学位論文

Investigation into New Catalytic Systems for Cross-Dehydrogenative Coupling Reactions under Aerobic Conditions

（酸素雰囲気下における脱水素クロスカップリング反応のための新規触媒系の研究）

平成２５年１２月博士（理学）申請

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化学専攻

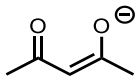
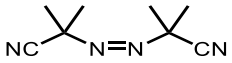
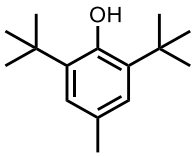
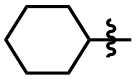
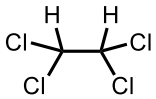
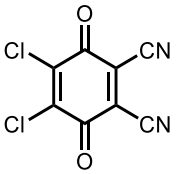
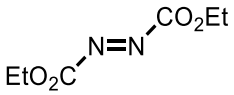
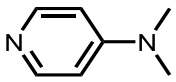
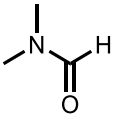
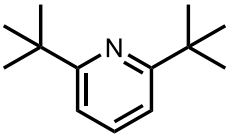
田上　新

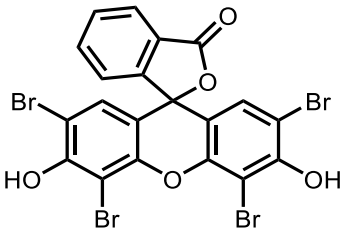
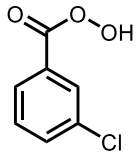
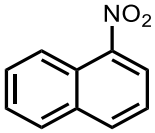
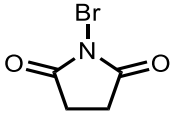
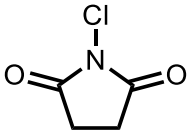
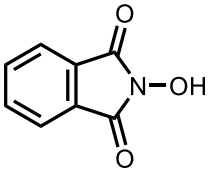
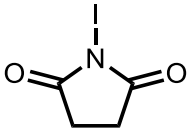
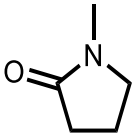
Abstract

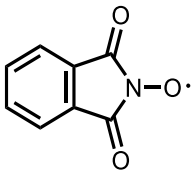
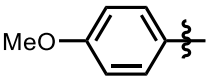
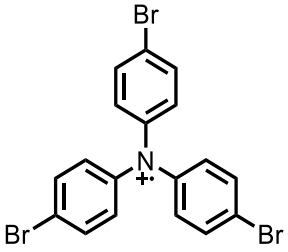
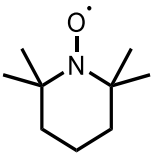
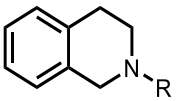
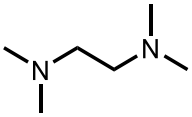
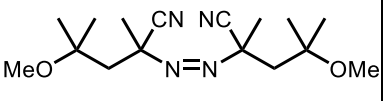
During the course of my Ph.D. studies, I investigated the metal-free cross-dehydrogenative coupling (CDC) reactions of amines using oxygen as a terminal oxidant. As a result, antimony, in the presence of *N*-hydroxyphthalimide as a co-catalyst, was unexpectedly found to be a novel catalyst for the cross-dehydrogenative coupling reactions of tertiary amines under very mild aerobic conditions. Although antimony is classified as a semi-metal, the use of antimony for CDC reactions was scientifically interesting since hexachloroantimonate anion has long been recognized as a stable and innocent counter anion in the field of organic chemistry. The present work dispels this widely regarded assumption. Based on this initial discovery, a metal antimonate was prepared and utilized as a novel type of bifunctional catalyst, which functions both as a Lewis acid and as an oxidation catalyst, for the oxidative α-functionalization of more synthetically useful glycine derivatives. Finally, my initial goal of developing a metal-free CDC reaction of tertiary amines was achieved by employing sulfuryl chloride as a non-metal initiator.

Contents

Abbreviation

acac	acetyl acetonate	
AcOH	acetic acid	CH_3COOH
AIBN	2,2'-azobisisobutyronitrile	
BHT	butylhydroxytoluene	
Bn	benzyl	$PhCH_2$-
CDC	cross-dehydrogenative coupling	-
Cy	cyclohexyl	
DCE	dichloroethane	
DCM	dichloromethane	CH_2Cl_2
DDQ	2,3-dichloro-5,6-dicyano-1,4-benzoquinone	
DEAD	diethyl azodicarboxylate	
DMAP	*N*,*N*-dimethyl-4-aminopyridine	
DMF	*N*,*N*-dimethylformamide	
DMSO	dimethylsulfoxide	
dTBP	2,6-di-*t*-butylpyridine	

DTBP	di-*t*-butylperoxide	^{t}BuOO^{t}Bu
eosin Y	2′,4′,5′,7′-tetrabromofluorescein	
EtCN	propionitrile	CH_3CH_2CN
*m*CPBA	*m*-chloroperbenzoic acid	
MeCN	acetonitrile	CH_3CN
MS4A	molecular sieve 4A	-
α-NaphNO_2	α-nitronaphthalene	
NBS	*N*-bromosuccinimide	
NCS	*N*-chlorosuccinimide	
NHPI	*N*-hydroxyphthalimide	
NIS	*N*-iodosuccinimide	
NMP	*N*-methylpyrrolidone	

PINO	phthalimide-*N*-oxyl	
PMP	*p*-methoxyphenyl	
TBHP	*t*-butyl hydroperoxide	*t*-BuOOH
TBPA	tris(*p*-bromophenyl)aminium	
TEMPO	2,2,6,6-tetramethylpiperidinyloxyl	
TFA	trifluoroacetic acid	CF_3COOH
TfO	trifluoromethanesulfonate	CF_3SO_3-
THIQ	tetrahydroisoquinoline	
T-HYDRO	*t*-butyl hydroperoxide (70 wt% in H_2O)	*t*-BuOOH
TMEDA	*N*,*N*,*N*',*N*'-tetramethyl-1,2-ethylenediamine	
TMS	trimethylsilyl	Me_3Si-
V-70	2,2'-azobis(4-methoxy-2.4-dimethylvaleronitrile)	

Introduction

0.1 Green and sustainable chemistry

In the 20th century, the life of mankind has been dramatically changed. The discovery of petroleum and electricity made life more convenient, and accordingly these and other related industries have grown significantly. In the past, society focused on developing their industrial capacity and innovation, without considering the consequence of their actions. As discharged industrial wastes adversely affect our health and environment, and with increase in prices of finite natural resources (petroleum, natural gas, rare metals), it is self-evident that current industrial practices cannot continue further. In order to solve these problems, sustainability must always be at the forefront. As organic chemists, we must become responsible and develop greener and more sustainable chemistry.[1]

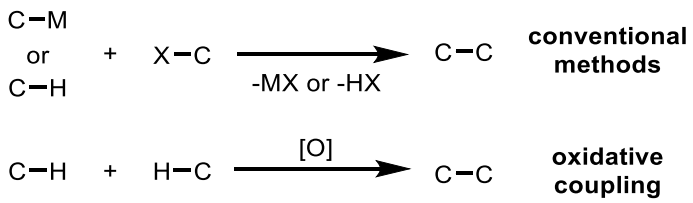
Although industries based on organic chemistry consume significant amounts of finite natural resources and produce considerable quantities of hazardous wastes, organic chemistry is vital for a healthy and thriving society since it produces the medicines and functional materials required for our daily lives. Thus, the goal to achieve a sustainable future is not to eliminate organic chemistry, but to re-invent and innovate to minimize the negative impact of our industries. Based on this motivation, chemists have accepted this challenge and have begun in earnest to invest their intellectual capital on advancing green and sustainable chemistry. For example, the use of water in organic synthesis, as a replacement for organic solvents, represents one approach to minimize the generation of hazardous chemical wastes. In a similar fashion, the development of efficient catalysts is a major focus in green chemistry since these molecular machines can lead to less energy-intensive synthetic methods that would produce less unwanted by-products. Another approach to sustainable chemistry is to employ substances that are readily available and to use them as replacements for toxic chemicals. For instance, oxidation reactions are fundamental organic transformations and many reagents have been invented to perform this operation. If these toxic reagents were replaced by readily available oxygen gas, the cost savings and reduced

environmental impact would be significant. Thus, the development of aerobic oxidation reactions is an important topic in the field of green and sustainable chemistry.

0.2 CDC reaction of tertiary amines

In conventional carbon−carbon bond forming reactions, the most common method is to react an organometallic nucleophile or an acidic pronucleophile with an alkyl halide as an electrophile (Scheme 0-1). However, in those reactions, the preparation of the organometallic nucleophile prior to the coupling event, and the formation of stoichiometric amount of metal salts or acid as co-product were problematic from the viewpoint of atom- and step-economy. Thus, if a carbon−carbon bond could be directly formed from two distinct carbon−hydrogen bonds, it would be more beneficial since: (i) it is not necessary to pre-activate the nucleophile, meaning the number of reaction steps can be reduced; and (ii) hydrocarbons are generally more available and environmentally benign compared with alkyl halides. In particular, the reduction of reaction steps is advantageous, since the purification of reaction mixtures is the most energy and waste intensive process in a chemical reaction. Thus, the oxidative coupling reaction of two distinct carbon-hydrogen bonds is highly beneficial for green and sustainable chemistry. This process can be rendered to be a particularly green process when oxygen gas is utilized as the terminal oxidant, since the sole by-product would be water. Such reactions, in which two distinct carbon−hydrogen bonds react together under oxidative conditions, are called “cross-dehydrogenative coupling” (CDC) reactions.

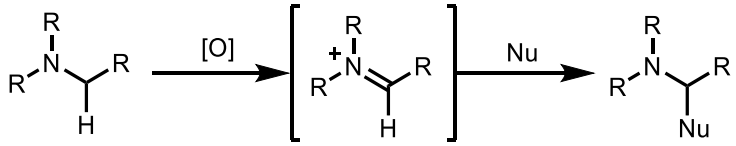
Scheme 0-1. C-C bond forming reactions



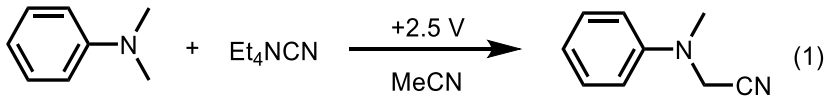
Among the various oxidative coupling reactions of two distinct carbon−hydrogen bonds, the functionalization of the C−H bond adjacent to the nitrogen atom is of great

importance, since the α-functionalization of unactivated C−H bonds of tertiary amines through the deprotonation process is generally difficult due to the low acidity of these C−H bonds. An alternative mechanism that does not rely on acid/base chemistry has been shown to overcome this challenge. Under oxidative conditions, tertiary amines can undergo oxidation to generate iminium intermediates, which are active electrophiles and reacts with various nucleophiles (Scheme 0-2). The CDC reactions of tertiary amines have been investigated predominantly over the past decade.[2-17] Herein, the historical background regarding the CDC reactions of tertiary amines will be presented.

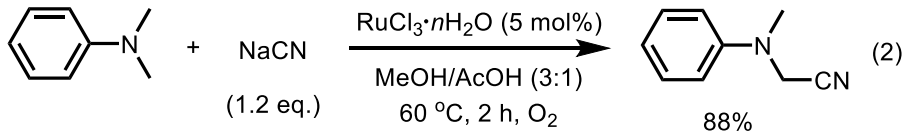
Scheme 0-2. CDC reaction of tertiary amines



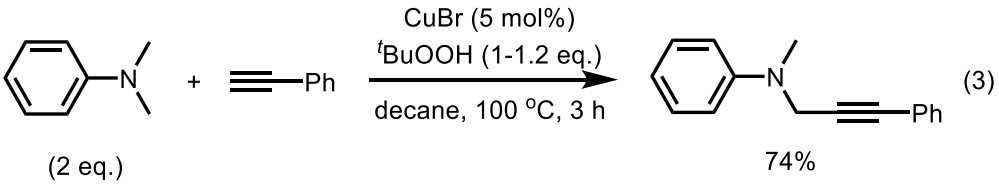
The initial stage of α-functionalization of tertiary amines through the oxidative coupling commenced from the late 1960s, utilizing electrochemical methods.[3] However, due to the gradual decomposition of nucleophiles under the electrochemical conditions, only cyanides could be employed as nucleophiles. The first example was reported by Andreades *et al*. in 1969, who attempted the oxidative cyanation of *N*,*N*-dimethylaniline under anodic conditions (eq.1).[3a]

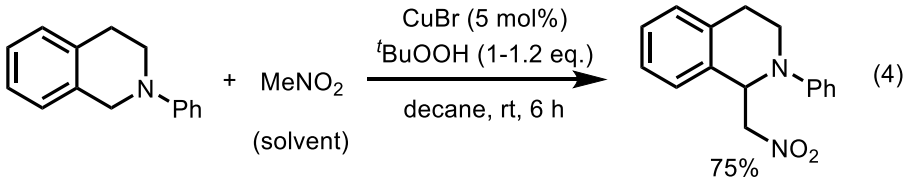


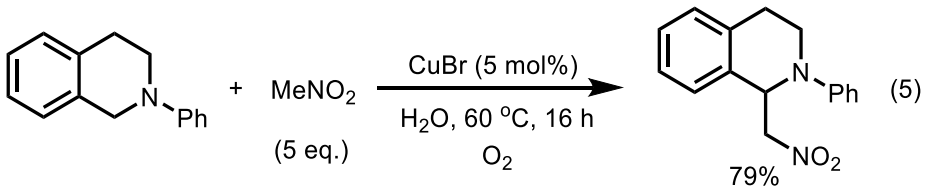
Apart from the electrochemical methods, the pioneering example of an oxidative coupling of tertiary amines was reported by Murahashi *et al*. in 2003 (eq. 2).[4a] The oxidative α-cyanation of *N*,*N*-dimethylaniline derivatives was achieved by utilizing NaCN/AcOH as a source of HCN in the presence of ruthenium(III) chloride using oxygen gas as a terminal oxidant.



Later, Li *et al*. reported the oxidative alkynylation reaction of *N*,*N*-dimethylaniline derivatives using copper(I) bromide as a catalyst and *t*-butyl hydroperoxide (TBHP) as an oxidant (eq. 3),[5a] and coined the term "cross-dehydrogenative coupling". An interesting feature of this oxidative alkynylation reaction was that the copper served as a catalyst for both the oxidation of amines and the activation of the alkynes. The same reaction system was also applied to other nucleophiles such as nitroalkanes (eq. 4)[5b] indoles[5c], malonates[5e], dialkylphosphites[5k], arylboronic acids[5i], and alkenes[5f] using *N*-aryl tetrahydroisoquinolines (THIQ) as more reactive tertiary amines. More importantly, in 2007, they disclosed that oxygen could be employed as a terminal oxidant for the copper-catalyzed oxidative nitromethylation and alkylation of tertiary amines in water (eq. 5).[5h]

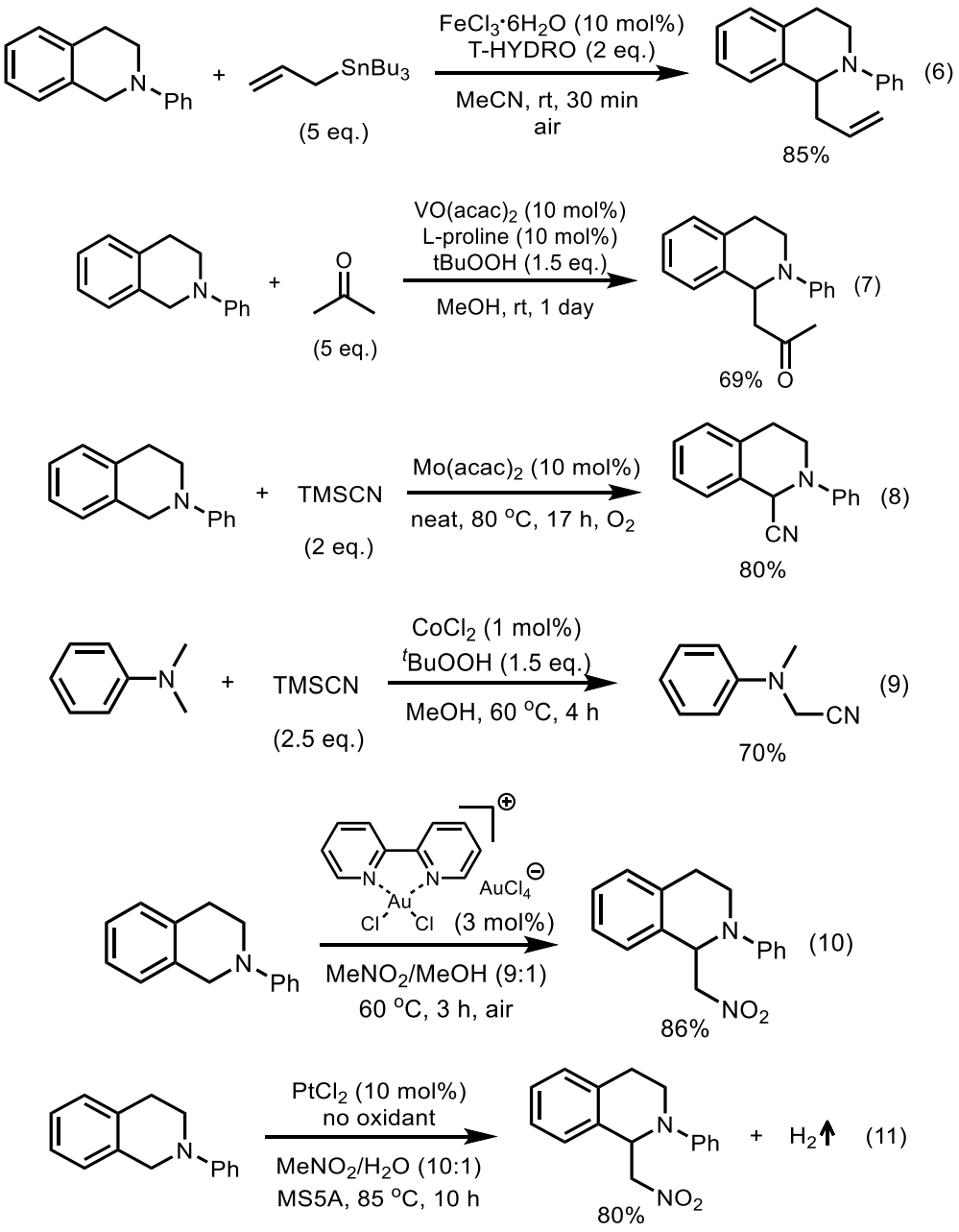




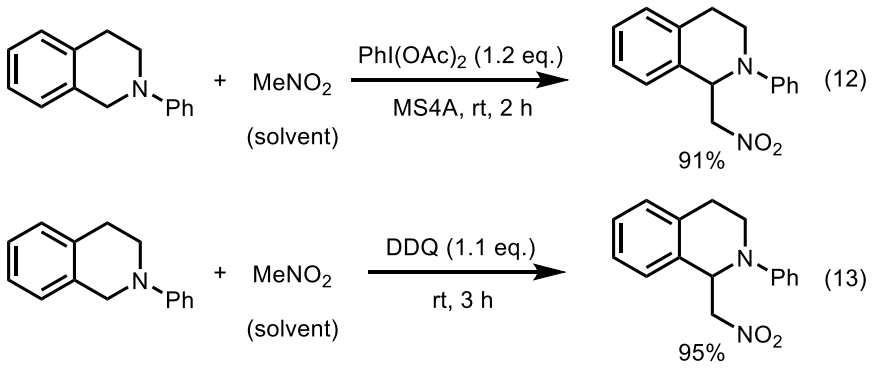


Although the initial examples of the CDC reaction of tertiary amines relied on copper or ruthenium salts as catalysts, other transition metals, such as Fe,[6] Au,[7] V,[8] Mo,[9]

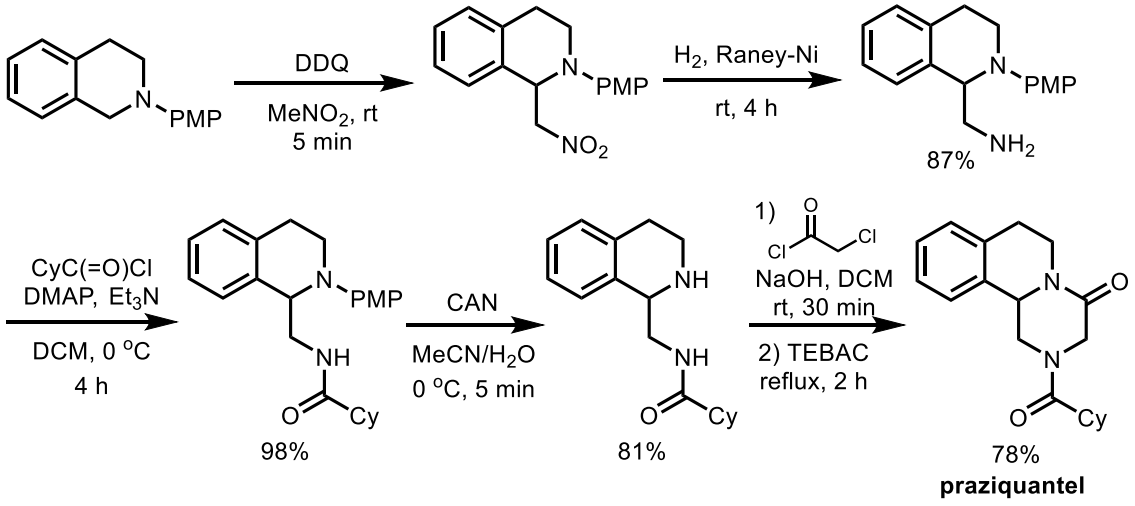
Co,[10] Pd[11] and Rh[12] have been reported for this reaction in the presence of oxygen or organic/inorganic oxidants (eqs. 6-10). An interesting example, in which no oxidant was required, was reported by Liang *et al*. in 2010.[13] They reported that the oxidative nitromethylation of THIQ in the presence of platinum(II) chloride proceeded, accompanied by the formation of hydrogen gas (eq. 11).



Although a variety of transition metal-catalyzed CDC reactions of tertiary amines have been reported to date, examples of metal-free system are not so many.[14,15] The stoichiometric use of strong oxidants, such as hypervalent iodines[14a] and DDQ[14b] have been reported to mediate CDC reactions of THIQ with nitroalkanes (eqs. 12, 13). It should be noted that metal-free synthetic methods are of interest due to the difficulty of removing metals completely from the product. Thus, despite the limited examples of metal-free CDC reactions reported in the literature, such methods are preferred in drug synthesis. For example, in 2013, Todd *et al*. reported the total synthesis of (±)-praziquantel, a racemate of a widely used anthelmintic drug, through the CDC reaction of a PMP protected THIQ mediated by DDQ (Scheme 0-3).[14i]

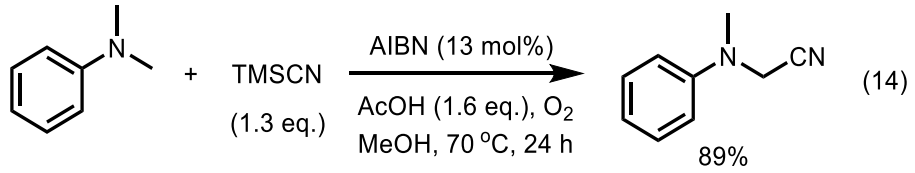


Scheme 0-3. Synthesis of praziquantel



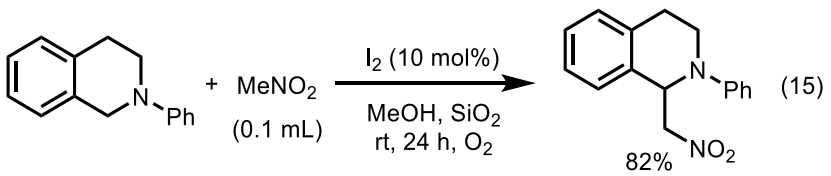
After the rapid CDC reaction of THIQ with nitromethane, the nitro moiety was reduced by Raney-Ni to provide the primary amine. The free amine was then acylated and the PMP group was removed by the oxidation using ceric ammonium nitrate (CAN). Subsequent cyclization with chloroacetyl chloride furnished the racemic praziquantel.

Examples of catalytic metal-free aerobic CDC reaction were only recently reported. Among these reactions, the use of oxygen as a terminal oxidant is especially rare. For example, in 2012, Fu *et al*. reported the oxidative cyanation reaction of *N*,*N*-dimethylanilines in the presence of AIBN as a radical initiator (eq. 14).[15c] The authors suggested that the reactions proceeded through a radical-initiated autoxidation mechanism.



(14)

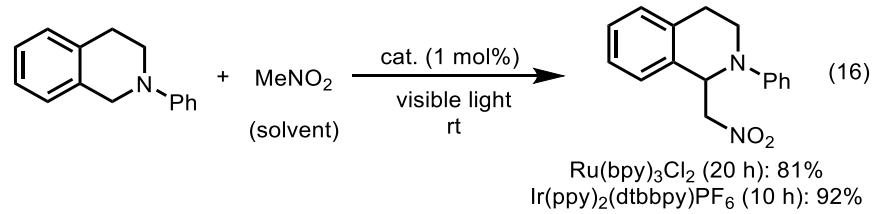
On the other hand, in 2013, Prabhu *et al*. reported the oxidative coupling reactions of THIQs with a variety of nucleophiles in an oxygen atmosphere by employing iodine as a catalyst (eq. 15).[15e] In this report, they proposed that the iodine was regenerated through the re-oxidation by oxygen gas. Since iodine is inexpensive and widely utilized in organic chemistry, iodine-catalyzed aerobic CDC reaction under very mild conditions appears to be one of the most ideal conditions for the CDC reactions of tertiary amines, although the catalyst loading of 10 mol% is relatively high.

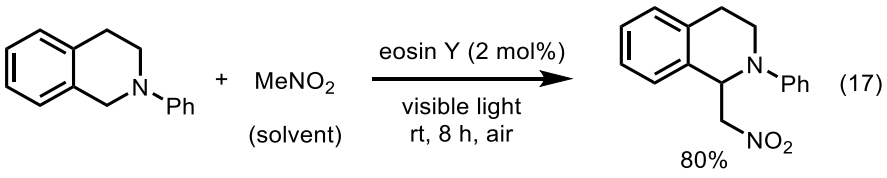


(15)

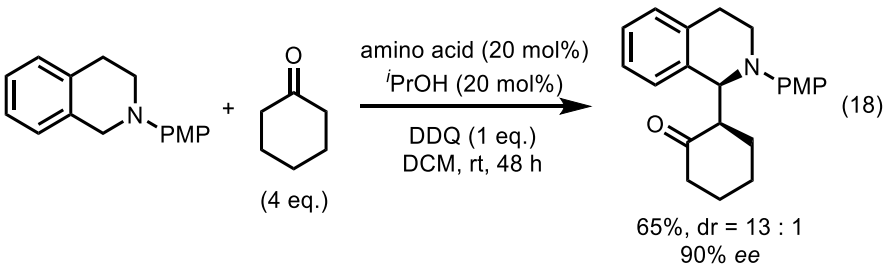
As a different class of the CDC reaction system, several examples of photocatalytic CDC reactions of tertiary amines have been reported.[16] For example, Stephenson *et al*. reported the oxidative nitromethylation reaction using ruthenium and iridium

photocatalysts under the irradiation of visible light (eq. 16).[16a] A similar reaction system was reported by König *et al*. by utilizing organic dyes, such as eosin Y, as a photocatalyst (eq. 17). [16b]





In addition, several examples of asymmetric CDC reactions of tertiary amines have also been reported. In 2013, Wang *et al*. reported a chiral amino acid-catalyzed asymmetric oxidative coupling reaction of tertiary amines with aliphatic ketones (eq. 18).[14h] Although the substrates were limited to THIQs and cyclohexanone, the products were obtained in moderate yields with good to high enantioselectivities.

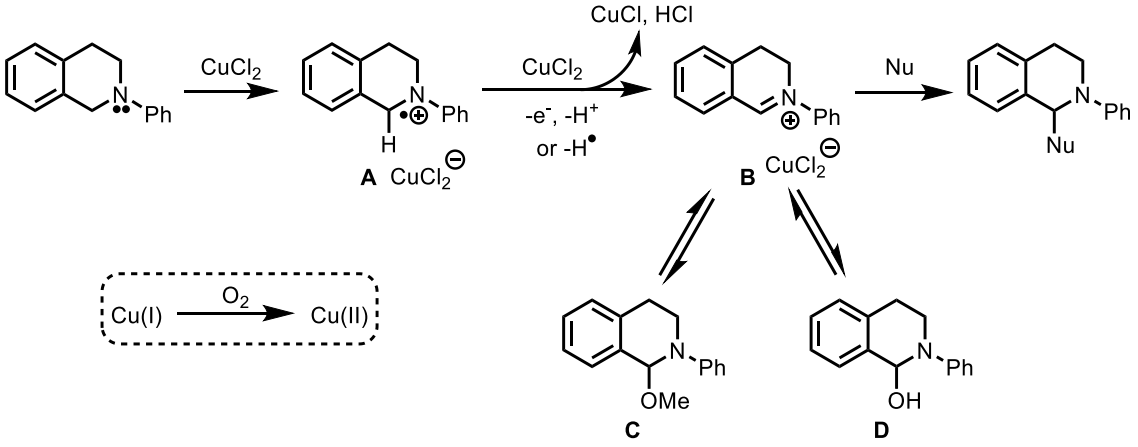


0.3 Reaction mechanisms of CDC reactions of tertiary amines

The detailed reaction mechanisms of copper-catalyzed CDC reactions were recently investigated by Klussmann *et al*.[17a,b] They examined the reaction mechanisms of the $CuCl_2 \cdot 2H_2O/O_2$ system and the CuBr/TBHP system. In the $CuCl_2 \cdot 2H_2O/O_2$ system, it was presumed that the reaction proceeded through the iminium intermediate formation

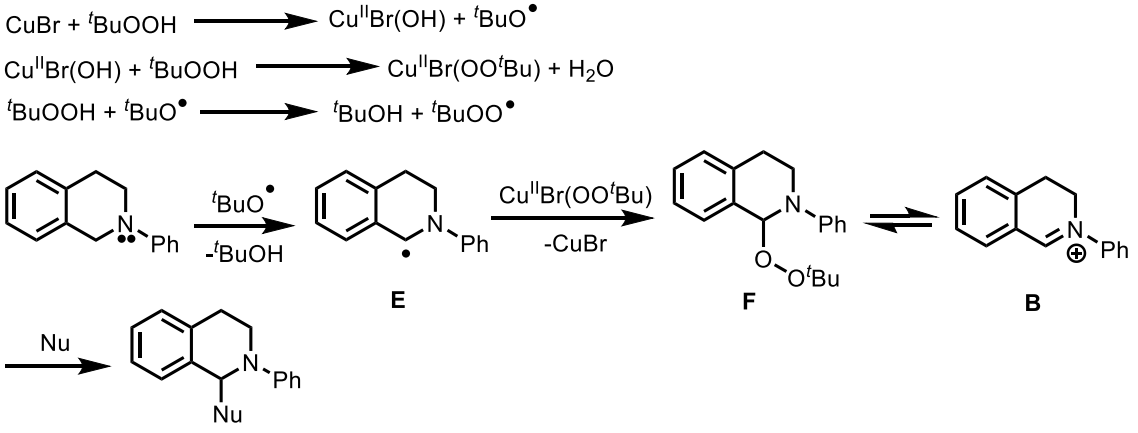
(Scheme 0-4). When $CuCl_2 \cdot 2H_2O$ was added to the *N*-phenyl tetrahydroisoquinoline in the absence of oxygen, yellow crystals immediately formed, which was determined to be the iminium intermediate **B** by X-ray analysis. Although the aminium radical intermediate **A** was not observed, it was proposed that the oxidation proceeded via a single electron oxidation (SET) of the substrate by Cu(II), and the subsequent hydrogen transfer or the combination of electron and proton transfer to afford the intermediate **B**. This intermediate **B** is in equilibrium with the hemiaminal ether **C** and the hemiaminal **D**, providing the reservoir of the iminium intermediate. Finally, the addition of nucleophile provides the oxidative coupling product. The role of oxygen is only for the regeneration of Cu(II) from Cu(I).

Scheme 0-4. Proposed mechanism of $CuCl_2/O_2$ system



On the other hand, the CuBr/TBHP system occurs through a different mechanism (Scheme 0-5). It was proposed that CuBr reacts with TBHP to generate ^{t}BuO·, which

Scheme 0-5. Proposed mechanism of CuBr/^{t}BuOOH system



abstract the α-hydrogen from the substrate to provide the carbon-centered radical intermediate **E**. Subsequently, this radical intermediate reacts with $Cu^{II}Br(OO^tBu)$ to give the peroxide intermediate **F**, which is in equilibrium with iminium intermediate **B**. Further addition of the nucleophile furnish the oxidative coupling product. During the reaction, a significant amount of the peroxide intermediate **F** was observed.

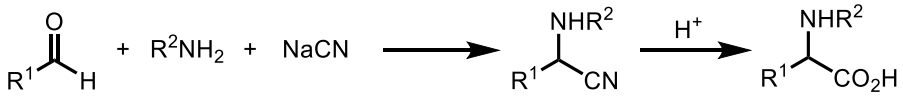
0.4 CDC reactions of α-amino acid derivatives

While the novel fashion of reactivity attracted much attention, the CDC reactions of tertiary amines suffered from the limitation of the amine structure. Namely, only substrates such as THIQs, *N*,*N*-dimethylanilines, *N*-phenylpyrrolidine or *N*-phenylpiperidine showed modest to high reactivity. To solve this problem, the idea to employ α-amino acid derivatives as substrates have recently emerged.[18,19]

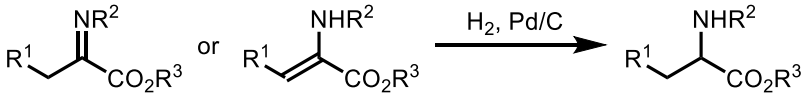
In order to synthesize α-functionalized amino acid derivatives, several methods have been reported, such as Strecker reaction, hydrogenation of imines or enamines, and oxidative amination of esters (Scheme 0-6). However the direct oxidative α-functionalization of amino acid derivatives is difficult since the acidity of the α-hydrogen of α-amino acid derivatives is comparatively low.[20]

Scheme 0-6. Synthetic pathways for α-alkylated amino acids

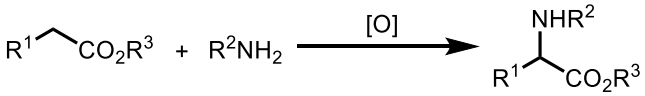
(a) Strecker reaction



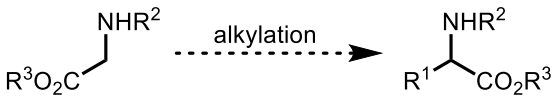
(b) hydrogenation of imines or enamines



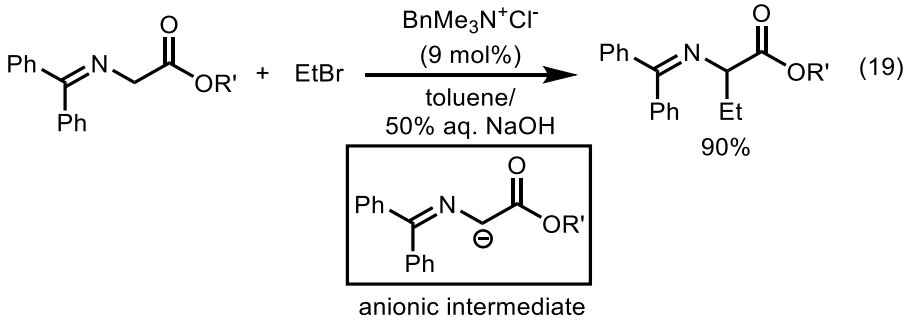
(c) amination of esters



(d) alkylation of amino acid derivatives

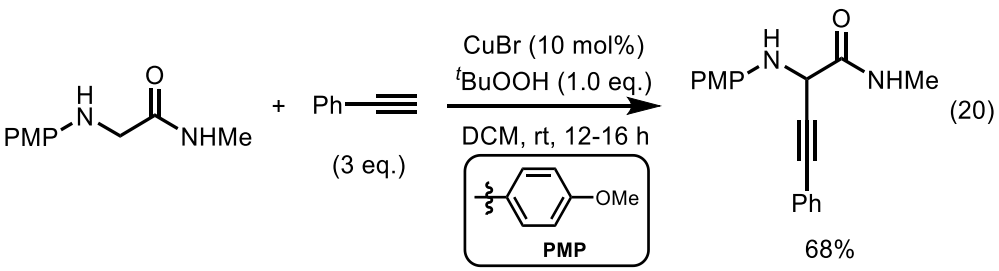


A rare example, in which α-alkylation of amino acid derivatives through the carbanion intermediates was achieved, was reported by O'Donnell *et al*. (eq. 19).[21] They increased the acidity of the α-hydrogen through the protection of α-hydrogen by a benzophenone moiety and the base-mediated alkylation occurred with a phase transfer catalyst. Later, Maruoka *et al*. developed the asymmetric variant of this reaction by employing chiral ammonium salts, and this is one of the most efficient and useful methodologies to synthesize chiral amino acid derivatives today.[22]

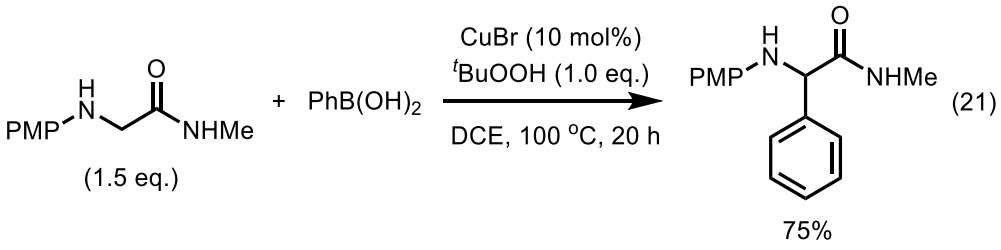


(19)

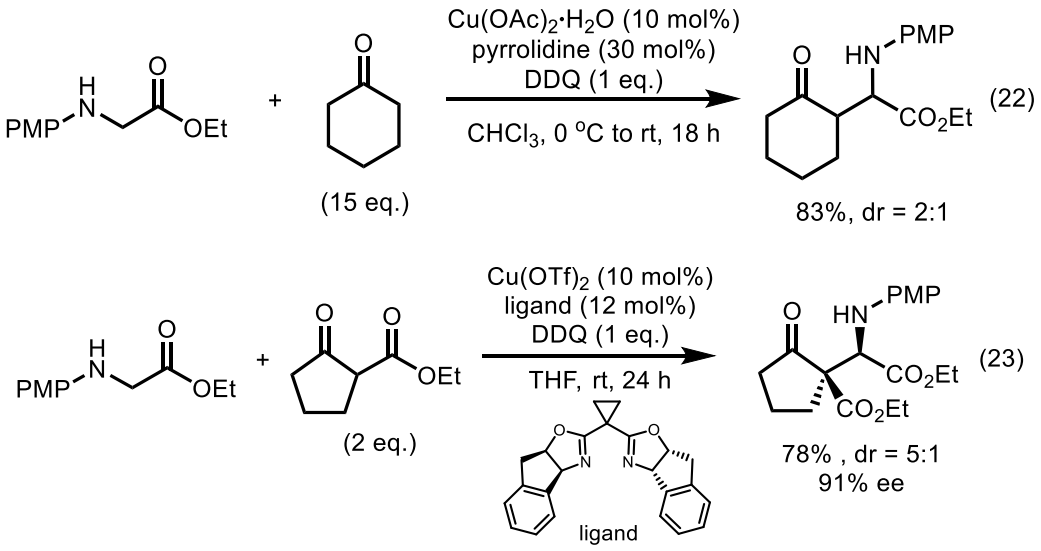
In contrast, Li *et al*. have recently attempted the direct functionalization of α-amino acid derivatives through the CDC-type reaction. In 2008, they reported the α-alkynylation of glycine amides, which were protected by *p*-methoxyphenyl (PMP) moiety, using copper(I) bromide as a catalyst and TBHP as a terminal oxidant (eq. 20).[18a] Although there was a disadvantage that the amine structure was restricted only to glycine amides, their reaction system represented a novel class of synthesis of α-functionalized amino acid derivatives. Although it was not exactly a *dehydrogenative* coupling reaction, they also reported the oxidative α-arylation of glycine amides under the similar reaction conditions using arylboronic acids as pronucleophiles (eq. 21).[18b]



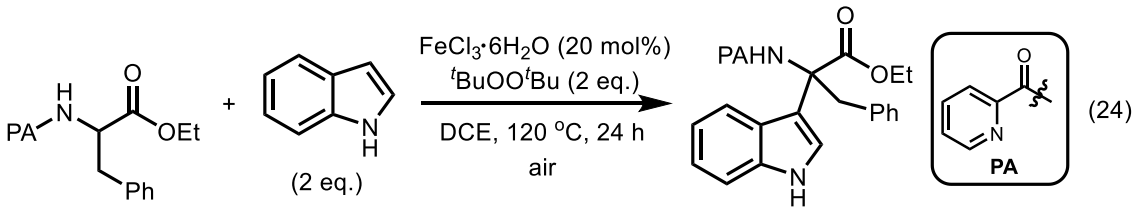
(20)



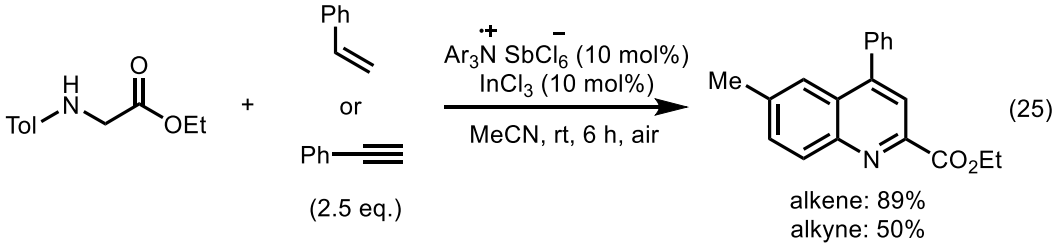
In 2010, Huang *et al*. reported the secondary amine-catalyzed oxidative Mannich reaction using copper(II) acetate as a catalyst and DDQ as a terminal oxidant (eq. 22).[18c] It is worth noting that not only glycine amides but also glycine esters were applicable in their reaction system. One year later, an asymmetric variant of this reaction was reported by Wang *et al*., which represented a truly useful methodology to synthesize chiral α-alkyl amino acid derivatives (eq. 23).[18d]

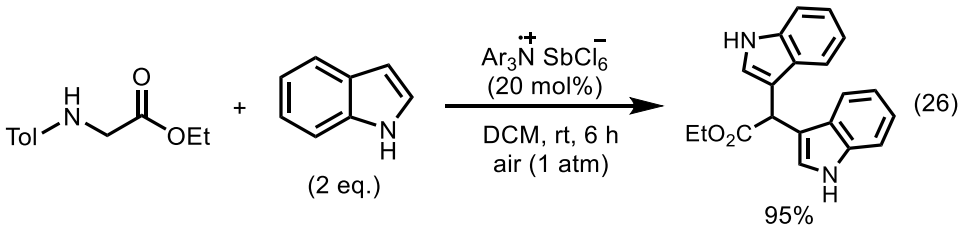


A rare example, in which α-alkylation of α-alkyl glycine derivatives were achieved, was recently reported by You *et al*. They attempted the oxidative addition of indoles to α-alkylated glycine esters using iron(III) chloride as a catalyst and DTBP as a terminal oxidant at high temperature (eq. 24).[18e] The protection of the nitrogen by a picolinamide (PA) was a key to achieve the efficient transformation, and air was also required to re-oxidize Fe(II) to Fe(III).

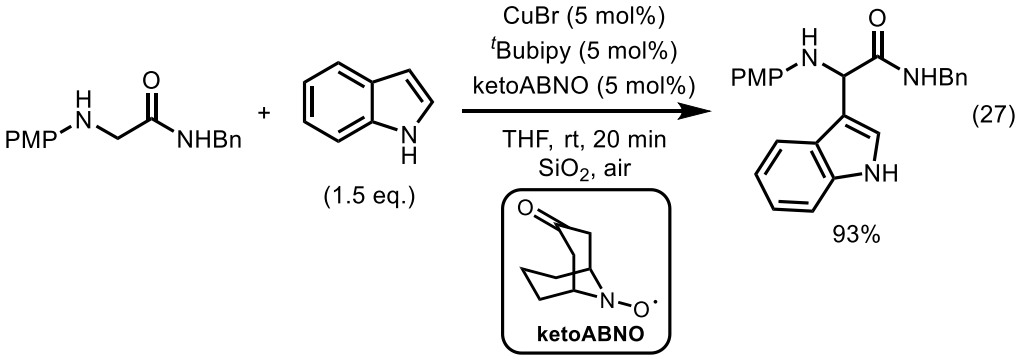


On the other hand, the examples of CDC-type reactions of α-amino acid derivatives using oxygen as a sole oxidant are scarce. In 2012, Wang *et al*. reported the oxidative Povarov reaction of glycine esters with alkenes or alkynes under air using tris(*p*-bromophenyl)aminium hexachloroantimonate as an aminium radical catalyst (eq. 25).[19b] In 2013, they also reported the double addition of indoles to the glycine esters employing the same catalyst (eq. 26).[19d]

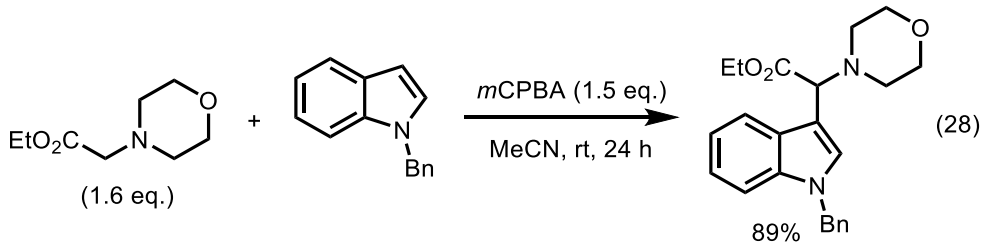




A different approach was recently made by Kanai *et al*. Based on the Cu/TEMPO-catalyzed oxidation reactions of alcohols, they developed a novel type of nitroxyl radical catalyst, ketoABNO, and succeeded in the highly efficient conversion of secondary amines to imines in the presence of the chiral copper co-catalyst under oxygen (eq. 27).[19a] When the reactions were performed in the presence of nucleophiles, a one-pot overall CDC reaction of glycine derivatives were accomplished. The reason for the highly efficient conversion to the imines seemed to be achieved by the rapid α-hydrogen abstraction through the coordination of copper with both the secondary amines and the nitroxyl radical.



Metal-free CDC reactions of glycine derivatives are almost non-existent. The only example was reported by Yu and Bao *et al*. in 2012 (eq. 28).[18e] They succeeded in the oxidative coupling reaction of *N*,*N*-dialkylglycine esters with indoles in the presence of a stoichiometric amount of *m*CPBA as an oxidant.



0.5 Purpose of my Ph.D. study

As shown in the introduction, examples of metal-free CDC reactions of tertiary amines and α-amino acid derivatives using oxygen as the terminal oxidant are scarce. The purpose of this research is to examine and explore novel reaction systems for metal-free CDC reactions of amines under aerobic conditions. This thesis will delineate the approach taken to achieve this goal and the unexpected discoveries that were found during the course of this study.

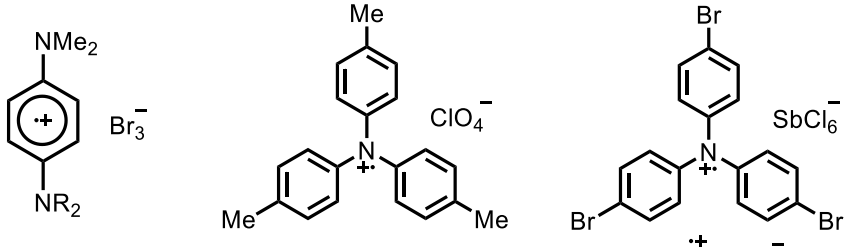
Chapter 1. Antimonate/NHPI-catalyzed CDC reaction of tertiary amines

1.1 Aminium radical cations

Since most metal catalysts that can facilitate the CDC reaction act as single electron oxidants, it was initially hypothesized that an aminium radical cation, an organic single electron oxidant, can serve as a catalyst to achieve the metal-free CDC reaction of tertiary amines.

Aminium radicals are radical cations of amines, which possess both an unpaired electron and a single unit of positive charge on the nitrogen atom.[23] Stable aminium radical cations were discovered as early as 1879, which are called Wurster's red and blue salts (Scheme 1-1, left).[24] Later, in 1907, Wieland prepared the tribromide salt of triarylaminium cation radical.[25] Weitz *et al*. also isolated the triarylaminium perchlorate (Scheme 1-1, middle) in 1926, demonstrated that the aminium radical cations possess monomeric structures,[26] and coined the term "cation radical" and "aminium" ion. The stability of these triarylaminium radicals is attributed to: (i) the delocalization of the cation to the aromatic moieties; (ii) the stability of the non-coordinating counter anions; and (iii) prevention of radical-based homocoupling on the aromatic ring by blocking the site of attack (substituents on the *p*-position). Currently, tris(*p*-bromophenyl)aminium hexachloroantimonate ($TBPA^{+\cdot}SbCl_6^-$; Scheme 1-1, right) is one of the most common aminium radical cations, and is a relatively strong oxidant that is readily available from the corresponding triarylamine. The oxidation potential of these aminium radical salts can be estimated from the reduction potential of the corresponding triarylamines (Table 1-1).[27]

Scheme 1-1. Examples of aminium salts

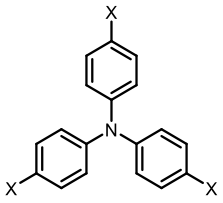
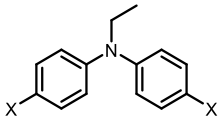


Wurster's red (R = H)
Wurster's blue (R = Me)

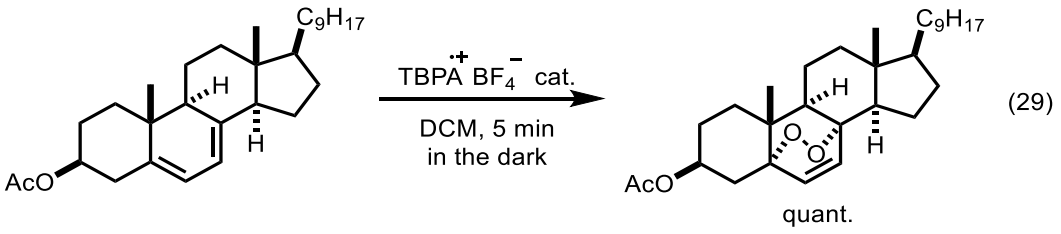
Weitz's aminium salt

TBPA $^{+\cdot}SbCl_6^-$

Table 1-1. Redox potentials of amines

amine	X	E vs SCE (V)
	MeO	0.52
	Me	0.75
	^{t}Bu	0.76
	F	0.95
	Cl	1.04
	Br	1.05
	I	1.01
	MeO_2C	1.26
	Ac	1.26
	Bz	1.25
	CN	1.44
	Me	0.74
	MeO	0.64
	^{t}Bu	1.25
	Cl	0.98

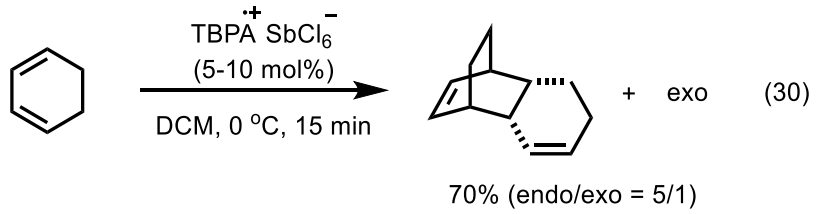
Triarylaminium radicals are known as strong single electron oxidants, whose oxidation potentials can be tuned by modifying their substituents. Although primarily used as stoichiometric single electron oxidants,[28] some catalytic applications of these species have been reported for: (i) oxygenation of dienes; (ii) Diels-Alder reactions; and (iii) cyclobutanation of alkenes. For example, Barton *et al*. discovered in 1972 that both tris(*p*-bromophenyl)aminium hexachloroantimonate and trityl tetrafluoroborate ($Ph_3C^+BF_4^-$) can catalyze the rapid oxygenation of cyclohexadiene in the ergosteryl benzoate (eq. 29).[29] While the trityl cation-catalyzed reaction proceeded through a photo-oxygenation, the aminium radical-catalyzed reaction seemed to be a thermal-oxygenation. The authors speculated that the oxygen adduct of the aminium radical (ArNOO·) is the key intermediate in this oxygenation reaction.



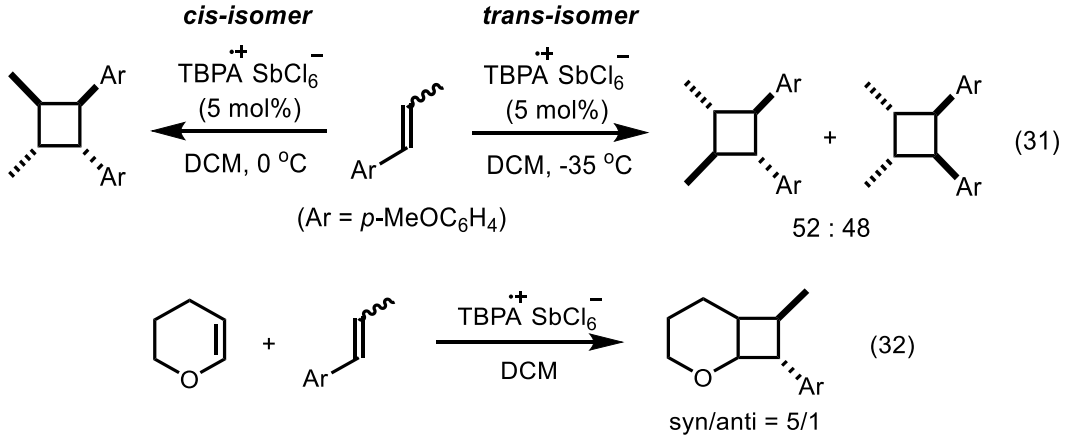
(29)

The first example of an aminium radical cation-initiated Diels−Alder reaction was reported by Bauld *et al*. in 1981 (eq. 30). [30] Although electron-deficient dienophiles are known to possess high reactivity for the Diels−Alder reaction and some Lewis acids can

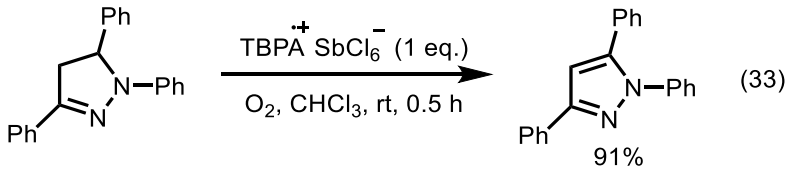
enhance the reactivity of heteroatom-containing dienophiles, neutral and electron-rich dienophiles are often poor substrates. The authors hypothesized that the conversion of the less reactive dienophiles to the corresponding radical cations, which are highly electron-deficient acceptors, would promote these reactions. Based on this hypothesis, they attempted the aminium radical cation-initiated Diels−Alder dimerization of cyclohexadiene, which immediately reacted at low temperature to provide the dimerized product in 70% yield, while the thermal reaction without the initiator provided the product in only 30% yield after 20 h at 200 °C.



The aminium salt initiated cyclobutanation was first reported by Bauld *et al*. in 1983 (eq. 31).[31] The authors investigated the cyclodimerization of *cis*- and *trans*-anethole in the presence of a catalytic amount of tris(*p*-bromophenyl)aminium hexachloroantimonate, and obtained the dimerized products as a mixture of stereoisomers. The cross-cycloaddition of anethole with dihydropyran was also successful (eq. 32).



Quite recently, the use of an aminium radical cation as a catalyst for the oxidation reaction under aerobic conditions was reported by Wu *et al*. (eq. 33).[32] Although a substoichiometric amount of catalyst was required, this example suggested the possibility that aminium radicals can be regenerated under aerobic conditions, and I hypothesized that these organic oxidants could be utilized to catalyze the cross-dehydrogenative coupling reaction of tertiary amines.

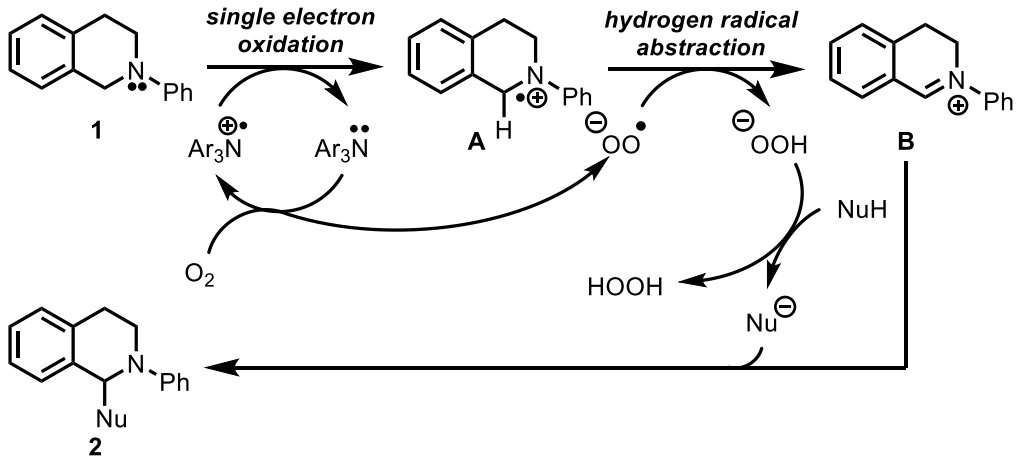


(33)

1.2 Initial hypothesis

In order to achieve the metal-free CDC reaction, I hypothesized the reaction mechanism as follows (Scheme 1-2). First, the aminium radical catalyst will oxidize the tertiary amine **1** through single electron oxidation to generate aminium radical intermediate **A**. On the other hand, the aminium radical catalyst will be regenerated through the oxidation by oxygen gas, accompanied by the formation of oxygen radical anion. Then, this radical anion will abstract the hydrogen radical from intermediate **A** to provide iminium intermediate **B** and release hydrogen peroxide anion, which can function as a base to activate the pronucleophile. Finally, iminium intermediate **B**

Scheme 1-2. Initial hypothesis using aminium radical as a catalyst

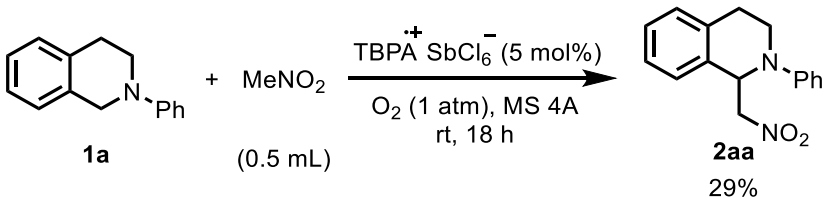


undergoes nucleophilic addition to furnish the product **2**.

1.3 Initial attempt of the aminium radical-catalyzed CDC reaction of tertiary amine

Based on this hypothesis, I attempted the oxidative coupling reaction of *N*-phenyl tetrahydroisoquinoline (**1**) and nitromethane using 5 mol% tris(*p*-bromophenyl)aminium hexachloroantimonate as a catalyst under an atmospheric pressure of oxygen gas (Scheme 1-3), and the oxidative aza-Mannich reaction proceeded under ambient temperature, albeit with a low yield. However, the initial reaction was considered a success, since catalytic turnover was achieved.

Scheme 1-3. Initial trial of aminium radical-catalyzed CDC reaction

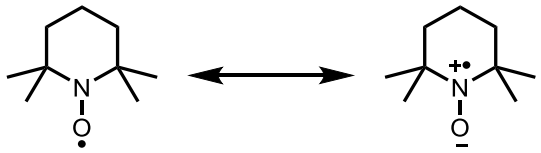


1.4 *N*-Hydroxyphthalimide

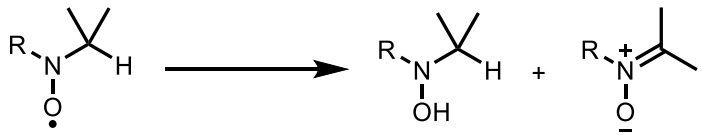
I hypothesized that the problem for the aminium radical-catalyzed CDC reaction was the hydrogen radical abstraction step. Thus, I assumed that the addition of *N*-hydroxyphthalimide (NHPI), which is known to facilitate hydrogen radical abstraction, would promote this reaction.

Nitroxyl radicals[33] were discovered in the early 20th century. One of the most common nitroxyl radicals used in organic chemistry is 2,2,6,6-tetramethyl-piperidinyloxyl (TEMPO), a stable radical that is known as a radical inhibitor and a catalyst for the oxidation of alcohols. This radical is stabilized by the equilibrium shown below (Scheme 1-4). In the nitroxyl radical structure, the absence of α-hydrogen is critical for its stability. In the presence of α-hydrogens, the nitroxyl radical undergoes disproportionation and decompose into the corresponding hydroxylamine and nitrone (Scheme 1-5).

Scheme 1-4. Stabilization of N-O radical

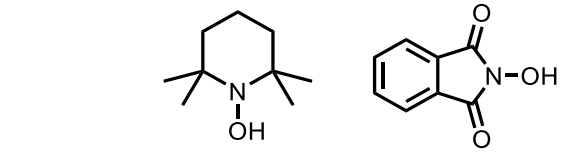


Scheme 1-5. Unstable N-O radical which contains α-hydrogen



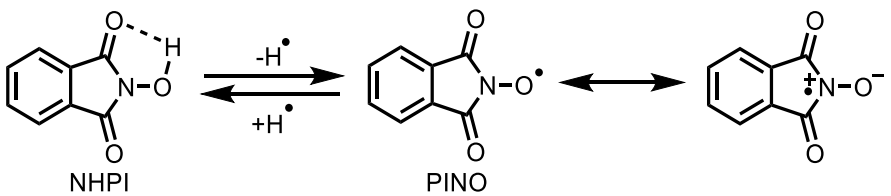
While TEMPO exhibits high stability, phthalimide-*N*-oxyl (PINO) radical does not possess such significant stability, thus it possesses high reactivity toward hydrogen atom abstraction. This nature is well substantiated by the bond dissociation energies of the O−H bonds. Compared with the bond dissociation energy of the O−H bond in TEMPOH, the dissociation energy for NHPI is much higher, suggesting the instability of PINO radical when compared to the TEMPO radical (Scheme 1-6). This can be explained by considering the effects of acyl moieties in the structures of NHPI and PINO radical. The PINO radical is in equilibrium with the aminium radical cation structure, which is destabilized by the electron-withdrawing double carbonyl moieties. In contrast, NHPI is stabilized by intramolecular hydrogen bonding (Scheme 1-7).

Scheme 1-6. BDEs of TEMPOH and NHPI



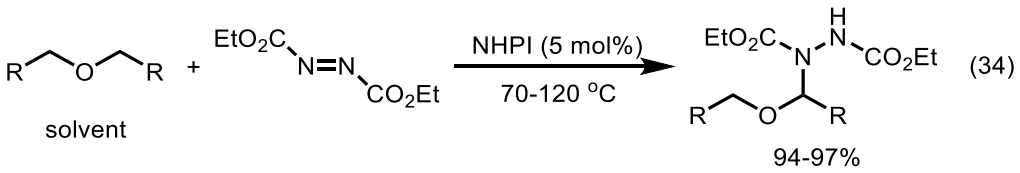
BDE (O-H) 292 kJ/mol 369 kJ/mol

Scheme 1-7. Stabilized NHPI and destabilized PINO radical



NHPI PINO

In 1977, Grochowski *et al*. reported the first radical reaction using NHPI as a catalyst (eq. 34).[34] During the course of their investigation into the Mitsunobu reaction of NHPI with alcohols in the presence of diethyl azodicarboxylate (DEAD) and triphenylphosphine in THF as a solvent, they discovered that the 1 : 1 adduct of DEAD and THF was obtained. They concluded that the reaction proceeded through a free-radical process initiated by NHPI. Further investigation revealed that several ethers can undergo radical addition to DEAD in the presence of a catalytic amount of NHPI at high temperature.

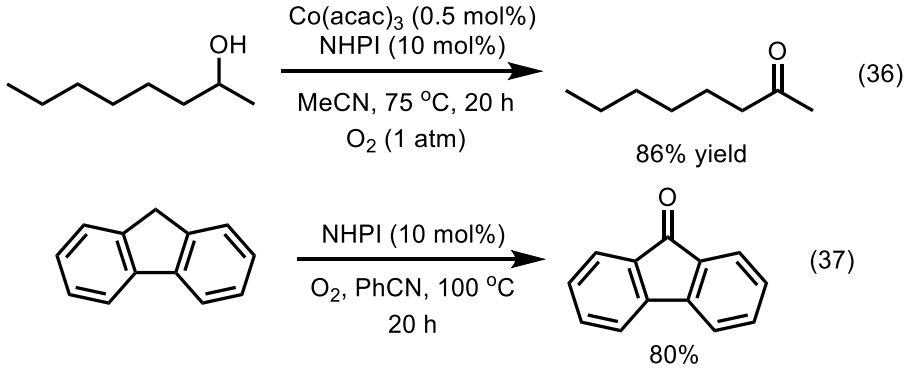


(34)

In the 1980s, Masui *et al*. found that NHPI serves as a good electron carrier with high current efficiency for anodic oxidations (eq. 35).[35] Electrochemical oxidation of secondary alcohols using a catalytic amount of NHPI successfully provided the corresponding ketones under mild conditions.

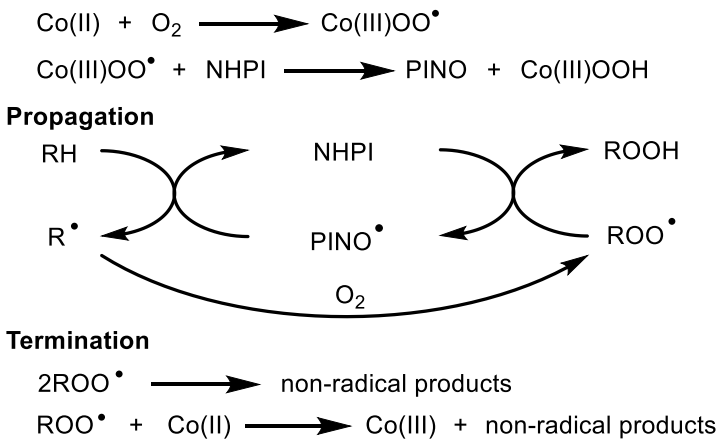
(35)

The chemistry of NHPI-catalyzed oxidation under aerobic conditions was developed extensively by Ishii *et al*.[36] In particular, he found that the addition of a small amount of transition metals, especially cobalt, leads to an effective catalyst system for the autoxidation of various organic substrates such as alcohols (eq. 36),[36a] alkyl aromatics and alkanes. It was also found that such autoxidation reactions could be performed at high temperatures in the absence of additional metal catalysts (eq. 37).[36b]



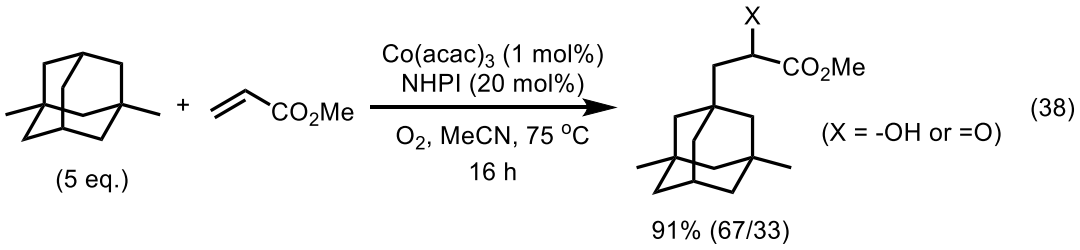
The reaction mechanism of the Co/NHPI system is proposed to be a cobalt-initiated autoxidation mechanism (Scheme 1-8).[33b] First, cobalt(II) reacts with oxygen to generate a radical species, which abstracts hydrogen atom of NHPI to generate PINO radical. In the propagation step, this PINO radical abstracts the hydrogen atom of the substrate to provide an alkyl radical and regenerate NHPI. Subsequently, this alkyl radical reacts with oxygen to afford alkylperoxy radical, which abstracts the hydrogen atom from NHPI to furnish the product and PINO radical. The termination of this reaction is the coupling of the alkylperoxy radical with itself or the Co(II) species.

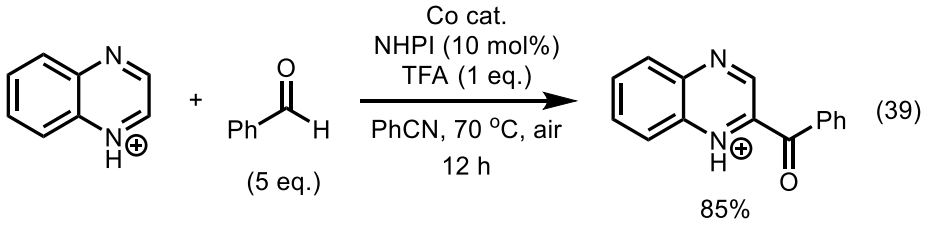
Scheme 1-8. Mechanism of Co/NHPI-catalyzed autoxidation



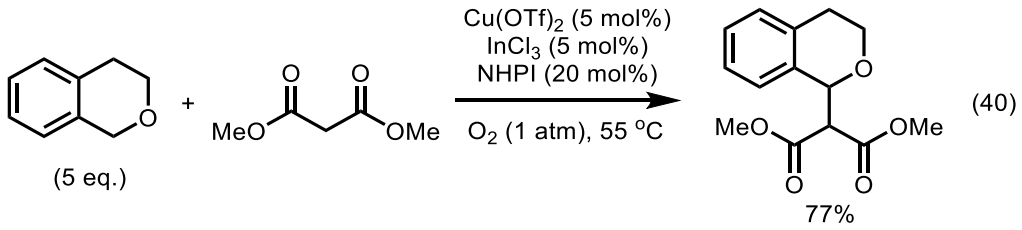
The Co/NHPI system can be also applied to intermolecular oxidative carbon−carbon bond forming reactions. In 2001, Ishii *et al*. reported the oxyalkylation of electron-deficient alkenes with unactivated alkanes under aerobic conditions through a radical process (eq. 38).[36c] Minisci *et al*. also reported that the free-radical acylation of

heteroaromatic bases could be catalyzed by NHPI and Co salts in air (eq. 39).[37]





A rare example in which NHPI was utilized as a catalyst for the cross-dehydrogenative coupling reaction was reported by Li *et al*. in 2009 (eq. 40).[5j] They demonstrated the oxidative alkylation of isochromans in the presence of copper(II) triflate, indium(III) chloride, and NHPI as catalysts by using oxygen gas as a terminal oxidant. However, due to the competing lactam formation, an excess amount of the isochroman was required in this reaction.

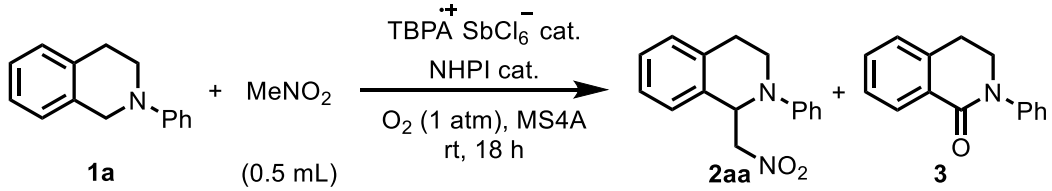


1.5 Optimization studies for the aminium radical cation catalyzed CDC reaction

The optimization for the aminium radical cation catalyzed CDC reaction was investigated. In the absence of any catalysts, a very slow reaction was observed (Table 1-2, entry 1). When 5 mol% of the aminium radical was employed, the desired product was obtained in a low yield, accompanied by a significant amount of amide **3** as a side-product (entry 2). According to my expectation, the addition of NHPI significantly

improved the reactivity (entry 3). In contrast, NHPI itself did not catalyze this reaction, indicating that the aminium radical catalyst plays a critical role in this reaction (entry 4). When only 1 mol% of both catalysts were employed, a very slow reaction was observed (entry 5). Although a comparable reactivity was observed when 10 mol% of both catalysts were employed, further addition of the catalysts began to suppress and stop the reaction (entries 7-9). Fixing the catalyst loading of the aminium radical to 5 mol%, the use of 2.5 mol% NHPI slightly suppressed the reactivity (entry 10), while the use of 10 mol% NHPI completed this oxidative nitromethylation reaction (entry 11). Also, by elevating the temperature, the CDC reaction was accelerated (entry 12). When the reaction vessel was protected from light, no suppression of reactivity was observed, which suggested that light is not involved in this reaction (entry 13). On the other hand, significant suppression of the reactivity was observed when the reaction was performed under an argon atmosphere (entry 14).

Table 1-2. Initial investigation of reactivity



1a **2aa** **3**

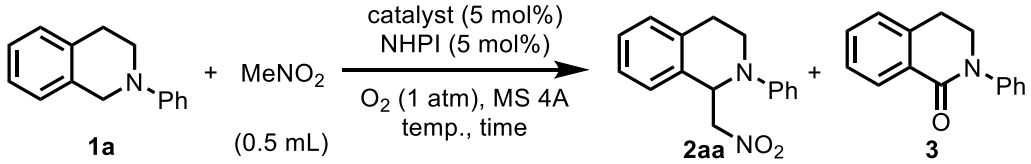
entry	TBPASbCl$_6$ (mol%)	NHPI (mol%)	modified conditions	**2aa** (%)[a]	**3** (%)[a]	rec. **1a** (%)[a]
1	-	-	-	5	1	>95
2	5	-	-	29	24	34
3	5	5	-	64	6	40
4	-	5	-	3	ND	>95
5	1	1	-	14	86	trace
6	10	10	-	63	19	7
7	20	20	-	31	ND	trace
8	30	30	-	32	ND	trace
9	60	60	-	ND	ND	ND
10	5	2.5	-	51	44	6
11	5	10	-	>95	ND	3
12	5	5	60 °C	88	ND	trace
13	5	5	protected from light	73	2	20
14	5	5	under Ar	9	ND	>95

[a] Determined by ^{1}H NMR analysis.

1.6 Effects of counter cations and anions

Then, the effect of the counter cations and anions were investigated. Compared with tris(*p*-bromophenyl)aminium hexachloroantimonate (Table 1-3, entry 1), when the counter anion was replaced with tetrafluoroborate and hexafluorophosphate, the CDC reaction proceed sluggishly (entries 2-3). However, when the counter anion was replaced with hexafluoroantimonate, the product was obtained in a moderate yield (entry 4). On the other hand, when the counter cation was replaced with tetraethylammonium and trityl cations, the desired product was obtained in moderate yields (entries 5 and 6). These results strongly suggested that *the true active catalyst was not an aminium radical cation, but the antimonate counter anion*. In order to confirm that antimony is truly the active catalyst, antimony(V) pentachloride was examined as a catalyst and the desired product was obtained in a moderate yield (entry 7). Thus, it was concluded that antimony was the true active catalyst for this oxidative coupling reaction. Finally, the optimization studies were completed, and sodium hexachloroantimonate was found to be the best catalyst (entry 8) and the reaction time was reduced to 4 hours by performing the reaction at 30 °C.

Table 1-3. Effects of counter anions and cations

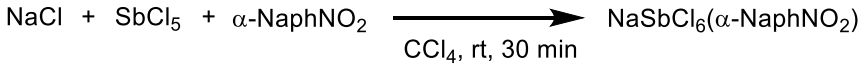


entry	catalyst	temp. (°C)	time (h)	**2a** (%)[a]	**3** (%)[a]	rec. **1a** (%)[a]
1	$TBPASbCl_6$	rt	18	64	6	40
2	$TBPABF_4$	rt	18	6	trace	>95
3	$TBPAPF_6$	rt	18	11	1	>95
4	$TBPASbF_6$	rt	18	41	3	55
5	Et_4NSbCl_6	rt	18	51	4	41
6	Ph_3CSbCl_6	rt	18	41	1	65
7	$SbCl_5$	rt	18	53	6	29
8	$NaSbCl_6$(α-$NaphNO_2$)	rt	18	>95	3	ND
9	$NaSbCl_6$(α-$NaphNO_2$)	30	4	>95	2	ND

[a] Determined by ^{1}H-NMR analysis.

