

博士論文

Lycopalhine A の合成研究

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目次

ABBREVIATIONS

第一章 序論 1

1-1	リコポジウムアルカロイドとは	2
1-2	リコポジウムアルカロイドの生合成仮説	3
1-3	Fawcettimine 型リコポジウムアルカロイドについて	5
1-4	Lycopalhine A について	6
1-5	Lycopalhine A の構造決定	7
1-6	Lycopalhine A の生合成経路について	9
1-7	過去の全合成例	10
1-8	本研究の目的	12

第二章 合成研究 13

2-1	合成計画	14
2-2	モデル基質を用いた3環性スルホンイミドの合成検討	15
2-3	逆合成解析の改良	18
2-4	鍵反応基質の調整	20
2-5	鍵反応(逆 Michael 反応と分子内 Michael 付加反応)	23
2-6	15 位炭素の増炭反応と 3 位炭素への側鎖の導入	24
2-7	β -ヒドロキシケトン部位及びアミナール部位の構築について	30
2-8	Lycopalhine A の全合成	39

第三章 結語 41

EXPERIMENTAL SECTION 45

SPECTRAL DATA 113

REFERENCES 171

謝辞

ABBREVIATIONS

Ac	acetyl	HMBC	
aq	aqueous		heteronuclear multiple bond correlation
Ar	aryl	HMQC	
9-BBN	9-borabicyclo[3.3.1]nonane		heteronuclear multiple quantum correlation
Boc	<i>t</i> -butoxycarbonyl	HRMS	high resolution mass spectroscopy
Bu	butyl	IR	infrared spectroscopy
Bz	benzoyl	LAH	lithium aluminium hydride
18-c-6	18-crown-6	<i>m</i>	meta
CDI	carbonyldiimidazole	min	minute(s)
COSY	correlation spectroscopy	Me	methyl
DAIB	(diacetoxyiodo)benzene	Ms	methanesulfonyl
DBU	diazabicyclo[5.4.0]undec-7-ene	MS	molecular sieves
decomp.	decomposition	<i>n</i>	normal
DEAD	diethyl azodicarboxylate	NMR	nuclear magnetic resonance
DEPT		Ns	nosyl, 2-nitrobenzenesulfonyl
distortionless enhancement by polarization transfer		nOe	nuclear Overhauser effect
DIBAL	diisobutylaluminium hydride	<i>o</i>	ortho
DMAP	4-(<i>N,N</i> -dimethylamino)pyridine	<i>p</i>	para
DMF	<i>N,N</i> -dimethylformamide	P	protecting group
DMP	Dess-Martin periodinane	Ph	phenyl
DMSO	dimethylsulfoxide	PMP	<i>p</i> -methoxyphenyl
dppf		PPTS	pyridinium <i>p</i> -toluenesulfonate
1,1-bis(diphenylphosphino)ferrocene		ppm	parts per million
d.r.	diastereo ratio	Py	pyridine
ECD	electronic circular dichroism	quant.	quantitative yield
ee	enantiomeric excess	R	alkyl
<i>epi</i> -	epimer	rt	room temperature
eq	equivalent	SM	starting material
ESI	electron-spray ionization	<i>t</i>	tertially
Et	ethyl	TASF	
h	hour(s)	tris(dimethylamino)sulfur	trimethylsilyl
HMPA	hexamethylphosphoric amide	difluoride	
		TBAF	tetra- <i>n</i> -butylammonium fluoride
		TBS	<i>t</i> -butyldimethylsilyl

TD-DFT

time-dependent density functional theory

Tf trifluoromethanesulfonyl

TFA trifluoroacetic acid

THF tetrahydrofuran

TLC thin layer chromatography

Ts *p*-toluenesulfonyl

第一章

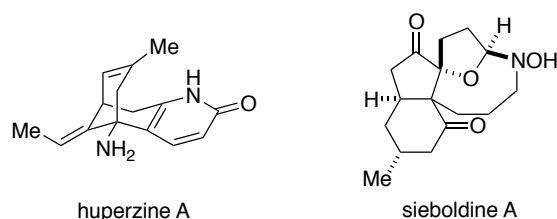
序論

1-1 リコポジウムアルカロイドとは

リコポジウムアルカロイドはヒカゲノカズラ科(Lycopodiaceae)の植物より産生されるアルカロイドの総称であり、多様でユニークな環構造を有する化合物群である¹。上記アルカロイドを含有するヒカゲノカズラ科はヒカゲノカズラ植物門に分類されるシダ植物であり、熱帯を中心に世界中に広く分布している。同科植物に分類される属、種は多く、*Lycopodium*属や*Palhinhaea*属など、計18属、約480種が確認されている¹。日本では、*Lycopodium*属のヒカゲノカズラ(*Lycopodium clavatum*)、トウゲシバ(*Lycopodium serratum*)の生息が見られ、それらを中心に約20種類が自生している¹。特に、ヒカゲノカズラは神事の際には髪飾りとして使用されたり、その神事の様子を見て”日陰の蔓”を詠んだ歌が万葉集に登場したり、更に身近なものとして、鏡餅の飾りとして用いたりするなど古来より日本人に深く親しまれてきた。

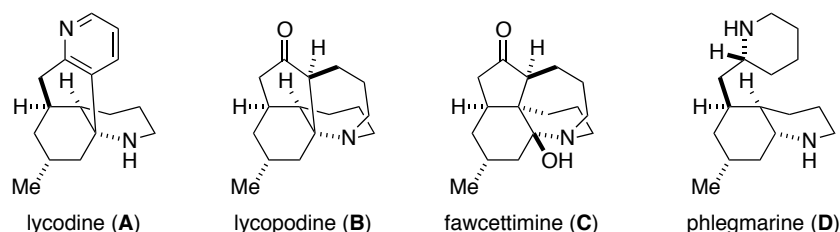
リコポジウムアルカロイドに関わる研究は古くから行われてきており、1881年のBödekerによるアスヒカズラ(*Lycopodium complanatum*)からのLycopodineの単離を皮きりに、ヒカゲノカズラ科の植物の成分研究が今日まで精力的に行われ、現在までに約50種の植物から、200種以上のリコポジウムアルカロイドが単離されている^{1,2}。その中でも特に、1980年代後半にトウゲシバ(*Lycopodium serratum*)より単離されたHuperzine Aは高いアセチルコリンエステラーゼ阻害活性とNMDA受容体拮抗作用を有し、神経変性疾患、特にアルツハイマー型認知症に対する有望な治療薬として研究が進められている³。最近では、*Lycopodium sieboldii*より単離されたSieboldine AがHuperzine Aとは異なる骨格を有するものの、Huperzine Aと同等のアセチルコリンエステラーゼ阻害活性を示したことからリコポジウムアルカロイドは創薬シーズとして脚光を浴びている⁴。

Figure 1



リコポジウムアルカロイドはその炭素骨格及び窒素数からlycodine class (A)、lycopodine class (B)、fawcettimine class (C)、miscellaneous class (D)の4つのクラスに分類されている¹⁾。その代表的な化合物をFigure 2に示す。

Figure 2

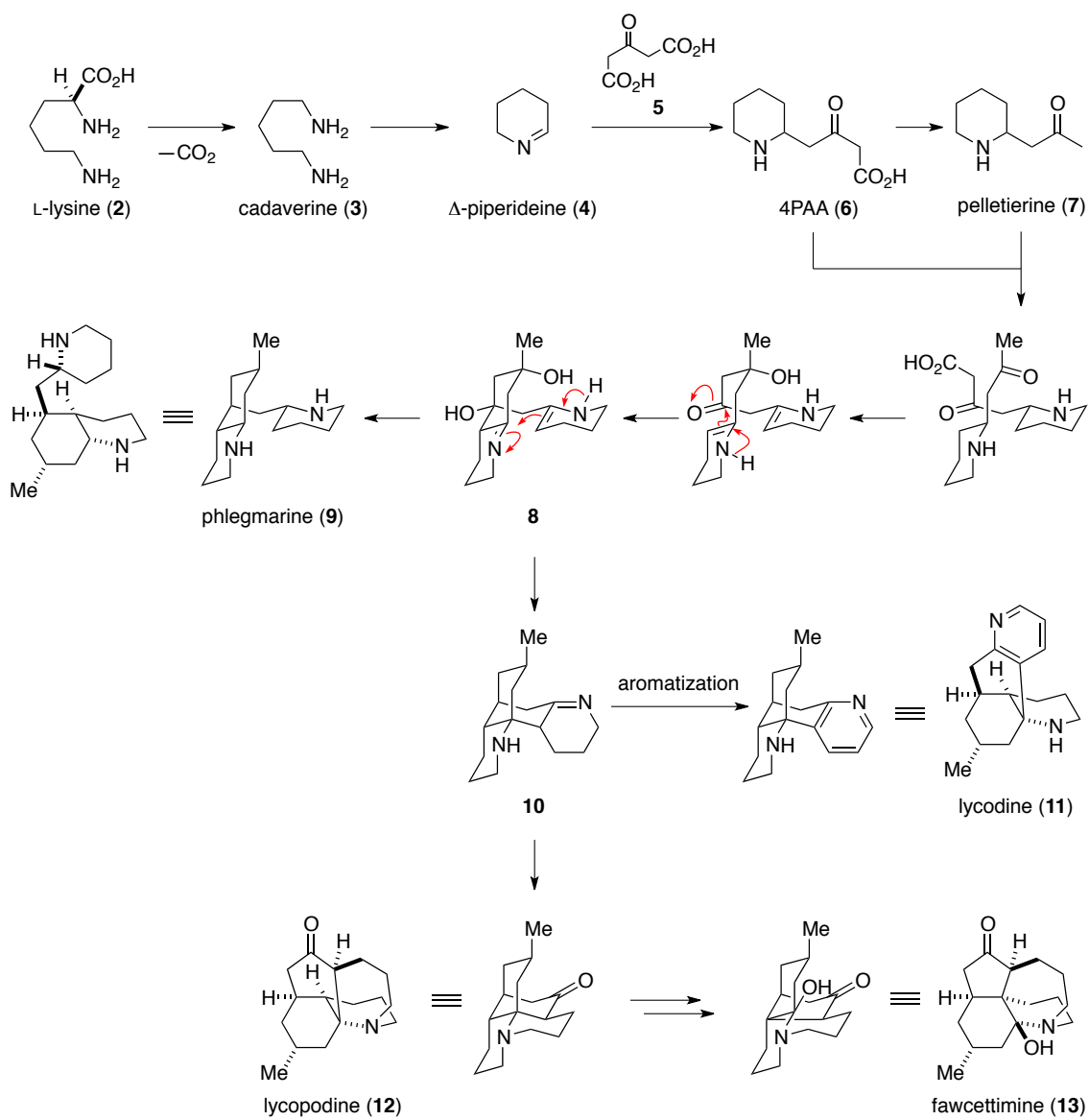


1-2 リコポジウムアルカロイドの生合成仮説

リコポジウムアルカロイドの生合成経路は Spencer らによる生合成実験を基に仮説が提唱されている。それによると、リコポジウムアルカロイドは脂肪族アミノ酸であるリジン由来の二次代謝産物であるとされている(Figure 3)⁵⁾。

まず、L-Lysine (2)の脱炭酸により cadaverine (3)が生成した後、一方のアミンの酸化と環化を経て Δ -piperidine (4)を与える。次に Δ -piperidine (4)は 3-oxoglutaric acid (5)と縮合し 4-(2-piperidyl)-acetoacetate (6)へと変換された後、脱炭酸により pelletierine (7)を生ずる。生成した 4-(2-piperidyl)-acetoacetate (6)と pelletierine (7)は縮合と酸化を経た後、炭素-炭素結合形成を伴う形で生合成中間体 8 へと変換される。中間体 8 は酸化、還元を繰り返すことで phlegmarine (9)へと変換される一方で、連続的に炭素-炭素結合が形成されることでリコポジウムアルカロイド群の重要な基本骨格となる 4 環性の生合成仮想中間体 10 へと変換される。その後、中間体 10 は一方ではテトラヒドロピリジン部位の酸化、芳香化が進行することで lycopodine (11)に、他方ではイミン部位の加水分解と酸化、更には再環化反応により lycopodine (12)となる。そして lycopodine (12)の炭素-炭素結合の転位が生ずることで fawcettimine (13)が生成する。以上のように生じた 4 つの代表的な化合物が、酸化、還元、転位などの代謝を受け多様なリコポジウムアルカロイドが生成すると考えられている。

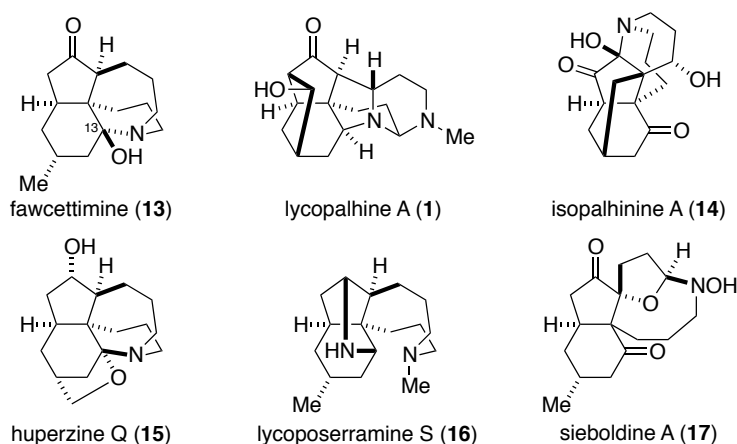
Figure 3



1-3 Fawcettimine 型リコポジウムアルカロイドについて

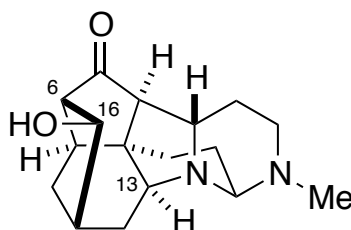
Fawcettimine 型に分類されるリコポジウムアルカロイドの中で、1959 年に Burnell らによってジャマイカのブルーマウンテン山脈に自生する *Lycopodium fawcetti* から単離された fawcettimine (**13**)が最も古い⁶。現在までに単離、構造決定された fawcettimine 型のリコポジウムアルカロイドは、80 種類を超える¹。この型に分類されるリコポジウムアルカロイドは窒素原子 1 つを含む 9 員環が縮環したヒドリンダン骨格を有する(Figure 4)。Fawcettimine (**13**)の分子内では 13 位炭素上でヘミアミナールを形成し、4 つの環が高度に縮環している。自然界ではこの化合物に新たな結合の形成や官能基変換が生じることで、より複雑な構造を有する化合物へと変換されている。そして、その複雑な構造故に多くの有機化学者の興味を引きつけ、現在までに多くの合成研究がなされている⁷。

Figure 4



1-4 Lycopalhine A について

Figure 5



lycopalhine A (1)

Lycopalhine A (1)は2012年に趙らによってヒカゲノカズラ科のミズスギ (*Palhinhaea cernua*, *Lycopodium cernuum*)より単離、構造決定されたリコポジウムアルカロイドであり、上記のようにfawcettimine型に分類される(Figure 5)⁸。

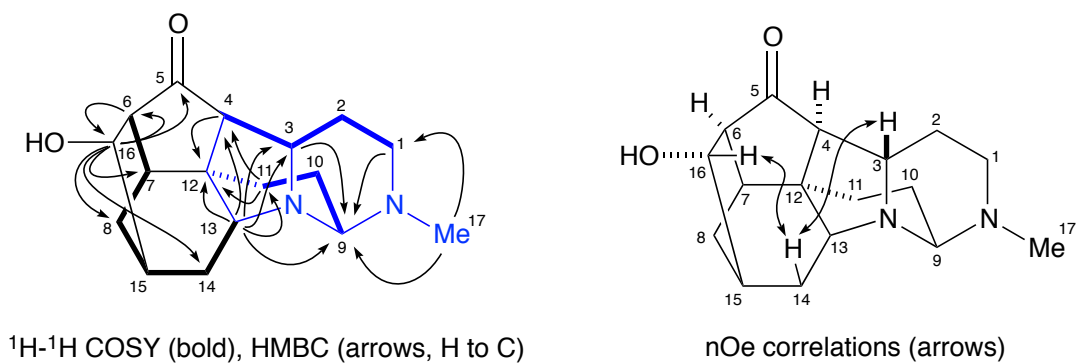
構造上の特徴としては、fawcettimine (13) と比較して、6位炭素と16位炭素で結合し分子内で β -ヒドロキシケトン及びシクロペンタン環を形成し、更に、13位炭素に新たに導入された窒素原子がピロリジン環並びにもう一方の窒素原子と一般的に不安定と考えられているアミナールを形成していることが挙げられる。また、構成する縮環構造は天然物ではほとんど見られないジアザトリシクロウンデカン骨格並びにトリシクロデカン骨格を含んでいる。このように、高度に縮環した特徴的な構造を有していることからlycopalhine A (1)は有機合成化学的に非常に興味深い化合物であると言える。筆者が合成研究を始めた2013年時点では本化合物の全合成や合成研究についての報告はなかったが、1-7で後述するように2016年にTraunerらにより初の全合成が報告された。

また、生物活性については、リコポジウムアルカロイドがしばしば有するようなアセチルコリンエステラーゼ阻害活性は全くなく、弱いながらもブチリルコリンエステラーゼ阻害活性を有することが報告されている(31.4% inhibition at 50 μ M)⁸。最近では、黄熱病ウイルスに対する増殖抑制活性を有することも確認されている⁹。

1-5 Lycopalhine A の構造決定

Lycopalhine A (**1**)の構造決定については分光学と計算科学を用いて以下のように行われた⁸。まず、質量分析より分子量 289.1920、分子式 $C_{17}H_{24}N_2O_2$ 不飽和度 7 と示された。次いで、3431、1716 cm^{-1} の IR 吸収帯を示したことより、水酸基とカルボニル基を有することが示唆された。 1H NMR よりその化学シフトと積分値より、窒素原子に結合したメチル基と第 2 級水酸基を有すること、また、 ^{13}C NMR、DEPT より、17 個ある炭素原子のうち、1 個がメチル基、6 個がメチレン炭素、8 個がメチン炭素、2 個が四置換炭素($\delta_c = 221.56, 54.38$)であることが明らかとなった。上記の情報と多くの fawcettimine 型リコポジウムアルカロイドの第四級炭素が ^{13}C NMR において 54.3 付近に化学シフトを示すことから、本化合物は 6 環性骨格を有する fawcettimine 型リコポジウムアルカロイドであると予想された。次に 1H - 1H COSY、HMBC スペクトルより 3 つの独立する spin-system(a,b,c)が存在し(Figure 6 実線)、HMBC スペクトルにおいて単にその繋がりだけでなく、本化合物が高度に縮環していることが示された。即ち、HMBC スペクトルにおいて H(17)-C(1, 9)、H(1)-C(9)、H(11)-C(4, 12)、H(4)-C(12)、H(3)-C(9)、H(13)-C(3, 4, 9, 11, 12)、との間での相関があることから spin-system (a)と(b)のつながりが示され、更に 5-メチル-5,9-ジアザトリシクロ[6.2.1.0^{4,9}]ウンデカン骨格 (Figure 6 青部分)を有することが示唆された。次いで、spin-system (c)について、H(8,14)-C(12)との間での相関からシクロヘキサン環、H(3,4,6)-C(5)との間での相関からシクロペンテノン環、そして、H(16)-C(5,6,7,8,14)、H(6)-C(16)との間での相関から β -ヒドロキシケトン部位を有することが示唆され、最後に(c)と(a),(b)とのつながりが H(13)-C(4,11)との間での相関より示されたことから平面構造として Figure 6 の構造が推測された。また、 β -ヒドロキシケトン部位の相対立体配置を決定することで分子全体の相対立体配置を決定している。即ち、H(3)-H(14b)、H(14b)-H16 の間にそれぞれ nOe 相関が観測され、更に 1H - 1H -COSY において H(6)-H(16)、H(15)-H(16)において相関が認められないことからその二面角がおおよそ 90° と示されたことから Figure 6 に示す相対立体配置であると導いている。絶対立体配置については、本化合物が結晶化できなかったことより、計算科学を用いて推測されている。即ち、TD-DFT 計算によって得られる両エナンチオマーの ECD スペクトルと実際に得られた ECD スペクトルのコットン効果の比較から Figure 6 に示した絶対立体配置であるとしている。

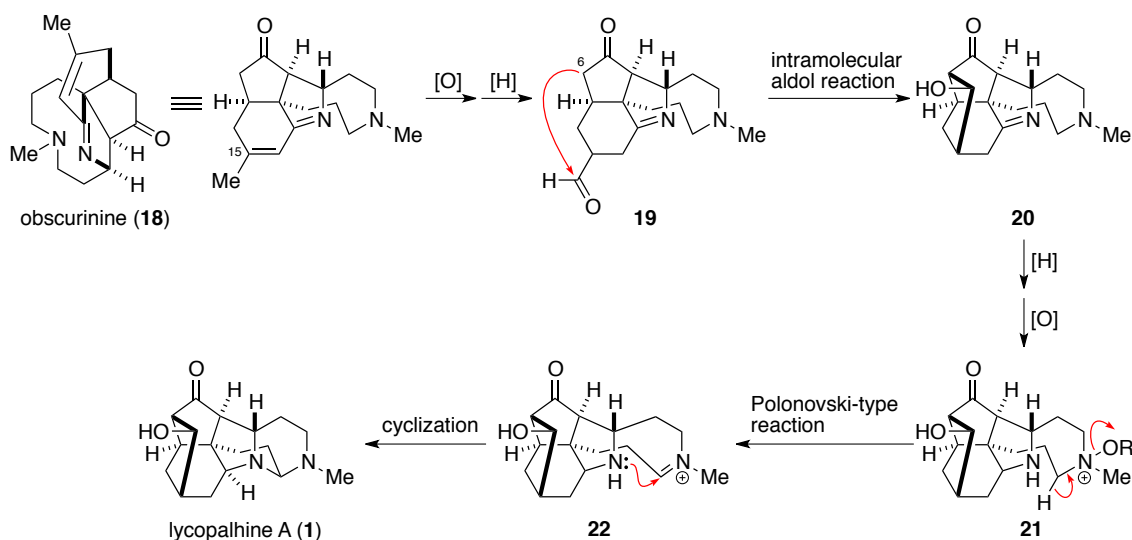
Figure 6



1-6 Lycopalhine A の生合成経路について

Lycopalhine A (**1**)の生合成については入手困難なため実験的に証明されておらず、同時に単離された obscurinine (**18**)の構造から次のように提唱されている (Figure 7)⁸。Obscurinine (**18**)の 15 位メチル基の酸化とオレフィンの還元が進行することで生合成中間体 **19** へと変換される。そして、中間体 **19** のホルミル基が concave 側に配向した時に、6 位炭素との分子内アルドール反応が起こることで中間体 **20** が生成する。その後、酸化、還元、アシル化を経て *N*-オキシドアシル化体へと変換された後、Polonovski 型の反応¹⁰が進行することでイミニウムカチオンが生じると近傍に存在するピロリジン環の窒素原子からの環化反応が起こり、lycopalhine A (**1**)が生成する。

Figure 7

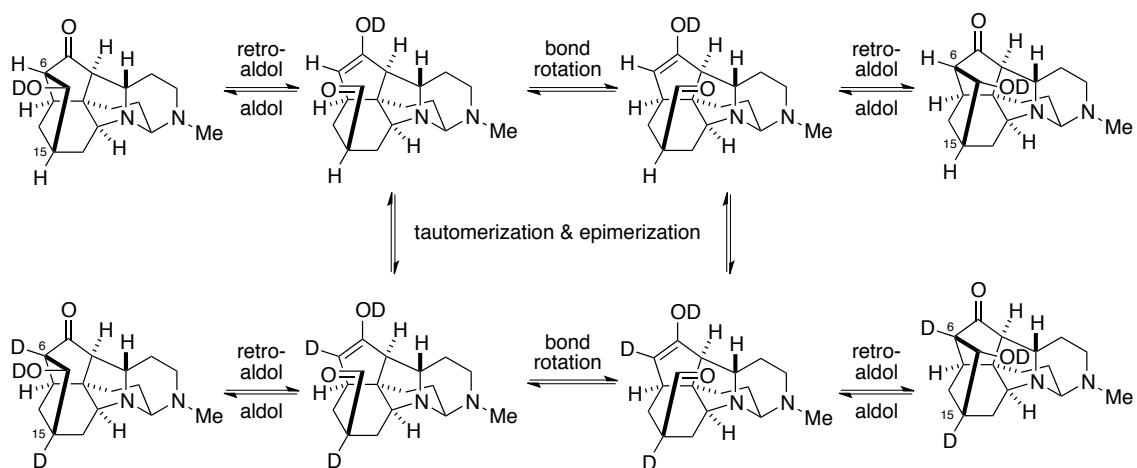
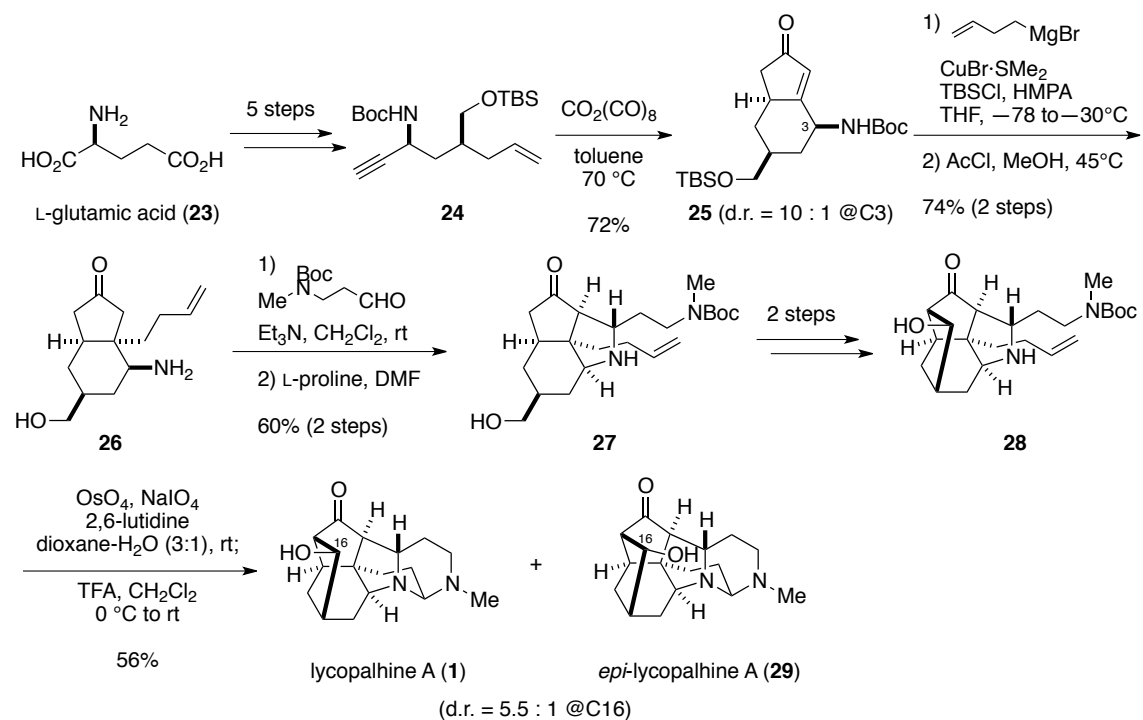


1-7 過去の全合成例

Lycopalhine A (**1**)は2012年に単離、構造決定されてから日が浅いためか全合成、合成研究含めてTraunerらによる1報に留まっている。

1-7-1 Trauner らによる全合成¹¹

Lycopalhine A (**1**)の初の全合成は2016年にTraunerらによって達成されている(Scheme 1)。L-グルタミン酸 (**23**)より5工程の変換を経て得られるエンイン **24** のPauson-Khand反応を行うことでインデノン **25** を得ている。次いで、クプラート反応剤を用いてブテニル基のMichael付加反応を行い、第四級炭素を構築した後、保護基を除去することでアミノアルコール **26** へと導いた後、5-endo-trigの形式で分子内Mannich反応を行うことでlycopalhine A (**1**)の中心骨格であるピロリジン環を含む3環性化合物 **27** を得ている。側鎖のアルコールの酸化と分子内アルドール反応を行うことで **28** とした後、側鎖のオレフィン部位を酸化的に開裂し、酸性条件に付すことで閉環反応が進行し、lycopalhine A(**1**)と16位の水酸基がエピ化した *epi*-lycopalhine A(**29**)を5.5 : 1の混合物として得ている。Lycopalhine A(**1**)が平衡混合物で存在しているかを確かめるため重水素化実験を行っている。Lycopalhine A(**1**)と *epi*-lycopalhine A(**29**)の混合物に対し、CH₃OD中、炭酸カリウムを作用させると6位と16位の水素が逆アルドール、互変異性、エピ化を経て重水素に置換されたことより、lycopalhine A(**1**)がβ-ヒドロキシケトン部位で平衡混合物であることを報告している(Scheme 2)。



1-8 本研究の目的

上述したように lycopalhine A (**1**)は天然物ではほとんど目にしないジアザトリシクロウンデカン骨格並びにトリシクロデカン骨格を有する特異な 6 環性化合物であり、分子内に β -ヒドロキシケトン部位及び一般的に不安定とされるアミナルを有していることから有機合成化学的に非常に魅力的な化合物である。また新規な骨格を有するため、新規な作用機序による有望な薬理作用を持つ可能性を秘めており、薬理学的見地からも興味深い化合物であると言える。

このような背景の下、筆者は lycopalhine A (**1**)の有する特異な縮環構造とその合成方法に興味を抱き、本天然物の骨格構築における独創的な合成経路の確立を目指し合成研究に着手した。

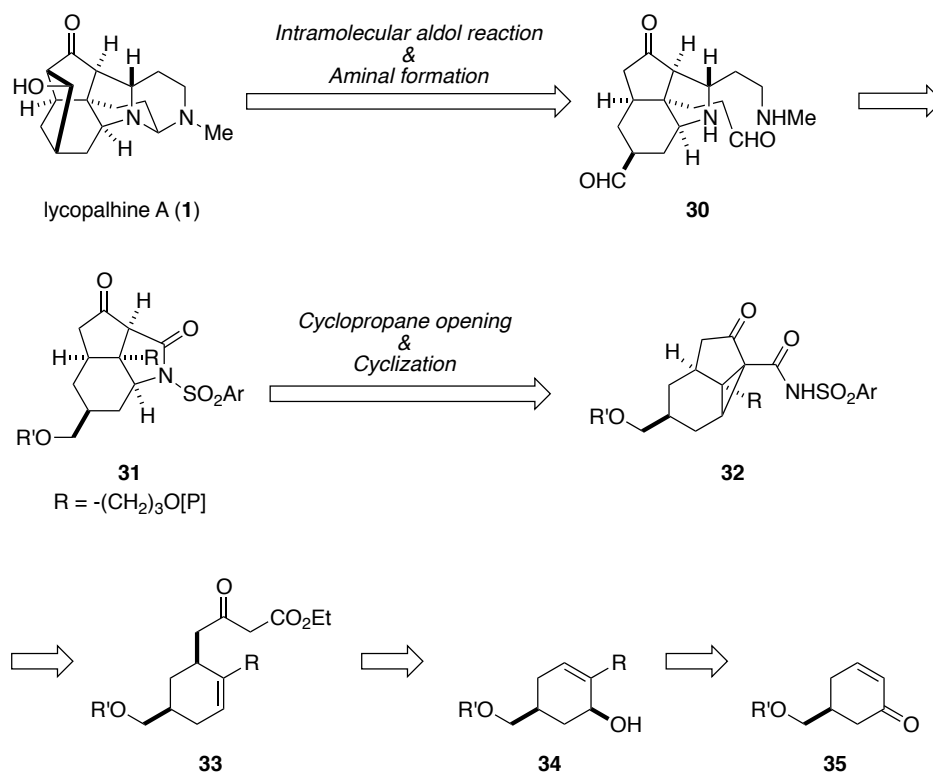
第二章

合成研究

2-1 合成計画

Lycopalhine A (**1**)の全合成に向けて、以下のように逆合成解析を行った(Scheme 3)。まず、本天然物の分子内に存在する β -ヒドロキシケトン部位及びアミナル部位を合成終盤にて構築するものとし、ピロリジン環を含む三環性化合物**30**へと逆合成した。次に**30**のアミノエチル基はスルホンイミドを足がかりとして導入できると考え、3環性スルホンイミド**31**を中間体として設定した。この中間体はシクロプロパンの開環と窒素原子からの閉環反応により合成することを計画した。そして、**32**はシクロヘキセノン**35**より1,2還元とJohnson-Claisen転位、更には β -ケトエステルのジアゾ化とシクロプロパン化より合成できるものとし、実際に合成検討を開始した。

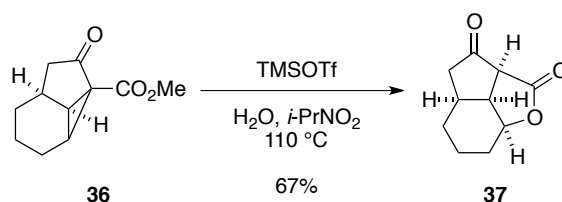
Scheme 3



2-2 モデル基質を用いた 3 環性スルホンイミドの合成検討

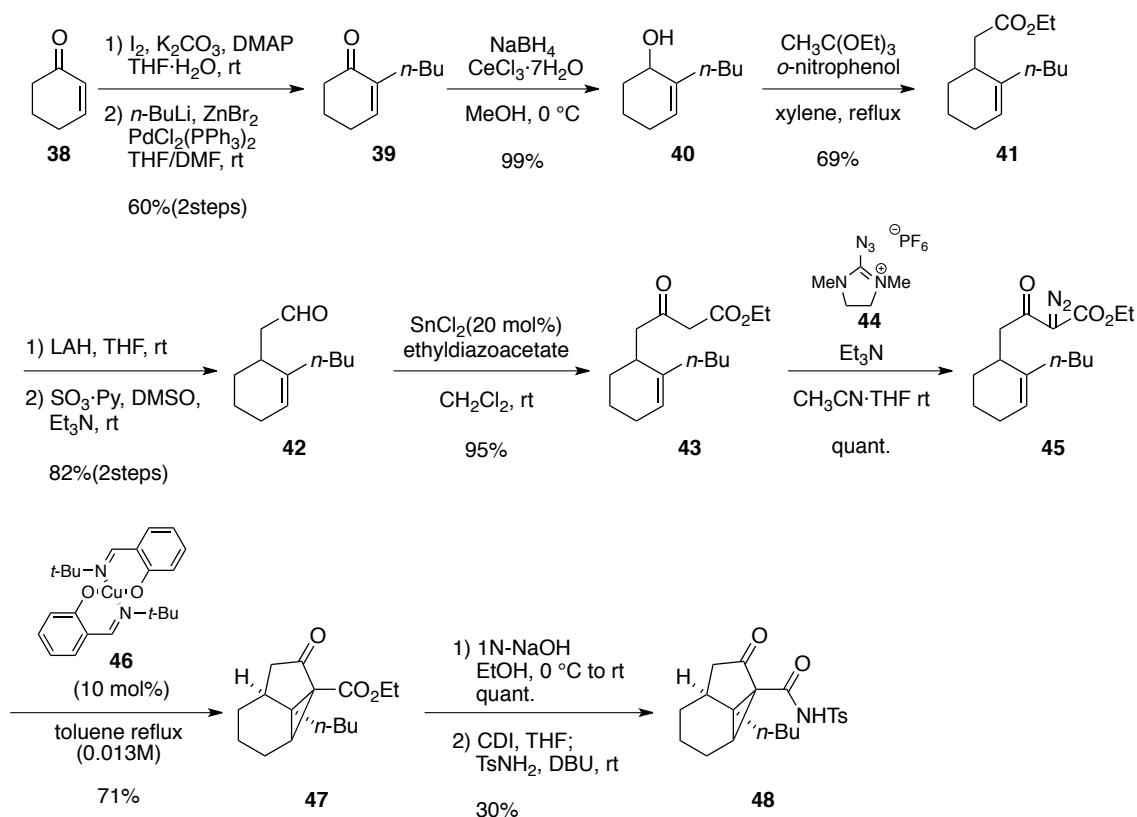
上記逆合成解析の中で示した中間体**31**を得るべく計画した反応はScheme 4に示すE. J. Coreyらによって報告された反応¹²より着想を得ている。即ち、シクロプロパンを有する三環性 β -ケトエステル**36**に対して少量の水存在下、TMSOTfを作用させることで三環性ラクトン**37**を得る反応である。この反応では、シクロプロパンの開環が進行した後、生じたカルボカチオンへエステル部分の酸素原子が攻撃することでラクトンが生成していると考えられる。3環性スルホンイミドの合成においては、 β -ケトエステル**36**のメチルエステル部分をスルホンイミドへと変換することでシクロプロパンの開環後、窒素原子より閉環することを期待した。そこでまずは、ラセミ体のモデル基質を用いて3環性スルホンイミドの合成を検討することとした。

Scheme 4



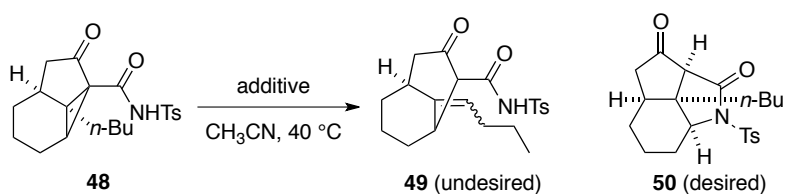
モデル基質として、**32**のアルコキシプロピル基を*n*-ブチル基へと変換し、ヒドリンダン骨格上に存在するヒドロキシメチル基を有さない基質を設定した。モデル基質の合成をScheme 5に示す。市販のシクロヘキセノン**38**をヨウ素化した後、Negishiカップリングを行うことで*n*-ブチル基を導入し**39**とした。次いで、Luche還元¹³を行いアリルアルコール**40**へと変換した後、Johnson-Claisen転位を用いることでエステル**41**へと導いた。このエステル部分を還元、酸化の工程を経てアルデヒドへと変換した後、Roskamp 反応¹⁴を用いることで β -ケトエステル**43**を得た。続いて、2-azido-1,3-dimethylimidazolinium hexafluorophosphate (ADMP) (**43**)¹⁵により収率良くジアゾ化体**45**を得た後、銅触媒**46**存在下、トルエン溶媒中で加熱還流することでシクロプロパン化¹⁶が進行し**47**を合成することができた。そして、エステル部分をトシルイミドへと変換しモデル基質**48**を得た。

Scheme 5



得られたモデル基質を用いて所望の反応の検討を行った(Scheme 6)。反応条件には、 β -ケトエステルもしくは1,3-ジケトンの β 位に存在するシクロプロパンの開環に用いられる条件を用いた¹⁷。行ったすべての条件において、期待した反応はまったく進行せず、代わりにカチオンをより安定化する方向でシクロプロパンが開環した考えられるエキソオレフィンを含む2環性化合物**49**が得られた。

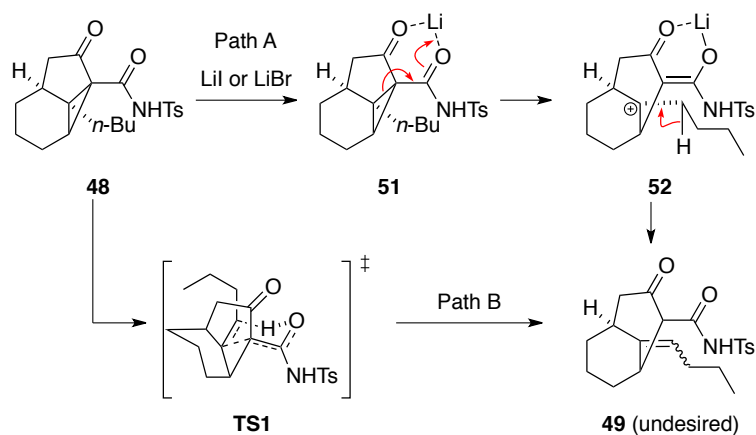
Scheme 6



entry	additive	result
1	Lil	49 (90%), 50 (0%)
2	LiBr	49 (82%), 50 (0%)
3	PhSH, $t\text{-BuOK}$	49 (75%), 50 (0%)
4	PhSeSePh, $NaBH_4$	49 (86%), 50 (0%)

望みの反応が進行しなかった理由について以下のように考察した(Scheme 7)。望まない化合物が得られる可能性として以下2つ(Path A, Path B)の経路を考えた。Path Aは、Li塩が添加されると1.3-ジケトンにリチウムイオンが配位し、次いで第3級カルボカチオンが生成する方向でシクロプロパンの開環が進行し、最後に生じたカチオンを解消する形でオレフィンが生成する経路である。Path Bは添加剤の影響はなく、協奏的にシクロプロパンの開環とオレフィンの生成が起こる経路である。両経路ともにオレフィンの生成する位置はBredt則に合致している。

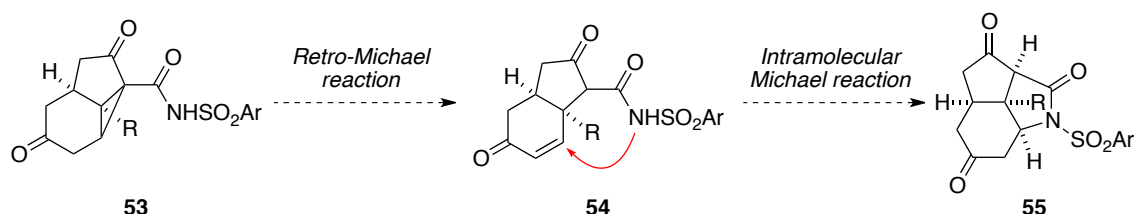
Scheme 7



2-3 逆合成解析の改良

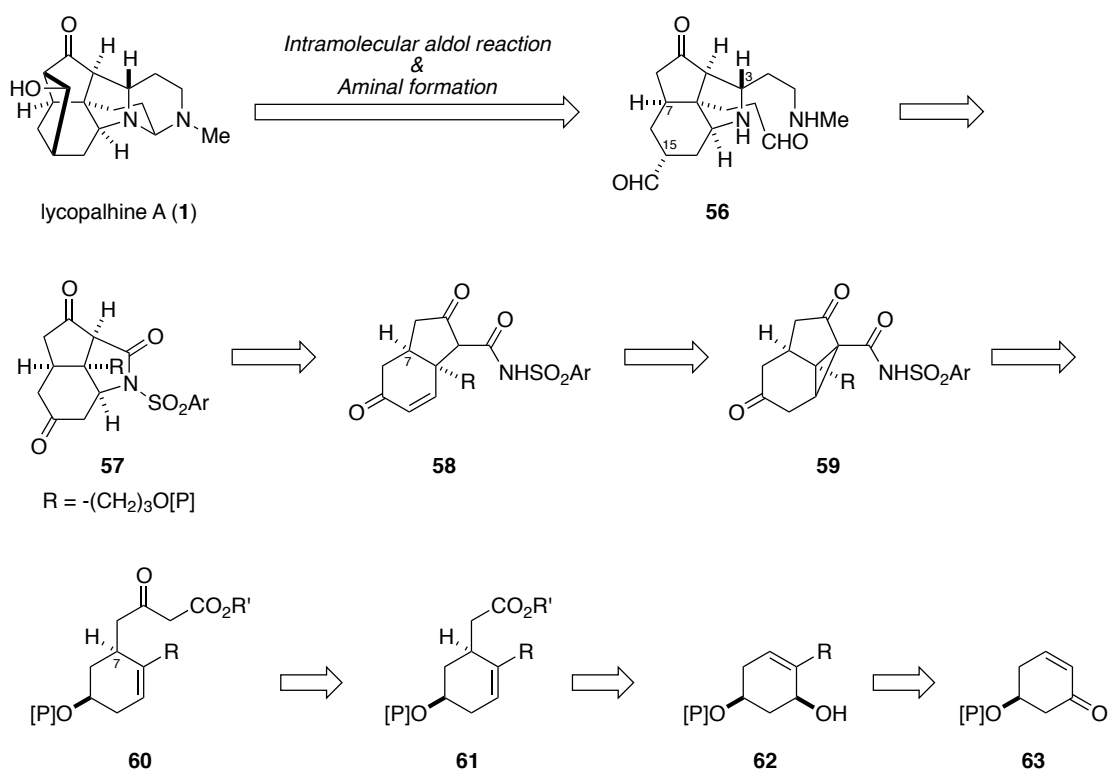
前述のモデル実験よりシクロプロパンの開環は確認できたものの、その位置選択性に問題があることが明らかとなったのでそれを解決する目的で以下のような分子設計を行った(Scheme 8)。シクロプロパンの β 位にカルボニル基を導入することで、歪みを解消するために逆Michael反応が進行し、生じたエノンへの分子内Michael反応により所望の3環性スルホンイミド中間体を合成できるものと考えた。

Scheme 8



上記の反応を鍵反応と位置づけ、再度逆合成解析を行った(Scheme 9)。先の逆合成解析と同様に56へと逆合成した。化合物56の15位炭素上のホルミル基は S_N2 反応などを用いた1炭素ユニットの導入により可能と考え、3位のアミノエチル基は、お椀型の立体構造を利用しconvex面より立体選択的に導入できるものとし、3環性スルホンイミド57を中間体として設定した。中間体57は上記の逆Michael反応と分子内Michael付加反応により59より導けるものとし、更に59はモデル基質の合成で用いた方法を適用することで β -ケトエステル60より合成可能と考えた。Lycopalhine A (1)の不斉合成を視野に入れると、化合物60の7位炭素の立体化学を制御する必要がある。その立体化学は、光学活性なシクロヘキセノン63のアルコキシ基の立体化学を利用した立体選択的な1,2-還元とJohnson-Claisen転位により制御可能であると考えた。

Scheme 9



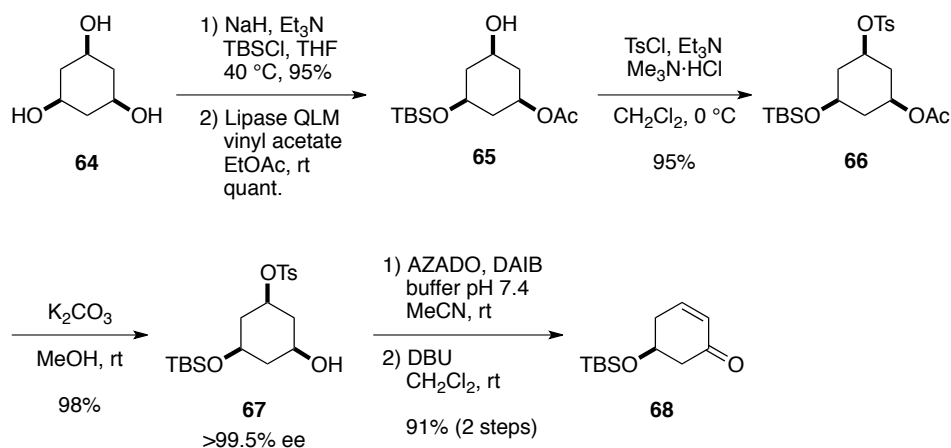
2-4 鍵反応基質の調整

まずは、光学活性な 5-シロキシ-シクロヘキセノンの合成を行い、その後 7 位炭素の立体化学が制御された鍵反応基質の調製を行うこととした。

2-4-1 光学活性な 5-シロキシ-シクロヘキセノンの合成

光学活性な 5-シロキシ-シクロヘキセノンは、市販のトリオール **64** から文献記載の方法¹⁸に従って導ける光学活性化合物 **65** より合成した(Scheme 10)。即ち *cis,cis*-1,3,5-シクロヘキサントリオールのモノ TBS 化を行った後、Lipase QLM を用いたジオールの非対称化を行うことで **65** を得た¹⁸。次いで、残余の水酸基に Ts 基を導入した後¹⁹、加溶媒分解を行うことでアルコール **67** へと導いた。続いて、**67** の水酸基を 2-azaadamantane-*N*-oxyl (AZADO) とヨードベンゼンジアセタートを用いてケトンへと酸化した後²⁰、DBU で処理することにより光学活性な 5-シロキシ-シクロヘキセノン **68** を収率良く得た。

Scheme 10



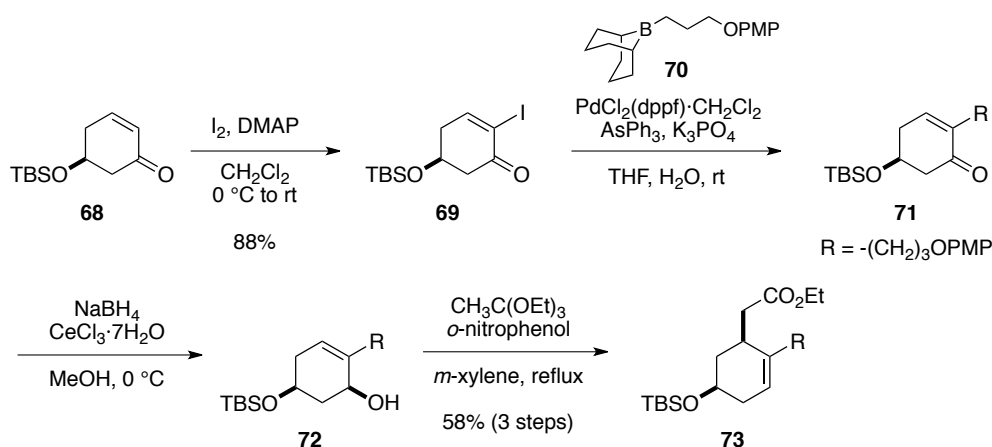
2-4-2 鍵反応前駆体の合成

光学活性な 5-シロキシ-シクロヘキセノンが得られたので、次に lycopalhine A (**1**)の 7 位に相当する炭素の立体化学が制御された基質への誘導化を行った。先に述べたように 7 位炭素の立体化学については、光学活性な 5-シロキシ-シクロヘキセノンのシロキシ基の立体化学を利用した 1,2-還元を行った後、

Johnson-Claisen 転位により制御可能だと判断し、実際に合成を行った(Scheme 11)。

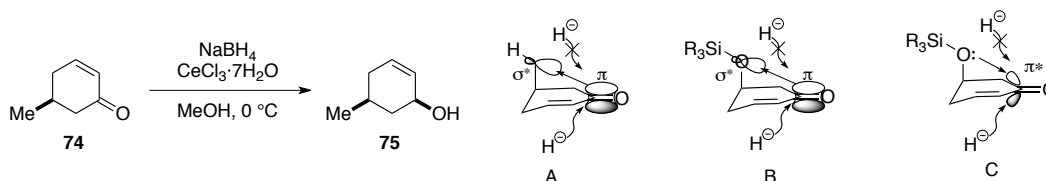
シクロヘキセノン **68** に対しヨウ素を作用させることでヨードエノン **69** へと収率良く変換し、アリルアルコールの水酸基を PMP 基で保護した化合物より調製可能なホウ素試薬 **70** を用いて鈴木-宮浦カップリングを行うことでエノン **71** へと導いた*。次いで、エノンの 1,2-還元を Luche 還元^{**}の条件で行った後**、Johnson-Claisen 転位を行うことで lycopalhine A (**1**)の7位に相当する炭素の立体化学が制御されたエステル **73** を得た***。

Scheme 11



* **71** 対し 20%程度生成した還元体 **68** が分離困難であったため、混合物のまま次の反応へと進めた。**68** 由来の生成物は 1,2 還元^{*}の工程でも分離できず、**73** を得る工程にて分離可能であった。

** 立体選択的に 1,2-還元が進行した理由として、以下のように考察している。以下の文献^aによると 5 位にメチル基を有するシクロヘキセノン **74** の 1,2-還元は立体選択的に **75** を与える、その理由としてメチル基 CH 結合の σ^* 軌道からカルボニル π 軌道への超共役(A)によりメチル基がアキシアルに配向しカルボニル基の一方が塞がれるためとされている。エノン **71** に対して同様に考えると、Si-O 結合 σ^* 軌道と π 結合への超共役(B)もしくは、酸素原子の非共有電子対と π^* 軌道の超共役(C)により TBSO 基がアキシアルに配向し立体障害のために立体選択的に還元が進行したと考察している。

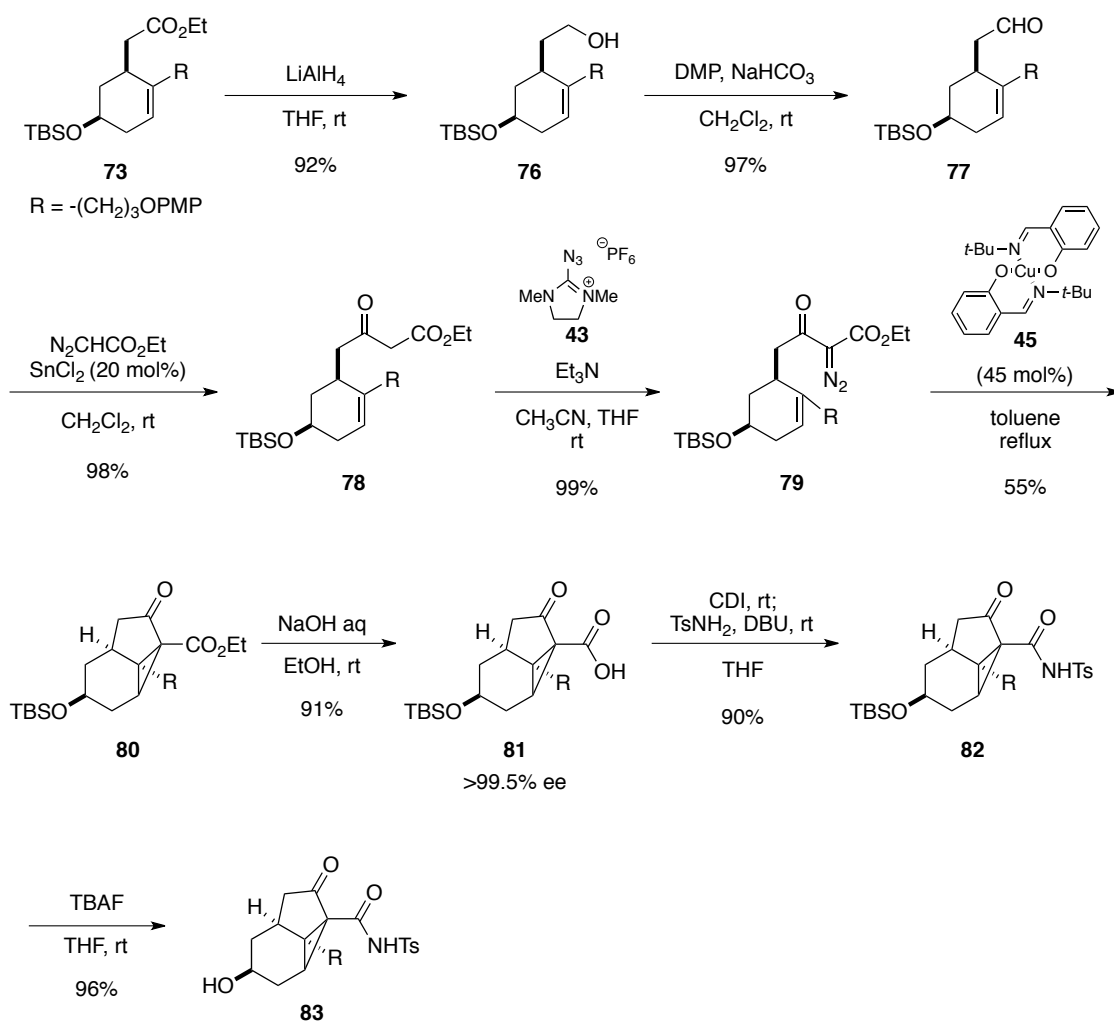


^a Gorthey, L.A.; Vairamani, M.; Djerassi, C. *J. Org. Chem.* **1985**, *50*, 4173.

*** エステル **73** の光学純度は両エナンチオマーの分離条件を見出せなかったため未決定であるが、一段階前のアリルアルコール **72** のジアステレオマーを確認できていないこと及びその後の誘導体で光学純度が 99.7% ee 以上であることより立体化学を制御して **73** を調製できたと考えている。

次に、モデル基質を合成した時と同様にシクロプロパン誘導体 **82** まで導いた (Scheme 12)。即ち、エステル **73** を還元、酸化の工程を経てアルデヒド **77** へと導いた後、Roskamp 反応¹⁴、ジアゾ化¹⁵を行い収率良く **79** を得た。続いて、銅触媒 **45** を用いてシクロプロパン化¹⁶を行い、**80** を得た後、エステル部分を加水分解し、光学活性なカルボン酸 **81** とした。次いで Ts イミド **82** へと導いた。最後に **82** の TBS 基を TBAF により除去することで鍵反応基質 **83** を得た。

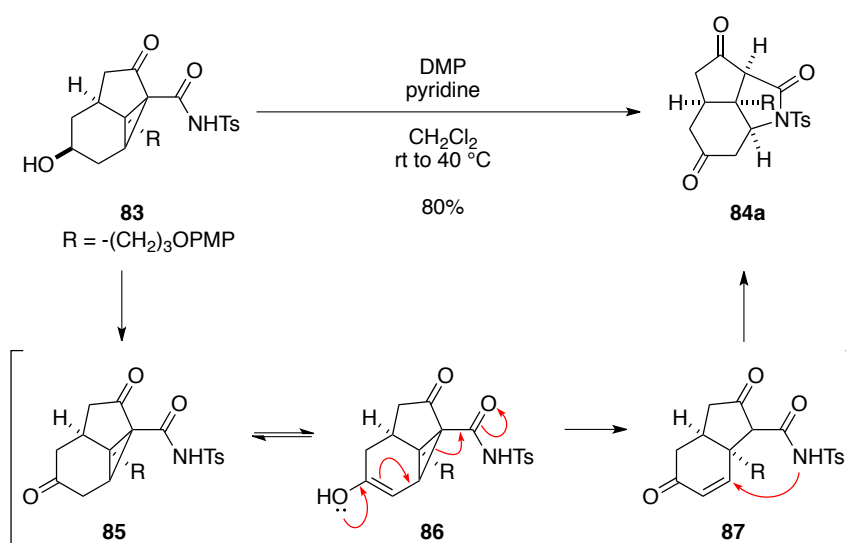
Scheme 12



2-5 鍵反応(逆 Michael 反応と分子内 Michael 付加反応)

次に逆 Michael 付加反応と分子内 Michael 反応を利用した 3 環性スルホンイミドの合成を試みた(Scheme 13)。シクロプロパン **83** の第 2 級アルコールを Dess-Martin 試薬により酸化したところ、望み通りカルボニル β 位のシクロプロパンの開環が起きた後、分子内 Michael 反応が速やかに進行することで所望の 3 環性スルホンイミド **84a** を収率良く得ることに成功した*。

Scheme 13



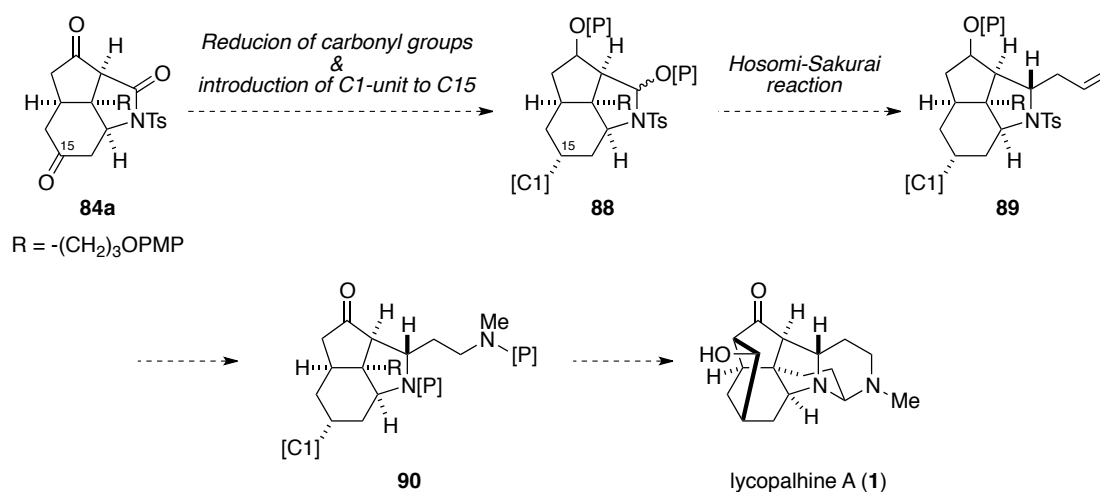
* 酸化反応開始後 5min 後では **84a** の生成は確認できないものの、1 時間後では一部生成が認められた。40 °C に加温することで **84a** へと収束させた。TLC 上で **85** もしくは **87** の存在が確認できるため単離を試みたが、反応速度が速いため、精製操作の間に **84a** へと変化した。

2-6 15 位炭素の増炭反応と 3 位炭素への側鎖の導入

天然物の全合成に向けて次なる課題は 15 位炭素への 1 炭素ユニットの導入と 3 位炭素へのアミノエチル基側鎖の導入である。前述のように 3 環性スルホニイミドを得ることに成功したので詳細に合成計画を立案した(Scheme 14)。

まず、15 位炭素への 1 炭素ユニットの導入を計画した。中間体 **84a** のカルボニル基をすべて還元し、得られる三つの水酸基のうち、C15 位の水酸基を適切な方法によって区別することとした。そして、区別できた C15 位の水酸基に対して S_N2 反応を行うことで 1 炭素ユニットの導入は可能であると考えた。3 位炭素への側鎖導入に関しては、**88** のヘミアミナル部位を足がかりとして細見-櫻井反応を用いてアリル基を導入することとし、その立体化学はお椀型の立体構造を利用することで制御できるものと予想した。そしてアリル基の官能基変換を行うことでアミノエチル基へと導けると考えた。その後は、上述したとおり β -ヒドロキシケトン部位及びアミナル部位を合成終盤に構築することとした。

Scheme 14

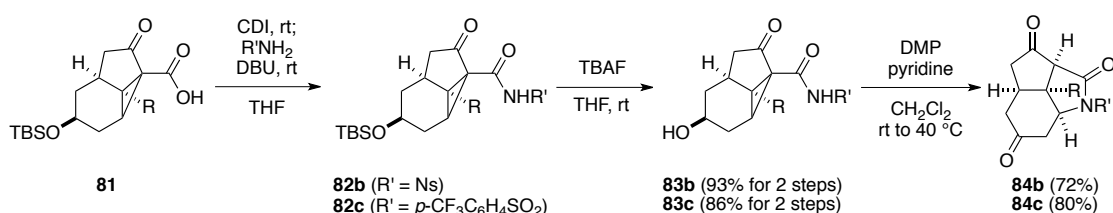


2-6-1 15 位炭素の増炭反応と窒素原子上保護基の検討

まずは、15 位炭素の増炭反応に取り組んだ(Scheme 15)。初めに **84a** の有する 3 つのカルボニル基の還元反応を DIBAL により行った。その結果、ヘミアミナル部分でのジアステレオ混合比が 2:1 かつ低収率ながらトリオール **91a** を得た。誘導化に問題が残るものの、とりあえず 15 位炭素への 1 炭素ユニットの導入を進めることとした。3,5 位の水酸基をアセトナイドで保護した後、15 位水酸基の

メシル化を行い、更に S_N2 反応にて立体選択的にシアノ基を導入することができた。15 位炭素への 1 炭素ユニットの導入には成功したものの、**94a** への誘導化において工程 **A**、**B** が低収率に留まる問題を解決しなければならない。工程 **A**、**B** の低収率の原因はヘミアミナル部位の安定性に起因していると考え、窒素原子上の保護基をより電子求引性を示す 2-ニトロベンゼンスルフォニル(Ns)基へ変換した。ノシル体 **84b** の DIBAL を用いた還元反応においては、ジアステレオ混合比が低下したものの、期待どおり収率の改善が認められた(**91b** ; 71%、**92b** ; 68%)*。その後、定法に従ってメシル化まで問題なく行えたものの、シアノ基の導入工程において目的とする化合物を全く得ることができなかった**。そこで、Ns 基と同様に電子求引性を示す窒素原子上の保護基として、4-トリフルオロメチル-ベンゼンスルフォニル基を新たに選択した。その結果、工程 **A**、**B** の両工程において良好な収率を示し***、その後のメシル化、シアノ化においても問題はないことがわかった。このように 15 位炭素への 1 炭素ユニットの堅牢な導入方法を確立することができた。

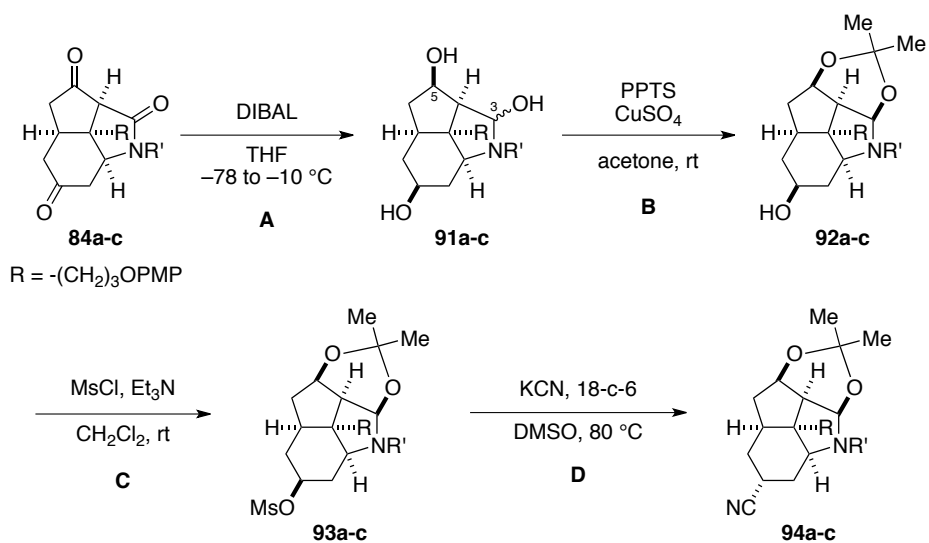
* 3 環性スルホンイミド **84b**、**84c** は **84a** と同様の方法によって合成した。