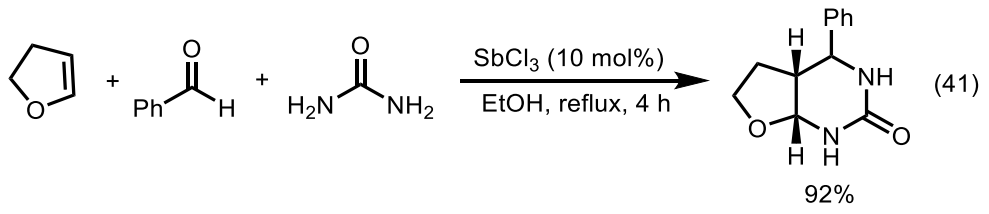
Sodium hexachloroantimonate was prepared according to the literature procedure.[38] In 1974, Drăgulescu *et al*. synthesized various hexachloroantimonate salts of Li, Na, K and Cu(I) using nitromethane, nitrobenzene, and α-nitronaphthalene as ligands (Scheme 1-9). In order to synthesize metal hexachloroantimonate salts, some ligands were required to coordinate the metals and stabilize the complexes. They reported that nitromethane complexes could not be synthesized due to their instability. When nitrobenzene was employed as a ligand, either one or two nitrobenzene coordinated to the metals. And when α-nitronaphthalene was employed, only one α-nitronaphthalene coordinated to the metal. Thus, I selected α-nitronaphthalene as a ligand. As for the metal, I selected sodium since sodium chloride is one of the most common inorganic salts. Finally, an α-nitronaphthalene-ligated sodium hexachloroantimonate was easily prepared by reacting sodium chloride, antimony pentachloride and α-nitronaphthalene in CCl_4.

Scheme 1-9. Preparation of antimonate salts



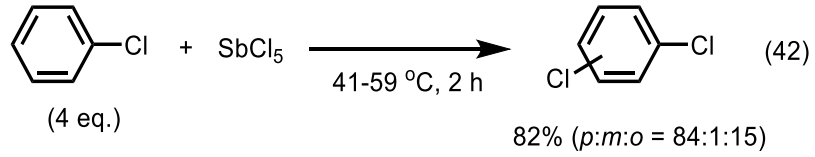
1.7 Antimony in organic chemistry

Antimony is an inexpensive element, which belongs to the group 15 elements and it is classified as a semi-metal. The stable valencies of antimony are III and V, and the most common usage of antimony species in organic chemistry is the use of antimony(III) trihalides or antimony(V) pentahalides as Lewis acids (eq. 41).[39]



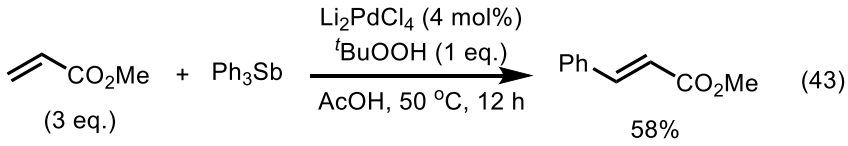
(41)

Antimony pentachloride is known not only as a strong Lewis acid, but also as an electrophilic chlorinating agent, which can induce the Friedel-Crafts type aromatic chlorination reaction as shown below (eq. 42).[40]



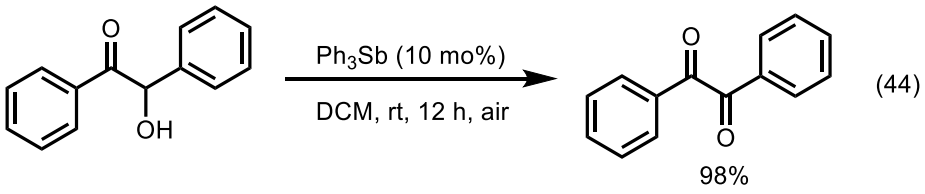
(42)

An interesting feature of antimony, when compared with transition metals, is the availability of arylantimony species. For instance, triarylantimonies are stable antimony(III) species which can undergo a transition metal-catalyzed oxidative arylation reactions (eq. 43).[41]



(43)

Although the use of antimony as an additive for the oxidation reaction has been reported, the use of antimony as a sole catalyst for oxidation, especially under aerobic conditions is almost non-existent. In 2005, Kurita *et al*. reported a rare example of an aerobic oxidation reaction with antimony as a catalyst by demonstrating the oxidation of benzoin by employing triphenylantimony as a catalyst in air (eq. 44).[42]



(44)

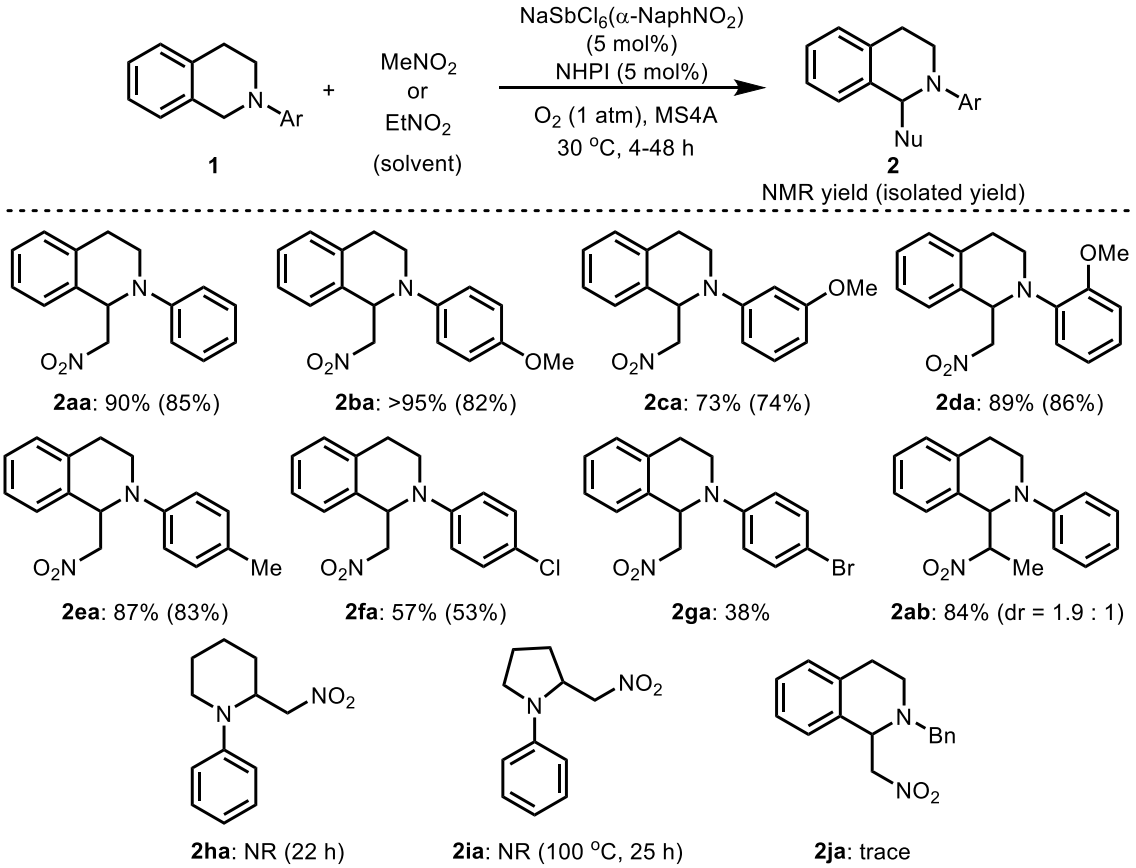
However, to the best of my knowledge, there are no reports on the use of antimony as a catalyst for the cross-dehydrogenative coupling reactions of tertiary amines. In

addition, hexahaloantimonate anions are commonly considered as stable and innocent non-coordinating anions, similar to other anions such as triflate, tetrafluoroborate, or hexafluorophosphate anions. Thus, it is scientifically interesting that such an innocent non-coordinating anion exhibited catalytic activity for the oxidative coupling reaction. Based on these backgrounds, I decided to focus on the use of antimonate and NHPI as a catalyst system for the cross-dehydrogenative coupling reaction of tertiary amines under aerobic conditions.

1.8 Substrate scope

After optimizing the reaction conditions, the scope of substrate was investigated (Scheme 1-10). In addition to the simple *N*-phenyl-substituted tetrahydroisoquinoline, *p*-, *m*- and *o*-methoxyphenyl substrates gave the corresponding products in high yields (**2ba**, **2ca**, **2da**). Also, the *p*-tolyl substrate exhibited a good reactivity (**2ea**). On the other hand, electron-deficient *p*-chlorophenyl and *p*-bromophenyl substrate gave the

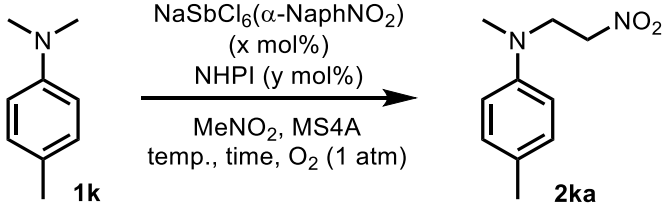
Scheme 1-10. Substrate scope



product in a modest yield (**2fa**, **2ga**), due to the fact that the single electron oxidation of electron-poor tertiary amines is more difficult. In addition to nitromethane, nitroethane also served as a reactive nucleophile (**2ab**). However, no reaction took place when *N*-phenylpiperidine and *N*-phenylpyrrolidine were employed as substrates (**2ha**, **2ia**), suggesting the importance of the reaction site to be a benzylic position. Also, an *N*-benzyl tetrahydroisoquinoline provided only a trace product (**2ja**).

To expand the substrate generality, an acyclic amine, *N*,*N*-dimethyl-*p*-toluidine, was examined as a substrate (Table 1-4). When the reaction was performed using 5 mol% sodium antimonate and 5 mol% NHPI at 30 °C, only a trace amount of the desired product **2ka** was obtained (entry 1). When the temperature was raised to 60 °C, a slight improvement of reactivity was observed (entry 2). Finally, when the reaction was performed at 100 °C, the desired product was obtained in 22% yield (entry 3). In order to improve the reactivity, the catalyst loadings were increased (entries 4-5). Unfortunately, this did not improve the reactivity further. Since higher catalyst loading can sometimes exhibit a negative effect, slow addition of the catalysts was tested (entry 6). However, only a slight improvement on reactivity was observed. In addition, when the reaction was performed in acetonitrile at a higher temperature, very poor reactivity was observed (entry 7).

Table 1-4. Nitromethylation of acyclic amine



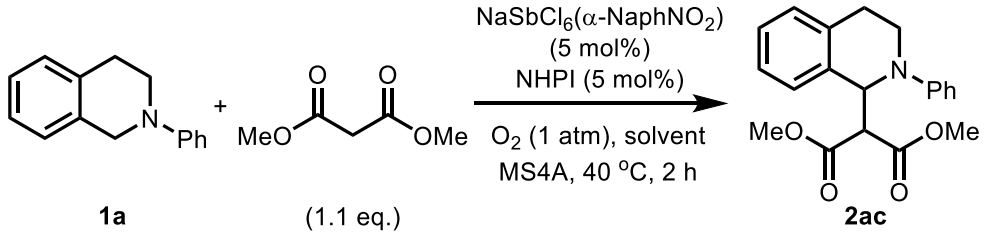
entry	x (mol%)	y (mol%)	temp (°C)	time (h)	**2ka** (%)[a]
1	5	5	30	20	4
2	5	5	60	20	11
3	5	5	100	20	22
4	10	10	100	20	19
5	20	20	100	20	18
6[b]	20	5	100	8 + 20	27
7[c]	5	5	80	20	3

[a] Determined by ^{1}H NMR analysis. [b] Slow addition of antimonate catalyst over 8 h. [c] MeCN as a solvent and 5 equivalents of $MeNO_2$.

1.9 Other nucleophiles

In order to apply this catalytic system other types of nucleophiles, further modification to the reaction conditions were made (Table 1-5). When several solvents were screened using 1.1 equivalents of dimethyl malonate as a nucleophile, surprisingly, only the reaction in acetonitrile gave the desired product in a high yield (entry 1), while the reactions in all the other solvents resulted in very poor yields (entries 2-5). I assume that the some of the radical species and the iminium intermediate were stabilized by acetonitrile. Although methanol is also a very polar solvent that has been used in the past for the CDC reaction, it is probable that the catalyst underwent solvolysis to lose its activity in this case.

Table 1-5. Effect of solvents



1a (1.1 eq.) **2ac**

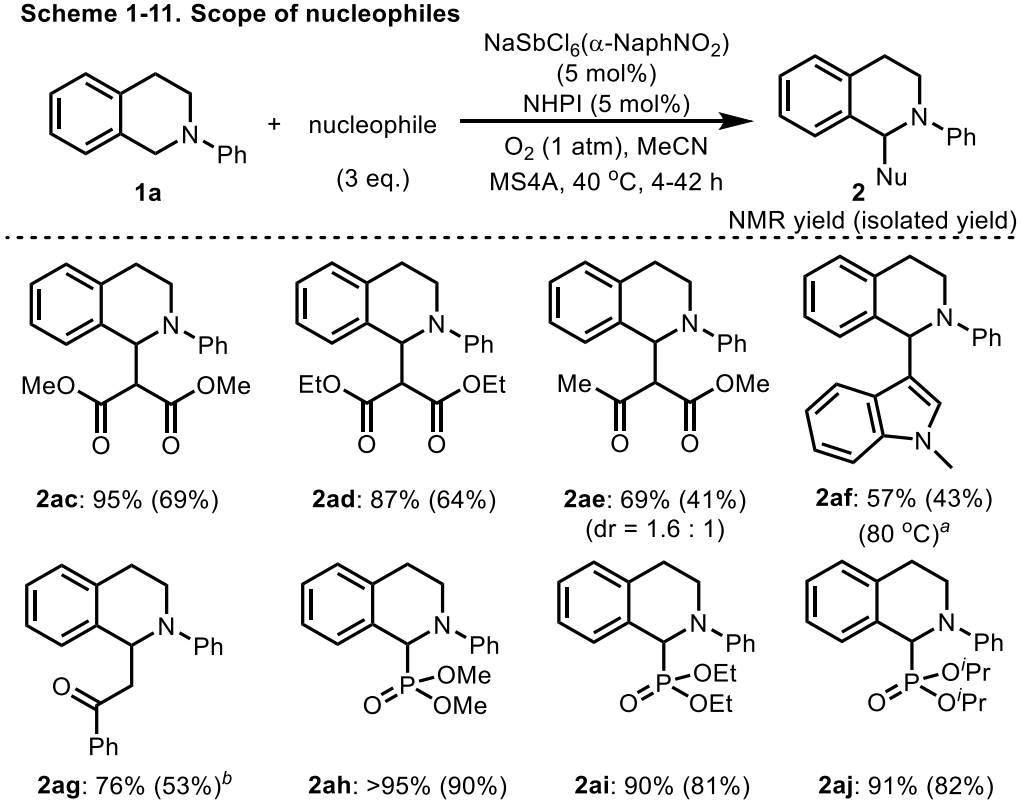
entry	solvent	**2ac** (%)[a]	rec. **1a** (%)[a]
1	MeCN	88	ND
2	$CHCl_3$	6	93
3	THF	4	99
4	MeOH	3	96
5	hexane	5	92

[a] Determined by ^{1}H-NMR analysis.

With the optimized conditions in hand, other nucleophiles were also examined using acetonitrile as a solvent under a slightly elevated temperature (Scheme 1-11). Both dimethyl and diethyl malonates gave the products in good yields (**2ad** and **2ae**). It was found that the reactivity of β-ketoester was modest (**2ae**). In addition to sp^3-hybridized carbon nucleophile, sp^2 carbon nucleophiles, such as *N*-methylindole and a acetophenone-derived silyl enolate, also reacted (**2af** and **2ag**). Furthermore, phosphine-based nucleophiles such as dimethyl, diethyl and diisopropyl phosphites

provided the corresponding products in high yields (**2ah**, **2ai** and **2aj**).

Scheme 1-11. Scope of nucleophiles



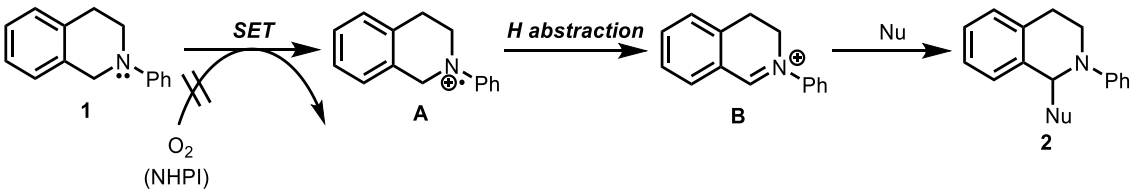
[a] 1.5 equivalents of nucleophile were employed. [b] Corresponding silyl enolate was used.

1.10 Insights into the reaction mechanism

Based on my experimental results and the previously reported mechanistic studies on the CDC reactions,[17] I believe that the Sb/NHPI-catalyzed CDC reaction proceeds through a single electron oxidation−hydrogen abstraction sequence.

In the absence of antimonate, with or without NHPI, the reactions were extremely sluggish (Scheme 1-12). This means that oxygen or the combination of oxygen and NHPI cannot induce the initial single electron transfer (SET) process. Therefore,

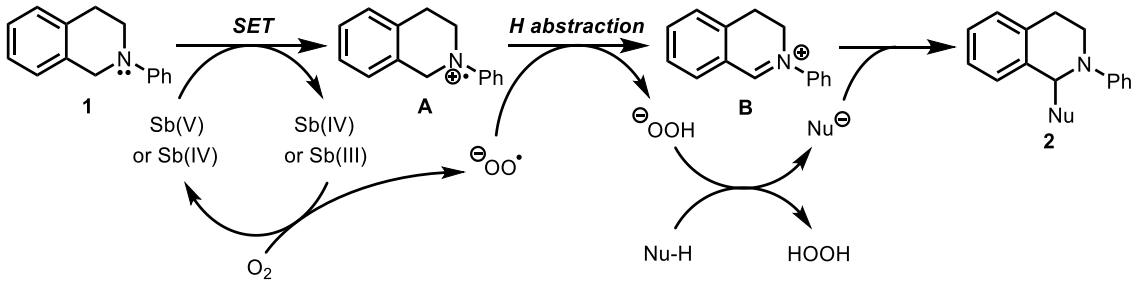
Scheme 1-12. O_2/(NHPI)



antimonate is responsible for the initial single electron oxidation of the tertiary amines.

On the other hand, when the reaction was performed in the presence of antimonate under oxygen atmosphere, catalytic turnover was observed. In this case, the initial catalytic single electron oxidation took place (Scheme 1-13). Since the antimonate-catalyzed CDC reaction was relatively slower than the Sb/NHPI system, it would suggest that although the subsequent hydrogen abstraction by the oxygen radical anion takes place, the rate of this abstraction is slow in the absence of NHPI.

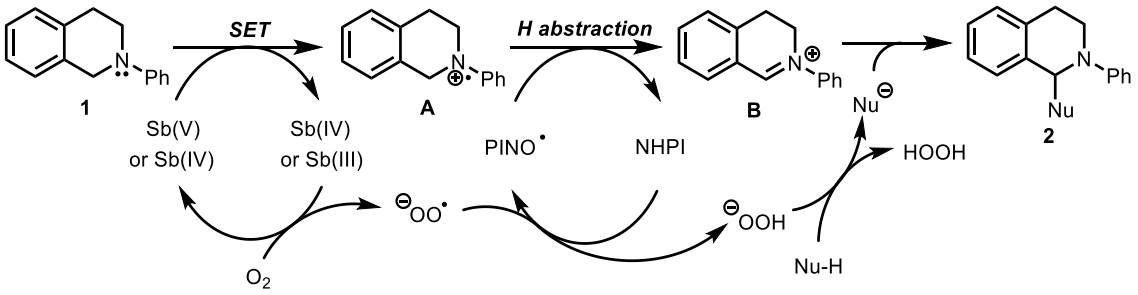
Scheme 1-13. Sb/O_2



Thus, in the presence of both antimonate and NHPI, I believe the reaction proceeds through the mechanism as shown below (Scheme 1-14). The initial single electron oxidation of the tertiary amine **1** was induced by the higher valent antimonies, Sb(V) or Sb(IV), which generates an aminium radical intermediate **A**. The resultant lower valent antimonies, Sb(IV) or Sb(III), are then oxidized by oxygen gas to regenerate the higher valent antimonies, accompanied by the formation of the oxygen radical anion. Since the oxidation potential of $SbCl_6^-$ is reported to be 0.2 V,[43] while the oxidation of the tertiary amine **1** requires 0.55 V,[3f] $SbCl_6^-$ is not the active catalyst but a reservoir of the true active species such as $SbCl_5$. Next, the radical anion of oxygen abstracts the hydrogen atom from NHPI to generate the PINO radical and the hydrogen peroxide anion, which functions as a base to deprotonate the pronucleophile. Subsequently, the PINO radical abstracts the hydrogen atom from intermediate **A** to afford iminium intermediate **B**. Finally, intermediate **B** undergoes nucleophilic addition to furnish the desired CDC product. Since hydrogen abstraction by PINO radical is known to be much faster than ROO· species, such acceleration may be possible when compared with the hydrogen abstraction by the oxygen radical anion, which explains the faster reaction

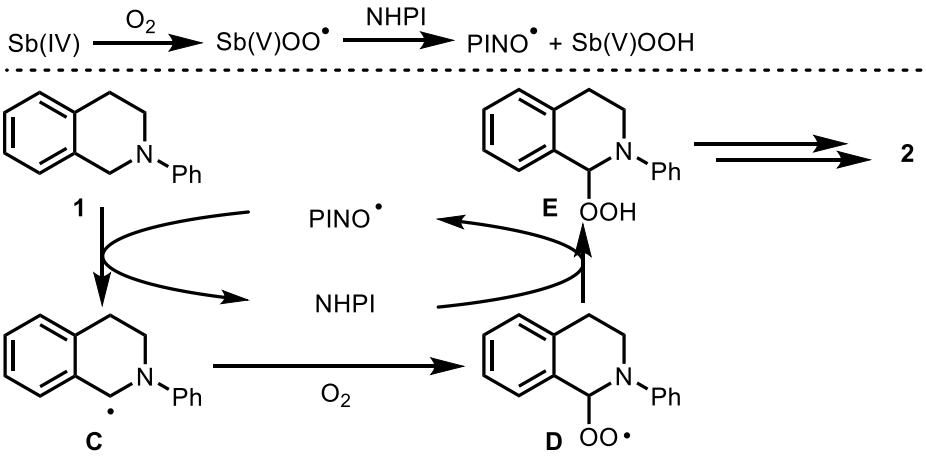
rate in the presence of NHPI. Although the possibility of the aminium radical catalysis in the initial SET process cannot be completely ruled out, this contribution would be very small, if any, since tetrafluoroborate and hexafluorophosphate salts of aminium radicals provided the oxidative aza-Mannich product in low yields.

Scheme 1-14. Sb/NHPI/O_2



In addition to a catalytic SET−hydrogen abstraction mechanism, the possibility of a radical-initiated autoxidation mechanism through the formation of carbon-centered radical intermediate should be considered. In the aerobic alcohol oxidation catalyzed by the Co/NHPI system, Ishii *et al*. suggested a NHPI-initiated radical-based autoxidation mechanism.[33b] More specifically, Co(III)OO· abstracts the hydrogen atom from NHPI to initiate the reaction, and the resultant PINO radical catalyzed the autoxidation to propagate the reaction. Similar event may be applicable in our reaction system. A lower valent antimony such as Sb(IV) can be generated by the single electron oxidation of the tertiary amine. Then, oxygen gas reacts with Sb(IV) provide Sb(V)OO·, which interacts with NHPI to generate a PINO radical to initiate the reaction (Scheme 1-15).

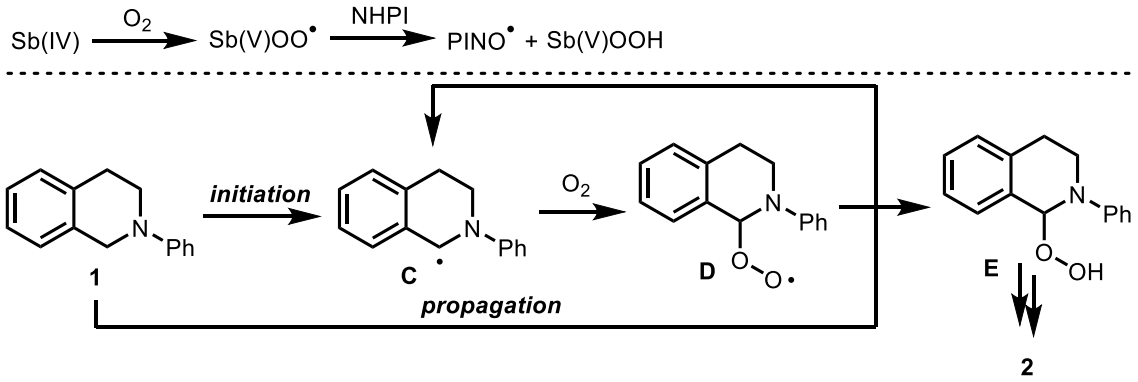
Scheme 1-15. Mechanism based on the Co/NHPI autoxidation system



Autoxidation proceeds through the initial hydrogen abstraction from **1** to generate the carbon-centered radical **C**, to which oxygen attacks to afford the radical intermediate **D** Subsequently, this radical intermediate abstracts the hydrogen atom from NHPI to regenerate the PINO radical and provide the intermediate **E**, which undergoes nucleophilic addition to furnish the product. Such a mechanism cannot be denied at this stage.

In a similar fashion, a more genuine radical-initiated autoxidation mechanism can be used to explain my current reaction system (Scheme 1-16). The initiation of the reaction follows the same manner (*vide supra*). After the hydrogen abstraction of **1** by the PINO radical, it also follows the same reaction pathway. However, the main difference is that under the genuine autoxidation mechanism, the reaction is propagated by the hydrogen abstraction of **1** by the radical intermediate **D**. Such a reaction mechanism also cannot be ruled out.

Scheme 1-16. Genuine autoxidation mechanism

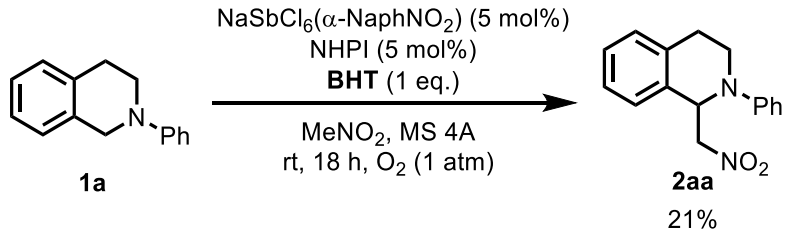


1.11 Effect of a radical inhibitor

To confirm the radical mechanism, the effect of radical inhibitor was examined (Scheme 1-17). When a stoichiometric amount of a radical inhibitor, 3,5-di-*t*-butyl-4-hydroxytoluene (BHT), was added, the oxidative nitromethylation reaction was significantly suppressed. Thus, the reaction is likely to proceed through the formation of radical intermediates. Although the reaction was not completely inhibited, similar phenomenon is sometimes observed in the CDC reactions of tertiary amines. For example, when Klussmann *et al*. added 2 equivalents of BHT to the CuBr/TBHP system,

the oxidative nitromethylation started to proceed after the complete consumption of TBHP.[17b] Thus, such an event may be also taking place in my reaction system.

Scheme 1-17. Addition of a radical inhibitor



1a **2aa** 21%

1.12 Conclusion

To summarize this chapter, during the course of my investigation to utilize aminium radical cations for the cross-dehydrogenative coupling reactions of tertiary amines under aerobic conditions, it was discovered that antimonate anion served as a catalyst for the CDC reaction. Moreover, the addition of NHPI as a hydrogen abstraction promoter significantly accelerated this transformation. Thus, a $NaSbCl_6$/NHPI system was found to be an efficient system for the oxidative coupling reaction of tertiary amines under mild aerobic conditions. Although there was no notable advantage compared with previously reported methodologies, it was worth disclosing that hexahaloantimonate anions, which are commonly regarded as innocent, non-coordinating counter anions, served as a catalyst for aerobic oxidation.

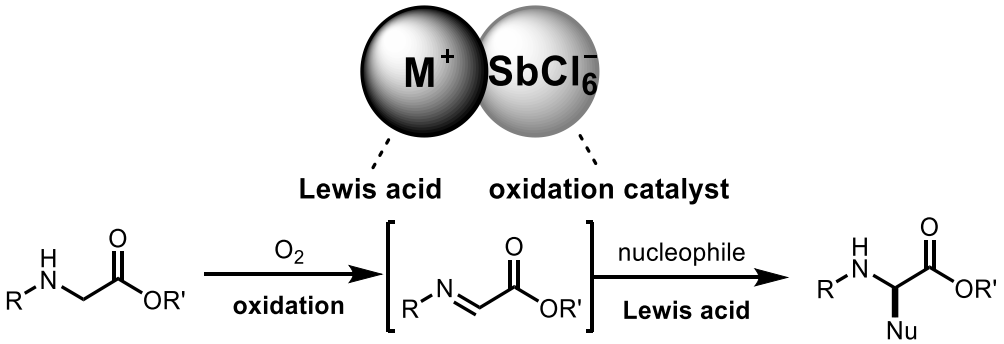
Chapter 2. Zinc antimonate-catalyzed oxidative allylation of α-amino acid derivatives

2.1 Introduction

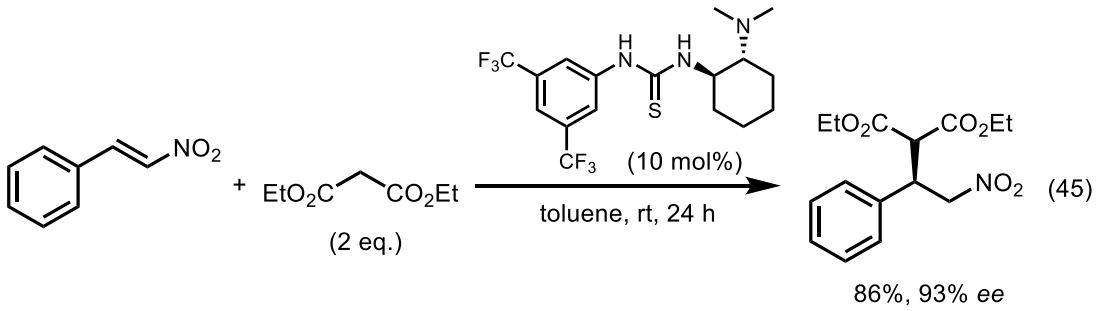
Although the antimonate/NHPI system exhibited an interesting transition metal-free CDC reaction, the scope of substrate was only limited to *N*-aryl tetrahydroisoquinolines. To solve the problem of substrate limitation, I hypothesized that some α-amino acid derivatives could serve as alternative substrates that are synthetically more useful. As previously discussed, several examples of CDC-type reactions of glycine derivatives have been reported.[18,19] However, among these oxidative coupling reactions, examples of using oxygen as a terminal oxidant were almost non-existent. Thus, I planned to develop the Sb/NHPI system for the oxidative coupling reaction of glycine derivatives.

Among the previously reported CDC-type reactions of α-amino acid derivatives, glycine esters or amides that were mono-protected by a PMP moiety on the nitrogen seemed to be good candidates of substrates. Unlike the CDC reactions of tertiary amines, which proceed through the formation of highly reactive iminium intermediates, secondary amines are oxidatively transformed into the less active imine intermediates. Therefore, in order to develop a more efficient CDC-type reaction with secondary amines, Lewis acids are required. Based on this consideration, in addition to the idea of using α-amino acid derivatives as substrates, I considered the possibility of employing a metal antimonate as a novel type of bifunctional catalyst that could serve both as an oxidation catalyst and a Lewis acid (Scheme 2-1).

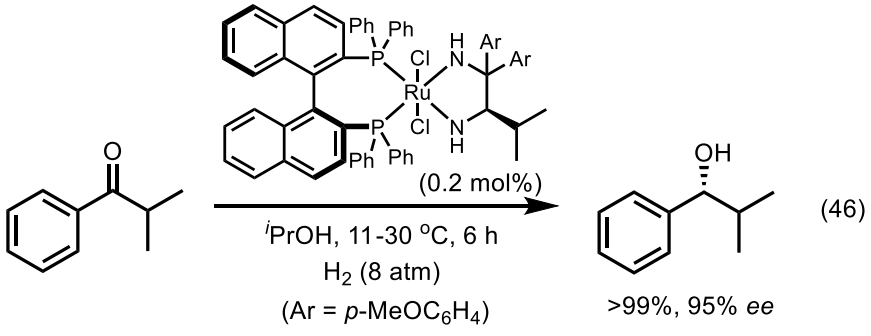
Scheme 2-1. Metal antimonate as a bifunctional catalyst



Bifunctional catalysts are catalysts that are designed to exhibit two roles cooperatively and various examples of bifunctional catalysts have been reported. For instance, in 2003, Takemoto *et al*. reported the enantioselective Michael reaction using a chiral thiourea that possesses both hydrogen bonding capability and Lewis basicity within the molecular catalyst (eq. 45).[44] This thiourea is now called the Takemoto catalyst.

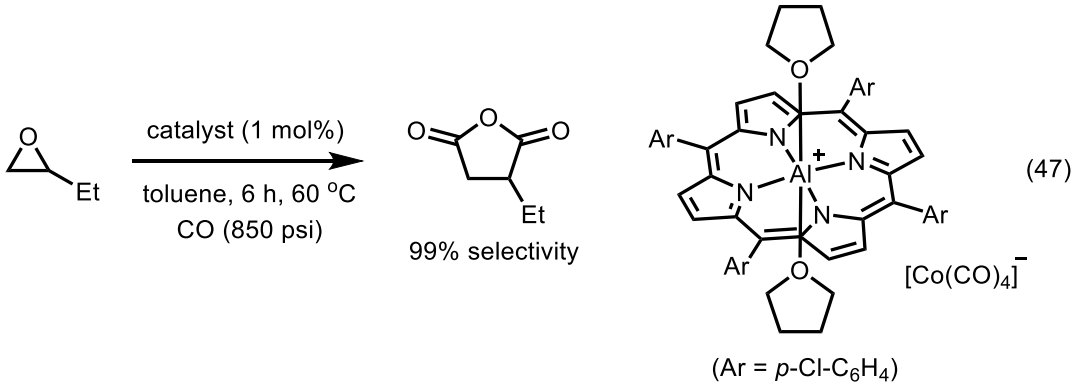


Noyori *et al*. has long studied the catalytic asymmetric hydrogenation reactions. In 1995, they found that chiral ruthenium catalysts that possess a chiral BINAP and a chiral diamine as ligands are highly effective for the asymmetric hydrogenation of ketones (eq. 46).[45] These active ruthenium complexes catalyzed the asymmetric hydrogenation through a metal-ligand bifunctional mechanism, in which the hydridic Ru-H and protic N-H are delivered to the carbonyl moiety via a six-membered pericyclic transition state.



A rare example of a bifunctional catalyst, a metal-ion pair with orthogonal characteristics, was reported by Coates *et al*. in 2007 (eq. 47).[46] In their reaction

system, the cationic aluminum served as a Lewis acid, while anionic cobalt serves as a carbonylation catalyst to achieve the selective dicarbonylation of epoxides to provide succinic imides.



(47)

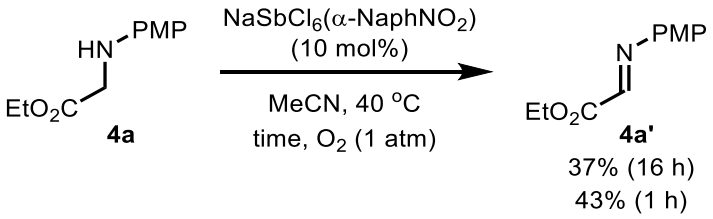
Compared with these bifunctional catalysts, metal antimonates could be considered as a new class of bifunctional catalyst, in which the metal cation plays the role of a Lewis acid and the metal anion plays the role of the oxidation catalyst. Furthermore, since non-coordinating counter anions are known to enhance the Lewis acidity of their counter cations,[47] it can be expected that the metal antimonate salts possess a strong Lewis acidity. Based on these hypotheses, I investigated the oxidative coupling reactions of α-amino acid derivatives using metal antimonate as a bifunctional catalyst.

2.2 Initial attempt on the oxidation of glycine ester

Since it is often employed as a model substrate for the CDC reactions of glycine derivatives and *p*-methoxyphenyl (PMP) group is one of the easiest protecting groups to remove among the various aromatic substituents (e.g., removal of phenyl group requires more harsh conditions than PMP requires), *p*-methoxyphenyl-substituted glycine ethyl ester **4a** was selected as a model substrate. Initially, I attempted the dehydrogenation of this glycine ester using 10 mol% of sodium hexachloroantimonate under oxygen gas at 40 °C over 16 hours (Scheme 2-2). As a result, the corresponding imino ester **4a'** was obtained in 37% yield after aqueous quenching. Then, it was found that this oxidation completed within only 1 hour and the corresponding imino ester could be obtained in 43% yield. Although this yield was relatively low, I decided to continue this work since:

(i) without aqueous quenching, the yield may be higher; (ii) this may be improved later; and (iii) in the presence of a nucleophile, side-reactions may be suppressed.

Scheme 2-2. Oxidation of glycine ester



2.3 Oxidative allylation of glycine ester

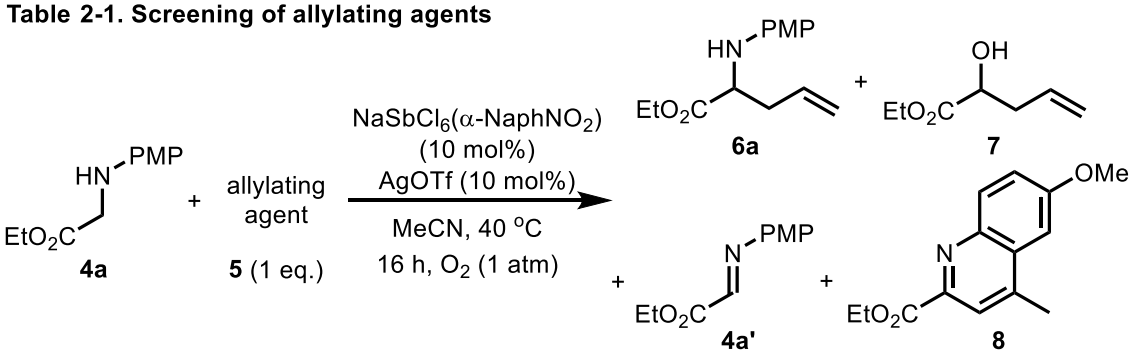
As a model reaction, an oxidative allylation reaction was chosen since: (i) the corresponding product can be further converted to a wide variety of compounds by already reported processes; (ii) during my master course, I investigated the allylation reactions of aldehydes; and (iii) other nucleophiles such as nitromethane did not work well.

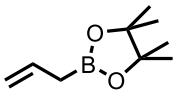
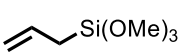
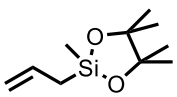
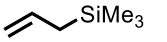
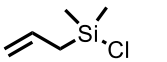
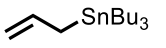
Thus, I initially examined the oxidative allylation reaction of PMP-substituted glycine ester with allylboronate in the presence of sodium antimonate (10 mol%) and silver triflate (10 mol%) as an alternative to silver antimonate (Table 2-1, entry 1). At this stage, I believed that the combination of sodium antimonate and metal triflate would allow for a more rapid screening of the appropriate metal-antimonate combination, and my plan was to determine the optimal paring before preparing the well-defined metal antimonate complex. When this reaction was performed in acetonitrile at 40 °C, homoallylic alcohol **7** was obtained in a modest yield instead of the desired allylated product **6a**, probably due to the hydrolysis of imino ester intermediate **4a'** and nucleophilic addition to the corresponding ethyl glyoxylate. When allyltrimethylsilane was examined as a nucleophile, the desired product was obtained in a low yield (entry 2). However, in this case, a side-product **8** was also produced in a comparable yield. Allylchlorodimethylsilane also exhibited similar reactivity (entry 3). Also, allylpinacolatosilane, previously used for the allylation of aldehydes, gave the desired product only in a low yield (entry 4). On the other hand, one of the most

common allylating agent, allyltrimethoxysilane, afforded only a trace amount of the desired product (entry 5). When allyltin was used as a nucleophile, the desired product was obtained only in a low yield (entry 6). Surprisingly, in this case, the oxidation of glycine ester was also suppressed and a significant amount of **4a** was recovered. Thus, I speculated that the addition of allyltin after the oxidation was completed could improve the reactivity. When allyltin was added after 1 hour, the desired product was obtained in a moderate yield, accompanied with the formation of the homoallylic alcohol **7** in a low yield (entry 7). When, 2 equivalents of glycine ester was employed, the reactivity slightly improved (entry 8).

Although the oxidative allylation of glycine ester with allyltin was found to be promising, I initially decided to focus on the use of allylsilanes since: (i) allylsilanes did not suppress oxidation, thus enabling the oxidation and allylation to occur at the same time; and (ii) it is desirable to avoid using toxic allyltin from the view point of

Table 2-1. Screening of allylating agents



entry	allylating agent		**6a** (%)[a]	**7** (%)[a]	**4a'** (%)[a]
1		**5a**	ND	24	trace
2		**5b**	trace	ND	17
3		**5c**	12	trace	13
4		**5d**	18	ND	trace
5		**5e**	12	ND	trace
6			7	ND	ND
7[b]		**5f**	51	11	ND
8[b,c]			56	15	ND

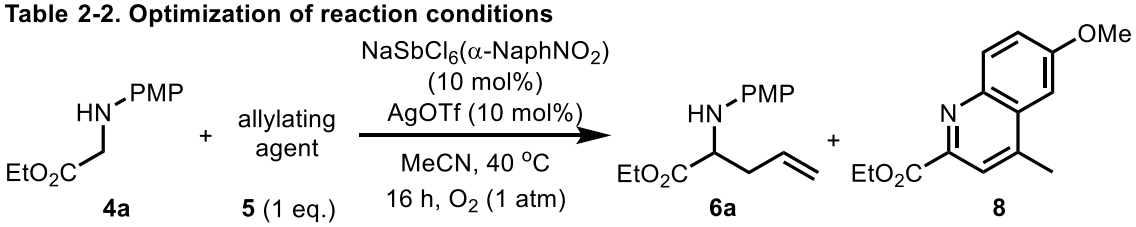
[a] Determined by ^{1}H NMR analysis. [b] Allylating agent was added after 1 h. [c] 2 eq. of **4a** were employed.

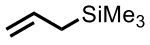
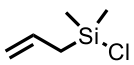
environmental protection.

2.4 Oxidative allylation with allylsilanes

The reaction conditions were optimized using allyltrimethylsilane as a nucleophile (Table 2-2). The problems associated with using allyltrimethylsilane were its low reactivity and the competing formation of the quinoline side-product **8** (entry 1). When the nucleophile was added after the oxidation was completed, only slight improvement on the distribution of the products was observed (entry 2). When the reaction was performed at room temperature, the reactivity was suppressed (entry 3) and at 60 °C, only quinoline **8** was obtained (entry 4). When the reaction was quenched after 1 hour, the yield of the desired product improved. This suggested that the reaction occurred rapidly and that the oxidatively allylated product gradually decomposed during the longer reaction time (entry 5). In order to improve the reactivity, the use of 2 equivalents of allylsilane was examined (entry 6). However, it resulted in the suppression of the reaction. Instead, when I employed 2 equivalents of the glycine ester,

Table 2-2. Optimization of reaction conditions



entry	allylating agent	modified conditions	**6a** (%)[a]	**8** (%)[a]
1		-	18	14
2[b]		-	23	14
3		rt	16	9
4		60 °C	ND	20
5		1 h	30	18
6	**5d**	1 h, 2 eq. allylTMS	21	13
7		1 h, 2 eq. glycine ester	37	28
8[b]		2 h, 2 eq. glycine ester	45	13
9[c]		3 h, 2 eq. glycine ester	41	9
10		-	12	27
11		1 h	28	26
12	**5e**	1 h, 2 eq. glycine ester	38	37
13[b]		2 h, 2 eq. glycine ester	54	18

[a] Determined by ^{1}H NMR analysis. [b] **5** was added after 1 h. [c] **5** was added after 2 h.

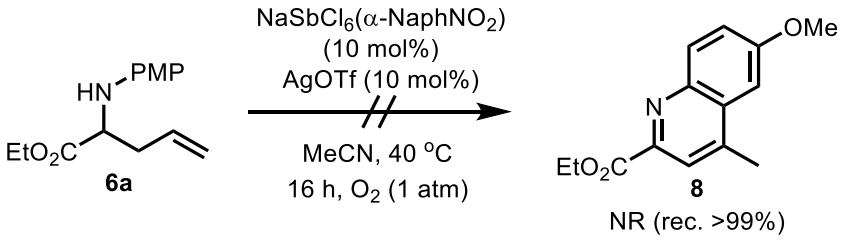
significant improvement on the reactivity was observed, but the product distribution did not improve (entry 7). Subsequently, I tested the addition of the nucleophile after 1 hour under the conditions used in entry 7 (entry 8). Surprisingly, this suppressed the formation of quinoline **8** and promoted the formation of the desired product (entry 9). The addition of nucleophile after 2 hours did not further improve the reactivity.

Then, I examined allylchlorodimethylsilane as a nucleophile, which gave more quinoline **8** than the desired product under the standard conditions (entry 10). When the reaction was quenched after 1 hour, more of the desired product was obtained, although the product distribution was almost 1 : 1 (entry 11). When 2 equivalents of the nucleophile were employed, both products were obtained in higher yields (entry 12). Finally, the nucleophile was added after the oxidation was completed (entry 13). Although it suppressed the formation of side-product and the desired product was obtained in a moderate yield, still there was a necessity to improve the reactivity.

2.5 Formation of quinoline **8**

In order to investigate the possibility that the allylated product was converted to the quinoline side-product **8**, the allylated glycine ester **6a** was subjected to the same reaction conditions employed for the oxidative allylation (Scheme 2-3). However, even under the oxidative reaction conditions, the glycine ester **6a** was not consumed at all. Thus, it was clarified that quinoline **8** was not generated from the allylated glycine ester **6a**.

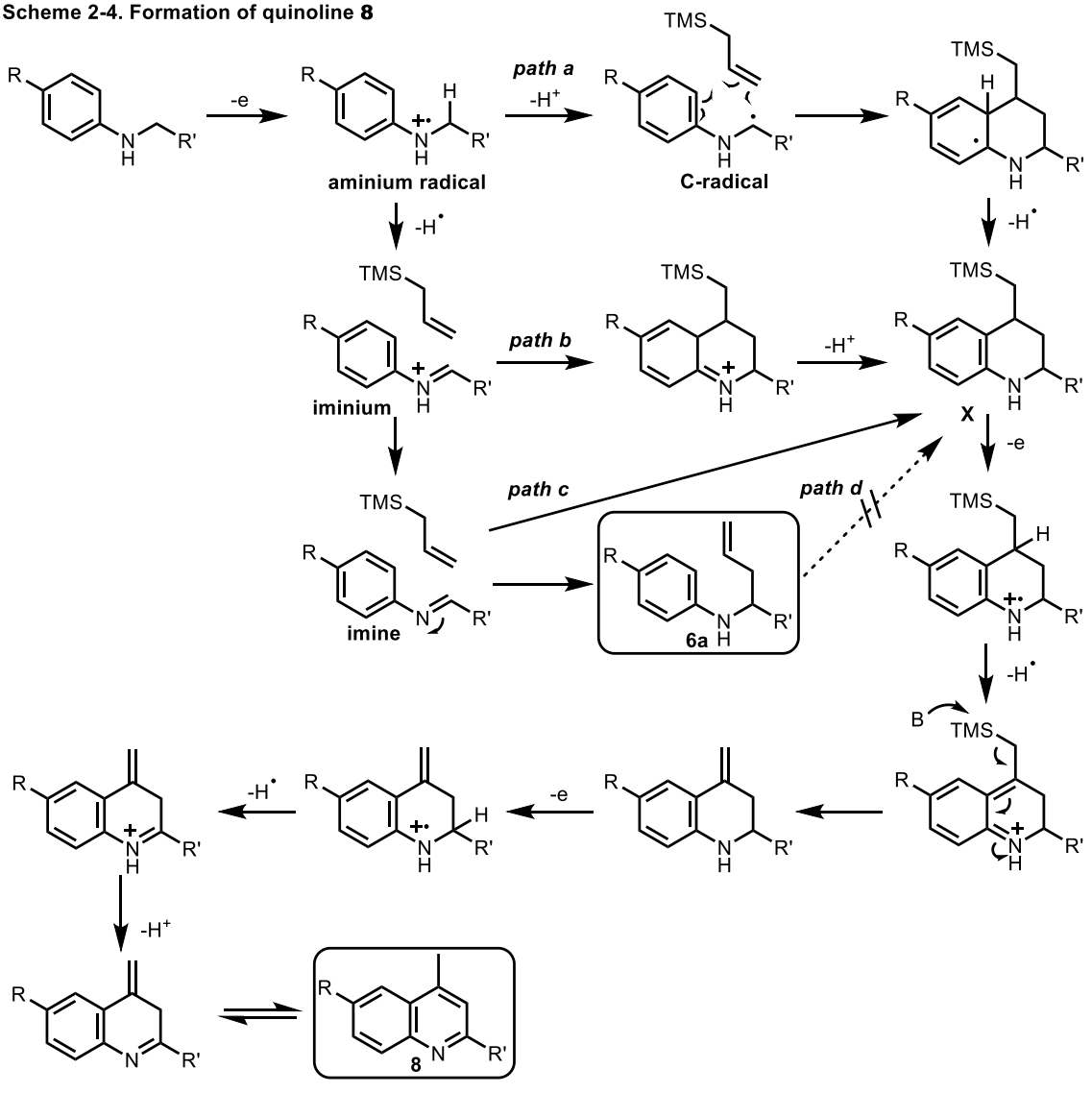
Scheme 2-3. Stability of the product



Although the exact mechanism to provide the quinoline by-product **8** is not clear, I consider three pathways (Scheme 2-4). The reaction starts from the single electron

oxidation of glycine ester to form aminium radical intermediate. If this intermediate undergoes deprotonation, the resultant carbon-centered radical may undergo the radical cyclization with allylsilane (***path a***). Subsequent abstraction of hydrogen provides intermediate **X**. On the other hand, if the aminium radical intermediate undergoes hydrogen radical abstraction, it generates an iminium intermediate. Thus, the Diels--Alder reaction of this intermediate with allylsilane and the subsequent deprotonation can provide the same intermediate **X** (***path b***). In the case where the iminium intermediate was deprotonated, the corresponding imino ester intermediate can undergo either the Diels-Alder reaction with the assistance of the Lewis acid to provide intermediate **X** (***path c***), or the nucleophilic addition would provide allylated product **6a**.

Scheme 2-4. Formation of quinoline 8

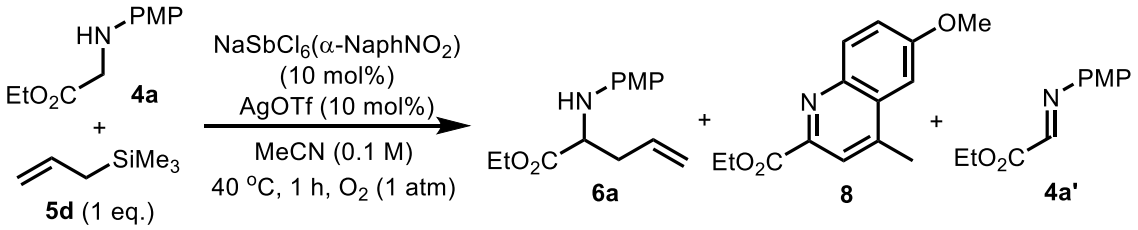


However, the possibility of generating intermediate **X** from product **6a** was experimentally denied (***path d***). Subsequently, intermediate **X** can furnish the quinoline **8** through single electron oxidation, hydrogen abstraction, elimination of TMS moiety and isomerization.

2.6 Effect of solvents

In order to improve the reactivity, the effect of solvents was investigated (Table 2-3). Based on the solvent screening study, acetonitrile was found to be the best solvent (entry 1). Although the reaction also proceeded in propionitrile, the reactivity was poorer than that in acetonitrile (entry 2). When the reaction was performed in dichloromethane, only the formation of quinoline was observed without formation of the desired product (entry 3). Other solvents such as THF, ethanol, toluene, NMP, DMF and DMSO gave no or only little desired product (entries 4-9). Next, the effect of concentration was examined. However, both lower and higher concentration in acetonitrile suppressed the reaction (entries 10 and 11).

Table 2-3. Effect of solvents



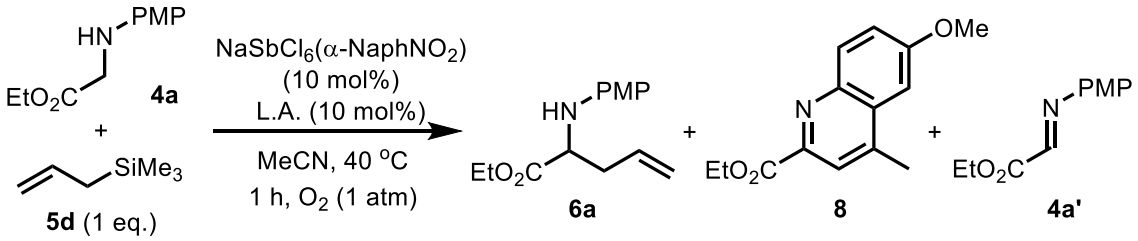
entry	solvent	**6a** (%)[a]	**8** (%)[a]	**4a'** (%)[a]
1	MeCN	30	18	2
2	EtCN	20	20	1
3	DCM	ND	18	7
4	THF	3	9	41
5	EtOH	ND	ND	24
6	toluene	trace	4	23
7	NMP	ND	ND	21
8	DMF	ND	ND	9
9	DMSO	ND	ND	11
10	MeCN (0.05 M)	22	17	3
11	MeCN (0.25 M)	19	11	4

[a] Determined by ^{1}H NMR analysis.

2.7 Effect of Lewis acids

Next, the effect of Lewis acids was tested (Table 2-4). Surprisingly, the reaction proceeded in the absence of any Lewis acids, suggesting that sodium antimonate itself served as a Lewis acid (entry 1). When silver triflate was employed, slight improvement on the reactivity was observed (entry 2). Among the metal triflates examined, cerium(IV) triflate was found to be the best Lewis acid, which provided the desired product and the quinoline by-product in a 2 : 1 ratio (entry 3). Other metals such as magnesium(II), copper(I) and aluminum(III) triflates provided the allylated product in comparable or slightly lower yields (entries 4-6). However other metals such as scandium(III), zinc(II), iron(III), indium(III) and copper(II) triflates furnished little to no amounts of the desired product (entries 7-11).

Table 2-4. Effect of Lewis acids



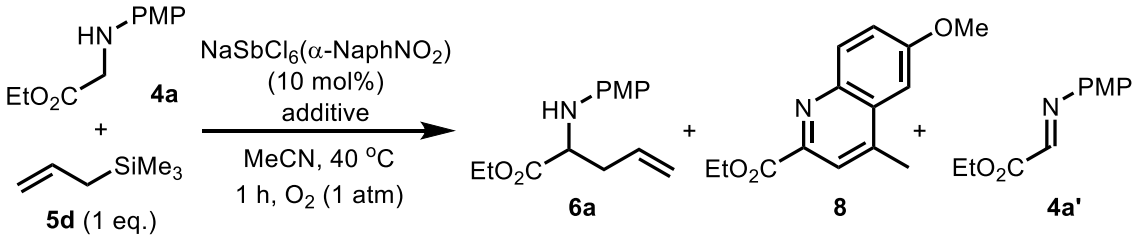
entry	Lewis acid	**6a** (%)[a]	**8** (%)[a]	**4a'** (%)[a]
1	-	21	15	1
2	AgOTf	30	18	2
3	$Ce(OTf)_4$	36	18	ND
4	$Mg(OTf)_2$	29	17	ND
5	CuOTf•0.5toluene	22	7	ND
6	$Al(OTf)_3$	16	11	2
7	$Sc(OTf)_3$	7	3	ND
8	$Zn(OTf)_2$	6	3	ND
9	$Fe(OTf)_3$	6	3	ND
10	$In(OTf)_3$	8	3	ND
11	$Cu(OTf)_2$	ND	4	ND

[a] Determined by ^{1}H NMR analysis.

2.8 Effect of additives

To improve the reactivity of the oxidative allylation of the PMP-protected glycine ester by allylsilane, several additives were tested (Table 2-5). When a catalytic amount of pyridine was added, the reaction was suppressed (entry 2). Also, acetic acid was found to inhibit the reaction (entry 3). In order to minimize the hydrolysis of the imino ester intermediate, drying agents were introduced. However, the use of MS4A significantly suppressed the CDC reaction (entry 4), while magnesium sulfate did not improve the reactivity (entry 5).

Table 2-5. Effect of additives



entry	additive	**6a** (%)[a]	**8** (%)[a]	**4a'** (%)[a]
1	-	21	15	1
2	pyr. (20 mol%)	11	6	27
3	AcOH (20 mol%)	17	10	1
4	MS4A	5	trace	ND
5	$MgSO_4$	23	18	4

[a] Determined by ^{1}H NMR analysis.

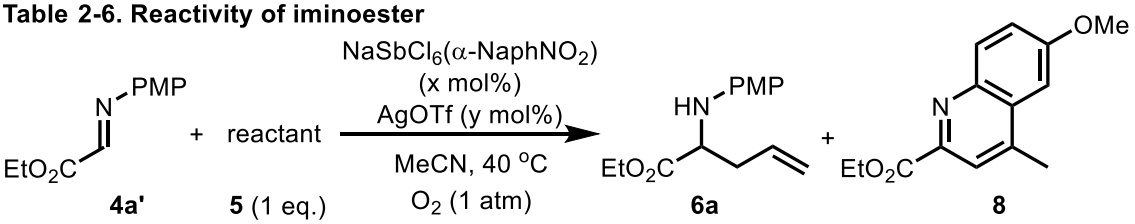
2.9 Comparison between allylsilane and allyltin

Because the oxidative allylation with allylsilane was not efficient, I decided to employ allyltin since it gave the desired product in a good yield. Before starting the optimization process, the reactivity of allylsilane and allyltin was compared using imino ester **4a'** as an electrophile (Table 2-6). Although it was not necessarily needed, the reactions were performed under oxygen atmosphere to see the effect of oxygen. In case of allyltrimethylsilane, no reaction took place in the absence of catalysts (entry 1). Also,

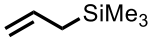
silver triflate itself did not induce any reaction (entry 2). When sodium antimonate was employed as a catalyst, the allylation reaction took place, accompanied by the formation of quinoline **8** (entry 3). Under argon atmosphere the formation of quinoline was significantly suppressed (entry 4). When both catalysts were added, no improvement on the reactivity was observed (entry 5). To summarize these results, only sodium antimonate could catalyze the allylation with allylsilane, while silver triflate did not possess enough activity to induce allylation of imino ester.

On the other hand, when allyltin was employed as a nucleophile, a very slow background reaction was observed in the absence of catalysts (entry 6). When silver triflate was used as a catalyst, the allylated product was obtained in a moderate yield (entry 7). However, when 20 mol% silver triflate was added, no improvement on the reactivity was observed (entry 8). In contrast, sodium antimonate provided the allylated product in a very low yield (entry 9). When both catalysts were employed, the reactivity was diminished compared with using only silver triflate as catalyst (entry 10). Thus, in contrast to allylsilane, only silver triflate exhibited good catalytic activity for the nucleophilic addition reactions of allyltin.

Table 2-6. Reactivity of iminoester



4a' **5** (1 eq.) **6a** **8**

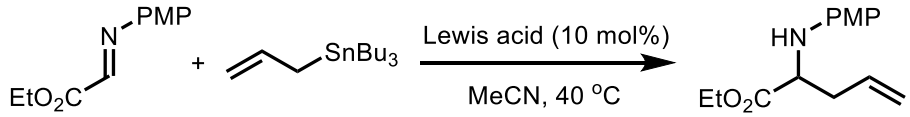
entry	reactant	x (mol%)	y (mol%)	**6a** (%)[a]	**8** (%)[a]	rec. **4a'** (%)[a]	rec. **5** (%)[a]
1	 **5d**: (1 h)	-	-	ND	ND	>99	ND
2		-	10	ND	ND	97	ND
3		10	-	31	22	2	ND
4[b]		10	-	40	5	2	ND
5		10	10	28	17	ND	ND
6	**5f**: (16 h)	-	-	2	ND	83	70
7		-	10	51	ND	15	35
8		-	20	49	ND	4	ND
9		10	-	7	ND	26	22
10		10	10	30	ND	27	35

[a] Determined by ^{1}H NMR analysis. [b] Under Ar.

2.10 Screening of Lewis acids

Next, the effect of Lewis acids was investigated (Table 2-7). In the absence of Lewis acids, only a very slow background reaction was observed (entry 1). As shown previously, silver triflate gave the desired product in a moderate yield (entry 2). When other metal triflates were examined, zinc(II) and indium(III) triflates were found to give the allylated product in high yields (entries 3 and 4). Other Lewis acids such as gallium(III), ytterbium(III), aluminum(III), lanthanum(III), cerium(IV), iron(III), scandium(III), tin(II) and magnesium(II) triflates provided the desired product in good to modest yields (entries 5-13). On the other hand, copper(I) and copper(II) triflate furnished the product only in low yields (entries 14 and 15). Based on these results, I selected zinc(II) as the best counter cation for the metal antimonate.

Table 2-7. Effect of Lewis acids



4a' **5f** (1 eq.) **6a**

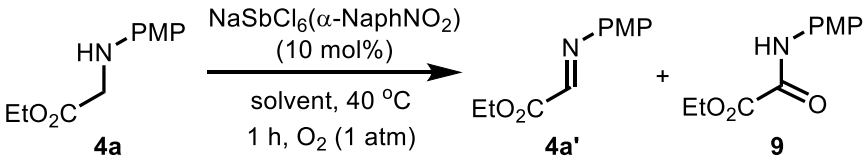
entry	Lewis acid	**6a** (%)[a]	rec. **4a'** (%)[a]	rec. **5f** (%)[a]
1	-	2	83	70
2	AgOTf	51	15	35
3	$Zn(OTf)_2$	74	ND	8
4	$In(OTf)_3$	71	ND	3
5	$Ga(OTf)_3$	62	10	20
6	$Yb(OTf)_3$	58	10	24
7	$Al(OTf)_3$	57	14	20
8	$La(OTf)_3$	54	10	33
9	$Ce(OTf)_4$	53	2	9
10	$Fe(OTf)_3$	42	3	6
11	$Sc(OTf)_3$	43	23	28
12	$Sn(OTf)_2$	44	17	25
13	$Mg(OTf)_2$	43	24	49
14	$Cu(OTf)_2$	21	7	ND
15	CuOTf·0.5toluene	9	23	5

[a] Determined by ^1H NMR analysis.

2.11 Effect of solvents in oxidation

Before starting the oxidative allylation reaction, the oxidation of glycine ester **4a** was investigated. First the effect of solvents was examined (Table 2-8). When the oxidation was performed in acetonitrile in the presence of 10 mol% sodium antimonate, the desired imino ester **4a'** was obtained in 43% yield, accompanied by the formation of amide **9** in a low yield (entry 1). In addition to acetonitrile, the oxidation in dichloromethane, THF and nitromethane provided the imino ester in similar yields (entries 2-4). On the other hand, the oxidation in toluene, DMSO and ethanol gave the imino ester in lower yields (entries 5-7). Thus, the efficiency of oxidation could not be improved by replacing the solvent.

Table 2-8. Effect of solvents



entry	solvent	**4a'** (%)[a]	**9** (%)[a]	rec. **4a** (%)[a]
1	MeCN	43	12	ND
2	DCM	44	6	ND
3	THF	43	5	ND
4	$MeNO_2$	44	3	ND
5	toluene	36	6	ND
6	DMSO	28	4	ND
7	EtOH	20	5	19

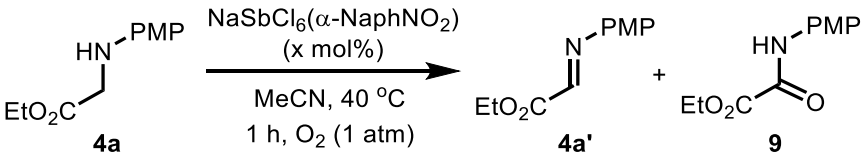
[a] Determined by ^{1}H NMR analysis.

2.12 Catalyst loading

Next, the effect of the catalyst loading was investigated (Table 2-9). The oxidation of glycine ester **4a** in the presence of 10 mol% sodium antimonate gave the imino ester **4a'** in 43% yield (entry 1). Although the catalyst loading was gradually reduced down to 1 mol%, the imino ester was still obtained in similar yields (entries 2-5). Thus, it turned out that only a small amount of antimony is required for the aerobic oxidation of glycine

ester **4a**.

Table 2-9. Catalyst loading



entry	x (mol%)	**4a'** (%)[a]	**9** (%)[a]	rec. **4a** (%)[a]
1	10	43	12	ND
2	5	41	14	ND
3	3	41	10	ND
4	2	45	17	ND
5	1	44	20	ND

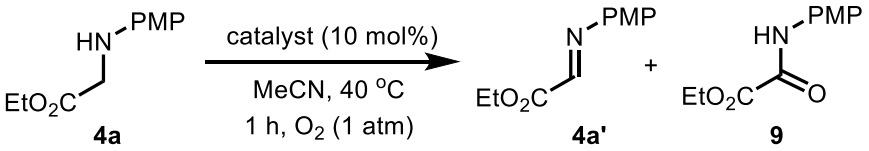
[a] Determined by ^{1}H NMR analysis.

2.13 Difference of antimony catalyst in oxidation

Next, the different antimony catalysts for the oxidation reaction were investigated (Table 2-10). Without catalyst, no oxidation took place (entry 1) and sodium hexachloroantimonate provided the imino ester in a modest yield (entry 2). When other neutral and anionic antimony(V) species were examined, tetraethylammonium hexachloroantimonate and antimony pentachloride gave the product in similar yields (entries 3 and 4), while antimony pentafluoride and sodium hexafluoroantimonate gave no or little product (entries 5 and 6). I assume that this difference is derived from the bond dissociation energies of Sb-Cl and Sb-F bonds (metal−halogen bond energy of SbF_3 is 444 kJ/mol, while that of $SbCl_3$ is only 312 kJ/mol).[48] Since an Sb-Cl bond is much weaker than that of an Sb-F bond, an Sb-Cl bond cleaves to provide some active catalyst, while a strong Sb-F bond does not generate such species. When antimony(III) species such as antimony trichloride, tribromide and triiodide were tested, extremely slow oxidation was observed except for antimony tribromide (entries 7-9). Also, triphenyl antimony and antimony(III) oxide did not catalyze the oxidation (entries 10 and 11). On the other hand, antimony(V) oxide catalyzed the oxidation, albeit with a slow reaction rate (entry 12). Thus, neglecting the result of antimony tribromide, it is likely that only Sb(V) species possess the activity to catalyze the oxidation, suggesting

the intermediacy of Sb(V) and Sb(IV) species, but not Sb(IV) and Sb(III) species.

Table 2-10. Comparison of antimony catalysts



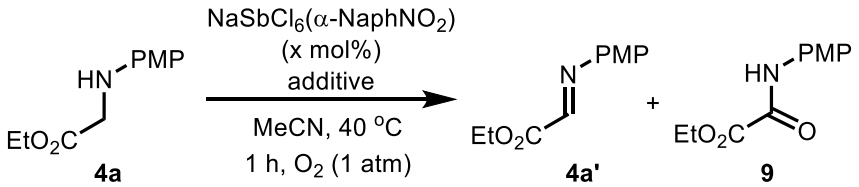
entry	catalyst	**4a'** (%)[a]	**9** (%)[a]	rec. **4a** (%)[a]
1	-	ND	ND	quant.
2	$NaSbCl_6$(α-$NaphNO_2$)	43	12	ND
3	Et_4NSbCl_6	38	26	ND
4	$SbCl_5$	39	2	ND
5	SbF_5	8	1	64
6	$NaSbF_6$	ND	ND	quant.
7	$SbCl_3$	1	ND	82
8	$SbBr_3$	37	3	6
9	SbI_3	trace	ND	85
10	Ph_3Sb	ND	ND	85
12	Sb_2O_3	ND	ND	86
13	Sb_2O_5	22	2	42

[a] Determined by ^1H NMR analysis.

2.14 The use of quinone derivatives

To improve the efficiency of oxidation, the effect of benzoquinones and a hydroquinone was investigated (Table 2-11). When 1 mol% sodium antimonate was employed as a catalyst, the imino ester **4a'** was obtained in a modest yield, accompanied by the formation of some amount of amide **9** (entry 1). On the other hand, when a stoichiometric amount of DDQ was employed under argon atmosphere, the imino ester was obtained in a high yield (entry 2). Then, the use of 1 mol% sodium antimonate and 20 mol% hydroquinone was tested, which provided the imino ester in a good yield (entry 3). However, the use of lower and higher amounts of sodium antimonate only suppressed the reactivity (entries 4 and 5). In contrast, the use of 40 mol% hydroquinone further improved the reactivity (entry 6). To decrease the loading of hydroquinone, the use of 20 mol% benzoquinone was attempted, which was less effective than 40 mol% hydroquinone (entry 7).

Table 2-11. Effect of quinone derivatives



4a **4a'** **9**

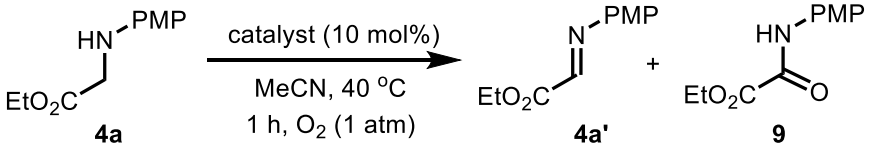
entry	x (mol%)	additive (mol%)	**4a'** (%)[a]	**9** (%)[a]	rec. **4a** (%)[a]
1	1	-	44	20	ND
2[b]	-	DDQ (100)	77	ND	ND
3	1	hydroquinone (20)	60	trace	ND
4	0.5	hydroquinone (20)	54	1	ND
5	10	hydroquinone (20)	43	trace	ND
6	1	hydroquinone (40)	73	trace	ND
7	1	benzoquinone (20)	60	6	ND

[a] Determined by ^{1}H NMR analysis. [b] Under Ar atmosphere.

2.15 Oxidation by other metal chlorides

In order to evaluate the oxidation ability of antimony, the oxidation of glycine ester derivative **4a** with other metal chlorides, which are known as potential oxidation catalysts, was investigated (Table 2-12). When antimony pentachloride was used as a catalyst, the imino ester **4a'** was obtained in 39% yield (entry 1). Among several metal chlorides examined, copper(II), cerium(III), rhodium(III) and gold(III) provided the

Table 2-12. Comparison of oxidation catalysts



4a **4a'** **9**

entry	catalyst	**4a'** (%)[a]	**9** (%)[a]	rec. **4a** (%)[a]
1	$SbCl_5$	39	2	ND
2	$CuCl_2 \cdot 2H_2O$	55	1	ND
3	$CeCl_3$	53	1	3
4	$RhCl_3 \cdot 3H_2O$	49	6	ND
5	$AuCl_3$	46	2	ND
6	$FeCl_3$	33	1	22
7	$PdCl_2$	33	3	10
8	$RuCl_3$	20	ND	57
9	CuCl	9	ND	68

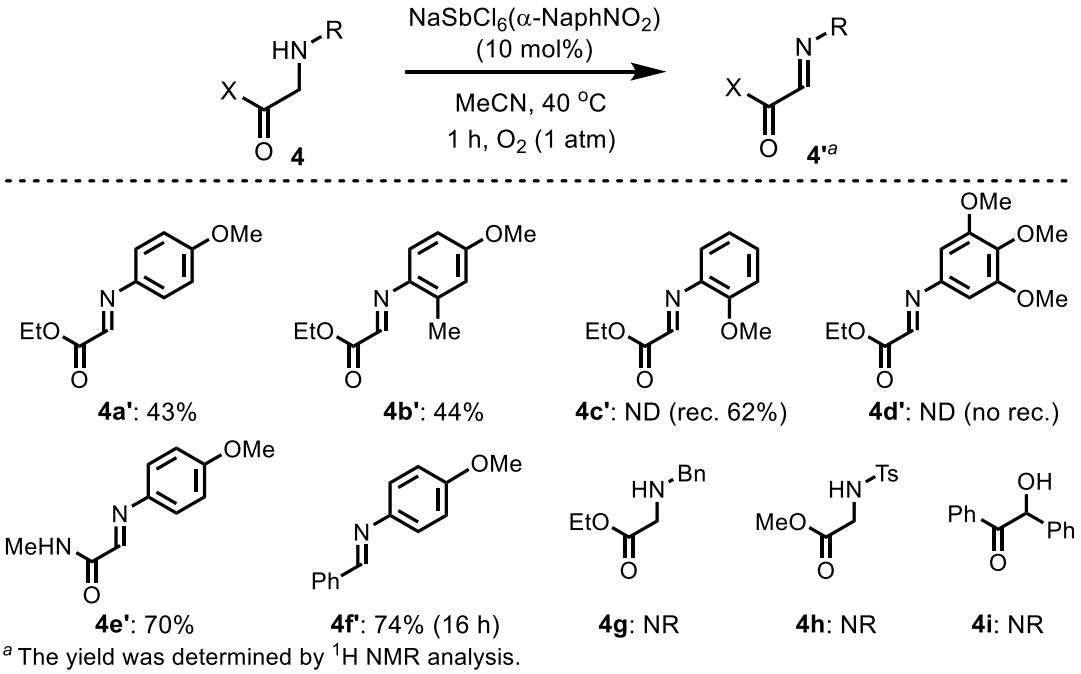
[a] Determined by ^{1}H NMR analysis.

imino ester in higher yields (entries 2-5). On the other hand, iron(III), palladium(II) and ruthenium(II) showed the poorer activity (entries 6-8) and the oxidation by copper(I) chloride was very sluggish (entry 9). To explain the poorer efficiency of oxidation toward imino ester by antimony pentachloride compared with other metals such as copper(II) chloride, I assume that a very strong Lewis acidity of antimony pentachloride induced some side-reactions, which was not the case with copper(II) chloride.

2.16 Effect of amine structure in oxidation

In order to improve the efficiency of oxidation, the effect of the amine structure was investigated (Scheme 2-5). When a PMP moiety on the nitrogen was replaced with a 2-methyl-4-methoxyphenyl moiety, no difference in the reactivity was observed (**4b'**). When the 2-methoxyphenyl substrate was employed, the desired imino ester **4c'** was not obtained, since a sterically crowded imino ester may favor hydrolysis. In the case of an electron-rich 3,4,5-trimethoxyphenyl substrate, no imino ester (**4d'**) was observed, although the oxidation was completed. In contrast, when a PMP-protected glycine methyl amide was employed in place of ethyl ester, significant improvement on the efficiency of the oxidation was observed (**4e'**). Also, when a PMP-protected benzyl

Scheme 2-5. Effect of the amine structure in oxidation



[a] The yield was determined by ^{1}H NMR analysis.

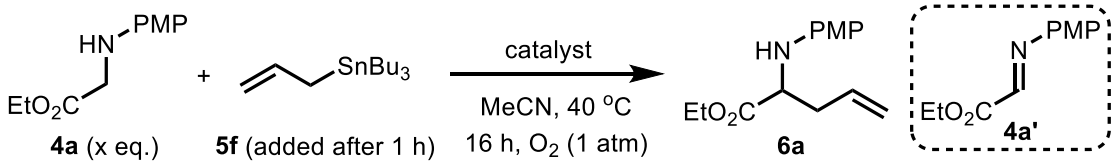
amine was employed, the corresponding imine **4f'** was obtained in a high yield, although the oxidation was very slow. On the other hand, no reaction took place when a PMP moiety was replaced with benzyl (**4g**) or tosyl (**4h**) moieties, suggesting the importance of an aromatic group on the nitrogen. Also, the oxidation of benzoin (**4i**) did not proceed at all, which was reported to be oxidized by Ph_3Sb/O_2 system,[42] indicating the difference in the reaction mechanisms.