** 反応の粗生成物を精査したところ、Ns 基の損壊が認められた。シアノ化物イオンが Ns 基の電子不足のベンゼン環を攻撃することが原因であると考えている

*** 薄層クロマトグラフィー上での **84a**、**b**、**c** の挙動を精査すると、**84a** は明らかにヘミアミナル部分での異性化が認められたが、**84b**、**c** に関しては認められなかったことから工程 **A**、**B** の収率の向上の要因はヘミアミナル部位の安定性の寄与が高いと考えられる。ジアステレオ混合比の違いは、窒素原子上の置換基の種類によるイミド部分の反応性の違いによって生じたのではないかと考えている。Hummet 則から考えると Ns 基が、一番反応性が高いと考えられるが、その反応性の高さ故に、5 位もしくは 15 位酸素原子上に配位した Al からの還元が起こることでジアステレオ混合比が低下した可能性がある。

Scheme 15

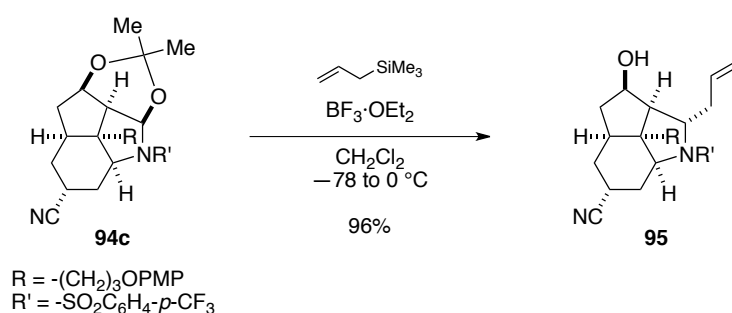


compound	R'	yield			
		A (d.r.)	B	C	D
a	Ts	32% (2:1)	50%	99%	84%
b	Ns	71% (1:1)	68%	97%	decomp.
c	p - $CF_3C_6H_4SO_2$	88% (3:1)	80%	93%	97%

2-6-2 細見-櫻井反応

次に、3 位炭素へのアリル基の導入を細見-櫻井反応にて行った(Scheme 16)。BF₃·OEt₂ でヘミアミナル部位を活性化させ、生じたスルフォニイミニウムカチオンにアリルトリメチルシランを作用させたところ、convex 面よりアリルトリメチルシランが攻撃し、立体選択的に 3 位炭素上へアリル基を導入することができた*。

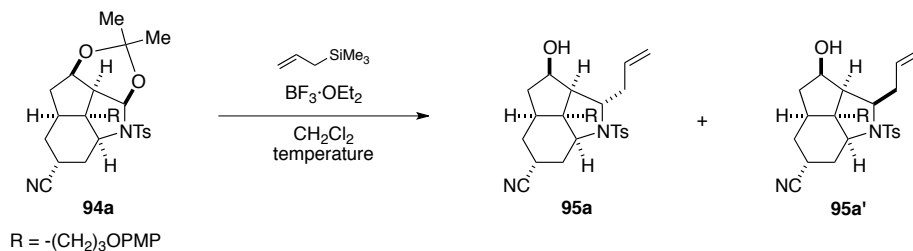
Scheme 16



2-6-3 窒素原子上の保護基の変換について(*p*-CF₃C₆H₄SO₂ 基→Boc 基)

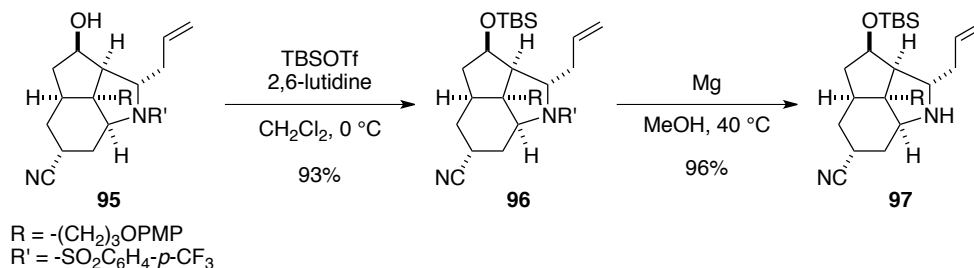
アリル基よりアミノエチル基側鎖への官能基変換の前に、天然物のアミナル部位の構築を見据えて、窒素原子上の *p*-トリフルオロメチル-ベンゼンスルフォニル基をより穏和な条件で除去できる Boc 基へと変換することとした。まず、**95** の第 2 級水酸基に TBS 基を導入した後、マグネシウム単体を用いて *p*-トリフルオロメチル-ベンゼンスルフォニル基を除去し、第 2 級アミン **97** を良好な収率にて得た(Scheme 17)。

* **95** の合成は **94a** を用いた反応条件の検討結果に従い行った。



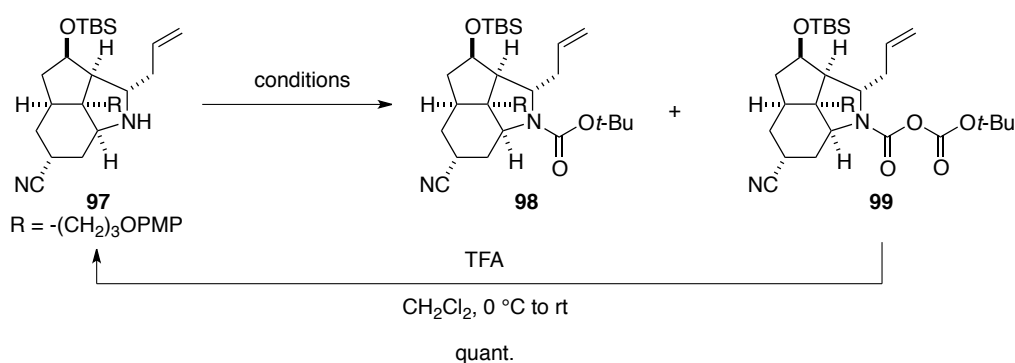
entry	temperature	result
1	0°C to rt	95a (40%), 95a' (16%)
2	-78°C to 0°C	95a (91%), 95a' (0%)

Scheme 17

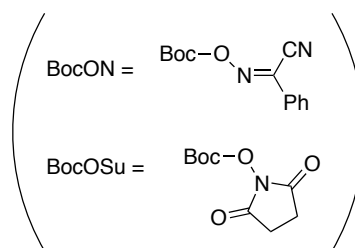


次に、第2級アミンへの Boc 基の導入を検討した(Scheme 18)。Boc₂O を用いて反応を行ったところ、低収率ながら目的の Boc 基導入体 **98** が得られたものの、二酸化炭素が挿入された **99** も同時に得られた(entry 1)。DMAP を加えることで **98** へ収束させることを期待したが、逆に **98** の収率が低下し、**99** の収率が向上する結果となった(entry 2)。反応を再考し、文献調査²¹を行い、Scheme 19 のように考察した。即ち、一旦 **97** と Boc₂O が反応すると **98**、二酸化炭素、そして *t*-BuOH が生成する。**97** の第2級アミンは両隣の炭素にトランス配置で置換基が導入されているため、立体的に嵩高く反応性が乏しい。そのため、未反応の **97** は余剰の Boc₂O と反応するよりも、立体的に小さい二酸化炭素と反応しカルバミン酸 **100** が生成する。**100** のカルバミン酸末端は立体的嵩高さが軽減されているため Boc₂O と反応し **99** が生成する。DMAP を加えても、**98** へ収束しなかった理由も **99** の立体的嵩高さで説明できると考察している。

Scheme 18

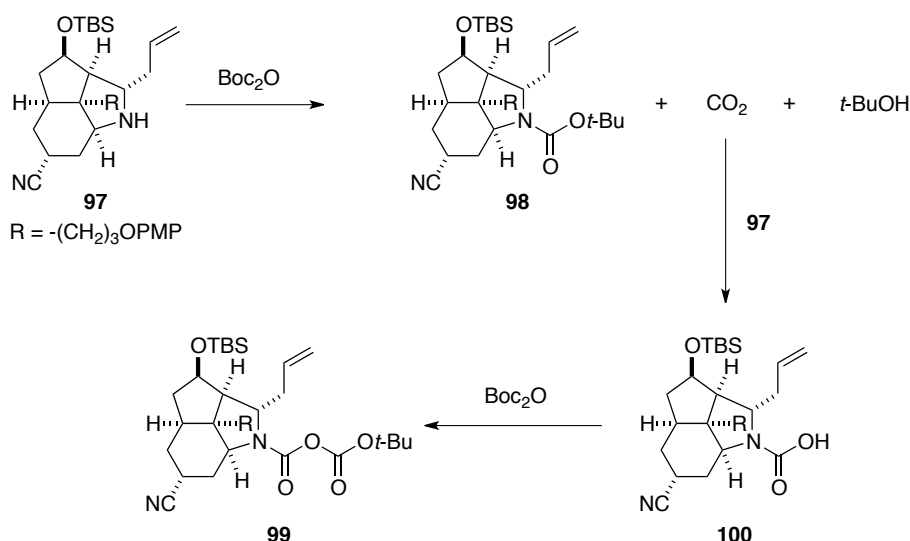


entry	conditions	result
1	Boc ₂ O, Et ₃ N, DMF 40 °C	98 (35%), 99 (60%)
2	Boc ₂ O, DMAP, DMF 40 °C	98 (20%), 99 (70%)
3	triphosgene, pyridine; <i>t</i> -BuOH	complex mixture
4	BocON, Et ₃ N, DMF, 40 °C	No reaction
5	BocOSu, Et ₃ N, DMF, 40 °C	98 (92%), 99 (0%)



上記のように、反応系内で二酸化炭素が発生しなければ、**99** の生成は起こらないと考え、entry 3~5 のように系中で二酸化炭素を生成しない Boc 化試薬を検討した。その結果、entry 5 のように BocOSu が良好な結果を示し、収率良く **98** を得ることに成功した。

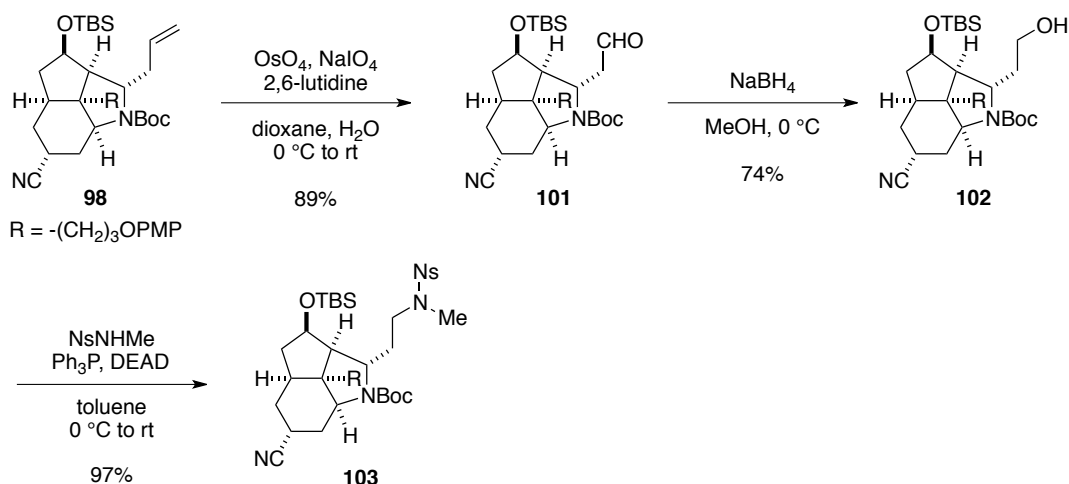
Scheme 19



2-6-4 3位アリル基のアミノエチルへの誘導化について

続いて **98** のアリル基をアミノエチル基側鎖へと変換した。即ち、**98** のオレフィン部位を Lemieux-Johnson 酸化によりアルデヒドへとした後、生じたアルデヒドを水素化ホウ素ナトリウムによりアルコールへと還元した。そして、*N*-メチルスルホンアミドとの光延反応^{22,23}により、**103** を収率良く得た(Scheme 20)。

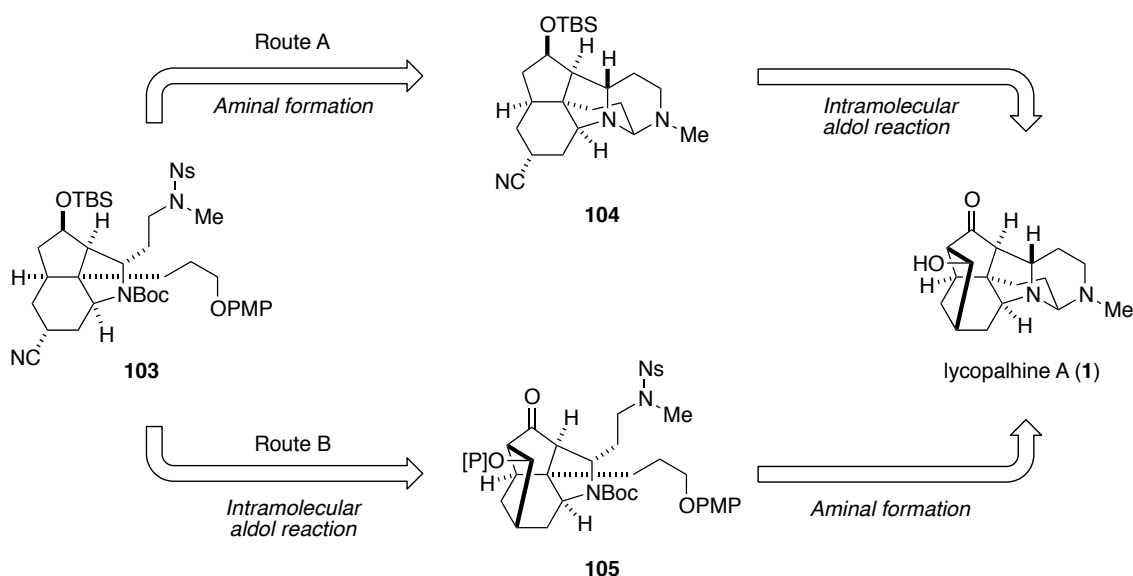
Scheme 20



2-7 β -ヒドロキシケトン部位及びアミナール部位の構築について

天然物の全合成に必要なとされる原子団はすべて導入することができたことから、天然物の全合成に向けて残す大きな課題である β -ヒドロキシケトン部位及びアミナール部位の構築に着手した。考えられる合成ルートは二つあり (Scheme 21)、先にアミナール部位を構築し、後に β -ヒドロキシケトン部位を構築するルート (Route A) と、先に β -ヒドロキシケトン部位を構築し、後にアミナール部位を構築するルート (Route B) である。Route B は、 β -ヒドロキシケトン部位を構築した後、生じたアルコールに保護基を導入する工程が Route A と比べて余分に必要である。なるべく少ない工程数で天然物に導くことを考え、まずは Route A の検討を行うこととした。

Scheme 21



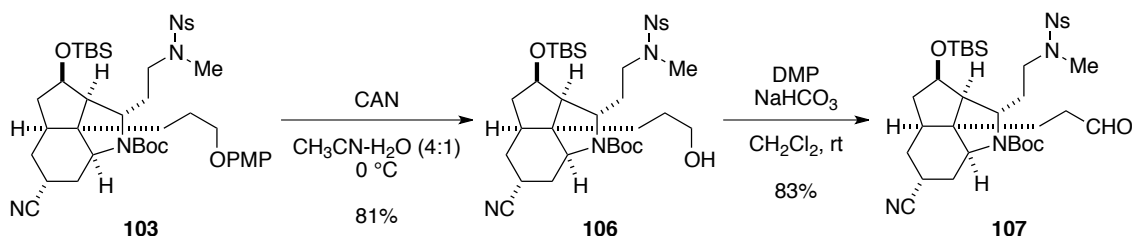
2-7-1 アミナール部位の構築(Route A)の検討

まずは、アミナール部位を構築するためにアルコキシプロピル基の保護基を除去した後、酸化を行うことでアルデヒドへと導くこととした。そして、骨格上及び側鎖上の窒素原子の保護基を段階的に除去することでアミナール部位を構築することを計画した。

中間体 **103** のアルコキシプロピル基の保護基である PMP 基をヘキサニトラトセリウム(IV)酸アンモニウム(CAN)を用いて除去した後、アルコール部分を

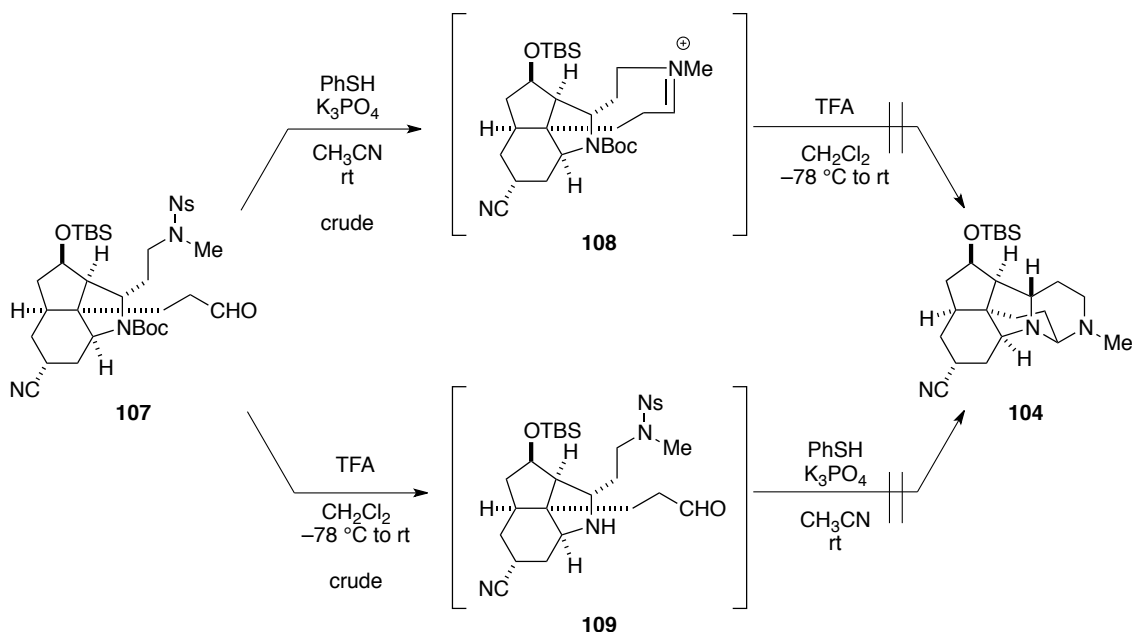
Dess-Martin 試薬を用いてアルデヒドへと変換し **107** を得た(Scheme 22)。

Scheme 22



次いで、アミナール部位の構築の検討を行った(Scheme 23)。まず、**107** の Ns 基をチオフェノールにより除去した。質量分析より反応系中を分析したところ、分子内でイミニウムカチオンを形成していることが予想されたので、分液操作を行った後、有機層をトリフルオロ酢酸で処理し、Boc 基を除去することでアミナールを形成するか検討した。しかしながら、反応は全く進行せず目的とするアミナール **104** は得られなかった。反応の加温も行ったが、反応系が複雑化するのみであった。窒素原子上の保護基を除去する順序を変更したものの、同様に **104** は得られなかった*。

Scheme 23



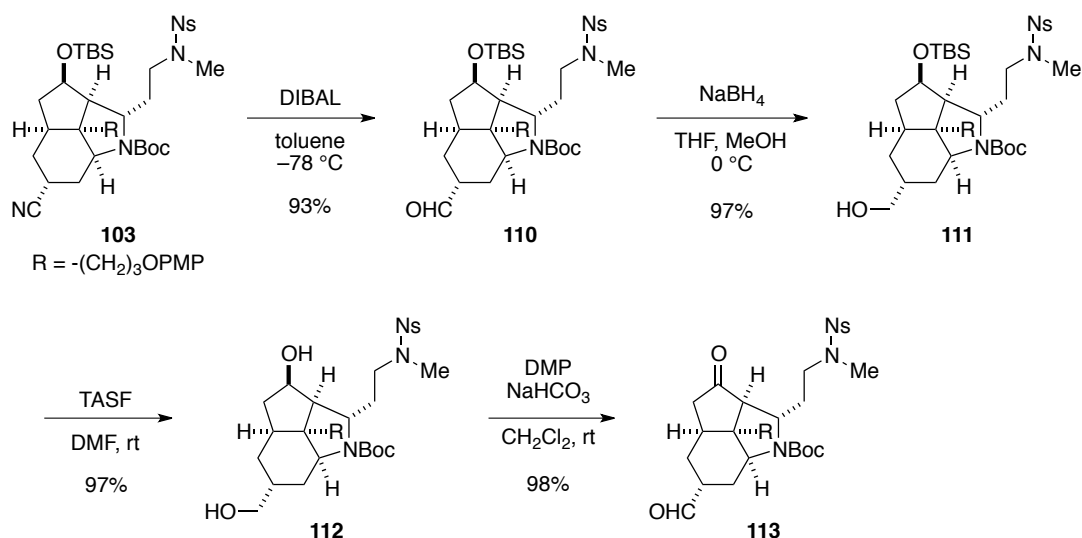
* **107** の Ns 基を除去すると **108** に相当するイオンピークが質量分析にて検出されたため、イミニウムカチオンを形成していると思われる。一方、**107** の Boc 基を除去すると、予想されたイミニウムカチオンに相当するイオンピークは検出されず、更に $^1\text{H-NMR}$ においてアルデヒドの存在が認められたため、**109** のように側鎖と母核の間での結合形成はなかったと考えている。

2-7-2 β -ヒドロキシケトン部位の構築(Route B)の検討

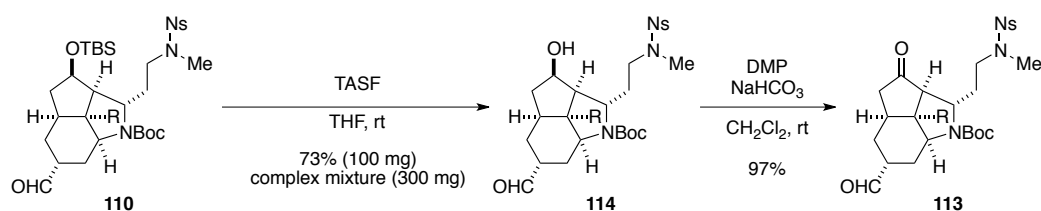
上述のように、Route A のアミナル構築は困難であったため、Route B での β -ヒドロキシケトン部位とそれに続くアミナル部位の構築に着手した。

β -ヒドロキシケトン部位を構築するため、分子内アルドール反応前駆体 **113** への誘導化を企図した(Scheme 24)。まず、**103** のニトリル基を DIBAL によりホルミル基へと変換した後、水素化ホウ素ナトリウムを用いてアルコールへと還元した。次いで、TASF により TBS 基を除去した後、Dess-Martin 試薬を用いて第 1 級アルコールと第 2 級アルコールをそれぞれアルデヒド、ケトンへと同時変換し、分子内アルドール反応前駆体 **113** を得た*。

Scheme 24



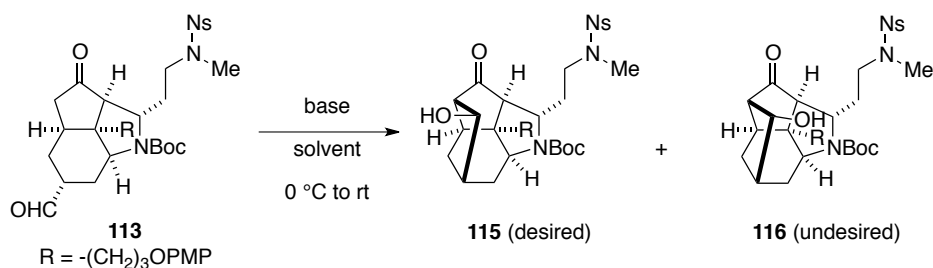
* 15 位のホルミル基をアルコールへと還元せずに、誘導化を進めると **113** を得られるものの、下記のスキームに示すようにスケールアップに問題があった。



2-7-3 分子内アルドール反応

分子内アルドール反応前駆体が得られたので、続いて分子内アルドール反応の検討を行った(Scheme 25)。溶媒をメタノールに固定し、塩基を無機塩基、有機塩基を用いて反応を行った(entry 1~4)。その結果、すべての条件において良好な収率にて望みのアルドール成績体 **115** を与えた。溶媒を非プロトン性極性溶媒のアセトニトリルに変更し、塩基を DBU に変更しても、同様に **115** を収率良く与えた(entry 5)。しかしながら、溶媒を非プロトン性かつアセトニトリルより極性が低い THF、トルエンを用いると、**115** と共に水酸基の立体化学が反対の β -ヒドロキシケトン **116** も得られてきた(entry 6,7)。

Scheme 25

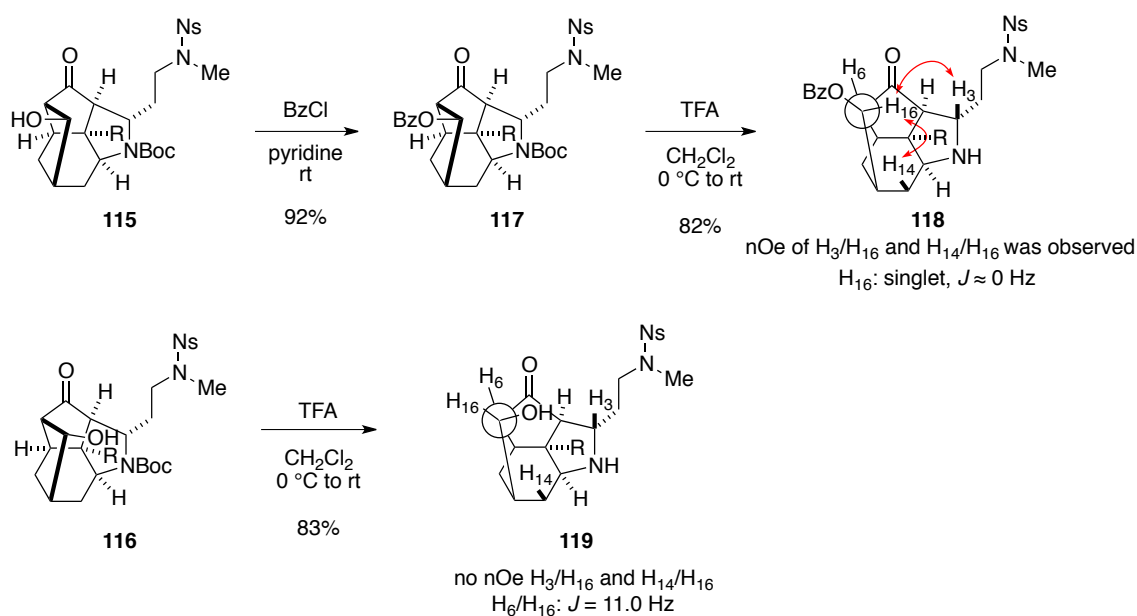


entry	solvent	base	result
1	MeOH	KOH	115 92%, 116 –
2	MeOH	LiOH	115 93%, 116 –
3	MeOH	NaOH	115 92%, 116 –
4	MeOH	Triton B	115 90%, 116 –
5	CH ₃ CN	DBU	115 82%, 116 –
6	THF	DBU	115 27%, 116 67%
7	Toluene	DBU	115 30%, 116 55%

得られたアルドール成績体 **115**、**116** は共に立体的に嵩高い窒素原子に Boc 基が導入されているため ¹H NMR において回転異性体が観察され、**115**、**116** そのものの水酸基の立体化学の同定は困難であった。そのため、両化合物とも Boc 基の除去を行った後、NOESY と ¹H NMR を用いて水酸基の立体化学を決定した(Scheme 26)。化合物 **115** に関しては、水酸基に Bz 基を導入した後、トリフルオロ酢酸を用いて Boc 基を除去して得た **118** の NOESY スペクトルにおいて H(3)-H(16)及び H(14)-H(16)との間で相関が認められた。更に ¹H NMR において H₁₆ のピークが singlet であることより H₆ と H₁₆ の二面角はおよそ 90°であることが示唆されたことから、**115** の水酸基は望みの立体化学であると決定した。一方、

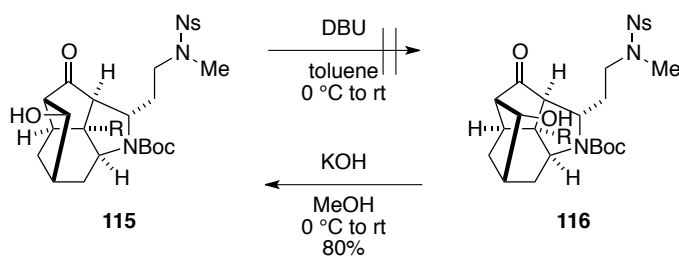
116 に関しては、水酸基に Bz 基が導入できなかったため、トリフルオロ酢酸を用いて Boc 基を除去し **119** を得た後、同様に NOESY と ^1H NMR を測定したところ、**118** で認められた nOe 相関は観測されず、更に ^1H NMR において H_6 と H_{16} の間のカップリング定数が 11.0 Hz であったことから **116** の水酸基の立体化学は望みの逆であると決定した。

Scheme 26



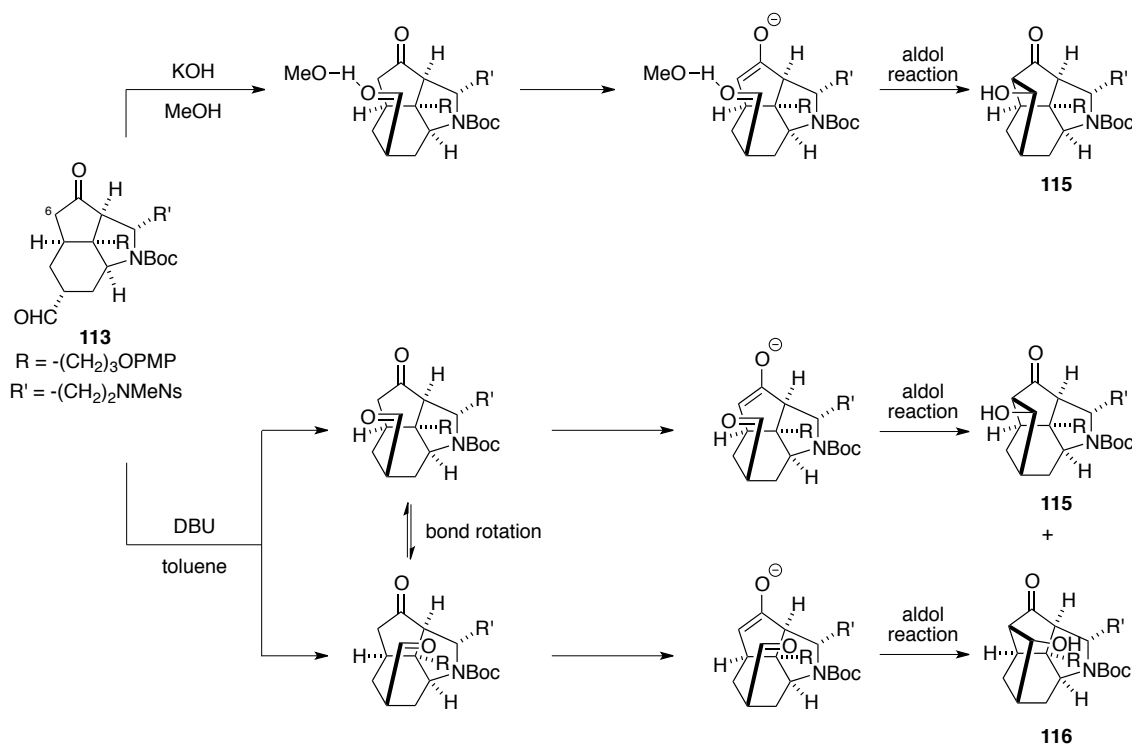
化合物 **115** と **116** の間に平衡が存在し、加える試薬を選ぶだけで相互変換が可能であるかに興味を抱いたので Scheme 27 に示したように、**115** もしくは **116** を得た条件をそのまま互いに適用することで変換可能であるか検討した。**115** に対してトルエン中 DBU を作用させたが、**116** の生成は認められなかったものの、**116** に対してメタノール中水酸化カリウムを作用させると **115** に収率良く変換できることが明らかとなった。これにより、**115** は **116** よりも熱力学的に安定であると考えている。

Scheme 27



以上を踏まえて、分子内アルドール反応の条件によって得られる β -ヒドロキシケトン の立体化学が異なることを次のように考察している(Scheme 28)。即ち、まず、塩基によりホルミル基の α 位のプロトンが引き抜かれた後、convex 面からプロトン化を受けることでホルミル基のエピ化が起こる。エピ化が生ずるとホルミル基と 6 位炭素が接近するため、アルドール反応が進行する。反応が進行するとき、溶媒によってホルミル基のカルボニルの配向性が異なると考えられる。極性溶媒中では、溶媒分子との水素結合によってホルミル基の酸素原子が convex 側に向くことで **115** が生成する。一方、非極性溶媒中では溶媒との水素結合形成が弱まり、ホルミル基が自由に回転できるようになり、ホルミル基の酸素原子が concave 側に配向する状態の分子も一部存在するために **115** と共に **116** も生成したと考えている。

Scheme 28

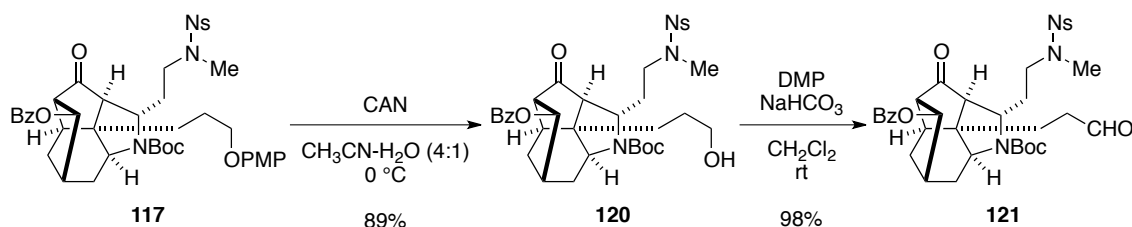


2-7-4 アミナール部位の構築(Route B)の検討

β -ヒドロキシケトン部位の構築を行うことができたことから、最後の課題であるアミナール部位の構築に取り掛かることとした。Route A と同様のアプローチでアミナール部位の構築を行うことを計画した。即ち、アルコキシプロピル基をアルデヒドへと酸化し、次いで段階的に窒素原子上の保護基を除去することでアミナール部位を構築することとした。

まず、**117** の PMP 基をヘキサニトラトセリウム(IV)酸アンモニウム(CAN)を用いて除去した後、Dess-Martin 試薬を用いてアルコール部位をアルデヒドへと変換し **121** を得た。(Scheme 29)。

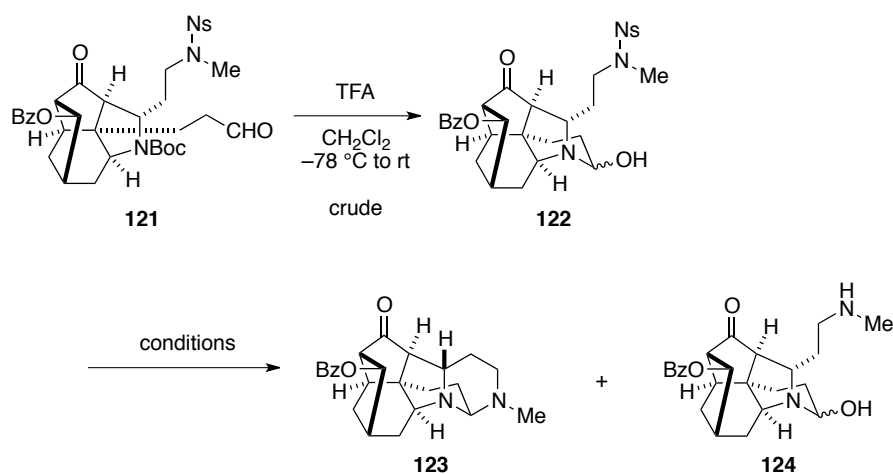
Scheme 29



次いでアミナール部位の構築を検討した(Scheme 30)。Boc 基をトリフルオロ酢酸により除去したところ、Route A では認められなかったアルデヒド側鎖とのヘミアミナール形成が ^1H NMR より示唆された。次いで、側鎖上の Ns 基をチオフェノールにより除去したところ*、低収率ながら目的のアミナール形成体 **123** が得られたが、アミナール形成前駆体 **124** も中程度の収率で得られた (entry 1)。中間体 **124** が残存していることから、反応系を塩基性から酸性へと変更することにした。チオフェノールによる Ns 基の除去を確認した後、リン酸カリウムに対して 2 等量の酢酸を添加し、更に $50\text{ } ^\circ\text{C}$ まで昇温させると反応は円滑に進行しアミナール **123** を高収率にて得ることに成功した。

* Ns 基の除去においてよく用いられる炭酸カリウムや炭酸セシウムを用いると Scheme 18 及び 19 で示したように反応系内で二酸化炭素が生成し、第 2 級アミンとカルバミン酸を形成することが懸念されたため、リン酸カリウムを用いた。

Scheme 30

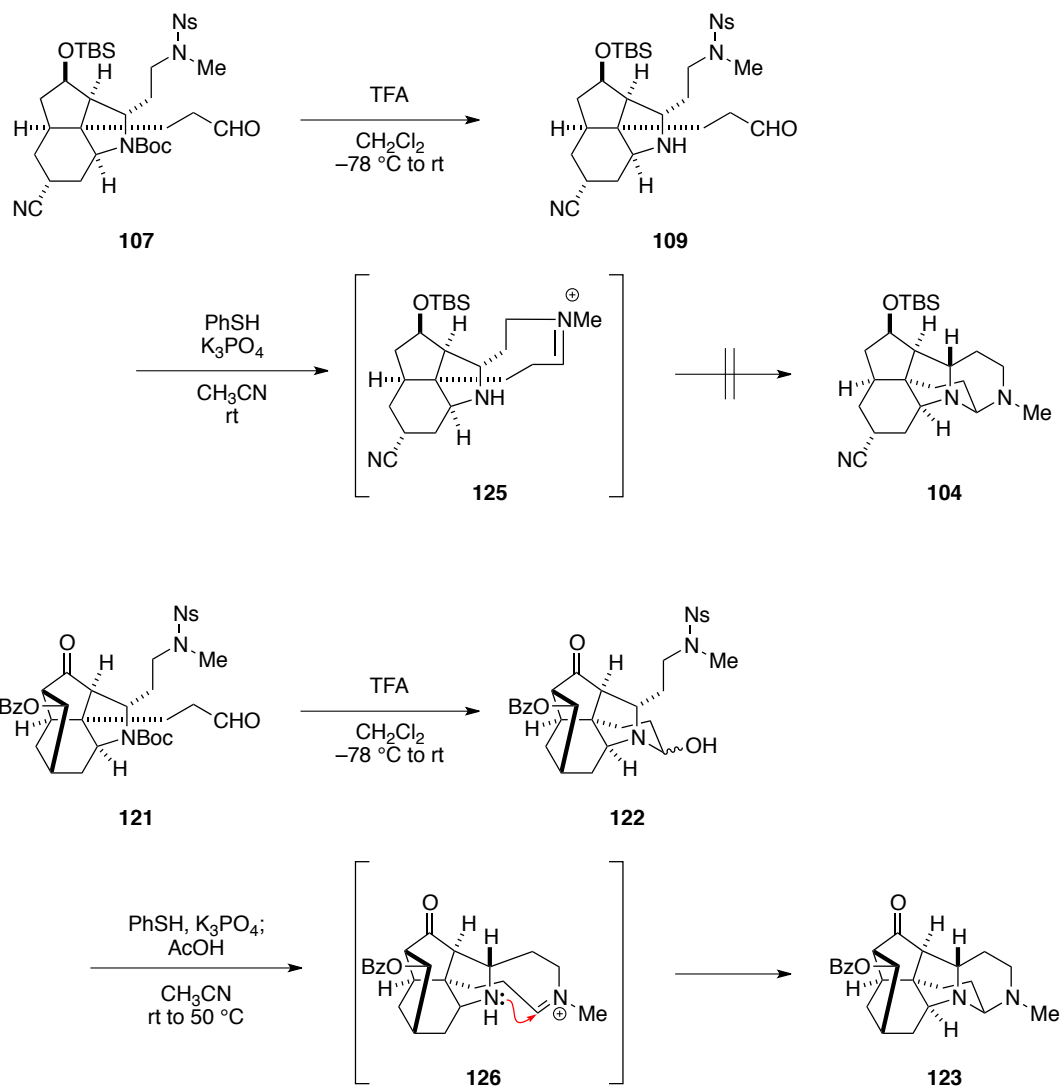


entry	conditions	result
1	PhSH, K ₃ PO ₄ (3 eq), CH ₃ CN, rt	123 (13%), 124 (35%) for 2 steps
2	PhSH, K ₃ PO ₄ (3 eq), CH ₃ CN, rt; AcOH, (6 eq) rt to 50 °C	123 (89% for 2 steps)

2-7-5 Route A もしくは Route B でのアミナール形成について

Route B にてアミナール部位を構築することができたことを踏まえて、Route A にてアミナール形成が進行しなかった理由について以下のように考察した (Scheme 31)。アミナール部位の構築において、Route A と Route B を比較した時、アルデヒド側鎖と母核上の窒素原子とのヘミアミナール形成が大きく影響していることが分かる。¹H NMR より化合物 **109** は分子内でヘミアミナールを形成していないが、化合物 **122** はヘミアミナールを形成していることが示唆されている。この違いは主骨格の構造の違いによる第 2 級アミンの非共有電子対の向きに起因していると考えている。分子模型より考えると、化合物 **122** では分子内で β -ヒドロキシケトンを形成していることから構造が剛直であり、窒素原子の非共有電子対が紙面奥側に向きやすくなっていると思われる。一方、化合物 **109** については **122** と比べて窒素原子の非共有電子対がより紙面手前側に配向すると思われる。上記の違いが最終的に二つの側鎖で形成されるイミニウムカチオンへの求核攻撃によるアミナール形成の有無につながると考えている。

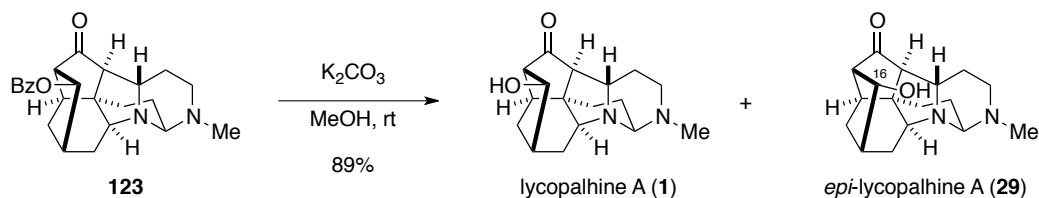
Scheme 31



2-8 Lycopalhine A の全合成

最後に水酸基の Bz 基を加溶媒分解にて除去したところ、lycopalhine A (**1**) と 16 位の水酸基がエピ化した **29** の混合物が得られた(Scheme 32)。Lycopalhine A (**1**) の単離、構造決定が行われた文献⁸記載の NMR を精査すると、記載はないもののエピ化体 **29** が含まれていることを確認できた。筆者が得た lycopalhine A (**1**) とエピ化体 **29** の混合物の NMR と化学シフト並びに積分値まで完全に一致していることも併せて確認した。上記の文献で lycopalhine A (**1**) は平衡混合物であることが言及されてはいなかったため、 β -ヒドロキシケトン部位での平衡が存在するかを検討することとした。

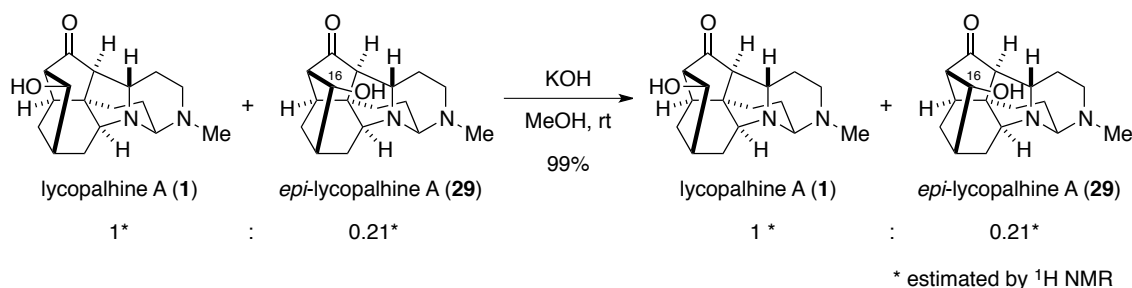
Scheme 32



2-8-1 Lycopalhine A が平衡混合物であることの確認実験

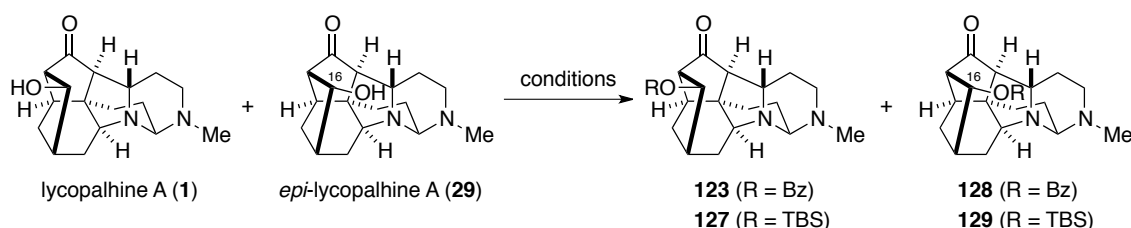
まず初めに、Scheme 27 で示したように、水酸基が convex 側に配向した化合物が熱力学的安定であることを利用して、lycopalhine A (**1**) に平衡を偏らせることが可能かどうか検討した(Scheme 33)。混合物 **1** と **29** に対しメタノール中水酸化カリウムを作用させたが、その比率に変化は認められなかった。

Scheme 33



次に水酸基に置換基を導入することで、平衡が存在するか確認した(Scheme 34)。まず、Bz 基の導入を行った(entry 1)。反応は完結し、Bz 基導入体を得たが、**123** のみであり **128** は全く得られなかった。次に TBS 基の導入を行った(entry 2, 3)。反応を 4 時間で終了させ、精製操作を行ったところ、**127** は収率 66%で得られたが、**129** は全く得られなかった。更に未反応の原料 (lycopalhine A (**1**)とエピ化体 **29** の混合物)を回収したところ、その混合比率にほとんど変化はなかった。収率 66%で **127** が得られていることから、平衡が存在しなければ、理論的にはその混合比率はおおよそ 1:1 になるはずであるが、変化が見られなかったことから平衡が存在すると考えられる。また、entry 3 のように反応時間を 11 時間に延長すると、**127** を収率 94%で与え、平衡が存在しなければ、計算上 82%を越えることがないため、このことから lycopalhine A (**1**)は **29** との平衡混合物あると言える。

Scheme 34



entry	conditions	result
1	BzCl, pyridine	123 (75%), 128 (0%)
2	TBSCl, imidazole, DMF, 4h	127 (66%), 129 (0%) SM was recovered (1 : 29 = 1 : 0.26)
3	TBSCl, imidazole, DMF, 11h	127 (94%), 129 (0%)

以上のように、Trauner らの重水素化実験(Scheme 2)に加えて、更に lycopalhine A (**1**)が平衡混合物であることを実験的に示すことができ、lycopalhine A (**1**)の全合成を達成した。

第三章

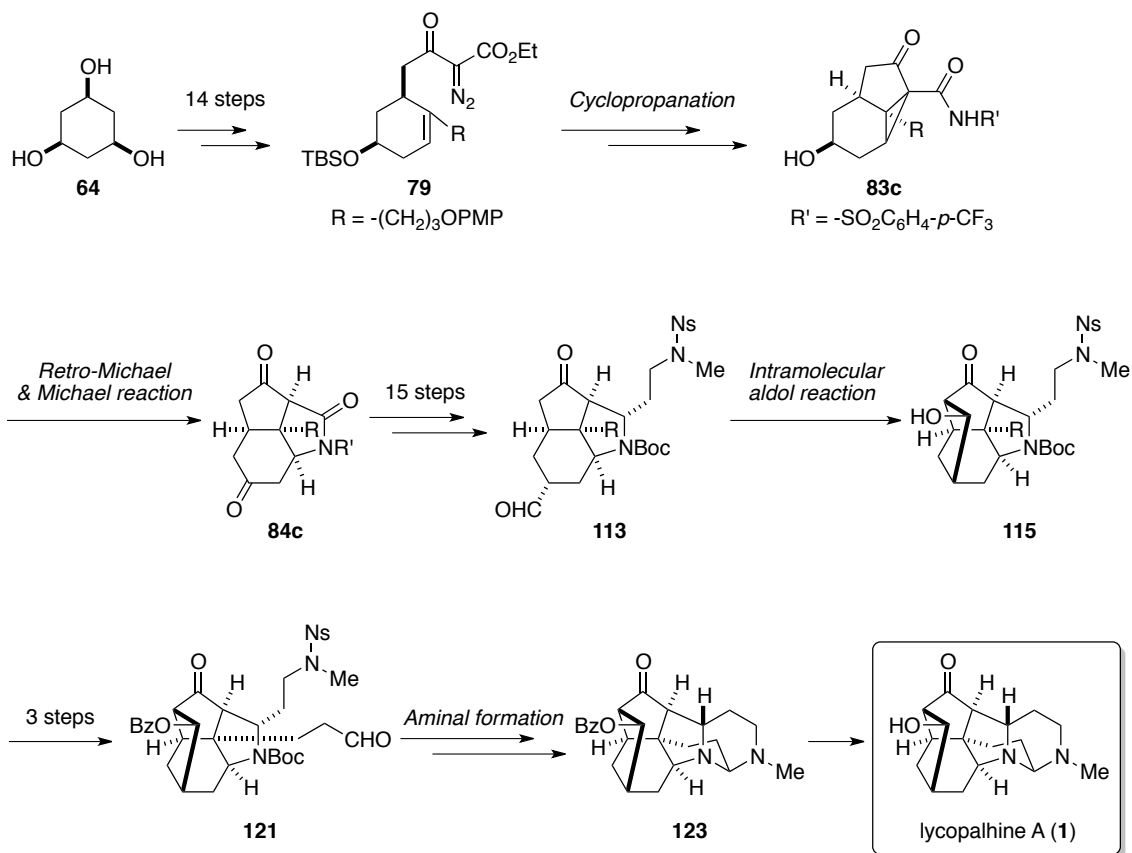
結語

以上を総括すると、今回筆者は、lycopalhine A (**1**)の有する特異な縮環構造とその合成方法に興味を抱き、本天然物の骨格構築における独創的な合成経路の確立を目指し、全合成研究を行った。

その中で、逆 Michael 反応と続く分子内 Michael 付加反応を行うことで天然物の主骨格であるピロリジン環を含む 3 環性化合物を合成し、更にその分子構造を活用した立体選択的な反応により本天然物の全合成を達成した。以下にその概要を示す(Scheme 35)。

cis,cis-1,3,5-シクロヘキサントリオール **64** より鈴木-宮浦カップリング、Johnson-Claisen 転位などを含む 14 段階にてジアゾ化合物 **79** へと導いた後、銅触媒を用いた分子内シクロプロパン化と置換基の変換を行うことで **83c** を得た。化合物 **83c** の第 2 級アルコールの酸化を行うと逆 Michael 反応と分子内 Michael 付加反応が一挙に進行し天然物の主骨格である 3 環性スルホンイミド **84c** を得ることに成功した。次に、**84c** の立体化学を利用し 15 段階にて **113** へと変換した。化合物 **113** に水酸化カリウムをメタノール中作用させるとホルミル基のエピ化と分子内アルドールが進行し、高い立体選択性にて β -ヒドロキシケトン部位を構築することができた。 β -ヒドロキシケトン **115** の立体化学は水酸基の Bz 基を導入後、Boc 基を除去した基質にて NOESY, ^1H NMR を測定し決定した。また、上記の分子内アルドール反応において塩基として DBU を用い、非プロトン性非極性溶媒中で反応を行うと第 2 級アルコールの立体化学が逆である化合物も同時に得られてくることを見出した。続いてアミナール部位の構築に向けて 3 段階にて **121** へと導いた。この中間体 **121** の保護基を段階的に除去し、反応系中を酸性とすることでアミナール形成を収率良く行うことに成功した。その後、アルコールの保護基を除去することで lycopalhine A (**1**)の全合成を達成した。更に、lycopalhine A (**1**)が平衡混合物であることも併せて見出した。

Scheme 35

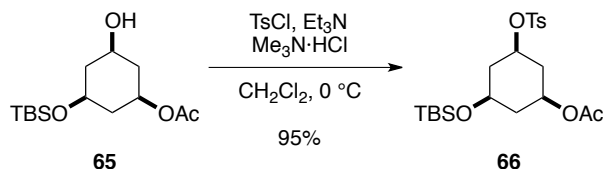


Experimental Section

General Remarks: Nuclear magnetic resonance (^1H NMR (400 MHz), ^{13}C NMR (100 MHz)) spectra were determined on a JEOL-ECS400 instrument unless otherwise noted. Chemical shifts for ^1H NMR are reported in parts per million (ppm) downfield from tetramethylsilane (δ) or relative to the singlet for residual chloroform at 7.26 ppm or pyridine at 7.19 ppm as the internal standard. Coupling constants are reported in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Chemical shifts for ^{13}C NMR were reported in ppm relative to the center line of a triplet at 77.0 ppm for deuteriochloroform or a triplet at 123.4 ppm for pyridine- d_5 . Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 Fourier Transform Infrared Spectrophotometer and were reported in wavenumbers (cm^{-1}). High resolution mass spectra (HRMS) were obtained on a JEOL JMS-T100LP AccuTOF LC-plus either in positive electrospray ionization (ESI) method or in positive direct analysis in real time (DART) ionization method, using PEG as the internal standard. Melting points (mp) were determined on a Yanaco Micro Melting Point Apparatus. Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F₂₅₄. Preparative TLC separations were performed on Merck analytical plates (0.25 or 0.50 mm thick) precoated with silica gel 60 F₂₅₄. Flash chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 (spherical, 40-100 mesh) unless otherwise noted. Reagents were commercial grades and were used without any purification. Dehydrated tetrahydrofuran, diethyl ether, toluene, and dichloromethane were purchased from Kanto Chemicals Co., Inc., and were purified using a Glass Contour Solvent System. Dehydrated benzene and *N,N*-dimethylformamide were purchased from Kanto Chemicals Co., Inc. and stored over activated MS4A*. Dehydrated methanol, ethanol and acetonitrile were also purchased from Kanto Chemicals Co., Inc. and stored over activated MS3A*. All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere.

* Molecular sieves were "activated" in the following manner: A round-bottom flask containing molecular sieves was heated in a regular microwave for 1.5-2.0 minute and the flask was immediately evacuated. When cooled to room temperature, the flask was backfilled with argon. The above procedure was repeated three times.

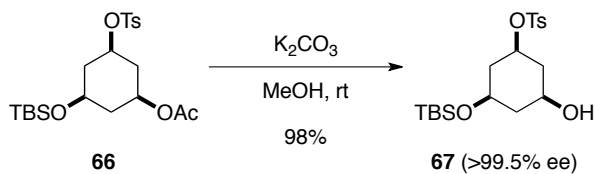
(1*R*,3*S*,5*S*)-1-Acetoxy-3-(*p*-toluenesulfonyloxy)-5-(*tert*-butyldimethylsilyloxy)-cyclohexane (66**)**



To a solution of **65** (29.7 g, 102 mmol), triethylamine (35.4 ml, 254 mmol) and trimethylammonium hydrochloride (9.7 g, 102 mmol) in CH₂Cl₂ (300 mL) was added TsCl (29.0 g, 152 mmol) at 0 °C. The mixture was stirred for 1 h. To decompose the remaining TsCl, *N,N*-dimethylethylenediamine (ca. 18.0 ml) was added to the reaction mixture. After stirring for another 10 min, water was added to the mixture. The resulting solution was extracted three times with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 10:1) to give **66** (44.9 g, 99%) as a colorless oil.

[α]_D²⁴ -1.88° (*c* = 1.00, CHCl₃); IR (film) 2954, 2930, 2857, 1738, 1598, 1471, 1365, 1241, 1178, 1099, 1036, 935, 861, 813, 778 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 7.78 (d, *J*=8.2 Hz, 2H), 7.34 (d, *J*=8.2 Hz, 2H), 4.61 (dddd, *J*=11.5, 11.5, 4.6, 4.6 Hz, 1H), 4.36 (dddd, *J*=11.5, 11.5, 4.6, 4.6 Hz, 1H), 3.53 (dddd, *J*=11.5, 11.5, 4.6, 4.6 Hz, 1H), 2.43 (s, 3H), 2.18 (ddd, *J*=11.5, 4.6, 4.6 Hz, 1H), 2.15-2.03 (m, 2H), 2.00 (s, 3H), 1.48 (ddd, *J*=11.5, 11.5, 11.5 Hz, 1H), 1.43 (ddd, *J*=11.5, 11.5, 11.5 Hz, 1H), 1.29 (ddd, *J*=11.5, 11.5, 11.5 Hz, 1H), 0.82 (s, 9H), -0.01 (s, 3H), -0.02 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.0 (C), 144.8 (C), 134.1 (C), 129.9 (CH), 127.6 (CH), 75.2 (CH), 66.6 (CH), 65.3 (CH), 41.4 (CH₂), 40.2 (CH₂), 37.1 (CH₂), 25.6 (CH₃), 21.6 (CH₃), 21.0 (CH₃), 17.9 (C), -4.9 (CH₃); HRMS (ESI+) 465.1744 (calcd for C₂₁H₃₄NaO₆SSi 465.1743).

(1*R*,3*S*,5*S*)-1-Hydroxy-3-(*p*-toluenesulfonyloxy)-5-(*tert*-butyldimethylsilyloxy)-cyclohexane (67**)**



To a solution of **66** (44.9 g, 101 mmol) in MeOH (1.00 L) was added potassium carbonate (21.4 g, 152 mmol) at room temperature and stirring was continued at room temperature for 2 h. The solution was evaporated and the residue was partitioned between EtOAc and water. The aqueous phase was further extracted with EtOAc and the combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 5:1~2:1) to afford **67** (39.6 g, 98%, >99.5% ee) as a colorless oil. The enantiomeric excess was determined by HPLC analysis with a chiral HPLC column (DAICEL CHIRALCEL AD-H, 4% 2-propanol in *n*-hexane, 1.0 mL/min at 25 °C, 210 nm). The retention times corresponding to **67** and its enantiomer are 30.9 and 27.1 min, respectively.

$[\alpha]_{\text{D}}^{25} -1.32^\circ$ ($c = 1.00$, CHCl₃);

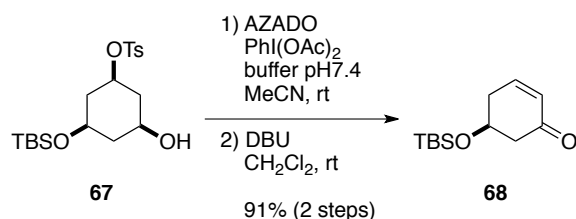
IR (film) 2953, 2930, 2857, 1598, 1470, 1360, 1256, 1176, 1099, 1049, 956, 931, 873, 836, 777 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.82 (d, $J=8.2$ Hz, 2H), 7.33 (d, $J=8.2$ Hz, 2H), 4.42 (dddd, $J=10.5, 10.5, 4.6, 4.6$ Hz, 1H), 3.57 (dddd, $J=10.5, 10.5, 4.6, 4.6$ Hz, 1H), 3.57 (dddd, $J=10.5, 10.5, 4.6, 4.6$ Hz, 1H), 2.44 (s, 3H), 2.18-2.08 (m, 1H), 2.08-1.94 (m, 2H), 1.91 (d, $J=5.0$ Hz, 1H), 1.50 (ddd, $J=12.0, 10.5, 10.5$ Hz, 1H), 1.48 (ddd, $J=12.2, 10.5, 10.5$ Hz, 1H), 1.33 (ddd, $J=12.0, 10.5, 10.5$ Hz, 1H), 0.82 (s, 9H), 0.00 (s, 3H), -0.03 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 144.7 (C), 134.3 (C), 129.8 (CH), 127.6 (CH), 75.8 (CH), 65.7 (CH), 65.1 (CH), 43.4 (CH₂), 40.8 (CH₂), 40.5 (CH₂), 25.7 (CH₃), 21.6 (CH₃), 18.0(C), -4.9(CH₃);

HRMS (ESI+) 423.1622 (calcd for C₁₉H₃₂NaO₅SSi 423.1637).

(5S)-5-*tert*-Butyldimethylsilyloxycyclohex-2-enone (68)



To a solution of **67** (56.0 g, 140 mmol) and PhI(OAc)₂ (98.0 g, 304 mmol) in acetonitrile (580 mL) and phosphate buffer (pH7.4, 580 mL) was added AZADO (1.58 g, 10.4 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature. After stirring for 2 h at room temperature, the reaction was quenched with aqueous Na₂S₂O₃. The resulting solution was extracted three times with EtOAc. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residue was dissolved in CH₂Cl₂ (1.00 L) and DBU (25.5 mL, 171 mmol) was added at 0 °C. After stirring for 1.5 h at 0 °C, aqueous NH₄Cl was added. The resulting mixture was extracted three times with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:0~10:1) to give **68** (28.5 g, 91%) as a pale yellow oil.

$[\alpha]_D^{25}$ 10.4° (*c* = 1.00, CHCl₃);

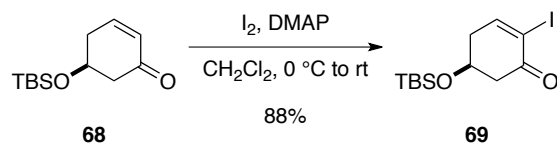
IR (film) 2955, 2930, 2894, 2857, 1682, 1472, 1389, 1253, 1103, 939, 836, 777 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.85 (ddd, *J*=10.1, 5.0, 3.2 Hz, 1H), 6.03 (d, *J*=10.1 Hz, 1H), 4.22 (dddd, *J*=9.6, 7.5, 4.7, 4.1 Hz, 1H), 2.64 (dd, *J*=16.0, 4.1 Hz, 1H), 2.58 (ddd, *J*=18.3, 5.0, 4.7 Hz, 1H), 2.46 (dd, *J*=16.0, 9.6 Hz, 1H), 2.36 (dddd, *J*=18.3, 7.5, 3.2, 2.7 Hz, 1H), 0.86 (s, 9H), 0.05 (s, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 198.6 (C), 146.8 (CH), 130.0 (CH), 67.5 (CH), 48.0 (CH₂), 35.5 (CH₂), 25.7 (CH₃), 17.9 (C), -4.8 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 249.1284 (calcd for C₁₂H₂₂NaO₂Si 249.1287).

(5*S*)-2-Iodo-5-*tert*-butyldimethylsilyloxycyclohex-2-enone (69)



To a solution of **68** (16.4 g, 72.4 mmol) and DMAP (17.7 g, 145 mmol) in CH₂Cl₂ (40.0 mL) was added iodine (20.5 g, 80.8 mmol) in CH₂Cl₂ (500 mL) slowly at 0 °C. The reaction mixture was allowed to warm to room temperature. After stirring for 2 h at room temperature, the reaction was quenched with aqueous Na₂S₂O₃. The resulting solution was extracted with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 50:1) to afford **69** (22.5 g, 88%) as a pale yellow oil.

[α]_D²⁶ 11.0° (*c* = 1.00, CHCl₃);

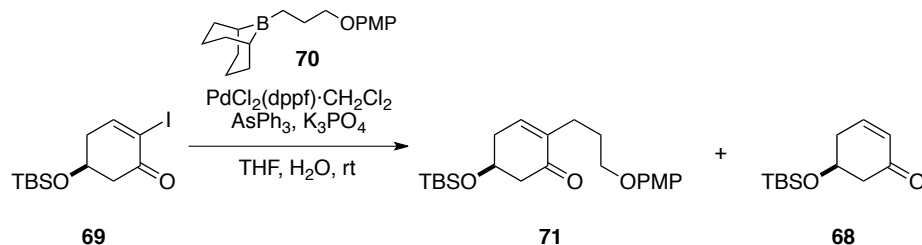
IR (film) 2953, 2929, 2893, 2856, 1690, 1591, 1471, 1322, 1254, 1106, 962, 837, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.61 (dd, *J*=5.3, 3.8 Hz, 1H), 4.27 (dddd, *J*=9.2, 6.9, 5.0, 3.7 Hz, 1H), 2.85 (dd, *J*=15.6, 5.0 Hz, 1H), 2.67 (dd, *J*=15.6, 9.2 Hz, 1H), 2.63 (ddd, *J*=18.3, 5.3, 3.7 Hz, 1H), 2.45 (ddd, *J*=18.3, 6.9, 3.8 Hz, 1H), 0.85 (s, 9H), 0.05 (s, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 191.2 (C), 155.1 (CH), 103.5 (C), 67.2 (CH), 46.7 (CH₂), 39.3 (CH₂), 25.6 (CH₃), 17.9 (C), -4.8 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 375.0249 (calcd for C₁₂H₂₁INaO₂Si 375.0253).