2.17 Oxidative allylation by sodium antimonate and other antimony catalysts

Initially, I tested the oxidative allylation reaction using sodium antimonate as a catalyst (Table 2-13). When 1 equivalent of glycine ester was oxidized with 10 mol% sodium antimonate and allyltin was subsequently added, surprisingly, the desired product **6a** was obtained in a modest yield, where a significant amount of allyltin was still recovered (entry 1). This was an interesting result, since the sodium antimonate previously gave the allylated product in a very low yield when imino ester **4a'** was used as an electrophile (Table 2-6, entry 9). This suggested that, although sodium antimonate does not possess enough Lewis acidity to catalyze the allylation of imino ester, it generated some active Lewis acid after oxidation of glycine ester. Next, the effect of additives was investigated. It was found that drying agents such as magnesium sulfate, calcium chloride and MS4A did not improve the reactivity at all (entries 2-4). A very strong drying agent, phosphorus pentoxide, significantly suppressed the reaction (entry 5). In some literature reports, it was suggested that hexachloroantimonate is in equilibrium with $SbCl_5$ and Cl^-, and that the antimonate, with trace amounts of water, can form protic acids as the true catalyst.[48] In order to determine if the allylation reaction occurs via a protic acid-catalyzed pathway, I added a sterically-hindered, non-nucleophilic base, 2,6-di-*t*-butylpyridine (entry 6). However, no difference in the reactivity was observed. In order to evaluate the possibility that antimony pentachloride is the real active Lewis acid for the allylation reaction, the addition of tetrabutylammonium chloride was considered since the addition of a Cl^- source would shift the equilibrium towards the hexachloroantimonate form via the common ion effect. When 20 mol% tetrabutylammonium chloride was added, the yield decreased slightly

(entry 7). When 1 equivalent of tetrabutylammonium chloride was added, the allylation was significantly suppressed (entry 8). Next, the use of 20 mol% sodium antimonate was tested (entry 9). As a result, the allylated product was obtained in a moderate yield, where imino ester intermediate **4a'** was fully consumed, while some amount of allyltin was still recovered. This suggested that only the amount of glycine ester was not sufficient. Thus, I employed 2 equivalents of the glycine ester **4a** in the presence of 10 mol% sodium antimonate (entry 10). Although the reactivity did not improve when compared with entry 1, a significant amount of imino ester intermediate **4a'** still remained, which suggested that the Lewis acidic aspect of the catalyst was not sufficient in this reaction. Thus, the loading of sodium antimonate was gradually increased. Whereas the use of 14 mol% and 15 mol% sodium antimonate gave the product still in modest yields (entries 11 and 12), the use of 18 mol% catalyst provided the product in a high yield (entry 13). However, further addition of the catalyst did not significantly improve the reactivity since the allyltin was fully consumed in this case (entry 14).

Table 2-13. Sodium antimonate-catalyzed oxidative allylation



4a (x eq.) **5f** (added after 1 h) **6a**

entry	catalyst (mol%)	x (eq.)	**6a** (%)[a]	**4a'** (%)[a]	rec. **5f** (%)[a]
1	$NaSbCl_6$(α-$NaphNO_2$) (10)	1	36	3	39
2	$NaSbCl_6$(α-$NaphNO_2$) (10), $MgSO_4$ (50 mg)	1	31	3	30
3	$NaSbCl_6$(α-$NaphNO_2$) (10), $CaCl_2$ (50 mg)	1	32	10	43
4	$NaSbCl_6$(α-$NaphNO_2$) (10), MS4A (50 mg)	1	30	19	40
5	$NaSbCl_6$(α-$NaphNO_2$) (10), P_2O_5 (50 mg)	1	4	ND	ND
6	$NaSbCl_6$(α-$NaphNO_2$) (10), dTBP (20)	1	37	5	30
7	$NaSbCl_6$(α-$NaphNO_2$) (10), $^nBu_4NCl$ (20)	1	20	7	52
8	$NaSbCl_6$(α-$NaphNO_2$) (10), $^nBu_4NCl$ (100)	1	6	23	27
9	$NaSbCl_6$(α-$NaphNO_2$) (20)	1	55	ND	11
10	$NaSbCl_6$(α-$NaphNO_2$) (10)	2	32	61	35
11	$NaSbCl_6$(α-$NaphNO_2$) (14)	2	40	59	24
12	$NaSbCl_6$(α-$NaphNO_2$) (15)	2	47	34	19
13	$NaSbCl_6$(α-$NaphNO_2$) (18)	2	71	23	2
14	$NaSbCl_6$(α-$NaphNO_2$) (30)	2	74	3	ND
15	$SbCl_5$ (10)	2	29	95	30
16	Et_4NSbCl_6 (10)	2	17	70	37

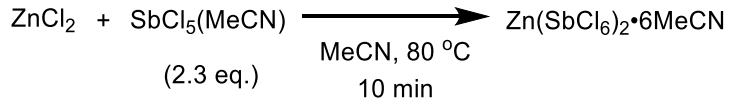
[a] Determined by ^1H NMR analysis.

Additionally, other antimony(V) species were examined as catalysts. Although antimony pentachloride exhibited similar reactivity as sodium antimonate (entry 15), tetraethylammonium antimonate showed lower activity (entry 16), probably due to the relative stability of the antimonate species to resist the formation of the active catalyst, $SbCl_5$.

2.18 Preparation of zinc antimonate

Based on our Lewis acidic metal screening studies, a well-defined metal antimonate, zinc(II) hexachloroantimonate, was synthesized. It was easily prepared according to the procedure reported by Zuur *et al*. in 1967, who synthesized a wide variety of metal hexachloroantimonate salts using acetonitrile as a ligand (Scheme 2-6).[50] Initially, antimony pentachloride, which is a viscous oil and difficult to handle, was purified by crystallizing in acetonitrile as an acetonitrile complex. Then, the reaction of zinc(II) chloride and an antimony pentachloride-acetonitrile complex in acetonitrile gave the zinc hexachloroantimonate-acetonitrile complex after recrystallization. They found that $Zn(SbCl_6)_2 \cdot 7MeCN$ was initially obtained, which was easily converted to $Zn(SbCl_6)_2 \cdot 6MeCN$ by sufficient drying of the salt.

Scheme 2-6. Preparation of zinc antimonate

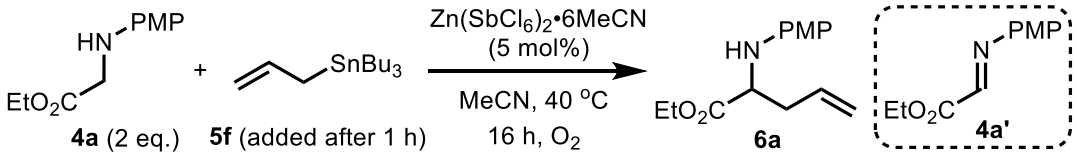


2.19 Oxidative allylation by zinc antimonate

Next, the oxidative allylation was attempted by utilizing zinc hexachloroantimonate as a catalyst (Table 2-14). When the reaction was performed in acetonitrile under oxygen using 5 mol% of zinc antimonate, the oxidatively allylated product **6a** was obtained in 58% yield (entry 1). Compared with the reaction catalyzed by 10 mol% sodium antimonate (Table 2-13, entry 10), there was a noticeable improvement by the presence of zinc species. Other solvents such as nitromethane, THF, dichloromethane,

which showed similar efficiency in oxidation (Table 2-8), did not give better results (entries 2-4). Thus, acetonitrile was selected as the best solvent. Expecting some stabilizing effect of the catalyst through the coordination of ligands, several ligands known for zinc, such as phenanthrolines, bipyridine and TMEDA, were tested (entries 5-8). However, only slight suppression of the reactivity was observed. Under dry air, the reactivity was almost the same (entry 9). When 5 mol% benzoic acid was added, no improvement in the reactivity was observed (entry 10). Conversely, the addition of a relatively strong base, *N*,*N*-dimethylaminopyridine (DMAP), suppressed the reactivity (entry 11). Also, the addition of an alcohol had no positive effect (entry 12). When a higher concentration was tested, the reaction was only suppressed (entry 13). Assuming that the catalyst was deactivated by allyltin, a slow addition of allyltin was attempted (entry 14). However, no improvement on the reactivity was achieved. Also, lower and higher temperatures did not improve the reactivity (entries 15 and 16).

Table 2-14. Zinc antimonate-catalyzed oxidative allylation



4a (2 eq.) **5f** (added after 1 h) **6a** **4a'**

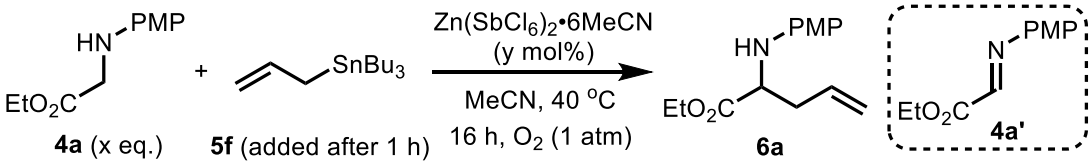
entry	modified conditions	**6a** (%)[a]	**4a'** (%)[a]	rec. **5f** (%)[a]
1	-	58	69	26
2	$MeNO_2$ as a solvent	57	11	29
3	THF as a solvent	46	59	38
4	CH_2Cl_2 as a solvent	45	9	37
5	phenanthroline (5 mol%)	45	41	30
6	Me_2-phenanthroline (5 mol%)	44	57	43
7	bipyridine (5 mol%)	42	47	32
8	TMEDA (5 mol%)	42	43	33
9[b]	-	56	21	31
10[b]	$PhCO_2H$ (5 mol%)[c]	55	19	29
11[b]	DMAP (20 mol%)[c]	26	26	50
12[b]	MeOH (1 eq.)[c]	50	3	23
13[b]	0.25 M	40	15	30
14[b]	slow addition of 5 over 2 h	49	25	30
15[b]	10 °C	52	34	34
16[b]	60 °C, 3 h	33	15	40

[a] Determined by ^1H NMR analysis. [b] Conditions: glycine ester **4a** (1.2 eq.), 25 °C, air (1 atm). [c] Added after 1 h.

2.20 Optimization of reaction conditions

Since there were no positive effects by adding some additives, the reaction conditions were optimized without any additives (Table 2-15). When the loading of zinc antimonate was gradually increased, the use of 7.5 mol% catalyst afforded the desired product **6a** in a high yield (entries 1-4). Since a significant amount of imino ester intermediate **4a'** was still observed, the amount of glycine ester **4a** could be reduced down to 1.3 equivalents (entries 5-7). Next, the reaction at 25 ^{o}C gave the similar result (entry 8). When the reaction vessel was opened to air, no loss of reactivity was observed (entry 9). Interestingly, when the oxidative allylation was performed in aqueous media, the allylated product was still obtained in a high yield, although it is not clear whether the catalyst was active or an acid generated through the hydrolysis of the catalyst promoted the reaction (entry 10). To exclude the effect of moisture, subsequent reactions were performed using the balloon of dry air (entry 11). Next, the amount of

Table 2-15. Optimization of reaction conditions



4a (x eq.) **5f** (added after 1 h) **6a**

entry	y (mol%)	x (eq.)	temp. (^{o}C)	O_2/air	time (h)	**6a** (%)[a]	**4a'** (%)[a]	rec. **5f** (%)[a]
1	5	2	40	O_2	16	58	69	26
2	6	2	40	O_2	16	64	48	18
3	7	2	40	O_2	16	73	57	13
4	7.5	2	40	O_2	16	81	42	5
5	7.5	1.5	40	O_2	16	77	19	5
6	7.5	1.4	40	O_2	16	79	11	5
7	7.5	1.3	40	O_2	16	74	7	4
8	7.5	1.3	25	O_2	16	72	4	7
9	7.5	1.3	25	air[b]	16	81	10	5
10[c]	7.5	1.3	25	air[b]	16	70	3	3
11	7.5	1.3	25	air	16	70	9	7
12	7.5	1.2	25	air	4	69	ND	14
13	**8**	**1.2**	**25**	air	**4**	**75 (71)**	**2**	**6**
14	8	1.4	25	air	4	75	3	6
15	8	1.6	25	air	4	75	ND	7
16	9	1.4	25	air	4	66	ND	5
17	9	1.6	25	air	4	64	ND	4
18	9	1.8	25	air	4	68	ND	4

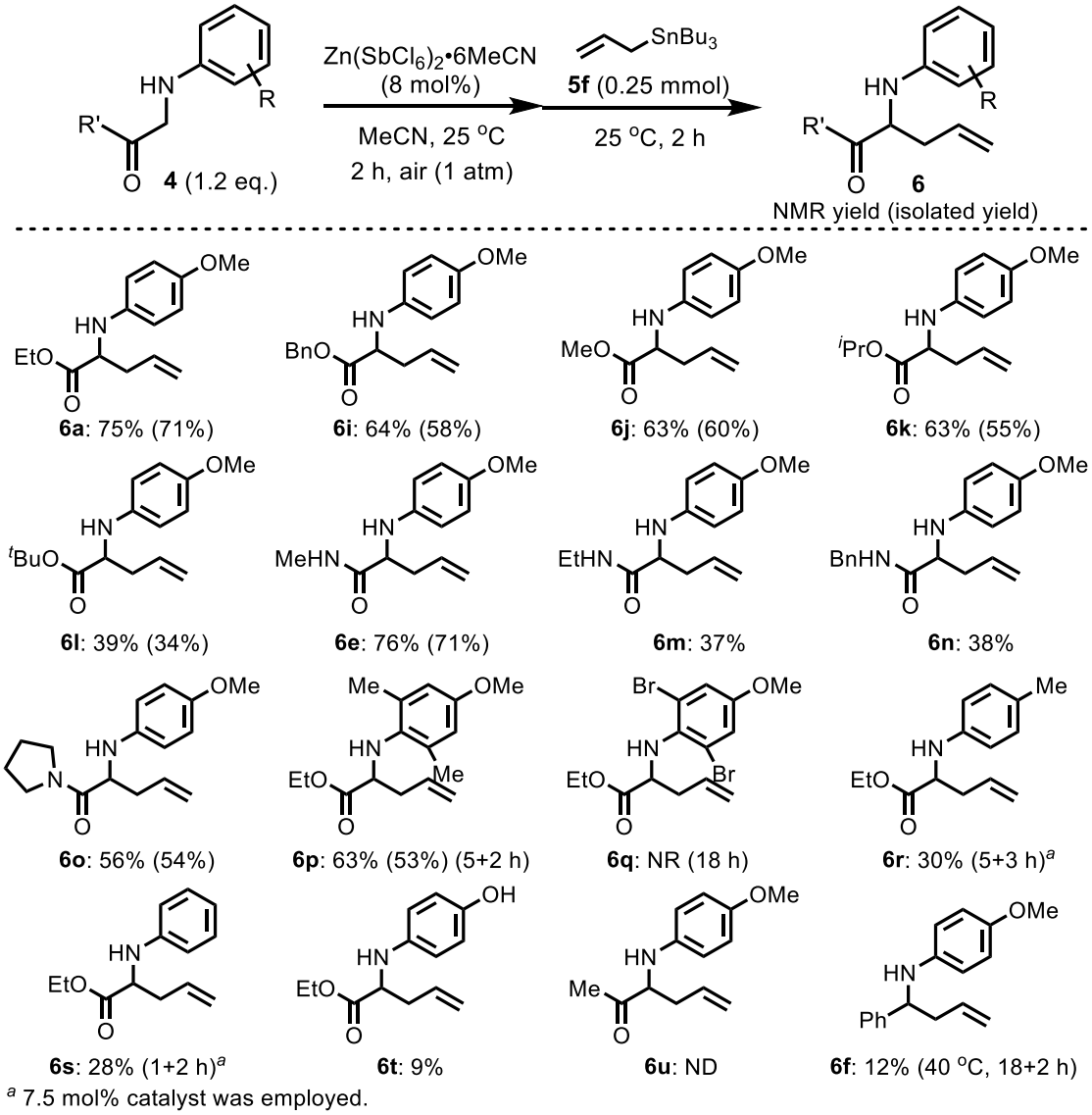
[a] Determined by ^{1}H NMR analysis. Isolated yield is shown in parentheses. [b] The flask was open to air. [c] Performed in MeCN/H_2O (19:1).

the glycine ester could be further reduced to 1.2 equivalents and the reaction time was shortened to 4 hours (entry 12). Finally, the loading of zinc antimonate was slightly raised to 8 mol% and was determined as the best reaction conditions (entry 13). Further addition of the catalyst or glycine ester did not improve the reactivity (entries 14-18).

2.21 Substrate scope

With the optimized reaction conditions in hand, the scope of the substrates was surveyed (Scheme 2-7). In addition to the PMP-protected glycine ethyl ester, benzyl, methyl and isopropyl esters provided the corresponding allylated products in good yields (**6i**, **6j**, **6k**), while the bulky *t*-butyl ester was less reactive (**6l**). When the ester moiety was replaced with methyl amide, the product **6e** was obtained in a high yield, while ethyl and benzyl amide gave the products in modest yields (**6m**, **6n**). Thus, it is likely that the reactivity is highly dependent on the substituents on the amide nitrogen. Then, a pyrrolidyl amide was examined and showed moderate reactivity (**6o**). To examine the effect of the structure of the aromatic moiety, a 2,6-dimethyl-4-methoxyphenyl substrate was prepared and tested (**6p**). This substrate was found to be less reactive than the standard substrate. On the other hand, a 2,6-dibromo-4-methoxyphenyl substrate did not undergo oxidation (**6q**). Thus, electron-deficient substrates cannot be utilized in this reaction. When a PMP moiety was replaced with *p*-tolyl or phenyl moieties, the desired products were obtained only in modest yields (**6r**, **6s**) and the oxidation of *p*-hydroxyphenyl substrate was very slow (**6t**). Thus, the existence of a PMP moiety appears to be critical to achieve higher efficiency of this oxidative allylation reaction. When an ester moiety was replaced with a ketone, no desired product (**6u**) was obtained, although the oxidation was completed. It is probably due to the instability of the corresponding imine intermediate. Finally, *N*-benzyl-*p*-anisidine was tested and the allylated product (**6f**) was obtained in a low yield with a significant amount of recovered **4f**, indicating the very slow oxidation of **4f** by zinc antimonate.

Scheme 2-7. Substrate scope

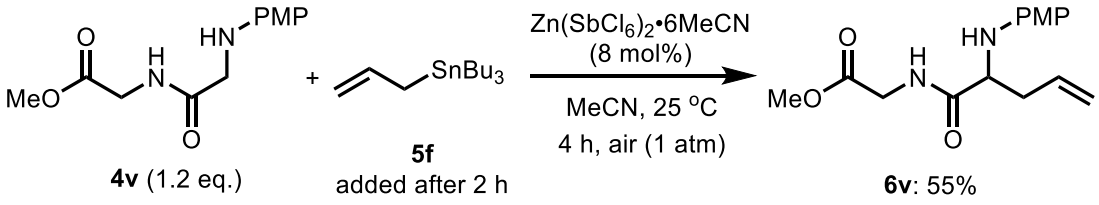


[a] 7.5 mol% catalyst was employed.

2.22 Oxidative allylation of a peptide

Finally, peptide **4v**, which contains two glycine moieties, was subjected to the oxidative allylation reaction using zinc(II) hexachloroantimonate as a catalyst (Scheme 2-8). It was found that the C−H bond adjacent to a nitrogen atom bearing a PMP moiety was selectively allylated in a moderate yield (**6v**). Thus, this reaction was found to be a good methodology to selectively functionalize peptides.

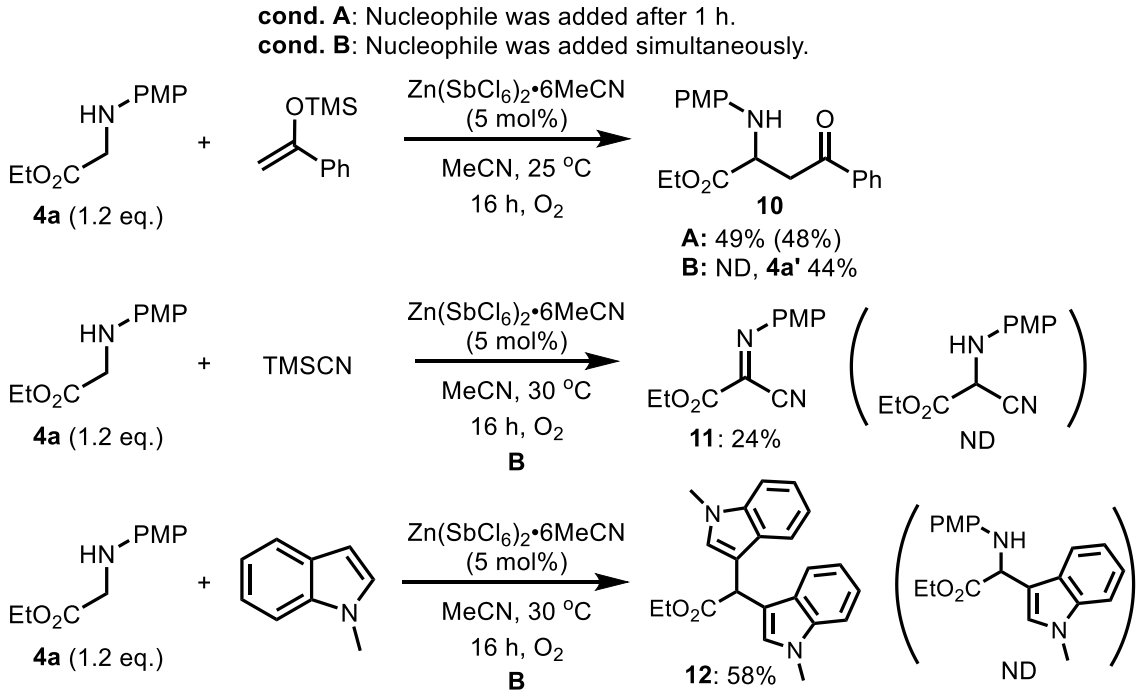
Scheme 2-8. Selective functionalization of peptide



2.23 Other nucleophiles

To expand the substrate scope of this reaction, other carbon nucleophiles were also examined (Scheme 2-9). Although a benzophenon-derived silyl enolate only resulted in the decomposition of the nucleophile, it gave the desired product **10** in a moderate yield when nucleophile was added after 1 hour. When trimethylsilylcyanide was employed as a nucleophile, simultaneous addition of nucleophile was possible. However, the desired product underwent further oxidation to provide the corresponding imino ester **11** in a low yield. Since X. Wang *et al*. recently reported the oxidative double addition of indoles to glycine esters in the presence of aminium radical antimonate catalyst.[19d], *N*-methylindole was tested as a nucleophile. As expected, *N*-methylindole underwent

Scheme 2-9. Other nucleophiles



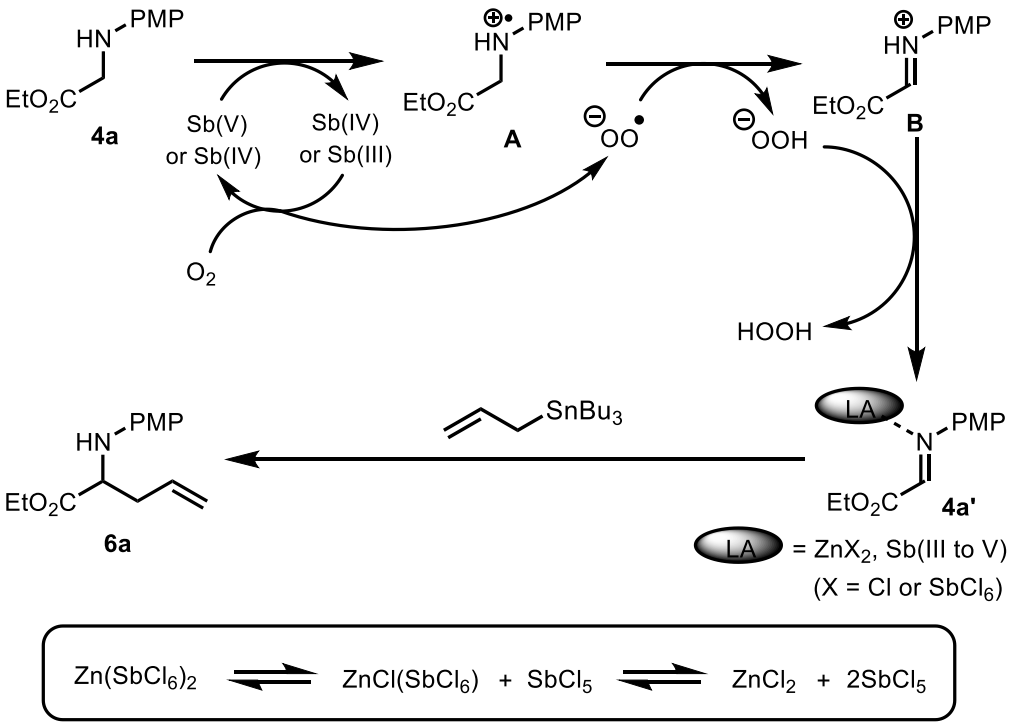
oxidative double addition to provide the double addition product **12** in a good yield. Thus, it seems likely that antimony is the true active species in Wang's reaction system.

2.24 Assumed reaction mechanism

I hypothesize the reaction mechanism as follows (Scheme 2-10). A glycine ester **4a** is initially oxidized by higher valent antimonies(V or IV) to provide an aminium radical cation intermediate **A**, while the resultant lower valent antimonies(IV or III) are oxidized by oxygen gas to regenerate the higher valent antimonies and form oxygen radical anion. Based on the experimental results that most antimony(III) species did not catalyze the oxidation, the intermediacy of Sb(V) and Sb(IV) is more likely than Sb(III). Subsequently, this radical anion abstracts a hydrogen radical from the intermediate **A** to afford an iminium intermediate **B** and generate a hydrogen peroxide anion, which serves as a base to deprotonate the intermediate **B** and provide the imino ester intermediate **4a'**. Finally, the imino ester undergoes allylation through the activation by Lewis acids.

Considering the results that sodium hexachloroantimonate and antimony pentachloride could catalyze the reaction, not only the zinc, but also antimony species

Scheme 2-10. Assumed reaction mechanism



released during the oxidation seem to be working as Lewis acids. Most likely the zinc antimonate decomposes into other zinc(II) and antimony(III-V) species such as $ZnCl_2$ and $SbCl_5$ under the oxidative reaction conditions either reversibly or irreversibly.

2.26 Conclusion

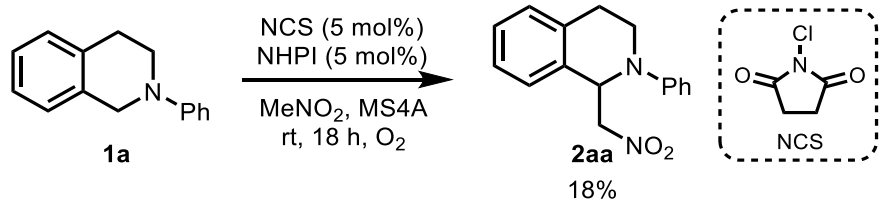
To solve the problem of substrate limitation in the antimonate/NHPI-catalyzed oxidative coupling reactions of tertiary amines, α-amino acid derivatives were chosen as more useful secondary amine substrates. Based on the hypothesis that a metal antimonate would serves as a bifunctional catalyst of a Lewis acid and an oxidation catalyst, zinc(II) hexachloroantimonate was prepared and utilized. As expected, the oxidative allylation reaction of glycine derivatives with allyltin proceeded in the presence of zinc antimonate under very mild aerobic conditions. Thus, the utility of antimony-catalyzed oxidative coupling reaction was significantly improved, and the concept of metal antimonate as a bifunctional catalyst succeeded. However, a couple of disadvantages also existed: (i) since the presence of allyltin inhibited the oxidation, it was necessary to add allyltin after the oxidation was completed; (ii) the oxidation of glycine derivatives to the corresponding imines were not efficient, thus leading to the relatively low yields of the allylated products; and (iii) not only zinc, but also antimony species released in the reaction system seemed to work as a Lewis acid. In spite of these drawbacks, this CDC-type reaction is still worth disclosing in that the oxidative allylation of glycine derivatives is synthetically useful and this is a rare example of the oxidative coupling reaction in which oxygen gas was utilized as the terminal oxidant.

Chapter 3. Sulfuryl Chloride-mediated CDC reaction of Tertiary *N*-Aryl Amines

3.1 Discovery of the metal-free CDC reaction

During the course of my investigation into the antimonate/NHPI-catalyzed CDC reaction of tertiary amines, I examined *N*-chlorosuccinimide (NCS) as a catalyst since hexachloroantimonate salt can potentially act as a source of antimony pentachloride, and antimony pentachloride is known to be an electrophilic chlorine source as previously shown in Scheme 3-1. When NCS was examined as a catalyst, the reaction proceeded, albeit with a low yield.

Scheme 3-1. Discovery of metal-free CDC reaction

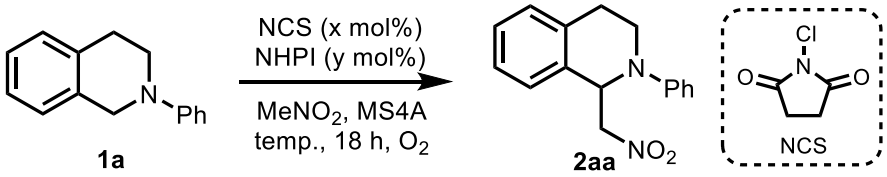


3.2 Investigation of oxidative coupling with NCS

Initially, the effect of NCS was evaluated using 5 mol% NCS and 5 mol% NHPI at room temperature over 18 hours (Table 3-1, entry 1). Under these conditions, the desired product was obtained in a low yield, accompanied by the recovery of a significant amount of *N*-phenyl tetrahydroisoquinoline. Although the turnover was very low, the combination of NCS and NHPI still could catalyze this reaction. Next, the effect of temperature was examined. However, no significant loss or enhancement of reactivity was observed within the temperature range of 20 to 60 ^{o}C (entries 2-4). Fixing the reaction temperature to 30 ^{o}C, in the absence of NCS, no reaction took place (entry 5). In contrast, slight improvement in reactivity was observed when NHPI was excluded (entry 6). These results suggested that unlike the antimonate/NHPI system, NHPI is not involved in the NCS-catalyzed CDC reaction. In order to improve the reactivity, the catalyst loading was raised to 10 mol%, which resulted in the significant improvement

on the reactivity (entry 7). The use of 15 mol% catalyst resulted in a further improvement (entry 8) and the use of 20 mol% catalyst was found to almost complete the reaction (entry 9).

Table 3-1. Oxidative coupling with NCS



entry	x	y	temp (^{o}C)	**2aa** (%)[a]	rec. **1a** (%)[a]
1	5	5	rt	18	81
2	5	5	20	16	81
3	5	5	30	14	85
4	5	5	60	14	82
5	-	5	30	ND	quant.
6	5	-	30	24	76
7	10	-	30	60	32
8	15	-	30	70	23
9	20	-	30	87	3

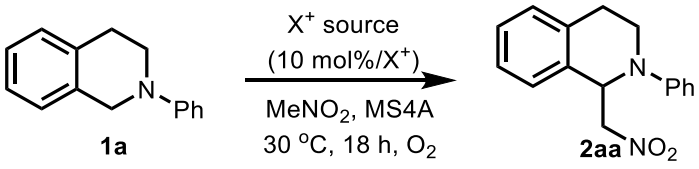
[a] Determined by ^{1}H NMR analysis.

3.3 Survey of electrophilic halogen sources

Although the use of NCS as a catalyst for metal-free CDC reaction seemed fascinating, the loading of 20 mol% catalyst was much higher than what was desired. Thus, other electrophilic halogen sources were examined (10 mol%) in order to find a more suitable catalyst and also to elucidate the reaction mechanism. In the absence of the catalyst, the reaction proceeded extremely slowly (Table 3-2, entry 1). Compared with the result of NCS (entry 2), sulfuryl chloride was found to be a superior catalyst that fully converted the tertiary amine, although the yield did not reach the desired level (entry 3). On the other hand, it was surprising that other electrophilic chlorine sources, such as *t*-butyl hypochlorite, chloramine T, dichloroamine T and trichloroisocyanuric acid provided the desired product in very low yields (entries 4-7). In addition to electrophilic chlorine sources, other electrophilic halogen sources were also examined. However, the reactions with *N*-bromosuccinimide (NBS), *N*-iodosuccinimide (NIS) and I_2 were also very sluggish (entries 8-10). Although it seemed strange that other halogen

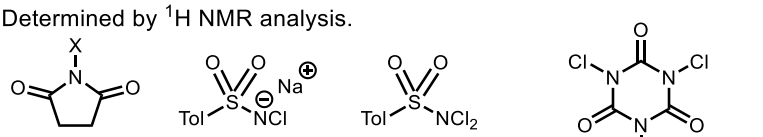
sources did not serve as efficient catalysts, I selected sulfuryl chloride as a catalyst for the metal-free CDC reactions since it is very cheap and a very common reagent in organic synthesis.

Table 3-2. Survey of electrophilic halogen sources



entry	X^+ source	**2aa** (%)[a]	rec. **1a** (%)[a]
1	-	5	97
2	NCS	60	32
3	SO_2Cl_2	75	trace
4	^{t}BuOCl	10	91
5	chloramine T	8	95
6	dichloramine T	4	95
7	trichloroisocyanuric acid	4	99
8	NBS	3	95
9	NIS	11	82
10	I_2	15	85

[a] Determined by ^{1}H NMR analysis.

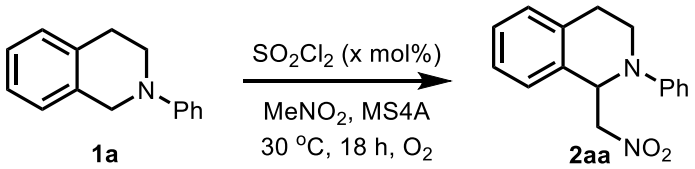


3.4 Optimization of reaction conditions

Next, the reaction conditions were optimized using sulfuryl chloride as a catalyst (Table 3-3). The use of 10 mol% catalyst fully converted the tertiary amine, but with a somewhat disappointing yield (entry 1). I speculated that this moderate yield was not due to the insufficient reactivity, but due to the side-reaction caused by the excess use of the catalyst. Based on this hypothesis, the use of only 5 mol% catalyst provided a higher yield of the desired CDC product with similar reactivity (entry 3). However, further lowering the loading of the catalyst only significantly diminished the reactivity (entry 4). And finally, the use of 6 mol% catalyst was found to be the best (entry 2). When sodium sulfate was employed in place of MS4A, slight suppression of the reactivity was observed (entry 5). To see if light is involved in the reaction mechanism, for example,

by inducing the generation of radical species from sulfuryl chloride, the reaction vessel was protected from light. However, this did not suppress the reactivity (entry 6). Based on this result, the light was not likely to be involved in the reaction mechanism. On the other hand, the reaction under argon atmosphere significantly suppressed the reaction, which suggested that oxygen is essential for this oxidative coupling reaction (entry 7).

Table 3-3. Optimization of reaction conditions



1a **2aa**

entry	x (mol%)	modified conditions	**2aa** (%)[a]	rec. **1a** (%)[a]
1	10	-	75	trace
2	6	-	93	ND
3	5	-	89	5
4	1	-	18	84
5	6	Na_2SO_4 instead of MS4A	65	21
6	6	protected from light	90	ND
7	6	under Ar atmosphere	1	98

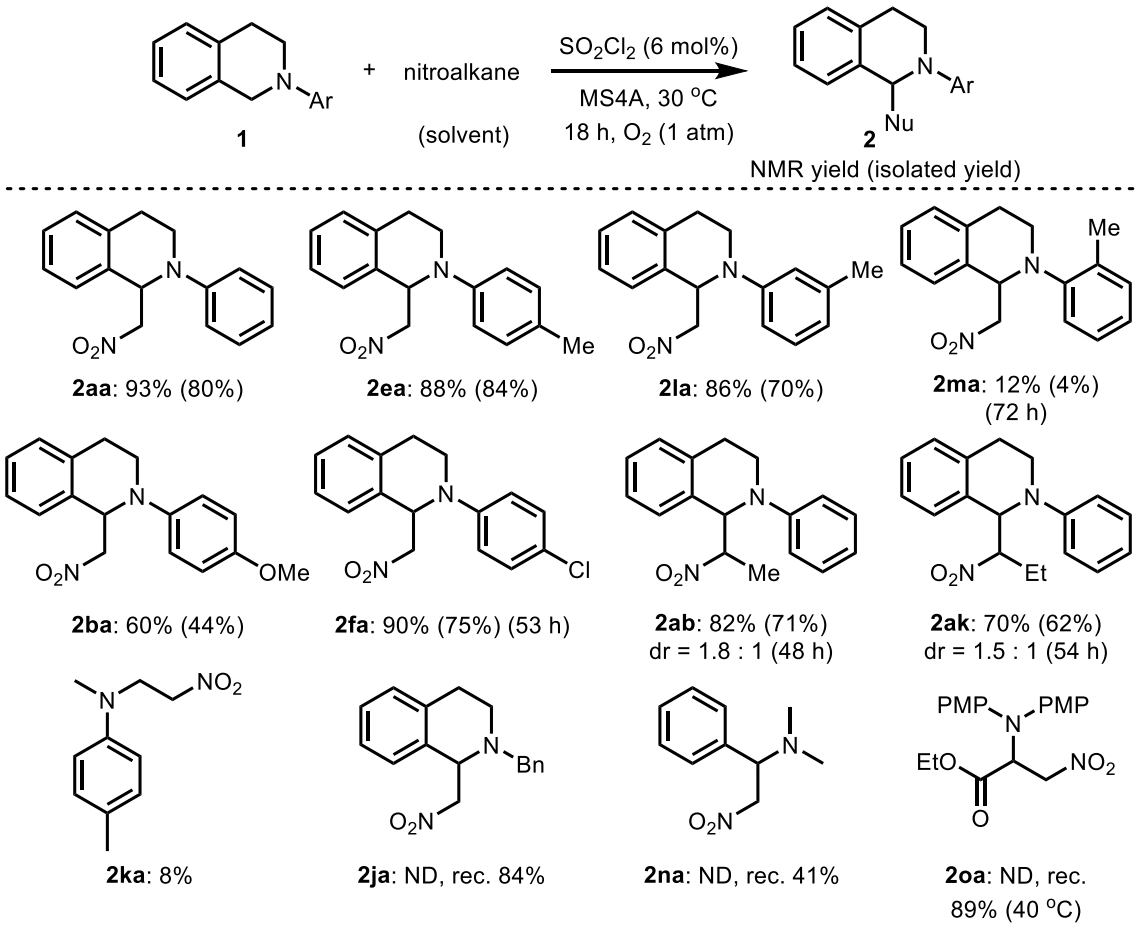
[a] Determined by ^{1}H NMR analysis.

3.5 Substrate scope

With the optimized reaction conditions in hand, the substrate scope was investigated (Scheme 3-2). In addition to the simple *N*-phenyl tetrahydroisoquinoline, *p*- and *m*-tolyl-substituted tetrahydroisoquinolines provided the desired products in high yields (**2ea**, **2la**). On the other hand, the nitromethylation of *o*-tolyl-substrate was extremely slow (**2ma**), probably due to the steric hindrance derived from the *o*-methyl substituent. In the case of *p*-methoxyphenyl substrate, the yield was modest, probably due to some competing side-reactions (**2ba**). When electron-deficient *p*-chlorophenyl substrate was employed, the desired product was obtained in a high yield (**2fa**), although the reaction was very sluggish. In addition to nitromethane, nitroethane and nitropropane served as good nucleophiles (**2ab**, **2ak**). When an acyclic amine, *N*,*N*-dimethyl-*p*-toluidine, was

examined, the desired product was obtained with a low yield (**2ka**). In addition, other tertiary amines such as *N*-benzyltetrahydroisoquinoline, benzyldimethylamine and *N*,*N*-bis(*p*-methoxyphenyl)-glycine ethyl ester did not undergo the oxidative nitromethylation (**2ja**, **2na**, **2oa**).

Scheme 3-2. Substrate scope

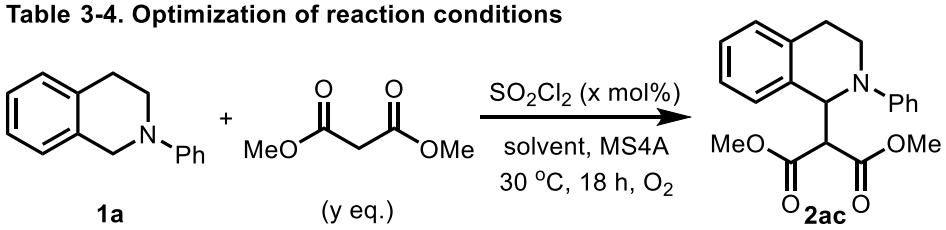


3.6 Optimization of reaction conditions for other nucleophiles

Since in the previous CDC reaction the nitroalkanes served as a nucleophile and as a solvent, expanding the substrate scope would require further modification of the reaction conditions. Thus, I re-optimized the reaction conditions using 1.5 equivalents of dimethyl malonate as the model nucleophile. In the presence of 5 mol% sulfuryl chloride, several solvents were tested and only acetonitrile gave the desired product **2ac**

in a high yield (Table 3-4, entries 1-6). Then, the loading of the catalyst was optimized (entries 7-11). To my delight, the use of 2 mol% sulfuryl chloride was found to give the best result (entry 10), while the use of 1 mol% catalyst gave the product in a very low yield (entry 11). Next, the amount of the nucleophile was reduced for the sake of easier purification (entries 13-15) and it was found that only 1.0 equivalent of the nucleophile was sufficient to provide the product in a high yield (entry 14).

Table 3-4. Optimization of reaction conditions



1a (y eq.) **2ac**

entry	solvent	x (mol%)	y (eq.)	**2ac** (%)[a]	rec. **1a** (%)[a]
1	MeOH	5	1.5	42	51
2	THF	5	1.5	9	93
3	DCM	5	1.5	9	86
4	toluene	5	1.5	13	86
5	DMF	5	1.5	46	37
6	MeCN	5	1.5	85	ND
7	MeCN	6	1.5	84	ND
8	MeCN	4	1.5	86	ND
9	MeCN	3	1.5	91	ND
10	MeCN	2	1.5	96	ND
11	MeCN	1	1.5	7 (12)[b]	98
12	MeCN	2	1.3	98	ND
13	MeCN	2	1.1	95	ND
14	MeCN	2	1.0	92 (77)[c]	ND

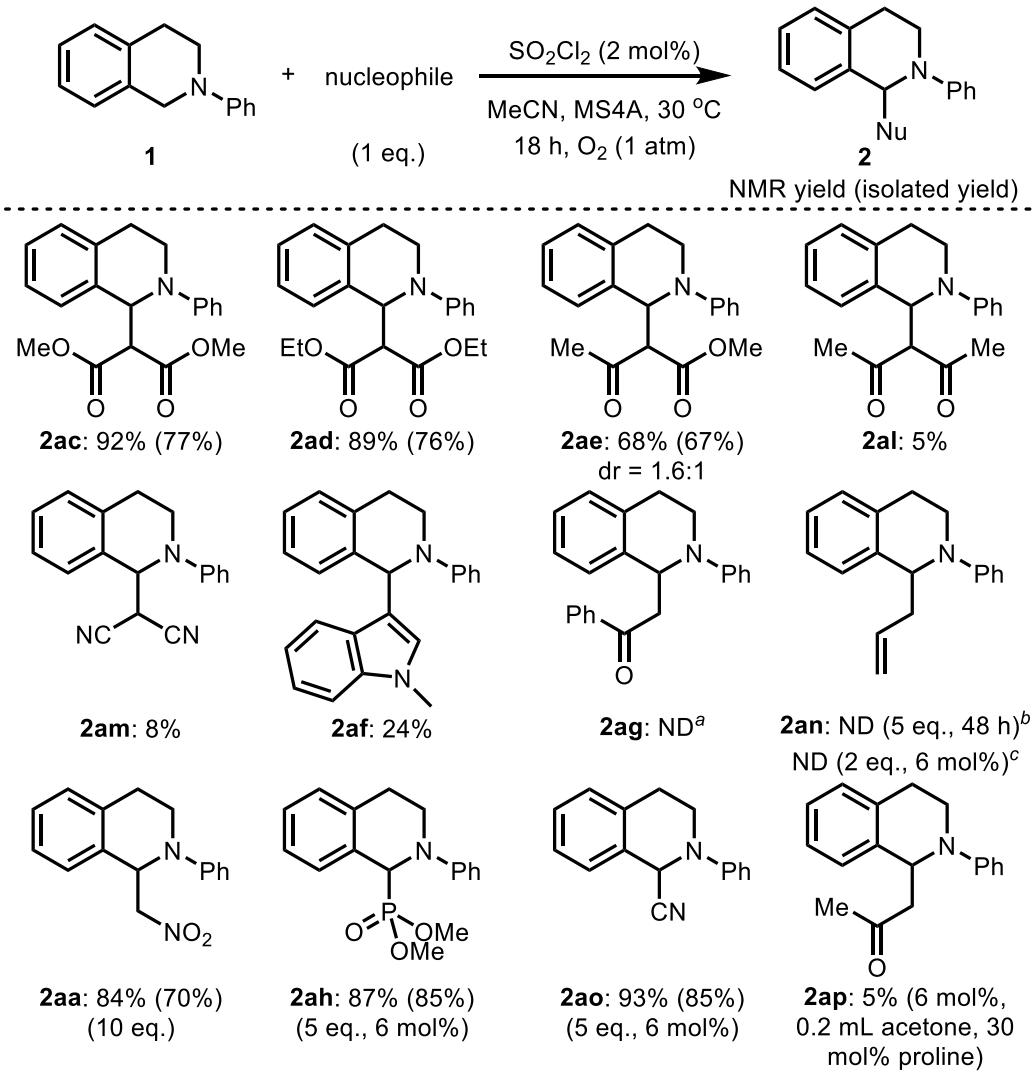
[a] Determined by ^{1}H NMR analysis. [b] Reproducibility. [c] Isolated yield.

3.7 Scope of nucleophiles

After re-optimizing the reaction conditions, several nucleophiles were investigated by utilizing only 2 mol% of the catalyst (Scheme 3-3). In addition to dimethyl malonate, diethyl malonate exhibited a comparable reactivity (**2ad**). Also, a β-ketoester showed a good reactivity (**2ae**), while the reactivity of a β-diketone and a malononitrile was very poor (**2al** and **2am**). Furthermore, *N*-methylindole gave the product in a modest yield (**2af**). When a acetophenone-derived silyl enolate, allyltrimethylsilane or allyltributyltin were employed as nucleophiles, the expected products were not obtained (**2ag**, **2an**).

When nitromethane was subjected to the similar reaction conditions, the nitromethylated product was obtained in a low yield (**2aa**). However, this result was significantly improved by using 10 equivalents of the nitromethane as a nucleophile. Also, the use of dimethyl phosphite and trimethylsilyl cyanide initially provided the corresponding products in modest yields, which was notably improved by using 5 equivalents of the nucleophiles and 6 mol% sulfuryl chloride (**2ah**, **2ao**). On the other hand, a proline-catalyzed Mannich reaction with acetone as a nucleophile provided only little product (**2ap**).

Scheme 3-3. Scope of nucleophiles

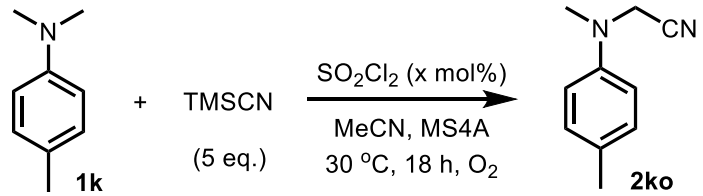


[a] Corresponding silyl enolate was used. [b] Allyltrimethylsilane was used. [c] Allyltributyltin was used.

3.8 Oxidative cyanation of an acyclic amine

To further broaden the scope of substrates, the oxidative coupling reaction of an acyclic amine was investigated (Table 3-5). In place of nitromethane, trimethylsilylcyanide was employed, since the corresponding cyanated product **2ka** is a more useful precursor of α-amino acids or 1,2-diamines. Surprisingly, the desired mono-cyanated product was obtained when 5 equivalents of the nucleophile and 6 mol% sulfuryl chloride were employed (entry 1). When the catalyst loading was increased, only slight improvement in the reactivity was observed (entries 2 and 3). Using 12 mol% sulfuryl chloride, I examined the addition of an excess amount of acetic acid, since acetic acid was sometimes utilized to promote this type of reactions in other reports. However, it only suppressed the reaction (entry 4). Expecting that alcohols would stabilize the iminium intermediate, methanol was added to the reaction system. Unfortunately, this suppressed the reaction and it was assumed that the alcohol slowly decomposed the catalyst (entry 5). Further attempts were made to improve the reactivity. Using 6 mol% sulfuryl chloride, the oxidative cyanation was suppressed at higher temperature (entry 6). Also, a longer reaction time and another portion of sulfuryl chloride did not improve the reactivity (entry 7 and 8). Further addition of the nucleophile only resulted in the suppression of the reactivity (entry 9).

Table 3-5. Acyclic amine as a substrate



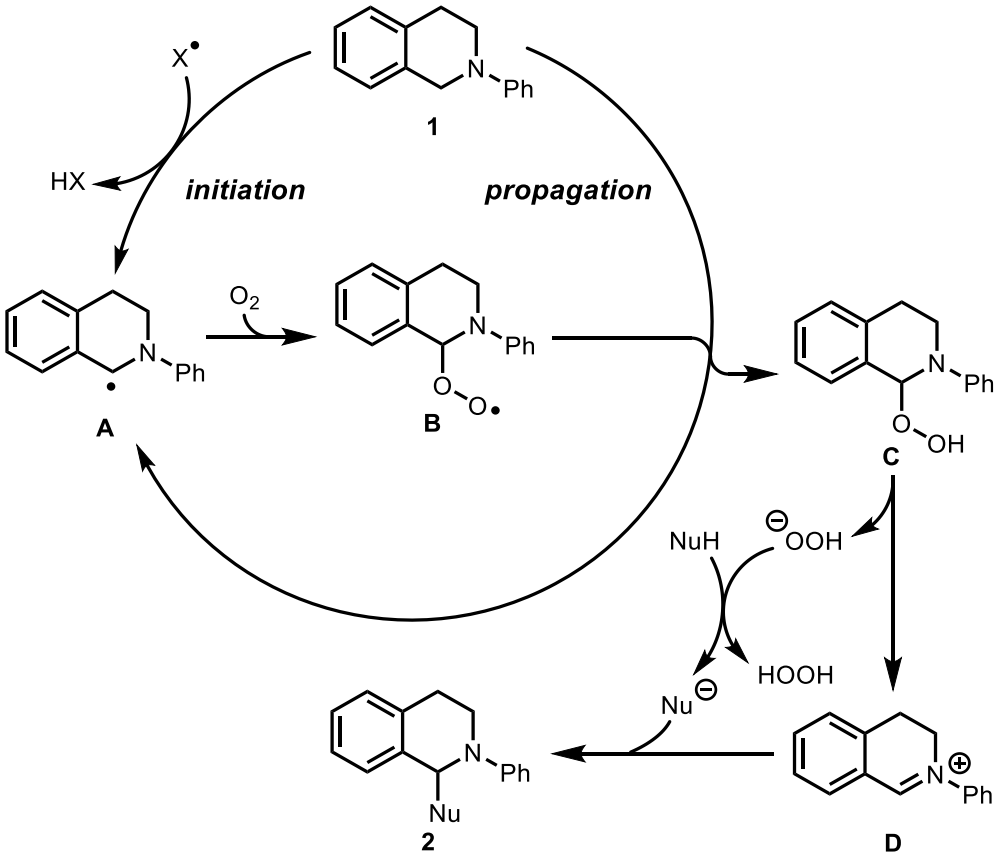
entry	conditions	**2ko** (%)[a]	rec. **1k** (%)[a]
1	6 mol%	40	~40
2	9 mol%	42	~20
3	12 mol%	47	ND
4	12 mol%, AcOH (1.6 eq.)	20	much
5	12 mol%, MeOH (10 eq.)	14	57
6	6 mol%, 40 °C	19	60
7	6 mol%, 42 h	38	33
8	6 mol%, 18 h; + 6 mol%, 24 h	37	~29
9	6 mol%, TMSCN (10 eq.)	11	69

[a] Determined by ^{1}H NMR analysis.

3.9 Elucidation of the reaction mechanism

Due to the high oxidation potential of chlorine, the re-oxidation of chlorine by oxygen gas is highly unlikely. As such, I propose a radical-initiated autoxidation mechanism[51] to explain how catalytic amounts of sulfuryl chloride could facilitate the CDC reaction (Scheme 3-4). Initially, I hypothesized that sulfuryl chloride generates some radical species such as a chlorine radical. Then, this radical species may abstract the hydrogen radical from the tertiary amine **1** to initiate the reaction, by providing a carbon-centered radical intermediate **A**, to which oxygen attacks to form radical intermediate **B**. Then, intermediate **B** can abstract the hydrogen atom from the starting material **1** to propagate the reaction and generate the intermediate **C**. Subsequently, this intermediate releases the hydrogen peroxide anion, which can serve as a base to activate a pronucleophile, to afford the electrophilic iminium intermediate **D**, which is finally intercepted by the nucleophile to furnish the desired product **2**.

Scheme 3-4. Proposed autoxidation pathway



Although this radical-initiated autoxidation mechanism seems likely, the initiation step requires further discussion. Initially, I hypothesized that sulfuryl chloride generated a chlorine radical either indirectly through the formation of chlorine gas (Scheme 3-5, ***path a***) or through the direct homolytic cleavage of the S−Cl bond (***path b***). However, these pathways are theoretically unlikely, since the homolytic cleavage of a Cl−Cl bond and a Cl−SO_2Cl bond requires relatively high energies, which is evidenced by their bond dissociation energies (Table 3-6).[52,53] In addition, if chlorine radical formation through ***path a*** or ***path b*** were true, then iodine, which has a much weaker bond dissociation energy,[52] should possess similar or higher activity (Table 3-2, entry 10). Also, the CDC reaction did not require any light (Table 3-3, entry 7). Thus, ***path a*** and ***path b*** may be inappropriate. An alternative pathway could be through an acid-promoted autoxidation (***path c***). In 2010, Klussmann *et al*. reported a methanesulfonic acid-promoted autoxidation of alkylarene or tertiary amine **1a** with ketones as pronucleophiles, whereas high pressure of oxygen gas was required and the products were obtained in low yields (Scheme 3-6).[15a] Although they did not mention how the initial insertion of oxygen gas was promoted, it seemed feasible that sulfuryl chloride underwent hydrolysis and generated sulfuric acid, which served as a true promoter of the reaction.

Scheme 3-5. Initiation of autoxidation

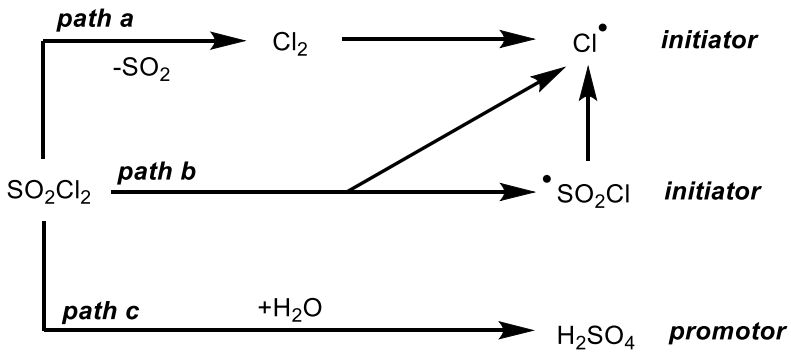
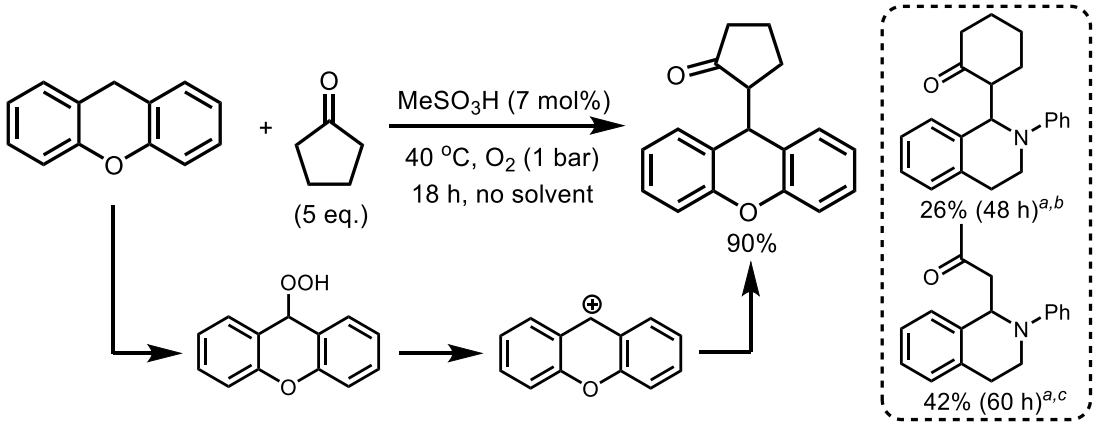


Table 3-6. Bond dissociation energies

bond	BDE (kJ/mol)
Cl-Cl	243
ClO_2S-Cl	193
I-I	151

Scheme 3-6. Sulfonic acid-promoted autoxidation reported by Klussmann



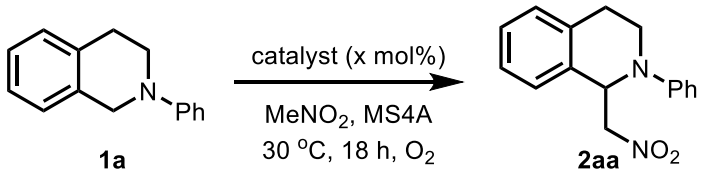
[a] O_2 (6 bar), rt. [b] In MeOH. [c] TfOH (7 mol%).

3.10 Examination of promoters to determine the reaction mechanism

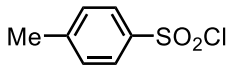
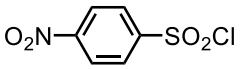
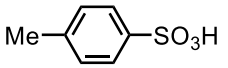
Thus, to experimentally elucidate the reaction mechanism, several experiments were performed (Table 3-7). First, I examined arylsulfonyl chlorides as initiators. Since they are not electrophilic halogen sources, these reactions suggest the possibility of either the direct cleavage of a Cl−SO_2R bond or the acid-promoted autoxidation via hydrolysis. When a *p*-toluenesulfonyl chloride was tested as an initiator, the oxidative coupling reaction proceeded, although the yield was low (entry 2). When the loading of *p*-toluenesulfonyl chloride was raised to 12 mol%, still the reaction was not complete (entry 3). To examine the electronic effect, an electron-deficient *p*-nitrobenzenesulfonyl chloride was tested and was found to possess better reactivity (entry 4). Then, some radical initiators were examined. When AIBN was utilized as an initiator, the desired product was obtained only in a very low yield (entry 5). Since the activation energy of AIBN (131 kJ/mol)[54] is even lower than the bond dissociation energy of iodine, this result suggested that the reaction through the chlorine radical formation via ***path a*** and ***path b*** was not likely. Finally, when a room temperature radical initiator V-70 was employed, the reaction was promoted (entry 6). Then, methanesulfonic acid was examined as a promoter, to investigate the acid-promoted pathway (entry 7). Indeed, the reaction proceeded, although the yield was modest. On the other hand, sulfuric acid only gave the product in a very low yield (entry 8), which strongly suggested that the

reaction did not proceed through the formation of sulfuric acid as the true active species via the hydrolysis of sulfuric chloride (***path c***). To confirm that point, *p*-toluenesulfonic acid was examined as a promoter, which also gave the product in a very low yield (entry 9). Since *p*-toluenesulfonic acid was much less active than *p*-toluenesulfonic chloride, an acid-promoted pathway was not likely.

Table 3-7. Mechanistic investigation



1a **2aa**

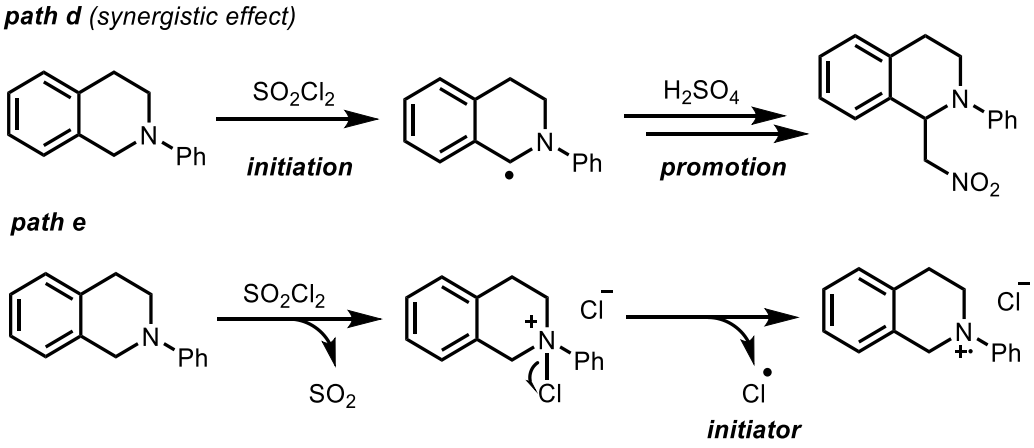
entry	catalyst	x (mol%)	**2aa** (%)[a]	rec. **1a** (%)[a]
1	SO_2Cl_2	6	93	ND
2		6	27	47
3		12	42	22
4		6	71	21
5	AIBN	6	7	80
6	V-70	6	38	55
7	$MeSO_3H$	6	40	57
8	H_2SO_4	6	7	93
9		6	8	60

[a] Determined by ^1H NMR analysis.

Since all the pathways I initially assumed (***paths a-c***) were denied, now I speculate two other possibilities (Scheme 3-7). The first possibility is that the existence of both sulfuryl chloride and sulfuric acid exhibits a synergic effect to facilitate the reaction (***path d***). Namely, sulfuryl chloride was responsible for the initiation of the autoxidation, and sulfuric acid, which was partly generated through the hydrolysis of sulfuryl chloride, promoted the subsequent autoxidation. It can explain why the reaction was slow when only sulfuric acid was employed. The second possibility is that a chlorine radical is generated through an alternative pathway, where the activation energy is lower than ***path a*** and ***path b***. One plausible pathway is that THIQ initially undergoes chlorination by sulfuryl chloride on the nitrogen atom to form a tetrasubstituted ammonium chloride intermediate. Subsequently, homolytic cleavage of the N−Cl bond would provide a

chlorine radical, which serves as an initiator of the autoxidation, and release an aminium radical salt of THIQ (***path e***). If the formation of such an ammonium cation intermediate was feasible, the subsequent homolytic cleavage may be favored due to the stability of the released aminium radical salt. This pathway might be supported by the fact that the benzyl-substituted THIQ did not undergo the oxidative nitromethylation. Namely, the homolytic cleavage of the N−Cl bond was not favored in the case of Bn-THIQ because of the instability of the corresponding aminium radical salt.

Scheme 3-7. Other possibilities of the reaction mechanism



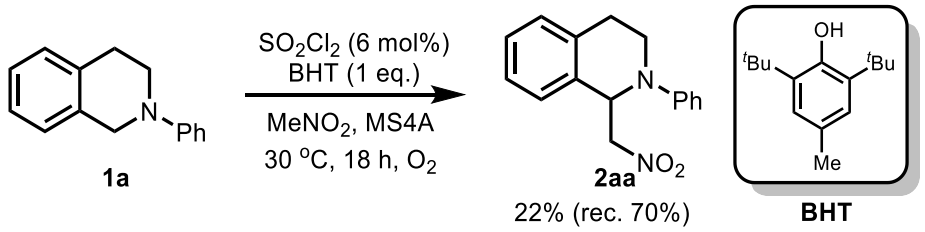
In addition, when 5 mol% sulfuryl chloride was added to Ph-THIQ (**1a**) in $MeNO_2$, the colorless solution turned yellow (in the case of *N*,*N*-dimethyltoluidine, the color turned blue). Although the color disappeared when a stoichiometric amount of sulfuryl chloride was added or when nucleophile was added, such color change may suggest the facile interaction of sulfuryl chloride with tertiary amines to generate some key radical species.

3.11 Effect of a radical inhibitor

To confirm the radical mechanism, the effect of radical inhibitor was examined (Scheme 3-8). When a stoichiometric amount of radical inhibitor, 3,5-di-*t*-butyl-4-hydroxytoluene (BHT), was added, the oxidative nitromethylation reaction was significantly suppressed, suggesting that the reaction proceeded through a

radical mechanism. The observed slow reaction may suggest that either radical species were not completely trapped by BHT, or the addition of a stoichiometric amount of radical inhibitor induced some other reaction pathways.

Scheme 3-8. Effect of radical inhibitor



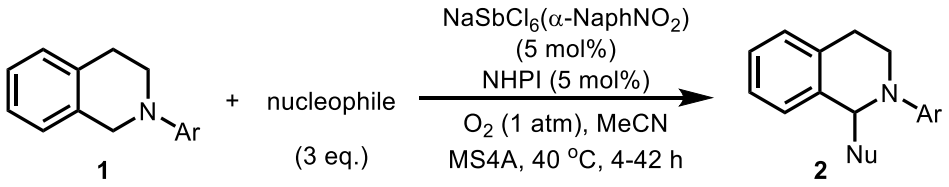
3.12 Conclusion

During the course of my investigation to explore a metal-free cross-dehydrogenative coupling reaction of tertiary amines under aerobic conditions, it was discovered that sulfuryl chloride, which is an inexpensive electrophilic chlorine source, served as a highly efficient initiator for the CDC reaction of tertiary amines under mild aerobic conditions. The reactions seemed to proceed through the autoxidation mechanism, yet the mechanism of the initiation step remains unclear. It is worth emphasizing that the CDC reactions of tertiary amines, investigated over a decade by a large number of chemists mostly using transition metal catalysts or photoredox catalysts in the presence or absence of synthetic oxidants, could be performed by utilizing a simple and inexpensive non-metal catalyst under truly mild aerobic conditions. Also, this reaction system is environment-friendly since only a small amount of catalyst is required and sulfuryl chloride generates only HCl and SO_2 or H_2SO_4 during the reaction, which can be easily removed by evaporation or aqueous work-up.

Summary

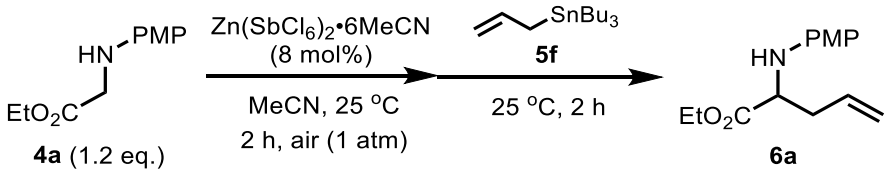
The CDC reactions of amines are highly useful methodologies that allow for the direct functionalization the α-position of amines without the necessity of pre-functionalization of the substrates. Despite a variety of examples of the CDC reactions of amines explored over the last decade, most examples employed transition metal catalysts and stoichiometric chemical oxidants. From the viewpoint of green and sustainable chemistry, it is more desirable if we could employ a non-metal catalyst and oxygen as a terminal oxidant. In order to achieve this goal, I have found several novel cross-dehydrogenative coupling reactions of tertiary amines and glycine derivatives with various nucleophiles using oxygen as a terminal oxidant.

In Chapter 1, I describe my first attempt to achieve the metal-free CDC reaction of tertiary amines using oxygen as a terminal oxidant. Based on the hypothesis that aminium radical cations could catalyze the CDC reactions under aerobic conditions, I investigated tris(*p*-bromophenyl)aminium hexachloroantimoate as a catalyst, and unexpectedly discovered that the antimony could catalyze the CDC reaction in the presence of NHPI as a co-catalyst. Although antimony is classified as a semi-metal, the use of antimony as a catalyst is interesting since: (i) the use of antimony in the CDC reactions of tertiary amines has not been reported; and (ii) the use of hexachloroantimonate anion as a catalyst overturns the commonly held belief that antimonate anions are stable and innocent counter anions in organic chemistry. After extensive optimization, sodium hexachloroantimonate was found to be the best catalyst and I demonstrated that the CDC reactions of *N*-aryl tetrahydroisoquinolines with various nucleophiles proceeded under very mild aerobic conditions.



One of the major limitations of the antimonate/NHPI-catalyzed CDC reaction was that only *N*-aryl tetrahydroisoquinolines could undergo the desired transformation in an

efficient manner. Thus, in Chapter 2, I hypothesized that the use of α-amino acid derivatives would solve this problem since the direct oxidative α-alkylation of α-amino acid derivatives is a highly useful methodology to synthesize natural and unnatural amino acid derivatives. In addition, I wanted to explore the possibility of utilizing metal antimonates, as a novel class of bifunctional catalysts, which can function as both a Lewis acid and as an oxidation catalyst. In order to advance my concept, I initially examined the oxidative allylation of *N*-aryl glycine ester, since allylated glycine derivatives are useful precursors for further transformation, and discovered that allyltin worked as a good nucleophile. After identifying zinc as an active Lewis acid for the allylation reaction, zinc hexachloroantimonate was synthesized and found to serve as a good bifunctional catalyst. Although my goal of utilizing a metal antimonate bifunctional catalyst for the CDC reaction of glycine ester derivatives was achieved, several disadvantages were also identified. For instance: (i) allyltin is toxic; (ii) it was necessary to add the allyltin after the oxidation was completed since it prevented the oxidation step; and (iii) not only zinc, but also antimony could catalyze the allylation reaction. To the best of my knowledge, this is the first example of the direct oxidative allylation of glycine derivatives reported thus far.



During the course of my investigation into the antimony-catalyzed CDC-type reactions of tertiary amines and glycine derivatives, I finally discovered a metal-free CDC reaction of tertiary amines under aerobic conditions, which is described in Chapter 3. Although the reaction mechanism remains unclear, I hypothesized that the reaction proceeded through the radical-based autoxidation mechanism initiated by sulfuryl chloride. Whereas the scope of nucleophile was slightly more limited compared with the antimonate/NHPI system, the sulfuryl chloride system is valuable since: (i) only 2-6 mol% of inexpensive sulfuryl chloride was required for the efficient transformation; and (ii) sulfuryl chloride only generates HCl and SO_2 or H_2SO_4 during the reaction, which

can be easily removed by aqueous treatment, thus leading to a highly environmental-friendly transformation. Although several examples of metal-free CDC reactions of tertiary amines under aerobic conditions have been reported during the course of my Ph.D. studies, such examples are rare and the system described in this chapter represents a significant advance in this field. Additionally, since the preliminary investigation to oxidize the glycine ester **4a** in the presence of sulfuryl chloride was successful, it would be an interesting future topic to oxidatively functionalize α-amino acid derivatives in the presence of sulfuryl chloride and a non-metal Lewis or Brønsted acid catalyst under aerobic conditions.

In conclusion, I have investigated antimony-catalyzed and metal-free CDC reactions of secondary and tertiary amines using oxygen as a terminal oxidant. Although there was no significant improvement in the reactivity compared with other reported reaction systems, the explored catalyst systems provided new insights in organic chemistry, and these CDC-type reactions proceeded under very mild aerobic conditions. For example, the use of antimony as an oxidation catalyst was worth disclosing since the hexachloroantimonate anion has been widely considered as an innocent counter anion in organic chemistry. The sulfuryl chloride-promoted CDC reaction is highly valuable from the viewpoint of green and sustainable chemistry, compared with the transition metal-catalyzed CDC reactions utilizing synthetic oxidants reported, due to its low catalyst loading, the low cost of sulfuryl chloride, and the low toxicity of by-products. Due to the consumption and depletion of finite natural resources such as petroleum products and rare metals, innovation through research is necessary to maintain the lifestyle we enjoy today for future generations. I believe that the studies disclosed in this thesis represents a small step along the long journey towards the never ending struggle towards green and sustainable chemistry required for the future prosperity of human beings.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a JEOL ECX-400, JEOL ECX-500 or a JEOL ECX-600 in $CDCl_3$ unless otherwise noted. Tetramethylsilane served as the internal standard ($\delta = 0$) for ^{1}H NMR and $CDCl_3$ was used as the internal standard ($\delta = 77.0$) for ^{13}C NMR. IR spectra were measured on a JASCO-4200 spectrometer. High Resolution Mass Spectra (HRMS) were recorded using a JEOL JMS-T100TD (DART) spectrometer. The compositions of Zn and Sb were determined by inductively coupled plasma (ICP) analysis with Shimadzu ICPS-7510 equipment. Elemental analysis was performed by Ms. Kamitsubo (The Univ. of Tokyo) to determine the compositions of C, H and N. Column chromatography was conducted on Silica gel 60 (Merck) and preparative thin-layer chromatography (PTLC) was carried out using Wakogel B-5F from Wako Pure Chemical Industries, Ltd.

$MeNO_2$ was commercially available and distilled before use, and acetonitrile was a commercially available dry solvent. $SbCl_5$ was purchased from Aldrich (>99.99% purity) and used without further purification unless otherwise noted. Sulfuryl chloride was purchased from Wako chemical (>99.0% purity) and used without further purification.

Chapter 1. Antimonate/NHPI-catalyzed CDC reaction of tertiary amines

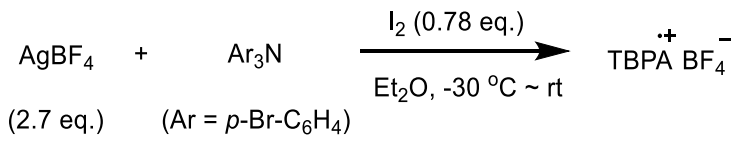
Preparation of $TBPASbCl_6$[55]

This salt was prepared by my co-worker (Woo-Jin Yoo). Into a dry round-bottomed flask, equipped with an argon balloon and a dropping funnel, was added DCM (10 mL) and tris(*p*-bromophenyl)amine (2.40 g, 4.98 mmol). After dissolving the amine, a solution of $SbCl_5$ (2.36 g, 7.89 mmol) in DCM (10 mL) was added dropwise. The reaction mixture turned blue upon the addition. Then, the mixture was stirred over 15 min and poured into Et_2O (40 mL). Filtration provided the desired salt as a dark blue precipitate (3.77 g, 93% yield).

Preparation of $TBPASbF_6$[56]

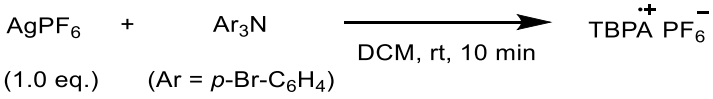
Into a dry round-bottomed flask, equipped with an argon balloon, was added dichloromethane (8 mL), tris(*p*-bromophenyl)amine (98.0 mg, 0.203 mmol) and $AgSbF_6$ (70.0 mg, 0.204 mmol). The reaction mixture immediately turned blue. After stirring the mixture over 10 min at room temperature, silver was removed by filtration through a pad of celite. Then, the filtrate was concentrated dried under high vacuum to provide the desired salt (162 mg, quant.).

Preparation of $TBPABF_4$[57]



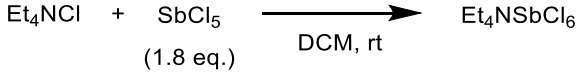
Into a dried round-bottomed flask, equipped with an argon balloon, was added $AgBF_4$ (438 mg, 2.25 mmol), tris(*p*-bromophenyl)amine (400 mg, 0.830 mmol) and Et_2O (21 mL). After cooling the reaction mixture to -30 ºC, to the suspension was added a solution of iodine (165 mg, 0.650 mmol) in Et_2O (3 mL). The reaction mixture immediately turned blue and it was warmed to room temperature over an hour, and the resulting solid was filtered. Then, the solid was extracted with dichloromethane (3 mL x 2) and the extract was poured into dry Et_2O (20 mL) at -20 ºC. The desired salt was obtained as blue crystals (139 mg, 29% yield).

Preparation of $TBPAPF_6$[58]



Into a dry round-bottomed flask, equipped with an argon balloon, was added dichloromethane (8 mL), tris(*p*-bromophenyl)amine (100 mg, 0.207 mmol) and $AgPF_6$ (55.0 mg, 0.218 mmol). The reaction mixture immediately turned blue. After stirring the reaction mixture over 10 min at room temperature, silver was removed by filtration. Then, the filtrate was concentrated and dried under high vacuum to provide the desired salt as black green powder (143 mg, quant.).