(S)-5-((*tert*-Butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenoxy)propyl)cyclohex-2-ene (71)



To a solution of 1-allyloxy-4-methoxybenzene (14.2 g, 86.5 mmol) in THF (120 mL) was added 9-BBN (0.5 M solution in THF, 152 mL, 76.0 mmol) at room temperature and the solution was heated at reflux for 2 h. In another flask **69** (20.6 g, 58.5 mmol) were dissolved in THF (240 mL). To this solution were added the above solution containing the boron reagent, $\text{PdCl}_2(\text{dppf})\cdot\text{CH}_2\text{Cl}_2$ (4.74 g, 5.80 mmol), potassium phosphate (24.0 g 113 mmol), triphenylarsine (1.81 g, 5.91 mmol) and water (120 mL) at 0 °C. After stirring for 2 h at room temperature, the reaction was quenched with aqueous NH_4Cl . The resulting solution was extracted with EtOAc. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified roughly by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 50:1~10:1) to afford 5:1 mixture of **71** and **68** (20.86 g) as a yellow oil, which was used for the next step without further purification. The spectroscopic data for **71** were collected after purification by PTLC (SiO_2 ; toluene:acetone = 100:1).

$[\alpha]_{\text{D}}^{26}$ 1.98° (c = 1.00, CHCl_3);

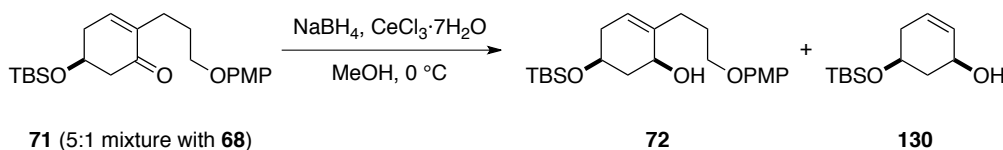
IR (film) 2953, 2929, 2896, 2856, 1676, 1508, 1471, 1380, 1231, 1106, 1041, 866, 835, 777 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 6.85 (s, 4H), 6.61 (dd, J =4.6, 3.2 Hz, 1H), 4.17 (dddd, J =9.6, 7.3, 4.6, 4.1 Hz, 1H), 3.88 (t, J =6.4 Hz, 2H), 3.75 (s, 3H), 2.66 (dd, J =16.0, 4.1 Hz, 1H), 2.57 (ddd, J =17.8, 4.6, 4.6 Hz, 1H), 2.47 (dd, J =16.0, 9.6 Hz, 1H), 2.42-2.30 (m, 3H), 1.86 (tt, J =7.6, 6.4 Hz, 2H), 0.86 (s, 9H), 0.05 (s, 6H);

^{13}C NMR (100 MHz, CDCl_3) δ 198.0 (C), 153.7 (C), 153.0 (C), 141.9 (CH), 139.3 (C), 115.4 (CH), 114.6 (CH), 67.8 (CH_2), 67.7 (CH), 55.7 (CH_3), 48.2 (CH_2), 35.9 (CH_2), 28.1 (CH_2), 26.0 (CH_2), 25.8 (CH_3), 17.9 (C), -4.8 (CH_3), -4.9 (CH_3);

HRMS (ESI+) 413.2112 (calcd for $\text{C}_{22}\text{H}_{34}\text{NaO}_4\text{Si}$ 413.2124).

(1*S*,5*S*)-5-((*tert*-Butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenoxy)propyl)cyclohex-2-enol (72**)**



To a solution of **71** containing a small amount of **68** in MeOH (500 mL) was added $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$ (28.3 g, 76.0 mmol) and NaBH_4 (2.43 g, 64.3 mmol) at 0 °C. After stirring for 2 h at 0 °C, the reaction was quenched with aqueous NH_4Cl . The solution was evaporated and the residue was partitioned between EtOAc and water. The aqueous phase was further extracted with EtOAc and the combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified roughly by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 20:1~10:1) to afford 5:1 mixture of **72** and **130** (20.4 g) as a yellow oil, which was used for the next step without further purification. The spectroscopic data for **72** were collected after purification by PTLC (SiO_2 ; toluene:acetone = 100:1).

$[\alpha]_{\text{D}}^{26} -3.04^\circ$ ($c = 1.00$, CHCl_3);

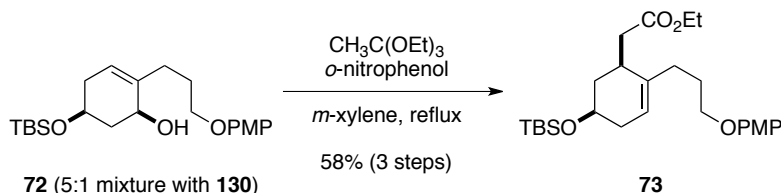
IR (film) 3445, 2950, 2928, 2857, 1508, 1470, 1322, 1231, 1044, 962, 835, 777 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 6.82 (s, 4H), 5.38 (m, 1H), 4.23 (d, $J=3.2$ Hz, 1H), 3.98 (m, 1H), 3.91 (t, $J=6.4$, Hz, 2H), 3.75 (s, 3H), 3.38 (d, $J=10.1$ Hz, 1H), 2.35-2.26 (m, 2H), 2.23-2.16 (m, 2H), 2.13 (ddd, $J=13.8, 4.1, 3.7$ Hz, 1H), 1.94 (m, 1H), 1.82 (ddd, $J=13.8, 5.0, 1.8$ Hz, 1H), 0.88 (s, 9H), 0.09 (s, 3H), 0.07 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 153.7 (C), 153.2 (C), 139.2 (C), 119.2 (CH), 115.5 (CH), 115.5 (CH), 114.6 (CH), 114.6 (CH), 68.3 (CH_2), 66.7 (CH), 66.7 (CH), 55.7 (CH_2), 37.5 (CH_2), 34.3 (CH_2), 30.7 (CH_2), 27.6 (CH_3), 25.8 (CH_3), 18.0 (C), -4.9 (CH_3), -5.1 (CH_3);

HRMS (ESI+) 415.2264 (calcd for $\text{C}_{22}\text{H}_{36}\text{NaO}_4\text{Si}$ 415.2281).

Ethyl 2-((1*S*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenoxy)propyl)cyclohex-2-en-1-yl)acetate (73**)**



To a solution of **72** containing a small amount of **130** in *m*-xylene (200 mL) was added triethyl orthoacetate (200 mL) and *o*-nitrophenol (400 mg, 2.88 mmol) at room temperature and the solution was heated at reflux for 13.5 h. After cooling to room temperature, the solvent was evaporated. The residual oil was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:0~20:1) to afford **73** (16.4 g, 58% for 3 steps) as a pale yellow oil.

$[\alpha]_{\text{D}}^{26} -34.8^\circ$ ($c = 1.00$, CHCl_3);

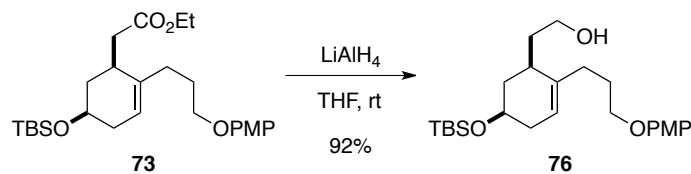
IR (film) 2951, 2929, 2856, 1733, 1508, 1471, 1232, 1105, 1039, 835, 775 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 6.82 (s, 4H), 5.38-5.37 (m, 1H), 4.14 (q, $J=7.4$ Hz, 2H), 3.96-3.80 (m, 2H), 3.76 (s, 3H), 2.80-2.65 (m, 1H), 2.61 (dd, $J=15.1, 4.1$ Hz, 1H), 2.28 (dd, $J=15.1, 9.6$ Hz, 1H), 2.25-2.15 (m, 1H), 2.13 (t, $J=7.6$ Hz, 1H), 2.05-19.2 (m, 2H), 1.90-1.85 (m, 1H), 1.85-1.75 (m, 1H), 1.46 (ddd, $J=12.4, 10.1, 10.1$ Hz, 1H), 1.25 (t, $J=7.4$ Hz, 3H), 0.88 (s, 9H), 0.06 (s, 6H);

^{13}C NMR (100 MHz, CDCl_3) δ 172.9 (C), 153.7 (C), 153.1 (C), 137.8 (C), 120.9 (CH), 115.4 (CH), 114.6 (CH), 68.0 (CH_2), 67.9 (CH), 60.2 (CH_2), 55.6 (CH_3), 38.4 (CH_2), 38.2 (CH_2), 35.3 (CH_2), 34.6 (CH), 30.5 (CH_2), 27.5 (CH_2), 25.9 (CH_3), 18.1 (C), 14.2 (CH_3), -4.7 (CH_3), -4.7 (CH_3);

HRMS (ESI+) 485.2714 (calcd for $\text{C}_{26}\text{H}_{42}\text{NaO}_5\text{Si}$ 485.2699).

2-((1*R*,5*R*)-5-((*tert*-Butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenoxy)propyl)cyclohex-2-en-1-yl)ethanol (76**)**



To a solution of **73** (28.0 g, 60.5 mmol) in THF (900 mL) was added LiAlH₄ (2.53 g, 66.6 mmol) at 0 °C. After stirring for 2 h at 0 °C, H₂O (2.60 mL), 3M aqueous NaOH (2.60 mL) and H₂O (7.80 mL) were successively added at the same temperature, and then the resulting mixture was filtered through a pad of Celite®. The filtrate was concentrated *in vacuo*. The residual oil was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 5:1~2:1) to afford **76** (23.1 g, 92%) as a pale yellow oil.

$[\alpha]_{\text{D}}^{27} -38.1^\circ$ ($c = 1.00$, CHCl₃);

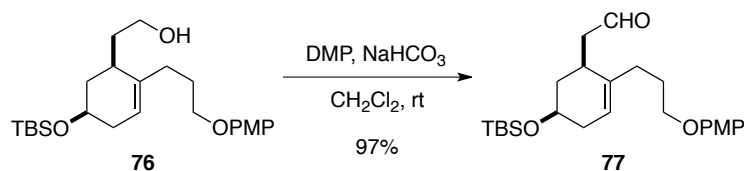
IR (film) 3409, 2950, 2929, 2856, 1508, 1231, 1105, 1041, 835, 775 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.82 (s, 4H), 5.36 (d, $J=5.5$ Hz, 1H), 3.89 (dd, $J=9.2, 6.4$ Hz, 2H), 3.85-3.78 (m, 1H), 3.76 (s, 3H), 3.74-3.60 (m, 2H), 2.50-2.35 (m, 1H), 2.25-2.05 (m, 3H), 2.05-1.85 (m, 4H), 1.85-1.70 (m, 1H), 1.56-1.44 (m, 2H), 1.37 (ddd, $J=12.3, 11.0, 10.6$ Hz, 1H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.7 (C), 153.1 (C), 137.8 (C), 120.3 (CH), 115.4 (CH), 114.6 (CH), 68.4 (CH), 68.1 (CH₂), 60.5 (CH₂), 55.7 (CH₃), 38.4 (CH₂), 35.7 (CH₂), 35.5 (CH₂), 34.4 (CH), 30.6 (CH₂), 27.6 (CH₂), 26.0 (CH₃), 18.1 (C), -4.6 (CH₃), -4.7 (CH₃);

HRMS (ESI+) 443.2584 (calcd for C₂₄H₄₀NaO₄Si 443.2594).

2-((1S,5R)-5-((*tert*-Butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenoxy)propyl)cyclohex-2-en-1-yl)acetaldehyde (77**)**



To a solution of **76** (23.0 g, 54.7 mmol) in CH₂Cl₂ (600 mL) was added sodium hydrogen carbonate (28.0 g, 333 mmol), Dess-Martine periodinane (25.5 g, 60.2 mmol) at 0 °C. After stirring for 1 h at room temperature, water was added at the same temperature. The resulting solution was extracted three times with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 10:1) to give **77** (22.2 g, 97%) as a colorless oil.

$[\alpha]_{\text{D}}^{26} -44.3^\circ$ ($c = 1.00$, CHCl₃);

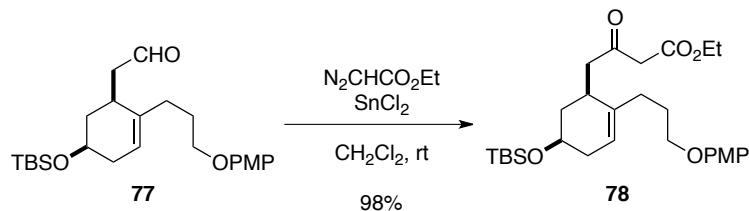
IR (film) 2951, 2928, 2856, 1724, 1508, 1231, 1106, 1040, 835, 775 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 9.78 (dd, $J=2.3, 1.4$ Hz, 1H), 6.82 (s, 4H), 5.48-5.36 (m, 1H), 3.96-3.82 (m, 3H), 3.76 (s, 3H), 2.90-2.75 (m, 1H), 2.63 (ddd, $J=17.0, 4.1, 1.4$ Hz, 1H), 2.52 (ddd, $J=17.0, 8.7, 2.3$ Hz, 1H), 2.23 (ddd, $J=18.3, 5.6, 5.6$ Hz, 1H), 2.12 (t, $J=7.6$ Hz, 2H), 2.06-1.94 (m, 2H), 1.93-1.85 (m, 1H), 1.84-1.73 (m, 1H), 1.47 (ddd, $J=12.4, 10.1, 9.6$ Hz, 1H), 0.88 (s, 9H), 0.06 (s, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 202.4 (CH), 153.7 (C), 153.0 (C), 137.2 (C), 121.3 (CH), 115.4 (CH), 114.6 (CH), 67.9 (CH₂), 67.4 (CH), 55.6 (CH₃), 47.24 (CH₂), 38.6 (CH₂), 35.2 (CH₂), 32.4 (CH), 30.6 (CH₂), 27.5 (CH₂), 25.8 (CH₃), 18.1 (C), -4.7 (CH₃), -4.7 (CH₃);

HRMS (ESI+) 441.2431 (calcd for C₂₄H₃₈NaO₄Si 441.2437).

Ethyl 4-((1*S*,5*R*)-5-((*tert*-butyldimethylsilyl)oxy)-2-(3-(4-methoxyphenoxy)propyl)cyclohex-2-en-1-yl)-3-oxobutanoate (78**)**



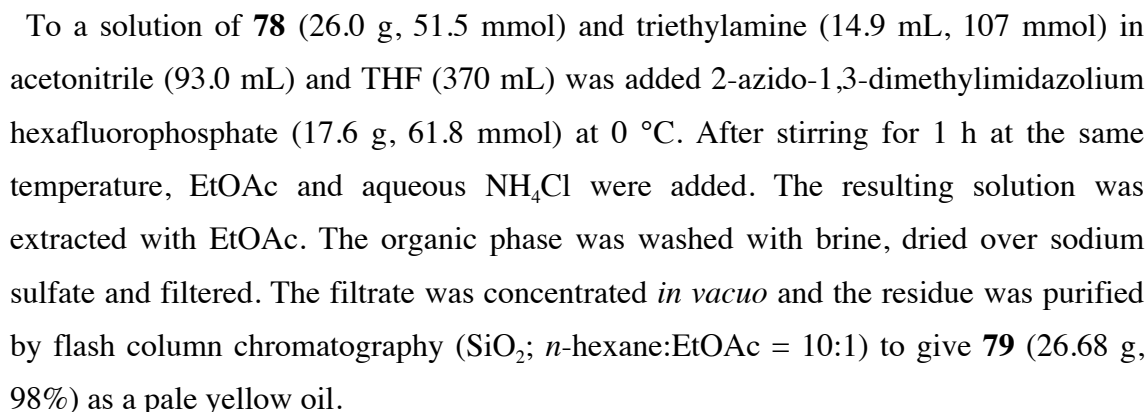
To a solution of **77** (22.2 g, 53.0 mmol) in CH_2Cl_2 (750 mL) was added SnCl_2 (1.12 g, 5.91 mmol) and ethyl diazoacetate (15% solution in toluene, 61.0 mL, 80.2 mmol) at 0 °C. After stirring for 1 h at room temperature, aqueous NH_4Cl was added at 0 °C. The resulting solution was extracted three times with CH_2Cl_2 . The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 10:1~5:1) to give **78** (26.1 g, 98%) as a pale yellow oil.

$[\alpha]_{\text{D}}^{26} -39.8^\circ$ ($c = 1.00$, CHCl_3);

IR (film) 2951, 2928, 2856, 1724, 1508, 1231, 1106, 1040, 835, 775 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 12.13 (s, 0.13H), 6.81 (s, 4H), 5.42-5.30 (m, 1H), 5.00 (s, 0.14H), 4.19 (q, $J=7.1$ Hz, 0.28H), 4.18 (q, $J=7.1$ Hz, 2.72H), 3.95-3.80 (m, 3H), 3.76 (s, 3H), 3.42 (s, 1.66H), 2.85-2.55 (m, 1.67H), 2.54-2.51 (m, 1.12H), 2.30-1.70 (m, 7H), 1.45-1.30 (m, 1H), 1.26 (t, $J=7.1$ Hz, 3H), 0.88 (s, 9H), 0.05 (s, 6H);

^{13}C NMR (100 MHz, CDCl_3) δ 202.1 (C), 177.2 (C), 172.5 (C), 167.0 (C), 153.7 (CH), 153.1 (CH), 138.2 (C), 137.6 (C), 120.9 (CH), 115.4 (CH), 114.6 (CH), 90.7 (CH), 68.0 (CH), 68.0 (CH_2), 67.4 (CH), 61.3 (CH_2), 59.9 (CH_2), 55.7 (CH_3), 50.0 (CH_2), 46.9 (CH_2), 39.1 (CH_2), 38.2 (CH_2), 37.9 (CH_2), 35.4 (CH_2), 35.2 (CH_2), 34.9 (CH), 33.0 (CH), 30.6 (CH_2), 27.5 (CH_2), 25.9 (CH_3), 18.2 (C), 14.2 (CH_2), 14.1 (CH_3), -4.7 (CH_3); HRMS (ESI+) 527.2789 (calcd for $\text{C}_{28}\text{H}_{44}\text{NaO}_6\text{Si}$ 527.2804).



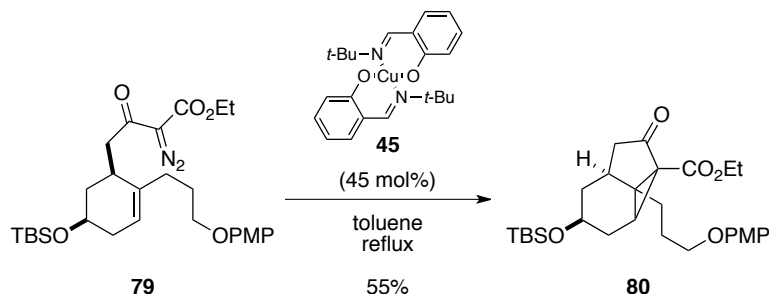
IR (film) 2952, 2929, 2856, 2132, 1718, 1654, 1508, 1470, 1306, 1231, 1106, 1070, 835, 775 cm^{-1} ;

¹H NMR (400 MHz, CDCl₃) δ 6.81 (s, 4H), 5.46-5.32 (m, 1H), 4.28 (q, *J*=7.3 Hz, 2H), 3.94-3.78 (m, 3H), 3.75 (s, 3H), 3.10 (dd, *J*=16.0, 3.2 Hz, 1H), 2.93 (dd, *J*=16.0, 9.6 Hz, 1H), 2.92-2.80 (m, 1H), 2.20 (ddd, *J*=17.0, 5.0, 5.0 Hz, 1H), 2.12 (t, *J*=7.6 Hz, 2H), 2.22-1.94 (m, 2H), 1.93-1.84 (m, 1H), 1.84-1.72 (m, 1H), 1.42 (ddd, *J*=12.4, 10.1, 10.1 Hz, 1H), 1.32 (t, *J*=7.3 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 192.0 (C), 161.2 (C), 153.6 (C), 153.1 (C), 138.1 (C), 120.8 (CH), 115.4 (CH), 114.5 (CH), 76.3 (C), 68.1 (CH₂), 67.9 (CH), 61.3 (CH₂), 55.7 (CH₃), 43.6 (CH₂), 38.6 (CH₂), 35.4 (CH₂), 33.8 (CH), 30.5 (CH₂), 27.6 (CH₂), 25.9 (CH₃), 18.1 (C), 14.3 (CH₃), -4.6 (CH₃), -4.7 (CH₃);

HRMS (ESI+) 553.2693 (calcd for $C_{28}H_{43}N_2NaO_6Si$ 553.2710).

(4*S*,5*aS*)-Ethyl 4-((*tert*-butyldimethylsilyl)oxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxylate (80**)**



To a solution of **79** (7.00 g, 9.42 mmol) in toluene (940 mL) was added bis(*N-tert*-butylsalicylaldiminato)copper(II) (1.80 g, 4.32 mmol) at room temperature, and the resulting solution was heated at 110 °C for 1 h. After cooling to room temperature, the solvent was evaporated. The residual oil was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 20:1~7:1) to afford **80** (3.65 g, 55%) as a white solid.

m.p. 72.1-73.0 °C;

[α]_D²⁷ 10.3° (*c* = 1.00, CHCl₃);

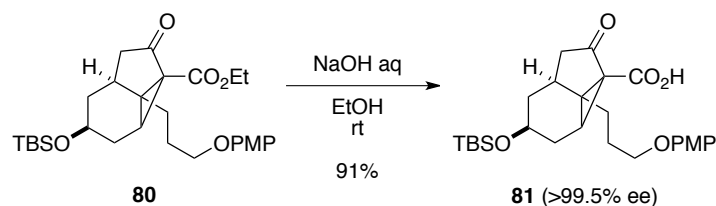
IR (film) 2951, 2931, 2856, 1732, 1508, 1231, 1106, 1033, 835, 775 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.80 (s, 4H), 4.15 (q, *J*=7.3 Hz, 2H), 4.05-3.95 (m, 2H), 3.87 (t, *J*=6.0 Hz, 2H), 3.74 (s, 3H), 2.78 (dd, *J*=17.8, 11.9 Hz, 1H), 2.70-2.60 (m, 1H), 2.40-2.22 (m, 3H), 1.96-1.70 (m, 5H), 1.56-1.45 (m, 2H), 1.23 (t, *J*=7.3 Hz, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 207.7 (C), 168.0 (C), 153.8 (C), 152.9 (C), 115.3 (CH), 114.6 (CH), 68.0 (CH₂), 64.5 (CH), 61.3 (CH₂), 55.6 (CH₃), 49.5 (C), 49.1 (CH₂), 46.7 (C), 34.2 (CH₂), 32.3 (CH), 30.0 (CH), 28.3 (CH₂), 28.2 (CH₂), 26.7 (CH₂), 25.7 (CH₃), 17.9 (C), 14.1 (CH₃), -4.9 (CH₃), -5.0 (CH₃);

HRMS (ESI+) 525.2623 (calcd for C₂₈H₄₂NaO₆Si 525.2648).

**(4*S*,5*aS*)-4-((*tert*-Butyldimethylsilyl)oxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-oxo-
ctahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxylic acid (81)**



To a solution of **80** (13.1 g, 26.1 mmol) in ethanol (250 mL) was added 1 M aqueous NaOH (125 mL) at 0 °C. After stirring for 1 h at room temperature, EtOAc and aqueous NH₄Cl were added. The mixture was partitioned between EtOAc and water. The aqueous phase was further extracted with EtOAc and the combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂, *n*-hexane:EtOAc = 7:1) to afford **81** (11.2 g, 91%, >99.5% ee) as a pale yellow oil. The enantiomeric excess was determined by HPLC analysis with a chiral HPLC column (DAICEL CHIRALCEL AD-H, 10% 2-propanol in *n*-hexane, 1.0 mL/min at 25 °C, 210 nm). The retention times corresponding to **81** and its enantiomer are 17.1 and 14.0 min, respectively.

$$[\alpha]_{\text{D}}^{27} -0.868^{\circ} (c = 1.00, \text{CHCl}_3);$$

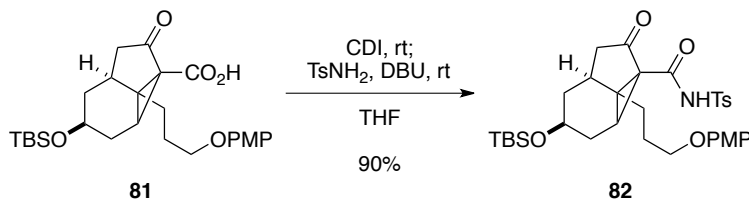
IR (film) 2951, 2930, 2856, 1751, 1685, 1508, 1231, 1089, 1040, 835, 776 cm^{-1} ;

¹H NMR (400 MHz, CDCl₃) δ 6.85-6.75 (m, 4H), 4.07 (dddd, *J*=6.1, 6.1, 6.1, 3.6 Hz, 1H), 3.96-3.82 (m, 2H), 3.75 (s, 3H), 2.78 (dd, *J*=17.4, 11.5 Hz, 1H), 2.76-2.68 (m, 1H), 2.63 (dd, *J*=7.6, 3.6 Hz, 1H), 2.57 (d, *J*=17.4 Hz, 1H), 2.37 (ddd, *J*=16.0, 7.6, 7.6 Hz, 1H), 2.18 (ddd, *J*=14.2, 10.5, 5.0 Hz, 1H), 2.06 (ddd, *J*=14.2, 10.5, 5.5 Hz, 1H), 1.95-1.75 (m, 3H), 1.67-1.55 (m, 2H), 0.86 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 216.1 (C), 169.2 (C), 153.8 (C), 152.9 (C), 115.3 (CH), 114.6 (CH), 68.2 (CH₂), 64.4 (CH), 55.6 (CH₃), 52.4 (C), 48.4 (C), 46.1 (CH₂), 41.5 (CH), 33.6 (CH₂), 29.9 (CH), 29.2 (CH₂), 27.5 (CH₂), 27.3 (CH₂), 25.7 (CH₃), 17.9 (C), -4.9 (CH₃), -5.0 (CH₃);

HRMS (ESI+) 519.2164 (calcd for $C_{26}H_{37}Na_2O_6Si$ 519.2154).

(4*S*,5*aS*)-4-((*tert*-Butyldimethylsilyl)oxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-oxo-*N*-tosyloctahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxamide (82**)**



To a solution of **81** (930 mg, 1.96 mmol) in THF (14.0 mL) was added 1,1'-carbonyldiimidazole (980 mg, 6.08 mmol) at room temperature and the solution was stirred at room temperature for 2 h. In another flask *p*-toluenesulfonamide (503 mg, 2.94 mmol) and DBU (410 μL , 2.74 mmol) were dissolved in THF (28 mL). To this solution was added above solution containing the acyl imidazole reagent. After stirring for 3 h at the same temperature, EtOAc and aqueous NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 4:1) to give **82** (1.10 g, 90%) as a white amorphous.

$[\alpha]_{\text{D}}^{27} -32.1^\circ$ ($c = 1.00$, CHCl_3);

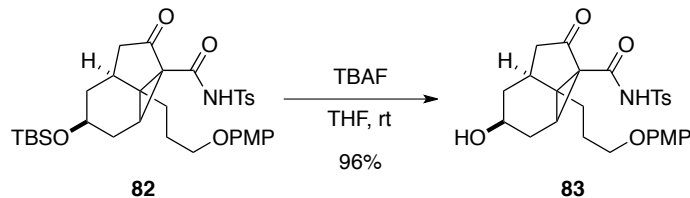
IR (film) 3185, 2951, 2930, 2856, 1709, 1508, 1437, 1350, 1231, 1173, 1088, 835, 775 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 10.83 (s, 1H), 7.93 (d, $J=8.3$ Hz, 2H), 7.28 (d, $J=8.3$ Hz, 2H), 6.82 (dd, $J=6.9, 2.7$ Hz, 2H), 6.75 (dd, $J=6.9, 2.7$ Hz, 2H), 4.01 (dddd, $J=6.6, 6.6, 6.6, 3.2$ Hz, 1H), 3.77 (s, 3H), 3.73 (t, $J=6.2$ Hz, 2H), 2.71 (dd, $J=18.0, 11.5$ Hz, 1H), 2.66-2.60 (m, 1H), 2.51 (dd, $J=8.0, 4.1$ Hz, 1H), 2.46 (dd, $J=18.0, 1.4$ Hz, 1H), 2.36 (s, 3H), 2.31 (ddd, $J=15.6, 8.0, 6.6$ Hz, 1H), 2.06 (ddd, $J=13.8, 10.5, 5.0$ Hz, 1H), 1.96-1.82 (m, 2H), 1.81-1.70 (m, 1H), 1.60-1.43 (m, 3H), 0.85 (s, 9H), 0.010 (s, 3H), 0.001 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 212.8 (C), 165.6 (C), 153.8 (C), 152.8 (C), 144.6 (C), 136.0 (C), 129.3 (CH), 128.4 (CH), 115.2 (CH), 114.6 (CH), 67.9 (CH_2), 64.4 (CH), 55.7 (CH_3), 53.1 (C), 49.2 (C), 46.6 (CH_2), 40.0 (CH), 33.6 (CH_2), 29.7 (CH), 29.1 (CH_2), 26.9 (CH_2), 26.7 (CH_2), 25.7 (CH_3), 17.9 (C), -4.9 (CH_3), -5.0 (CH_3);

HRMS (ESI+) 672.2419 (calcd for $\text{C}_{33}\text{H}_{44}\text{N}_1\text{Na}_2\text{O}_7\text{SSi}$ 672.2403).

(4*S*,5*aS*)-4-Hydroxy-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-oxo-*N*-tosyloctahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxamide (83)



To a solution of **82** (1050 mg, 1.67 mmol) in THF (30.0 mL) was added TBAF (30.0 ml, 30.0 mmol, 1.0 M in THF) at 0 °C. After stirring for 3 h at room temperature, EtOAc and aqueous NH₄Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 0:1) to give **83** (820 mg, 96%) as a pale yellow amorphous.

$$[\alpha]_{\text{D}}^{27} -31.2^{\circ} (c = 1.00, \text{CHCl}_3);$$

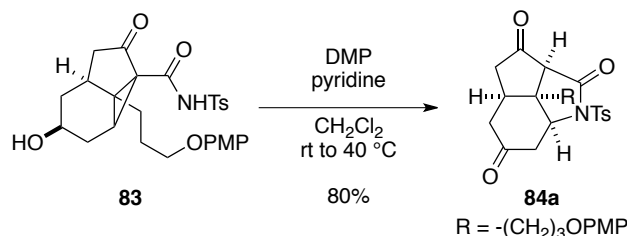
IR (film) 3531, 3109, 2937, 1707, 1508, 1438, 1347, 1230, 1172, 1087, 866, 825 cm^{-1} ;

¹H NMR (400 MHz, CDCl₃) δ 10.81 (s, 1H), 7.92 (d, *J*=8.2 Hz, 2H), 7.28 (d, *J*=7.8 Hz, 2H), 6.82 (dd, *J*=6.9, 2.7 Hz, 2H), 6.75 (dd, *J*=6.9, 2.7 Hz, 2H), 4.07 (dddd, *J*=7.7, 7.7, 7.7, 4.1 Hz, 1H), 3.76 (s, 3H), 3.72 (t, *J*=6.4 Hz, 1H), 2.78 (dd, *J*=19.2, 11.9 Hz, 1H), 2.72-2.64 (m, 1H), 2.54 (dd, *J*=8.7, 4.6 Hz, 1H), 2.42-2.37 (m, 1H), 2.36 (s, 3H), 2.35 (dd, *J*=19.2, 2.3 Hz, 1H), 2.20-1.95 (m, 3H), 1.89 (ddd, *J*=14.4, 10.3, 5.5 Hz, 1H), 1.80-1.70 (m, 1H), 1.57-1.45 (m, 2H), 1.40 (ddd, *J*=15.6, 7.7, 4.6 Hz, 1H);

¹³C NMR (100 MHz, CDCl₃) δ 212.9 (C), 165.4 (C), 153.7 (C), 152.8 (C), 144.7 (C), 135.8 (C), 129.3 (CH), 128.3 (CH), 115.2 (CH), 114.6 (CH), 67.8 (CH₂), 64.1 (CH), 55.6 (CH₃), 52.8 (C), 49.1 (C), 46.9 (CH₂), 39.7 (CH), 33.0 (CH₂), 29.8 (CH), 28.3 (CH₂), 26.8 (CH₂), 26.5 (CH₂);

HRMS (ESI+) 558.1558 (calcd for C₂₇H₃₀NNa₂O₇S 558.1538).

(2a*S*,2a¹*S*,4a*S*,7a*S*)-2a¹-(3-(4-Methoxyphenoxy)propyl)-1-tosyltetrahydro-1*H*-cyclopenta[*cd*]indole-2,3,6(2a*H*,2a¹*H*,4*H*)-trione (84a)



To a solution of **83** (660 mg, 1.29 mmol) and pyridine (1.00 ml) in CH_2Cl_2 (30.0 mL) was added Dess-Martine periodinane (572 mg, 1.35 mmol) at 0 °C and the solution was stirred for 1h at room temperature. After checking the reaction by TLC, the reaction mixture was stirred at 40 °C for 30 min. After cooling to 0 °C, EtOAc and aqueous NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:1~1:3) to give **84a** (520 mg, 80%) as a pale yellow amorphous.

$[\alpha]_{\text{D}}^{27} 29.6^\circ$ ($c = 1.00$, CHCl_3);

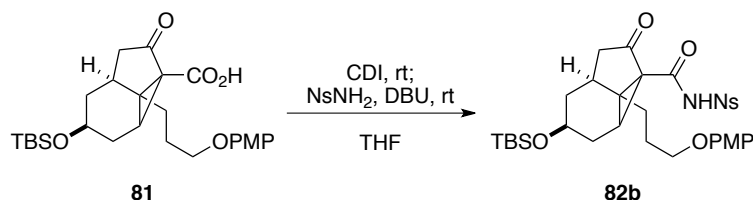
IR (film) 2931, 1765, 1719, 1508, 1361, 1231, 1170, 1086, 826 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 7.86 (d, $J=8.2$ Hz, 2H), 7.28 (d, $J=8.2$ Hz, 2H), 6.90-6.72 (m, 4H), 4.60 (dd, $J=6.4, 3.7$ Hz, 1H), 3.93 (t, $J=5.5$ Hz, 2H), 3.76 (s, 3H), 3.30 (s, 1H), 3.13 (dd, $J=18.3, 6.4$ Hz, 1H), 2.86 (dd, $J=18.3, 3.7$ Hz, 1H), 2.78 (dd, $J=19.0, 9.2$ Hz, 1H), 2.71-2.60 (m, 1H), 2.45-2.34 (m, 4H), 2.12 (dd, $J=19.0, 3.2$ Hz, 1H), 2.05-1.89 (m, 3H), 1.88-1.75 (m, 2H);

^{13}C NMR (100 MHz, CDCl_3) δ 205.9 (C), 205.5 (C), 165.8 (C), 154.0 (C), 152.5 (C), 145.8 (C), 134.8 (C), 129.7 (CH), 128.3 (CH), 115.3 (CH), 114.7 (CH), 67.6 (CH_2), 59.9 (CH), 59.6 (CH), 55.7 (CH_3), 46.4 (C), 44.2 (CH_2), 41.6 (CH_2), 41.1 (CH_2), 36.4 (CH), 34.4 (CH_2), 24.6 (CH_2), 21.6 (CH_3);

HRMS (ESI+) 534.1560 (calcd for $\text{C}_{27}\text{H}_{29}\text{NNaO}_7\text{S}$ 534.1562).

(4*S*,5*aS*)-4-((*tert*-Butyldimethylsilyl)oxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-*N*-((2-nitrophenyl)sulfonyl)-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxamide (82b)



To a solution of **81** (930 mg, 1.96 mmol) in THF (14.0 mL) was added 1,1'-carbonyldiimidazole (980 mg, 6.08 mmol) at room temperature and the solution was stirred at room temperature for 2 h. In another flask *o*-nitrobenzenesulfonamide (594 mg, 2.94 mmol) and DBU (410 μ L, 2.74 mmol) were dissolved in THF (28 mL). To this solution was added above solution containing the acyl imidazole reagent. After stirring for 3 h at the same temperature, EtOAc and aqueous NH_4Cl was added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 4:1) to give inseparable products which contained **82b** and *o*-nitrobenzenesulfonamide as a yellow oil, which was used for the next step without further purification. The spectroscopic data for **82b** were collected after purification by PTLC (SiO_2 ; *n*-hexane:EtOAc = 3:1).

$[\alpha]_{\text{D}}^{27}$ 10.6° (c = 1.00, CHCl_3);

IR (film) 3100, 2951, 2931, 1712, 1542, 1508, 1423, 1362, 1231, 1182, 1036, 835, 779 cm^{-1} ;

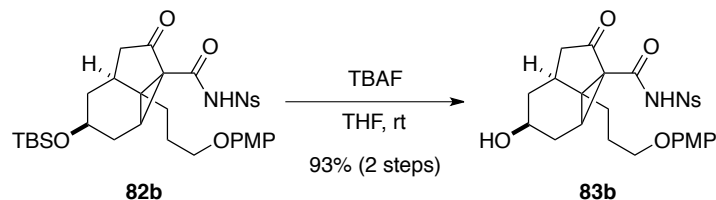
^1H NMR (400 MHz, CDCl_3) δ 11.32 (brs, 1H), 8.34 (dd, J =7.6, 1.6 Hz, 1H), 7.75 (dd, J =7.6, 1.6 Hz, 1H), 7.68 (ddd, J =7.5, 1.6, 1.6 Hz, 1H), 7.65 (ddd, J =7.5, 1.6, 1.6 Hz, 1H), 6.81 (dd, J =6.9, 2.7 Hz, 2H), 6.73 (dd, J =6.9, 2.7 Hz, 2H), 4.02 (dddd, J =6.5, 6.5, 6.5, 3.2 Hz, 1H), 3.74 (s, 3H), 3.72-3.67 (m, 2H), 2.78 (dd, J =18.8, 11.4 Hz, 2H), 2.70-2.62 (m, 1H), 2.55-2.45 (m, 2H), 2.32 (ddd, J =15.8, 8.0, 6.5 Hz, 1H), 2.03 (ddd, J =12.6, 11.0, 4.6 Hz, 1H), 1.95-1.72 (m, 3H), 1.62-1.45 (m, 3H), 0.84 (s, 9H), 0.02 (s, 3H), 0.01 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 212.0 (C), 166.1 (C), 153.8 (C), 152.8 (C), 148.2 (C), 134.6 (C), 133.3 (CH), 132.1 (CH), 131.8 (C), 124.7 (CH), 115.2 (CH), 114.6 (CH),

67.8 (CH₂), 64.4 (CH), 55.7 (CH₃), 53.5 (C), 49.2 (C), 46.6 (CH₂), 40.7 (CH), 33.7 (CH₂), 29.8 (CH), 29.1 (CH₂), 26.9 (CH₂), 26.7 (CH₂), 25.7 (CH₃), 17.9 (C), -4.9 (CH₃), -5.0 (CH₃);

HRMS (ESI+) 703.2119 (calcd for C₃₂H₄₁N₂Na₂O₉SSi 703.2097).

(4*S*,5*aS*)-4-Hydroxy-2*a*¹-(3-(4-methoxyphenoxy)propyl)-*N*-((2-nitrophenyl)sulfonyl)-2-oxooctahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxamide (83b)



To a solution of crude **82b** in THF (30.0 mL) was added TBAF (30.0 ml, 30.0 mmol, 1.0 M in THF) at 0 °C. After stirring for 3 h at room temperature, EtOAc and aqueous NH₄Cl was added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 0:1) to give **83b** (950 mg, 89% for 2 steps) as a pale yellow amorphous.

$$[\alpha]_{\text{D}}^{27} 4.12^\circ (c = 1.00, \text{CHCl}_3);$$

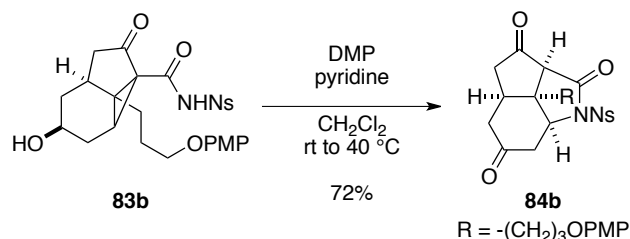
IR (film) 3546, 3100, 2937, 1711, 1541, 1508, 1426, 1362, 1230, 1182, 1056, 827 cm^{-1} .

¹H NMR (400 MHz, CDCl₃) δ 11.27 (brs, 1H), 8.34 (dd, *J*=7.6, 1.6 Hz, 1H), 7.75 (dd, *J*=7.6, 1.6 Hz, 1H), 7.68 (ddd, *J*=7.5, 1.6, 1.6 Hz, 1H), 7.65 (ddd, *J*=7.5, 1.6, 1.6 Hz, 1H), 6.81 (d, *J*=8.7 Hz, 2H), 6.73 (d, *J*=9.2 Hz, 2H), 4.20-4.11 (m, 1H), 3.75 (s, 3H), 3.74-3.65 (m, 2H), 2.85 (dd, *J*=19.5, 11.7 Hz, 1H), 2.56 (dd, *J*=8.3, 4.6 Hz, 1H), 2.55-2.53 (m, 1H), 2.50-2.46 (m, 2H), 2.25-1.95 (m, 3H), 1.90 (ddd, *J*=14.1, 10.5, 5.2 Hz, 1H), 1.85-1.75 (m, 1H), 1.66-1.45 (m, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 212.4 (C), 165.8 (C), 153.7 (C), 152.7 (C), 148.1 (C), 134.7 (CH), 132.2 (CH), 132.1 (CH), 131.7 (C), 124.8 (CH), 115.2 (CH), 114.6 (CH), 67.8 (CH₂), 64.1 (CH), 55.7 (CH₃), 53.3 (C), 49.3 (C), 47.1 (CH₂), 40.3 (CH), 33.0 (CH₂), 29.9 (CH), 28.4 (CH₂), 26.8 (CH₂), 26.6 (CH₂);

HRMS (ESI+) 589.1219 (calcd for $C_{26}H_{27}N_2Na_2O_9Si$ 589.1233).

(2a*S*,2a¹*S*,4a*S*,7a*S*)-2a¹-(3-(4-Methoxyphenoxy)propyl)-1-((2-nitrophenyl)sulfonyl)tetrahydro-1*H*-cyclopenta[*cd*]indole-2,3,6(2a*H*,2a¹*H*,4*H*)-trione (84b)



To a solution of **83b** (810 mg, 1.49 mmol) and pyridine (1.10 ml) in CH_2Cl_2 (30.0 mL) was added Dess-Martine periodinane (662 mg, 1.56 mmol) at 0 °C and the solution was stirred for 1h at room temperature. After checking the reaction by TLC, the reaction mixture was stirred at 40 °C for 30 min. After cooling to 0 °C, EtOAc and aqueous NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:1~1:3) to give **84b** (580 mg, 72%) as a pale yellow amorphous.

$[\alpha]_{\text{D}}^{27} 263^\circ$ ($c = 1.00$, CHCl_3);

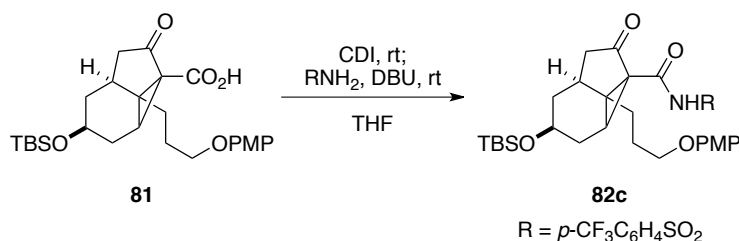
IR (film) 2934, 1766, 1722, 1541, 1508, 1368, 1231, 1177, 1037, 827 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.40-8.36 (m, 1H), 7.85-7.75 (m, 3H), 6.86-6.76 (m, 4H), 4.75 (dd, $J=4.6, 3.2$ Hz, 1H), 4.05-3.95 (m, 1H), 3.77 (s, 3H), 3.30 (s, 1H), 3.26 (dd, $J=18.3, 4.6$ Hz, 1H), 2.84 (dd, $J=18.3, 3.2$ Hz, 1H), 2.83 (dd, $J=19.0, 9.2$ Hz, 1H), 2.76-2.66 (m, 1H), 2.55 (dd, $J=18.3, 4.6$ Hz, 1H), 2.26 (dd, $J=19.0, 1.4$ Hz, 1H), 2.22 (dd, $J=18.3, 12.8$ Hz, 1H), 2.20-1.96 (m, 3H), 1.95-1.82 (m, 1H);

^{13}C NMR (100 MHz, CDCl_3) δ 205.0 (C), 165.8 (C), 154.1 (C), 152.6 (C), 147.9 (C), 135.8 (CH), 135.6 (CH), 132.3 (CH), 130.7 (C), 124.6 (CH), 115.4 (CH), 114.7 (CH), 67.8 (CH_2), 60.4 (CH), 58.6 (CH), 55.7 (CH_3), 46.9 (C), 44.2 (CH_2), 41.9 (CH_2), 41.4 (CH_2), 37.0 (CH), 33.5 (CH_2), 24.5 (CH_2);

HRMS (ESI+) 565.1237 (calcd for $\text{C}_{26}\text{H}_{26}\text{N}_2\text{NaO}_9\text{S}$ 565.1257).

(4*S*,5*aS*)-4-((*tert*-Butyldimethylsilyl)oxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-oxo-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)octahydro-1*H*-cyclopropa[*cd*]indene-2*a*-carboxamide (82c**)**



To a solution of **81** (9.00 g, 19.0 mmol) in THF (130 mL) was added 1,1'-carbonyldiimidazole (6.15 g, 38.0 mmol) at room temperature and the solution was stirred at room temperature for 2 h. In another flask 4-(trifluoromethyl)benzenesulfonamide (6.40 g, 28.5 mmol) and DBU (4.00 mL, 26.6 mmol) were dissolved in THF (260 mL). To this solution was added the above solution containing the acyl imidazole reagent. After stirring for 4 h at the same temperature, EtOAc and aqueous NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified roughly by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 4:1) to give a mixture of **82c** and 4-(trifluoromethyl)benzenesulfonamide as a yellow oil, which was used for the next step without further purification. The spectroscopic data for **82c** were collected after purification by PTLC (SiO_2 ; *n*-hexane:EtOAc = 3:1).

$[\alpha]_D^{27} -13.1^\circ$ ($c = 1.00$, CHCl_3);

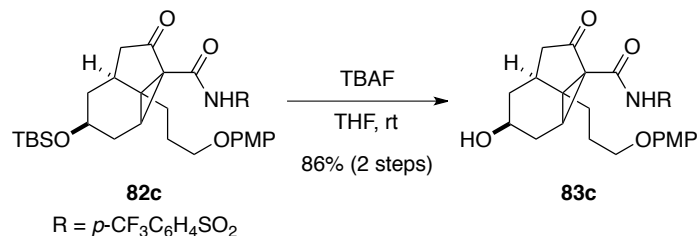
IR (film) 3105, 2952, 2931, 2857, 1710, 1508, 1322, 1231, 1175, 1062, 835, 777 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 11.02 (s, 1H), 8.19 (d, $J=8.3$ Hz, 1H), 7.76 (d, $J=8.3$ Hz, 1H), 6.82 (dd, $J=6.8, 2.8$ Hz, 2H), 6.74 (dd, $J=6.8, 2.8$ Hz, 2H), 4.02 (dddd, $J=6.5, 6.5, 6.5, 3.2$ Hz, 1H), 3.80-3.70 (m, 5H), 2.73 (dd, $J=18.1, 10.9$ Hz, 1H), 2.68-2.63 (m, 1H), 2.55-2.45 (m, 2H), 2.32 (ddd, $J=15.8, 8.0, 8.0$ Hz, 1H), 2.10 (ddd, $J=14.2, 10.1, 4.6$ Hz, 1H), 2.00-1.81 (m, 2H), 1.80-1.70 (m, 1H), 1.62-1.45 (m, 3H), 0.85 (s, 9H), 0.02 (s, 3H), 0.00 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 212.9 (C), 165.9 (C), 153.8 (C), 152.8 (C), 142.7 (C), 135.5 (C, q, $J=32.4$ Hz), 129.0 (CH), 125.9 (CH, q, $J=3.8$ Hz), 122.8 (CF_3 , q, $J=271.7$ Hz), 115.2 (CH), 114.7 (CH), 67.8 (CH_2), 64.3 (CH), 55.7 (CH_3), 53.5 (C), 49.3 (C),

46.6 (CH₂), 40.7 (CH), 33.6 (CH₂), 29.7 (CH), 29.2 (CH₂), 26.9 (CH₂), 26.8 (CH₂), 25.7 (CH₃), 17.9 (C), -4.9 (CH₃), -5.0 (CH₃);
HRMS (ESI+) 726.2147 (calcd for C₃₃H₄₁F₃NNa₂O₇SSi 726.2121).

(4*S*,5*aS*)-4-Hydroxy-2a¹-(3-(4-methoxyphenoxy)propyl)-2-oxo-*N*-((4-(trifluoromethyl)phenyl)sulfonyl)octahydro-1*H*-cyclopropa[*cd*]indene-2a-carboxamide (83c**)**



To a solution of a mixture containing **82c** and 4-(trifluoromethyl)benzenesulfonamide in THF (250 mL) was added TBAF (190 ml, 190 mmol, 1.0 M in THF) at 0 °C. After stirring for 1 h at room temperature, EtOAc and aqueous NH₄Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 0:1) to give **83c** (9.25 g, 86% for 2 steps) as a pale yellow amorphous solid.

$[\alpha]_{\text{D}}^{27} -32.1^\circ$ ($c = 1.00$, CHCl₃);

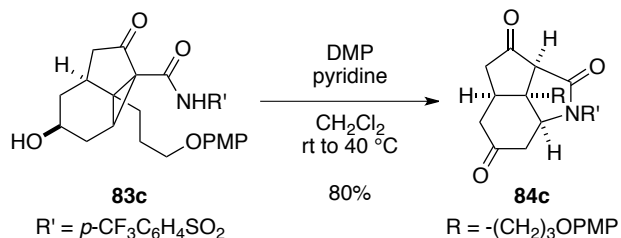
IR (film) 3538, 2938, 1709, 1508, 1433, 1356, 1322, 1230, 1133, 1062, 826 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 10.98 (s, 1H), 8.18 (d, $J=8.2$ Hz, 2H), 7.76 (d, $J=8.2$ Hz, 2H), 6.84-6.80 (m, 2H), 6.78-6.70 (m, 2H), 4.15-4.05 (m, 1H), 3.80-3.70 (m, 4H), 2.81 (dd, $J=19.3, 11.7$ Hz, 1H), 2.74-2.62 (m, 1H), 2.54 (dd, $J=8.3, 4.6$ Hz, 1H), 2.44-2.34 (m, 2H), 2.10 (ddd, $J=14.2, 9.6, 4.6$ Hz, 1H), 2.04-1.90 (m, 2H), 1.88-1.69 (m, 2H), 1.65-1.50 (m, 2H), 1.44 (ddd, $J=15.6, 7.8, 4.6$ Hz, 1H);

¹³C NMR (100 MHz, CDCl₃) δ 212.9 (C), 165.7 (C), 153.8 (C), 152.7 (C), 142.3 (C), 135.0 (C, q, $J=32.4$ Hz), 125.9 (CH, q, $J=3.8$ Hz), 123.0 (CF₃, q, $J=271.7$ Hz), 115.2 (CH), 114.7 (CH), 67.8 (CH₂), 64.1 (CH), 55.7 (CH₃), 53.1 (C), 49.3 (C), 47.0 (CH₂), 40.3 (CH), 33.0 (CH₂), 29.8 (CH), 28.5 (CH₂), 26.8 (CH₂);

HRMS (ESI+) 612.1231 (calcd for C₂₇H₂₇F₃NNa₂O₇S 612.1258).

(2a*S*,2a¹*S*,4a*S*,7a*S*)-2a¹-(3-(4-Methoxyphenoxy)propyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)tetrahydro-1*H*-cyclopenta[*cd*]indole-2,3,6(2a*H*,2a¹*H*,4*H*)-trione (84c)



To a solution of **83c** (2.20 g, 3.88 mmol) and pyridine (3.80 mL) in CH_2Cl_2 (130 mL) was added Dess-Martine periodinane (1.73 g, 4.07 mmol) at 0 °C and the solution was stirred for 1 h at room temperature. After checking the reaction by TLC, the reaction mixture was stirred at 40 °C for 30 min. After cooling to 0 °C, EtOAc and aqueous NH_4Cl were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:1) to give **84c** (1.75 g, 80%) as a pale orange amorphous solid.

$[\alpha]_{\text{D}}^{27} 32.9^\circ$ ($c = 1.00$, CHCl_3);

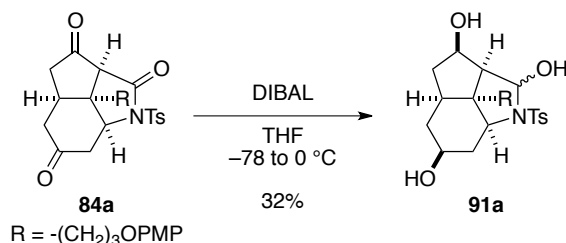
IR (film) 2934, 1768, 1720, 1508, 1405, 1370, 1322, 1231, 1174, 1133, 1062, 827 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, $J=8.2$ Hz, 2H), 7.77 (d, $J=8.2$ Hz, 2H), 6.87-6.75 (m, 4H), 4.65 (dd, $J=6.0, 3.6$ Hz, 1H), 3.95 (t, $J=5.5$ Hz, 2H), 3.77 (s, 3H), 3.35 (s, 1H), 3.16 (dd, $J=18.3, 6.0$ Hz, 1H), 2.88 (dd, $J=18.3, 3.6$ Hz, 1H), 2.80 (dd, $J=19.0, 9.2$ Hz, 1H), 2.64-2.54 (m, 1H), 2.42 (dd, $J=18.3, 4.8$ Hz, 1H), 2.15 (dd, $J=19.0, 3.0$ Hz, 1H), 2.10-1.95 (m, 2H), 1.89 (dd, $J=18.3, 11.0$ Hz, 1H), 1.95-1.55 (m, 2H);

^{13}C NMR (100 MHz, CDCl_3) δ 205.6 (C), 205.0 (C), 166.1 (C), 154.1 (C), 152.5 (C), 141.1 (C), 136.0 (C, q, $J=32.4$ Hz), 129.1 (CH), 126.3 (CH, q, $J=3.8$ Hz), 122.9 (CF_3 , q, $J=271.7$ Hz), 115.4 (CH), 114.7 (CH), 67.6 (CH_2), 60.1 (CH), 59.4 (CH), 55.7 (CH_3), 46.6 (C), 44.1 (CH_2), 41.6 (CH_2), 41.0 (CH_2), 36.4 (CH), 34.4 (CH_2), 24.6 (CH_2);

HRMS (ESI+) 588.1253 (calcd for $\text{C}_{27}\text{H}_{26}\text{F}_3\text{NNaO}_7\text{S}$ 588.1280).

(2*R*,2*aS*,2*a*¹*S*,3*R*,4*aS*,6*S*,7*aS*)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-1-tosyldecahydro-1*H*-cyclopenta[*cd*]indole-2,3,6-triol (91a**)**



To a solution of **84a** (460 mg, 0.900 mmol) in THF (100 mL) was added DIBAL (8.1 ml, 8.1mmol, 1 M in *n*-hexane) at -78°C . After stirring for 10min at the same temperature, the mixture was stirred for 1 h at -10°C . aqueous NaOH (1 M, 2.00 ml) was added at -40°C . The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered through a pad of Celite[®]. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:3~0:1) to afford a 2:1 diastereomeric mixture of **91a** (150 mg, 32%) as a white amorphous solid.

$[\alpha]_{\text{D}}^{27} -7.42^{\circ}$ ($c = 1.00$, CHCl₃);

IR (film) 3473, 2935, 1508, 1468, 1325, 1231, 1156, 1038, 823 cm⁻¹;

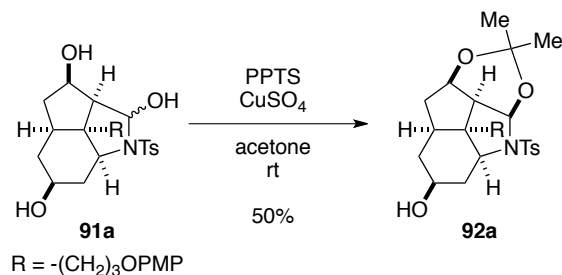
¹H NMR (400 MHz, CDCl₃) δ 7.87 (d, $J=8.2$ Hz, 1H), 7.74 (dd, $J=8.2$, 2.3 Hz, 1H), 7.32-7.26 (m, 2H), 6.82-6.71 (m, 4H), 5.96 (d, $J=4.6$ Hz, (2/3)1H), 5.80 (d, $J=10.6$ Hz, (1/3)1H), 5.59 (dd, $J=7.3$, 4.1 Hz, (1/3)1H), 5.45-5.30 (m, (2/3)1H), 5.28 (dd, $J=6.9$, 6.9 Hz, (1/3)1H), 4.35-4.20 (m, (2/3)3H), 4.10-4.00 (m, (1/3)1H), 3.86-3.76 (m, (2/3)2H), 3.76-3.72 (m, 3H), 3.63 (dd, $J=6.0$, 6.0 Hz, (2/3)1H), 3.52 (dd, $J=6.0$, 6.0 Hz, (1/3)1H), 3.46-3.34 (m, (2/3)1H+(2/3)1H), 2.53 (d, $J=8.0$ Hz (2/3)1H), 2.41-2.37 (m, (2/3)3H+(1/3)3H), 2.36-2.33 (br s, (1/3)2H), 2.33-2.10 (m, (2/3)4H), 2.10-1.40 (m, (2/3)6H+(1/3)4H), 1.25-1.07 (m, (1/4)2H), 0.98-0.95 (m, (1/3)1H);

¹³C NMR (100 MHz, CDCl₃) δ 153.9 (C), 153.8 (C), 153.1 (C), 153.0 (C), 144.1 (C), 143.4 (C), 137.0 (C), 135.4 (C), 132.6 (CH), 130.0 (CH), 129.8 (CH), 128.2 (CH), 127.2 (CH), 127.0 (CH), 115.5 (CH), 115.4 (CH), 115.3 (CH), 114.7 (CH), 86.6 (CH), 85.2 (CH), 73.3 (CH), 72.3 (CH), 72.0 (CH), 68.8 (CH₂), 68.7 (CH₂), 68.4 (CH₂), 66.3 (CH), 64.3 (CH), 63.8 (CH), 60.0 (CH), 58.8 (CH), 58.3 (CH), 55.8 (CH₃), 53.5 (CH), 51.9 (C), 51.2 (C), 45.6 (CH), 44.6 (CH), 41.3 (CH₂), 40.0 (CH₂), 39.1 (CH), 38.6 (CH₂),

36.8 (CH), 36.4 (CH₂), 35.0 (CH₂), 31.0 (CH₂), 30.2 (CH₂), 25.6 (CH₂), 25.2 (CH₂), 25.1 (CH₂), 21.6 (CH);

HRMS (ESI+) 540.2006 (calcd for C₂₇H₃₅NNaO₇S 540.2032).

(3a*R*,3a'*S*,4a*S*,4a'*S*,6*S*,7a*S*,8a*R*)-4a'-((3-(4-Methoxyphenoxy)propyl)-2,2-dimethyl-4-tosyldecahydro-3a*H*-1,3-dioxo-4-azacyclopenta[*def*]fluoren-6-ol (92a)



To a solution of **91a** (100 mg, 0.193 mmol) in acetone (14.0 mL) was added copper (II) sulfate anhydrous (230 mg, 1.44 mmol) and PPTS (64 mg, 0.255 mmol) at 0 °C and the solution was stirred for 2.5 h at room temperature. After cooling to 0 °C, EtOAc and aqueous NaHCO_3 were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 3:1~1:2) to give **92a** (54 mg, 50%) as a white amorphous.

$[\alpha]_{\text{D}}^{27} -34.7^\circ$ ($c = 1.00$, CHCl_3);

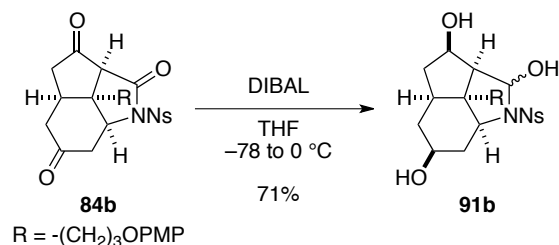
IR (film) 3502, 2938, 1508, 1470, 1382, 1339, 1232, 1162, 1040, 947, 827 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 7.85 (d, $J=8.2$ Hz, 2H), 7.23 (d, $J=8.2$ Hz, 2H), 6.86-6.76 (m, 4H), 5.86 (d, $J=6.9$ Hz, 2H), 4.40 (dd, $J=6.0, 4.6$ Hz, 1H), 3.93 (dd, $J=10.5, 8.2$ Hz, 1H), 3.82 (t, $J=6.0$ Hz, 2H), 3.39-3.30 (m, 1H), 2.27 (dd, $J=6.9, 6.0$ Hz, 1H), 2.18 (ddd, $J=13.3, 7.8, 4.6$ Hz, 1H), 2.10-2.02 (m, 1H), 2.00-1.60 (m, 8H), 1.50-1.42 (m, 5H), 1.33 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 153.8 (C), 153.0 (C), 143.2 (C), 138.7 (C), 129.2 (CH), 127.7 (CH), 115.4 (CH), 114.6 (CH), 97.5 (C), 82.2 (CH), 72.4 (CH), 68.5 (CH_2), 67.1 (CH), 62.3 (CH), 55.8 (C), 55.7 (CH_3), 51.9 (CH), 42.1 (CH_2), 41.5 (CH), 40.6 (CH_2), 39.0 (CH_2), 38.7 (CH_2), 29.3 (CH_3), 25.6 (CH_2), 21.5 (CH_3), 20.7 (CH_3);

HRMS (ESI+) 580.2364 (calcd for $\text{C}_{30}\text{H}_{39}\text{NNaO}_7\text{S}$ 580.2345).

(2*R*,2*aS*,2*a*¹*S*,3*R*,4*aS*,6*S*,7*aS*)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-1-((2-nitrophenyl)sulfonyl)decahydro-1*H*-cyclopenta[*cd*]indole-2,3,6-triol (91b**)**



To a solution of **84b** (500 mg, 0.922 mmol) in THF (26 mL) was added DIBAL (8.3 ml, 8.3mmol, 1 M in *n*-hexane) at $-78\text{ } ^\circ\text{C}$. After stirring for 10min at the same temperature, the mixture was stirred for 1 h at $-10\text{ } ^\circ\text{C}$. aqueous NaOH (1 M, 2.00 ml) was added at $-40\text{ } ^\circ\text{C}$. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered through a pad of Celite[®]. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:3~0:1) to afford a 1:1 diastereomeric mixture of **91b** (360 mg, 71%) as a white amorphous solid.

$[\alpha]_{\text{D}}^{27} 46.2^\circ$ ($c = 1.00$, CHCl_3);

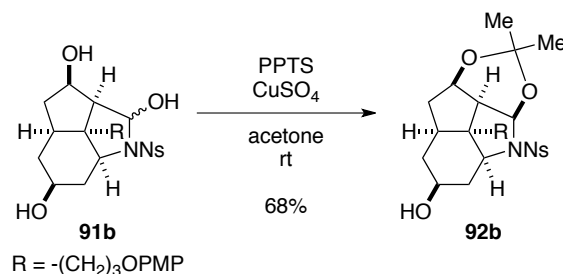
IR (film) 3395, 2935, 2360, 1717, 1541, 1508, 1468, 1371, 1230, 1169, 1036, 826, 761 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.20-8.02 (m, 1H), 7.82-7.55 (m, 3H), 6.85-6.70 (m, 4H), 5.96 (d, $J=4.1\text{ Hz}$, (1/2)1H), 5.76 (d, $J=6.6\text{ Hz}$, (1/2)1H), 5.50-5.38 (m, (1/2)1H), 4.35-4.11 (m, (1/2)3H), 3.98-3.83 (m, (1/2)5H), 3.83-3.76 (m, (1/2)2H), 3.75 (s, (1/2)3H), 3.74 (s, (1/2)3H), 3.72-3.65 (m, (1/2)2H), 2.87-2.61 (m, (1/2)2H), 2.54 (dd, $J=7.6, 7.6\text{ Hz}$, (1/2)1H), 2.46-2.28 (m, (1/2)4H), 2.21 (ddd, $J=12.4, 6.4, 6.4\text{ Hz}$, (1/2)1H), 2.51-1.61 (m, (1/2)20H), 1.58-1.47 (m, (1/2)2H), 1.46-1.11 (m, (1/2)4H), 0.97-0.85 (m, (1/2)1H);

^{13}C NMR (100 MHz, CDCl_3) δ 153.9 (C), 153.8 (C), 153.0 (C), 152.9 (C), 148.1 (C), 135.2 (CH), 134.2 (C), 134.0 (CH), 133.9 (CH), 133.3 (C), 132.3 (C), 132.1 (CH), 132.0 (CH), 131.1 (CH), 130.7 (CH), 129.5 (CH), 124.6 (CH), 124.5 (CH), 124.2 (CH), 115.5 (CH), 115.4 (CH), 114.7 (CH), 86.7 (CH), 86.1 (CH), 77.2 (CH), 73.1 (CH), 71.9 (CH), 68.7 (CH_2), 68.4 (CH_2), 67.8 (CH_2), 66.2 (CH), 65.0 (CH), 64.5 (CH), 63.1 (CH), 62.2 (CH), 61.2 (CH), 58.5 (CH), 58.2 (CH), 55.7 (CH_3), 52.2 (C), 51.8 (C), 45.4 (CH_2),

42.6 (CH₂), 41.7 (CH₂), 40.6 (CH₂), 39.3 (CH₂), 38.9 (CH₂), 38.1 (CH₂), 37.1 (CH), 37.0 (CH), 35.7 (CH₂), 35.4 (CH₂), 34.2 (CH₂), 31.5 (CH₂), 30.9 (CH₂), 30.6 (CH₂), 29.0 (CH₂), 25.5 (CH₂), 25.1 (CH₂), 23.9 (CH₂), 22.9 (CH₂), 14.0 (CH), 11.1 (CH);
HRMS (ESI+) 571.1710 (calcd for C₂₆H₃₂N₂NaO₉S 571.1726).