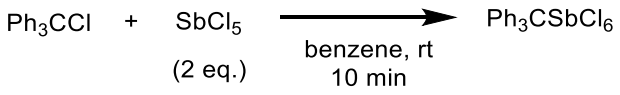
Preparation of Et_4NSbCl_6[59]



Tetraethylammonium chloride (1.10 g, 6.64 mmol) was dissolved in dichloromethane (7.5 mL). The solution was dried with sodium sulfate (0.5 g) and filtered through a filter paper. Into the reaction mixture was slowly added a solution of $SbCl_5$ (1.5 mL, 11.8 mmol) in dichloromethane (5 mL). Then, the reaction mixture was poured into Et_2O (50

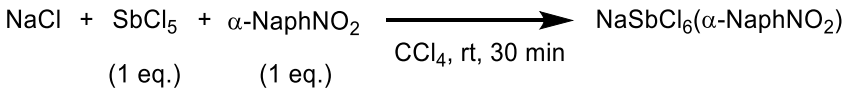
mL) and the precipitates were filtered. Recrystallization of the precipitates from Et_2O/MeCN provided the desired salt as white needles (2.15 g, 70% yield).

Preparation of Ph_3CSbCl_6[60]



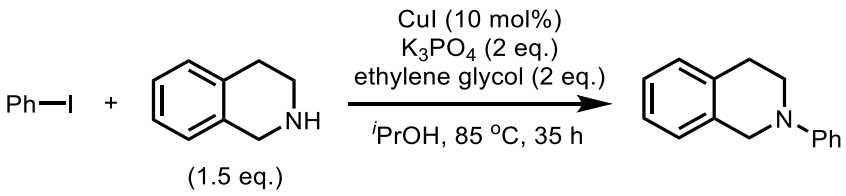
Into a dry round-bottomed flask, equipped with an argon balloon was added benzene (2.5 mL) and trityl chloride (556 mg, 1.99 mmol). Into the reaction mixture was added $SnCl_5$ (1.18 g, 3.95 mmol) and this was stirred over 20 minutes at room temperature. The suspension was washed with Et_2O (5 mL x 3) by decantation to remove unreacted $SbCl_5$. Then, the solvents were removed under reduced pressure and dried under high vacuum to provide the desired salt as an orange powder (1.17 g, quant.).

Preparation of $NaSbCl_6(\alpha\text{-}NaphNO_2)$[38]



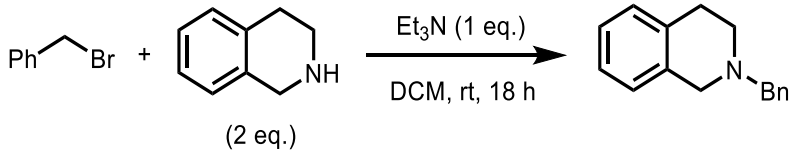
To a dried 10 mL round-bottomed flask, equipped with an argon balloon, was added sodium chloride (91.0 mg, 1.56 mmol), α-nitronaphthalene (272 mg, 1.57 mmol) and CCl_4 (5 mL). Into this suspension was added $SbCl_5$ (0.2 mL, 1.58 mmol) dropwise. Immediate formation of red precipitate was observed. After stirring for 30 minutes at room temperature, the stirring was stopped and the solids were allowed to settle to the bottom. Then, CCl_4 was removed by using a syringe and the suspension was dried under reduced pressure. The product was obtained as red precipitate (761 mg, 91% yield). Anal. Calcd for $NaSbCl_6C_{10}H_7NO_2$: C, 22.63; H, 1.33; N, 2.64. Found: C, 22.73; H, 1.70; N, 2.12.

Preparation of tertiary amines[61]



To a dried round-bottomed flask, equipped with an argon balloon, was added anhydrous K_3PO_4 (25.3 g, 116 mmol), ^{i}PrOH (60 mL), ethylene glycol (7.44 g, 120 mmol), 1,2,3,4-tetrahydroisoquinoline (12.0 g, 89.9 mmol), and iodobenzene (12.3 g, 60.1 mmol). Then, CuI (1.14 g, 5.99 mmol) was added and the reaction mixture was stirred over 35 h at 85 °C. After cooling to room temperature, Et_2O (120 mL) and water (120 mL) was added and extracted with Et_2O (120 mL x 2). Then, the combined organic layer was washed with brine (120 mL). The organic layer was dried over sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography on SiO_2 using hexane/AcOEt = 15/1 as an eluent to provide **1a** as a white solid (9.46 g, 75%). The product was further purified by recrystallization in hexane/Et_2O to furnish the pure product (5.97 g, 47% yield). ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.28 (t, 2H, J = 8.6 Hz), 7.18-7.15 (m, 4H), 6.98 (d, 2H, J = 8.6 Hz), 6.82 (t, 1H, J = 7.5 Hz), 4.41 (s, 2H), 3.56 (t, 2H, J = 6.3 Hz), 2.98 (t, 2H, J = 6.3 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 150.5, 134.8, 134.4, 129.2, 128.5, 126.5, 126.3, 126.0, 118.6, 115.1, 50.7, 46.5, 29.1 ppm

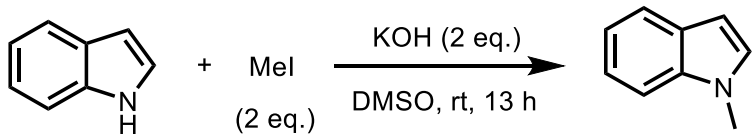
Preparation of *N*-benzyl tetrahydroisoquinoline[8d]



***N*-benzyl-1,2,3,4-tetrahydroisoquinoline (1j).** Into a dry round-bottomed flask, equipped with an argon balloon, was added dichloromethane (40 mL), 1,2,3,4-tetrahydroisoquinoline (2.55 mL, 20 mmol), and triethylamine (1.4 mL, 10 mmol). Then, benzyl bromide (1.2 mL, 10 mmol) was added dropwise to the solution at 0 °C. After stirring over 18 hours at room temperature, the reaction mixture was washed

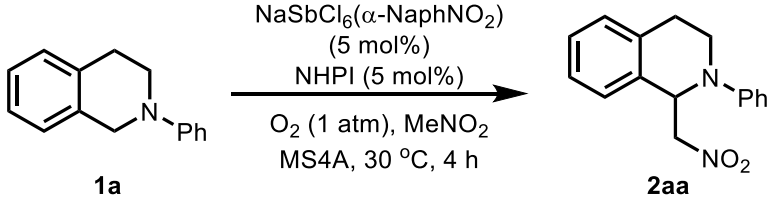
with brine (40 mL) and dried with magnesium sulfate. Then, the mixture was filtered and purified by flash chromatography on silica gel using hexane/AcOEt (4:1 to 1:1). The product was obtained as a yellow oil (1.89 g, 85% yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.38 (d, 2H, *J* = 7.2 Hz), 7.32 (t, 2H, *J* = 7.6 Hz), 7.26 (t, 2H, *J* = 6.9 Hz), 7.12-7.08 (m, 3H), 6.97 (d, 1H, *J* = 6.9 Hz), 3.67 (s, 2H), 3.62 (s, 2H), 2.89 (t, 2H, *J* = 6.2 Hz), 2.73 (t, 2H, *J* = 6.2 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.4, 134.9, 134.3, 129.0, 128.6, 128.2, 127.0, 126.5, 126.0, 125.5, 62.8, 56.1, 50.6, 29.1 ppm.

Preparation of *N*-methylindole[62]

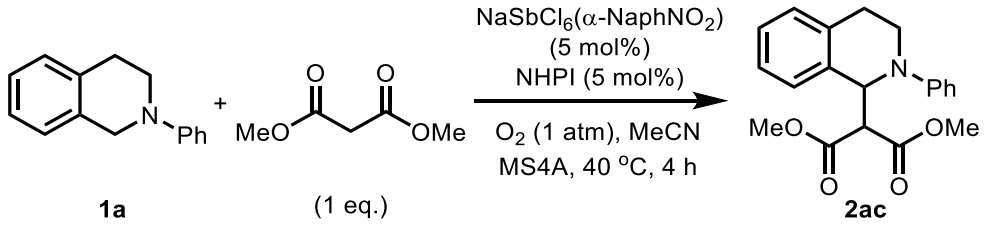


***N*-Methylindole.** Into a dry round-bottomed flask was added DMSO (50 mL), indole (1.74 g, 14.9 mmol), KOH (1.67 g, 29.8 mmol) and methyl iodide (1.85 mL, 29.7 mmol). The reaction mixture was stirred over 13 hours at room temperature. After the reaction, ethyl acetate (10 mL) was added and the organic layer was washed with water (20 mL x 4). Then, the organic layer was dried with sodium sulfate, filtered and concentrated to provide the product as a yellow oil (1.80 g, 92% yield). The compound was used without further purification. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.61 (d, 1H, *J* = 8.3 Hz), 7.28 (d, 1H, *J* = 8.3 Hz), 7.20 (t, 1H, *J* = 6.8 Hz), 7.09 (t, 1H, *J* = 6.9 Hz), 6.98 (d, 1H, *J* = 2.8 Hz), 6.46 (d, 1H, *J* = 3.5 Hz), 3.69 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 136.7, 128.7, 128.4, 121.4, 120.8, 119.2, 109.1, 100.8, 32.7 ppm.

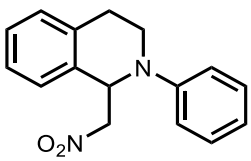
General procedure of the CDC reaction of tertiary amines



In nitroalkanes: To a dried 10 mL round-bottomed flask, equipped with an oxygen balloon, was added MS4A (50 mg), $MeNO_2$ (0.5 mL), and **1a** (52.2 mg, 0.249 mmol). Then, NHPI (2.0 mg, 0.0123 mmol) and $NaSbCl_6(\alpha\text{-}NaphNO_2)$ (6.8 mg, 0.0128 mmol) were successively added. After stirring the reaction mixture for 4 hours at 30 °C, the solvent was removed under reduced pressure and the NMR yield was determined with 1,1,2,2-tetrachloroethane (13 μL) as an internal standard (90% yield). The crude mixture was filtered through silica gel, and the filtrate was concentrated under reduced pressure. Flash chromatography on silica gel with hexane/ethyl acetate (15 : 1) afforded **2a** (56.6 mg, 85% yield).

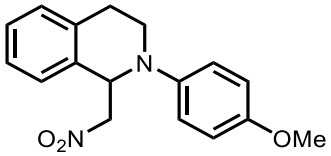


In acetonitrile: To a dried 10 mL round-bottomed flask, equipped with an oxygen balloon, was added MS 4A (50 mg), MeCN (0.5 mL), and **1a** (86 μL, 0.753 mmol). Then, **4a** (86 μL, 0.753 mmol), NHPI (2.0 mg, 0.0123 mmol), and $NaSbCl_6(\alpha\text{-}NaphNO_2)$ (6.8 mg, 0.0128 mmol) were successively added. After stirring the reaction mixture for 4 hours at 40 °C, the solvent was removed under reduced pressure and the NMR yield was determined with 1,1,2,2-tetrachloroethane (13 μL) as an internal standard (95% yield). The crude mixture was filtered through silica gel, and the filtrate was concentrated under reduced pressure. Flash chromatography on silica gel with hexane/ethyl acetate (10 : 1) afforded **5a** (58.2 mg, 69% yield).

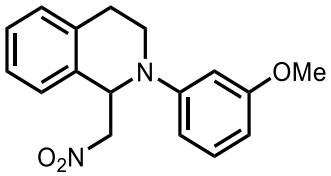


1-(Nitromethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (2aa).[5c] ^1H NMR ($CDCl_3$, 500 MHz) δ 7.28-7.18 (m, 5H), 7.12 (d, 1H, *J* = 6.8 Hz), 6.97 (d, 2H, *J* = 7.9 Hz), 6.84

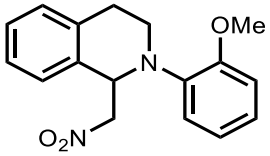
(t, 1H, *J* = 7.4 Hz), 5.54 (t, 1H, *J* = 7.4 Hz), 4.86 (dd, 1H, *J* = 7.9, 11.9 Hz), 4.55 (dd, 1H, *J* = 6.8, 11.9 Hz), 3.68-3.58 (m, 2H), 3.07 (ddd, 1H, *J* = 5.1, 8.5, 15.9 Hz), 2.78 (dt, 1H, J = 4.6, 15.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 148.4, 135.2, 132.9, 129.5, 129.2, 128.1, 127.1, 126.7, 119.4, 115.1, 78.8, 58.2, 42.0, 26.4 ppm.



2-(4-Methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (2ba).[5c] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.17-7.11 (m, 2H), 7.09-7.05 (m, 2H), 6.83 (d, 2H, *J* = 9.1 Hz), 6.72 (d, 2H, *J* = 9.1 Hz), 5.30 (dd, 1H, *J* = 6.2, 9.1 Hz), 4.74 (dd, 1H, *J* = 9.1, 11.9 Hz), 4.47 (dd, 1H, *J* = 5.7, 11.9 Hz), 3.66 (s, 3H), 3.49-3.46 (m, 2H), 2.96-2.89 (m, 1H), 2.60 (dt, 1H, *J* = 4.5, 16.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.9, 143.0, 135.4, 132.8, 129.4, 127.8, 126.9, 126.6, 118.8, 114.6, 78.9, 58.8, 55.5, 43.0, 25.7 ppm.

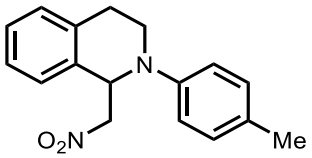


2-(3-Methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (2ca).[6f] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.24 (t, 1H, *J* = 7.4 Hz), 7.20-7.16 (m, 3H), 7.11 (d, 1H, *J* = 7.4 Hz), 6.58 (dd, 1H, *J* = 2.8, 8.2 Hz), 6.52 (t, 1H, *J* = 2.0 Hz), 6.40 (dd, 1H, *J* = 2.0, 8.2 Hz), 5.53 (t, 1H, *J* = 7.4 Hz), 4.85 (dd, 1H, *J* = 7.4, 11.5 Hz), 4.54 (dd, 1H, *J* = 6.8, 11.6 Hz), 3.79 (s, 3H), 3.57-3.65 (m, 2H), 3.08 (ddd, 1H, *J* = 5.4, 8.2, 15.6 Hz), 2.79 (dt, 1H, *J* = 4.8, 16.3 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 160.8, 149.7, 135.2, 132.9, 130.2, 129.1, 128.1, 127.0, 126.7, 107.5, 104.1, 101.4, 78.7, 58.2, 55.2, 42.1, 26.6 ppm.

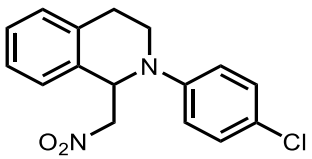


2-(2-Methoxyphenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (2da).[5c] ^{1}H

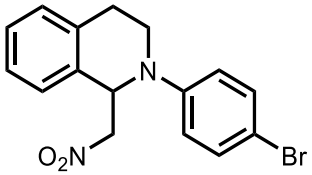
NMR ($CDCl_3$, 500 MHz) δ 7.17-7.13 (m, 2H), 7.08 (dd, 2H, *J* = 2.8, 6.2 Hz), 6.94 (t, 1H, *J* = 7.9 Hz), 6.80 (t, 2H, *J* = 7.9 Hz), 6.76 (t, 1H, *J* = 7.4 Hz), 5.42 (dd, 1H, *J* = 5.1, 8.5 Hz), 4.74 (dd, 1H, *J* = 8.5, 11.9 Hz), 4.45 (dd, 1H, *J* = 5.1, 11.9 Hz), 3.74 (s, 3H), 3.52 (dd, 1H, *J* = 6.3, 13.6 Hz), 3.41 (dt, 1H, *J* = 4.5, 11.3 Hz), 2.91 (ddd, 1H, *J* = 6.2, 11.9, 17.0 Hz), 2.62 (dt, 1H, *J* = 2.3, 15.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 153.1, 138.8, 135.3, 133.6, 129.5, 127.5, 126.8, 126.4, 124.1, 121.9, 121.0, 112.4, 79.1, 58.1, 55.7, 42.9, 26.8 ppm.



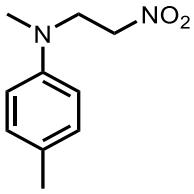
1-(Nitromethyl)-2-(*p*-tolyl)-1,2,3,4-tetrahydroisoquinoline (2ea).[4d] ^1H NMR ($CDCl_3$, 500 MHz) δ 7.25-7.06 (m, 6H), 6.88 (d, 2H, *J* = 7.9 Hz), 5.49 (t, 1H, *J* = 7.4 Hz), 4.84 (dd, 1H, *J* = 6.8, 11.9 Hz), 4.55 (dd, 1H, *J* = 5.1, 11.9 Hz), 3.66-3.55 (m, 2H), 3.05 (ddd, 1H, *J* = 5.7, 9.7, 15.9 Hz), 2.74 (dt, 1H, *J* = 4.0, 16.4 Hz), 2.25 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 146.4, 135.3, 132.9, 130.0, 129.3, 129.1, 128.0, 127.0, 126.6, 116.0, 78.8, 58.4, 42.4, 26.3, 20.3 ppm.



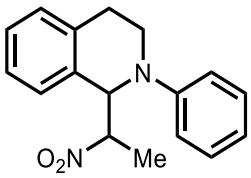
2-(4-Chlorophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (2fa).[4d] ^1H NMR ($CDCl_3$, 500 MHz) δ 7.28-7.11 (m, 6H), 6.90-6.87 (m, 2H), 5.47 (t, 1H, *J* = 7.4 Hz), 4.83 (dd, 1H, *J* = 7.9, 11.9 Hz), 4.55 (dd, 1H, *J* = 7.9, 11.9 Hz), 4.55 (dd, 1H, *J* = 6.2, 11.9 Hz), 3.63- 3.56 (m, 2H), 3.04 (ddd, 1H, *J* = 6.2, 8.5, 15.9 Hz), 2.76 (dt, 1H, *J* = 5.1, 16.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 147.1, 135.0, 132.4, 129.3, 128.2, 126.9, 126.8, 124.3, 116.4, 116.1, 78.6, 58.2, 42.1, 26.1 ppm.



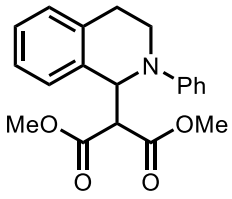
2-(4-bromophenyl)-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (2ga).[14a] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.34 (d, 2H, *J* = 8.9 Hz), 7.27-7.18 (m, 3H), 7.13 (d, 1H, *J* = 6.8 Hz), 6.84 (d, 2H, *J* = 8.9 Hz), 5.48 (t, 1H, *J* = 7.6 Hz), 4.84 (dd, 1H, *J* = 8.3, 12.4 Hz), 4.56 (dd, 1H, *J* = 6.8, 12.4 Hz), 3.65-3.57 (m, 2H), 3.09-3.04 (m, 1H), 2.78 (dt, 1H, *J* = 4.5, 16.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 147.5, 135.0, 132.4, 132.2, 129.3, 128.3, 127.0, 126.8, 116.8, 111.6, 78.6, 58.1, 42.1, 26.2 ppm.



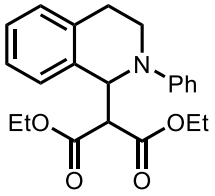
***N*,4-dimethyl-*N*-(2-nitroethyl)aniline (2ka).**[5c] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.08 (d, 2H, *J* = 8.9 Hz), 6.66 (d, 2H, *J* = 8.2 Hz), 4.55 (t, 2H, *J* = 6.2 Hz), 3.95 (t, 2H, *J* = 6.2 Hz), 2.94 (s, 3H), 2.26 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 145.8, 130.0, 127.4, 113.1, 72.6, 51.0, 38.9, 20.2 ppm.



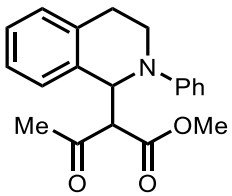
1-(1-Nitroethyl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (2ab).[5c] ^{1}H NMR ($CDCl_3$, 500 MHz, 1.6 : 1 mixture of diastereoisomers) δ 7.18 -6.98 (m, 6H), 6.92-6.87 (m, 2H), 6.73-6.69 (m, 1H), [5.15 (d, *J* = 8.5 Hz), 5.12 (d, *J* = 8.5 Hz), 1H], [4.93 (quintet, *J* = 6.8 Hz), 4.78 (quintet, *J* = 7.4 Hz), 1H], [3.74-3.69 (m), 3.49-3.40 (m), 2H], 2.92 (quintet, 1H, *J* = 6.8 Hz), 2.82-2.72 (m, 1H), [1.57 (d, *J* = 6.8 Hz), 1.41 (d, *J* = 6.8 Hz), 3H] ppm; ^{13}C NMR ($CDCl_3$, 125 MHz, 1.6 : 1 mixture of diastereoisomers) δ 149.1, 148.8, 135.5, 134.7, 133.8, 132.0, 129.3, 129.2, 129.0, 128.6, 128.2, 128.1, 127.2, 126.5, 126.0, 119.2, 118.7, 115.4, 114.5, 88.8, 85.4, 62.6, 61.1, 43.4, 42.6, 26.6, 26.3, 17.3, 16.3 ppm.



Dimethyl 2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (2ac).[5e] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.24-7.16 (m, 4H), 7.12 (dd, 2H, *J* = 2.8, 6.8 Hz), 6.98 (d, 2H, *J* = 8.5 Hz), 6.76 (t, 1H, *J* = 7.4 Hz), 5.70 (d, 1H, *J* = 9.6 Hz), 3.94 (d, 1H, *J* = 9.6 Hz), 3.71-3.60 (m, 5H), 3.06 (ddd, 1H, *J* = 6.8, 9.1, 16.4 Hz), 2.86 (dt, 1H, *J* = 5.0, 16.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 168.2, 167.3, 148.8, 135.6, 134.7, 129.0, 128.9, 127.6, 127.0, 126.0, 118.6, 115.2, 59.1, 58.1, 52.4, 52.4, 42.2, 26.0 ppm.

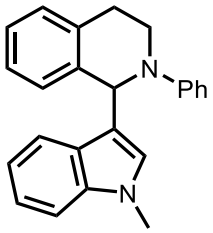


Diethyl 2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)malonate (2ad).[5e] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.18-7.02 (m, 6H), 6.90 (d, 2H, *J* = 8.2 Hz), 6.67 (t, 1H, *J* = 6.7 Hz), 5.64 (d, 1H, *J* = 8.9 Hz), 4.09-3.94 (m, 4H), 3.82 (d, 1H, *J* = 8.9 Hz), 3.64-3.53 (m, 2H), 2.98 (ddd, 1H, *J* = 6.2, 8.9, 15.6 Hz), 2.80 (dt, 1H, *J* = 4.8, 16.3 Hz), 1.08 (t, 3H, *J* = 7.4 Hz), 1.00 (t, 3H, *J* = 6.7 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 167.9, 167.1, 148.8, 135.9, 134.8, 129.0, 128.8, 127.5, 127.1, 125.9, 118.4, 115.0, 61.5, 59.5, 57.8, 42.2, 26.1, 13.9, 13.8 ppm.

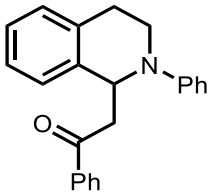


Methyl 3-oxo-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)butanoate (2ae).[14b] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.23-7.08 (m, 6H), 6.97 (t, 2H, *J* = 8.9 Hz), [6.85 (t, *J* = 7.4 Hz), 6.76 (t, *J* = 6.8 Hz), 1H], [5.76 (d, *J* = 9.6 Hz), 5.62 (d, *J* = 9.6 Hz), 1H], [4.17 (d, *J* = 8.9 Hz), 4.01 (d, *J* = 9.6 Hz), 1H], 3.73-3.53 (m, 5H), 3.10-2.67 (m, 2H), [2.17 (s), 2.10 (s), 3H] ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 201.1, 200.2, 169.0, 167.2, 149.2,

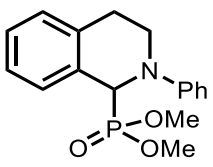
148.9, 136.4, 135.2, 134.7, 134.5, 129.4, 129.3, 129.0, 129.0, 127.5, 127.2, 126.8, 126.2, 126.1, 120.0, 118.5, 117.1, 115.2, 67.3, 66.9, 57.6, 57.2, 52.4, 52.4, 42.8, 42.5, 31.1, 27.4, 26.0, 25.0 ppm.



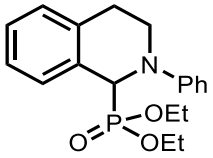
1-(1-Methyl-1*H*-indol-3-yl)-2-phenyl-1,2,3,4-tetrahydroisoquinoline (2af).[5d] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.46 (d, 1H, *J* = 8.0 Hz), 7.21-7.04 (m, 8H), 6.95-6.92 (m, 3H), 6.68 (t, 1H, *J* = 7.4 Hz), 6.41 (s, 1H), 6.09 (s, 1H), 3.58-3.53 (m, 5H), 2.97 (dt, 1H, *J* = 6.2, 15.8 Hz), 2.71 (dt, 1H, *J* = 4.6, 9.1, 15.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 149.7, 137.5, 137.3, 135.5, 129.2, 128.8, 128.0, 126.8, 126.6, 125.6, 121.6, 120.1, 119,1, 117.9, 117.6, 115.5, 109.1, 56.5, 42.1, 32.6, 26.5 ppm.



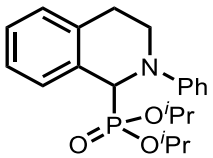
1-Phenyl-2-(2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)ethanone (2ag).[5l] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.75 (dd, 2H, *J* = 1.1, 8.5 Hz), 7.42 (t, 1H, *J* = 7.4 Hz), 7.30 (t, 2H, *J* = 7.9 Hz), 7.15 (t, 3H, *J* = 7.4 Hz), 7.06-7.00 (m, 3H), 6.88 (d, 2H, *J* = 8.5 Hz), 6.66 (t, 1H, *J* = 7.4 Hz), 5.58 (t, 1H, *J* = 5.1 Hz), 3.59-3.51 (m, 2H), 3.48 (dd, 1H, *J* = 4.5, 16.4 Hz), 3.30 (dd, 1H, *J* = 7.4, 17.0 Hz), 3.02 (ddd, 1H, *J* = 5.7, 7.9, 13.6 Hz), 2.83 (dt, 1H, *J* = 5.1, 15.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 198.6, 148.7, 138.5, 137.1, 134.4, 133.0, 129.3, 128.5, 128.0, 127.1, 126.8, 126.2, 117.8, 114.2, 54.9, 45.3, 42.1, 27.5 ppm.



Dimethyl (2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (2ah).[5k] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.28 (d, 1H, *J* = 6.8 Hz), 7.18 (t, 2H, *J* = 7.4 Hz), 7.14-7.06 (m, 3H), 6.89 (d, 2H, *J* = 7.9 Hz), 6.73 (t, 1H, *J* = 7.4 Hz), 5.12 (d, 1H, *J* = 19.8 Hz), 3.94 (ddd, 1H, *J* = 4.6, 8.5, 13.0 Hz), 3.59-3.53 (m, 7H), 3.02-2.88 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 149.2, 136.3 (d, *J* = 6.0 Hz), 130.3, 129.2, 128.8 (d, *J* = 2.4 Hz), 127.9 (d, *J* = 4.8 Hz), 127.5 (d, *J* = 3.6 Hz), 126.0 (d, *J* = 3.6 Hz), 118.6 114.7, 59.2 (d, *J* = 124 Hz), 53.9 (d, *J* = 7.2 Hz), 52.9 (d, *J* = 7.2 Hz), 4.35, 26.6 ppm.

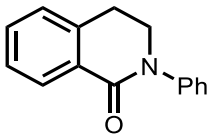


Diethyl (2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (2ai).[5k] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.29 (d, 1H, *J* = 6.8 Hz), 7.17 (t, 2H, *J* = 6.8 Hz), 7.15-7.06 (m, 3H), 6.90 (d, 2H, *J* = 8.5 Hz), 6.71 (t, 1H, *J* = 6.8 Hz), 5.10 (d, 1H, *J* = 19.8 Hz), 4.05-3.78 (m, 5H), 3.54 (dt, 1H, *J* = 11.3 Hz), 3.01-2.90 (m, 2H), 1.17 (t, 3H, *J* = 7.4 Hz), 1.06 (t, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 149.3 (d, *J* = 6.0 Hz), 136.4 (d, *J* = 6.0 Hz), 130.6, 129.1, 128.7 (d, *J* = 3.6 Hz), 128.1 (d, *J* = 4.8 Hz), 127.4 (d, *J* = 3.6 Hz), 125.8 (d, *J* = 2.4 Hz), 118.4, 114.7, 63.2 (d, *J* = 7.2 Hz), 62.2 (d, *J* = 8.4 Hz), 58.7 (d, *J* = 160 Hz), 43.4, 26.7, 16.4 (d, *J* = 4.8 Hz), 16.3 (d, *J* = 6.0 Hz) ppm.



Diisopropyl (2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)phosphonate (2aj).[5k] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.32 (d, 1H, *J* = 6.8 Hz), 7.17-7.04 (m, 5H), 6.87 (d, 2H, *J* = 8.5 Hz), 6.69 (t, 1H, *J* = 7.4 Hz), 5.06 (d, 1H, *J* = 21.5 Hz), 4.58-4.51 (m, 2H), 3.97 (ddd, 1H, *J* = 4.5, 8.5, 13.0 Hz), 3.58 (dt, 1H, *J* = 5.1, 11.3 Hz), 2.98-2.86 (m, 2H), 1.23-1.20 (m, 6H), 1.08 (d, 3H, *J* = 6.2 Hz), 0.87 (d, 3H, *J* = 6.2 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 149.5 (d, *J* = 7.2 Hz), 136.4 (d, *J* = 4.8 Hz), 130.9, 128.9, 128.6 (d, *J* = 39.9 Hz), 128.4 (d, *J* = 4.8 Hz), 127.2 (d, *J* = 3.6 Hz), 125.6 (d, *J* = 2.4 Hz), 118.2,

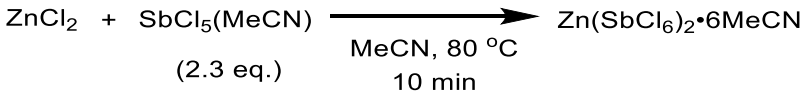
115.0, 72.2 (d, J = 7.2 Hz), 70.8 (d, J = 7.2 Hz), 58.7 (d, J = 162 Hz), 43.4, 26.5, 24.6 (d, J = 2.4 Hz), 24.1 (d, J = 3.6 Hz), 23.7 (d, J = 6.0 Hz), 23.3 (d, J = 6.0 Hz) ppm.



2-Phenyl-3,4-dihydroisoquinolin-1(2*H*)-one (3).[62] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.14 (d, 1H, J = 7.3 Hz), 7.45 (dt, 1H, J = 1.7, 7.4 Hz), 7.41-7.34 (m, 5H), 7.23 (t, 2H, J = 6.8 Hz), 3.98 (t, 2H, J = 6.8 Hz), 3.13 (t, 2H, J = 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 164.2, 143.1, 138.3, 132.0, 129.7, 128.7, 127.2, 126.9, 126.2, 125.3, 49.4, 28.6 ppm.

Chapter 2. Zinc antimonate-catalyzed oxidative allylation of α-amino acid derivatives

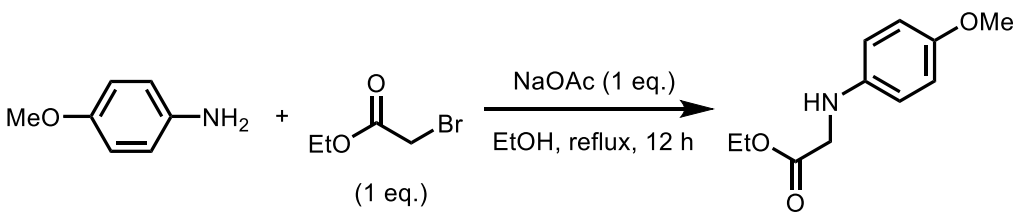
Preparation of $Zn(SbCl_6)_2 \cdot 6MeCN$[50]



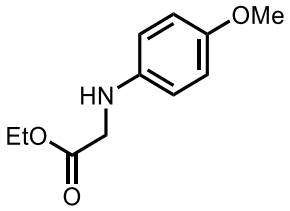
Antimony pentachloride was purified by recrystallization in acetonitrile. Into acetonitrile (20 mL) was slowly added antimony pentachloride (18.9 g, 63.1 mmol) and the reaction mixture was stirred for 10 minutes at room temperature. When the solution was cooled to -20 °C, white crystalline precipitates gradually formed. These crystals were filtered under argon atmosphere and dried under high vacuum to provide a light yellow powder (11.6 g). The powder was further purified by recrystallized from acetonitrile to provide the pure $SbCl_5 \cdot MeCN$ as white crystals (6.06 g, 28% yield).

Into a dry round-bottomed flask, equipped with an argon balloon, was added zinc chloride (308 mg, 2.26 mmol) and acetonitrile (4.0 mL). To the suspension was added $SbCl_5 \cdot MeCN$ (1.80 g, 5.20 mmol) in one portion at ambient temperature. After stirring for 10 minutes at 80 °C, the supernatant solution was quickly transferred to another flask while it is hot to remove the unreacted zinc chloride. Upon standing, white crystalline precipitates formed, which was filtered under argon atmosphere, washed with cold acetonitrile, and dried under high vacuum. $Zn(SbCl_6)_2 \cdot 6MeCN$ was obtained as hygroscopic white crystals (527 mg, 24% yield). Anal. Calcd for $ZnSb_2Cl_{12}C_{12}H_{18}N_6$: Zn, 6.67; Sb, 24.83; C, 14.70; H, 1.85; N, 8.57. Found: Zn, 6.58; Sb, 24.50; C, 14.55; H, 1.94; N, 8.36.

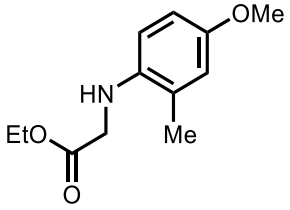
Preparation of *N*-aryl glycine esters[18c]



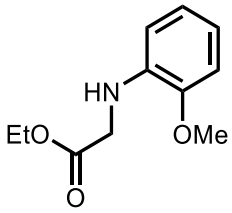
To a dried round-bottomed flask was added *p*-anisidine (12.3 g, 100 mmol), sodium acetate (8.22 g, 100 mmol), ethanol (26 mL), and ethyl bromoacetate (11.2 mL, 102 mmol). The suspension was refluxed over 12 hours. After the reaction, Et_2O (200 mL) was added and the organic layer was washed with water (100 mL x 2). Then, the organic layer was dried over sodium sulfate and purified by flash chromatography on silica gel using hexane/AcOEt = 10/1 to provide the crude product as a pale yellow solid (19.7 g, 94%), which was further recrystallized from hexane/DCM to furnish the product as a pale pink powder (14.5 g, 69% yield).



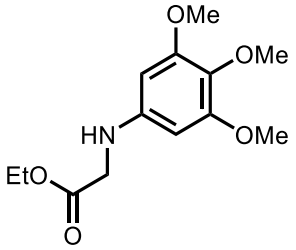
Ethyl (4-methoxyphenyl)glycinate (4a).[18c] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.78 (d, 2H, *J* = 9.1 Hz), 6.57 (d, 2H, *J* = 9.1 Hz), 4.22 (q, 2H, *J* = 7.4 Hz), 3.99 (br, 1H), 3.84 (s, 2H), 3.73 (s, 3H), 1.28 (t, 3H, *J* = 7.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 171.3, 152.6, 141.3, 114.9, 114.3, 61.1, 55.7, 46.8, 14.1 ppm.



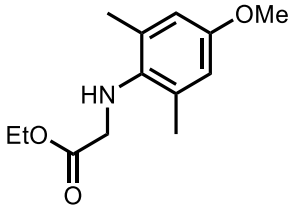
Ethyl (4-methoxy-2-methylphenyl)glycinate (4b). Colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.71-6.67 (m, 2H), 6.42 (d, 1H, *J* = 8.9 Hz), 4.23 (q, 2H, *J* = 6.8 Hz), 3.88 (s, 2H), 3.73 (s, 3H), 2.20 (s, 3H), 1.29 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.4, 152.1, 139.3, 124.4, 117.0, 111.4, 111.1, 61.1, 55.6, 46.6, 17.6, 14.1 ppm; HRMS (DART) calcd. for $C_{12}H_{18}NO_3$ ($[M+H]^+$): 224.1287, found: 224.1286; IR (neat) 3412, 2985, 1741, 1515, 1446, 1373, 1348, 1292, 1229, 1204, 1160, 1096, 1051, 1025, 866, 800 cm^{-1}



Ethyl (2-methoxyphenyl)glycinate (4c).[18g] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.86 (t, 1H, *J* = 7.6 Hz), 6.79 (d, 1H, *J* = 8.2 Hz), 6.71 (t, 1H, *J* = 7.6 Hz), 6.49 (d, 1H, *J* = 8.2 Hz), 4.24 (q, 1H, *J* = 6.8 Hz), 3.92 (s, 2H), 3.86 (s, 3H), 1.29 (t, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 600 MHz) δ 171.1, 147.1, 137.1, 121.1, 117.4, 109.9, 109.6, 61.2, 55.4, 45.7, 14.2 ppm.

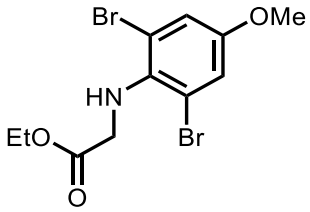


Ethyl (3,4,5-trimethoxyphenyl)glycinate (4d). White solid; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.85 (s, 2H), 4.26 (t, 2H, *J* = 6.2 Hz), 4.24 (br, 1H), 3.89 (s, 2H), 3.82 (s, 6H), 3.76 (s, 3H), 1.31 (t, 3H, *J* = 6.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.0, 153.9, 143.8, 130.5, 90.5, 61.3, 61.0, 55.8, 46.2, 14.1 ppm; HRMS (DART) calcd. for $C_{13}H_{20}NO_5$ ($[M+H]^+$): 270.1342, found: 270.1337; IR (KBr) 2980, 2935, 2824, 1731, 1595, 1516, 1453, 1380, 1345, 1283, 1219, 1126, 1012, 868, 811, 779, 604 cm^{-1}



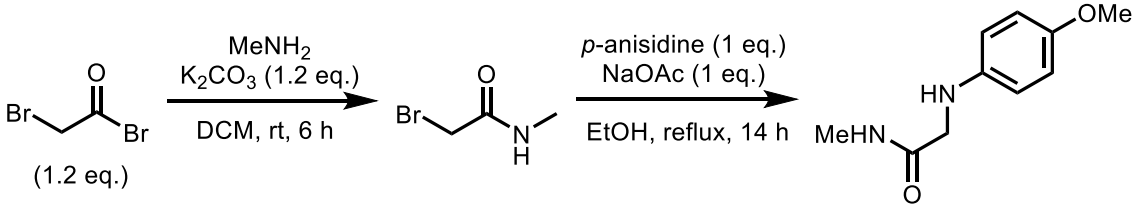
Ethyl (4-methoxy-2,6-dimethylphenyl)glycinate (4p). Purple oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.56 (s, 2H), 4.20 (q, 2H, *J* = 6.9 Hz), 3.72 (s, 3H), 3.69 (s, 2H), 3.60 (br, 1H), 2.30 (s, 6H), 1.27 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.2, 154.7, 138.8, 131.0, 113.9, 61.0, 55.2, 50.4, 18.6, 14.1 ppm; HRMS (DART) calcd. for $C_{13}H_{20}NO_3$ ($[M+H]^+$): 238.1443, found: 238.1442; IR (neat) 2946, 1738, 1604, 1488,

1371, 1342, 1317, 1210, 1153, 1113, 1066, 1030, 857 cm^{-1}



Ethyl (2,6-dibromo-4-methoxyphenyl)glycinate (4q). Light pink solid; ^1H NMR ($CDCl_3$, 600 MHz) δ 7.07 (s, 2H), 4.23 (q, 2H, *J* = 7.6 Hz), 3.97 (s, 2H), 3.74 (s, 3H), 1.29 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 155.3, 137.7, 118.4, 117.5, 61.2, 55.9, 49.6, 14.2 ppm; HRMS (DART) calcd. for $C_{11}H_{14}Br_2NO_3$ ($[M+H]^+$): 365.9340, found: 365.9335; IR (KBr) 3328, 2979, 1740, 1602, 1479, 1436, 1341, 1244, 1213, 1181, 1106, 1044, 744, 706 cm^{-1}

Preparation of *N*-aryl glycine amides[18a]

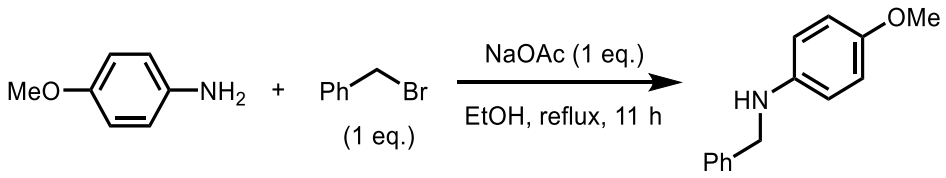


2-((4-Methoxyphenyl)amino)-*N*-methylacetamide (4e). Into a dry round-bottomed flask was added potassium carbonate (16.7 g), water (100 mL), dichloromethane (300 mL), and a solution of $MeNH_2$ in MeOH (40 wt%, 7.77 g, 100 mmol). To the reaction mixture was added a solution of bromoacetyl bromide (24.5 g, 119 mmol) in dichloromethane (100 mL). After stirring the reaction mixture over 6 hours at room temperature, the products were extracted with dichloromethane (50 mL x 3). The combined organic layer was dried with sodium sulfate and filtered. The bromoamide was used without further purification (14.7 g).

Into a dry round-bottomed flask was added the amide (14.7 g, 96.7 mmol), *p*-anisidine (12.3 g, 99.9 mmol), sodium acetate (8.20 g, 100 mmol), and ethanol (50 mL). The suspension was refluxed over 14 hours. After cooling to room temperature, the reaction mixture was filtered and the filtrate was concentrated. Further purification

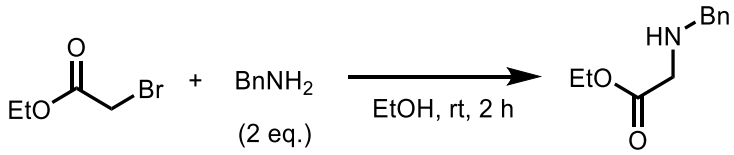
by flash chromatography gave the product as yellow powder (2.15 g). Recrystallization provided the product as pale brown crystals (1.83 g, 9% yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.78 (d, 2H, *J* = 8.9 Hz), 6.57 (d, 2H, *J* = 8.9 Hz), 3.86 (s, 2H), 3.75 (s, 3H), 3.73 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 600 MHz) δ 171.8, 152.5, 141.1, 114.8, 114.3, 55.6, 52.1, 46.5 ppm.

Preparation of *N*-benzyl-*p*-anisidine



***N*-Benzyl-4-methoxyaniline (4f).**[64] To a dried round-bottomed flask, equipped with an argon balloon, was added *p*-anisidine (3.69 g, 30.0 mmol), sodium acetate (2.46 g, 30.0 mmol), EtOH (15 mL), and benzyl bromide (3.55 mL, 29.9 mmol). The reaction mixture refluxed over 11 hours. Then, ethyl acetate was added, and the suspension was filtered and concentrated under reduce pressure. Purification by flash chromatography provided the crude product as a yellow oil (3.21 g, <50%) and it was recrystallized from hexane/DCM to provide the product as light yellow crystals (1.51 g, 24 % yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.37-7.25 (m, 5H), 6.77 (d, 2H, *J* = 8.2 Hz), 6.59 (d, 2H, *J* = 8.9 Hz), 4.27 (s, 2H), 3.73 (m, 4H) ppm; ^{13}C NMR ($CDCl_3$, 600 MHz) δ 152.1, 142.4, 139.6, 128.5, 127.5, 127.1, 114.8, 114.0, 55.7, 49.2 ppm.

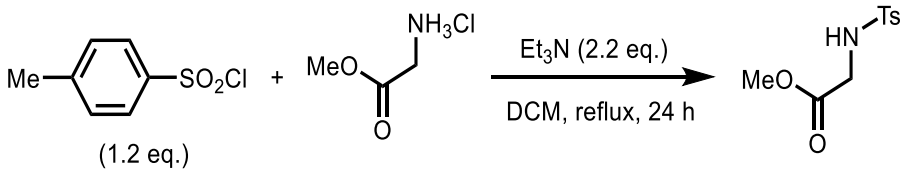
Preparation of *N*-benzyl glycine ethyl ester



Ethyl benzylglycinate (4g).[65] Into a dry round-bottomed flask, equipped with an argon balloon, was added ethanol (100 mL), benzylamine (10.8 g, 101 mmol), and ethyl bromoacetate (8.43 g, 50.5 mmol). The solution was stirred for 2 hours at room

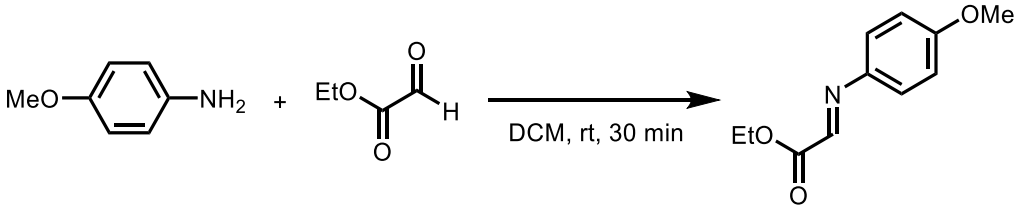
temperature. After the removal of the solvent, ether (100 mL) was added and filtered to remove the ammonium salt by-product. Flash chromatography on silica gel using hexane/AcOEt = 4/1 gave the product as a colorless oil (6.69 g, 69% yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.33-7.24 (m, 5H), 4.18 (q, 2H, *J* = 7.6 Hz), 3.80 (s, 2H), 3.40 (s, 2H), 1.92 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.3, 139.4, 128.3, 128.1, 127.0, 60.6, 53.2, 50.0, 14.1 ppm.

Preparation of *N*-tosyl glycine methyl ester



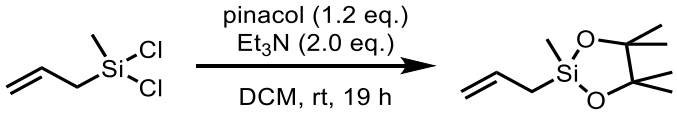
Methyl tosylglycinate (4h).[66] To dried round-bottomed flask, filled with argon gas, was added *p*-toluenesulfonyl chloride (7.4 g, 38 mmol), glycine methyl ester hydrogen chloride salt (4.00 g, 31.8 mmol), DCM (20 mL), and triethylamine (30 mL, 70 mmol). The reaction mixture was refluxed over 24 hours and poured into water (100 mL). After extracting with Et_2O (100 mL x 3) the combined organic layer was dried over sodium sulfate. The residue was purified by flash chromatography on silica gel using hexane/AcOEt (4/1~1/1). The product was obtained as a pale yellow solid (5.22 g, 67% yield), which was further purified by recrystallization in hexane/DCM to provide white crystals (4.16 g, 54% yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.75 (d, 2H, *J* = 8.3 Hz), 7.31 (d, 2H, *J* = 8.2 Hz), 5.28 (t, 1H, *J* = 5.5 Hz), 3.79 (d, 2H, *J* = 5.5 Hz), 3.64 (s, 3H), 2.43 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 169.3, 143.8, 136.1, 129.7, 127.2, 52.5, 44.0, 21.5 ppm.

Preparation of imino ester 4a' [67]



Ethyl 2-((4-methoxyphenyl)imino)acetate (4a').[67] Into a dried round-bottomed flask was added DCM (150 mL), sodium sulfate (15g), *p*-anisidine (3.69 g, 30.0 mmol), and a solution of ethyl glyoxylate in toluene (ca. 50%, 6.0 mL). The suspension was stirred over 30 minutes at room temperature. After filtration, the solution was concentrated to afford a yellow oil (6.39 g, quant). The imino ester was used without further purification. ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.94 (s, 1H), 7.37 (d, 2H, J = 8.3 Hz), 6.93 (d, 2H, J = 8.9 Hz), 4.42 (q, 2H, J = 7.6 Hz), 3.84 (s, 3H), 1.41 (t, 3H, J = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 163.6, 160.5, 148.0, 141.3, 123.6, 114.5, 61.9, 55.5, 14.2 ppm.

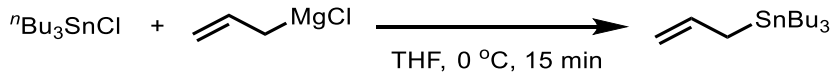
Preparation of allylpinacolatosilane



2-Allyl-2,4,4,5,5-pentamethyl-1,3,2-dioxasilolane (5c). To a dried two-necked 300 mL round-bottomed flask, equipped with a dropping funnel and an argon balloon, was added allyldichloromethylsilane (7.44 g, 48.0 mmol) and CH_2Cl_2 (70 mL). Into the reaction mixture was added Et_3N (9.80 g, 96.9 mmol) in one portion at 0 °C. Then, a solution of pinacol (7.19 g, 57.8 mmol; assay >95.0%(GC)) in CH_2Cl_2 (18 mL) was added dropwise at 0 °C over 15 minutes. The reaction mixture was stirred at room temperature over 19 hours. After concentration, hexane (80 mL) was poured and stirred at room temperature over 1 hour. The suspension was filtered through a pad of celite and the filtrate was washed with cold water (15 mL x 2), and then dried over anhydrous Na_2SO_4. After filtration, the solvent was removed and the resultant residue was purified by distillation to afford the desired compound as a colorless oil (6.85 g, 71%). ^{1}H NMR ($CDCl_3$) δ 0.27 (s, 3H), 1.25 (s, 6H), 1.26 (s, 6H), 1.71 (d, 2H, J = 8.0 Hz), 4.94 (d, 1H, J = 10.3 Hz), 4.98 (d, 1H, J = 17.2 Hz), 5.80 (ddt, 1H, J = 8.0, 10.3, 17.2 Hz); ^{13}C NMR ($CDCl_3$) δ -1.6, 24.8, 25.6, 81.3, 115.2, 132.2; HRMS (DART) calcd. for $C_{10}H_{21}O_2Si$

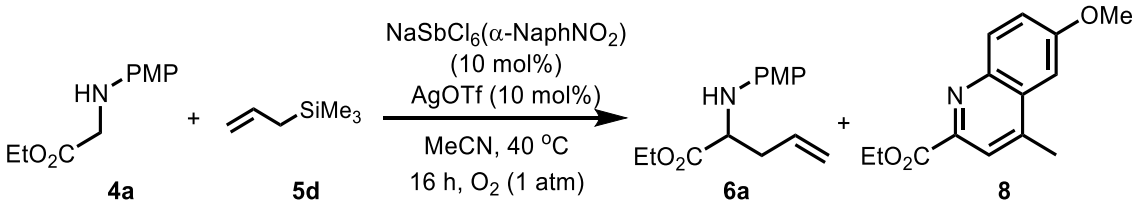
([M+H]$^+$): 201.1311, found: 201.1319; IR (neat) 790, 869, 925, 969, 1038, 1160, 1258, 1370, 1631, 2935, 2978 cm^{-1}

Preparation of allyltributyltin[68]



Allyltributyltin (5f). To a dried round-bottomed flask, filled with argon gas, was added Et_2O (100 mL) and ^{n}Bu$_3$SnCl (10 mL, 36.9 mmol). Into the reaction mixture was added dropwise a 2.0 M solution of allylmagnesium chloride in THF (20 mL, 40 mmol) at 0 °C. After stirring for 15 min at 0 °C, saturated aqueous $NaHCO_3$ (100 mL) and hexane (200 mL) were added. The aqueous layer was extracted with hexane (100 mL x 2) and dried over sodium sulfate. The product was obtained as a colorless oil (11.9 g, 98% yield). ^{1}H NMR ($CDCl_3$, 600 MHz) δ 5.97-5.90 (m, 1H), 4.78 (d, 1H, *J* = 17.2 Hz), 4.64 (d, 1H, *J* = 9.7 Hz), 1.77 (d, 2H, *J* = 8.3 Hz), 1.52-1.46 (m, 6H), 1.33-1.27 (m, 6H), 0.90-0.86 (m, 15H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 138.2, 109.1, 29.1, 27.3, 16.2, 13.4, 9.1 ppm.

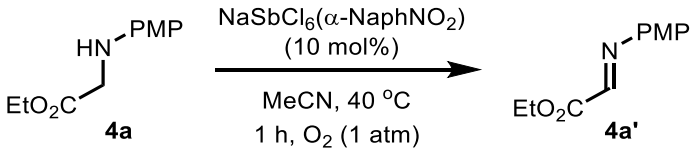
General procedure of oxidative allylation using allylsilanes



To a dry round-bottomed flask, equipped with an argon balloon, was added, MS4A (50 mg), glycine ester **4a** (51.8 mg, 0.25 mmol), allyltrimethylsilane (40 μL, 0.25 mmol) and MeCN (2.5 mL). To the solution was added silver triflate (6.3 mg, 0.025 mmol) and $NaSbCl_6$(α-$NaphNO_2$) (13.0 mg, 0.025 mmol). After stirring over 16 hours

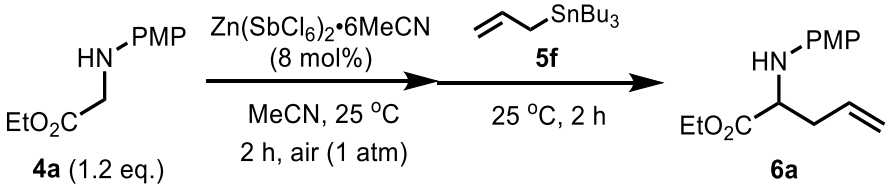
at 40 °C, saturated aqueous $NaHCO_3$ (5 mL) was added. The aqueous layer was extracted with DCM (5 mL x 3) and dried over sodium sulfate. After filtration and concentration, 1,1,2,2-tetrachloroethane (13.2 μL, 0.125 mmol) was added and the yield was determined by ^1H NMR.

General procedure of oxidation of glycine ester



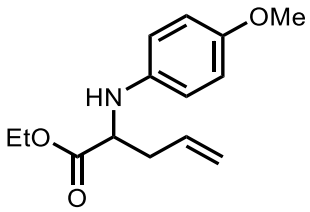
To a dry round-bottomed flask, equipped with an argon balloon, was added glycine ester **4a** (52.6 mg, 0.25 mmol), MeCN (2.5 mL) and $NaSbCl_6(\alpha\text{-}NaphNO_2)$ (13.0 mg, 0.025 mmol). The solution was heated at 40 °C over 1 hour. After the reaction, solvent was removed and 1,1,2,2-tetrachloroethane (13.2 μL, 0.125 mmol) was added. The yield was determined by ^1H NMR.

General procedure of oxidative allylation using allytion

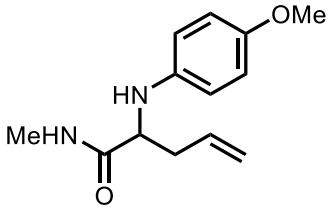


To a dry round-bottomed flask, equipped with a balloon of dry air, was added glycine ester **4a** (62.7 mg, 0.300 mmol) and MeCN (2.5 mL). To the solution was added zinc hexachloroantimonate (19.7 mg, 0.0201 mmol) and the brown reaction mixture was stirred over 2 hours at 25 °C. Then, allyltin (82.8 mg, 0.250 mmol) was added and the solution was stirred over 2 hours. After the reaction, saturated aqueous $NaHCO_3$ (5 mL) was added and extracted with DCM (5 mL x 3). Then, the combined organic layer was dried with sodium sulfate, filtered and concentrated. The yield was determined by using

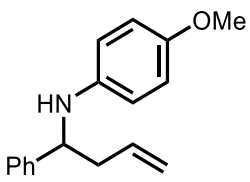
1,4-bis(trimethylsilyl)benzene (13.9 mg, 0.25 eq.) as an internal standard (75% yield). Further purification by PTLC using hexane/AcOEt (4 : 1) as an eluent provided the product as a colorless oil (44.5 mg, 71% yield).



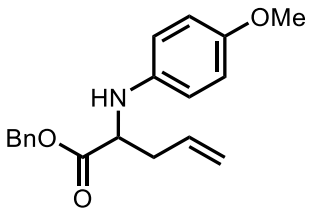
Ethyl 2-((4-methoxyphenyl)amino)pent-4-enoate (6a).[69] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.76 (d, 2H, *J* = 8.9 Hz), 6.59 (d, 2H, *J* = 8.9 Hz), 5.83-5.76 (m, 1H), 5.16 (d, 1H, *J* = 13.7 Hz), 5.14 (d, 1H, *J* = 6.8 Hz), 4.20-4.14 (m, 2H), 4.05 (dt, 1H, *J* = 6.2, 8.9 Hz), 3.92 (d, 1H, *J* = 9.6 Hz), 3.73 (s, 3H), 2.60-2.52 (m, 2H), 1.23 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.5, 153.0, 140.6, 132.9, 118.7, 115.1, 114.8, 60.9, 57.1, 55.6, 37.1, 14.2 ppm.



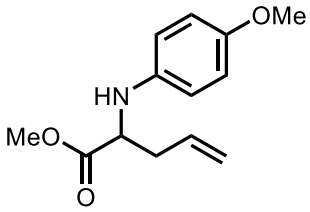
2-((4-Methoxyphenyl)amino)-*N*-methylpent-4-enamide (6e). Light brown oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.69 (d, 2H, *J* = 8.9 Hz), 6.51 (d, 2H, *J* = 8.9 Hz), 5.74-5.67 (m, 1H), 5.09 (d, 1H, *J* = 11.6 Hz), 5.07 (d, 1H, *J* = 3.4 Hz), 3.99 (t, 1H, *J* = 6.2 Hz), 3.83 (br, 1H), 3.65 (s, 3H), 3.63 (s, 3H), 2.53-2.44 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 174.1, 152.7, 140.6, 132.8, 118.8, 115.1, 114.8, 57.1, 55.6, 52.0, 37.1 ppm; HRMS (DART) calcd. for $C_{13}H_{19}N_2O_2$ ($[M+H]^+$): 235.1447, found: 235.1440; IR (neat) 2952, 2835, 1739, 1515, 1441, 1242, 1151, 1038, 997, 922, 824, 756 cm^{-1}



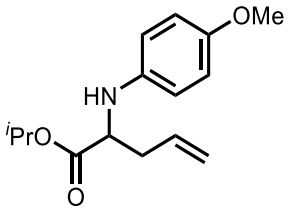
4-Methoxy-*N*-(1-phenylbut-3-en-1-yl)aniline (6f).[70] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.21 (m, 5H), 6.67 (d, 2H, *J* = 9.2 Hz), 6.45 (d, 2H, *J* = 9.2 Hz), 5.81-5.71 (m, 1H), 5.20-5.13 (m, 2H), 4.30 (dt, 1H, *J* = 5.0, 3.2 Hz), 3.68 (s, 3H), 2.63-2.43 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 151.9, 143.8, 141.6, 134.8, 128.5, 126.9, 126.3, 118.2, 114.7, 114.6, 57.9, 55.7, 43.4 ppm



Benzyl 2-((4-methoxyphenyl)amino)pent-4-enoate (6i).[69] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.34-7.26 (m, 5H), 6.74 (d, 2H, *J* = 8.9 Hz), 6.57 (d, 2H, *J* = 8.9 Hz), 5.79-5.72 (m, 1H), 5.15-5.10 (m, 2H), 4.11 (t, 1H, *J* = 6.2 Hz), 3.72 (s, 3H), 2.61-2.52 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 600 MHz) δ 173.5, 152.9, 140.6, 135.5, 132.7, 128.5, 128.3, 128.3, 118.8, 115.3, 114.9, 66.7, 57.3, 55.7, 37.1 ppm.

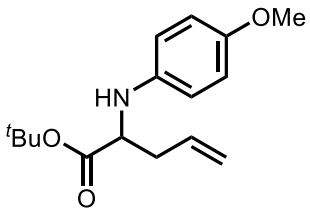


Methyl 2-((4-methoxyphenyl)amino)pent-4-enoate (6j).[69] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.77 (d, 2H, *J* = 8.9 Hz), 6.59 (d, 2H, *J* = 8.9 Hz), 5.82-5.75 (m, 1H), 5.18-5.15 (m, 2H), 4.07 (t, 1H, *J* = 6.2 Hz), 3.91 (br, 1H), 3.73 (s, 3H), 3.71 (s, 3H), 2.61-2.52 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 174.1, 152.7, 140.5, 132.8, 118.8, 115.1, 114.8, 57.1, 55.6, 52.0, 37.1 ppm.

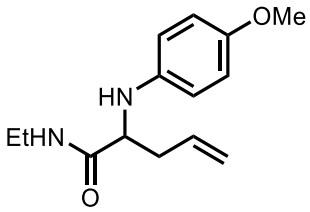


Isopropyl 2-((4-methoxyphenyl)amino)pent-4-enoate (6k).[69] ^{1}H NMR ($CDCl_3$,

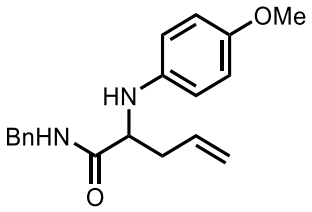
400 MHz) δ 6.68 (d, 2H, *J* = 9.2 Hz), 6.52 (d, 2H, *J* = 8.7 Hz), 5.77-5.67 (m, 1H), 5.09 (d, 1H, *J* = 10.0 Hz), 5.07 (d, 1H, *J* = 9.2 Hz), 4.99-4.93 (m, 1H), 3.94 (t, 1H, *J* = 6.0 Hz), 3.83 (br, 1H), 3.65 (s, 3H), 2.50-2.46 (m, 2H), 1.13 (t, 3H, *J* = 6.4 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.0, 152.7, 140.7, 132.9, 118.6, 115.1, 114.8, 68.5, 57.2, 55.6, 37.1, 21.8, 21.7 ppm.



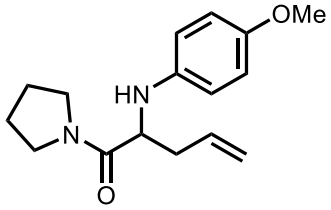
***tert*-Butyl 2-((4-methoxyphenyl)amino)pent-4-enoate (6l).** Colorless oil; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.69 (d, 2H, *J* = 9.2 Hz), 6.51 (d, 2H, *J* = 8.7 Hz), 5.78-5.68 (m, 1H), 5.09 (d, 1H, *J* = 9.6 Hz), 5.06 (d, 1H, *J* = 9.2 Hz), 3.87 (t, 1H, *J* = 6.4 Hz), 3.83 (br, 1H), 3.66 (s, 3H), 2.48-2.44 (m, 2H), 1.35 (s, 9H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.7, 152.6, 140.1, 133.1, 118.5, 115.1, 114.8, 81.5, 57.5, 55.7, 37.1, 28.0 ppm; HRMS (DART) calcd. for $C_{16}H_{24}NO_3$ ($[M+H]^+$): 278.1756, found: 278.1762; IR (neat) 2980, 2933, 2833, 1729, 1515, 1461, 1367, 1296, 1241, 1151, 1039, 918, 823, 756 cm^{-1}



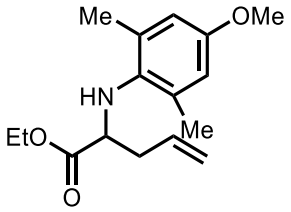
***N*-Ethyl-2-((4-methoxyphenyl)amino)pent-4-enamide (6m).** Light brown oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.94 (br, 1H), 6.78 (d, 2H, *J* = 8.9 Hz), 6.55 (d, 2H, *J* = 8.9 Hz), 5.80-5.73 (m, 1H), 5.21-5.18 (m, 2H), 3.74 (s, 3H), 3.62 (dt, 1H, *J* = 3.4, 8.2 Hz), 3.33-3.24 (m, 2H), 2.78-2.43 (m, 2H), 1.08 (t, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 172.8, 153.2, 140.8, 133.9, 119.0, 115.0, 114.9, 59.2, 55.7, 37.8, 34.0, 14.8 ppm; HRMS (DART) calcd. for $C_{14}H_{21}N_2O_2$ ($[M+H]^+$): 249.1603, found: 249.1595; IR (neat) 2979, 2933, 1651, 1514, 1444, 1300, 1240, 1179, 1149, 1037, 921, 824, 645 cm^{-1}



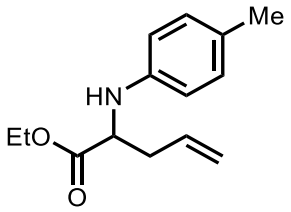
***N*-Benzyl-2-((4-methoxyphenyl)amino)pent-4-enamide (6n).** Light brown oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.29-7.23 (m, 3H), 7.18 (d, 2H, *J* = 6.8 Hz), 6.77 (d, 2H, *J* = 8.9 Hz), 6.56 (d, 2H, *J* = 8.9 Hz), 5.81-5.74 (m, 1H), 5.22-5.19 (m, 2H), 4.53 (dd, 1H, *J* = 6.2, 14.5 Hz), 4.37 (dd, 1H, *J* = 6.2, 15.1 Hz), 3.76-3.70 (m, 5H), 2.83-2.79 (m, 1H), 2.52-2.47 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.0, 153.3, 140.6, 138.1, 133.8, 128.6, 127.5, 127.3, 119.2, 115.1, 114.8, 59.2, 55.7, 43.1, 37.8 ppm; HRMS (DART) calcd. for $C_{19}H_{23}N_2O_2$ ($[M+H]^+$): 311.1760, found: 311.1769; IR (neat) 1655, 1514, 1457, 1241, 1036, 914, 824, 758, 732, 699 cm^{-1}



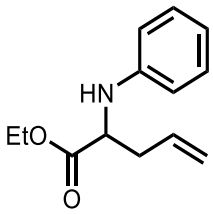
2-((4-Methoxyphenyl)amino)-1-(pyrrolidin-1-yl)pent-4-en-1-one (6o). Light brown solid; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.67 (d, 2H, *J* = 8.2 Hz), 6.53 (d, 2H, *J* = 8.9 Hz), 5.81-5.74 (m, 1H), 5.06 (d, 1H, *J* = 16.5 Hz), 5.02 (d, 1H, *J* = 10.3 Hz), 4.05 (t, 1H, *J* = 6.2 Hz), 3.65 (s, 3H), 3.65-3.34 (m, 4H), 2.44-2.37 (m, 2H), 1.89-1.79 (m, 2H), 1.78-1.74 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 171.1, 152.6, 141.0, 133.7, 118.0, 115.6, 114.8, 56.6, 55.6, 46.3, 45.8, 37.0, 26.0, 24.0 ppm; HRMS (DART) calcd. for $C_{16}H_{23}N_2O_2$ ($[M+H]^+$): 275.1760, found: 275.1751; IR (KBr) 3034, 2953, 2876, 1638, 1511, 1440, 1344, 1311, 1235, 1170, 1143, 1106, 1030, 919, 821, 793, 748, 594, 522 cm^{-1}



Ethyl 2-((4-methoxy-2,6-dimethylphenyl)amino)pent-4-enoate (6p). Colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.53 (s, 2H), 5.85-5.78 (m, 1H), 5.13 (d, 1H, *J* = 18.6 Hz), 5.11 (d, 1H, *J* = 10.3 Hz), 4.13-4.06 (m, 1H), 3.85 (t, 1H, *J* = 6.2 Hz), 3.72 (s, 3H), 3.53 (br, 1H), 2.55-2.46 (m, 2H), 2.28 (s, 6H), 1.17 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 174.3, 154.4, 137.1, 133.2, 130.6, 118.3, 114.0, 60.7, 59.8, 55.2, 38.1, 19.0, 14.1 ppm; HRMS (DART) calcd. for $C_{16}H_{24}NO_3$ ($[M+H]^+$): 278.1756, found: 278.1756; IR (neat) 2982, 1735, 1604, 1487, 1437, 1371, 1318, 1228, 1187, 1151, 1067, 1030, 920, 857 cm^{-1}

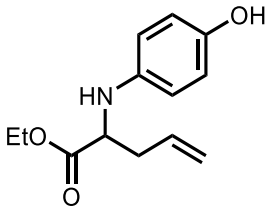


Ethyl 2-(*p*-tolylamino)pent-4-enoate (6r). Colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 6.98 (d, 2H, *J* = 8.2 H), 6.54 (d, 2H, *J* = 8.3 Hz), 5.82-5.75 (m, 1H), 5.16 (d, 1H, *J* = 13.7 Hz), 5. 14 (d, 1H, *J* = 10.3 Hz), 4.18 (q, 2H, *J* = 6.9 Hz), 4.10 (t, 1H, *J* = 6.2 Hz), 2.62-2.53 (m, 2H), 2.23 (s, 3H), 1.25 (t, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.5, 144.3, 132.9, 129.8, 127.6, 118.8, 113.7, 61.0, 56.4, 37.0, 20.3, 14.3 ppm; HRMS (DART) calcd. for $C_{14}H_{20}NO_2$ ($[M+H]^+$): 234.1494, found: 234.1504; IR (neat) 2920, 1734, 1619, 1522, 1370, 1184, 1149, 1027, 920, 809 cm^{-1}

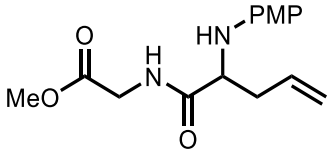


Ethyl 2-(phenylamino)pent-4-enoate (6s). Colorless oil; ^{1}H NMR ($CDCl_3$, 500

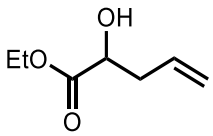
MHz) δ 7.17 (t, 2H, *J* = 7.4 Hz), 6.73 (t, 1H, *J* = 7.5 Hz), 6.61 (d, 2H, *J* = 8.6 Hz), 5.83-5.75 (m, 1H), 5.17 (d, 1H, *J* = 10.9 Hz), 5.14 (d, 1H, *J* = 2.9 Hz), 4.21-4.12 (m, 4H), 2.64-2.53 (m, 2H), 1.25 (t, 3H, *J* = 8.1 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.3, 146.5, 132.7, 129.3, 118.9, 118.3, 113.5, 61.1, 56.0, 37.0, 14.2 ppm; HRMS (DART) calcd. for $C_{13}H_{18}NO_2$ ($[M+H]^+$): 220.1338, found: 220.1328; IR (neat) 2982, 1734, 1604, 1507, 1438, 1371, 1316, 1189, 1150, 1028, 922, 751, 693 cm^{-1}



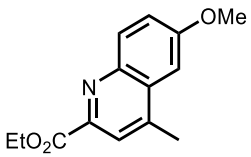
Ethyl 2-((4-hydroxyphenyl)amino)pent-4-enoate (6t). Light brown oil; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.62 (d, 2H, *J* = 8.6 Hz), 6.50 (d, 2H, *J* = 8.6 Hz), 5.82-5.73 (m, 1H), 5.16 (d, 1H, *J* = 10.9 Hz), 5.13 (d, 1H, *J* = 1.7 Hz), 4.20-4.15 (m, 2H), 4.04 (t, 1H, *J* = 6.32 Hz), 2.55 (t, 2H, *J* = 6.3 Hz), 1.22 (t, 3H, *J* = 6.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.1, 148.8, 140.1, 132.7, 118.9, 116.2, 115.5, 61.2, 57.4, 37.1, 14.1 ppm; HRMS (DART) calcd. for $C_{13}H_{18}NO_3$ ($[M+H]^+$): 236.1287, found: 236.1277; IR (neat) 2982, 1728, 1516, 1437, 1372, 1304, 1209, 1148, 1098, 1023, 919, 825, 757 cm^{-1}



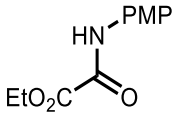
Methyl (2-((4-methoxyphenyl)amino)pent-4-enoyl)glycinate (6v). Colorless oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.43 (br, 1H), 6.78 (d, 2H, *J* = 8.9 Hz), 6.59 (d, 2H, *J* = 8.9 Hz), 5.84-5.77 (m, 1H), 5.23-5.20 (m, 2H), 4.14 (dd, 1H, *J* = 6.9, 18.5 Hz), 3.93 (dd, 1H, *J* = 5.5, 17.9 Hz), 3.79-3.68 (m, 8H), 2.78-2.73 (m, 1H), 2.55-2.49 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.7, 170.0, 153.3, 140.7, 133.7, 119.3, 115.2, 114.8, 59.1, 55.6, 52.2, 40.8, 37.7 ppm; HRMS (DART) calcd. for $C_{15}H_{21}N_2O_4$ ($[M+H]^+$): 293.1501, found: 293.1494; IR (neat) 2951, 1750, 1665, 1514, 1440, 1408, 1371, 1240, 1180, 1037, 915, 824, 757 cm^{-1}



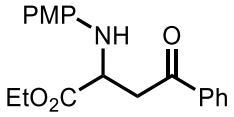
Ethyl 2-hydroxypent-4-enoate (7).[71] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.86-5.77 (m, 1H), 5.15 (d, 1H, *J* = 15.5 Hz), 5.13 (d, 1H, *J* = 9.2 Hz), 4.30-4.19 (m, 3H), 3.05 (d, 1H, *J* = 6.3 Hz), 2.60-2.42 (m, 2H), 1.30 (t, 3H, *J* = 6.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.3, 132.4, 118.4, 69.9, 61.5, 38.6 14.1 ppm



Ethyl 6-methoxy-4-methylquinoline-2-carboxylate (8). Light yellow solid; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 8.21 (d, 1H, *J* = 9.7 Hz), 8.02 (s, 1H), 7.42 (dd, 1H, *J* = 2.0, 8.9 Hz), 7.20 (d, 1H, *J* = 2.0 Hz), 4.54 (q, 2H, *J* = 6.2 Hz), 3.98 (s, 3H), 2.73 (s, 3H), 1.49 (t, 3H, *J* = 7.6 Hz) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.8, 159.2, 145.4, 143.8, 143.4, 133.0, 130.6, 122.5, 122.1, 101.4, 62.0, 55.6, 19.0, 14.4 ppm; HRMS (DART) calcd. for $C_{14}H_{15}NO_3$ ($[M+H]^+$): 246.1130, found: 246.1134; IR (KBr) 3351, 1734, 1696, 1616, 1507, 1477, 1434, 1368, 1284, 1255, 1223, 1178, 1148, 1107, 1025, 857, 833 cm^{-1}

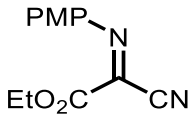


Ethyl 2-((4-methoxyphenyl)amino)-2-oxoacetate (9).[72] ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.86 (br, 1H), 7.57 (d, 2H, *J* = 9.2 Hz), 6.89 (d, 2H, *J* = 9.2 Hz), 4.40 (q, 2H, *J* = 6.9 Hz), 3.80 (s, 3H), 1.42 (t, 3H, *J* = 7.5 Hz) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 161.1, 157.1, 153.6, 129.5, 121.3, 114.2, 63.6, 55.4, 13.9 ppm.

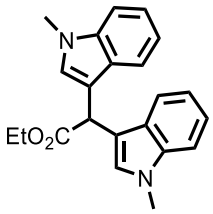


Ethyl 2-((4-methoxyphenyl)amino)-4-oxo-4-phenylbutanoate (10).[73] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.93 (d, 2H, *J* = 7.5 Hz), 7.56 (t, 1H, *J* = 7.6 Hz), 7.45 (t, 2H, *J* =

7.6 Hz), 6.76 (d, 2H, *J* = 8.9 Hz), 6.68 (d, 2H, *J* = 8.9 Hz), 4.53 (t, 1H, *J* = 5.5 Hz), 4.17 (q, 1H, *J* = 6.8 Hz), 3.72 (s, 3H), 3.51 (d, 2H, *J* = 5.5 Hz), 1.19 (t, 3H, *J* = 6.8 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 197.3, 173.1, 153.0, 140.5, 136.5, 133.4, 128.6, 128.1, 115.7, 114.8, 61.4, 55.6, 54.5, 41.0, 14.0 ppm.



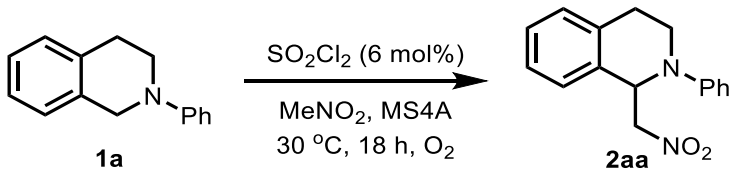
Ethyl 2-cyano-2-((4-methoxyphenyl)imino)acetate (11). Yellow oil; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.71 (d, 2H, *J* = 8.9 Hz), 7.01 (d, 2H, *J* = 8.9 Hz), 4.50 (q, 2H, *J* = 7.6 Hz), 3.89 (s, 3H), 1.45 (t, 3H, *J* = 6.9 Hz) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 162.7, 160.0, 138.6, 126.4, 124.9, 114.7, 111.7, 63.6, 55.7, 14.1 ppm; HRMS (DART) calcd. for $C_{12}H_{13}N_2O_3$ ($[M+H]^+$): 233.0926, found: 233.0924; IR (neat) 1754, 1722, 1612, 1552, 1502, 1466, 1371, 1305, 1256, 1211, 1165, 1095, 1023, 843 cm^{-1}



Ethyl 2,2-bis(1-methyl-1H-indol-3-yl)acetate (12).[18d] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.65 (d, 2H, *J* = 8.2 Hz), 7.29 (d, 2H, *J* = 8.3 Hz), 7.22 (t, 2H, *J* = 6.9 Hz), 7.10 (t, 2H, *J* = 6.8 Hz), 7.03 (s, 2H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 173.6, 137.1, 127.9, 127.1, 121.6, 119.3, 119.0, 112.3, 109.2, 61.0, 40.4, 32.7, 14.2 ppm.

Chapter 3. Sulfuryl Chloride-mediated CDC reaction of Tertiary *N*-Aryl Amines

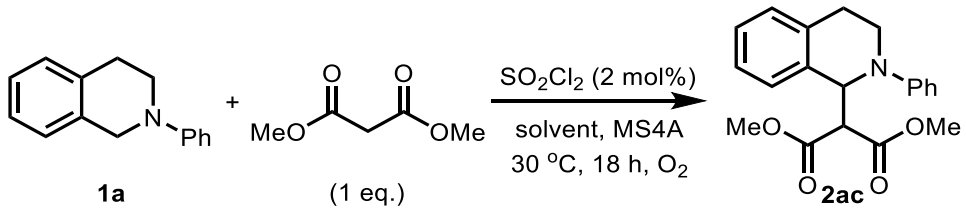
General procedure of oxidative nitroalkylation



A solution of sulfuryl chloride in nitromethane was prepared beforehand by adding 10 μL of sulfuryl chloride in 5 mL of nitromethane (0.025 M).

To a dried flask equipped with an oxygen balloon was added MS4A (100 mg), *N*-phenyl tetrahydroisoquinoline (105 mg, 0.50 mmol). Then, a 0.025 M solution of sulfuryl chloride in nitromethane 1.2 mL (0.030 mmol) was added and stirred for 18 hours at 30 °C. After concentration under reduced pressure, the yield was determined by ^{1}H NMR analysis using 1,4-bis(trimethylsilyl)benzene (13.9 mg, 0.25 eq.) as an internal standard. Then, the mixture was filtered and purified by flash chromatography to provide the nitro-Mannich product (107 mg, 80% yield).

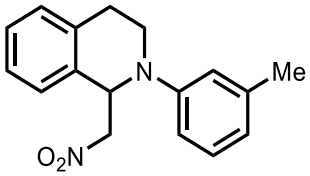
General procedure of the CDC reaction in MeCN



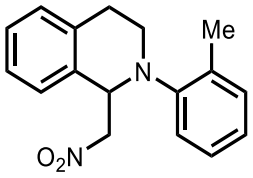
A solution of sulfuryl chloride in acetonitrile was prepared beforehand by adding 10 μL of sulfuryl chloride in 5 mL of acetonitrile (0.025 M).

To a dried flask, equipped with a balloon of oxygen, was added MS4A (50 mg), *N*-phenyl tetrahydroisoquinoline (52.3 mg, 0.25 mmol), acetonitrile (0.3 mL), and dimethyl malonate (33.6 μL, 0.25 mmol). Then, a 0.025 M solution of sulfuryl chloride in acetonitrile 0.2 mL (0.005 mmol) was added and stirred for 18 hours at 30 °C. After

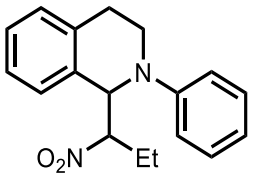
concentration under reduced pressure, the yield was determined by ^{1}H NMR analysis using 1,4-bis(trimethylsilyl)benzene (13.9 mg, 0.5 eq.) as an internal standard. Then, the mixture was filtered and purified by PTLC (hexane/AcOEt = 4/1). Contaminated dimethyl malonate was removed by drying under high vacuum at 100 ^{o}C over 1 hour and provided the product (65.2 mg, 77% yield).



1-(Nitromethyl)-2-(*m*-tolyl)-1,2,3,4-tetrahydroisoquinoline (2la).[16f] ^{1}H NMR ($CDCl_3$, 600 MHz) δ 7.16-7.02 (m, 5H), 6.70-6.68 (m, 2H), 6.58 (d, 1H, *J* = 6.8 Hz), 5.44 (t, 1H, *J* = 7.6 Hz), 4.77-4.30 (m, 2H), 3.57-3.47 (m, 2H), 3.00-2.66 (m, 2H), 2.23 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 148.5, 139.2, 135.3, 133.0, 129.3, 129.1, 128.0, 126.9, 126.6, 120.3, 115.9, 112.2, 78.7, 58.1, 42.1, 26.5, 21.8 ppm.

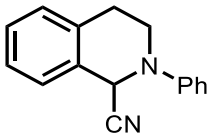


1-(Nitromethyl)-2-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinoline (2ma).[16f] ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.16 (m, 5H), 7.00-6.98 (m, 2H), 6.72 (t, 1H, *J* = 4.6 Hz), 5.13 (dd, 1H, *J* = 4.6, 10.5 Hz), 4.81 (t, 1H, *J* = 11.9 Hz), 4.59 (dd, 1H, *J* = 4.1, 11.9 Hz), 3.49 (dt, 1H, *J* = 3.7, 13.8 Hz), 3.21 (dt, 1H, *J* = 4.6, 13.7 Hz),2.83 (dt, 1H, *J* = 5.5, 17.0 Hz), 2.53 (d, 1H, *J* = 15.1 Hz), 2.26 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 125 MHz) δ 149.0, 136.3, 134.1, 133.1, 131.2, 129.8, 127.6, 126.6, 126.5, 126.3, 124.4, 122.8, 79.4, 59.6, 43.2, 24.4, 17.7 ppm.

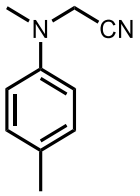


1-(1-Nitropropyl)-2-(*o*-tolyl)-1,2,3,4-tetrahydroisoquinoline (2ak).[15b] ^{1}H NMR

($CDCl_3$, 600 MHz, 1.5 : 1 mixture of diastereoisomers) δ 7.27-7.12 (m, 6H), 6.97 (t, 1H, *J* = 8.9 Hz), 6.93 (d, 1H, *J* = 8.3 Hz), 6.82-6.76 (m, 1H), [5.23, (d, *J* = 8.9 Hz); 5.12 (d, *J* = 9.7 Hz), 1H], [4.85 (t, *J* = 11.7 Hz), 4.67 (t, *J* = 12.4 Hz), 1H], 3.86-3.50 (m, 2H), 3.08-3.02 (m, 1H), 2.91-2.83 (m, 1H), 2.19-1.79 (m, 2H), 0.94-0.91 (m, 3H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz, 1.5 : 1 mixture of diastereoisomers) δ 149.1, 149.0, 135.5, 134.7, 133.9, 132.6, 129.4, 129.3, 129.2, 128.6, 128.6, 128.2, 128.1, 127.2, 126.6, 125.9, 119.4, 118.6, 115.8, 114.2, 96.1, 93.0, 62.2, 60.7, 43.5, 42.3, 26.8, 25.7, 25.0, 24.6, 10.6 ppm.



2-Phenyl-1,2,3,4-tetrahydroisoquinoline-1-carbonitrile (2ao).[4f] ^1H NMR ($CDCl_3$, 600 MHz) δ 7.36-7.21 (m, 6H), 7.07 (d, 2H, *J* = 8.9 Hz), 7.00 (t, 1H, *J* = 6.2 Hz), 5.49 (s, 1H), 3.77-3.44 (m, 2H), 3.16-2.93 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 150 MHz) δ 148.3, 134.5, 129.5, 129.3, 128.7, 127.0, 126.8, 121.8, 117.7, 117.5, 53.1, 44.1, 28.4 ppm.



2-(Methyl(*p*-tolyl)amino)acetonitrile (2ko).[4f] ^1H NMR ($CDCl_3$, 600 MHz) δ 7.12 (d, 2H, *J* = 8.2 Hz), 6.80 (d, 2H, *J* = 8.3 Hz), 4.14 (s, 2H), 2.97 (s, 3H), 2.29 (s, 3H) ppm; ^{13}C NMR ($CDCl_3$, 400 MHz) δ 145.6, 130.0, 129.9, 115.4, 115.4, 42.8, 39.5, 20.3 ppm.

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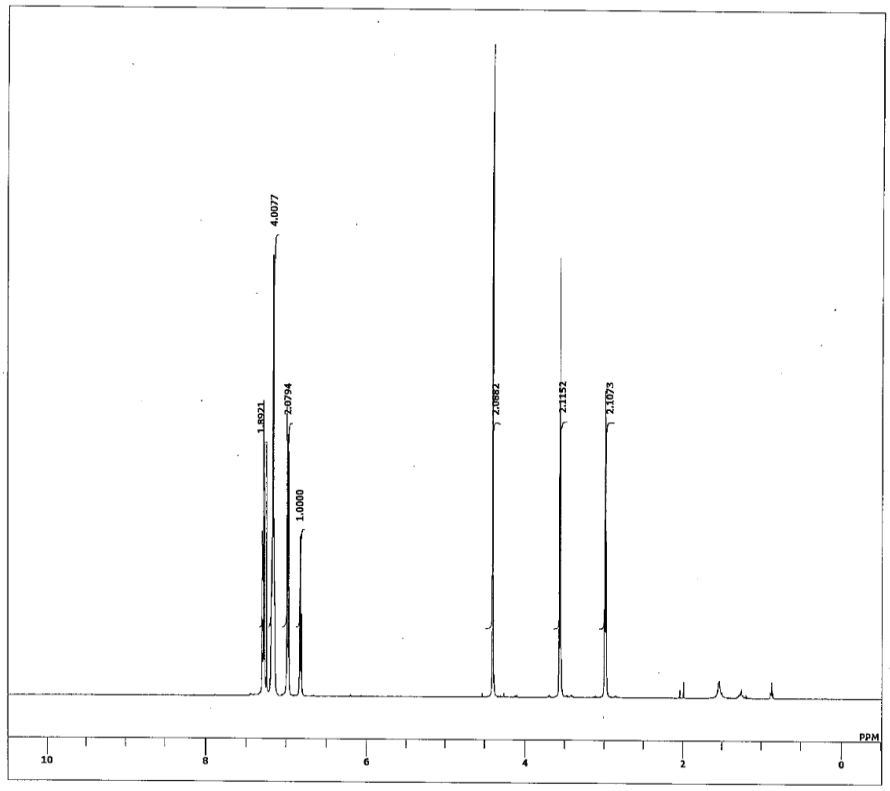

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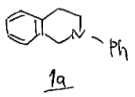

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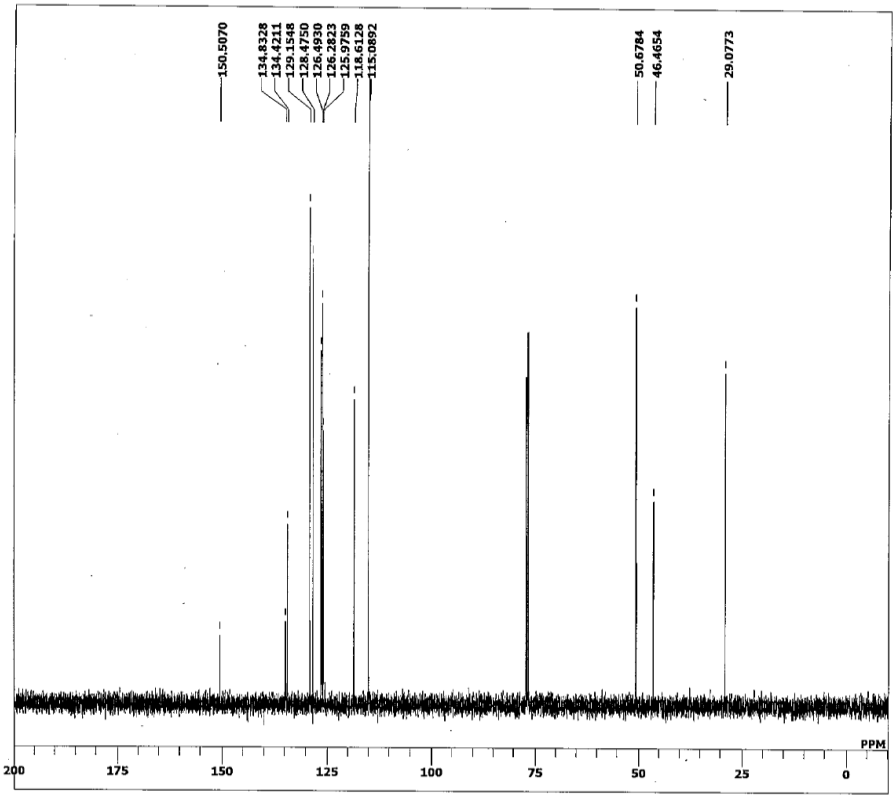

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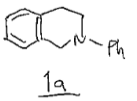
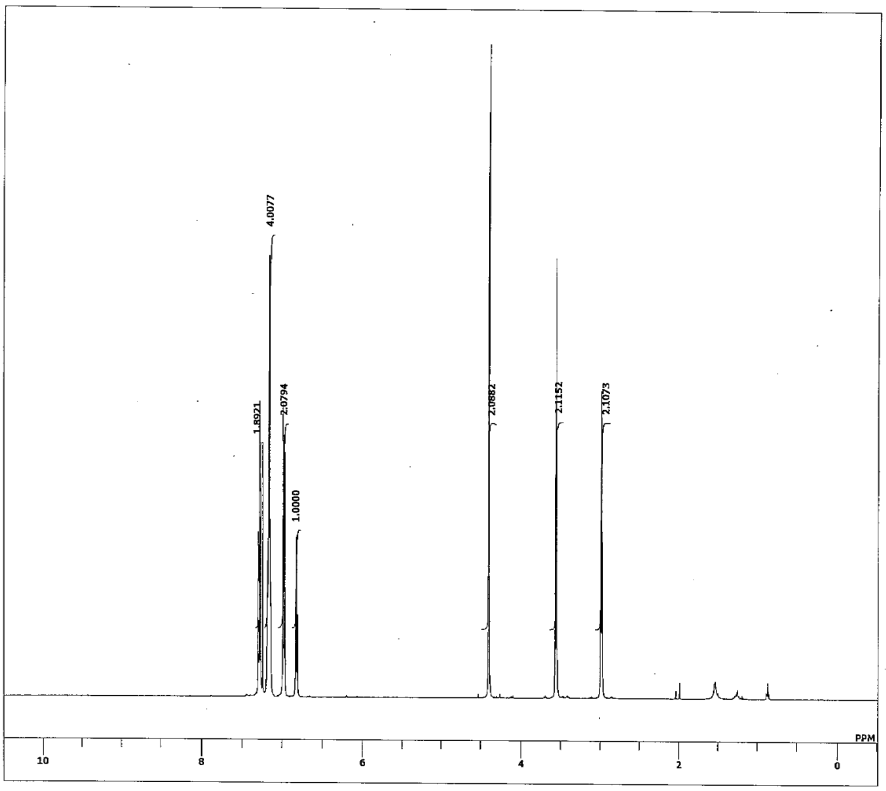
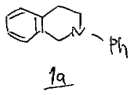


1a

D:¥Documents and Settings¥Kobayashilab¥Desktop¥1005-H-recryst-1.jdf

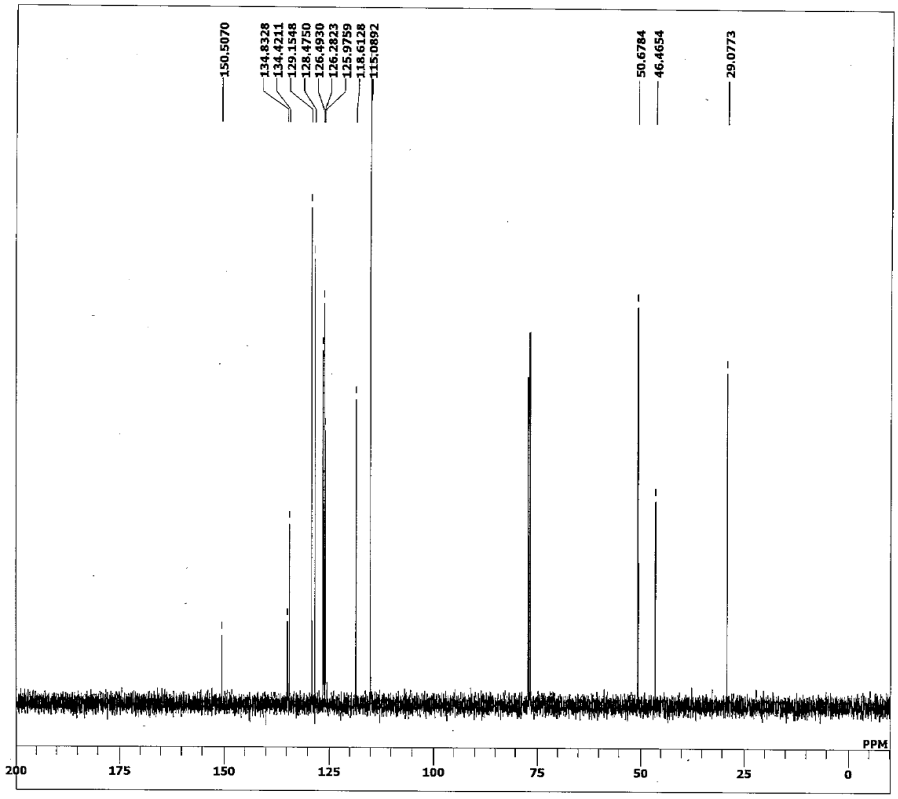


DFILE	D:¥Documents and Settings¥Kobayashilab¥Desktop¥1005-H
COMNT	
DATIM	10-03-2012 20:55:01
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	16384
FREQU	9286.78 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	21.0 c
SLVNT	CDCL3
EXREF	7.24 ppm
BF	0.12 Hz
RGAIN	46

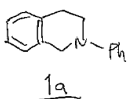


1a

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥811-C-1.als

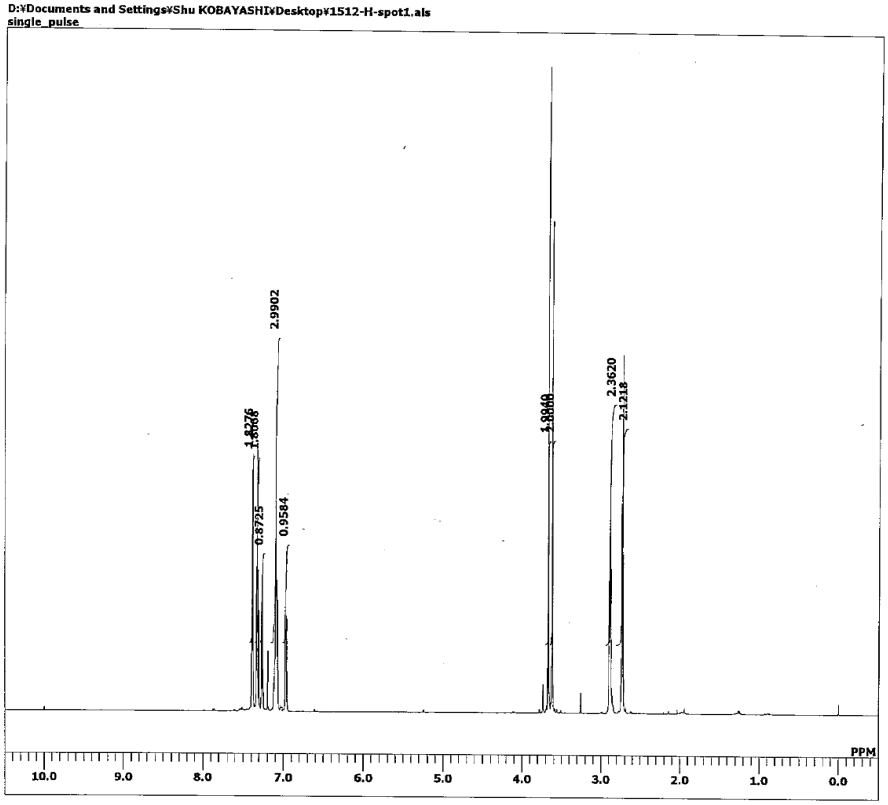


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	24-11-2011 23:30:48
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	74
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	23.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

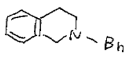


1a

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1512-H-spot1.als
single_pulse

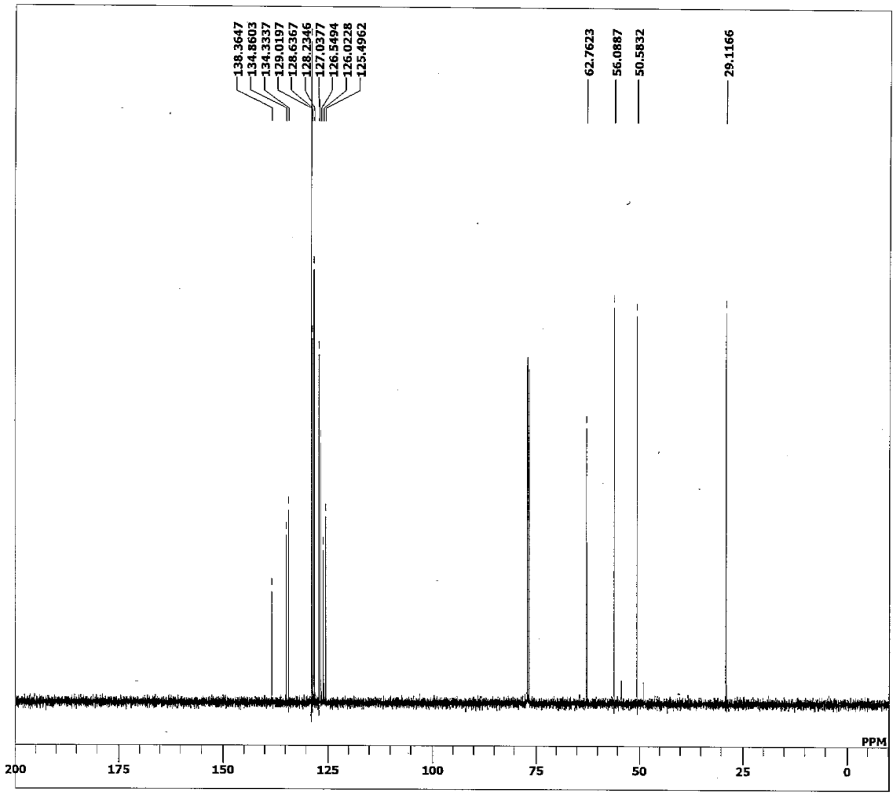


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	24-12-2012 02:50:33
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	18.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	1.20 Hz
RGAIN	30

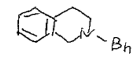


1j

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1512-C-spot1.als

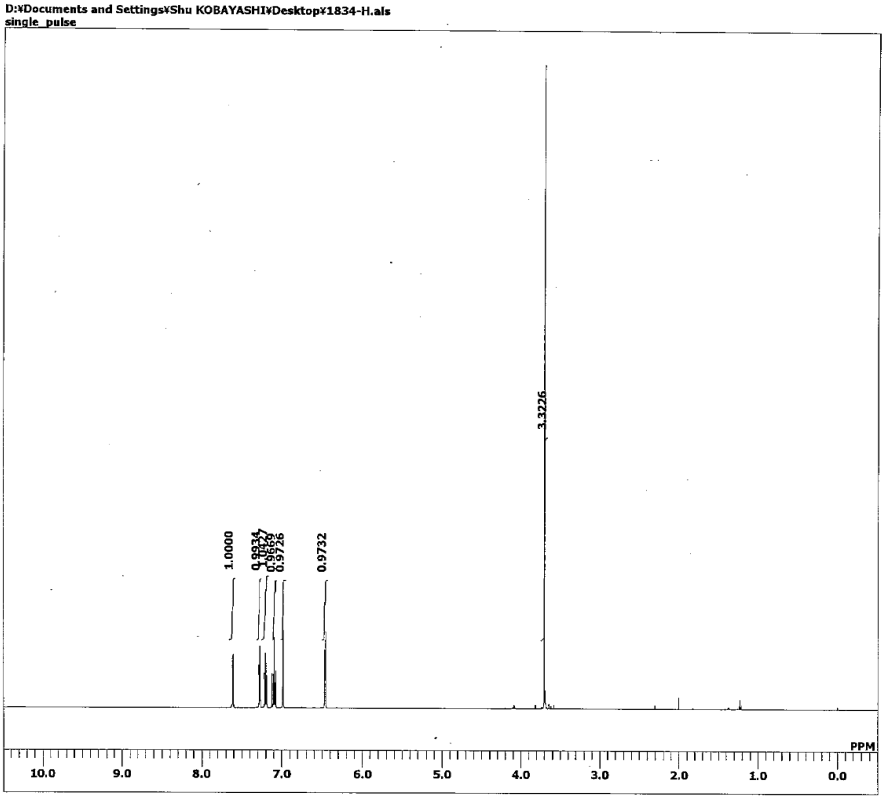


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	24-12-2012 02:57:46
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	100
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	19.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	60



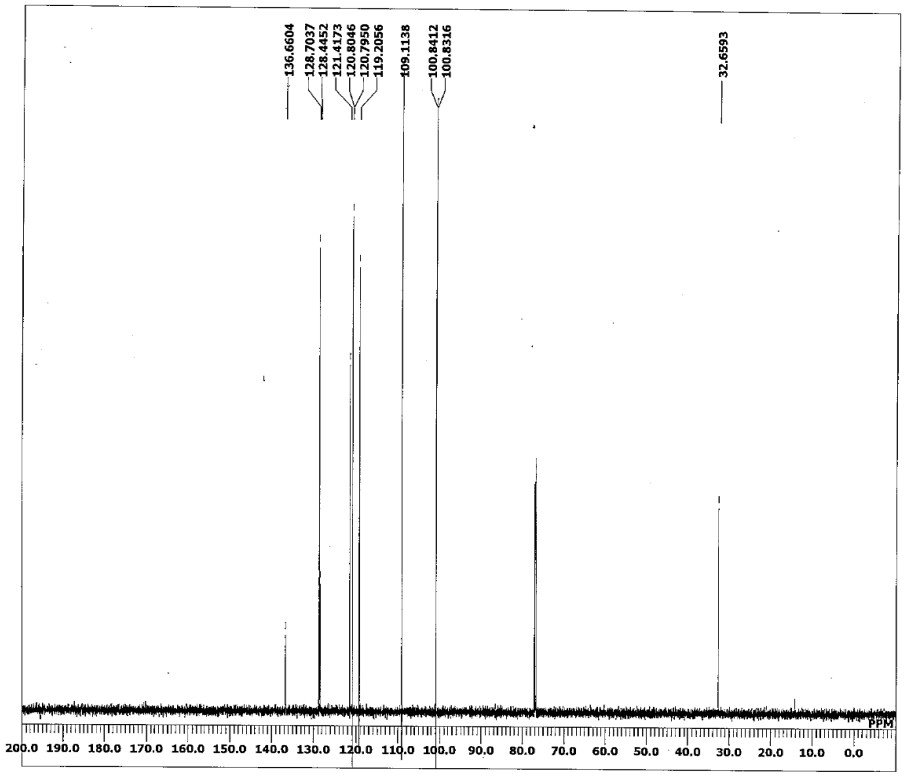
1j

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1834-H.als
single_pulse



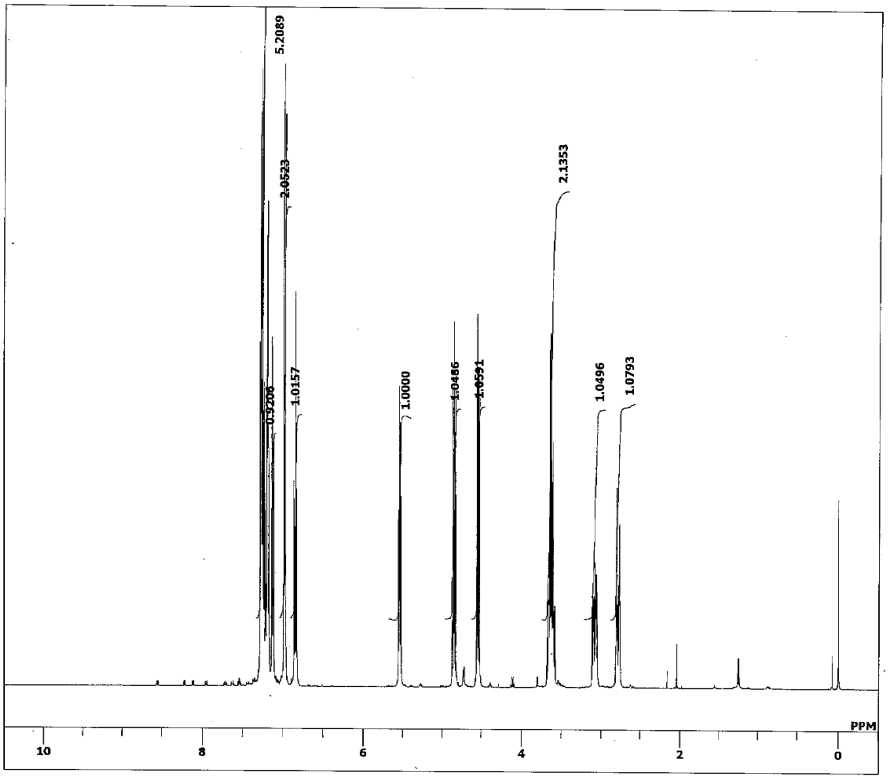
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	20-07-2013 04:27:56
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	28.0 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	1.20 Hz
RGAIN	34

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1834-C.als

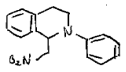


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	20-07-2013 04:35:02
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	96
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	28.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	60

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1093-H-final-1.als

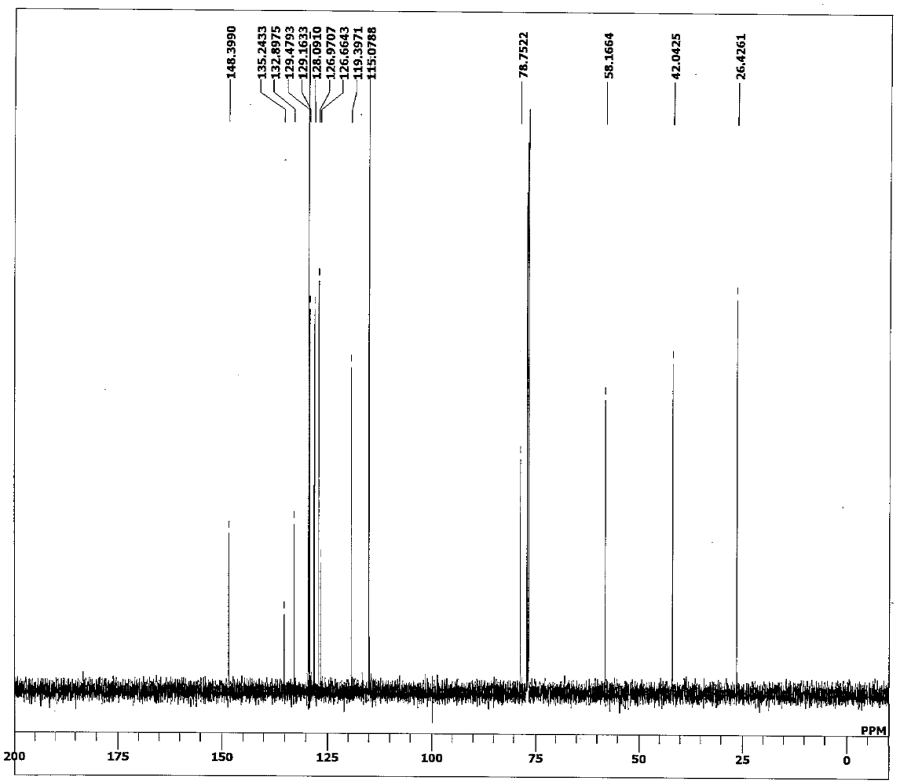


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	17-05-2012 13:09:46
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	23.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

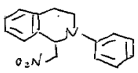


2aa

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥807-C.als

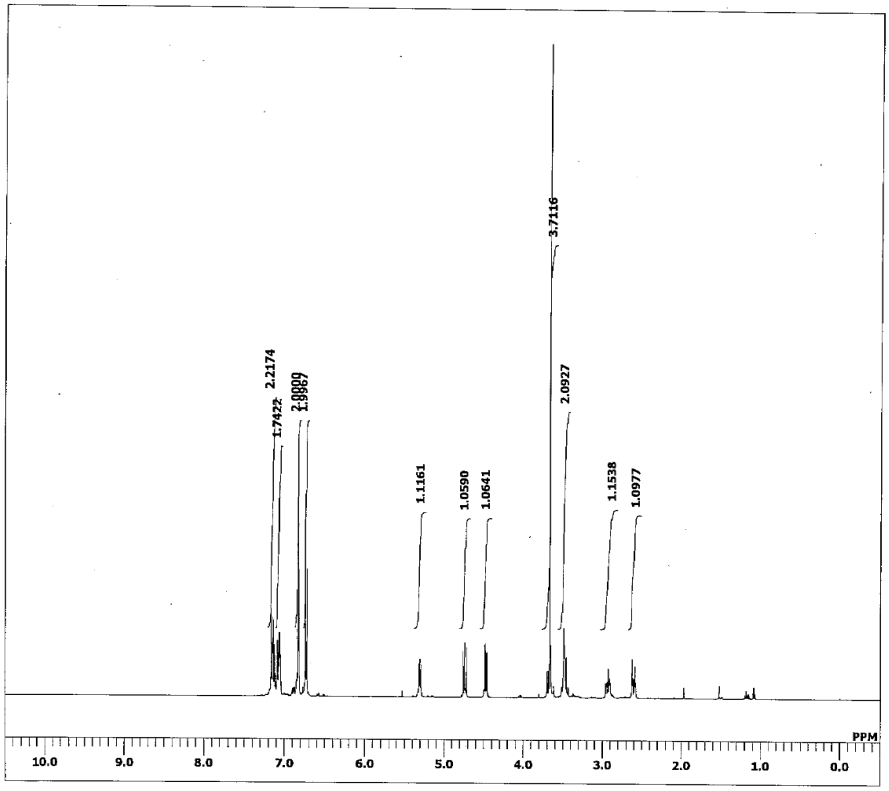


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-11-2011 00:49:47
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	90
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	49.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

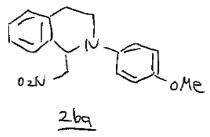


2aa

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥938-H-1.als

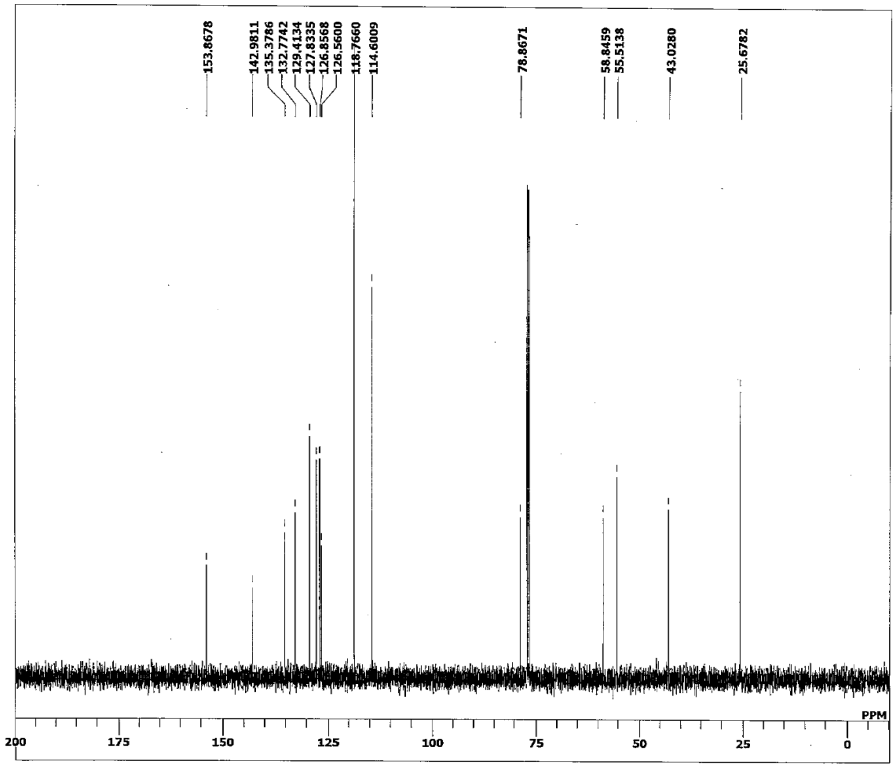


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-01-2012 21:34:05
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	18.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

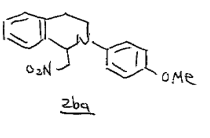


2bq

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥738-C-1.als

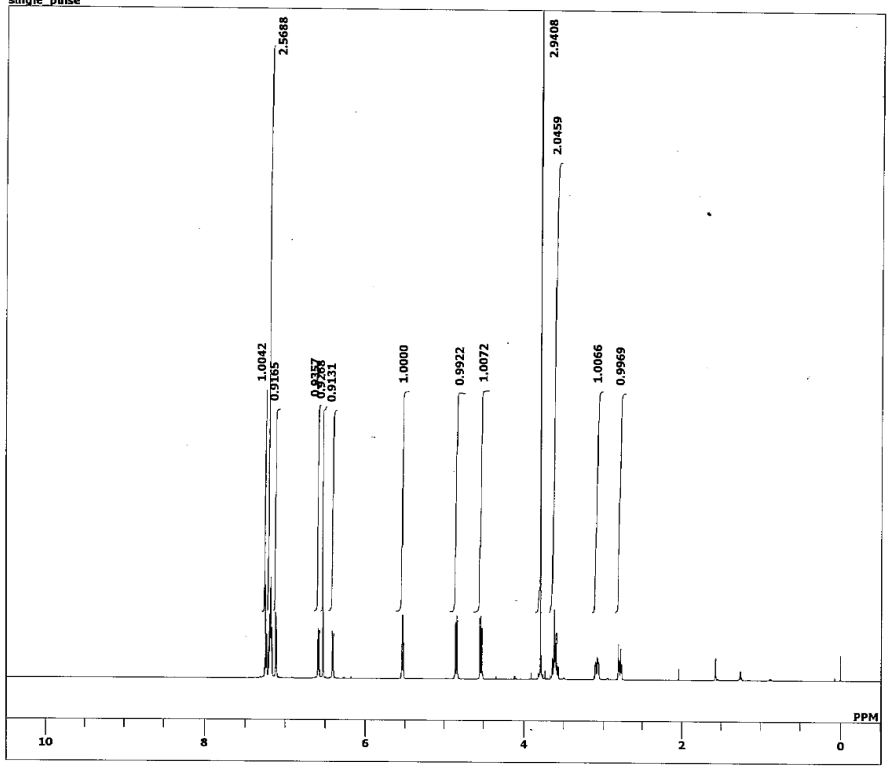


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-01-2012 21:38:55
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	87
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	18.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

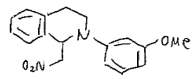


2bq

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1092-H.als
single_pulse

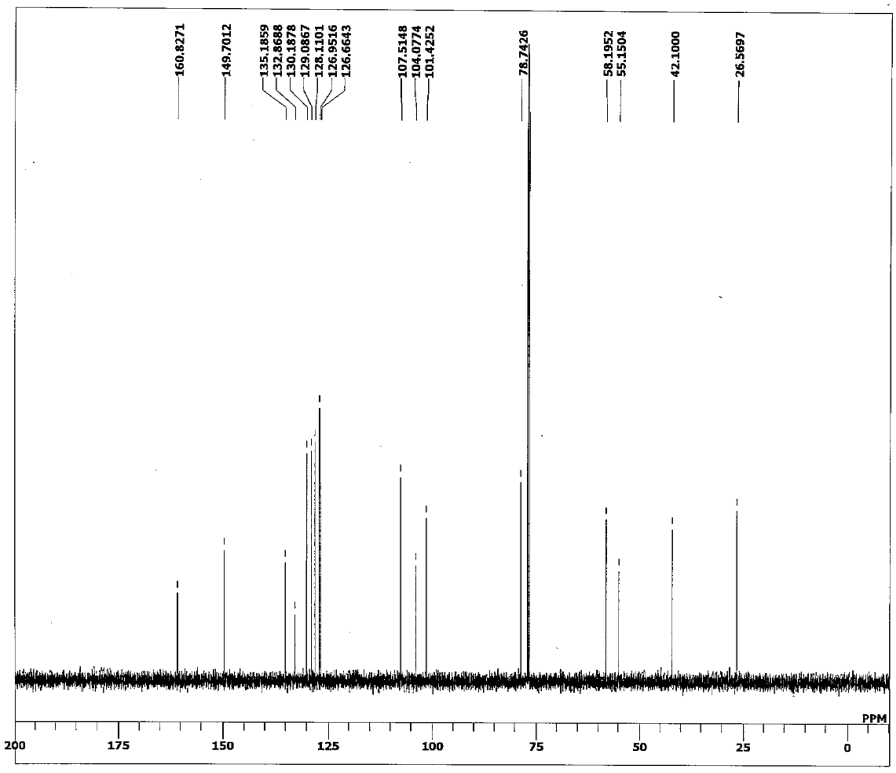


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	17-05-2012 23:48:52
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	23.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

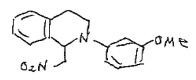


2ca

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1092-C.als

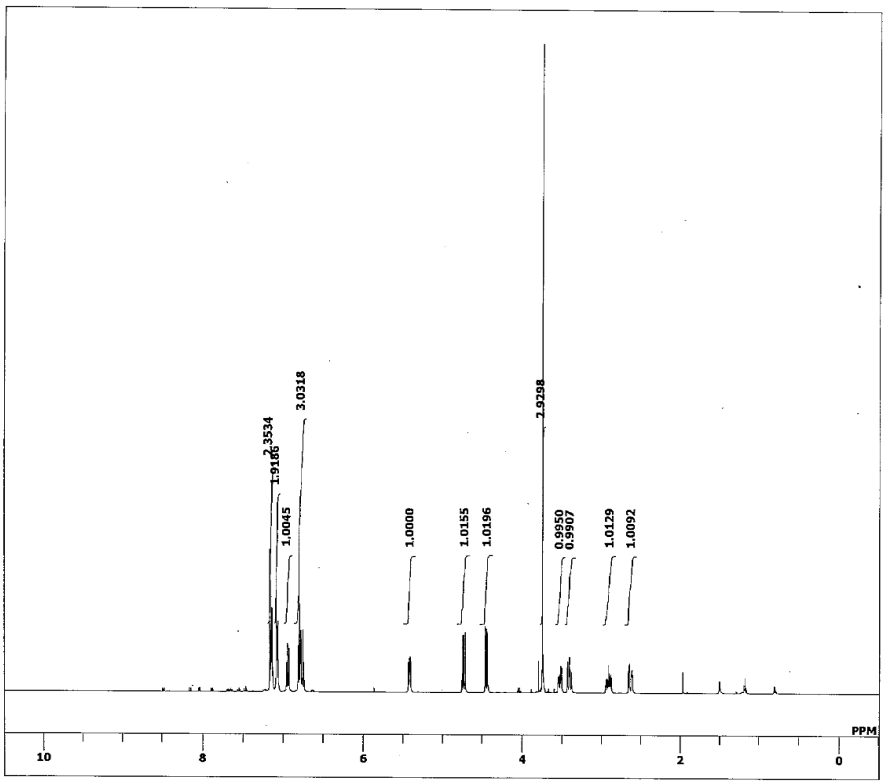


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	17-05-2012 23:56:17
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	109
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	24.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

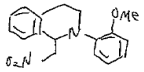


2ca

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1000-H-1.als

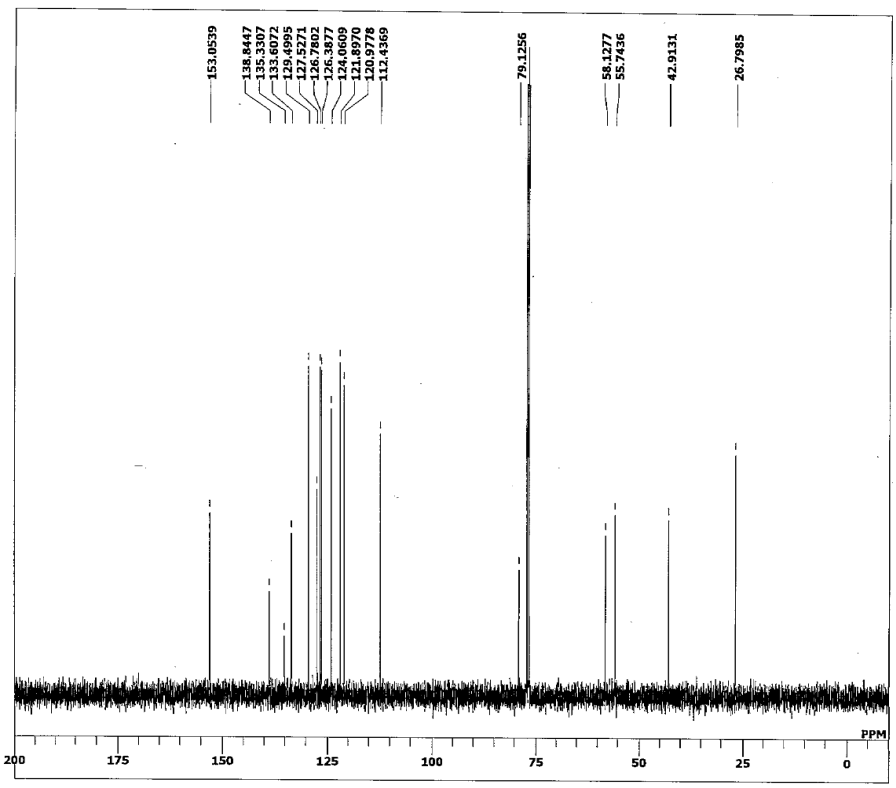


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-03-2012 17:36:28
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

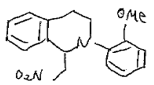


2da

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1000-C-1.als

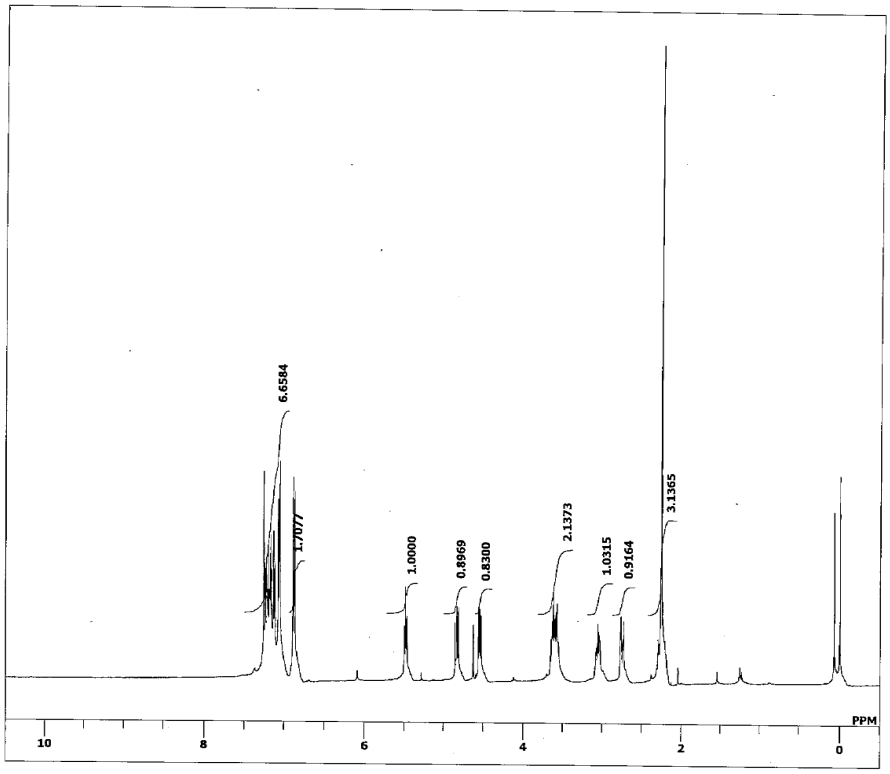


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-03-2012 17:42:10
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	105
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	21.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

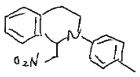


2da

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1209h-2.als

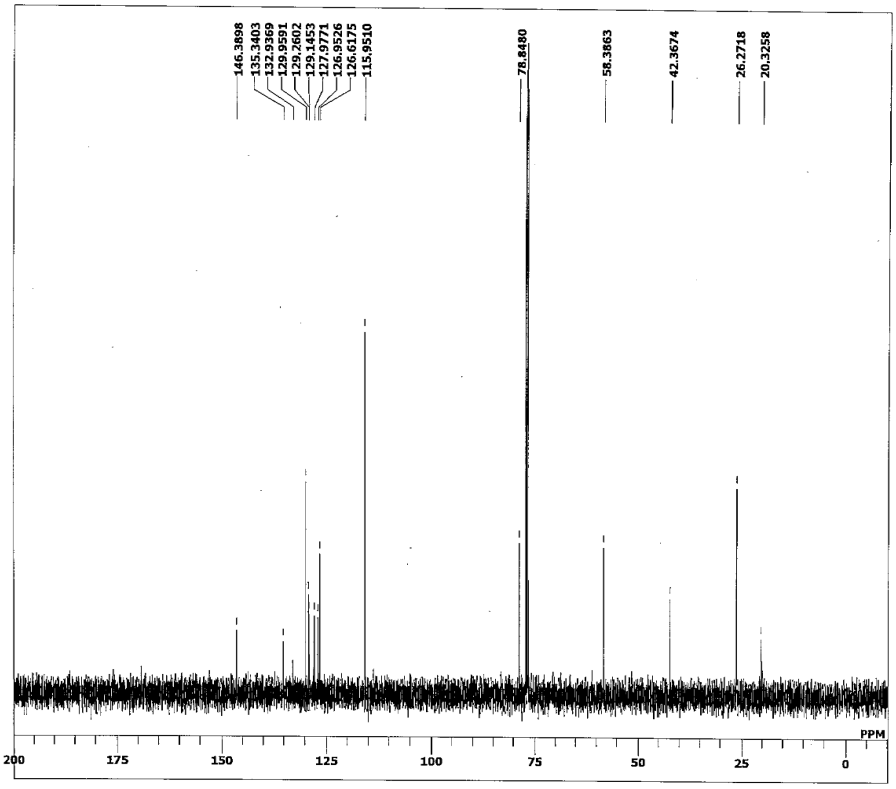


DFILE D:¥Documents and Settings¥Shu KOBAYASHI
COMNT
DATIM 23-07-2012 20:44:28
OBNUC 1H
EXMOD 1H NMR.ex2
OBFRQ 495.13 MHz
OBSET 4.38 KHz
OBFIN 9.64 Hz
POINT 13107
FREQU 7429.31 Hz
SCANS 8
ACQTM 1.7642 sec
PD 5.0000 sec
PW1 3.65 usec
IRNUC 1H
CTEMP 29.3 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 40

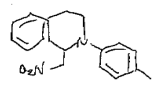


2eq

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1209C-1.als

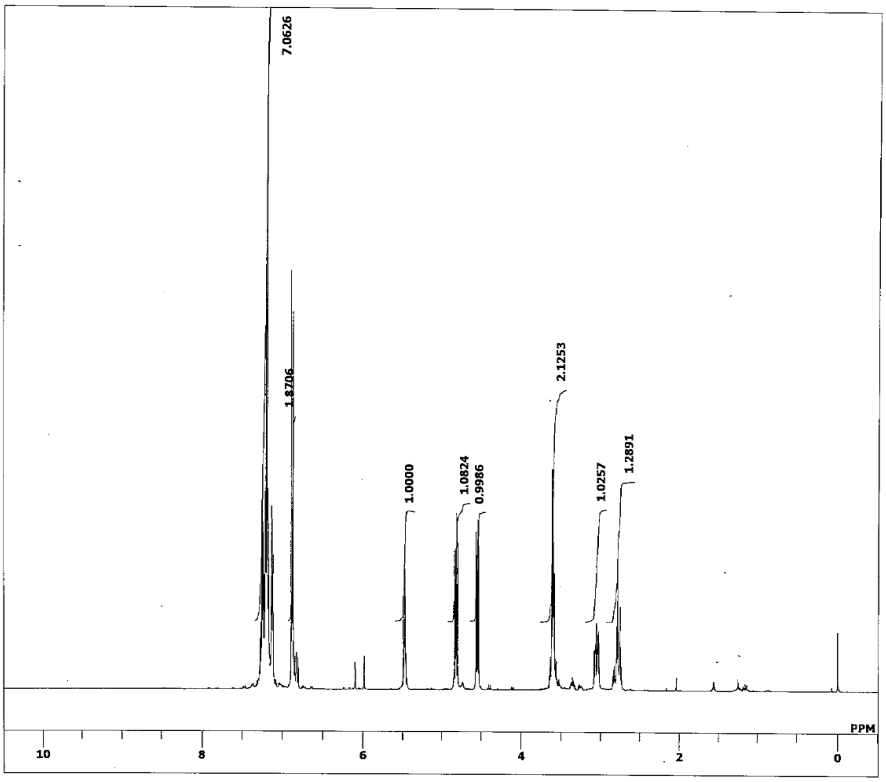


DFILE D:¥Documents and Settings¥Shu KOBAYASHI
COMNT
DATIM 23-07-2012 19:34:17
OBNUC 13C
EXMOD 13C NMR.ex2
OBFRQ 124.51 MHz
OBSET 3.45 KHz
OBFIN 6.00 Hz
POINT 26214
FREQU 31249.52 Hz
SCANS 80
ACQTM 0.8389 sec
PD 2.0000 sec
PW1 3.42 usec
IRNUC 1H
CTEMP 28.9 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 54

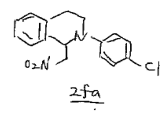


2eq

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1095-H-again-1.als

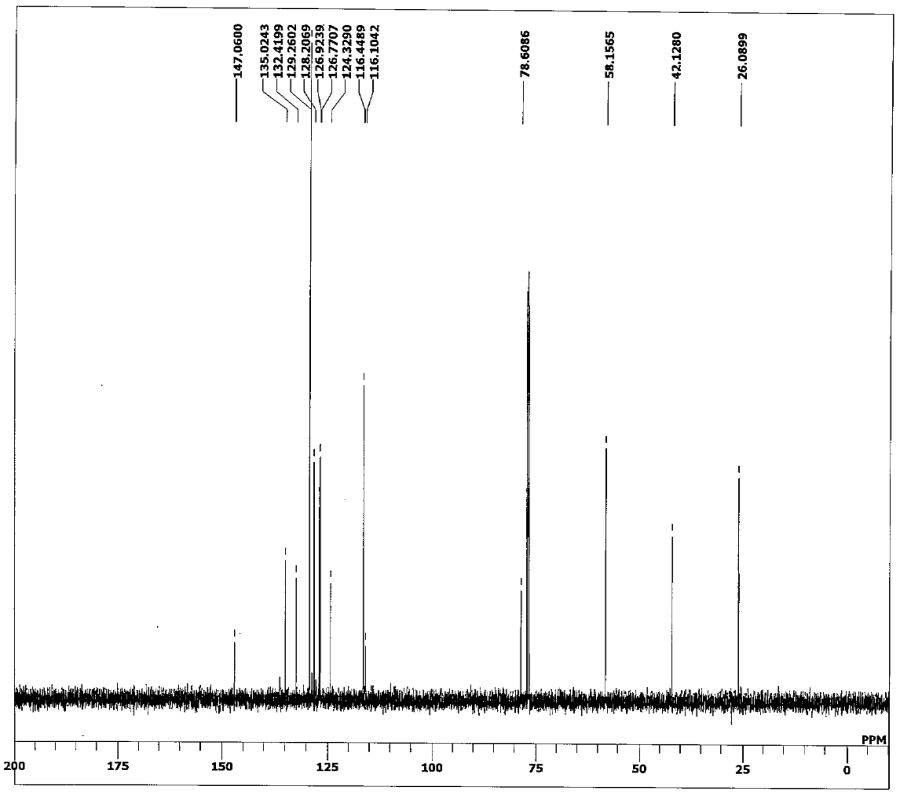


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	17-05-2012 13:13:16
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	23.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

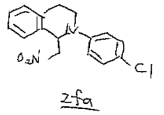


2-fa

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1095-C-again-1.als

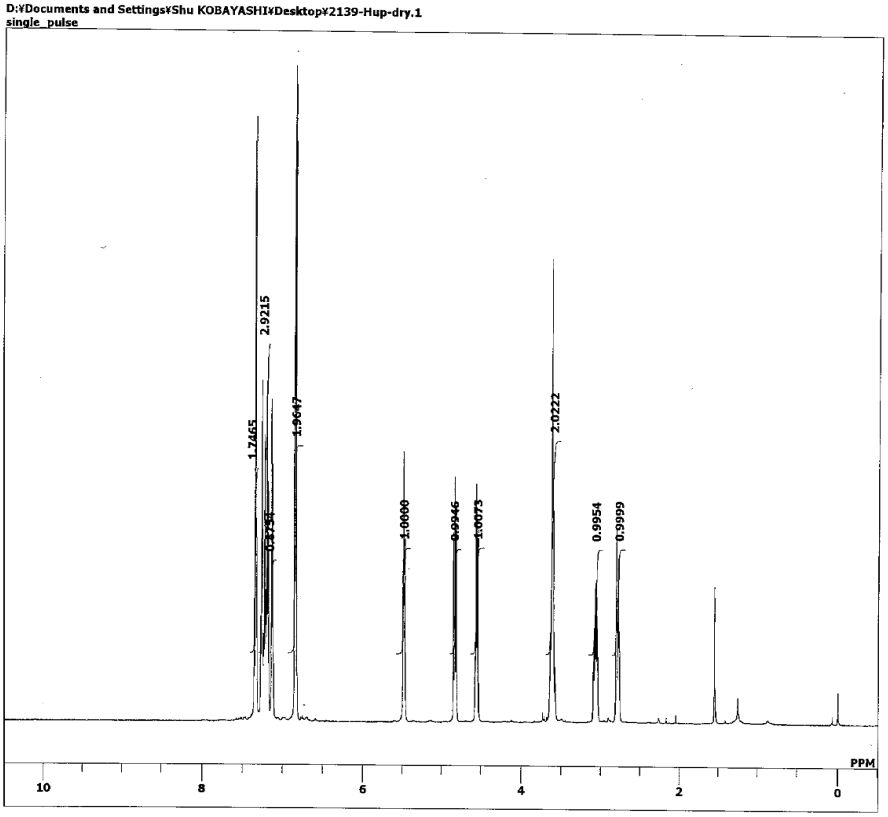


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	17-05-2012 13:19:08
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	108
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	23.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

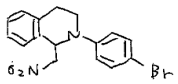


2-fa

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2139-Hup-dry.1
single_pulse

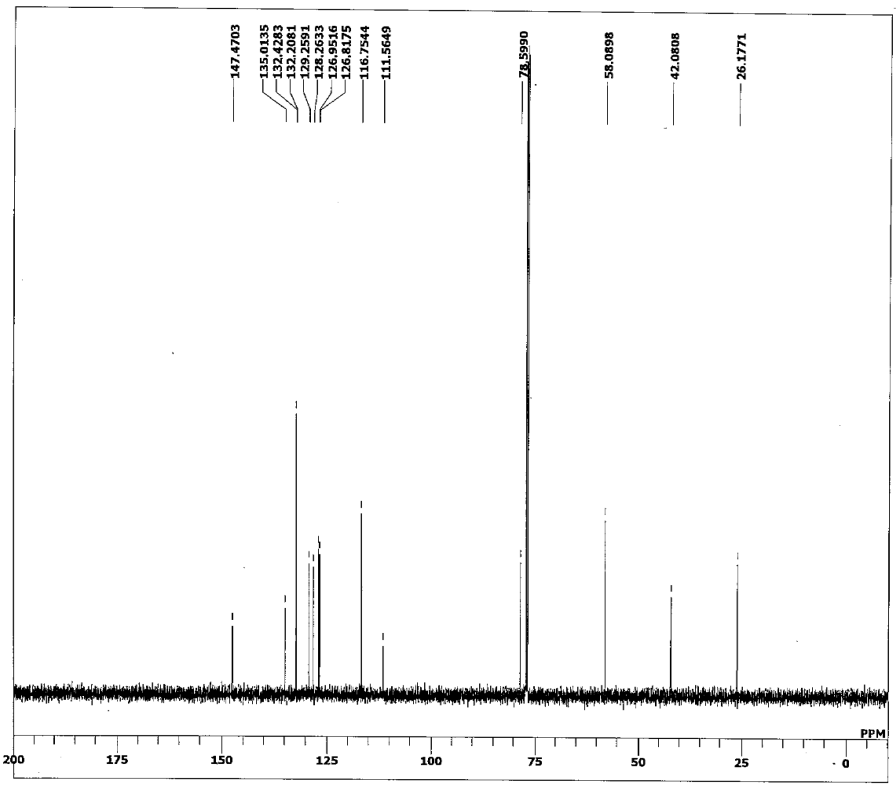


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	13-01-2014 00:05:28
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	16384
FREQU	11261.26 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.52 Hz
RGAIN	40

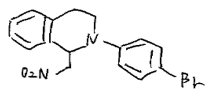


2gq

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2139-C-up-dry.1

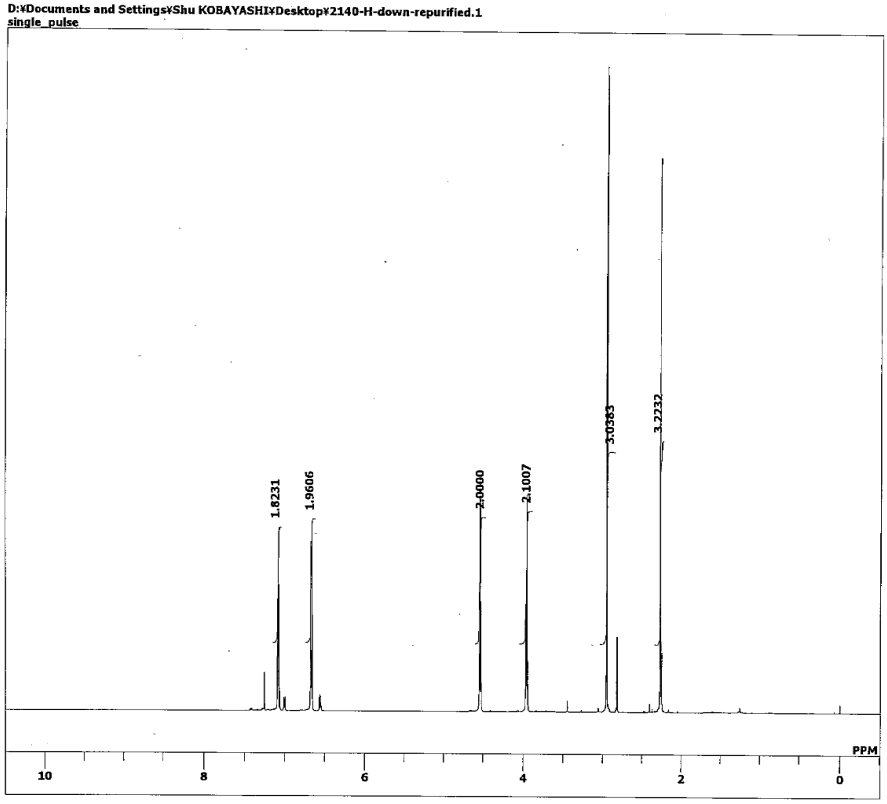


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	13-01-2014 00:14:10
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	32768
FREQU	47348.49 Hz
SCANS	141
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.52 Hz
RGAIN	60

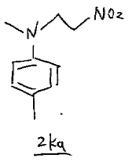


2gq

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2140-H-down-repurified.1
single_pulse

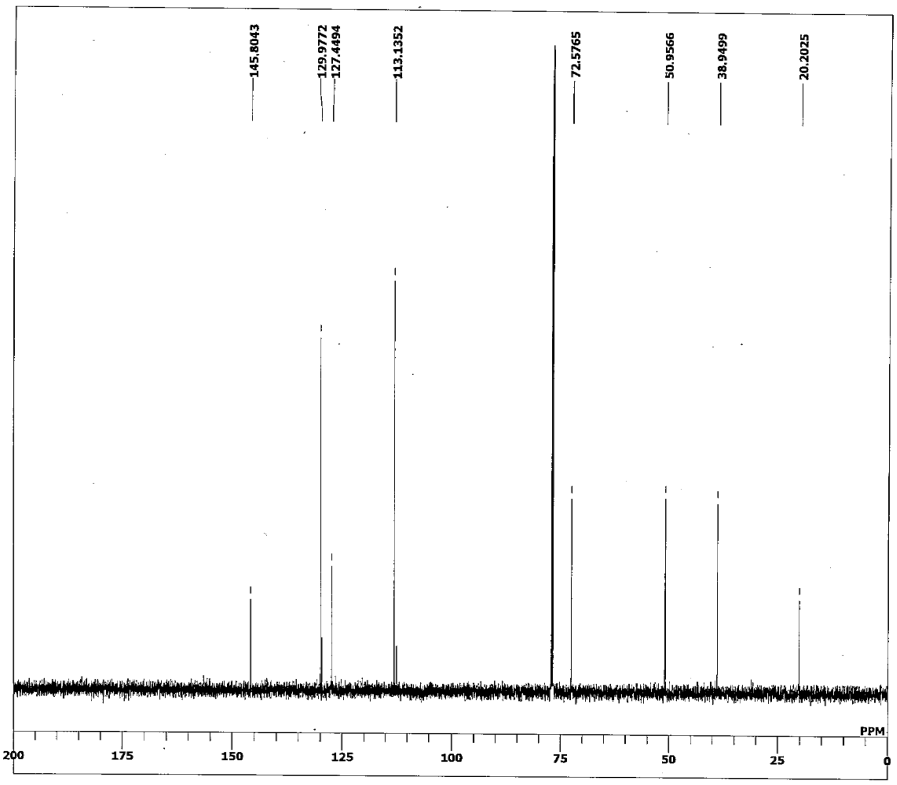


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	13-01-2014 00:18:01
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	16384
FREQU	11261.26 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.52 Hz
RGAIN	40

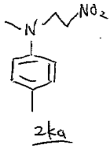


2ka

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2140-C-down-repurified.1

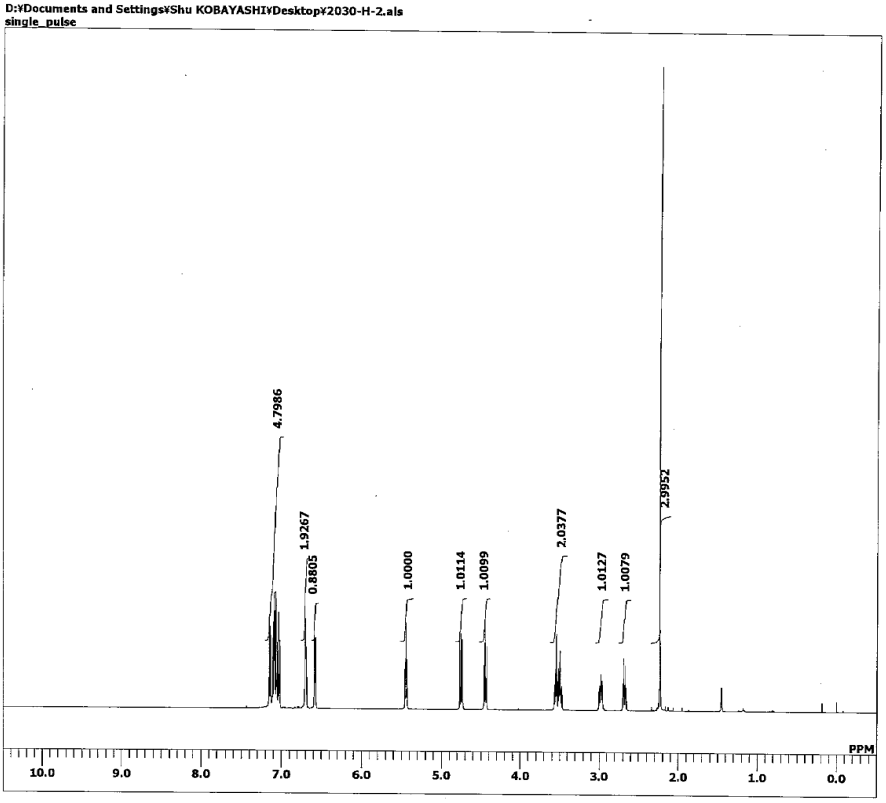


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	13-01-2014 00:26:25
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26213
FREQU	37878.21 Hz
SCANS	129
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.52 Hz
RGAIN	60

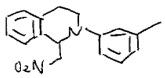


2ka

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2030-H-2.als
single_pulse

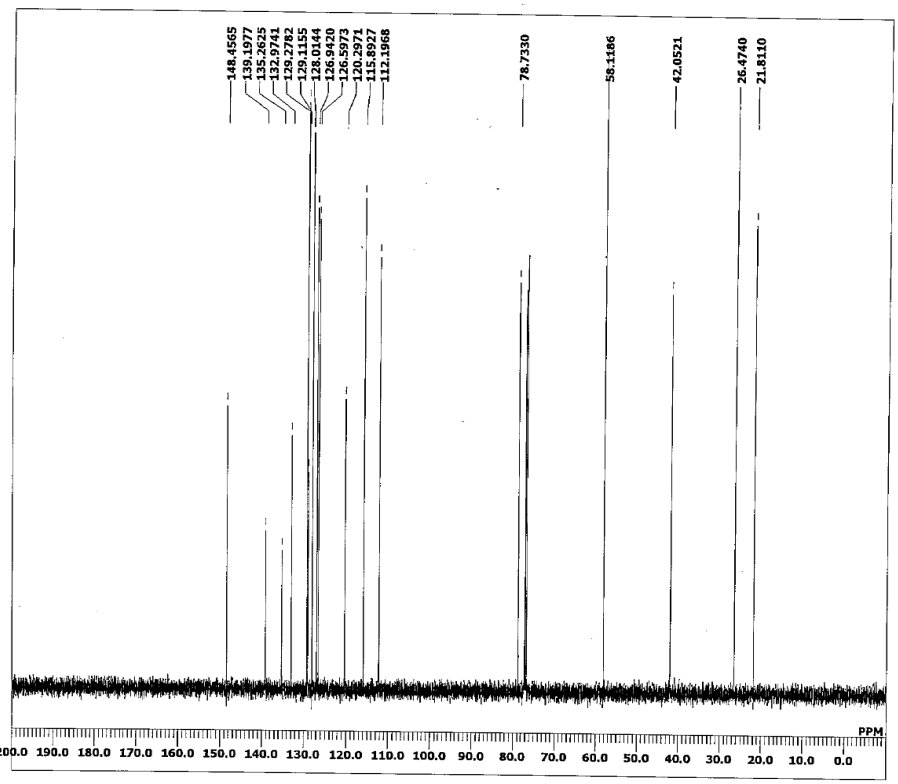


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	15-10-2013 01:59:57
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	26.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

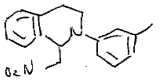


2la

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2033-C.als

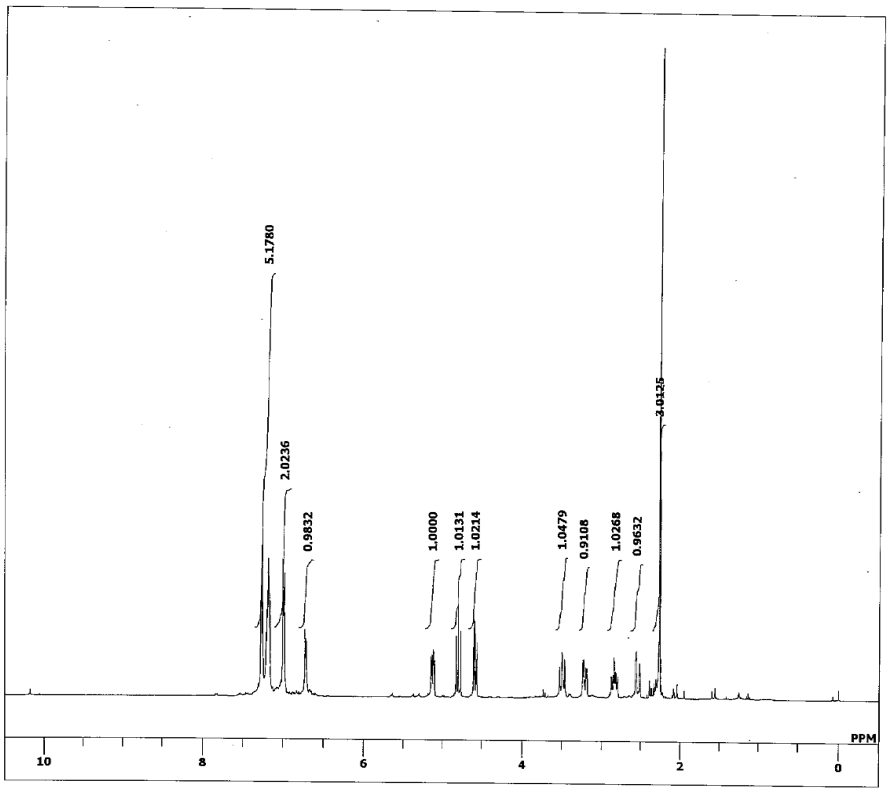


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	15-10-2013 02:06:06
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	84
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	27.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

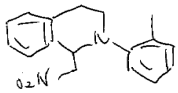


2la

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2135-H-dry.als

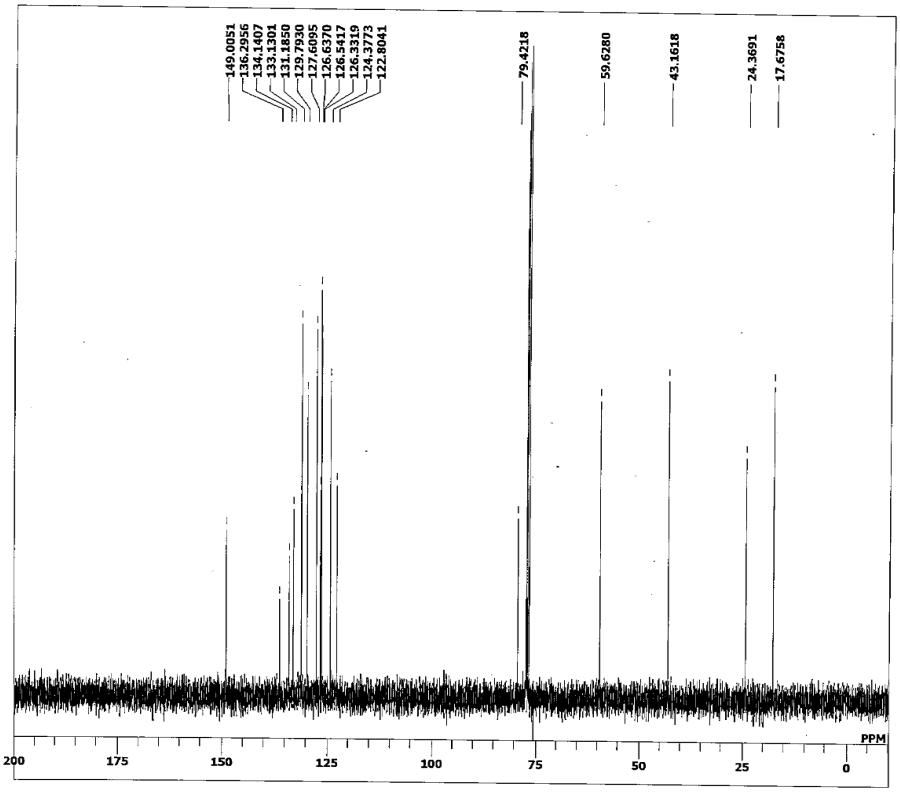


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-01-2014 20:59:00
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	399.78 MHz
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	6002.31 Hz
SCANS	8
ACQTM	2.1837 sec
PD	2.0000 sec
PW1	6.62 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