(3a*R*,3a¹*S*,4a*S*,4a¹*S*,6*S*,7a*S*,8a*R*)-4a¹-(3-(4-Methoxyphenoxy)propyl)-2,2-dimethyl-4-((2-nitrophenyl)sulfonyl)decahydro-3a*H*-1,3-dioxo-4-azacyclopenta[*def*]fluoren-6-ol (92b)



To a solution of **91b** (220 mg, 0.401 mmol) in Acetone (33.0 mL) was added Copper (II) sulfate anhydrous (530 mg, 3.32 mmol) and PPTS (150 mg, 0.598 mmol) at 40 °C and the solution was stirred for 12 h at the same temperature. After cooling to 0 °C, EtOAc and aqueous NaHCO₃ was added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1~1:2) to give **92b** (160 mg, 68%) as a white amorphous.

$[\alpha]_{\text{D}}^{27} -32.2^\circ$ ($c = 1.00$, CHCl₃);

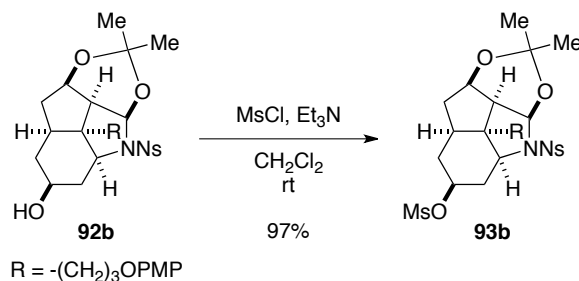
IR (film) 3420, 2938, 1717, 1542, 1508, 1470, 1372, 1232, 1164, 1078, 1039, 947, 827, 781 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 8.26-8.22 (m, 1H), 7.80-7.75 (m, 3H), 6.81 (d, $J=9.2$ Hz, 2H), 6.73 (d, $J=9.2$ Hz, 2H), 5.85 (d, $J=6.9$ Hz, 1H), 4.44 (dd, $J=5.5, 4.5$ Hz, 1H), 3.92 (dd, $J=10.3, 8.5$ Hz, 1H), 3.76 (s, 3H), 3.69 (t, $J=6.2$ Hz, 2H), 3.50-3.30 (m, 1H), 2.36 (dd, $J=6.9, 5.5$ Hz, 1H), 2.29-2.15 (m, 2H), 2.15-2.07 (m, 1H), 2.07-1.85 (m, 4H), 1.75-1.50 (m, 3H), 1.46 (s, 3H), 1.39 (s, 6H), 1.40-1.30 (m, 2H);

¹³C NMR (100 MHz, CDCl₃) δ 153.8 (C), 152.9 (C), 148.1 (C), 133.6 (C), 133.5 (CH), 131.5 (CH), 131.0 (CH), 123.9 (CH), 115.4 (CH), 114.6 (CH), 97.8 (C), 82.6 (CH), 72.3 (CH), 68.4 (CH₂), 67.0 (CH), 62.7 (CH), 56.2 (C), 55.7 (CH₃), 52.0 (CH), 42.2 (CH₂), 41.2 (CH), 40.3 (CH₂), 39.4 (CH₂), 38.7 (CH₂), 29.4 (CH₃), 25.5 (CH₂), 20.5 (CH₃);

HRMS (ESI+) 611.2047 (calcd for C₂₉H₃₆N₂NaO₉S 611.2039).

(3a*R*,3a¹*S*,4a*S*,4a¹*S*,6*S*,7a*R*,8a*R*)-4a¹-(3-(4-Methoxyphenoxy)propyl)-2,2-dimethyl-4-((2-nitrophenyl)sulfonyl)decahydro-3a*H*-1,3-dioxo-4-azacyclopenta[*def*]fluoren-6-yl methanesulfonate (93b)



To a solution of **92b** (100 mg, 0.170 mmol) and triethylamine (28.5 mL, 0.204 mmol) in CH₂Cl₂ (5.00 mL) was added methanesulfonyl chloride (14.5 μL, 0.187 mmol) at 0 °C. After stirring for 30min at the same temperature, aqueous NaHCO₃ aq was added. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1) to afford **93b** (110 mg, 97%) as a white amorphous.

[α]_D²⁷ −55.7° (*c* = 1.00, CHCl₃);

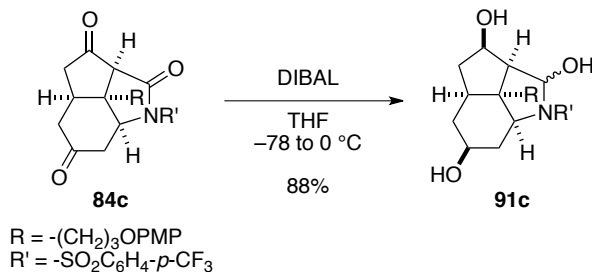
IR (film) 2989, 2938, 1544, 1508, 1471, 1440, 1355, 1232, 1175, 1078, 1034, 852, 828, 778 cm^{−1}

¹H NMR (400 MHz, CDCl₃) δ 8.25-8.16 (m, 1H), 7.70-7.55 (m, 3H), 6.84-6.78 (m, 2H), 6.74-6.68 (m, 2H), 5.84 (d, *J*=6.4 Hz, 1H), 4.44 (dd, *J*=6.0, 4.5 Hz, 1H), 4.44-4.36 (m, 1H), 3.90 (dd, *J*=10.0, 8.7 Hz, 1H), 3.76 (s, 3H), 3.70-3.58 (m, 2H), 3.00 (s, 3H), 2.55-2.45 (m, 1H), 2.38 (dd, *J*=6.4, 6.0 Hz, 1H), 2.38-2.05 (m, 5H), 1.94 (d, *J*=15.6 Hz, 1H), 1.65-1.50 (m, 2H), 1.46 (s, 3H), 1.40 (s, 3H), 1.43-1.23 (m, 2H);

¹³C NMR (100 MHz, CDCl₃) δ 153.8 (C), 152.8 (C), 147.9 (C), 133.8 (CH), 133.0 (C), 131.6 (CH), 131.0 (CH), 124.0 (CH), 115.4 (CH), 114.6 (CH), 97.9 (C), 82.9 (CH), 77.3 (CH), 72.1 (CH), 68.2 (CH₂), 61.9 (CH), 56.1 (C), 55.7 (CH₃), 51.7 (CH), 42.1 (CH₂), 40.8 (CH), 40.0 (CH₂), 38.8 (CH₃), 36.6 (CH₂), 35.7 (CH₂), 29.3 (CH₃), 25.4 (CH₂), 20.3 (CH₃);

HRMS (ESI⁺) 689.1807 (calcd for C₃₀H₃₈N₂NaO₁₁S₂ 689.1815).

(2*R*,2*aS*,2*a*¹*S*,3*R*,4*aS*,6*S*,7*aS*)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)decahydro-1*H*-cyclopenta[*cd*]indole-2,3,6-triol (91c**)**



To a solution of **84c** (2.20 g, 4.01 mmol) in THF (100 mL) was added DIBAL (37 mL, 37 mmol, 1 M in *n*-hexane) at -78°C . After stirring for 10 min at the same temperature, the mixture was stirred for 1 h at -10°C . aqueous NaOH (1 M, 2.00 mL) was added at -40°C . The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered through a pad of Celite®. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:3~0:1) to afford a 3:1 diastereomeric mixture of **91c** (2.20 g, 88%) as a white amorphous solid.

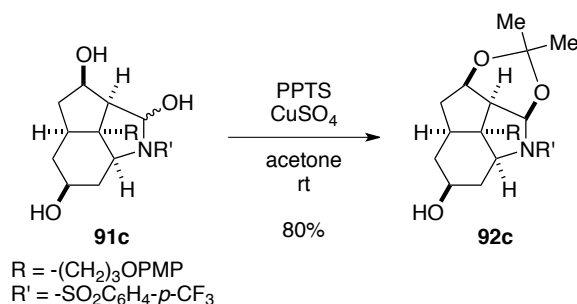
$[\alpha]_D^{27} 20.5^\circ$ ($c = 1.00$, CHCl_3);

IR (film) 3389, 2945, 1508, 1469, 1403, 1355, 1323, 1231, 1164, 1132, 1062, 826 cm^{-1} ;
 ^1H NMR (400 MHz, CDCl_3) δ 8.13 (d, $J=8.3$ Hz, (3/4)2H), 8.03 (d, $J=8.3$ Hz, (1/4)2H), 7.83-7.73 (m, 2H), 6.87-6.71 (m, 4H), 6.10-5.96 (m, (3/4)1H), 5.85 (d, $J=5.5$ Hz, (1/4)1H), 5.76-5.65 (m, (1/4)1H), 4.90-4.76 (m, (3/4)1H), 4.32-4.15 (m, 1H), 4.15-4.03 (m, (3/4)1H), 4.02-3.89 (m, (1/4)1H+(1/4)1H), 3.89-3.80 (m, (3/4)2H), 3.77 (s, (1/4)3H), 3.74 (s, (3/4)3H), 3.72-3.61 (m, (1/4)2H+(1/4)1H), 3.51 (br s, (3/4)1H), 3.48-3.42 (m, (3/4)1H), 3.33-3.21 (br s, (1/4)1H), 2.61 (d, $J=17.0$ Hz, (3/4)10.69H), 2.42 (d, $J=8.2$ Hz, (3/4)1H), 2.40-2.28 (m, (3/4)3H), 2.27-2.18 (m, (1/4)2H), 2.14 (s, 1H), 2.11-1.73 (m, (3/4)6H+(1/4)4H), 1.73-1.54 (m, (3/4)2H+(1/4)1H), 1.54-1.38 (m, (1/4)2H), 1.38-1.20 (m, (1/4)2H), 1.15-0.99 (m, (1/4)1H);

^{13}C NMR (100 MHz, CDCl_3) δ 153.9 (C), 153.8 (C), 152.8 (C), 152.7 (C), 142.8 (C), 141.9 (C), 134.4 (C, q, $J=32.4$ Hz), 134.5 (C, q, $J=32.4$ Hz), 129.0 (CH), 127.7 (CH), 126.3 (CH, q, $J=3.8$ Hz), 126.1 (CH, q, $J=3.8$ Hz), 123.2 (CF_3 , q, $J=271.7$ Hz), 123.1 (CF_3 , q, $J=271.7$ Hz), 115.4 (CH), 115.3 (CH), 114.6 (CH), 114.6 (CH), 86.6 (CH), 85.3 (CH), 73.2 (CH), 71.9 (CH), 68.6 (CH_2), 68.2 (CH_2), 66.0 (CH), 64.3 (CH), 63.0 (CH),

60.1 (CH), 58.9 (CH), 58.4 (CH), 55.7 (2CH₃), 51.9 (C), 51.4 (C), 44.8 (CH₂), 41.2 (CH₂), 41.0 (CH₂), 37.8 (CH₂), 37.2 (CH), 36.4 (CH), 34.8 (CH₂), 34.5 (CH₂), 30.4 (CH₂), 30.0 (CH₂), 25.5 (CH₂), 25.1 (CH₂); HRMS (ESI+) 594.1746 (calcd for C₂₇H₃₂F₃NNaO₇S 594.1745).

(3a*R*,3a'*S*,4a*S*,4a'*S*,6*S*,7a*S*,8a*R*)-4a'-((3-(4-Methoxyphenoxy)propyl)-2,2-dimethyl-4-((4-(trifluoromethyl)phenyl)sulfonyl)decahydro-3a*H*-1,3-dioxo-4-azacyclopenta[def]fluoren-6-ol (92c)



To a solution of a mixture of **91c** (1.93 g, 3.38 mmol) in acetone (140 mL) was added anhydrous copper (II) sulfate (1.8 g, 11.3 mmol) and PPTS (850 mg, 3.38 mmol) at room temperature and the solution was stirred for 16 h at the same temperature. The solution was evaporated and the residue was partitioned between EtOAc and aqueous NaHCO₃. The aqueous phase was further extracted with EtOAc and the combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1) to give **92c** (1.65 g, 80%) as a white amorphous solid.

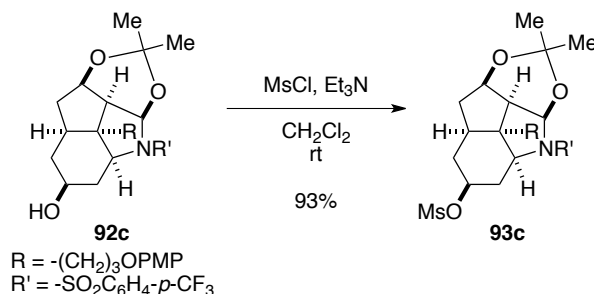
$[\alpha]_{\text{D}}^{27} -43.4^\circ$ ($c = 1.00$, CHCl₃);

IR (film) 3504, 2939, 1508, 1470, 1403, 1355, 1323, 1232, 1166, 1107, 1062, 948, 826 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 8.13 (d, $J=8.5$ Hz, 2H), 7.72 (d, $J=8.5$ Hz, 2H), 6.85-6.77 (m, 4H), 5.89 (d, $J=6.4$ Hz, 1H), 4.42 (dd, $J=6.4, 4.4$ Hz, 1H), 4.03 (dd, $J=10.5, 8.2$ Hz, 1H), 3.87 (t, $J=6.0$ Hz, 2H), 3.77 (s, 3H), 3.42-3.30 (m, 1H), 2.33 (dd, $J=6.4, 6.4$ Hz, 1H), 2.20 (ddd, $J=14.0, 7.8, 4.4$ Hz, 1H), 2.13-2.07 (m, 1H), 1.94 (d, $J=14.0$ Hz, 1H), 1.91-1.50 (m, 9H), 1.45 (s, 3H), 1.31 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.8 (C), 153.0 (C), 145.5 (C), 134.1 (C, q, $J=32.4$ Hz), 128.3 (CH), 125.6 (CH, q, $J=3.8$ Hz), 123.3 (CF₃, q, $J=271.7$ Hz), 115.4 (CH), 114.6 (CH), 97.6 (C), 82.3 (CH), 72.4 (CH), 68.4 (CH₂), 66.9 (CH), 62.8 (CH), 55.7 (C), 55.7 (CH₃), 51.7 (CH), 42.0 (CH₂), 41.7 (CH), 40.8 (CH₂), 38.8 (CH₂), 38.7 (CH₂), 29.2 (CH₃), 25.6 (CH₂), 20.6 (CH₃); HRMS (ESI+) 634.2059 (calcd for C₃₀H₃₆F₃NNaO₇S 634.2062).

(3a*R*,3a'*S*,4a*S*,4a'*S*,6*S*,7a*R*,8a*R*)-4a¹-(3-(4-Methoxyphenoxy)propyl)-2,2-dimethyl-4-((4-(trifluoromethyl)phenyl)sulfonyl)decahydro-3a*H*-1,3-dioxo-4-azacyclopenta[*de*]fluoren-6-yl methanesulfonate (93c**)**



To a solution of **92c** (1.54 g, 2.52 mmol) and triethylamine (528 mL, 3.78 mmol) in CH_2Cl_2 (70 mL) was added methanesulfonyl chloride (216 μL , 2.77 mmol) at 0 °C. After stirring for 30 min at the same temperature, aqueous NaHCO_3 was added. The resulting solution was extracted with CH_2Cl_2 . The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:1) to afford **93c** (1.62 g, 93%) as a white amorphous solid.

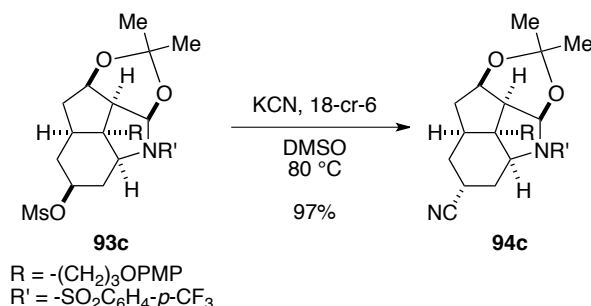
$[\alpha]_{\text{D}}^{27} -37.2^\circ$ ($c = 1.00$, CHCl_3);

IR (film) 3449, 2940, 1508, 1350, 1232, 1172, 1062, 943, 827 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.12 (d, $J=8.2$ Hz, 2H), 7.74 (d, $J=8.2$ Hz, 2H), 6.86-6.75 (m, 4H), 5.89 (d, $J=6.9$ Hz, 1H), 4.44 (dd, $J=6.0, 4.6$ Hz, 1H), 4.38-4.27 (m, 1H), 4.06 (dd, $J=10.1, 8.2$ Hz, 1H), 3.86 (t, $J=5.9$ Hz, 2H), 3.77 (s, 3H), 2.91 (s, 3H), 2.35 (dd, $J=6.9, 6.0$ Hz, 1H), 2.25-2.06 (m, 5H), 1.95 (d, $J=14.2$ Hz, 1H), 1.97-1.87 (m, 1H), 1.85-1.64 (m, 2H), 1.58-1.52 (m, 2H), 1.45 (s, 3H), 1.32 (s, 3H);

^{13}C NMR (100 MHz, CDCl_3) δ 153.9 (C), 152.9 (C), 145.2 (C), 134.1 (C, q, $J=32.4$ Hz), 128.3 (CH), 125.6 (CH, q, $J=3.8$ Hz), 123.3 (CF_3 , q, $J=271.7$ Hz), 115.4 (CH), 114.6 (CH), 97.7 (C), 82.3 (CH), 72.4 (CH), 68.4 (CH_2), 66.9 (CH), 62.8 (CH), 55.7 (C), 55.7 (CH_3), 51.7 (CH), 42.0 (CH_2), 41.7 (CH), 40.8 (CH_2), 38.8 (CH_2), 38.7 (CH_2), 29.2 (CH_3), 25.5 (CH_2), 20.5 (CH_3); HRMS (ESI+) 712.1848 (calcd for $\text{C}_{31}\text{H}_{38}\text{F}_3\text{NNaO}_9\text{S}_2$ 712.1838).

(3a*R*,3a'*S*,4a*S*,4a'*S*,6*R*,7a*S*,8a*R*)-4a'-((3-(4-Methoxyphenoxy)propyl)-2,2-dimethyl-4-((4-(trifluoromethyl)phenyl)sulfonyl)decahydro-3a*H*-1,3-dioxo-4-azacyclopenta[*def*]fluorene-6-carbonitrile (**94c**)



To a solution of **93c** (1.83 g, 2.52 mmol) in DMSO (30 mL) was added 18-crown-6 (4.36 g, 16.5 mmol) and potassium cyanide (4.36 g, 66.7 mmol) at room temperature and the solution was stirred for 5 h at 80 °C. After cooling to room temperature, EtOAc and aqueous NaHCO₃ were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residual oil was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 3:1~2:1) to afford **94c** (1.69 g, 97%) as a white amorphous solid.

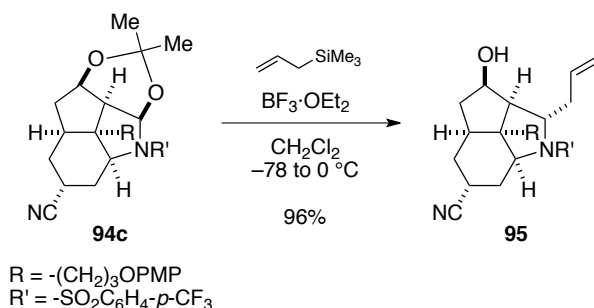
$[\alpha]_{\text{D}}^{27} -79.4^\circ$ ($c = 1.00$, CHCl₃);

IR (film) 3483, 2990, 2939, 1508, 1468, 1403, 1383, 1350, 1323, 1232, 1172, 1132, 1062, 943, 828 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 8.13 (d, $J=8.3$ Hz, 2H), 7.73 (d, $J=8.3$ Hz, 2H), 6.85-6.76 (m, 4H), 5.89 (d, $J=6.4$ Hz, 1H), 4.45 (dd, $J=6.4, 5.0$ Hz, 1H), 4.10 (dd, $J=10.1, 8.2$ Hz, 1H), 3.90-3.83 (m, 2H), 3.77 (s, 3H), 2.82-2.75 (m, 1H), 2.43 (dd, $J=6.4, 6.4$ Hz, 1H), 2.31-2.20 (m, 2H), 2.09 (ddd, $J=13.3, 11.5, 3.2$ Hz, 1H), 2.00-1.65 (m, 8H), 1.46 (s, 3H), 1.28 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.8 (C), 153.0 (C), 145.3 (C), 134.3 (C, q, $J=32.4$ Hz), 128.3 (CH), 125.8 (CH, q, $J=3.8$ Hz), 123.2 (CF₃, q, $J=271.7$ Hz), 120.8 (C), 115.5 (CH), 114.6 (CH), 97.8 (C), 82.5 (CH), 72.6 (CH), 68.4 (CH₂), 60.0 (CH), 55.7 (CH₃), 55.6 (C), 55.4 (CH), 41.8 (CH₂), 41.3 (CH₂), 40.2 (CH), 31.5 (CH₂), 30.9 (CH₂), 29.3 (CH₃), 24.8 (CH₂), 24.0 (CH), 20.5 (CH₃); HRMS (ESI+) 643.2058 (calcd for C₃₁H₃₅F₃N₂NaO₆S 643.2066).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-2-Allyl-3-hydroxy-2*a*¹-(3-(4-methoxyphenoxy)propyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)decahydro-1*H*-cyclopenta[*cd*]indole-6-carbonitrile (95**)**



To a solution of **94c** (1.21 g, 4.01 mmol) in CH_2Cl_2 (60 mL) was added allyltrimethylsilane (6.30 mL, 39.6 mmol) and $\text{BF}_3\cdot\text{OEt}_2$ (2.90 mL, 22.9 mmol) at -78°C . After stirring for 10 min at -78°C , the mixture was stirred for 30 min at 0°C . The reaction was quenched with aqueous NaHCO_3 . The resulting solution was extracted with CH_2Cl_2 . The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residual oil was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:1) to afford **95** (1.13 g, 96%) as a white amorphous solid.

$[\alpha]_{\text{D}}^{27} -0.812^\circ$ ($c = 1.00$, CHCl_3);

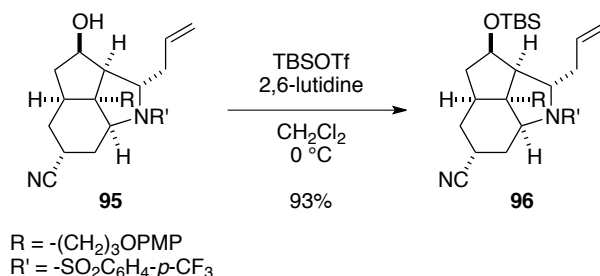
IR (film) 3504, 2947, 2388, 2241, 1508, 1366, 1402, 1323, 1231, 1161, 1134, 1062, 923, 827 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 8.04 (d, $J=8.2$ Hz, 2H), 7.84 (d, $J=8.2$ Hz, 2H), 6.90-6.76 (m, 4H), 5.63 (dddd, $J=16.9, 11.5, 3.2, 1.8$ Hz, 1H), 5.10 (dd, $J=11.5, 0.9$ Hz, 1H), 5.06 (dd, $J=16.9, 0.9$ Hz, 1H), 4.68 (dd, $J=10.1, 3.2$ Hz, 1H), 4.24-4.10 (m, 1H), 3.96-3.85 (m, 2H), 3.77 (s, 3H), 3.65-3.60 (m, 1H), 2.78 (dd, $J=15.3, 2.1$ Hz, 1H), 2.70-2.63 (m, 1H), 2.52-2.10 (m, 2H), 2.28 (d, $J=7.8$ Hz, 1H), 2.04 (d, $J=4.1$ Hz, 1H), 2.02-2.00 (m, 1H), 1.97-1.86 (m, 1H), 1.82-1.57 (m, 8H);

^{13}C NMR (100 MHz, CDCl_3) δ 154.0 (C), 152.7 (C), 145.2 (C), 134.7 (C, q, $J=33.4$ Hz), 133.7 (CH), 127.6 (CH), 126.7 (CH, q, $J=2.9$ Hz), 123.2 (CF_3 , q, $J=271.7$ Hz), 121.6 (C), 118.7 (CH_2), 115.3 (CH), 114.7 (CH), 71.9 (CH), 68.1 (CH_2), 61.7 (CH), 60.2 (CH), 55.7 (CH_3), 52.1 (CH), 51.7 (C), 38.4 (CH_2), 37.9 (CH_2), 36.4 (CH), 34.2 (CH_2), 28.8 (CH_2), 28.1 (CH_2), 25.8 (CH_2), 19.0 (CH);

HRMS (ESI+) 627.2091 (calcd for $\text{C}_{31}\text{H}_{35}\text{F}_3\text{N}_2\text{NaO}_5\text{S}$ 627.2117).

(2*S*,2*aR*,2*a'S*,3*R*,4*aS*,6*R*,7*aS*)-2-Allyl-3-((*tert*-butyldimethylsilyl)oxy)-2*a'*-(3-(4-methoxyphenoxy)propyl)-1-((4-(trifluoromethyl)phenyl)sulfonyl)decahydro-1*H*-cyclopenta[*cd*]indole-6-carbonitrile (**96**)**



To a solution of **95** (2.00 g, 3.30 mmol) in CH₂Cl₂ (60 mL) were added 2,6-lutidine (6.90 mL, 59.6 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.53 mL, 6.60 mmol) at 0 °C. After stirring for 1 h at the same temperature, aqueous NaHCO₃ was added. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residual oil was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 20:1~1:1) to afford **96** (2.20 g, 93%) as a white amorphous solid.

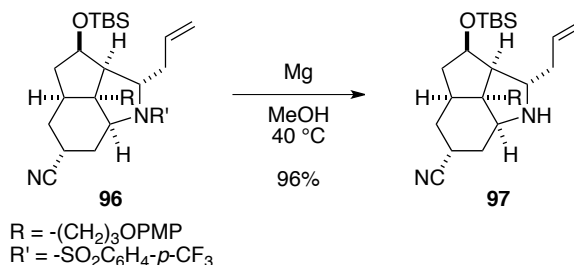
$[\alpha]_{\text{D}}^{27} -5.20^\circ$ ($c = 1.00$, CHCl₃);

IR (film) 2952, 2857, 2239, 1508, 1471, 1402, 1323, 1232, 1163, 1135, 1062, 835, 778 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, $J=8.2$ Hz, 2H), 7.83 (d, $J=8.2$ Hz, 2H), 6.85-6.76 (m, 4H), 5.60 (dddd, $J=16.5, 10.1, 3.2, 1.8$ Hz, 1H), 5.08 (d, $J=10.1$ Hz, 1H), 5.04 (d, $J=16.5$ Hz, 1H), 4.64 (dd, $J=10.8, 3.0$ Hz, 1H), 4.04 (ddd, $J=17.8, 8.2, 2.8$ Hz, 1H), 3.95-3.85 (m, 2H), 3.77 (s, 3H), 3.68-3.63 (m, 1H), 2.82 (dd, $J=15.4, 2.1$ Hz, 1H), 2.74-2.66 (m, 1H), 2.30-2.20 (m, 1H), 2.22 (d, $J=8.2$ Hz, 1H), 2.05-1.92 (m, 2H), 1.90-1.85 (m, 1H), 1.85-1.46 (m, 8H), 0.92 (s, 9H), 0.07 (s, 3H), 0.05 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 154.0 (C), 152.7 (C), 145.4 (C), 134.6 (C, q, $J=32.4$ Hz), 134.0 (CH), 127.6 (CH), 126.5 (CH, q, $J=2.9$ Hz), 124.4 (CH), 123.0 (CF₃, q, $J=271.7$ Hz), 121.6 (C), 118.4 (CH₂), 115.3 (CH), 114.7 (CH), 72.3 (CH), 68.1 (CH₂), 61.7 (CH), 55.7 (CH₃), 52.5 (CH), 50.9 (C), 39.0 (CH₂), 38.2 (CH₂), 36.3 (CH), 34.2 (CH₂), 28.7 (CH₂), 28.1 (CH₂), 25.8 (CH₂), 25.7 (CH₃), 19.0 (CH), 18.0 (C), -4.6 (CH₃), -5.0 (CH₃); HRMS (ESI+) 741.3003 (calcd for C₃₇H₄₉F₃N₂NaO₅SSi 741.2981).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-2-Allyl-3-((*tert*-butyldimethylsilyl)oxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)decahydro-1*H*-cyclopenta[*cd*]indole-6-carbonitrile (97**)**



To a solution of **96** (1.84 g, 2.56 mmol) in MeOH (200 mL) was added Mg (6.00 g, 247 mmol) at room temperature and the solution was heated at 40 °C for 3 h. After cooling to room temperature, EtOAc was added and then the solution was concentrated. The residue was partitioned between EtOAc and water. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 2:1) to afford **97** (1.26 g, 96%) as a pale yellow oil.

$[\alpha]_{\text{D}}^{27} 5.47^\circ$ ($c = 1.00$, CHCl₃);

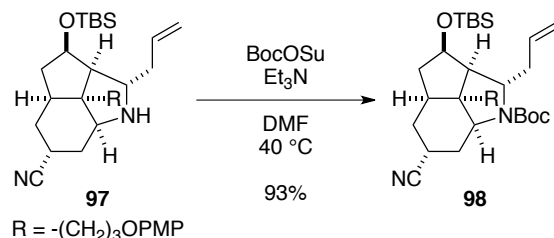
IR (film) 3464, 2929, 2856, 2237, 1639, 1508, 1470, 1413, 1359, 1231, 1143, 1044, 914, 835, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.83 (s, 4H), 5.70 (dddd, $J=17.0, 13.4, 8.2, 1.4$ Hz, 1H), 5.07 (dd, $J=8.2, 1.4$ Hz, 1H), 5.02 (dd, $J=17.0, 1.4$ Hz, 1H), 4.05 (ddd, $J=10.8, 8.0, 2.8$ Hz, 1H), 3.91 (t, $J=6.2$ Hz, 2H), 3.77 (s, 3H), 3.66 (dd, $J=6.9, 6.9$ Hz, 1H), 3.36-3.32 (m, 1H), 3.22 (dddd, $J=12.4, 12.4, 2.8, 2.8$ Hz, 1H), 2.14-2.05 (m, 2H), 2.02-1.86 (m, 5H), 1.85-1.68 (m, 4H), 1.65-1.51 (m, 3H), 0.88 (s, 9H), 0.04 (s, 6H), 0.03 (s, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 153.9 (C), 152.9 (C), 136.2 (CH), 123.8 (C), 117.2 (CH₂), 115.4 (CH), 114.7 (CH), 72.9 (CH), 68.8 (CH₂), 59.0 (CH), 58.5 (CH), 55.7 (CH₃), 54.3 (CH), 48.6 (C), 41.0 (CH₂), 39.6 (CH₂), 36.3 (CH), 35.3 (CH₂), 31.7 (CH₂), 29.4 (CH₂), 26.3 (CH₂), 25.8 (CH₂), 18.2 (CH), 18.0 (C), -4.7 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 511.3354 (calcd for C₃₀H₄₇N₂O₃Si 511.3356).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl-2-allyl-3-((*tert*-butyldimethylsilyl)oxy)-6-cyano-2*a*¹-(3-(4-methoxyphenoxy)propyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (**98**)



To a solution of **97** (1.74 g, 3.41 mmol) and triethylamine (1.43 mL, 10.2 mmol) in *N,N*-dimethylformamide (20.0 mL) was added *N*-(*tert*-butoxycarbonyloxy)succinimide (1.47 g, 6.82 mmol) at room temperature and the solution was heated at 40 °C for 3 h. After cooling to 0 °C, EtOAc and aqueous NaHCO₃ were added. The resulting solution was extracted with EtOAc. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 5:1) to give **98** (1.91 g, 92%) as a white amorphous solid.