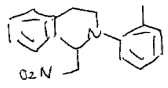


2ma

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2135C.als

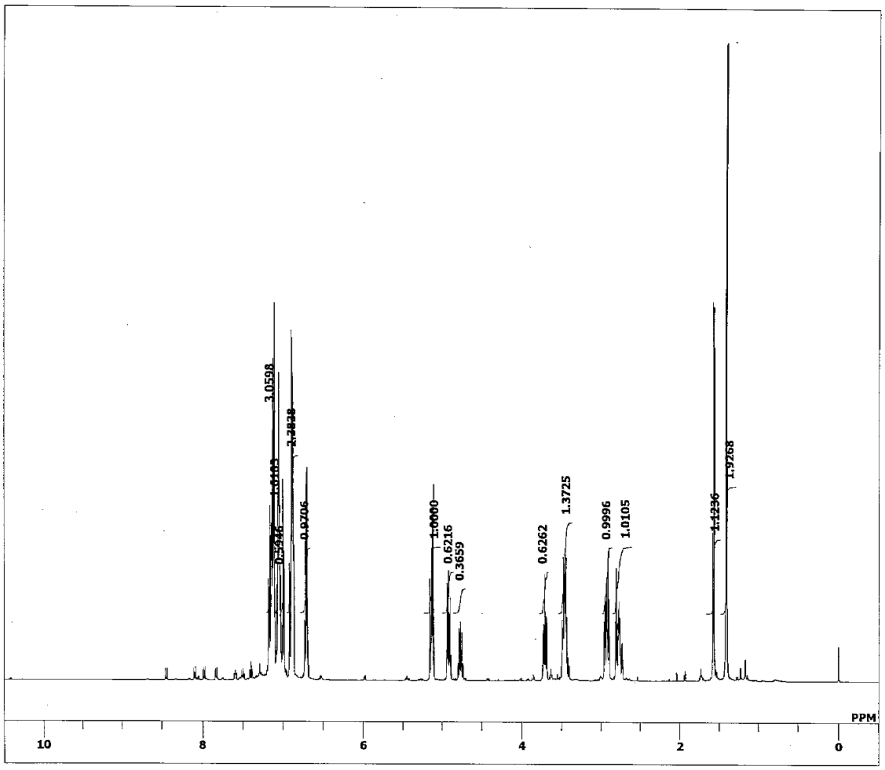


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-01-2014 20:57:28
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	100.53 MHz
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25125.24 Hz
SCANS	102
ACQTM	1.0433 sec
PD	2.0000 sec
PW1	3.50 usec
IRNUC	1H
CTEMP	20.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

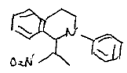


2ma

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥940H-1.als



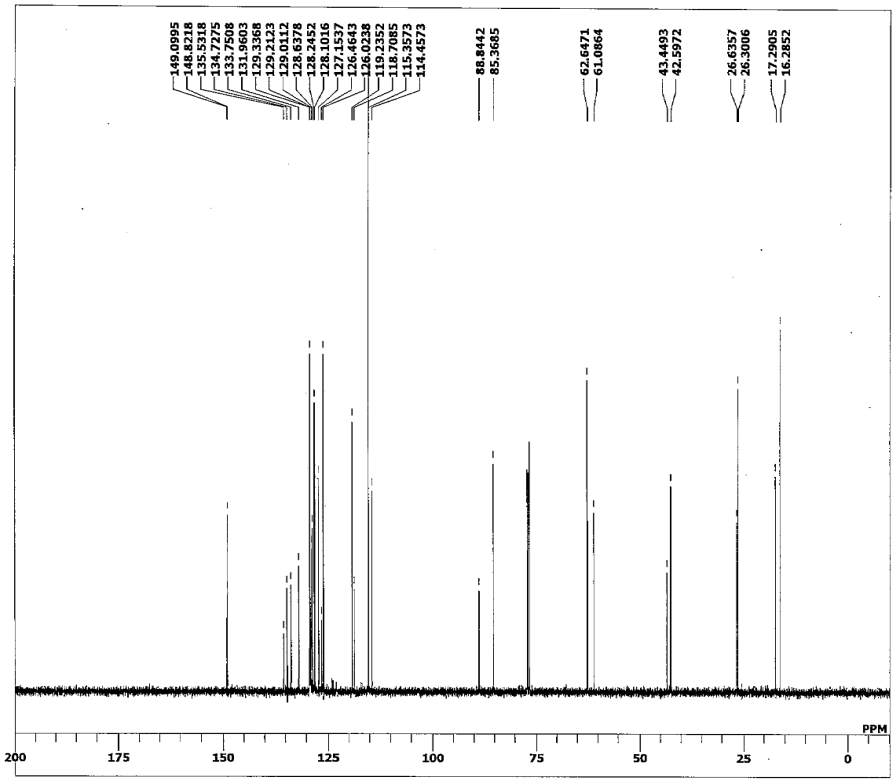
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	20-07-2012 15:07:40
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	3.65 usec
IRNUC	1H
CTEMP	28.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	24



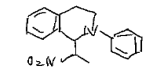
2ab

mixture of diastereomers

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥940C-1.als



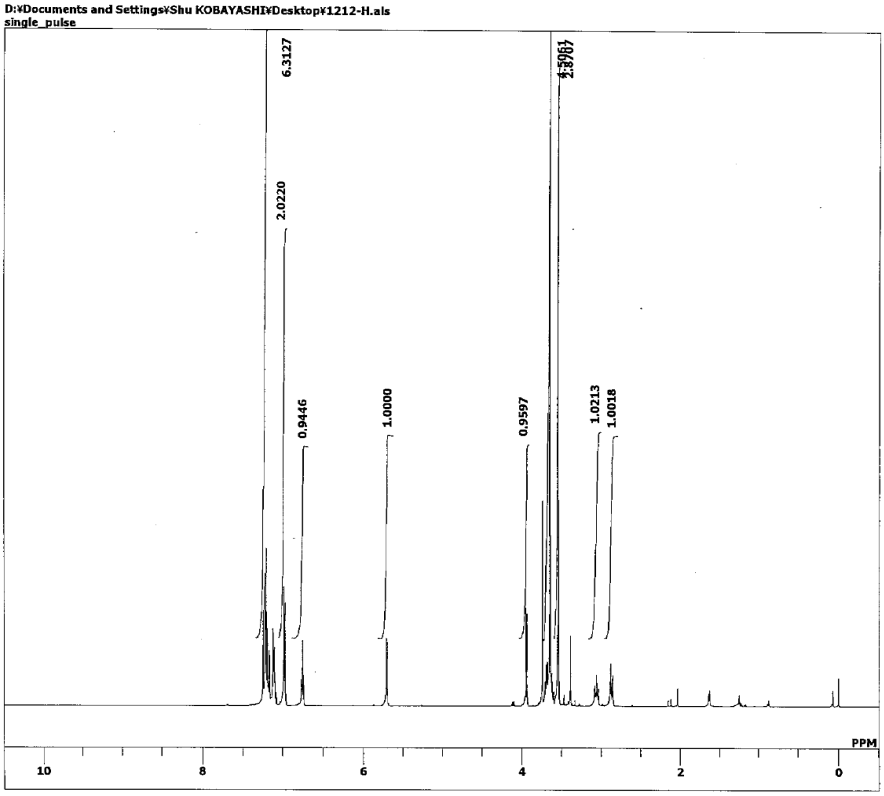
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	20-07-2012 15:15:22
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	144
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	29.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	52



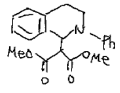
2ab

mixture of diastereomers

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1212-H.als
single_pulse

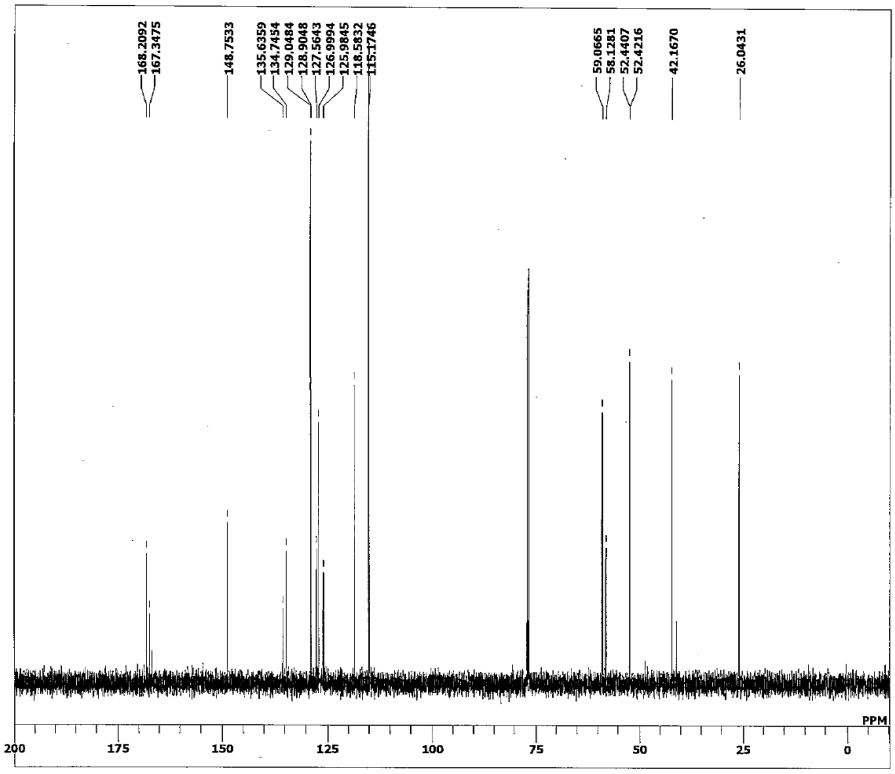


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	24-07-2012 22:11:27
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	30.0 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

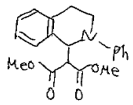


2ac

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1212-C.als

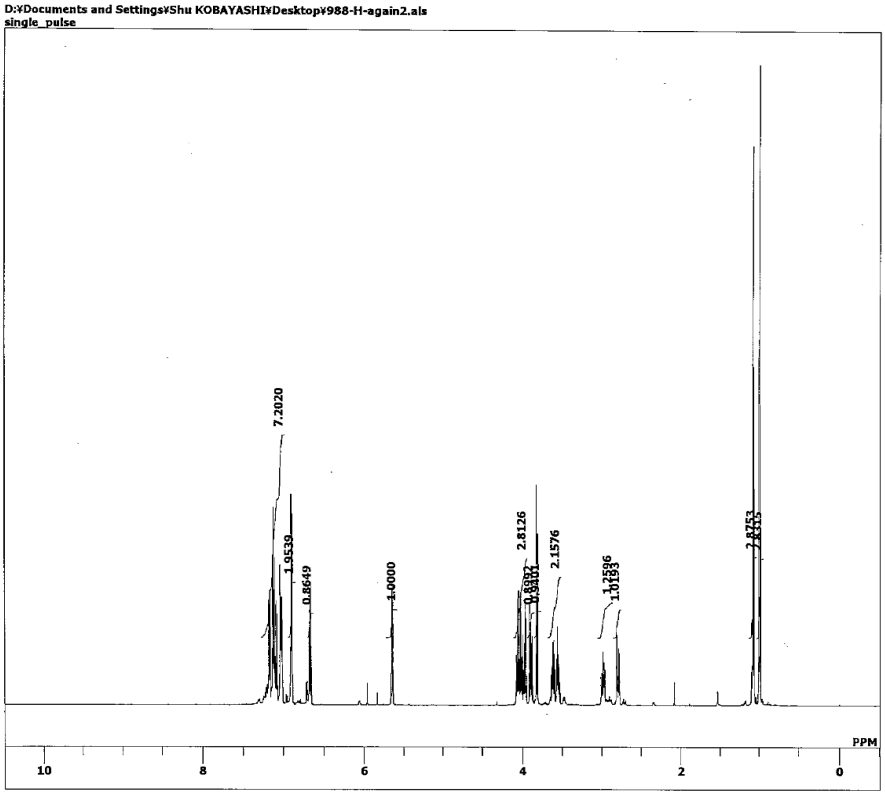


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	24-07-2012 22:15:50
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	41
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	30.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

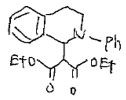


2ac

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥988-H-again2.als
single_pulse

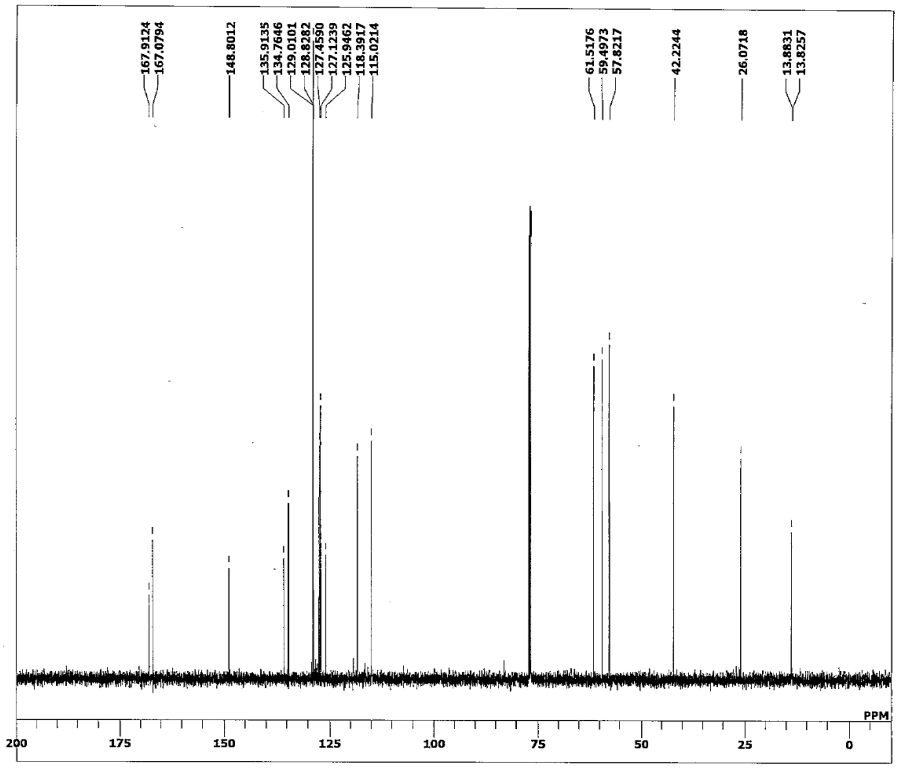


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	24-02-2012 01:24:17
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

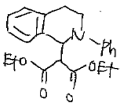


2ad

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥988-C-again2.als

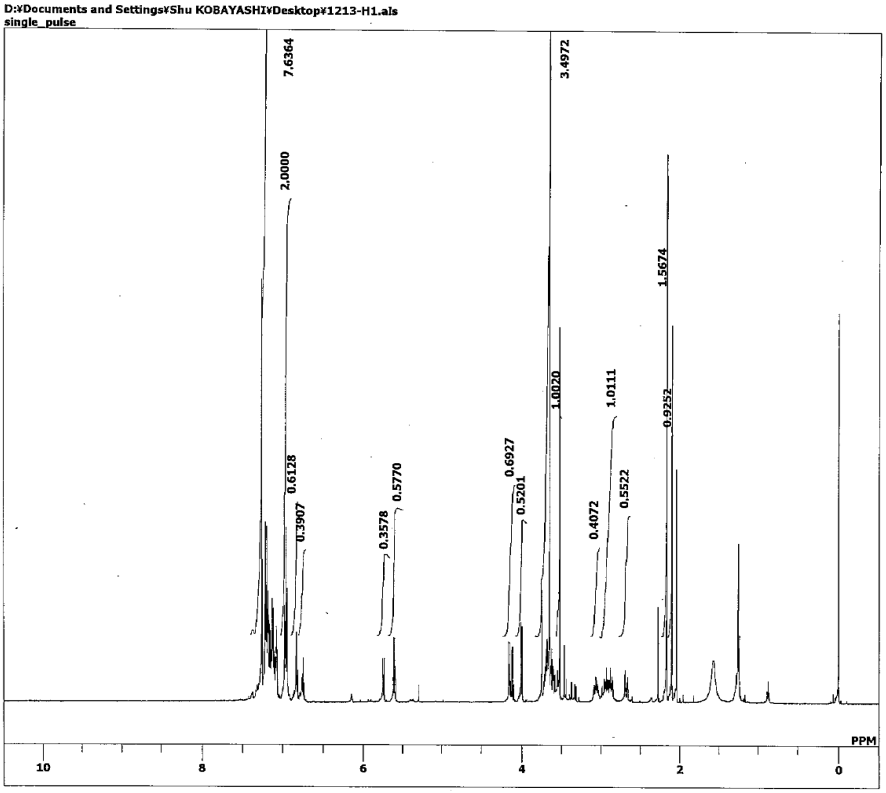


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	24-02-2012 01:31:47
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	99
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

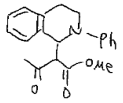


2ad

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1213-H1.als
single_pulse



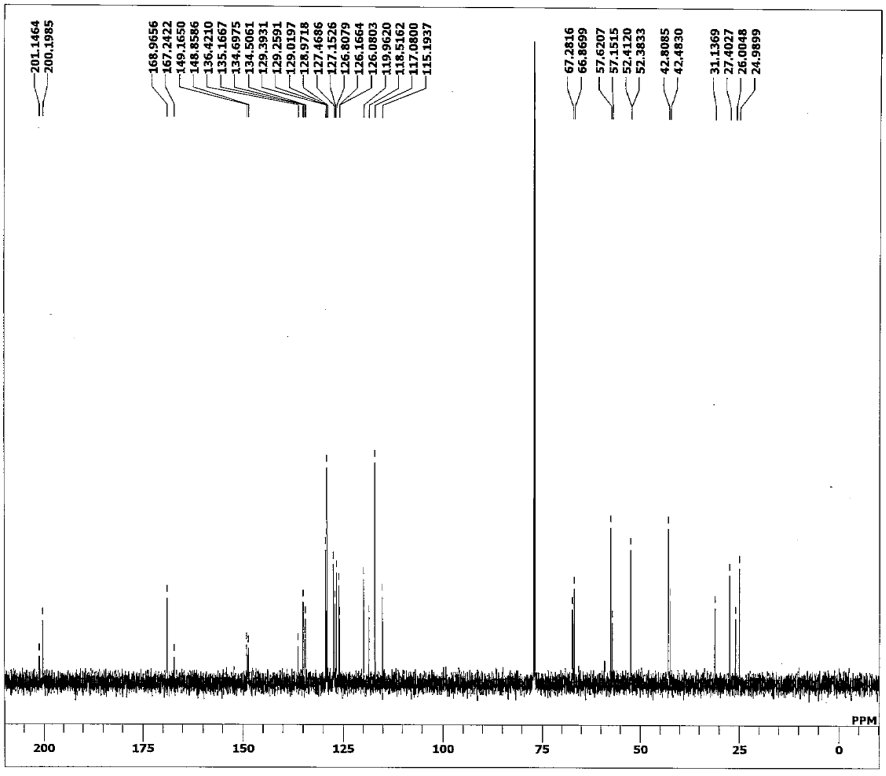
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	25-07-2012 04:39:19
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	29.3 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	44



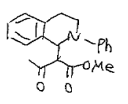
2ae

mixture of diastereomers

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1213-C.als



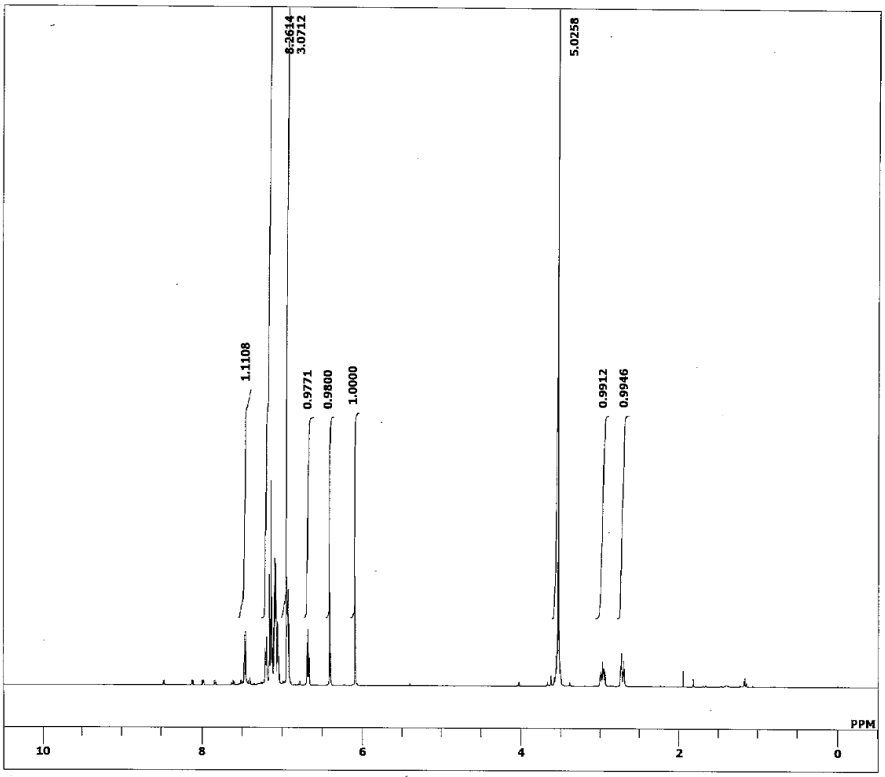
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	25-07-2012 00:45:11
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	137
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	31.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60



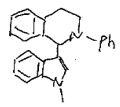
2ae

mixture of diastereomers

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥983-H-all-1.als

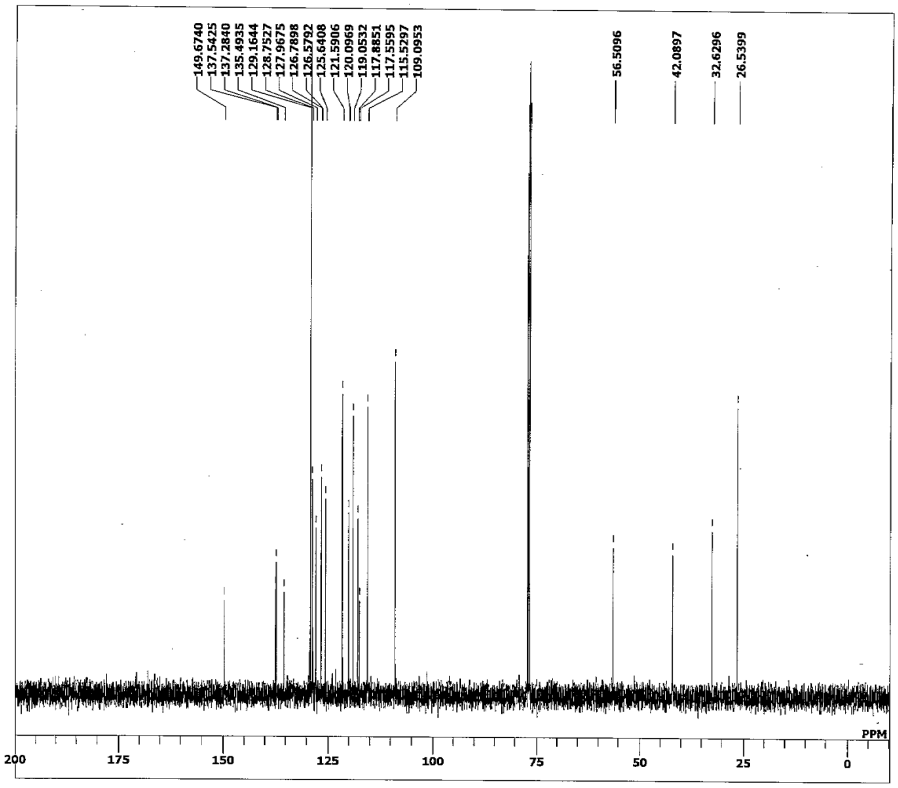


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	21-02-2012 13:57:31
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	20.4 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

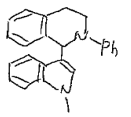


2af

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥983-C-all-1.als

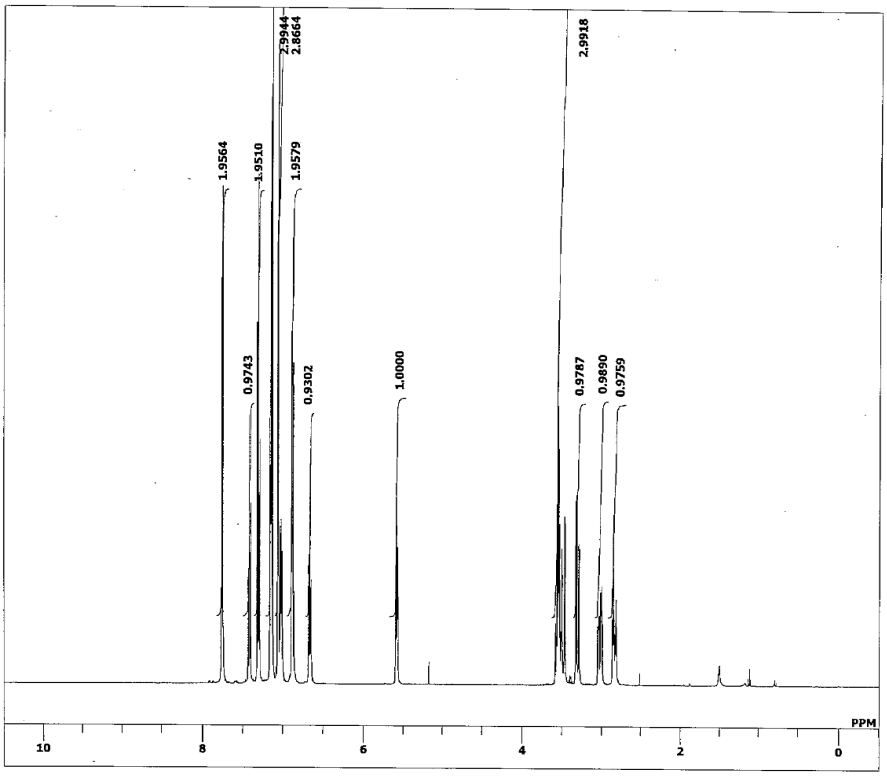


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	21-02-2012 14:03:21
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	106
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	20.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

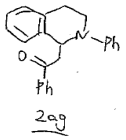


2af

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥993-H-cryst1-1.als

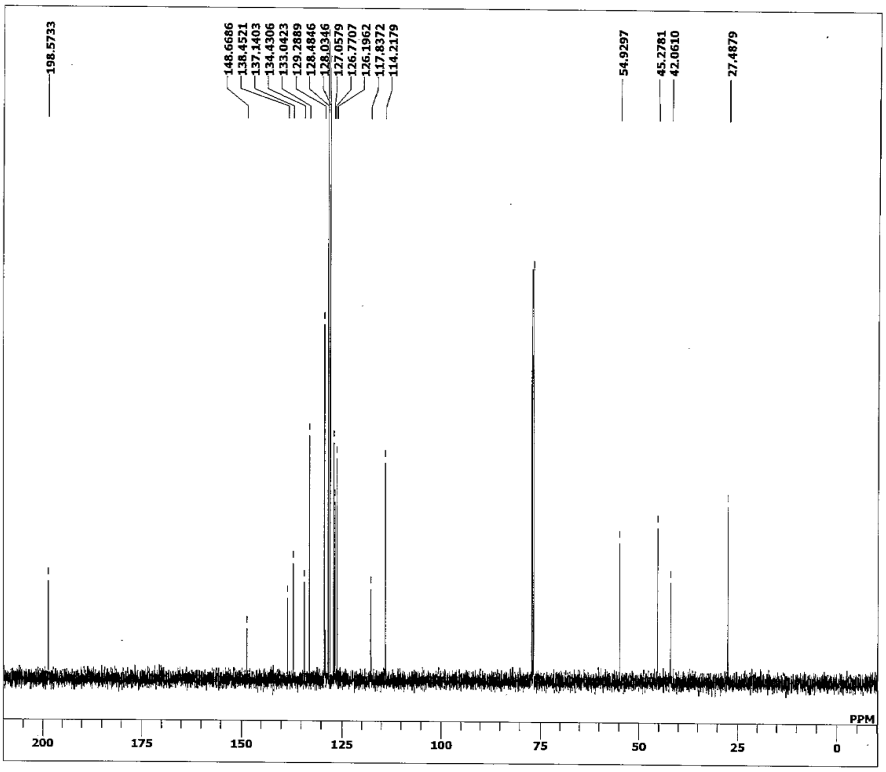


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	25-02-2012 17:11:39
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	20.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

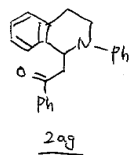


2ag

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥993-C-cryst1-1.als

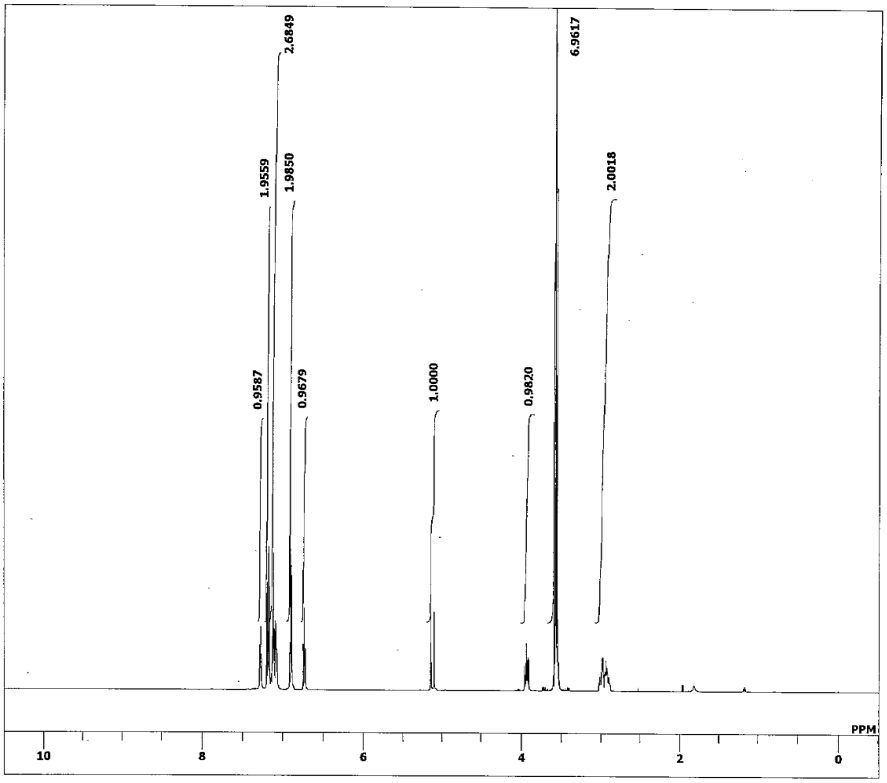


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	25-02-2012 17:19:21
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	109
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	21.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

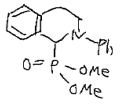


2ag

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥991-H-1.als

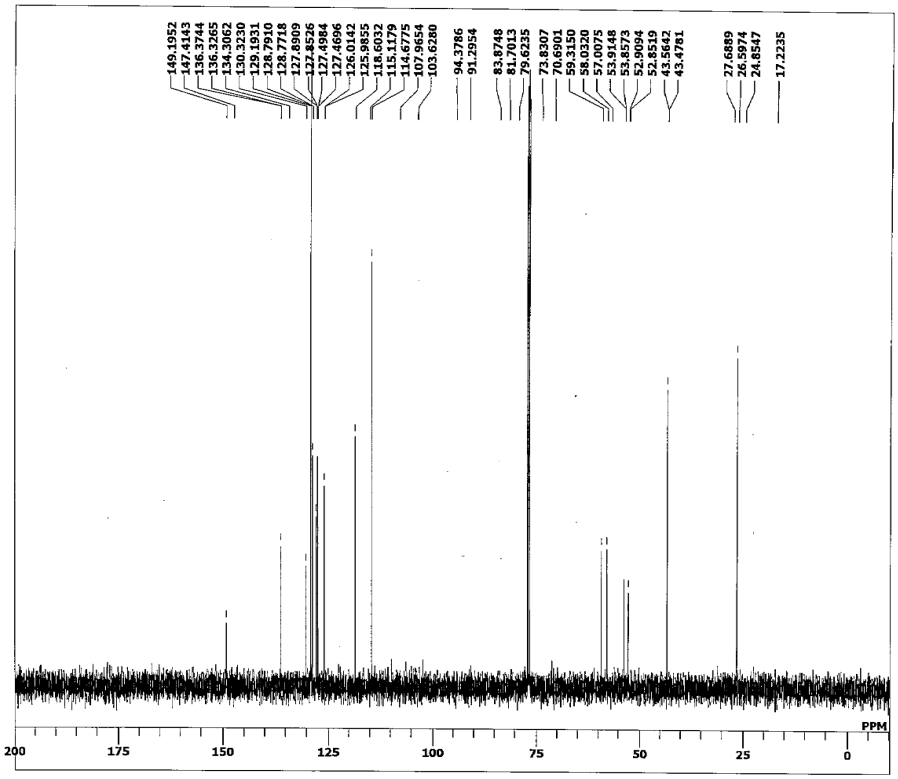


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-02-2012 18:16:27
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	20.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

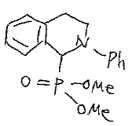


2ah

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥991-C-1.als

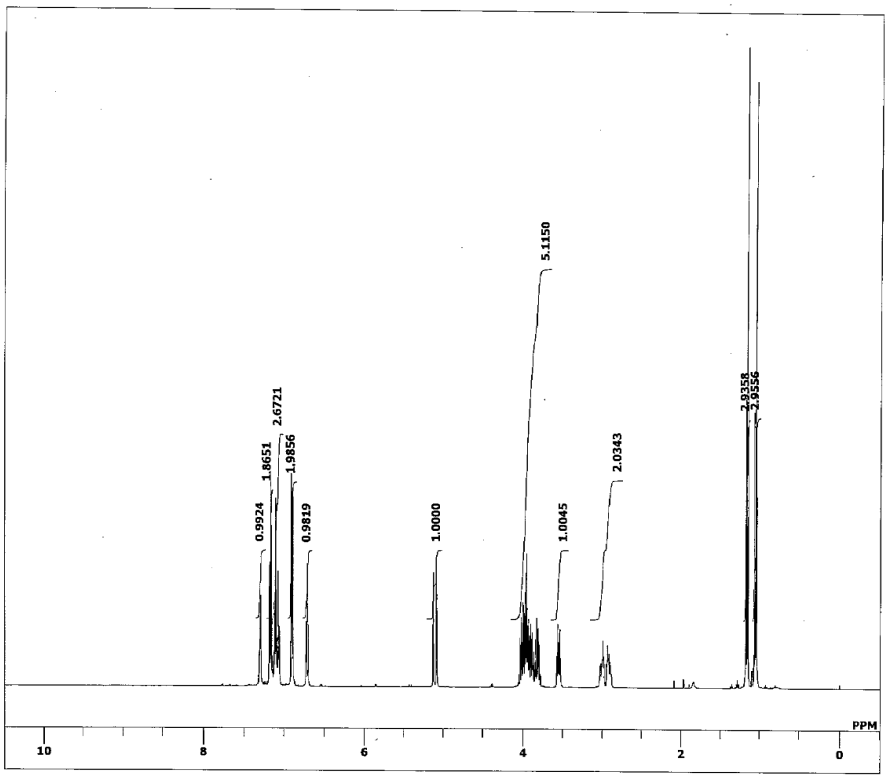


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-02-2012 18:22:22
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	73
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	21.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

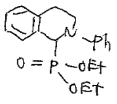


2ah

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1015-H-again-1.als

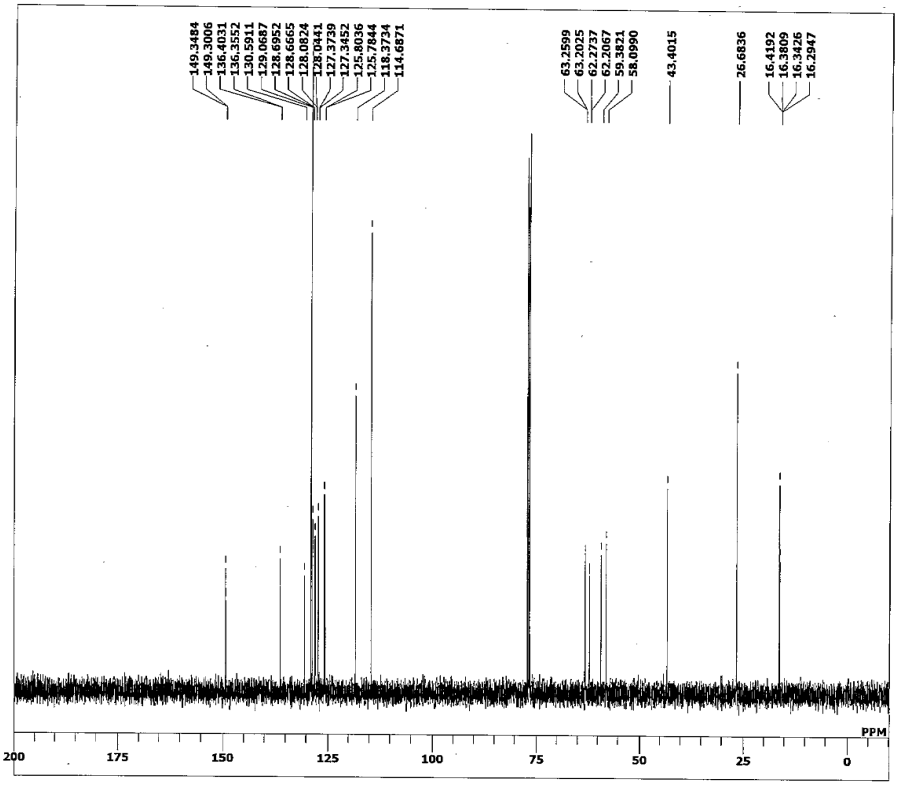


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	13-03-2012 11:03:57
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	20.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

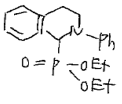


2ai

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1015-C-1.als

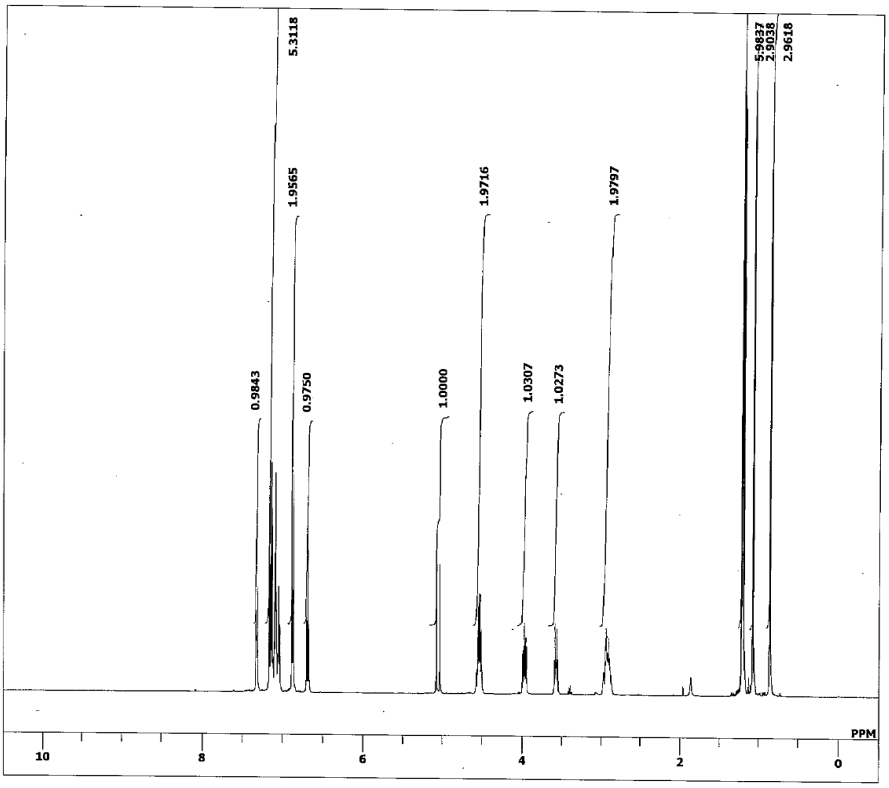


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	13-03-2012 11:09:31
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	103
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	21.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

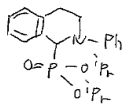


2ai

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥992-H-1.als

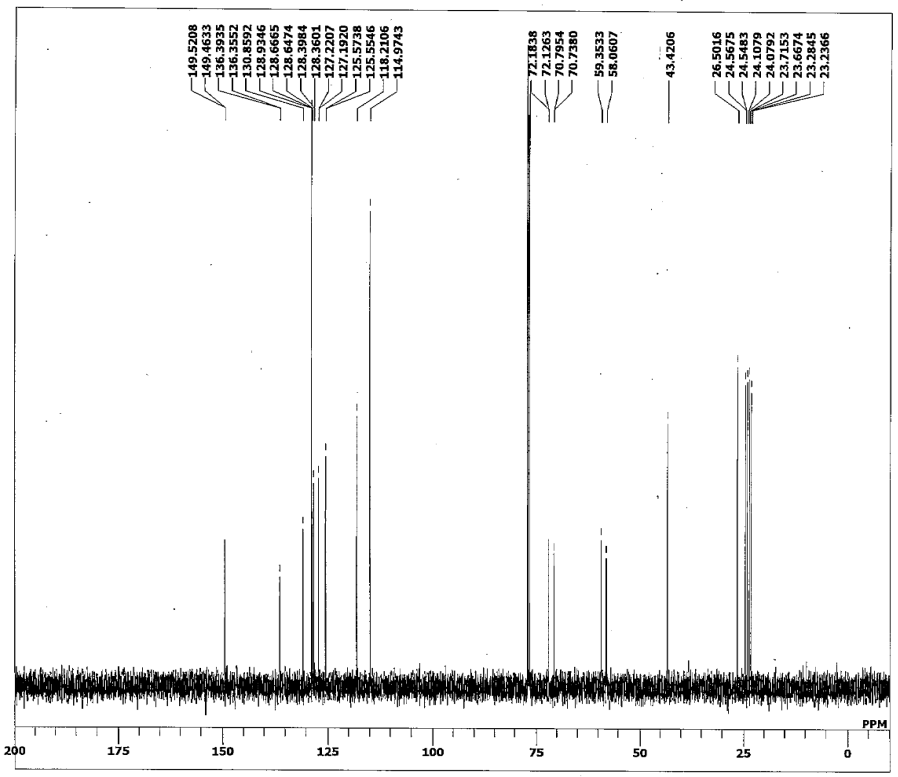


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-02-2012 18:25:36
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	21.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	30

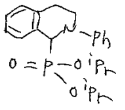


2aj

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥992-C-1.als

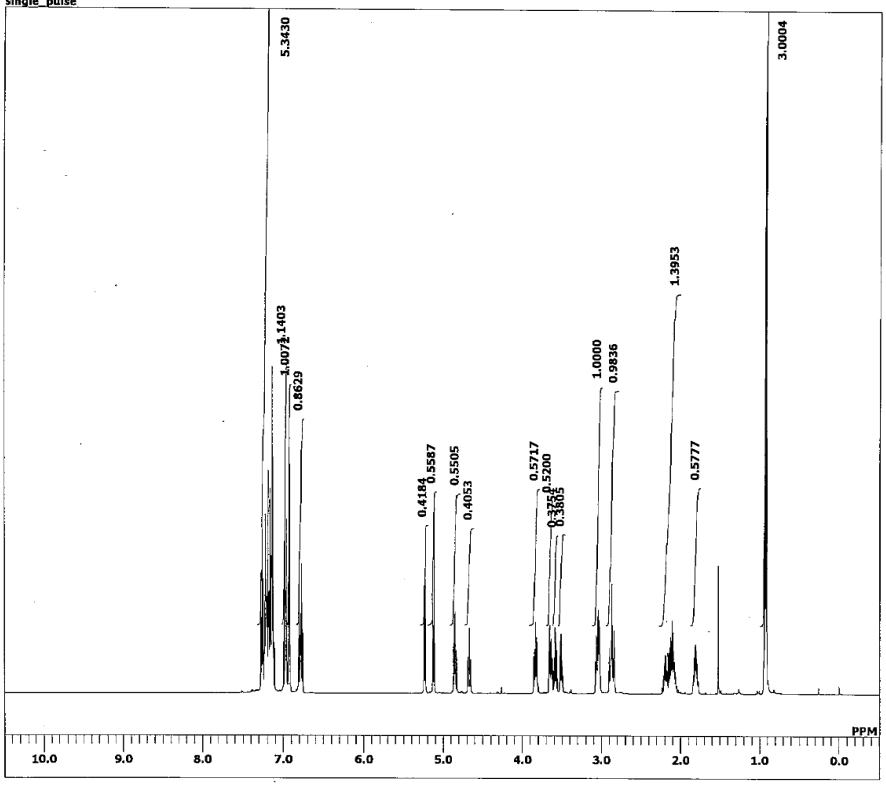


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-02-2012 18:30:53
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	96
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	21.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	50

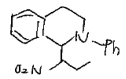


2aj

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2024-H.als
single_pulse



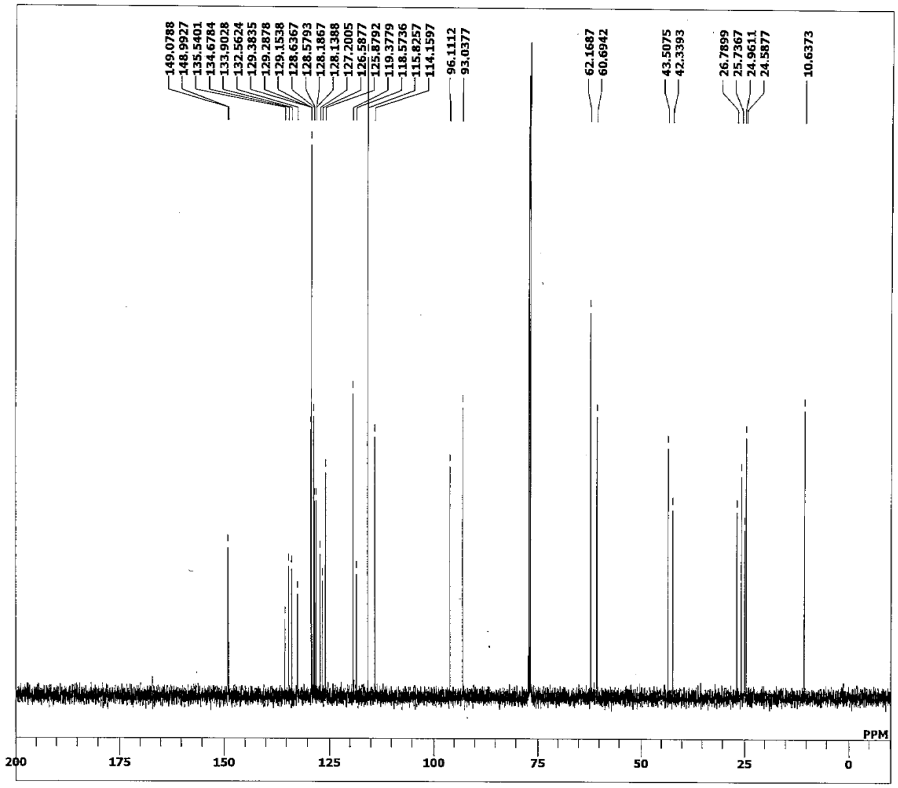
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	10-10-2013 10:52:52
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	10485
FREQU	7206.99 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	28.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.42 Hz
RGAIN	34



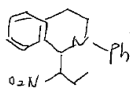
2ak

mixture of diastereomers

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2024-C.als



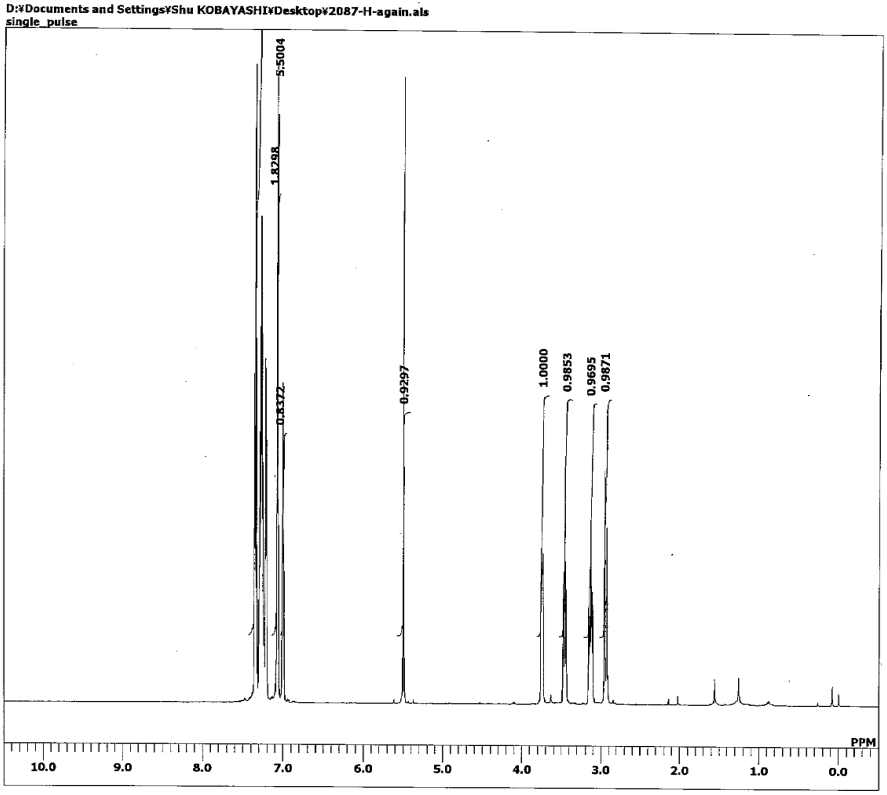
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	10-10-2013 11:04:05
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	128
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	29.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.42 Hz
RGAIN	60



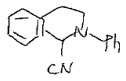
2ak

mixture of diastereomers

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2087-H-again.als
single_pulse

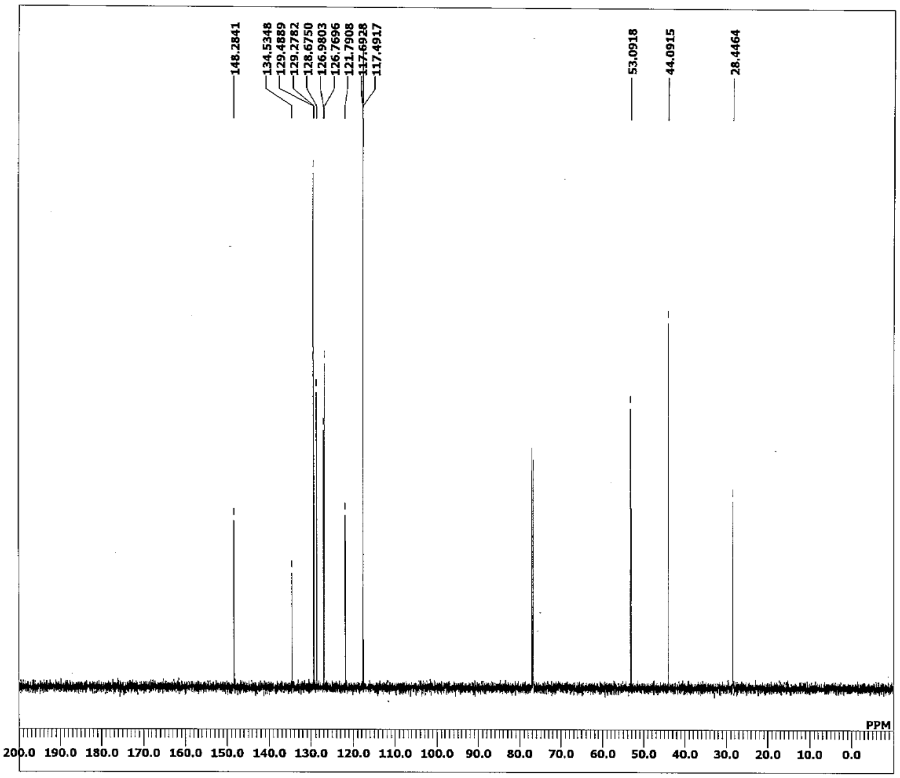


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	08-11-2013 07:02:52
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	23.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

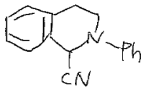


2ao

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2087-C-again.als

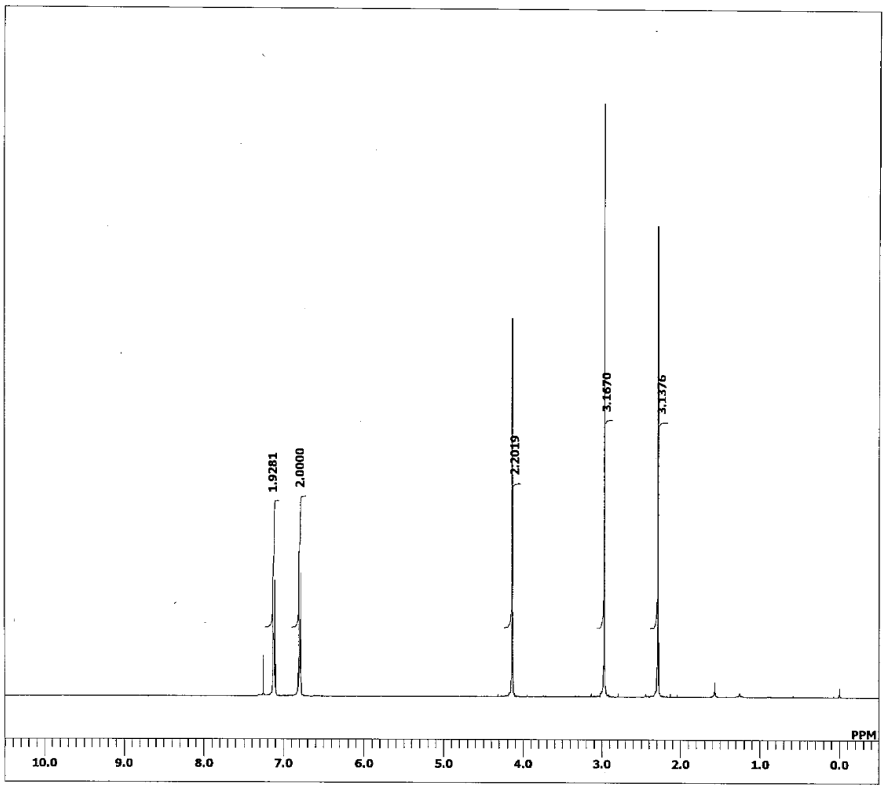


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	08-11-2013 07:08:17
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	68
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	24.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	58

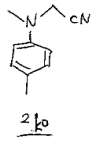


2ao

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2130-H.als

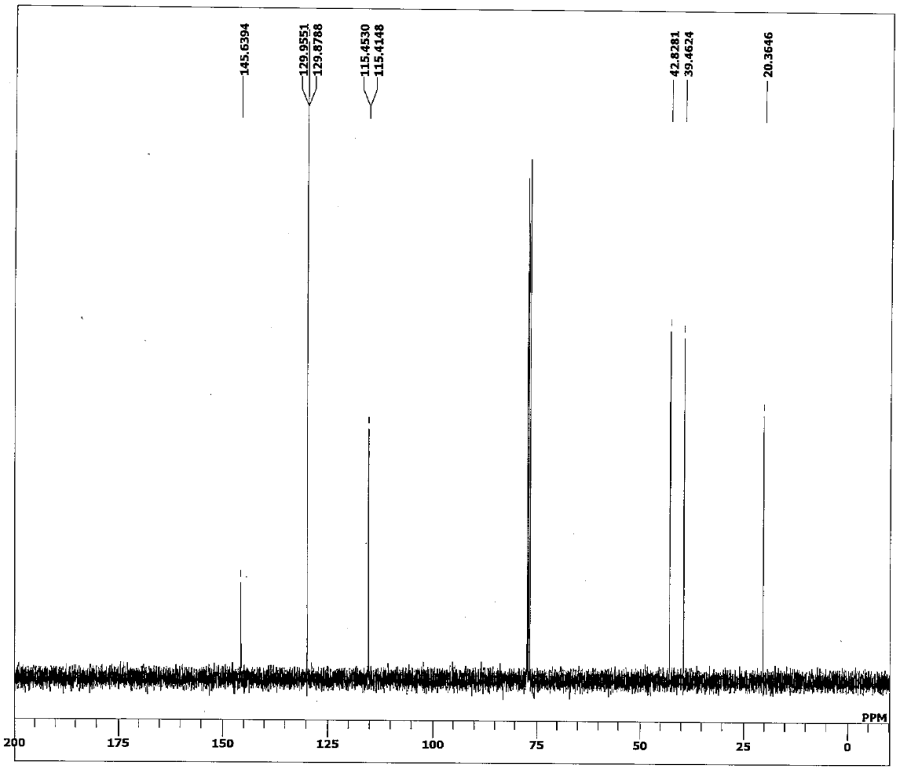


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	04-01-2014 03:19:23
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	399.78 MHz
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	6002.31 Hz
SCANS	8
ACQTM	2.1837 sec
PD	2.0000 sec
PW1	6.62 usec
IRNUC	1H
CTEMP	19.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

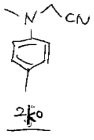


2Ko

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2130-C.als

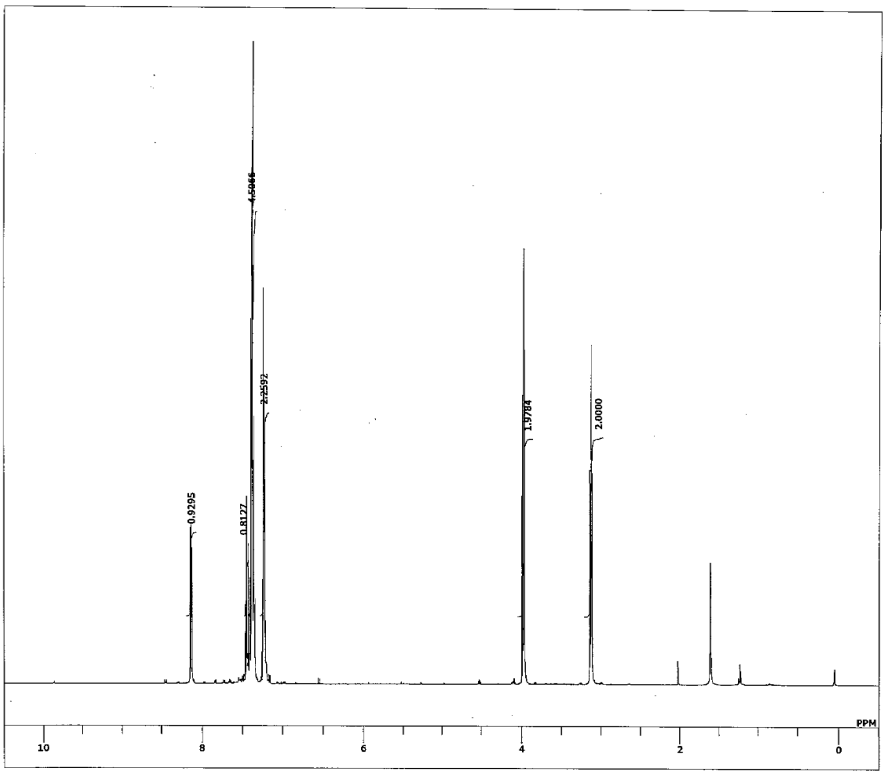


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	04-01-2014 03:28:46
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	100.53 MHz
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25125.24 Hz
SCANS	141
ACQTM	1.0433 sec
PD	2.0000 sec
PW1	3.50 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	56

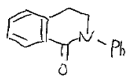


2Ko

D:¥Documents and Settings¥Kobayashilab¥Desktop¥WY-1024-1H-1.als

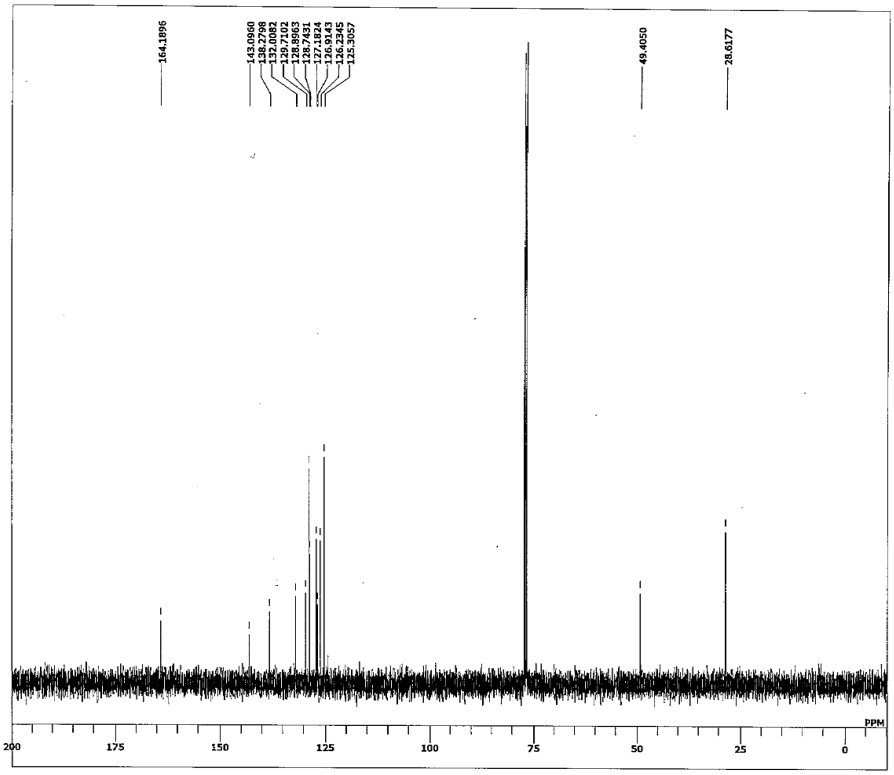


DFILE D:¥Documents and Settings¥Kobayashilab¥Desktop¥WY-10
COMNT
DATIM 04-11-2011 19:29:14
OBNUC 1H
EXMOD 1H NMR.ex2
OBFRQ 495.13 MHz
OBSET 4.38 KHz
OBFIN 9.64 Hz
POINT 13107
FREQU 7429.31 Hz
SCANS 8
ACQTM 1.7642 sec
PD 5.0000 sec
PW1 5.80 usec
IRNUC 1H
CTEMP 23.8 c
SLVNT CDCL3
EXREF 0.00 ppm
BF 0.12 Hz
RGAIN 46

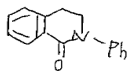


3

D:¥Documents and Settings¥Kobayashilab¥Desktop¥WY-1024-13C-1.als

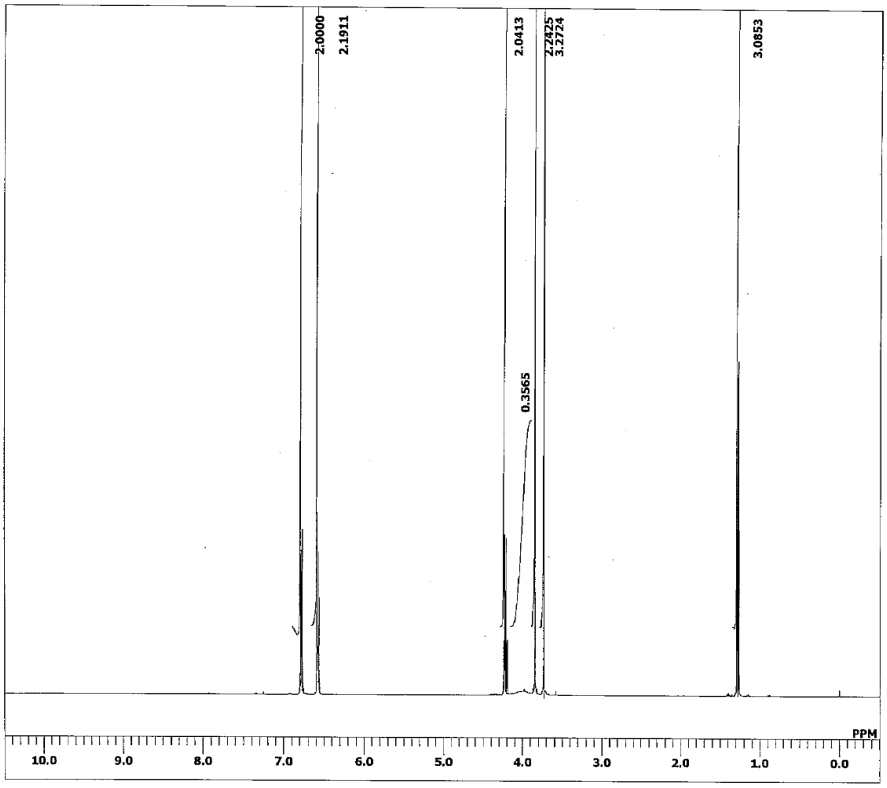


DFILE D:¥Documents and Settings¥Kobayashilab¥Desktop¥WY-10
COMNT
DATIM 04-11-2011 19:36:52
OBNUC 13C
EXMOD 13C NMR.ex2
OBFRQ 124.51 MHz
OBSET 3.45 KHz
OBFIN 6.00 Hz
POINT 26214
FREQU 31249.52 Hz
SCANS 139
ACQTM 0.8389 sec
PD 2.0000 sec
PW1 3.67 usec
IRNUC 1H
CTEMP 24.2 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 0.12 Hz
RGAIN 50

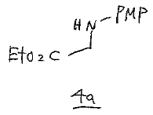


3

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1283-H-1.als

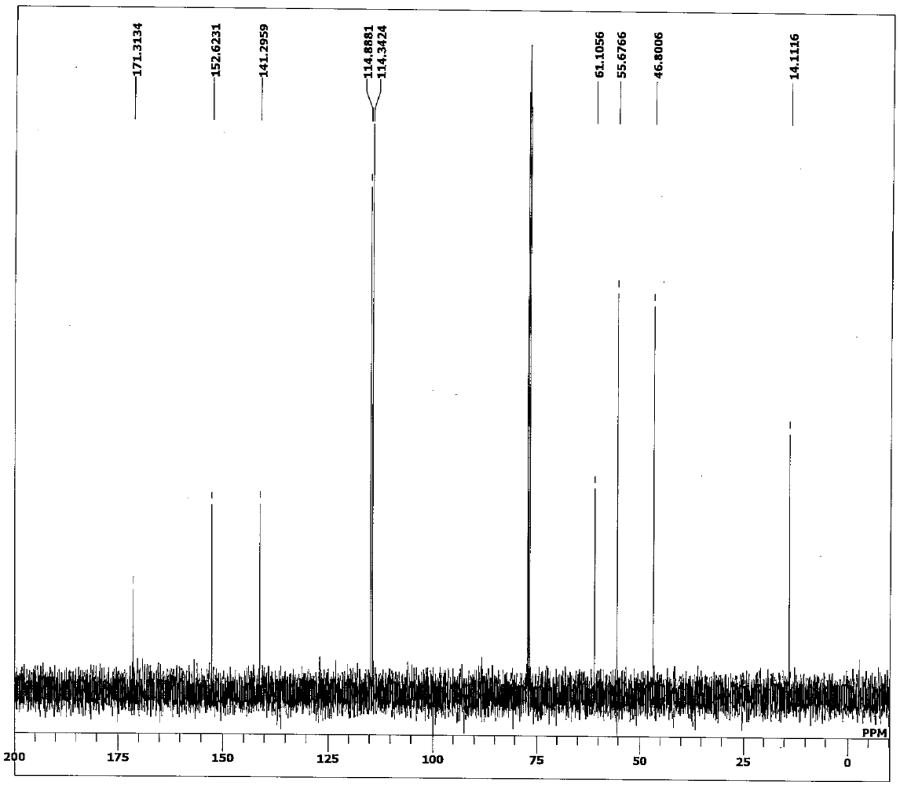


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	07-09-2012 18:59:40
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	3.65 usec
IRNUC	1H
CTEMP	30.3 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	26

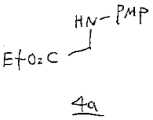


4a

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1283-C-1.als

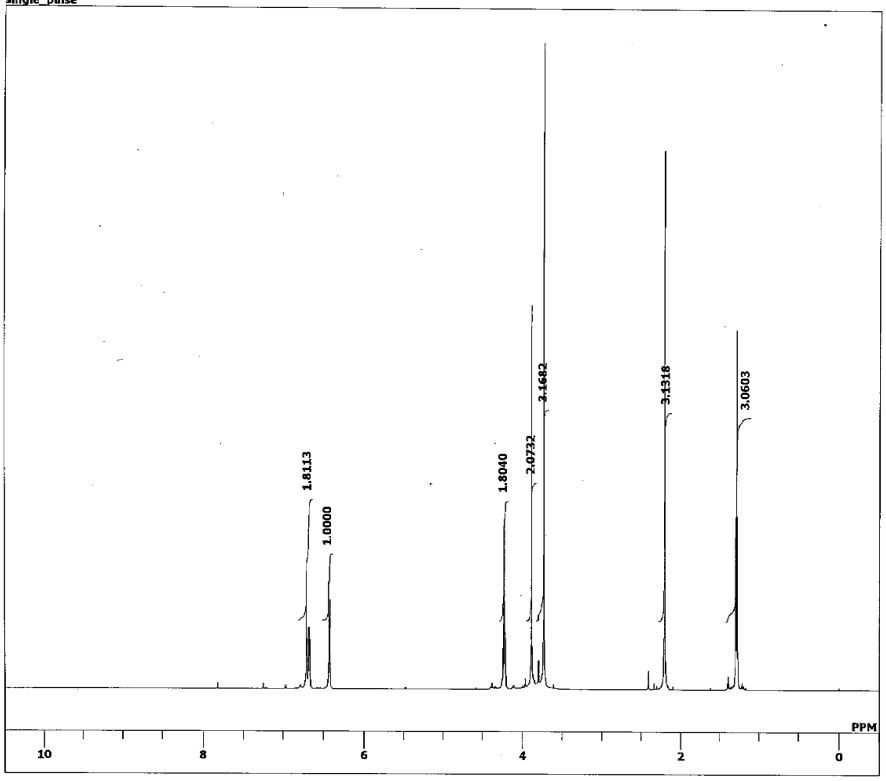


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	07-09-2012 19:03:57
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	70
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	30.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	54

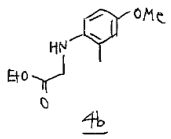


4a

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1648ab-H-dry.1
single_pulse

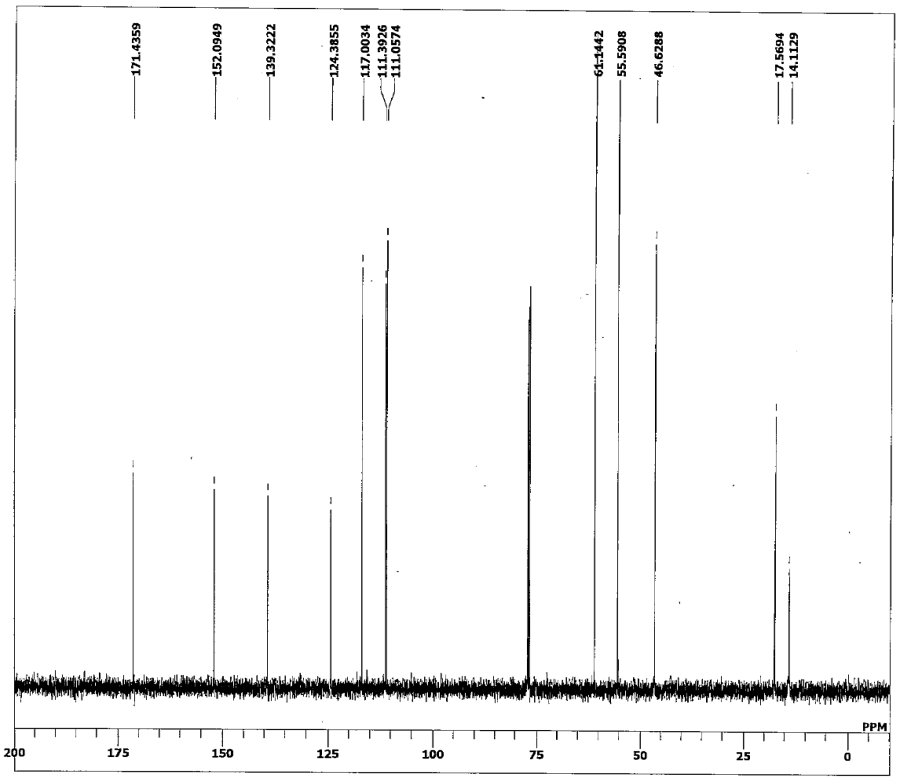


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	13-01-2014 03:55:57
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	16384
FREQU	11261.26 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.52 Hz
RGAIN	32

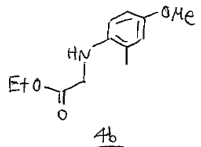


4b

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1648ab-C-dry.1

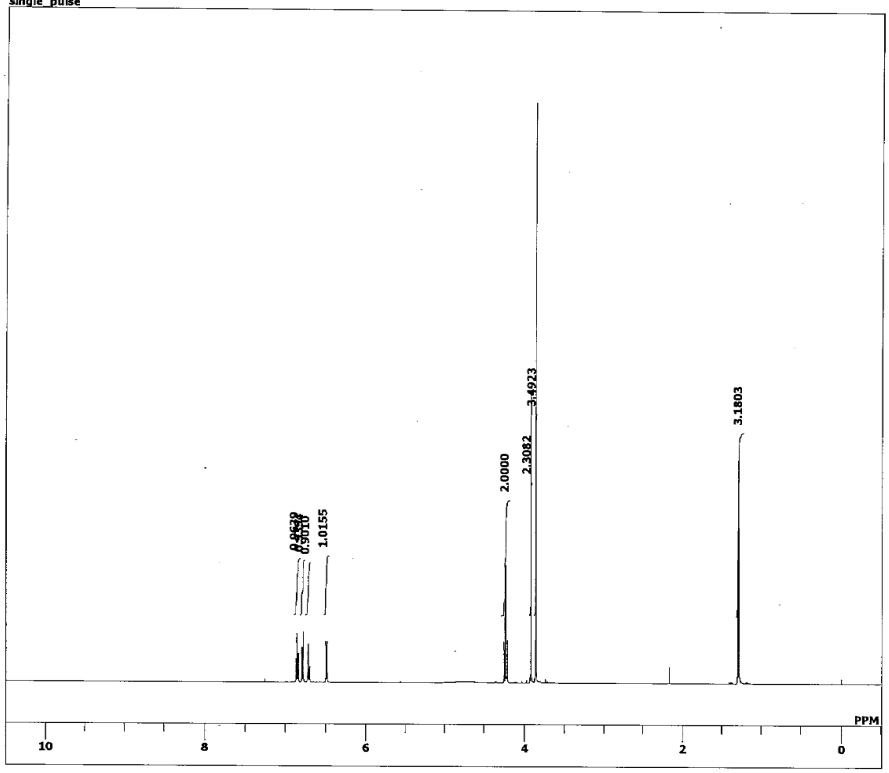


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	13-01-2014 04:01:36
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	32768
FREQU	47348.49 Hz
SCANS	73
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.52 Hz
RGAIN	58

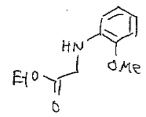


4b

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1635H.als
single_pulse

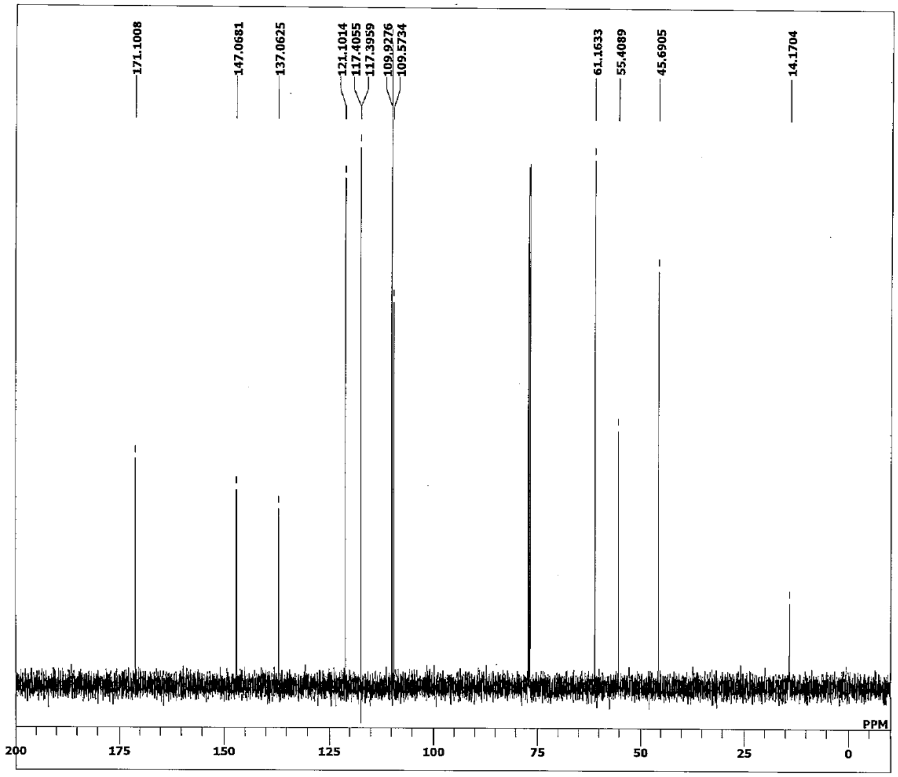


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	03-01-2014 15:33:26
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.7 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

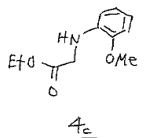


4c

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1635C.als

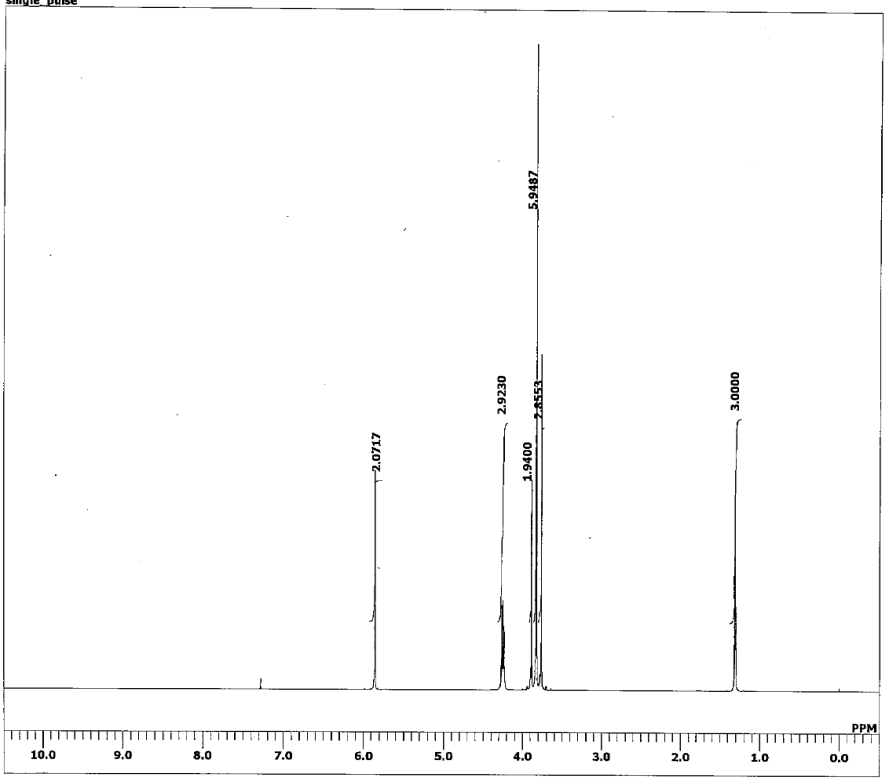


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	03-01-2014 15:40:33
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	107
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

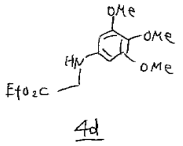


4c

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1572-H-again.als
single_pulse

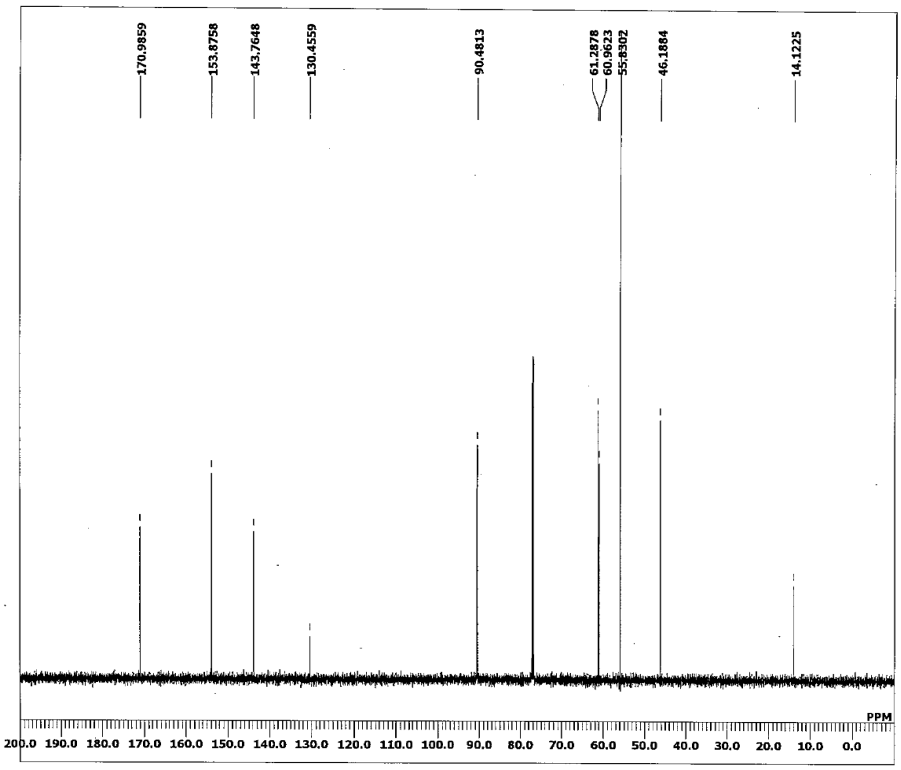


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	22-02-2013 01:36:58
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	19.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

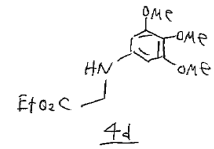


4d

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1572-C-again.als

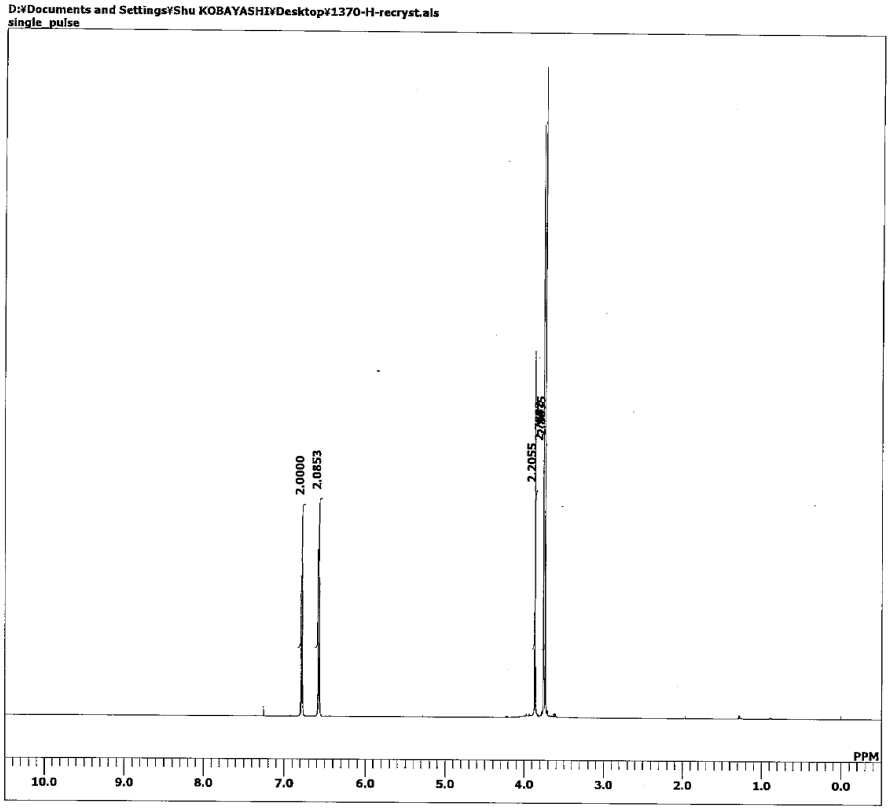


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	22-02-2013 01:43:51
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	96
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	20.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

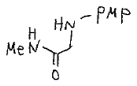


4d

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1370-H-recryst.als
single_pulse

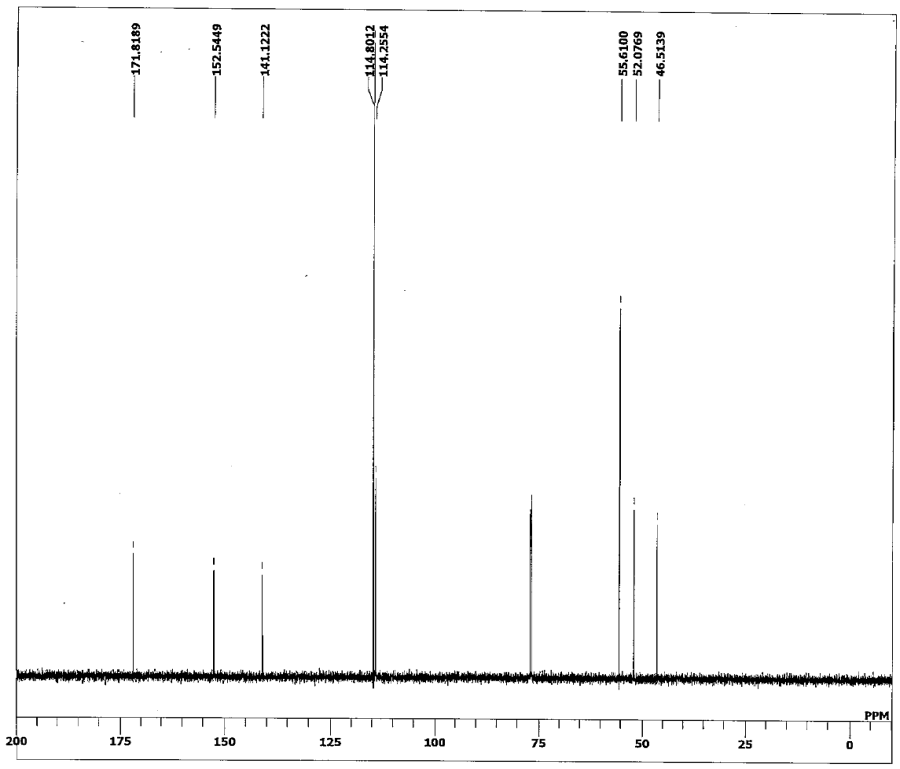


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	09-11-2012 00:41:05
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	20.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

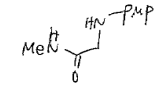


4e

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1370-C-recryst.als

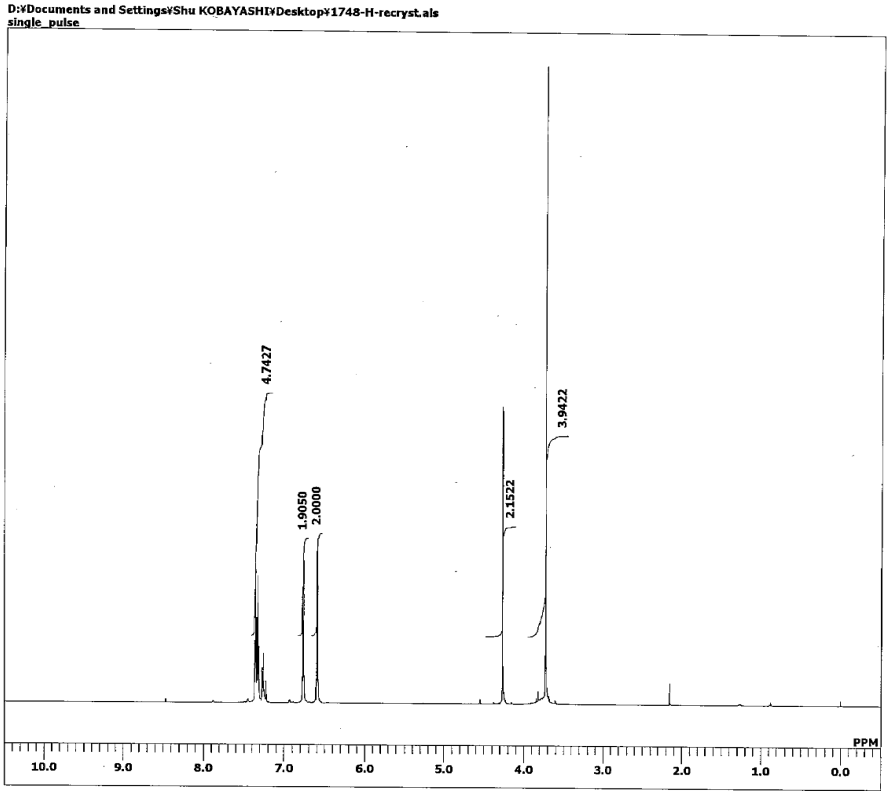


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	09-11-2012 00:46:18
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	37
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	21.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

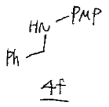


4e

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1748-H-recryst.als
single_pulse

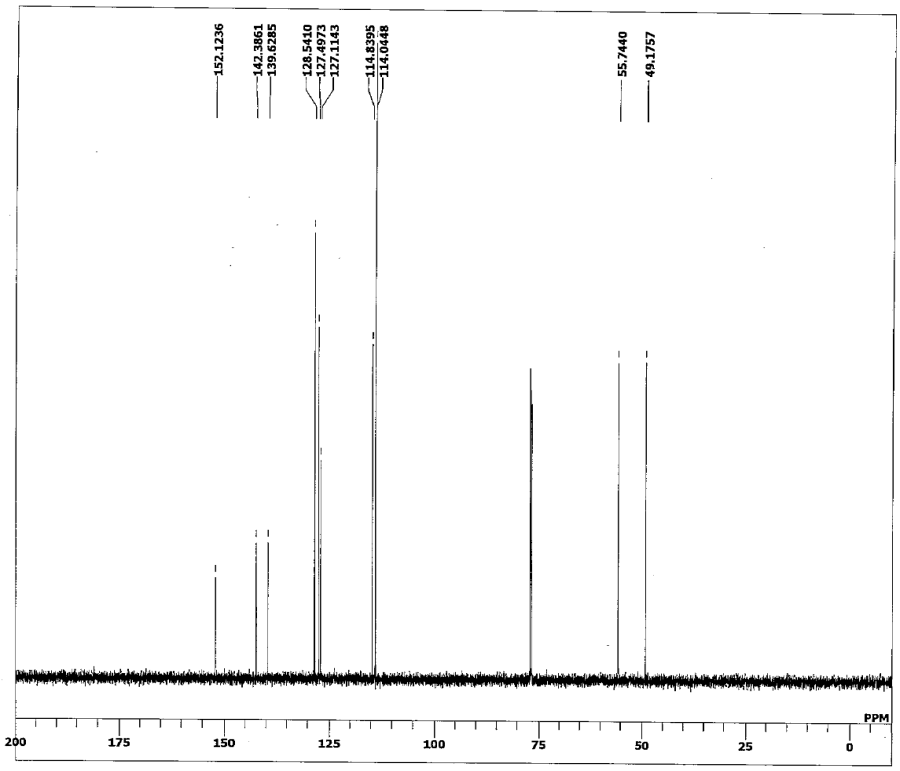


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	03-01-2014 15:22:35
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.3 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

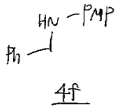


4f

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1748-C-recryst.als

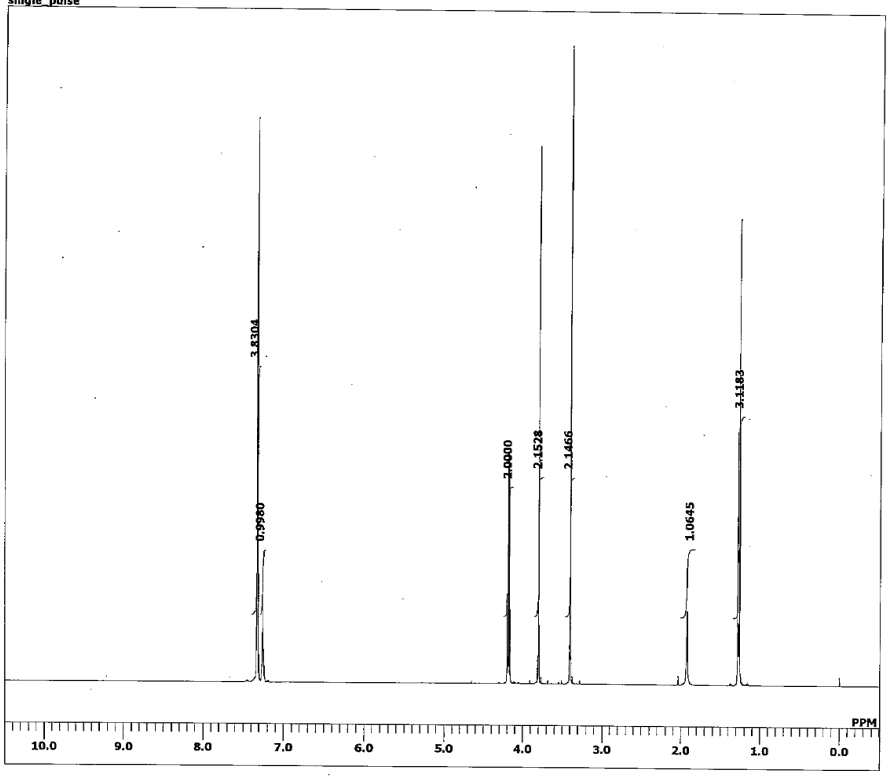


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	03-01-2014 15:29:33
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	98
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

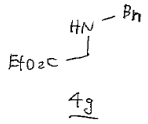


4f

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1557-H.als
single_pulse

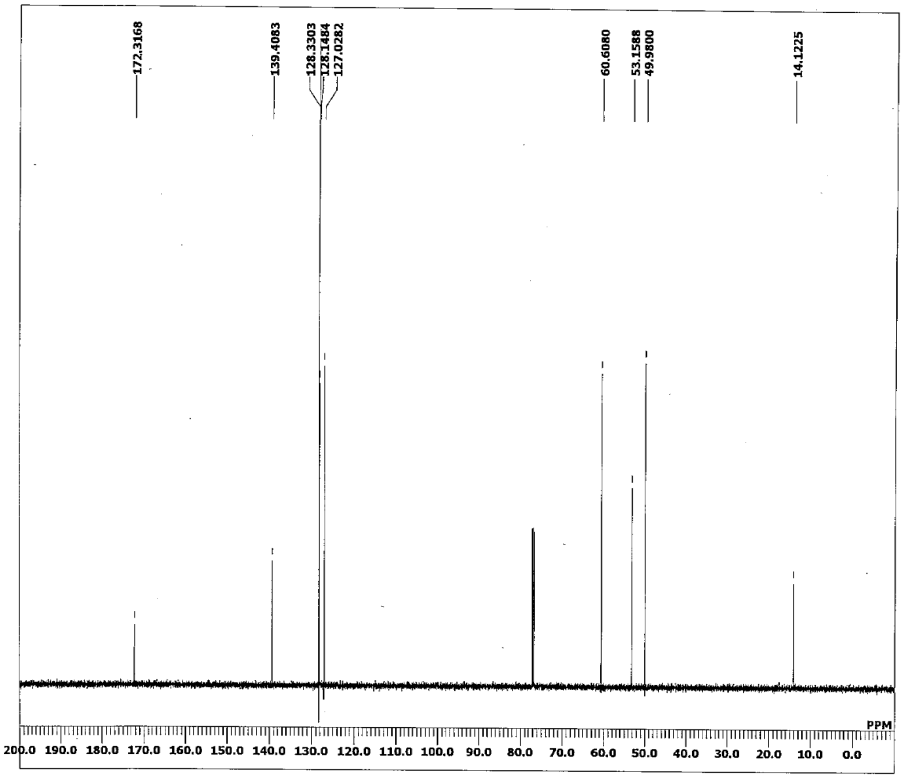


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	07-02-2013 01:47:15
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	20.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	30

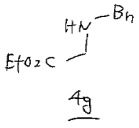


4g

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1557-C.als

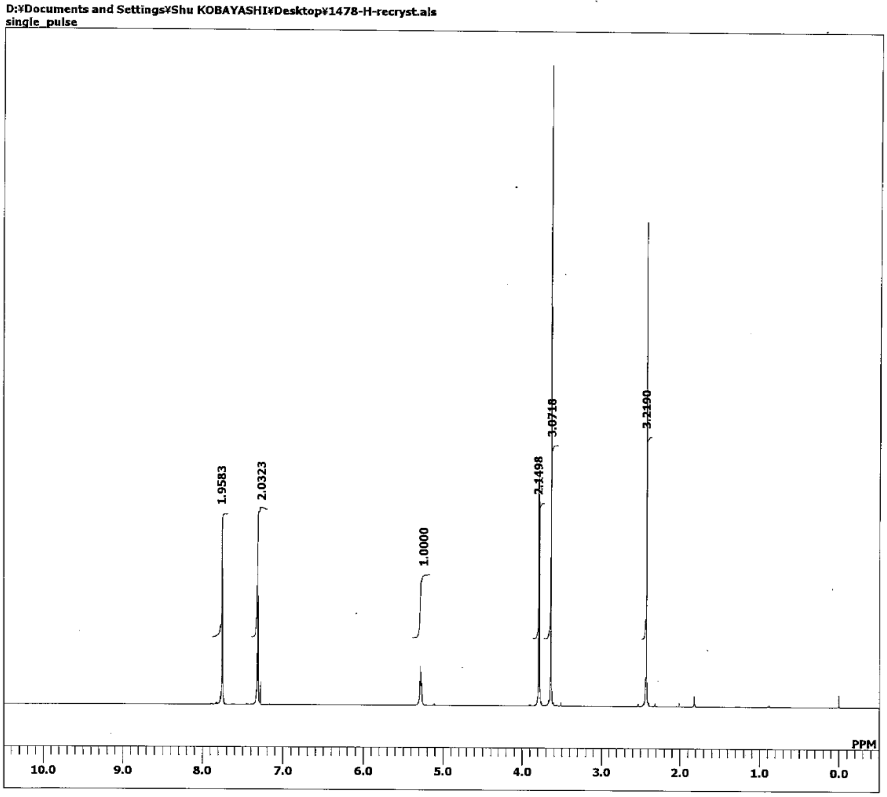


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	07-02-2013 01:51:55
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	48
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	20.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

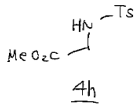


4g

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1478-H-recryst.als
single_pulse

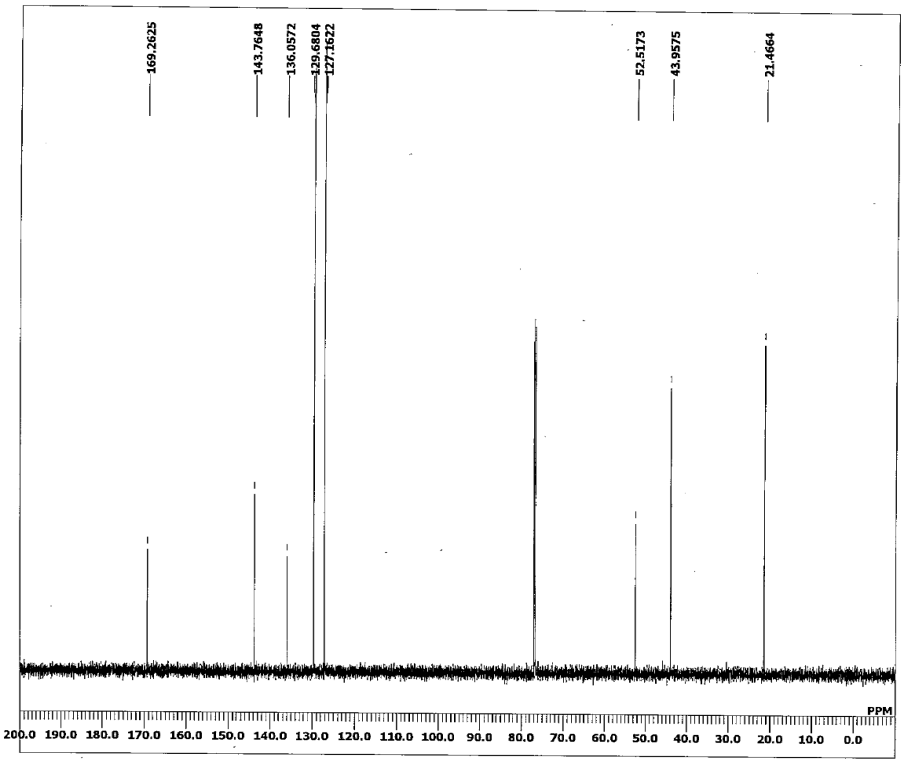


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	08-02-2013 05:41:08
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

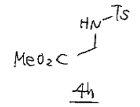


4h

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1478-C-recryst.als

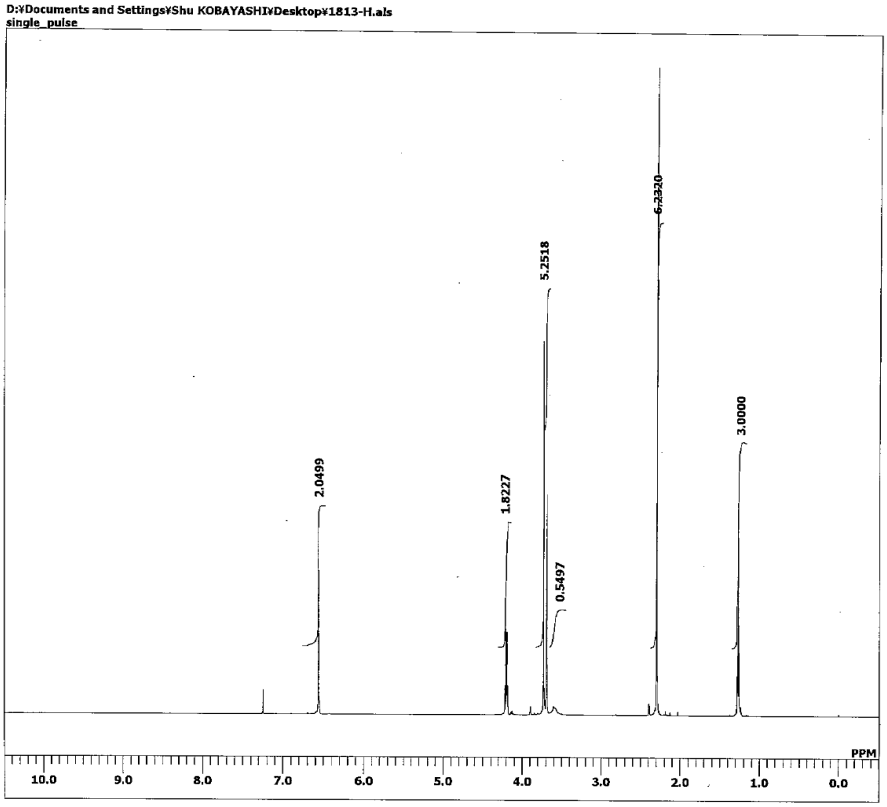


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	08-02-2013 05:46:57
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	70
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	21.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

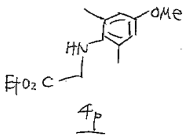


4h

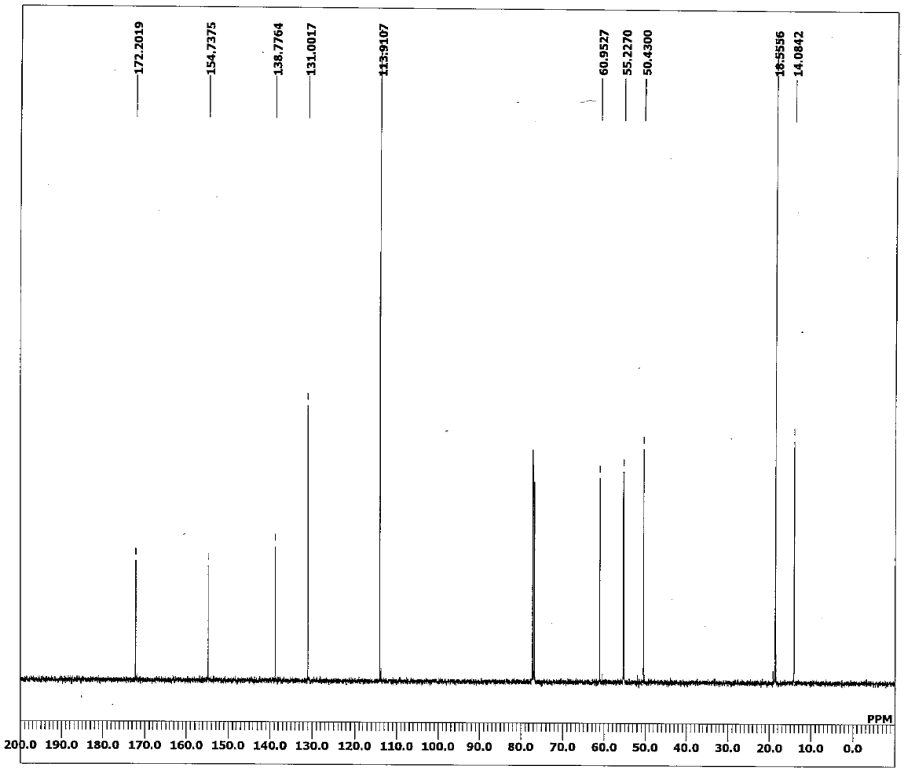
D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1813-H.als
single_pulse



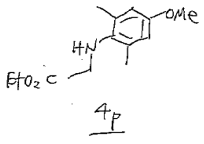
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	10-07-2013 00:50:49
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	31.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	1.20 Hz
RGAIN	30



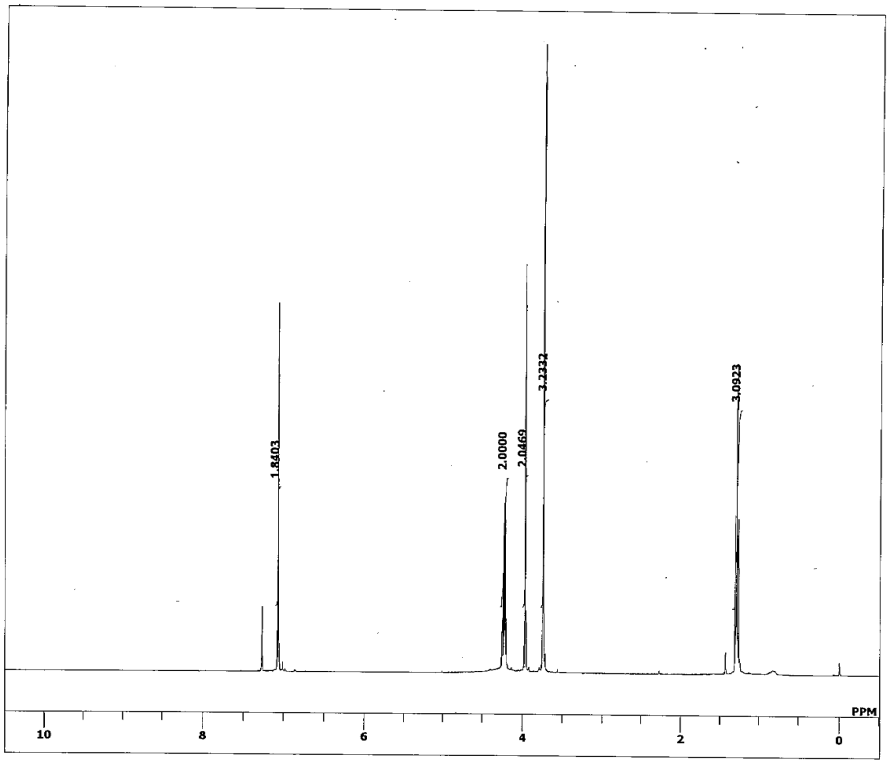
D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1813-C.als



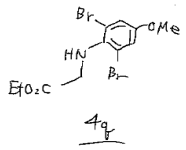
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	10-07-2013 00:58:27
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	117
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	31.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	1.20 Hz
RGAIN	60



D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1811H.als

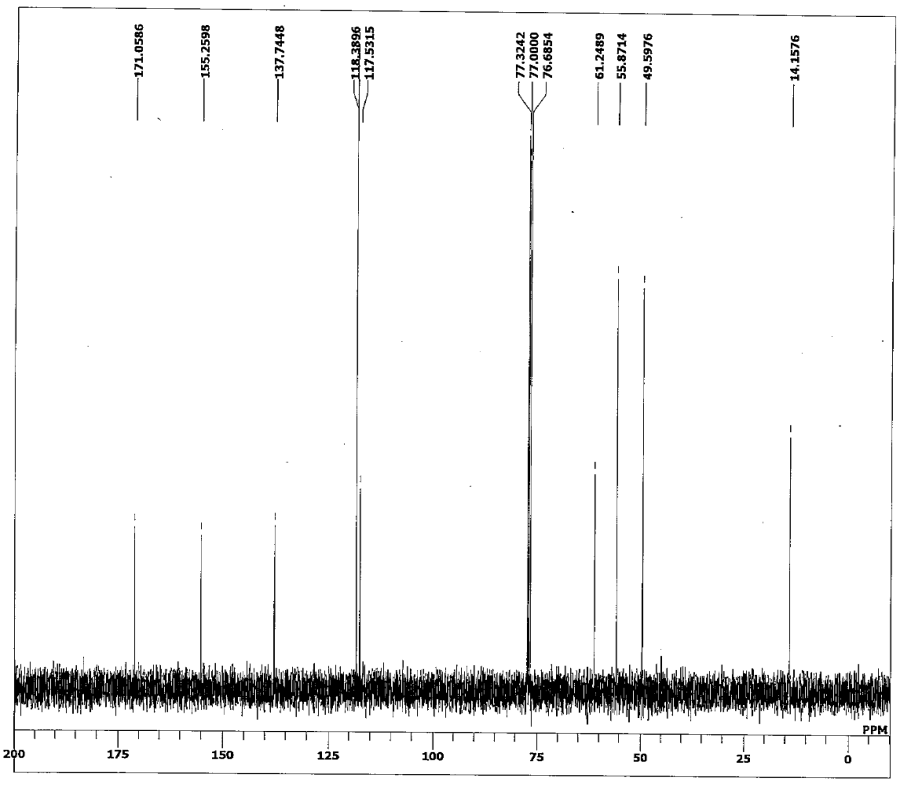


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-01-2014 01:30:59
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	399.78 MHz
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	6002.31 Hz
SCANS	8
ACQTM	2.1837 sec
PD	2.0000 sec
PW1	6.62 usec
IRNUC	1H
CTEMP	20.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

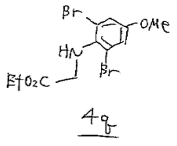


4q

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1811C.als

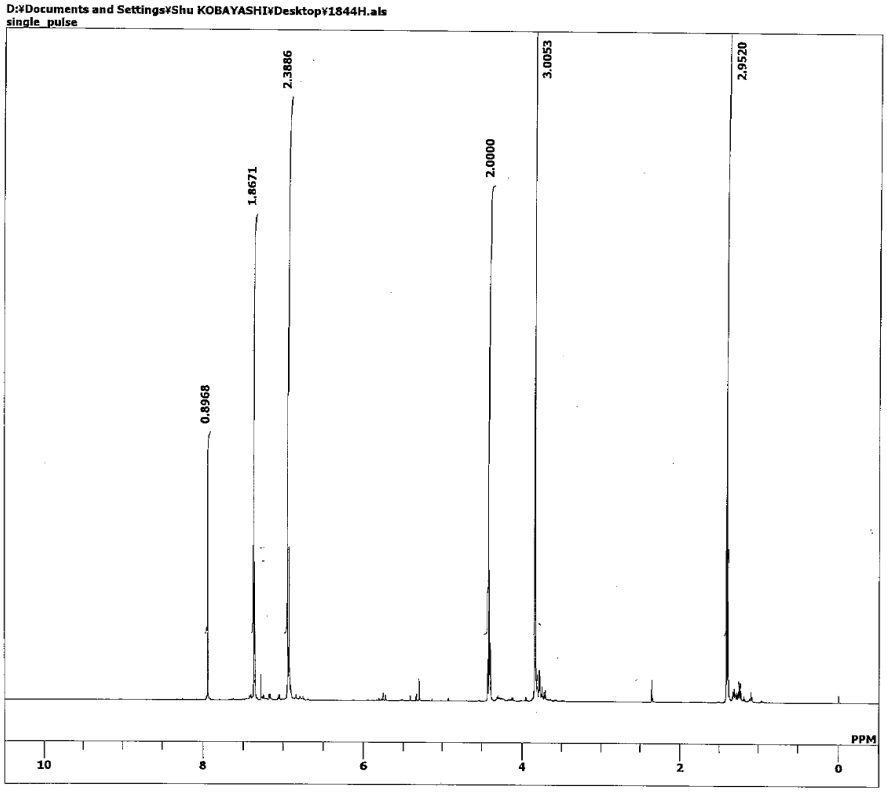


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-01-2014 01:37:18
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	100.53 MHz
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25125.24 Hz
SCANS	73
ACQTM	1.0433 sec
PD	2.0000 sec
PW1	3.50 usec
IRNUC	1H
CTEMP	20.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	56

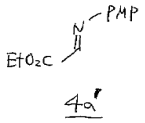


4q

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1844H.als
single_pulse

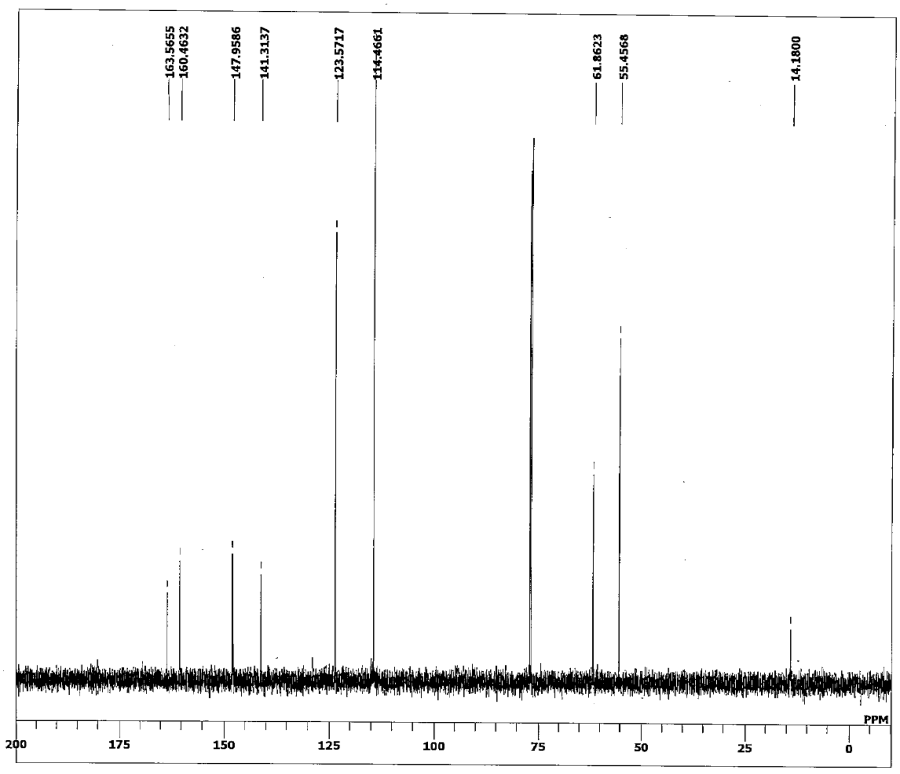


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	25-12-2013 01:41:32
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

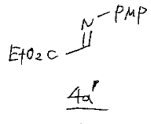


4a'

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1844C.als

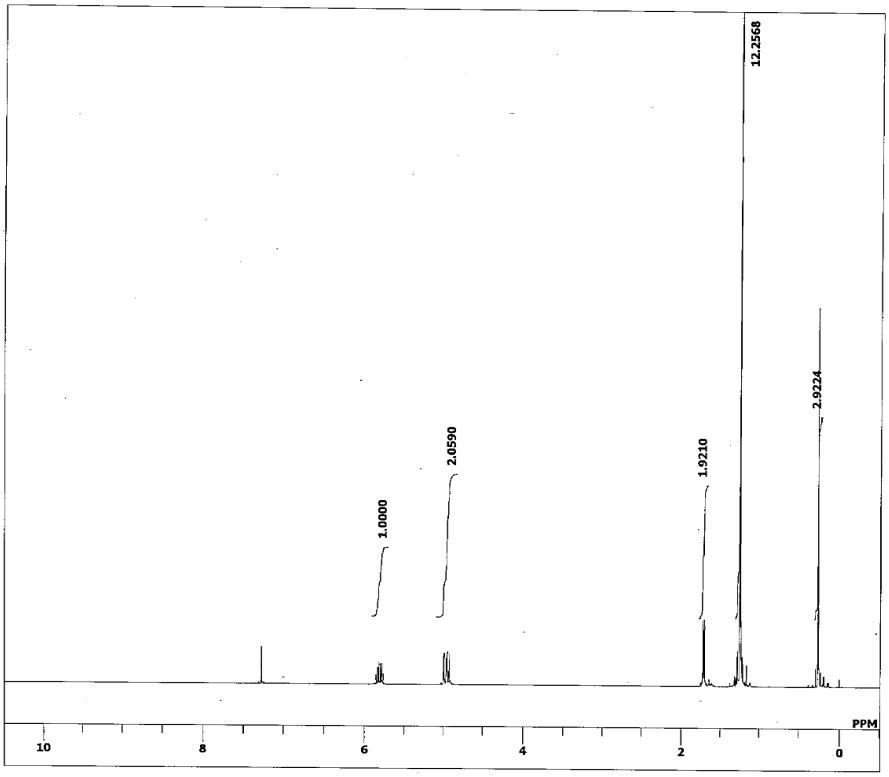


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	25-12-2013 01:47:04
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	76
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

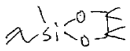


4a'

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥519-H-dist1-1.jdf

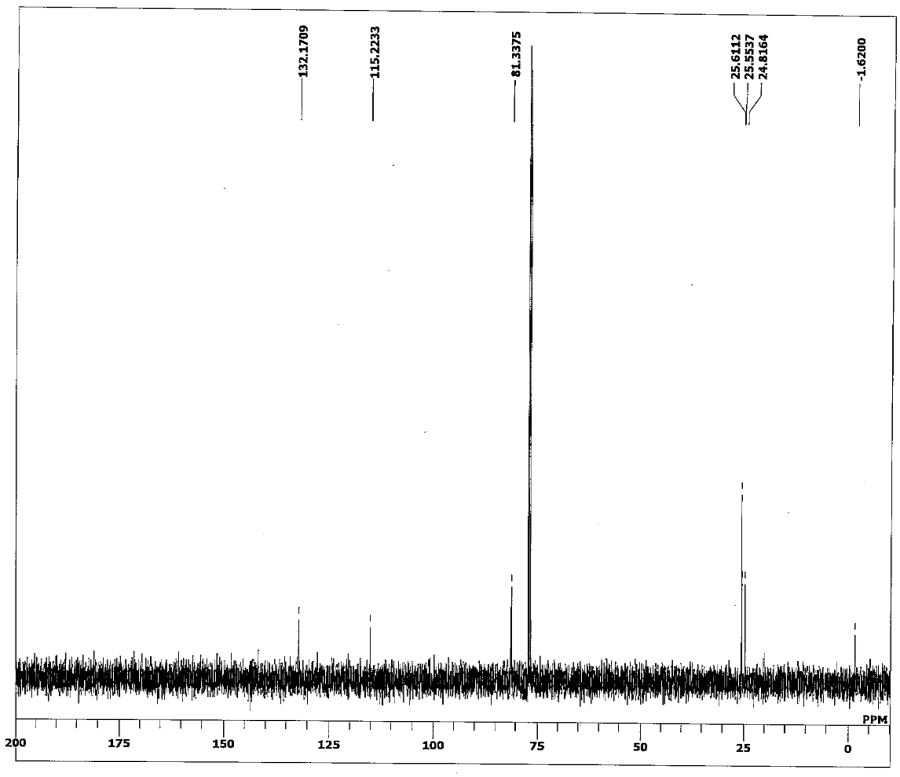


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	28-12-2010 13:52:06
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	16384
FREQU	9286.78 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	5.80 usec
IRNUC	1H
CTEMP	18.3 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	40

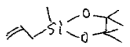


5c

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥519-C-dist1-1.jdf

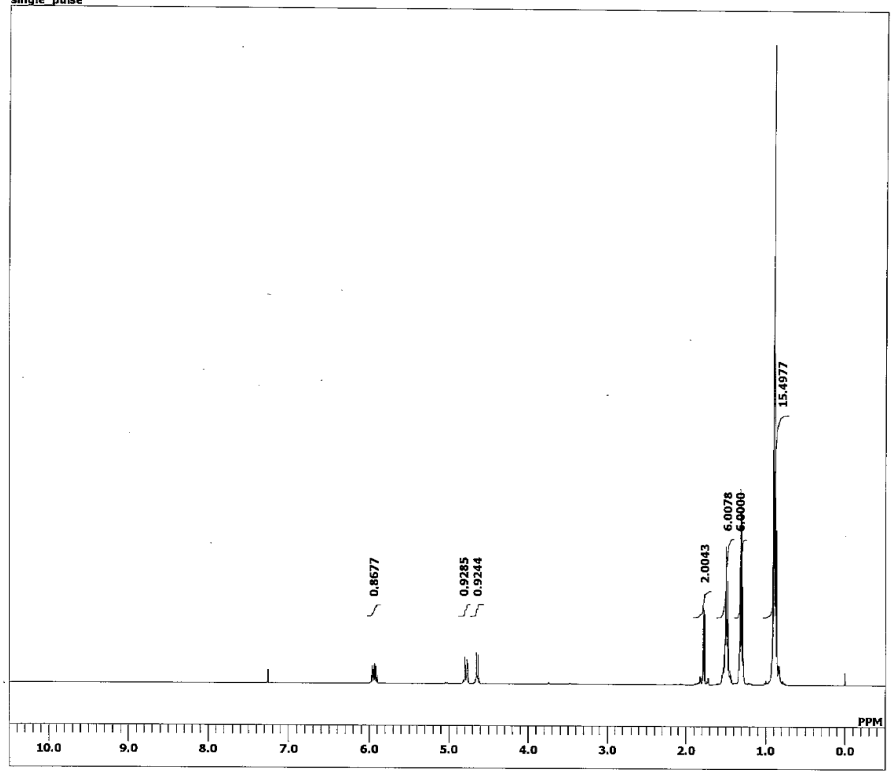


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	28-12-2010 14:00:48
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	32768
FREQU	39062.50 Hz
SCANS	167
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.67 usec
IRNUC	1H
CTEMP	18.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60



5c

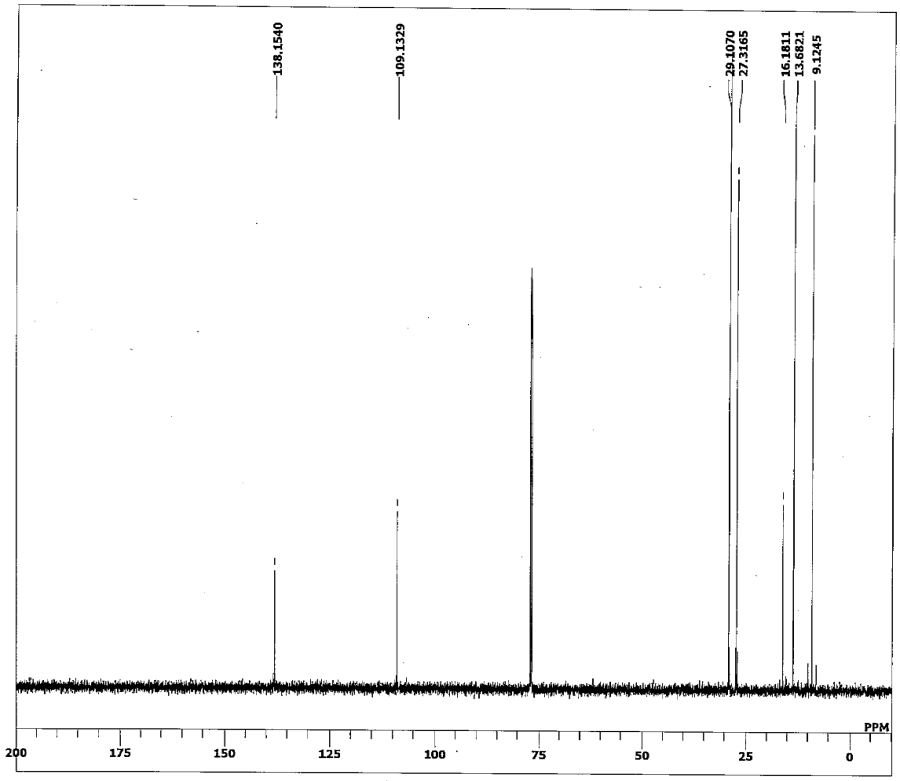
D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1335-H.als
single_pulse



DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	18-09-2012 04:27:43
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	27.9 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.52 Hz
RGAIN	32

5f

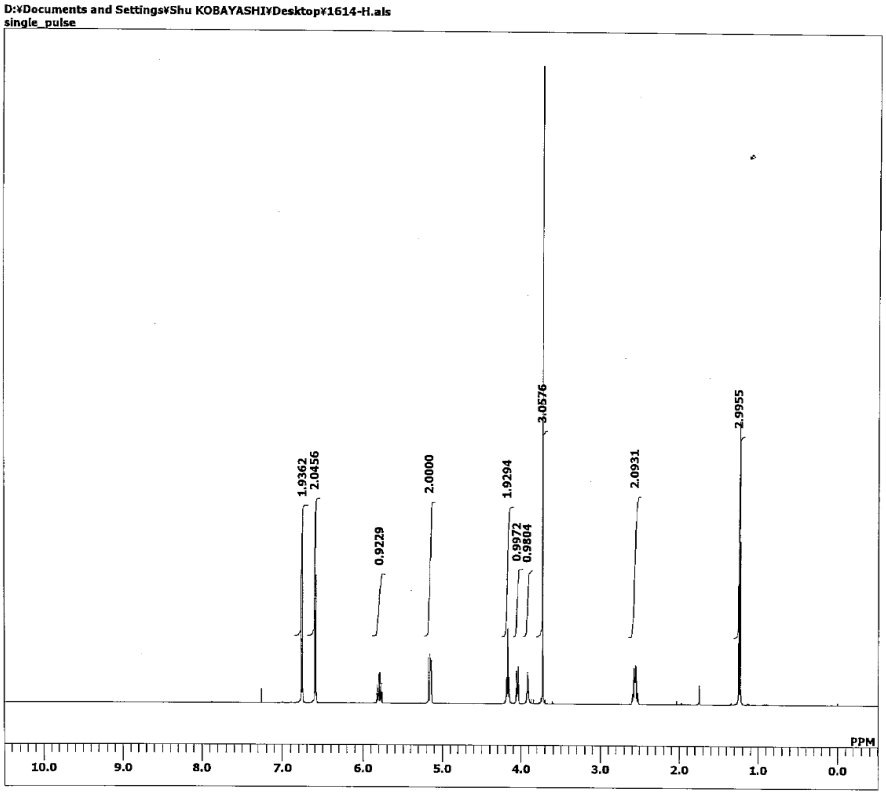
D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1335-C.als



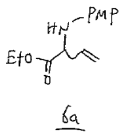
DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	18-09-2012 04:33:51
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	81
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	28.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.52 Hz
RGAIN	60

5f

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1614-H.als
single_pulse

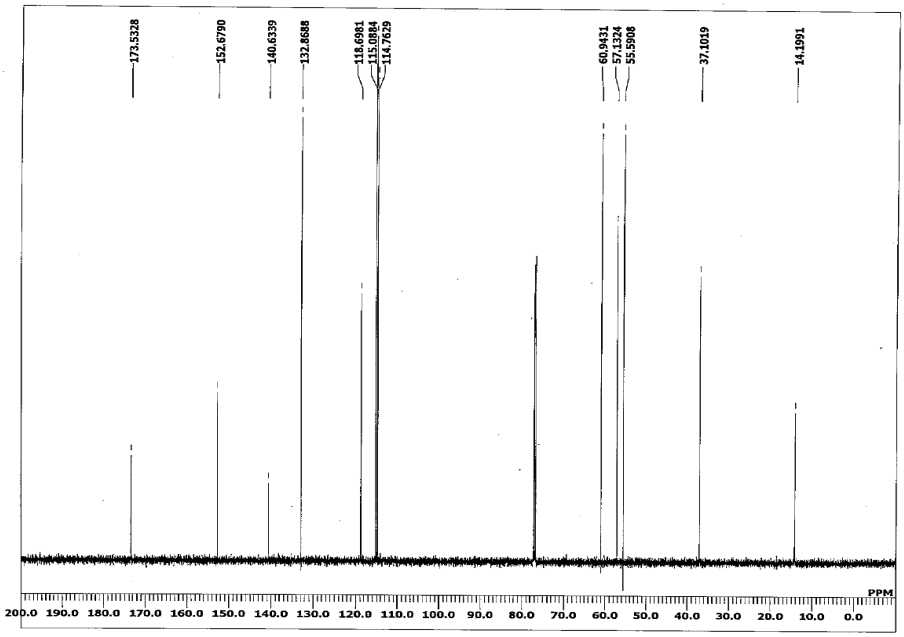


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	18-03-2013 01:38:08
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.0 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

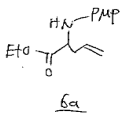


6a

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1614-C.als

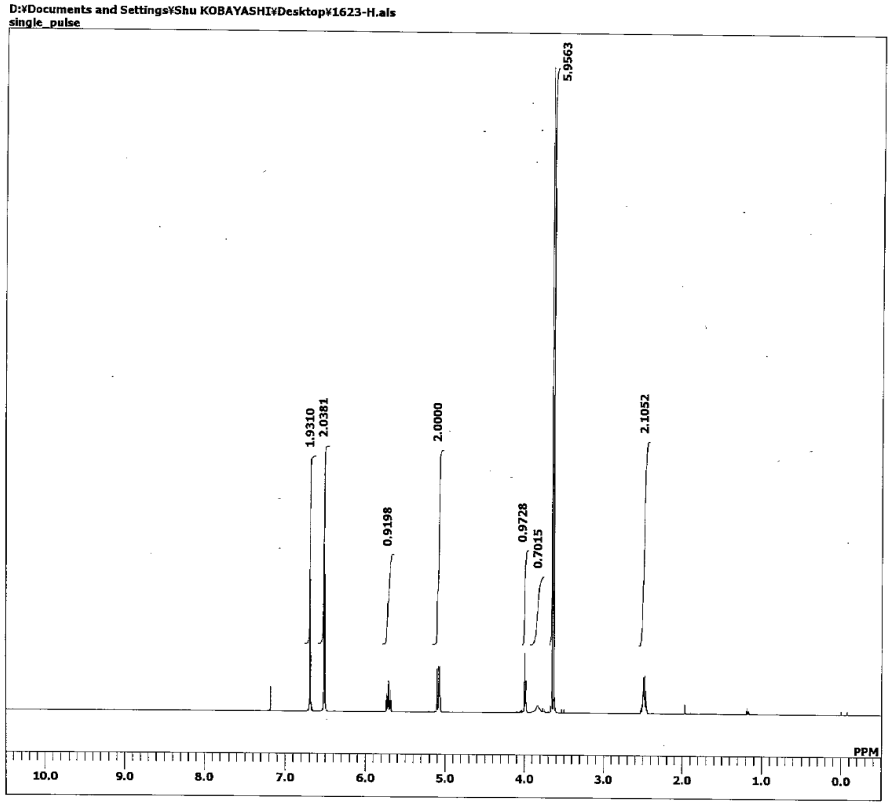


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	18-03-2013 01:46:53
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	122
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

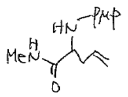


6a

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1623-H.als
single_pulse

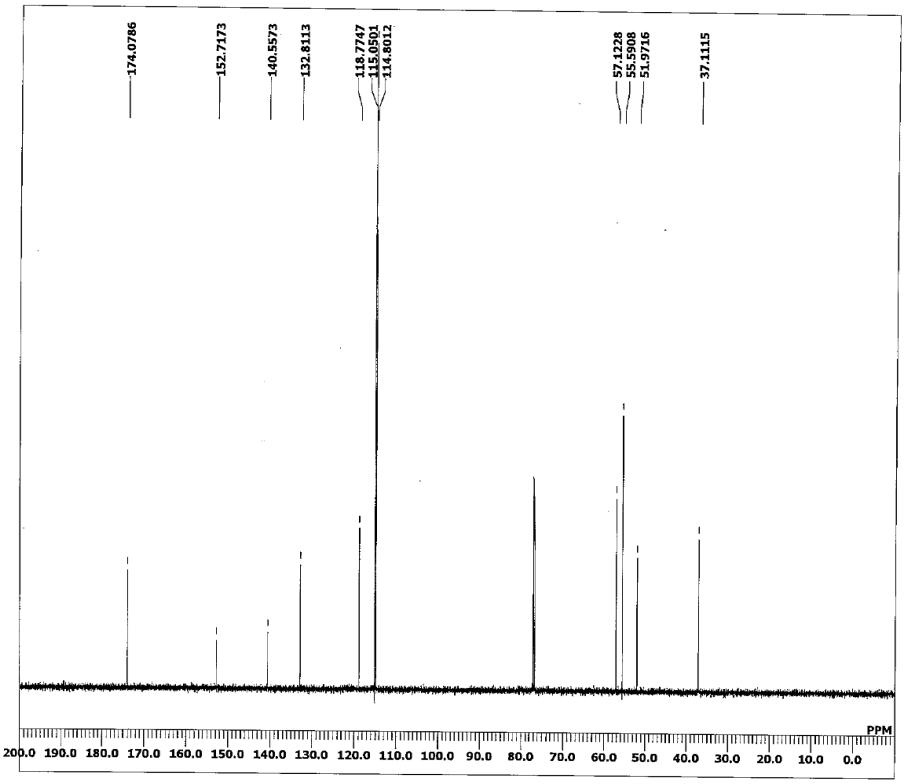


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	18-03-2013 08:35:52
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

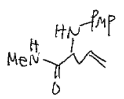


6e

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1623-C.als

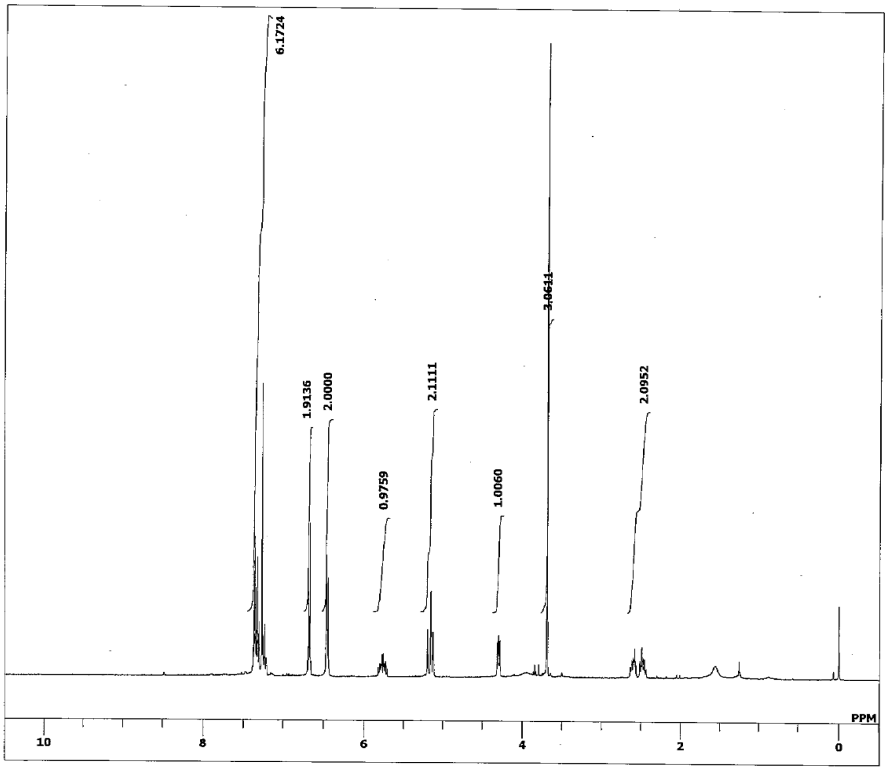


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	18-03-2013 08:42:56
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	102
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

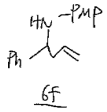


6e

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2129-H-moredry.als

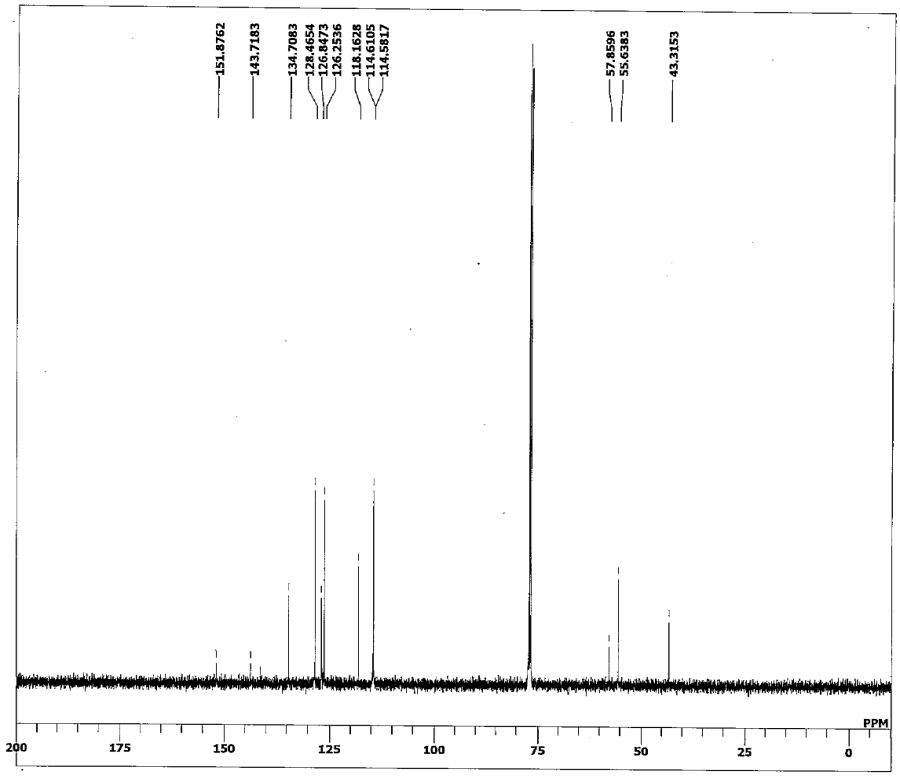


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-01-2014 01:13:55
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	399.78 MHz
OBSET	4.19 KHz
OBFIN	7.29 Hz
POINT	13107
FREQU	6002.31 Hz
SCANS	8
ACQTM	2.1837 sec
PD	2.0000 sec
PW1	6.62 usec
IRNUC	1H
CTEMP	19.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

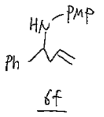


6f

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2136-C-true-1.jdf

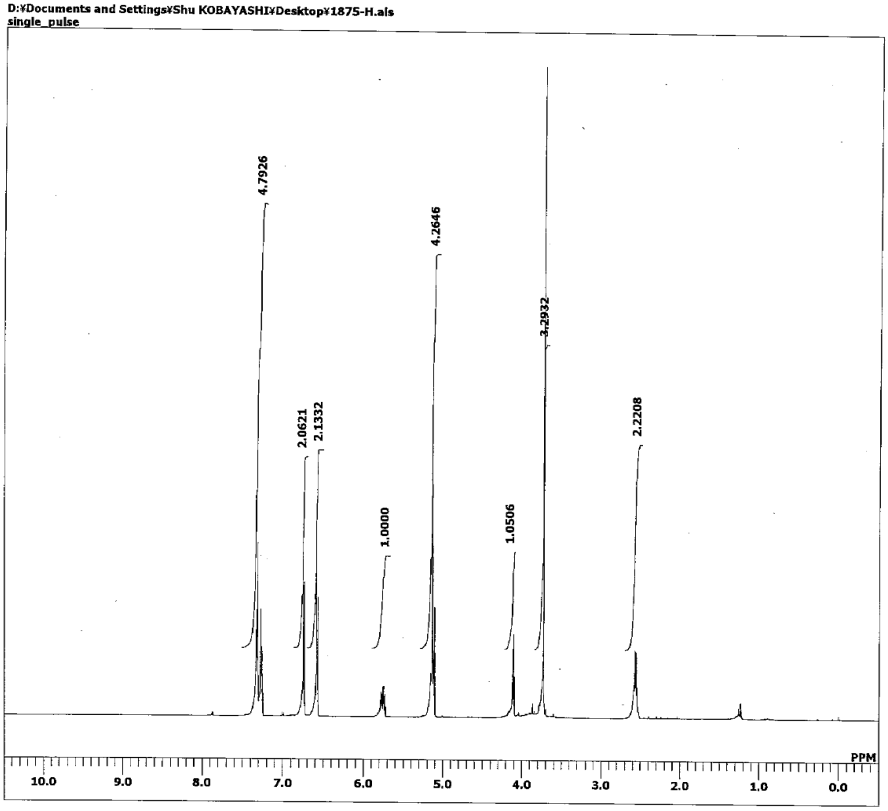


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	07-01-2014 23:50:25
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	32768
FREQU	39062.50 Hz
SCANS	1000
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	20.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	46

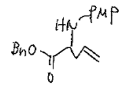


6f

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1875-H.als
single_pulse

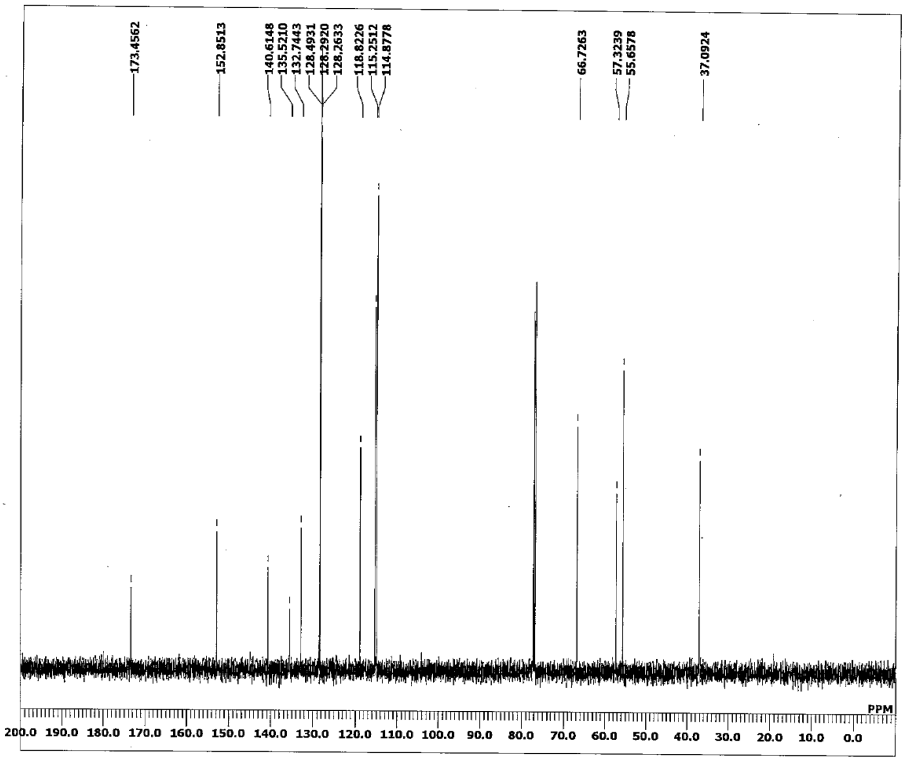


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	05-08-2013 02:51:59
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	29.6 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

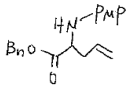


6i

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1875-C.als

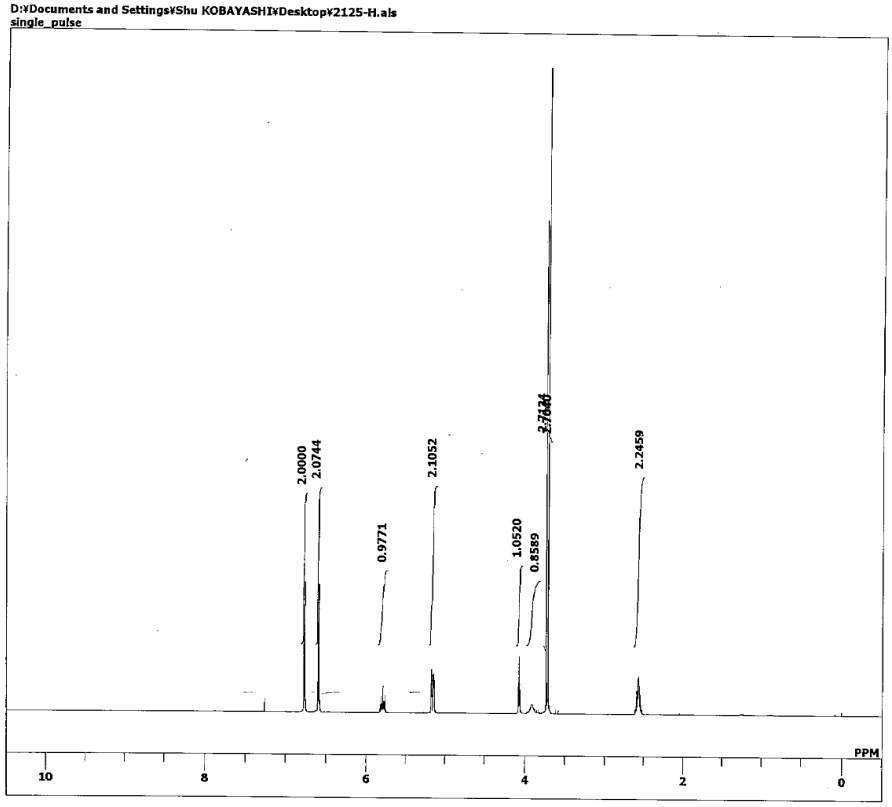


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	05-08-2013 02:58:45
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	97
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	30.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

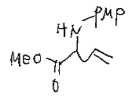


6i

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2125-H.als
single_pulse

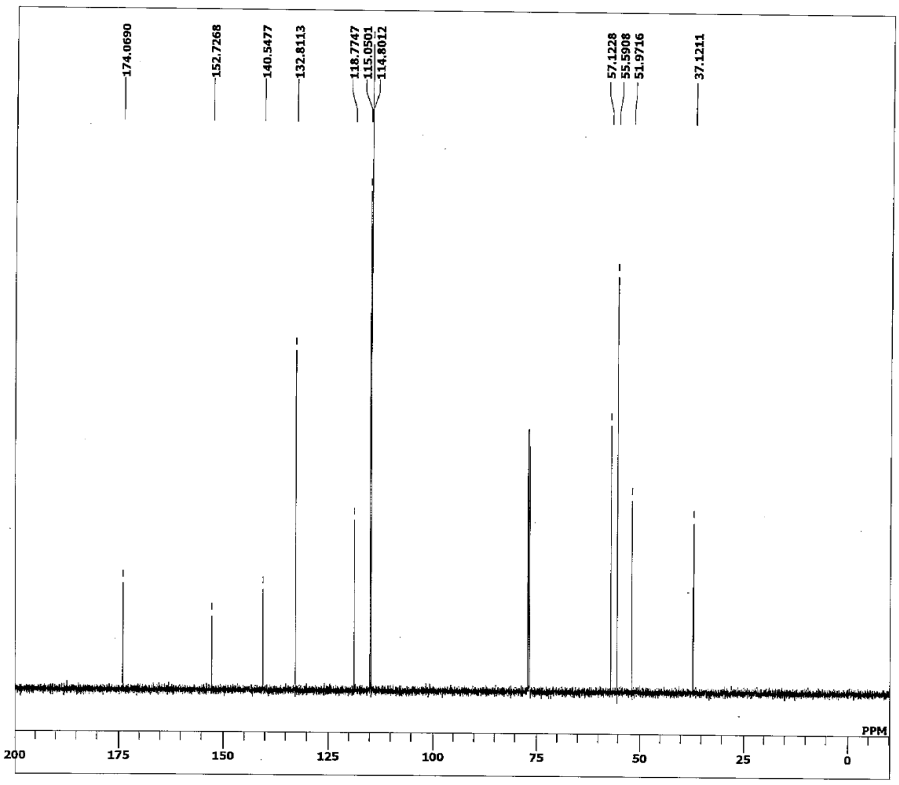


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	23-12-2013 06:43:49
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.8 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	34

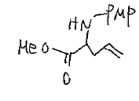


6j

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2125-C.als

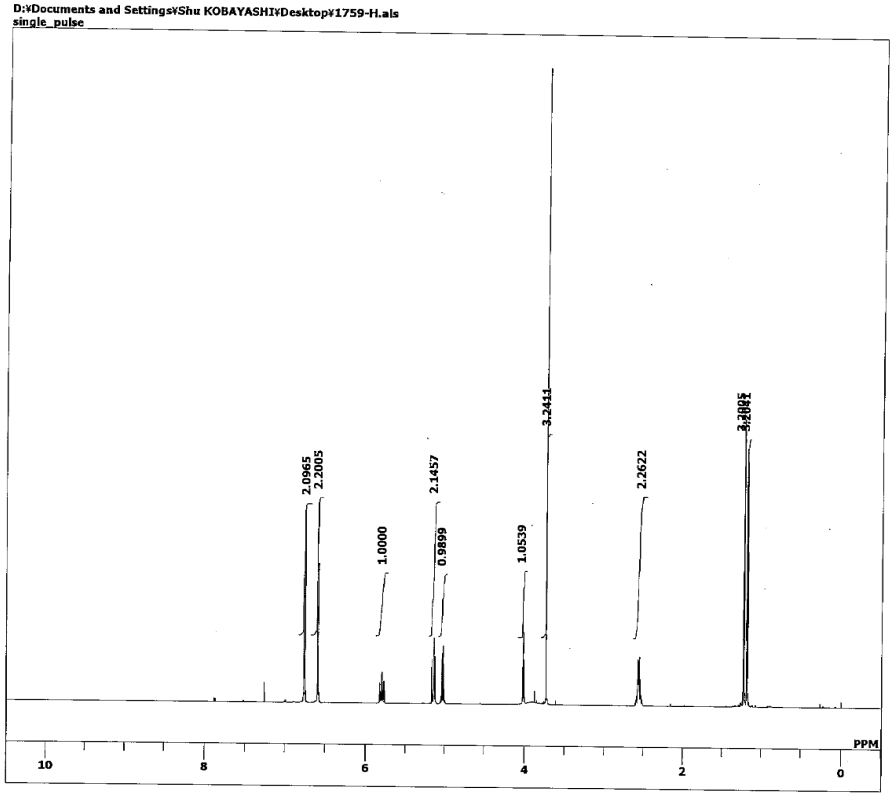


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-12-2013 06:50:33
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	97
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

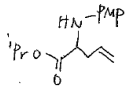


6j

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1759-H.als
single_pulse

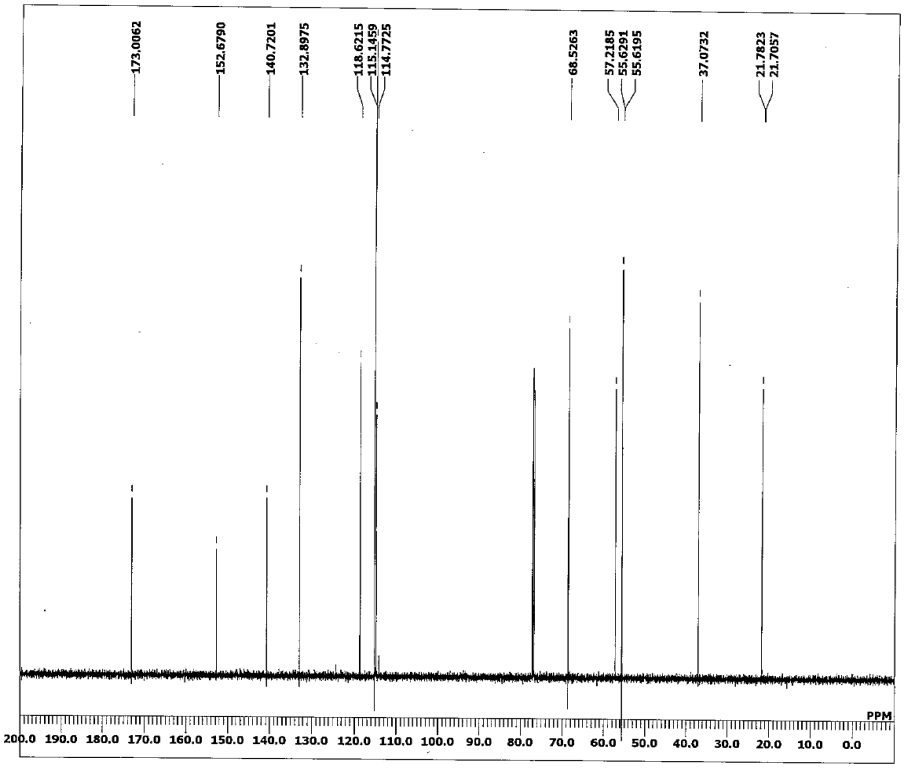


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	04-06-2013 03:43:54
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	25.4 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	32

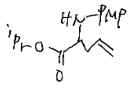


6k

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1759-C.als

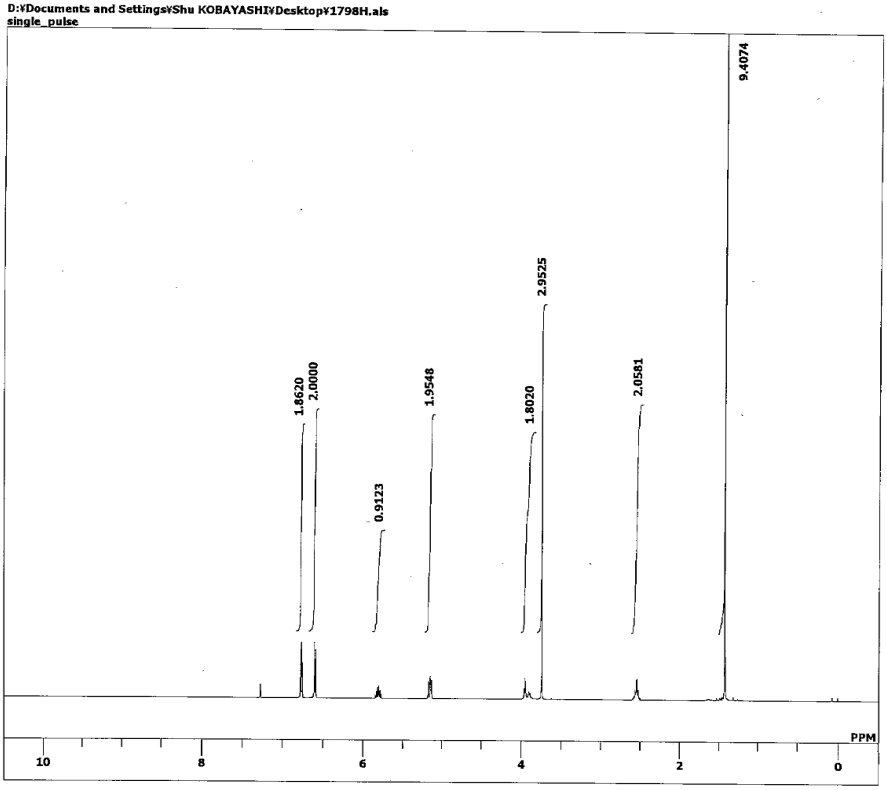


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	04-06-2013 03:53:41
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	165
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	26.4 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

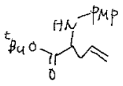


6k

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1798H.als
single_pulse

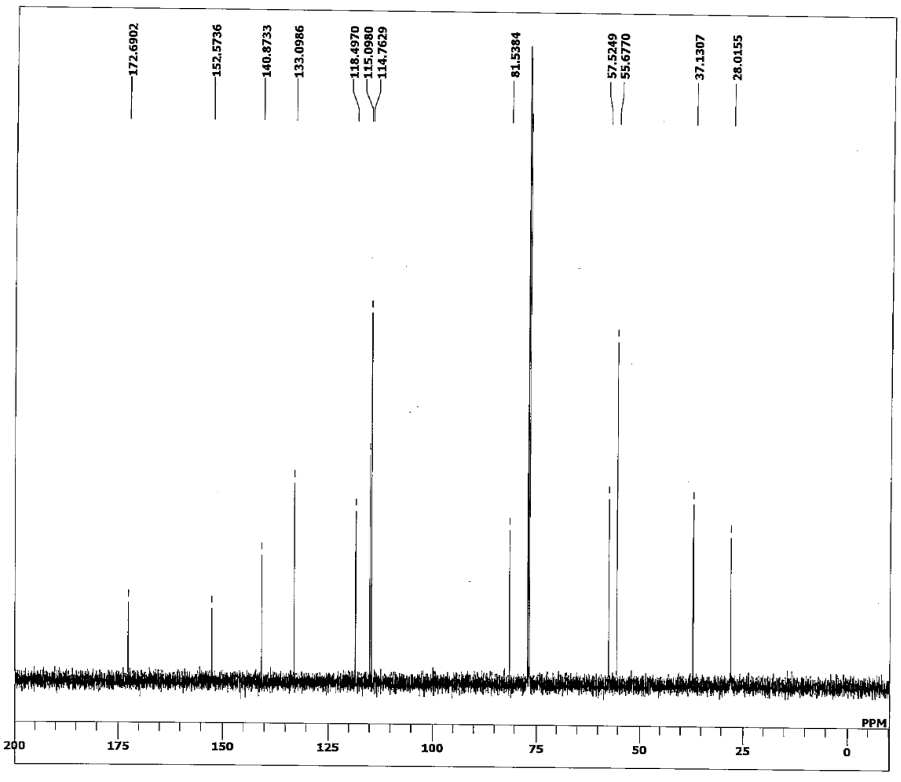


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	21-12-2013 08:14:33
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

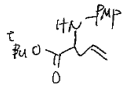


6l

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1798C.als

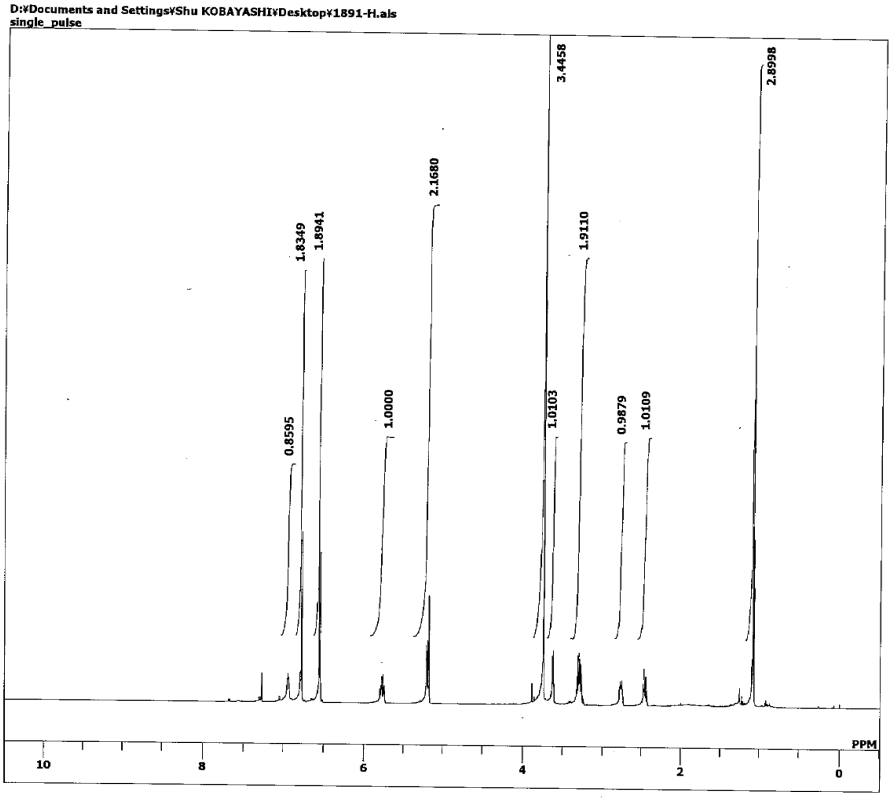


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	21-12-2013 08:22:35
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	125
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

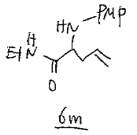


6l

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1891-H.als
single_pulse

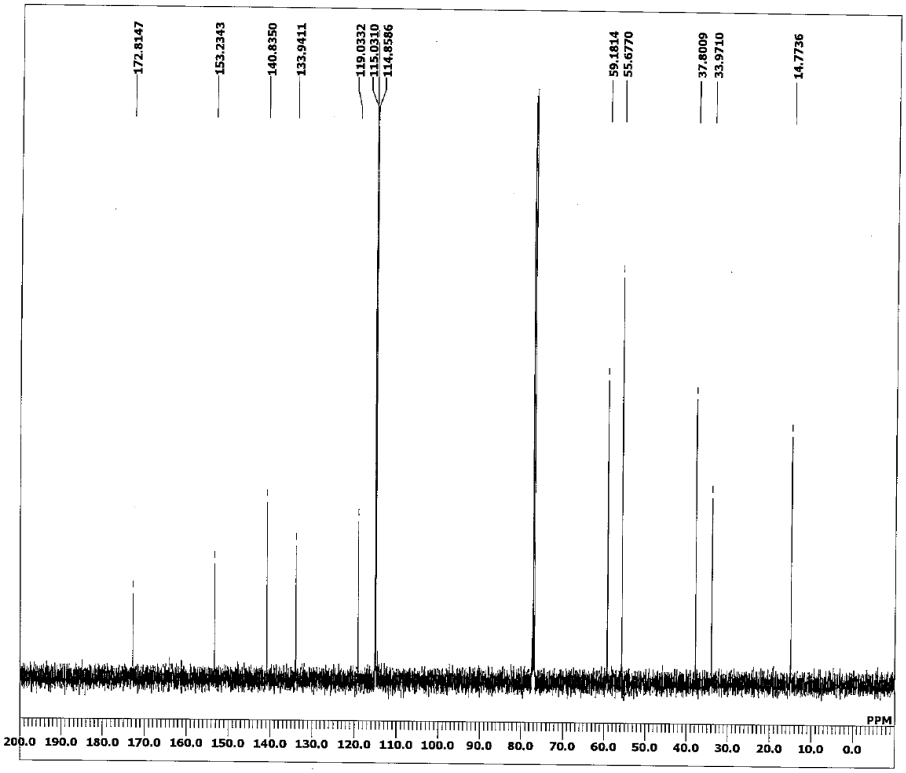


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	22-08-2013 08:07:41
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	27.7 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

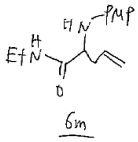


6m

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1891-C.als

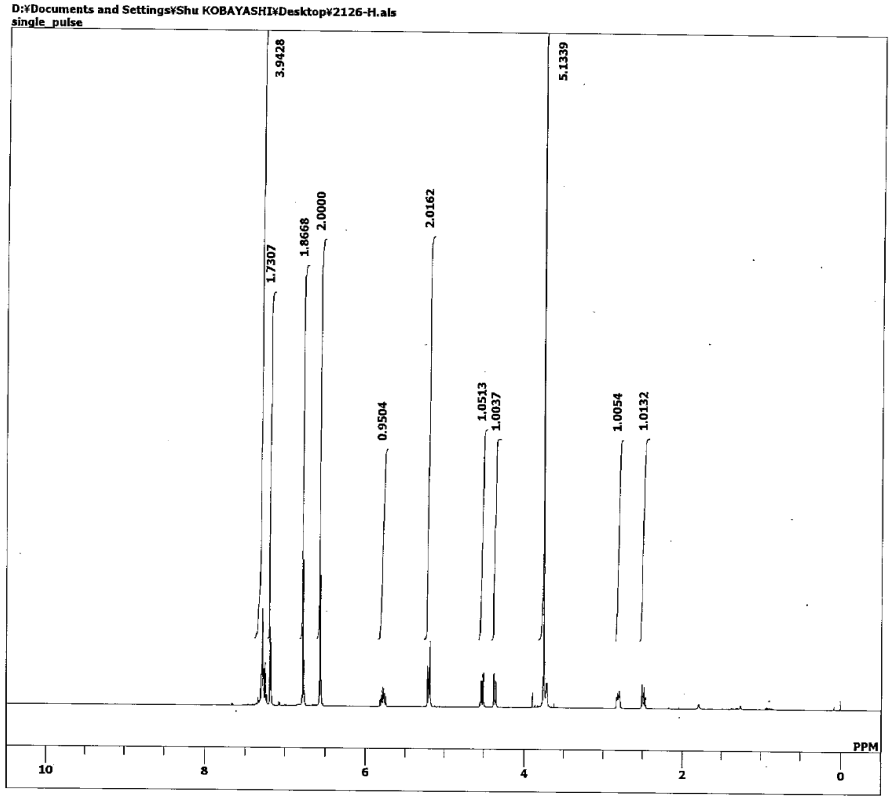


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	22-08-2013 08:15:49
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	128
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	28.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

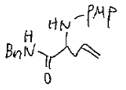


6m

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2126-H.als
single_pulse

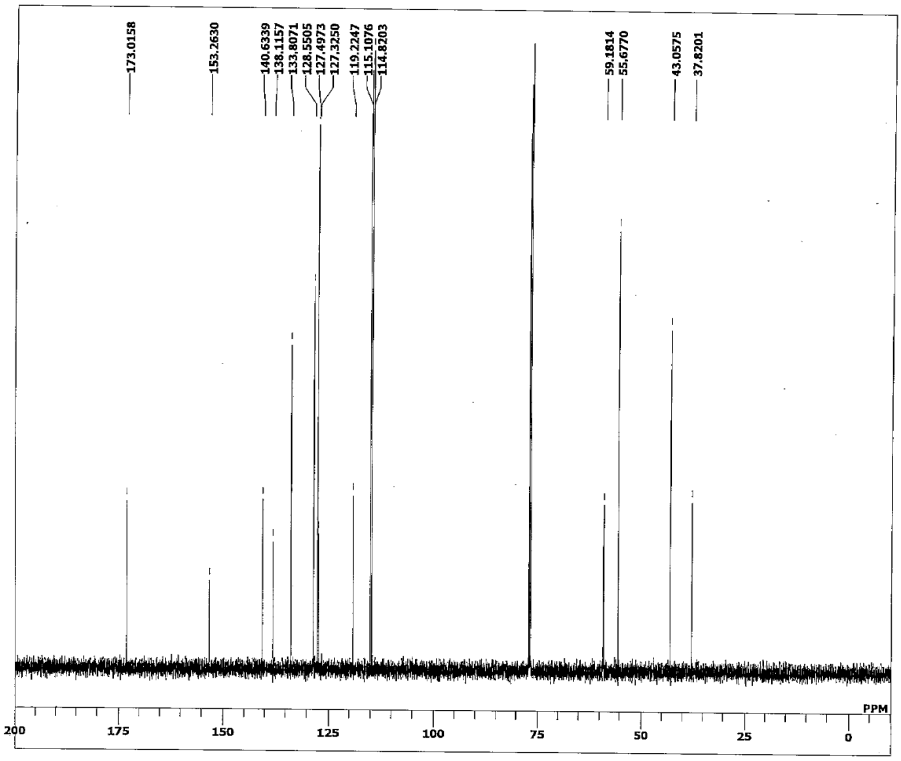


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	23-12-2013 06:54:10
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

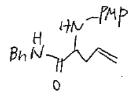


6h

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2126-C.als

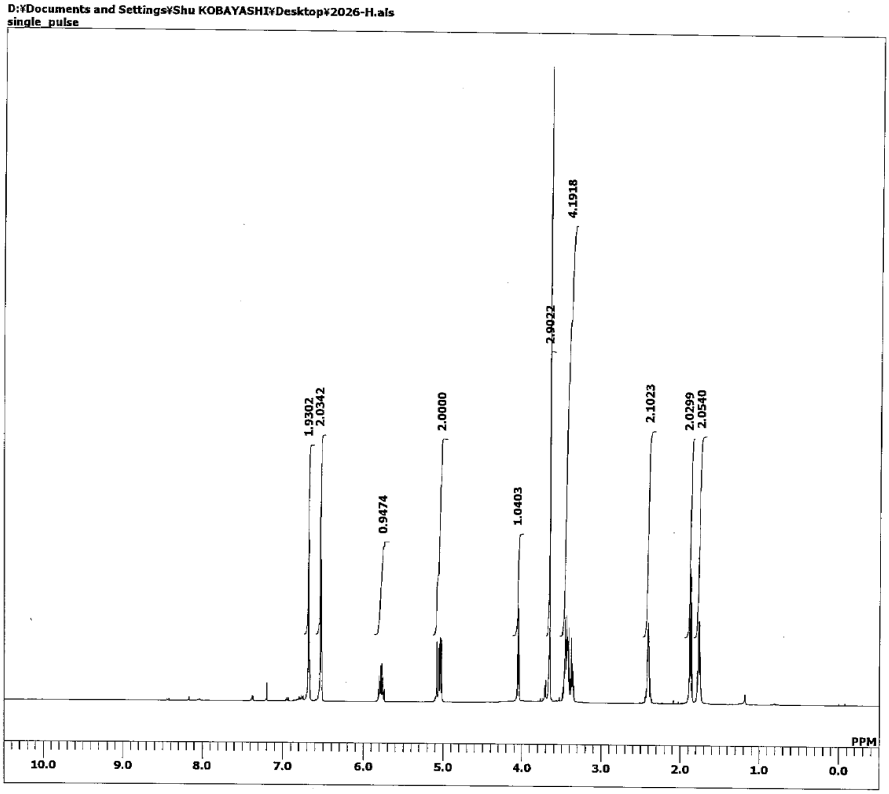


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-12-2013 07:02:32
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	134
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.7 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	58

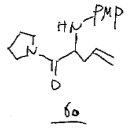


6h

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2026-H.als
single_pulse

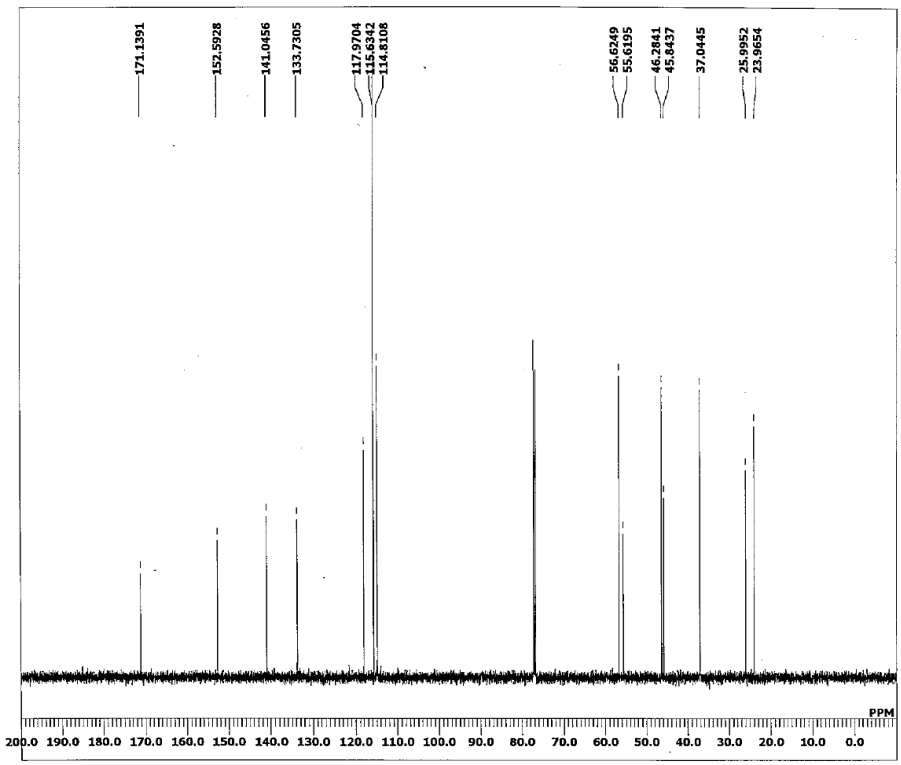


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	09-10-2013 03:45:29
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	27.3 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.42 Hz
RGAIN	34

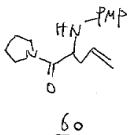


60

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2026-C.als

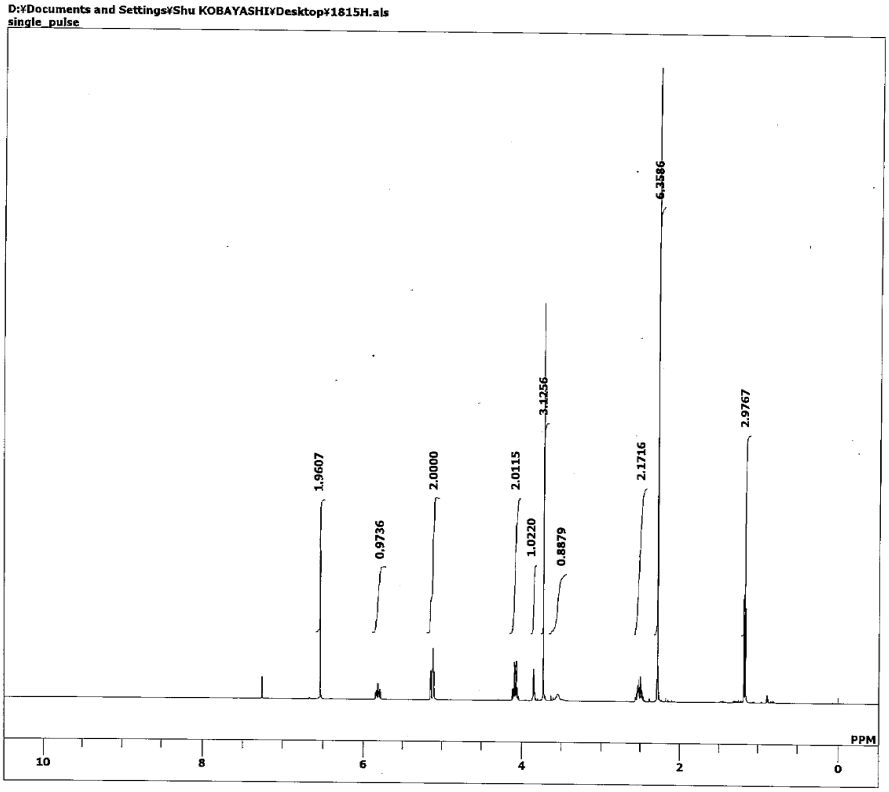


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	09-10-2013 03:53:25
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	100
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	27.9 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.42 Hz
RGAIN	60

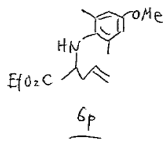


60

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1815H.als
single_pulse

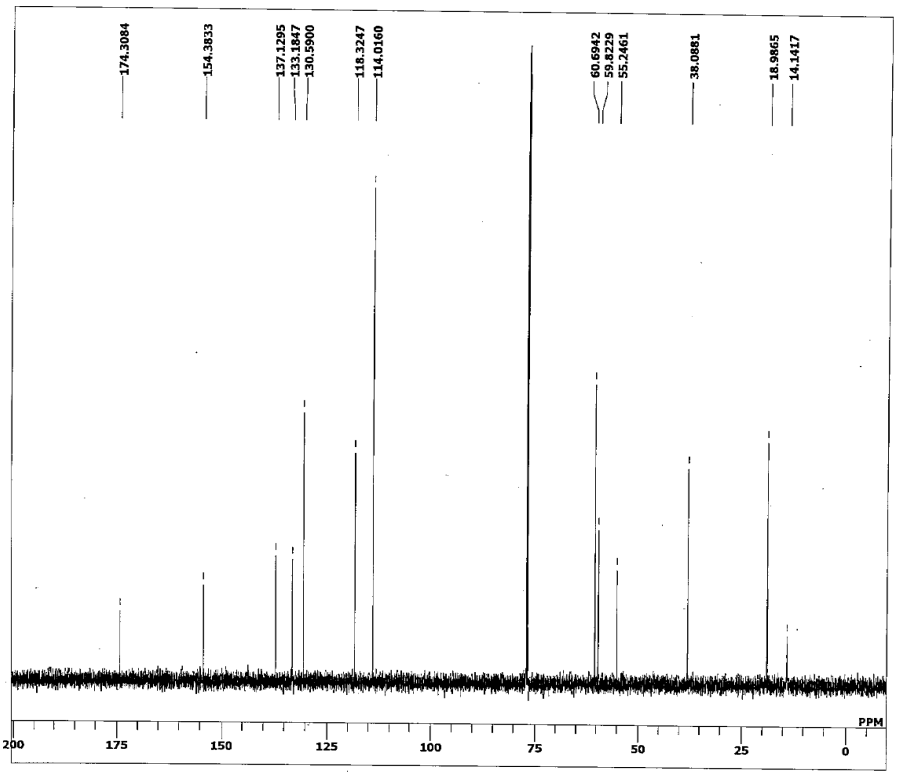


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	21-12-2013 08:25:56
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36

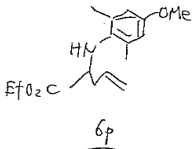


6p

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1815C.als

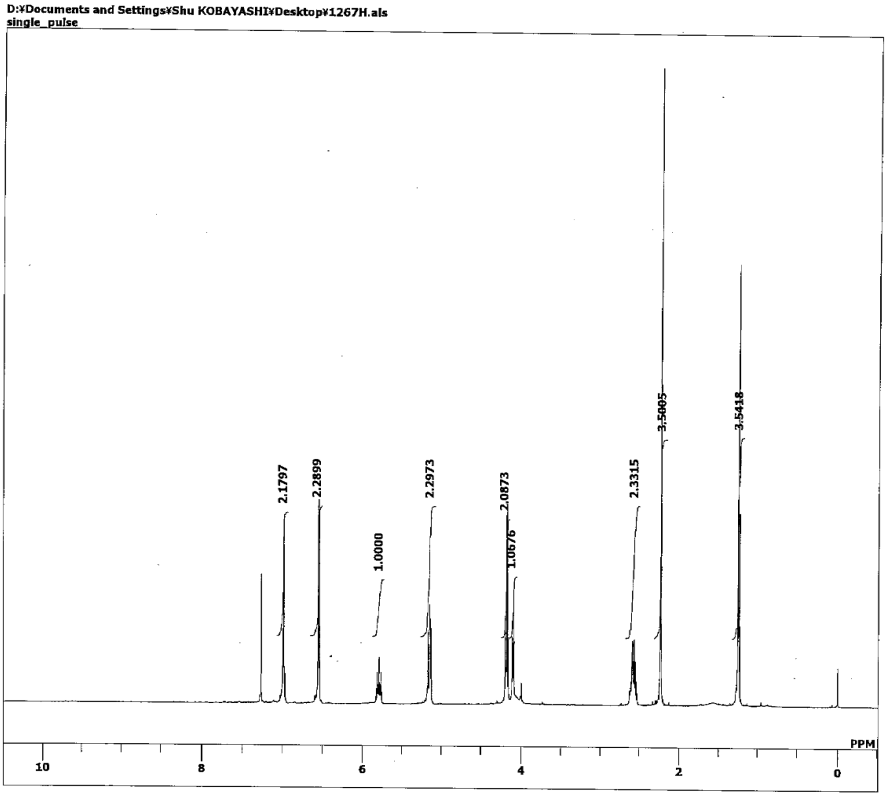


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	21-12-2013 08:33:46
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	122
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

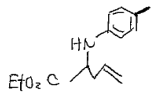


6p

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1267H.als
single_pulse

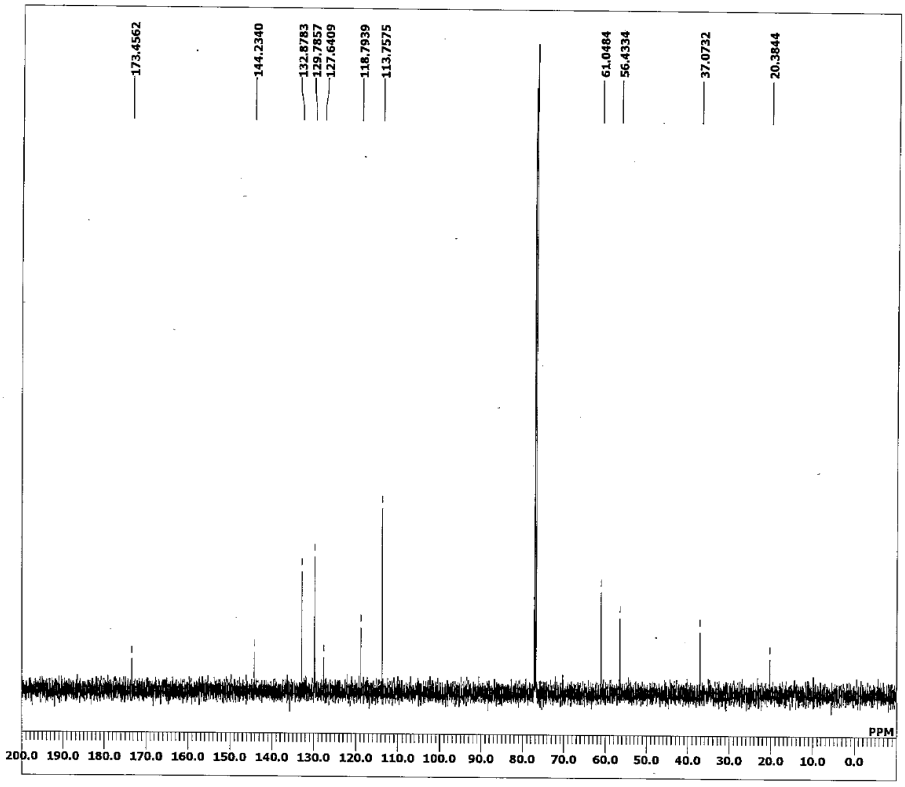


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	21-12-2013 08:37:48
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.2 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	42

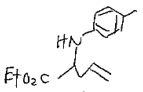


6r

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1267C.als

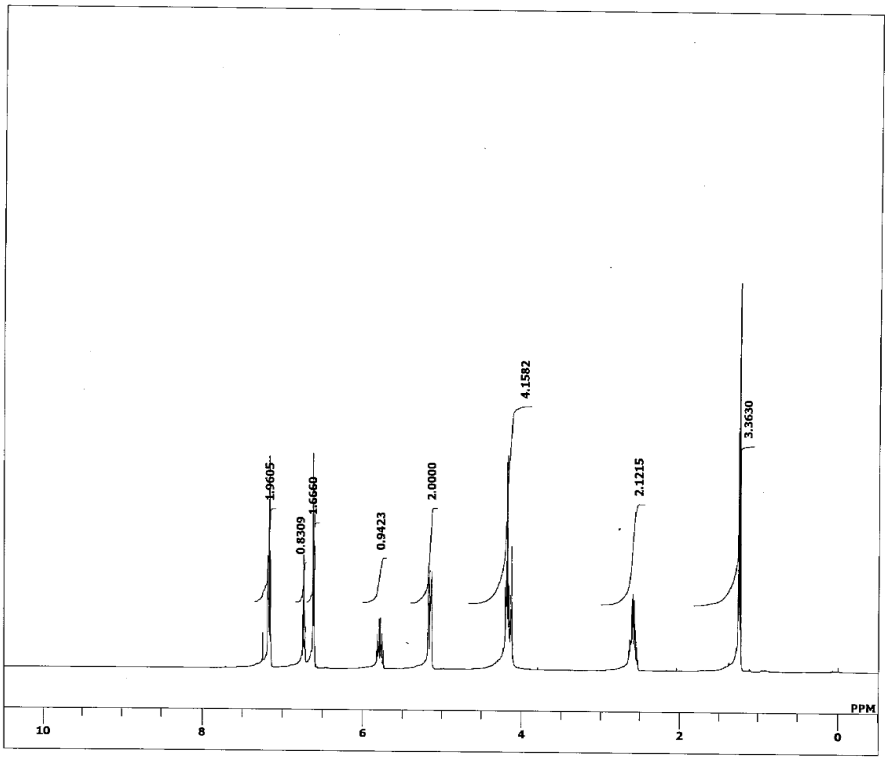


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	21-12-2013 08:46:55
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	150
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

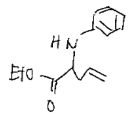


6r

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2135-H-PTLC2-1.als

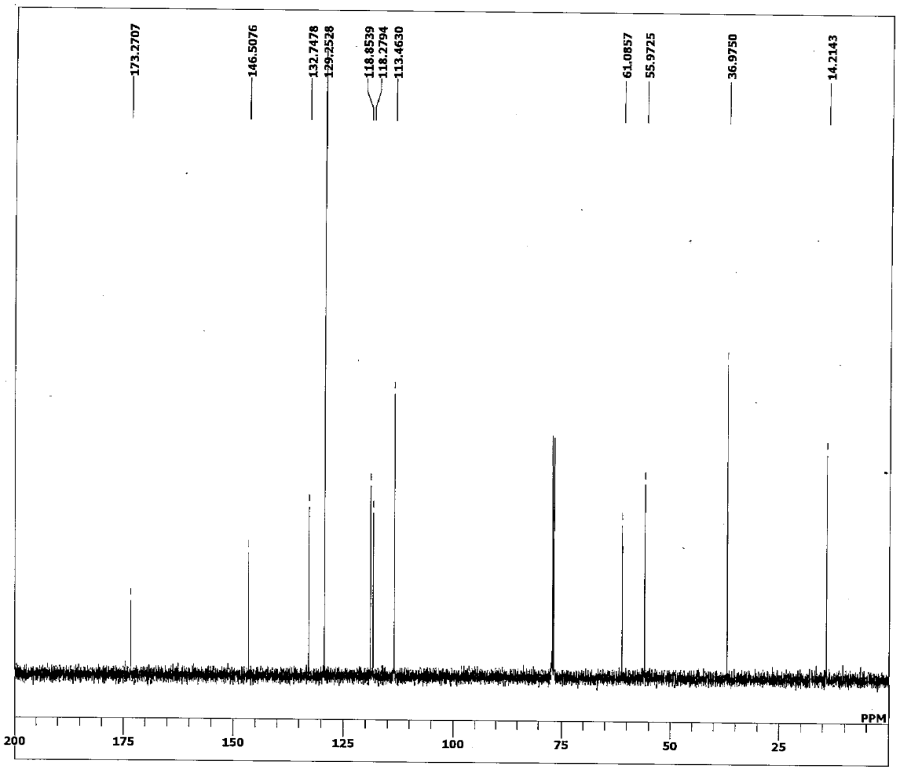


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	08-01-2014 08:22:34
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	10485
FREQU	5943.35 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	3.38 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	30

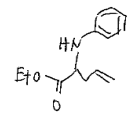


6s

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2135-C-PTLC2-1.als

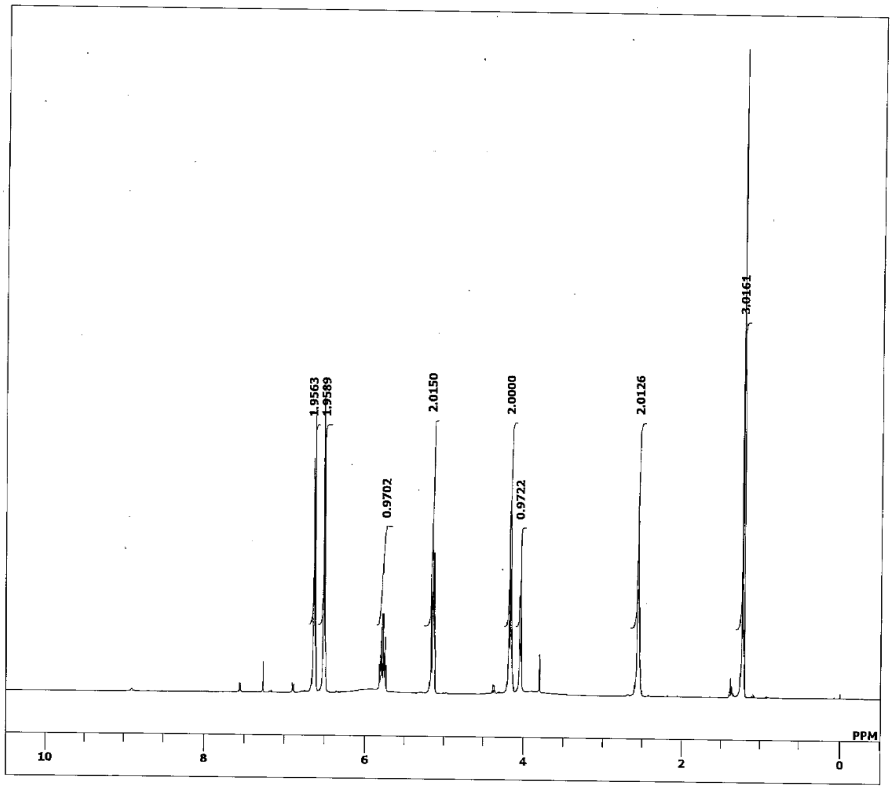


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	08-01-2014 08:27:07
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	20970
FREQU	24999.24 Hz
SCANS	82
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	20.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	46

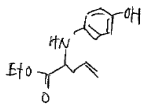


6s

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2136-H-repurified-1.als

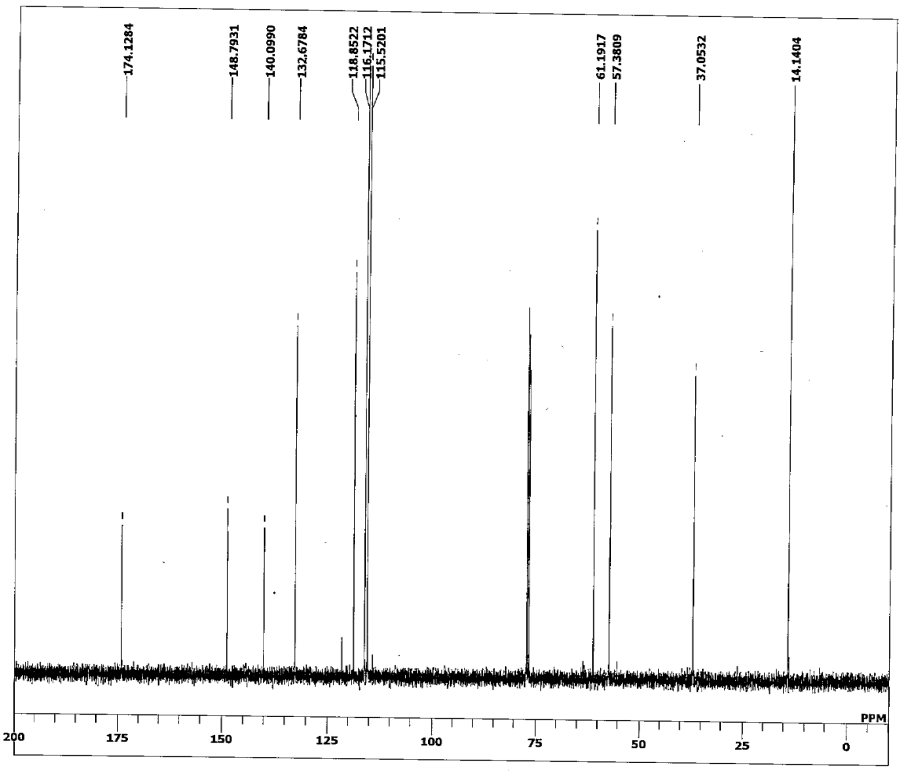


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	08-01-2014 08:31:27
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	13107
FREQU	7429.31 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	3.38 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	24

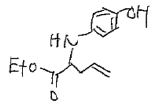


6t

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2136-C-repurified-1.als

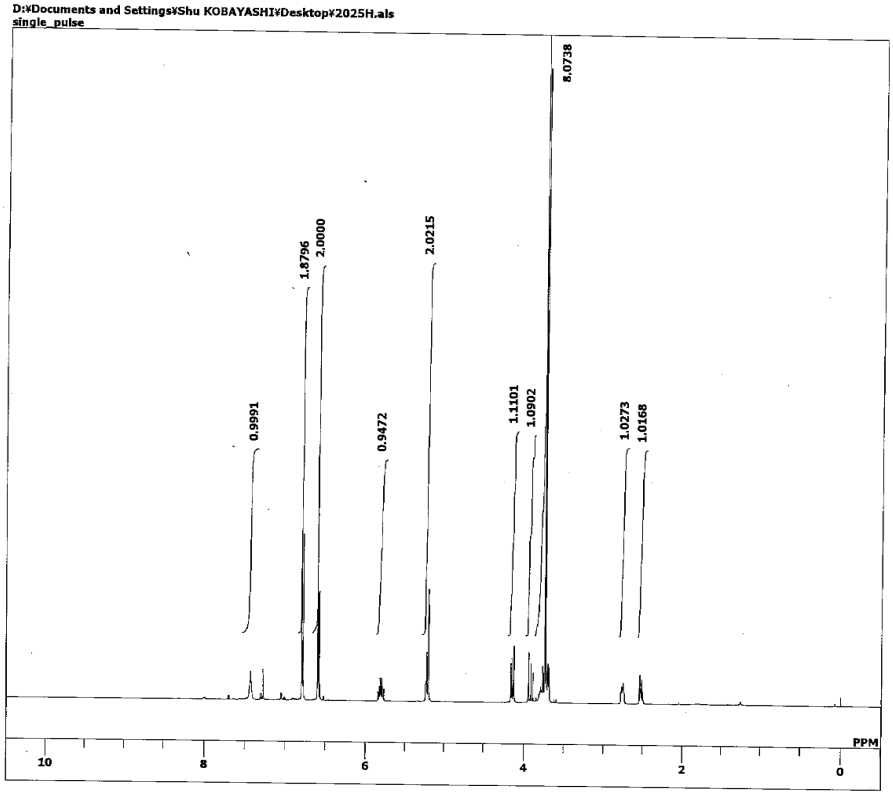


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	08-01-2014 08:36:18
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	88
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	20.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	48

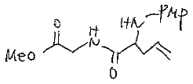


6t

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2025H.als
single_pulse

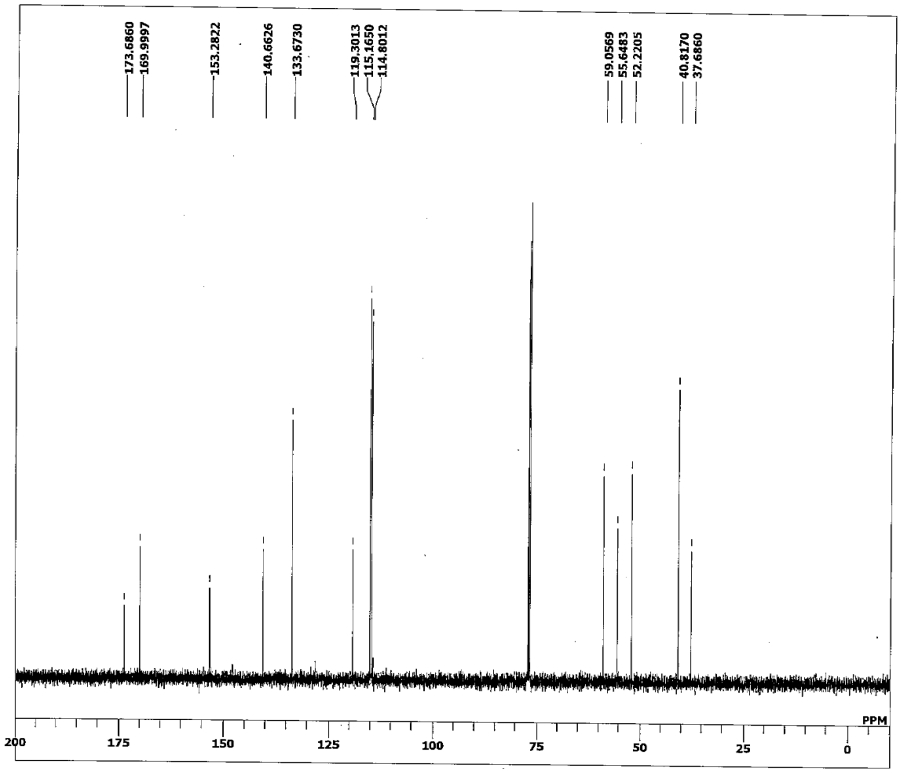


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	23-12-2013 07:05:52
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.7 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38

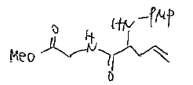


6v

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2025C.als

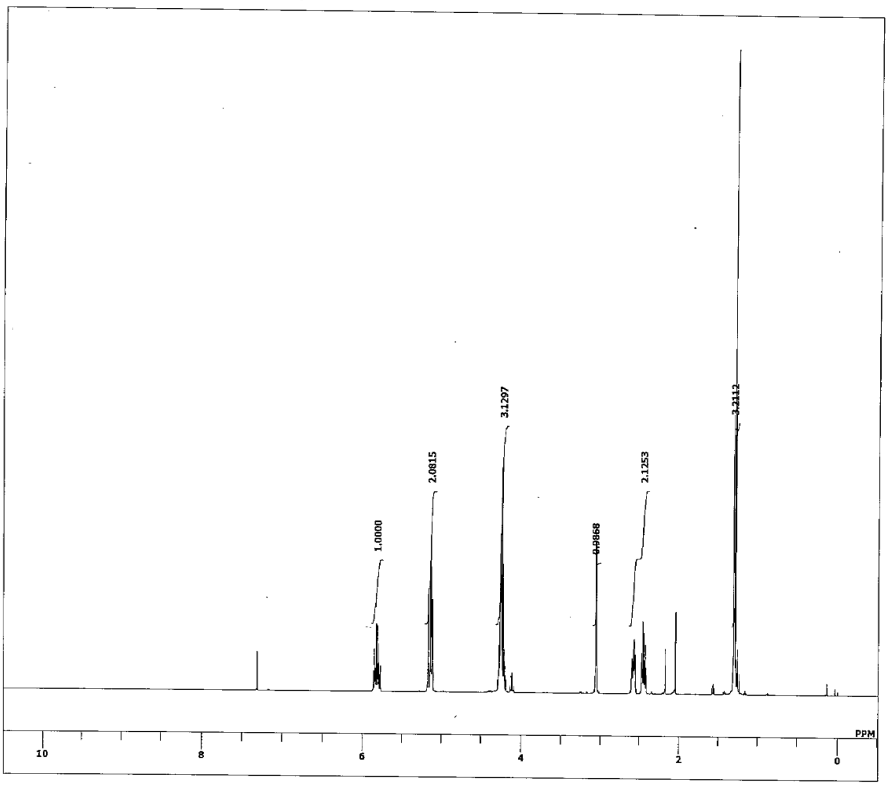


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	23-12-2013 07:13:59
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	127
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	22.8 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60

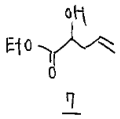


6v

D:¥Documents and Settings¥Kobayashilab¥Desktop¥2143-H-1.jdf

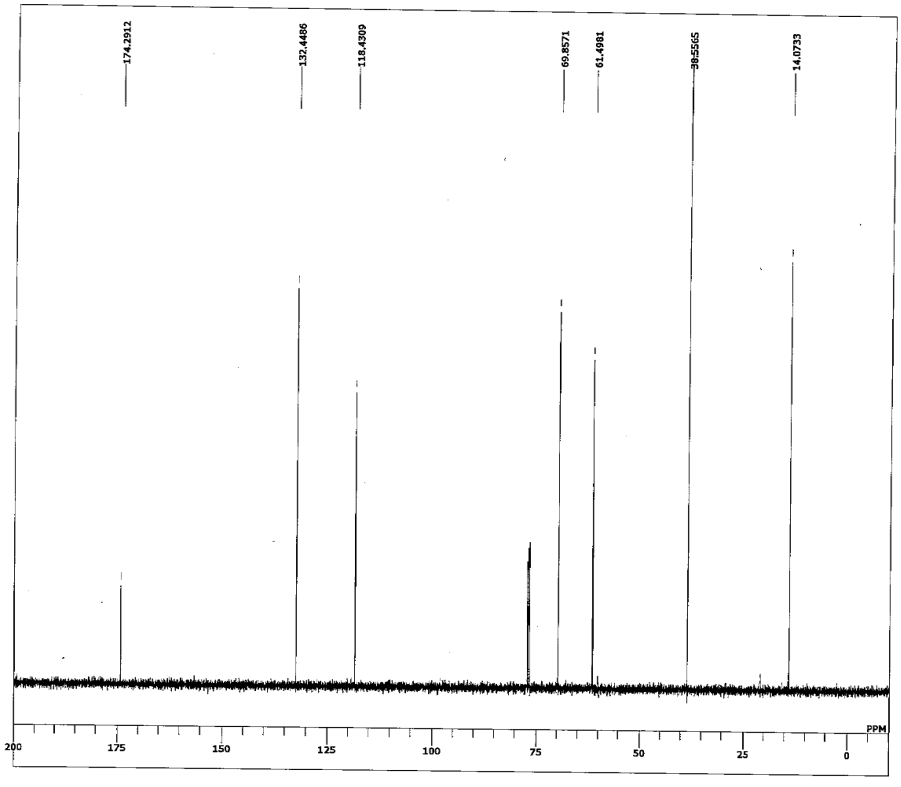


DFILE	D:¥Documents and Settings¥Kobayashilab¥Desktop¥2143-H
COMNT	
DATIM	14-01-2014 13:40:03
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	16384
FREQU	9286.78 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	3.38 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	22

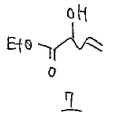


7

D:¥Documents and Settings¥Kobayashilab¥Desktop¥2143-C-1.jdf

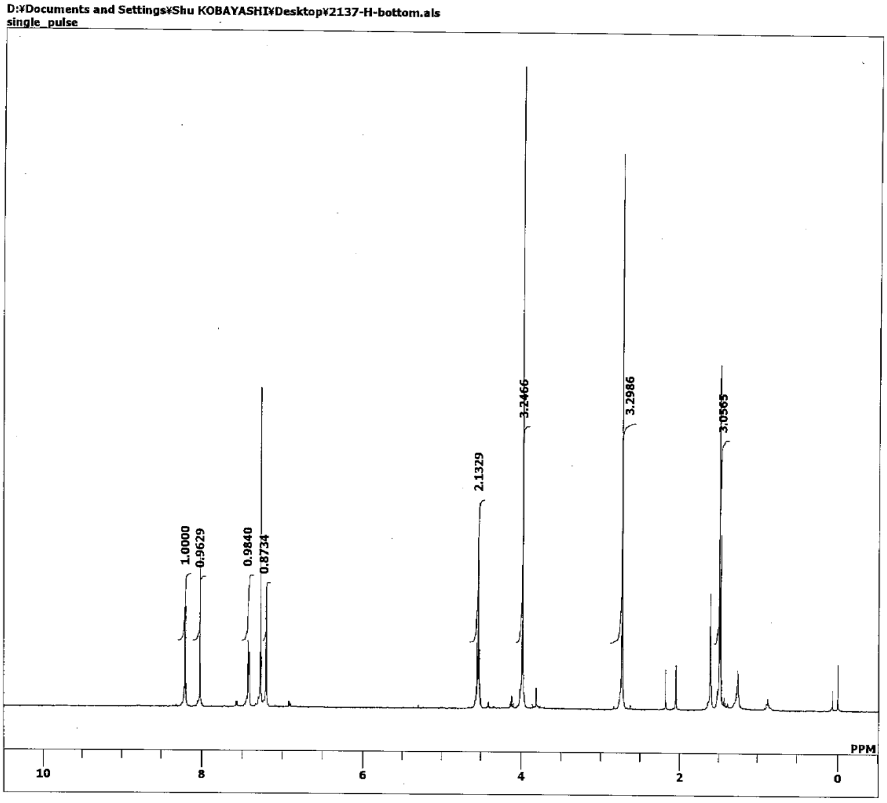


DFILE	D:¥Documents and Settings¥Kobayashilab¥Desktop¥2143-C
COMNT	
DATIM	14-01-2014 13:42:45
OBNUC	13C
EXMOD	13C NMR.ex2
OBFRQ	124.51 MHz
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	32768
FREQU	39062.50 Hz
SCANS	27
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	20.5 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	48

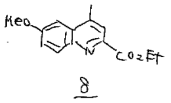


7

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2137-H-bottom.als
single_pulse

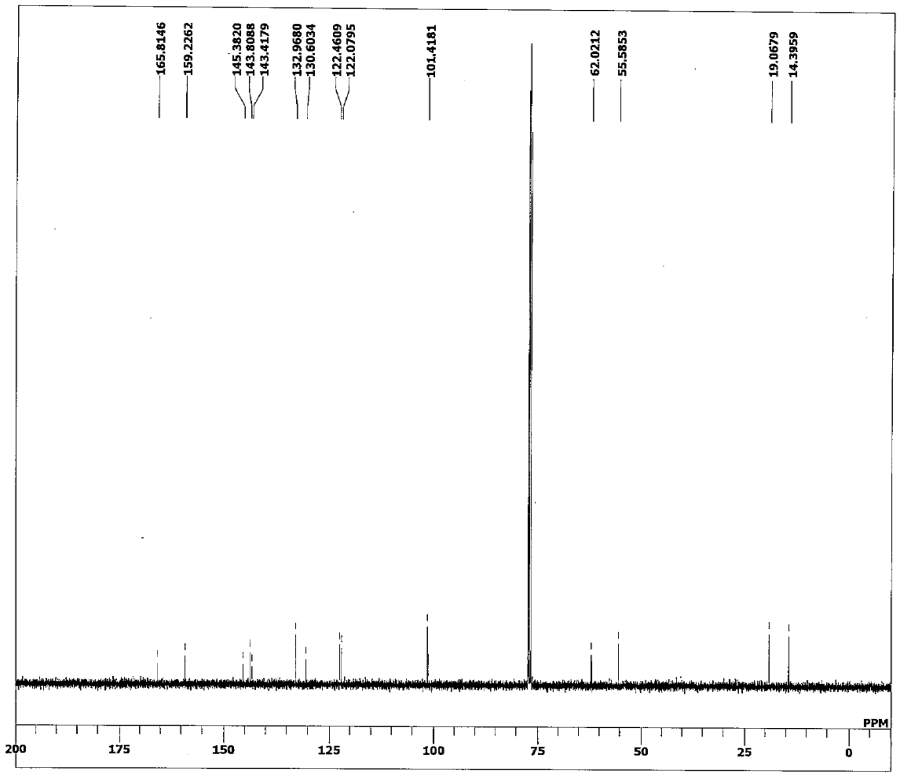


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	single_pulse
DATIM	10-01-2014 06:18:49
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	21.7 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	46

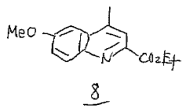


8

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2137-C-bottom.als

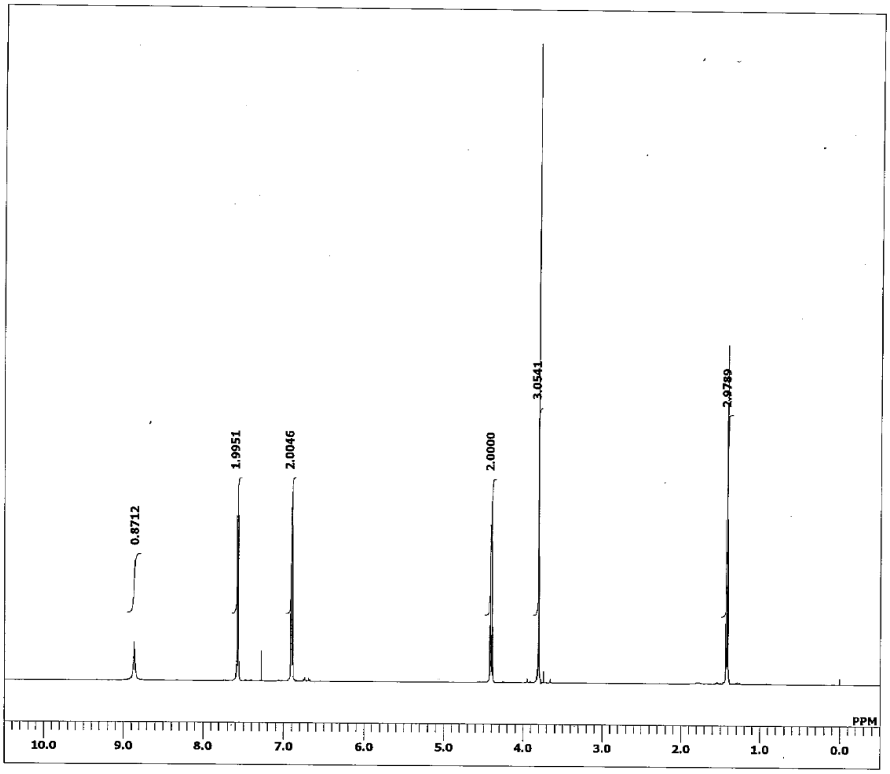


DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	10-01-2014 20:59:36
OBNUC	13C
EXMOD	single_pulse_dec
OBFRQ	100.53 MHz
OBSET	5.35 KHz
OBFIN	5.86 Hz
POINT	26214
FREQU	25125.24 Hz
SCANS	1000
ACQTM	1.0433 sec
PD	2.0000 sec
PW1	3.50 usec
IRNUC	1H
CTEMP	21.6 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	56

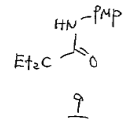


8

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥2136-H-1.als



DFILE	D:¥Documents and Settings¥Shu KOBAYASHI
COMNT	
DATIM	07-01-2014 22:44:01
OBNUC	1H
EXMOD	1H NMR.ex2
OBFRQ	495.13 MHz
OBSET	4.38 KHz
OBFIN	9.64 Hz
POINT	10485
FREQU	5943.35 Hz
SCANS	8
ACQTM	1.7642 sec
PD	5.0000 sec
PW1	3.38 usec
IRNUC	1H
CTEMP	20.3 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	30



9

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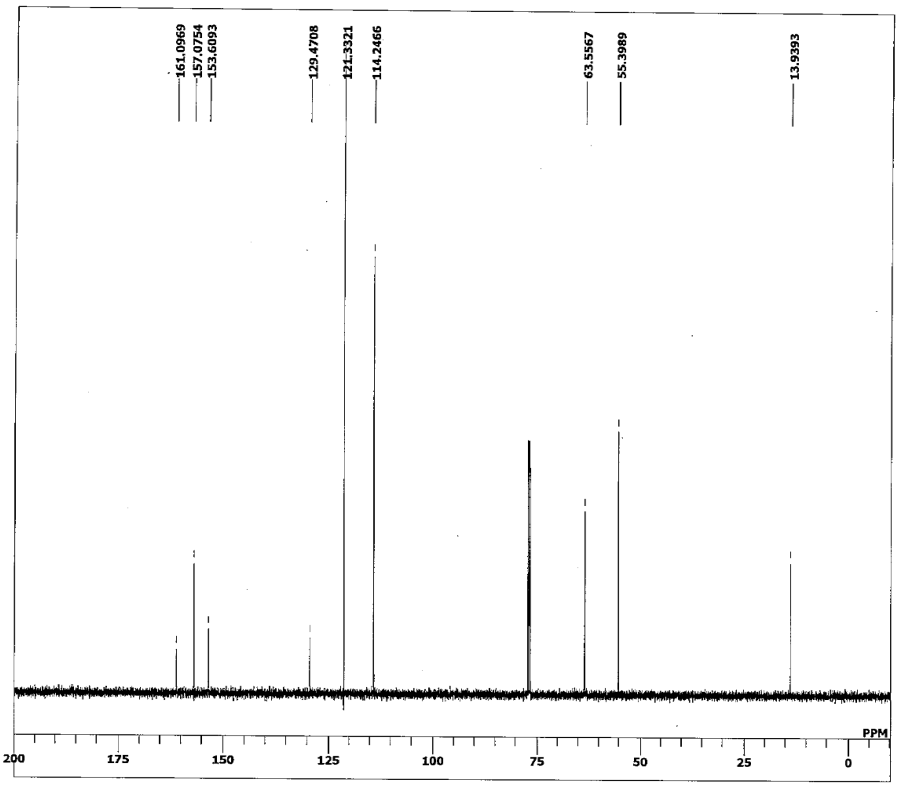

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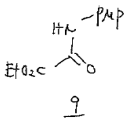
OBSET	3.45 KHz
OBFIN	6.00 Hz
POINT	26214
FREQU	31249.52 Hz
SCANS	85
ACQTM	0.8389 sec
PD	2.0000 sec
PW1	3.42 usec
IRNUC	1H
CTEMP	20.3 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	46



9

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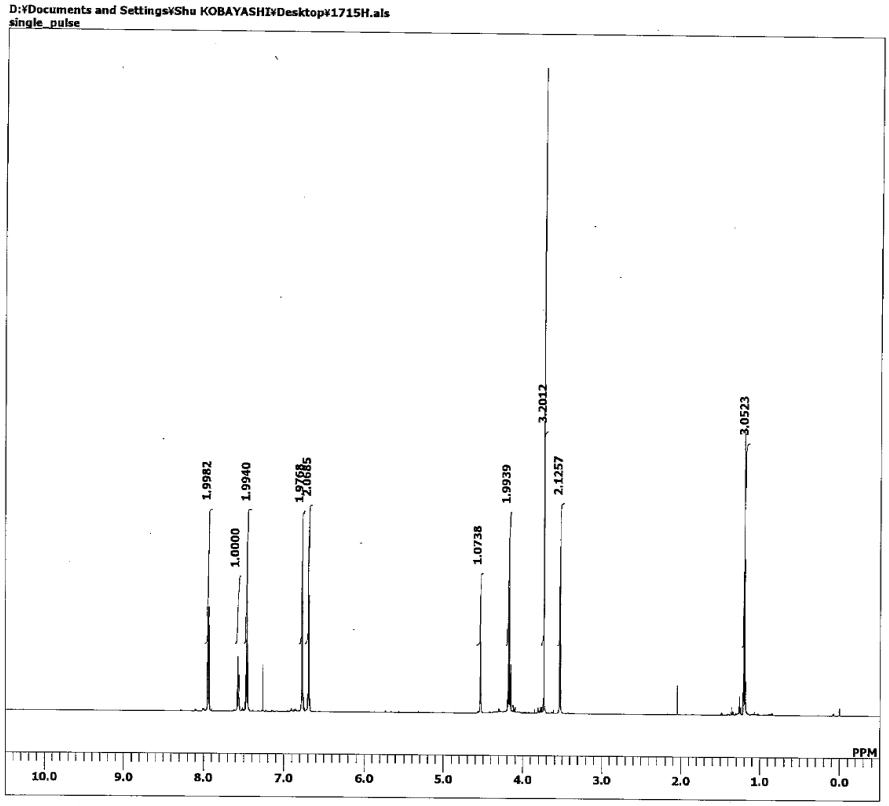

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EXMOD	single_pulse.ex2
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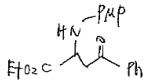
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.1 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	36



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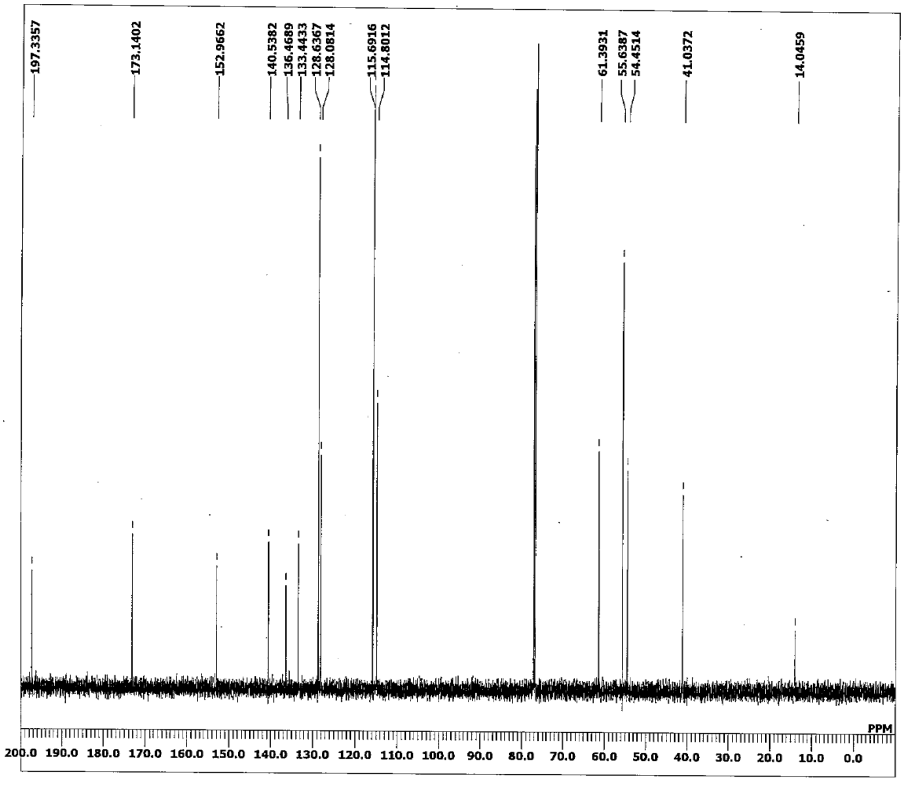
D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1715C.als



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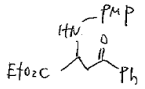
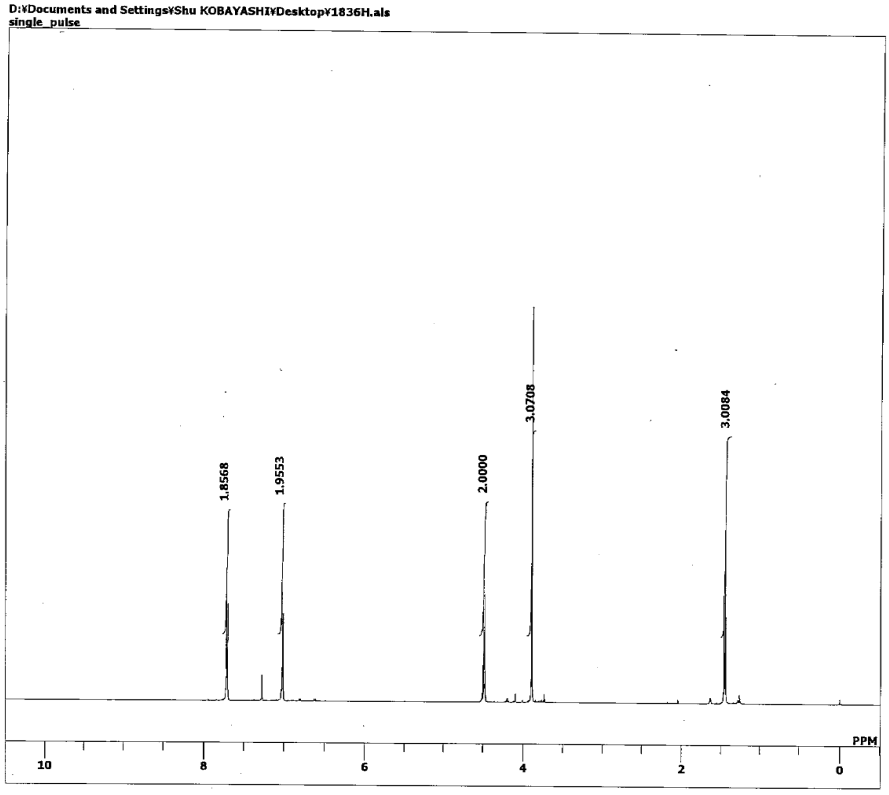
EXMOD	single_pulse_dec
OBFRQ	150.92 MHz
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	120
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.1 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60



10

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1836H.als
single_pulse



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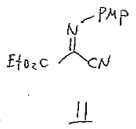
OBNUC	1H
EXMOD	single_pulse.ex2
OBFRQ	600.17 MHz
OBSET	5.30 KHz
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.0 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	40



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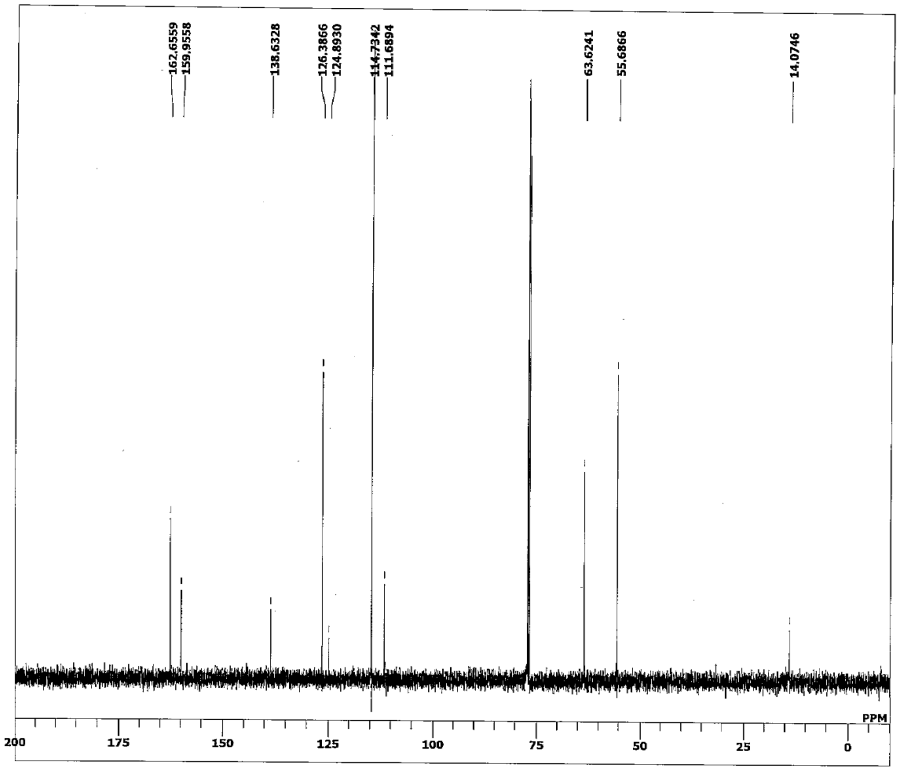
D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1836C.als



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EXMOD	single_pulse_dec
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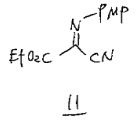
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	142
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.0 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60



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D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1835H.als
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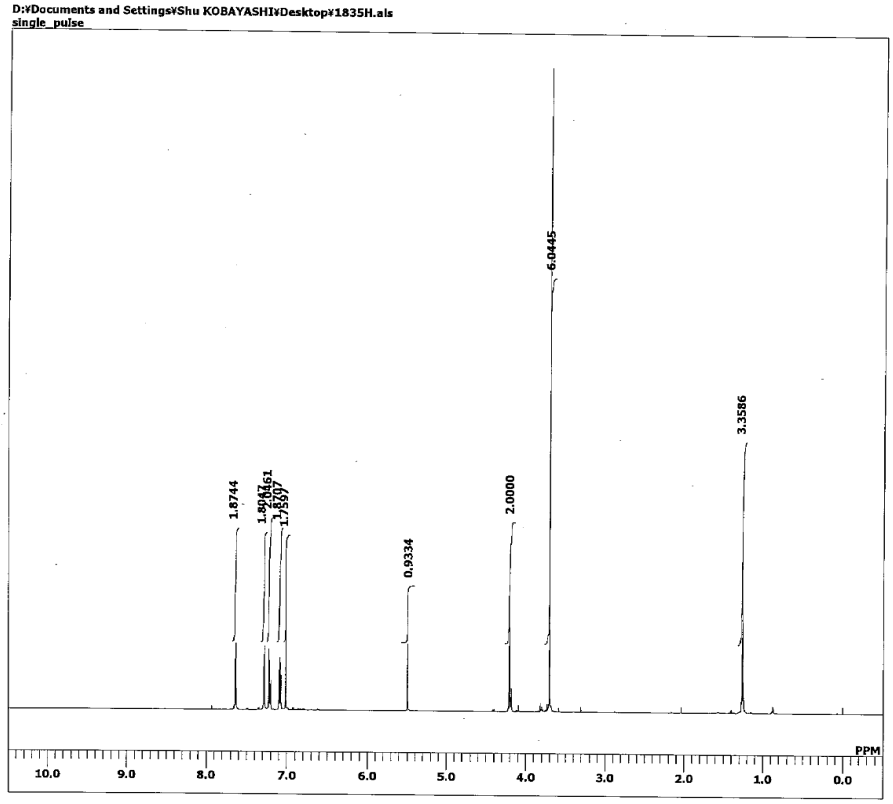

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EXMOD	single_pulse.ex2
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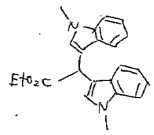
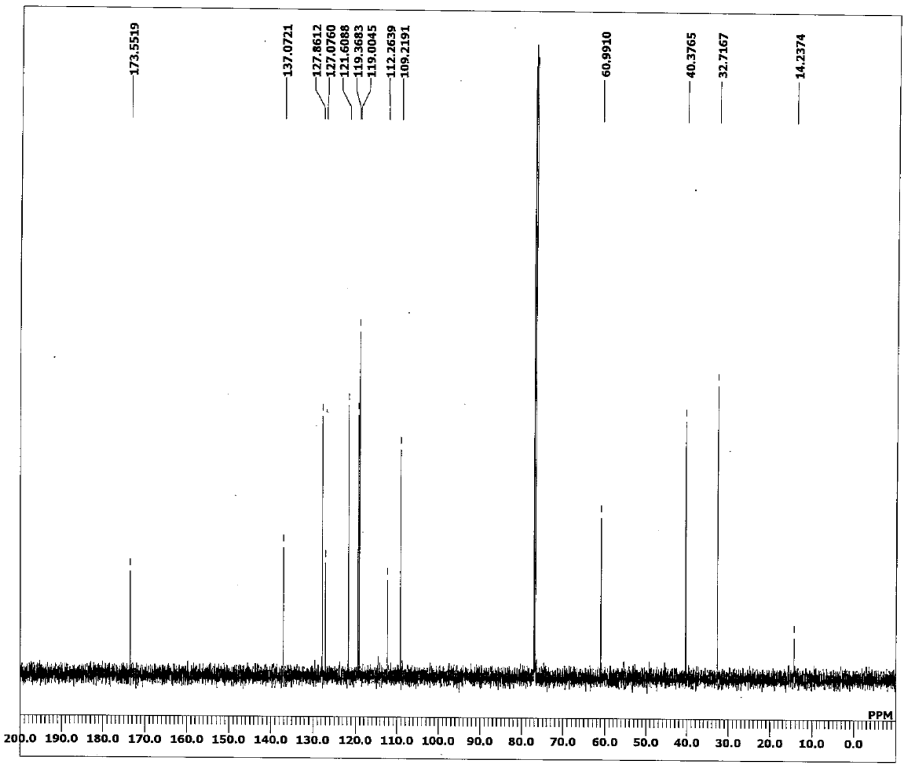
OBFIN	5.47 Hz
POINT	13107
FREQU	9008.87 Hz
SCANS	8
ACQTM	1.4549 sec
PD	2.0000 sec
PW1	6.50 usec
IRNUC	1H
CTEMP	22.4 c
SLVNT	CDCL3
EXREF	0.00 ppm
BF	0.12 Hz
RGAIN	38



12

D:¥Documents and Settings¥Shu KOBAYASHI¥Desktop¥1835C.als



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EXMOD	single_pulse_dec
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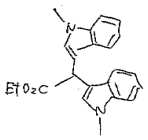
OBSET	8.52 KHz
OBFIN	1.74 Hz
POINT	26214
FREQU	37878.21 Hz
SCANS	127
ACQTM	0.6921 sec
PD	2.0000 sec
PW1	2.87 usec
IRNUC	1H
CTEMP	23.2 c
SLVNT	CDCL3
EXREF	77.00 ppm
BF	0.12 Hz
RGAIN	60



12

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Zhan. Tan, C.-C. Guo, *Chem*. *Commun*. **2009**, 953; (m) F. Yang, J. Li, Z.-Z. Huang, *Org*. *Lett*. **2010**, *12*, 5214; (n) L. Huang, T. Niu, J. Wu, Y. Zhang, *J*. *Org*. *Chem*. **2011**, *76*, 1759; (o) G. Zhang, Y. Ma, S. Wang, Y. Zhang, R. Wang, *J*. *Am*. *Chem*. *Soc*. **2012**, *134*, 12334.

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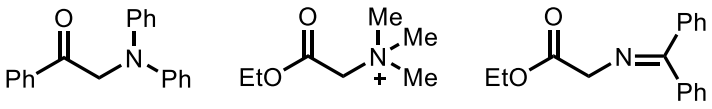

20.3 (ref. 20a) 20.0 (ref. 20b) 18.7 (ref. 20c)

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