[α]_D²⁷ 17.9° (*c* = 1.00, CHCl₃);

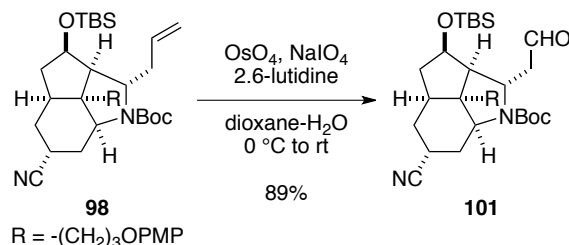
IR (film) 2932, 2857, 2362, 2238, 1695, 1508, 1472, 1394, 1232, 1174, 1130, 1045, 884, 835, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.82 (s, 4H), 5.67 (dddd, *J*=18.4, 13.4, 7.3, 2.3 Hz, 1H), 5.05 (d, *J*=15.6 Hz, 1H), 5.04 (d, *J*=12.4 Hz, 1H), 4.43 (ddd, *J*=8.2, 4.1, 2.3 Hz, 1H), 4.04 (ddd, *J*=13.2, 8.2, 7.3 Hz, 2H), 3.91 (t, *J*=6.0 Hz, 2H), 3.76 (s, 3H), 3.58 (dd, *J*=3.2, 2.7 Hz, 1H), 2.68 (dddd, *J*=12.4, 12.4, 3.0, 3.0 Hz, 1H), 2.36-2.20 (m, 2H), 2.07 (dd, *J*=7.3, 2.3 Hz, 1H), 2.02-1.90 (m, 2H), 1.85-1.70 (m, 3H), 1.69-1.54 (m, 6H), 1.47 (s, 9H), 0.89 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.9 (C), 153.5 (C), 152.8 (C), 134.7 (CH), 123.0 (C), 117.2 (CH₂), 115.4 (CH), 114.6 (CH), 79.7 (C), 72.6 (CH), 68.5 (CH₂), 60.5 (CH), 57.0 (CH), 55.7 (CH₃), 53.6 (CH), 50.2 (C), 39.2 (CH₂), 38.6 (CH₂), 36.7 (CH), 34.8 (CH₂), 29.3 (CH₂), 29.0 (CH₂), 28.4 (CH₃), 25.8 (CH₂), 25.8 (CH₃), 19.1 (CH), 18.0 (C), -4.6 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 633.3719 (calcd for C₃₅H₅₄N₂NaO₅Si 633.3700).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl-3-((*tert*-butyldimethylsilyl)oxy)-6-cyano-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-oxoethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (101**)**



To a solution of **98** (820 mg, 1.34 mmol) in 1,4-dioxane (70.0 mL) and H₂O (23.0 mL) was added 2,6-lutidine (1.37 mL, 11.8 mmol), NaIO₄ (5.73 g, 26.8 mmol) and OsO₄ (33.6 mL, 1.34 mmol, 0.04 M in *t*-BuOH) at 0 °C. The mixture was stirred for 3 h at room temperature. After cooling to 0 °C, CH₂Cl₂ and aqueous NaHCO₃ were added. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 2:1) to give **101** (730 mg, 89%) as a white amorphous solid.

$[\alpha]_{\text{D}}^{27}$ 30.6° (*c* = 1.00, CHCl₃);

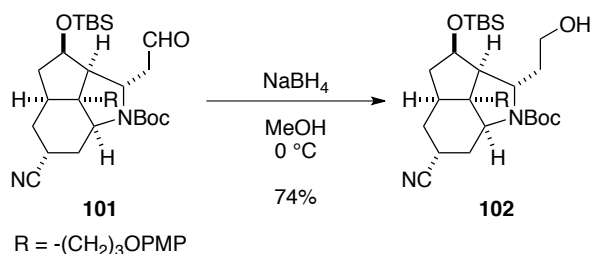
IR (film) 2932, 2857, 2238, 1725, 1697, 1508, 1471, 1393, 1366, 1231, 1172, 1127, 1043, 836, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 9.70 (t, *J*=2.5 Hz, 1H), 6.83 (s, 4H), 4.80 (m, 1H), 4.09 (ddd, *J*=10.5, 6.9, 6.9 Hz, 1H), 3.92 (t, *J*=5.7 Hz, 2H), 3.77 (s, 3H), 3.69 (m, 1H), 2.74-2.64 (m, 2H), 2.54 (ddd, *J*=14.6, 5.5, 2.5 Hz, 1H), 2.04-1.93 (m, 3H), 1.88-1.58 (m, 9H), 1.47 (s, 9H), 0.89 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 200.2 (CH), 154.0 (C), 153.1 (C), 152.8 (C), 122.7 (C), 115.5 (CH), 114.7 (CH), 80.8 (C), 72.6 (CH), 68.4 (CH₂), 60.4 (CH), 56.1 (CH), 55.7 (CH₃), 53.3 (CH), 50.2 (C), 49.0 (CH₂), 39.1 (CH₂), 36.9 (CH), 35.5 (CH₂), 29.4 (CH₂), 29.4 (CH₂), 28.4 (CH₃), 25.7 (CH₂), 25.7 (CH₃), 19.2 (CH), 17.9 (C), -4.6 (CH₃), -5.0 (CH₃);

HRMS (ESI+) 635.3509 (calcd for C₃₄H₅₂N₂NaO₆Si 635.3492).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl-3-((*tert*-butyldimethylsilyl)oxy)-6-cyano-2-(2-hydroxyethyl)-2*a*¹-(3-(4-methoxyphenoxy)propyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (**102**)



To a solution of **101** (685 mg, 1.12 mmol) in MeOH (20.0 mL) was added NaBH₄ (96.0 mg, 2.46 mmol) at 0 °C. The solution was stirred for 30 min at the same temperature. To this solution was added CH₂Cl₂ and aqueous NaHCO₃. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1) to give **102** (510 mg, 74%) as a white amorphous solid.

[α]_D²⁶ 7.71° (*c* = 1.00, CHCl₃);

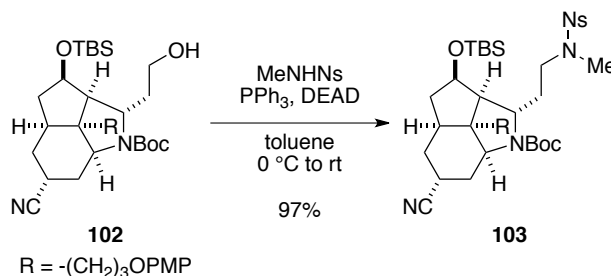
IR (film) 3481, 2932, 2857, 2238, 1692, 1508, 1472, 1393, 1366, 1313, 1231, 1173, 1128, 1044, 836, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 6.83 (s, 4H), 4.61 (br s, 1H), 4.07 (ddd, *J*=6.4, 6.4, 10.6 Hz, 1H), 3.92 (t, *J*=6.0 Hz, 2H), 3.77 (s, 3H), 3.68-3.45 (m, 4H), 2.70 (dddd, *J*=12.4, 12.4, 2.5, 2.5 Hz, 1H), 2.10-1.91 (m, 3H), 1.89-1.49 (m, 11H), 1.46 (s, 9H), 0.91 (s, 9H), 0.07 (s, 6H);

¹³C NMR (100 MHz, CDCl₃) δ 153.9 (C), 153.6 (C), 152.8 (C), 122.7 (C), 115.4 (CH), 114.7 (CH), 80.9 (C), 72.9 (CH), 68.4 (CH₂), 59.6 (CH), 59.5 (CH), 55.7 (CH), 55.3 (CH₃), 54.6 (C), 50.6 (CH₂), 38.9 (CH₂), 38.0 (CH₂), 36.8 (CH), 34.3 (CH₂), 28.8 (CH₂), 28.7 (CH₂), 28.4 (CH₃), 25.8 (CH₂), 25.8 (CH₃), 19.5 (CH), 18.0 (C), -4.5 (CH₃), -4.8 (CH₃);

HRMS (ESI+) 637.3658 (calcd for C₃₄H₅₄N₂NaO₆Si 637.3649).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl 3-((*tert*-butyldimethylsilyl)oxy)-6-cyano-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (103**)**



To a solution of **102** (470 mg, 0.764 mmol) in toluene (11.0 mL) was added *N*-methyl-2-nitrobenzenesulfonamide (181 mg, 0.840 mmol), triphenylphosphine (260 mg, 0.993 mmol) and diethyl azodicarboxylate (451 μ L, 0.993 mmol, 2.2 M in toluene) at 0 °C. The solution was stirred for 1 h at the room temperature. To this solution was added CH₂Cl₂ and aqueous NaHCO₃. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 5:1~2:1) to give **103** (600 mg, 97%) as a white amorphous solid.

$[\alpha]_D^{26}$ 13.5° (*c* = 1.00, CHCl₃);

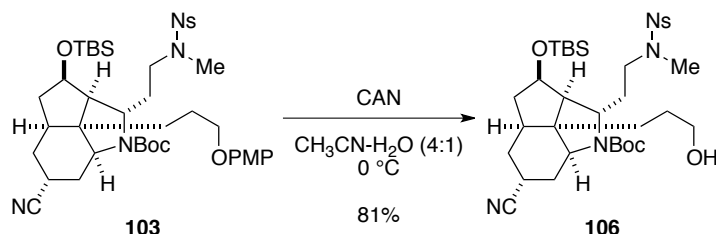
IR (film) 2932, 2857, 2238, 1692, 1545, 1508, 1471, 1367, 1231, 1169, 1126, 1042, 835, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.96 (m, 1H), 7.68-7.59 (m, 2H), 7.58 (m, 1H), 6.84 (s, 4H), 4.30 (m, 1H), 4.07 (ddd, *J*=10.5, 6.4, 6.4 Hz, 1H), 3.94 (t, *J*=5.7 Hz, 2H), 3.76 (s, 3H), 3.58 (m, 1H), 3.23 (ddd, *J*=13.1, 13.1, 4.1 Hz, 1H), 3.07 (ddd, *J*=13.1, 12.8, 5.3 Hz, 1H), 2.89 (s, 3H), 2.68 (dddd, *J*=13.0, 13.0, 2.8, 2.8 Hz, 1H), 2.03-1.92 (m, 4H), 1.87-1.61 (m, 7H), 1.61-1.51 (m, 3H), 1.46 (s, 9H), 0.85 (s, 9H), 0.04 (s, 3H), 0.02 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.9 (C), 153.3 (C), 152.9 (C), 148.1 (C), 133.5 (CH), 132.6 (C), 131.6 (CH), 130.7 (CH), 124.1 (CH), 122.9 (C), 115.5 (CH), 114.7 (CH), 80.1 (C), 72.6 (CH), 68.5 (CH₂), 60.1 (CH), 55.7 (CH₃), 55.3 (CH), 54.9 (CH), 50.5 (C), 47.3 (CH₂), 39.1 (CH₂), 36.9 (CH), 34.6 (CH₃), 34.6 (CH₂), 34.6 (CH₂), 32.9 (CH₂), 29.1 (CH₂), 28.4 (CH₃), 25.8 (CH₃), 25.7 (CH₂), 19.3 (CH), 17.9 (C), -4.5 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 835.3735 (calcd for $\text{C}_{41}\text{H}_{60}\text{N}_4\text{NaO}_9\text{SSi}$ 835.3748).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl 3-((*tert*-butyldimethylsilyl)oxy)-6-cyano-2*a*¹-(3-hydroxypropyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (**106**)



To a solution of **103** (137 mg, 0.168 mmol) in CH₃CN (4.0 mL) and H₂O (1.0 mL) was added cerium(IV) ammonium nitrate (110 mg, 0.202 mmol) at 0 °C and the solution was stirred for 2.5 h at the same temperature. To this solution was added CH₂Cl₂ and aqueous NaHCO₃ at 0 °C and then the resulting solution was extracted three times with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1) to afford **106** (97 mg, 81%) as a pale orange amorphous.

$[\alpha]_D^{27}$ 20.6° (*c* = 1.50, CHCl₃);

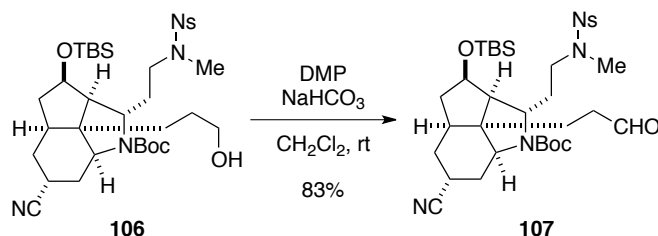
IR (film) 3488, 2932, 2857, 2239, 1692, 1546, 1459, 1368, 1349, 1252, 1168, 1126, 1057, 971, 898, 837, 776 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 7.94 (dd, *J*=7.3, 2.3 Hz, 1H), 7.71-7.60 (m, 2H), 7.60 (dd, *J*=7.3, 2.3 Hz, 1H), 4.29-4.24 (m, 1H), 4.04 (ddd, *J*=10.5, 6.4, 6.4 Hz, 1H), 3.73-3.59 (m, 2H), 3.59-3.48 (m, 1H), 3.23 (ddd, *J*=13.1, 13.1, 4.2 Hz, 1H), 3.07 (ddd, *J*=13.1, 13.1, 5.2 Hz, 1H), 2.88 (s, 3H), 2.67 (dddd, *J*=13.1, 13.1, 2.8, 2.8 Hz, 1H), 2.12-2.00 (m, 1H), 2.00-1.85 (m, 3H), 1.84-1.48 (m, 11H), 1.46 (s, 9H), 0.84 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.3 (C), 148.9 (C), 133.5 (CH), 132.4 (C), 131.6 (CH), 130.6 (CH), 124.1 (CH), 122.8 (C), 80.0 (C), 72.5 (CH), 62.8 (CH₂), 59.8 (CH₂), 55.3 (CH), 54.7 (CH), 50.5 (C), 47.2 (CH₂), 39.1 (CH₂), 37.1 (CH), 34.7 (CH₃), 34.2 (CH₂), 32.8 (CH₂), 29.1 (CH₂), 28.9 (CH₂), 28.4 (CH₃), 25.8 (CH₃), 19.2 (CH), 17.9 (C), -4.5 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 729.3328 (calcd for C₃₄H₅₄N₄NaO₈SSi 729.3329).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-tert-Butyl 3-((*tert*-butyldimethylsilyl)oxy)-6-cyano-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-2*a*¹-(3-oxopropyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (107**)**



To a solution of **106** (100.0 mg, 0.098 mmol) in CH₂Cl₂ (4.0 mL) was added sodium hydrogen carbonate (130 mg, 1.55 mmol), Dess-Martine periodinane (48 mg, 0.114 mmol) at 0 °C. After stirring for 1 h at room temperature, water was added at the same temperature. The resulting solution was extracted twice with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:2) to give **107** (56.0 mg, 83%) as a colorless oil.

$[\alpha]_D^{27}$ 20.6° (*c* = 1.60, CHCl₃);

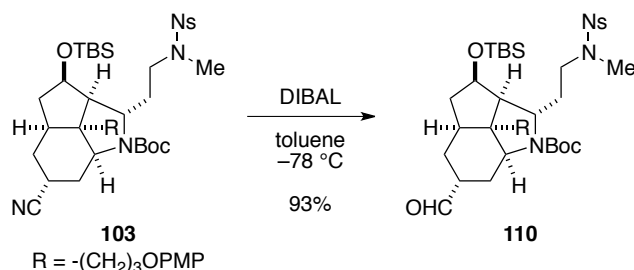
IR (film) 2931, 2857, 2384, 2239, 1723, 1692, 1546, 1460, 1367, 1311, 1252, 1167, 1127, 1058, 897, 837, 776 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 9.83 (s, 1H), 7.94 (dd, *J*=7.3, 1.8 Hz, 1H), 7.73-7.62 (m, 2H), 7.60 (dd, *J*=7.3, 1.8 Hz, 1H), 4.30-4.22 (m, 1H), 4.04 (dd, *J*=10.6, 5.3, 5.3 Hz, 1H), 3.56-3.43 (m, 1H), 3.25 (ddd, *J*=13.1, 13.1, 4.2 Hz, 1H), 3.00 (ddd, *J*=13.1, 13.1, 5.2 Hz, 1H), 2.88 (s, 3H), 2.67 (dddd, *J*=13.1, 13.1, 2.8, 2.8 Hz, 1H), 2.56 (dd, *J*=7.6, 7.6 Hz, 2H), 2.06-1.90 (m, 3H), 1.89-1.75 (m, 5H), 1.72-1.52 (m, 5H), 1.45 (s, 9H), 0.87 (s, 9H), 0.03 (s, 3H), 0.01 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 201.0 (CH), 153.2 (C), 148.0 (C), 133.5 (CH), 132.4 (C), 131.6 (CH), 130.6 (CH), 124.1 (CH), 122.6 (C), 80.1 (C), 72.4 (CH), 59.6 (CH), 55.2 (CH), 54.2 (CH), 50.0 (C), 47.2 (CH₂), 40.3 (CH₂), 38.9 (CH₂), 37.3 (CH), 34.7 (CH₃), 32.7 (CH₂), 29.1 (CH₂), 28.8 (CH₂), 28.4 (CH₃), 25.7 (CH₃), 19.2 (CH), 17.9 (C), -4.5 (CH₃), -5.0 (CH₃);

HRMS (ESI+) 727.3139 (calcd for C₃₄H₅₂N₄NaO₈SSi 727.3173).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl 3-((*tert*-butyldimethylsilyl)oxy)-6-formyl-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (**110**)



To a solution of **103** (544 mg, 0.669 mmol) in toluene (14.0 mL) was added DIBAL (1.0 M in toluene, 1.34 mL, 1.34 mmol) at -78°C . The solution was stirred for 1 h at the same temperature. To this solution was added H₂O carefully. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 2:1~5:1) to give **110** (510 mg, 93%) as a pale yellow amorphous solid.

$[\alpha]_{\text{D}}^{26} 13.9^{\circ}$ ($c = 0.600$, CHCl₃);

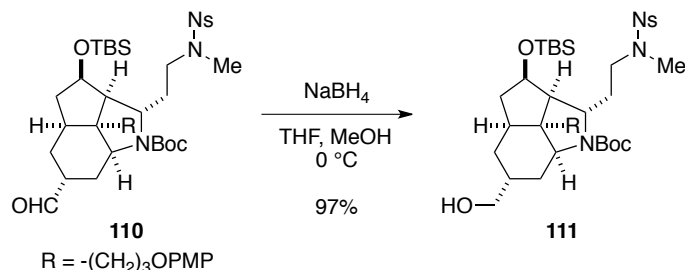
IR (film) 2930, 2857, 2390, 1722, 1693, 1546, 1508, 1470, 1366, 1231, 1169, 1126, 1043, 835, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 9.69 (s, 1H), 7.97 (m, 1H), 7.70-7.60 (m, 2H), 7.59 (m, 1H), 6.83 (s, 4H), 4.33 (m, 1H), 4.08 (ddd, $J=10.5, 6.4, 6.4$ Hz, 1H), 3.93 (t, $J=5.7$ Hz, 2H), 3.77 (s, 3H), 3.64 (m, 1H), 3.24 (ddd, $J=13.1, 13.1, 4.1$ Hz, 1H), 3.09 (ddd, $J=13.1, 12.7, 4.6$ Hz, 1H), 2.90 (s, 3H), 2.50 (m, 1H), 2.05-1.70 (m, 7H), 1.70-1.50 (m, 6H), 1.44 (s, 9H), 1.32 (ddd, $J=13.3, 13.3, 2.7$ Hz, 1H), 0.86 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 204.7 (CH), 153.9 (C), 153.3 (C), 153.0 (C), 148.1 (C), 133.4 (CH), 132.7 (C), 131.5 (CH), 130.7 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 79.6 (C), 72.8 (CH), 68.7 (CH₂), 60.9 (CH), 55.7 (CH₃), 55.5 (CH), 55.2 (CH), 51.3 (C), 47.3 (CH₂), 40.2 (CH), 39.5 (CH₂), 37.2 (CH), 34.9 (CH₂), 34.6 (CH₃), 33.7 (CH₂), 28.4 (CH₂), 28.4 (CH₃), 25.8 (CH₃), 25.8 (CH₂), 25.0 (CH₂), 17.9 (C), -4.5 (CH₃), -4.9 (CH₃);

HRMS (ESI+) 838.3752 (calcd for C₄₁H₆₁N₃NaO₁₀SSi 838.3745).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-*tert*-Butyl 3-((*tert*-butyldimethylsilyl)oxy)-6-(hydroxymethyl)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (**111**)



To a solution of **110** (1.41 g, 1.73 mmol) in THF (10.0 mL) and MeOH (10.0 mL) was added NaBH₄ (130 mg, 3.46 mmol) at 0 °C. The solution was stirred for 1 h at the same temperature. To this solution were added CH₂Cl₂ and aqueous NH₄Cl. The resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1) to give **111** (1.37 g, 97%) as a pale yellow amorphous solid.

$[\alpha]_{\text{D}}^{27}$ 20.9° (*c* = 1.70, CHCl₃);

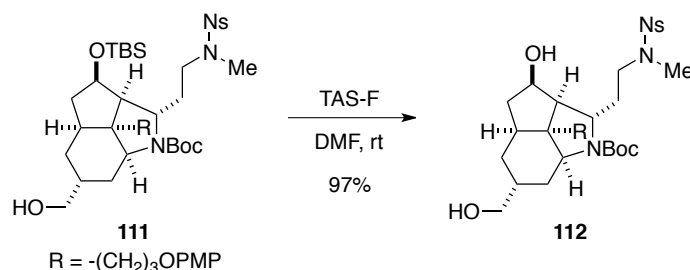
IR (film) 3464, 2930, 2857, 1681, 1545, 1508, 1471, 1366, 1231, 1169, 1125, 1042, 971, 898, 835, 776 cm⁻¹;

¹H NMR (400 MHz, CDCl₃) δ 7.97 (m, 1H), 7.70-7.60 (m, 2H), 7.58 (m, 1H), 6.84 (s, 4H), 4.32 (m, 1H), 4.07 (ddd, *J*=9.6, 7.3, 7.3 Hz, 1H), 3.93 (t, *J*=6.2 Hz, 2H), 3.76 (s, 3H), 3.57 (m, 1H), 3.53-3.40 (m, 2H), 3.22 (ddd, *J*=12.8, 12.8, 4.3 Hz, 1H), 3.18-3.00 (m, 2H), 2.90 (s, 3H), 2.00-1.84 (m, 3H), 1.84-1.51 (m, 10H), 1.44 (s, 9H), 1.27 (ddd, *J*=13.3, 13.3, 6.4 Hz, 1H), 1.08 (ddd, *J*=14.2, 11.9, 2.7 Hz, 1H), 0.86 (s, 9H), 0.04 (s, 3H), 0.01 (s, 3H);

¹³C NMR (100 MHz, CDCl₃) δ 153.9 (C), 153.3 (C), 153.1 (C), 148.1 (C), 133.4 (CH), 132.8 (C), 131.5 (CH), 130.7 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 79.3 (C), 73.0 (CH), 68.9 (CH₂), 68.1 (CH₂), 61.8 (CH), 55.7 (CH₃), 55.4 (CH), 55.4 (CH), 51.2 (C), 47.5 (CH₂), 39.7 (CH₂), 37.9 (CH), 35.1 (CH₂), 34.6 (CH₃), 33.5 (CH₂), 29.4 (CH), 28.8 (2CH₂), 28.5 (CH₃), 26.0 (CH₂), 25.8 (CH₃), 18.0 (C), -4.4 (CH₃), -4.8 (CH₃);

HRMS (ESI+) 840.3923 (calcd for C₄₁H₆₃N₃NaO₁₀SSi 840.3901).

(2*S*,2*aR*,2*a*¹*S*,3*R*,4*aS*,6*R*,7*aS*)-tert-Butyl 3-hydroxy-6-(hydroxymethyl)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)decahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (112**)**



To a solution of **111** (650 mg, 0.795 mmol) in *N,N*-dimethylformamide (4.50 mL) was added tris(dimethylamino)sulfonium difluorotrimethylsilicate (1.20 g, 4.36 mmol) in *N,N*-dimethylformamide (3.00 mL) at room temperature. The solution was stirred for 3 h at the same temperature. To this solution was added CH_2Cl_2 and H_2O . The resulting solution was extracted with CH_2Cl_2 . The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 0:1) to afford **112** (540 mg, 97%) as a pale yellow amorphous solid.

$[\alpha]_{\text{D}}^{27}$ 13.6° ($c = 1.00$, CHCl_3);

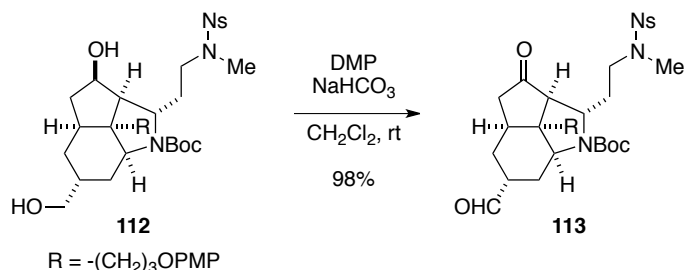
IR (film) 3444, 2932, 1671, 1543, 1508, 1456, 1405, 1367, 1347, 1231, 1165, 1137, 1041, 826, 758 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 7.96 (m, 1H), 7.70-7.65 (m, 2H), 7.59 (m, 1H), 6.83 (s, 4H), 4.38 (m, 1H), 4.21 (ddd, $J=8.0, 8.0, 8.0$ Hz, 1H), 3.92 (t, $J=6.2$ Hz, 2H), 3.77 (s, 3H), 3.60 (m, 1H), 3.52-3.42 (m, 2H), 3.36 (ddd, $J=13.3, 8.2, 8.2$ Hz, 1H), 3.19 (ddd, $J=13.3, 8.2, 4.1$ Hz, 1H), 2.92 (s, 3H), 2.49 (br s, 1H), 2.10 (dd, $J=7.3, 1.8$ Hz, 1H), 2.05-1.93 (m, 2H), 1.85-1.51 (m, 11H), 1.46 (s, 9H), 1.28 (m, 1H), 1.10 (ddd, $J=14.2, 11.9, 2.8$ Hz, 1H);

^{13}C NMR (100 MHz, CDCl_3) δ 153.8 (C), 153.5 (C), 153.0 (C), 148.2 (C), 133.6 (CH), 131.8 (C), 131.6 (CH), 130.8 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 79.6 (C), 72.3 (CH), 68.9 (CH_2), 68.1 (CH_2), 61.7 (CH), 55.7 (CH_3), 54.9 (CH), 54.1 (CH), 52.4 (C), 47.1 (CH_2), 38.8 (CH_2), 37.9 (CH), 35.3 (CH_2), 34.4 (CH_3), 31.8 (CH_2), 29.2 (CH), 28.9 (2CH_2), 28.6 (CH_3), 26.0 (CH_2);

HRMS (ESI+) 726.3032 (calcd for $\text{C}_{35}\text{H}_{49}\text{N}_3\text{NaO}_{10}\text{S}$ 726.3036).

(2*S*,2*aR*,2*a*¹*S*,4*aS*,6*R*,7*aS*)-*tert*-Butyl 6-formyl-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxodecahydro-1*H*-cyclopenta[*cd*]indole-1-carboxylate (113**)**



To a solution of **112** (510 mg, 0.725 mmol) in CH_2Cl_2 (25.0 mL) was added sodium hydrogen carbonate (1.90 g, 22.6 mmol), Dess-Martine periodinane (677 mg, 1.56 mmol) at 0 °C and the solution was stirred for 3 h at the same temperature. To this solution was added CH_2Cl_2 and H_2O and then the resulting solution was extracted with CH_2Cl_2 . The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:2) to afford **113** (497 mg, 98%) as a white amorphous solid.

$[\alpha]_{\text{D}}^{27}$ 16.3° (c = 1.00, CHCl_3);

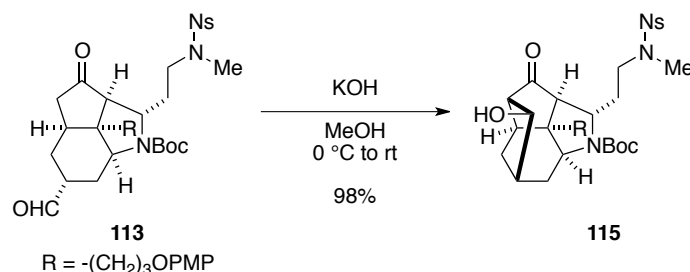
IR (film) 2933, 2360, 1737, 1687, 1545, 1508, 1468, 1368, 1232, 1166, 1125, 1038, 982, 826, 760 cm^{-1} ;

^1H NMR (400 MHz, CDCl_3) δ 9.70 (s, 1H), 7.96 (m, 1H), 7.70-7.64 (m, 2H), 7.58 (m, 1H), 6.82 (s, 4H), 4.00-3.91 (m, 2H), 3.86 (m, 1H), 3.76 (s, 3H), 3.60 (br s, 1H), 3.38 (m, 1H), 3.14 (ddd, J =15.6, 10.1, 5.5 Hz, 1H), 2.94 (s, 3H), 2.77-2.61 (m, 2H), 2.60-2.20 (m, 3H), 2.13 (dd, J =18.5, 6.0 Hz, 1H), 2.18-1.53 (m, 9H), 1.46 (s, 9H);

^{13}C NMR (100 MHz, CDCl_3 ; one sp^3 carbon signal missing, possibly due to broadening) δ 217.1 (C), 202.3 (CH), 153.9 (C), 153.5 (C), 152.9 (C), 148.2 (C), 133.5 (CH), 132.1 (C), 131.6 (CH), 130.7 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 80.4 (C), 68.3 (CH_2), 60.2 (CH), 58.3 (CH), 58.2 (CH), 55.7 (CH_3), 52.1 (C), 47.1 (CH_2), 44.0 (CH_2), 41.1 (CH), 35.1 (CH_3), 34.6 (CH_2), 33.6 (CH_2), 32.3 (CH_2), 28.4 (CH_3), 24.8 (CH_2), 22.6 (CH);

HRMS (ESI+) 722.2705 (calcd for $\text{C}_{35}\text{H}_{45}\text{N}_3\text{NaO}_{10}\text{S}$ 722.2723).

(2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*S*)-*tert*-Butyl 8-hydroxy-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (**115**)



To a solution of **113** (497 mg, 0.710 mmol) in MeOH (27.0 mL) was added KOH (8.70 mL, 15.5 mmol, 10% w/w in MeOH) at 0 °C and the solution was stirred for 1.5 h at room temperature. To this solution was added CH₂Cl₂ and aqueous NH₄Cl at 0 °C and then the resulting solution was extracted with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:3) to afford **115** (490 mg, 98%) as a white amorphous solid.

$[\alpha]_{\text{D}}^{27}$ 40.1° (*c* = 1.00, CHCl₃);

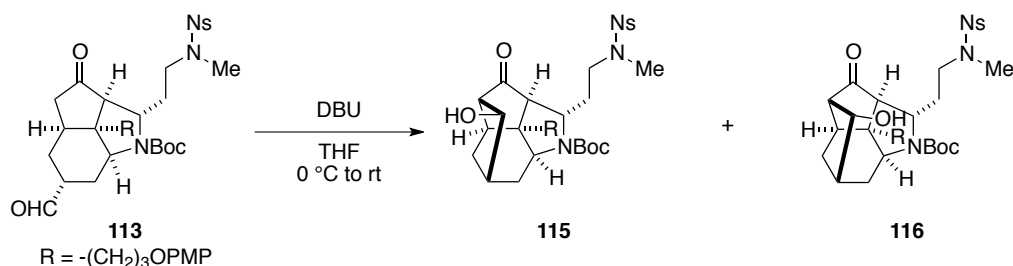
IR (film) 3466, 2946, 2391, 1731, 1683, 1544, 1508, 1455, 1370, 1348, 1231, 1164, 1132, 1033, 826, 760 cm⁻¹;

¹H NMR (400 MHz, CDCl₃; this material was observed as a 3:2 mixture of rotamers) δ 8.00-7.91 (m, 1H), 7.68-7.60 (m, 2H), 7.58-7.52 (m, 1H), 6.84 (s, 4H), 4.05-3.94 (m, 3H), 3.85 (m, (3/5)1H), 3.80-3.73 (m, 3H+(2/5)1H), 3.63 (t, *J*=9.1 Hz, (2/5)1H), 3.47 (t, *J*=9.1 Hz, (3/5)1H), 3.41-3.25 (m, 1H), 3.22-3.08 (m, 1H), 2.94 (s, (3/5)3H), 2.92 (s, (2/5)3H), 2.84-2.72 (m, 3H), 2.69-2.36 (m, 3H), 2.17-2.10 (m, 1H+(3/5)1H), 2.6-1.84 (m, 4H+(3/5)1H), 1.78-1.43 (m, 1H), 1.70 (br s, (3/5)1H), 1.67 (br s, (2/5)1H), 1.44 (s, (2/5)9H), 1.42 (s, (3/5)9H), 0.38 (m, 1H);

¹³C NMR (100 MHz, CDCl₃; this material was observed as a mixture of rotamers) δ 218.0 (C), 217.6 (C), 154.5 (C), 154.1 (C), 153.9 (2C), 153.0 (2C), 148.3 (C), 148.1 (C), 133.6 (CH), 133.4 (CH), 132.2 (C), 131.6 (CH), 130.7 (CH), 130.6 (CH), 124.2 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 84.5 (CH), 84.4 (CH), 80.3 (C), 79.9 (C), 68.5 (2CH₂), 60.9 (CH), 60.8 (CH), 60.5 (CH), 59.2 (CH), 58.2 (CH), 58.1 (CH), 57.4 (CH), 57.0 (CH), 55.8 (CH₃), 54.0 (C), 53.0 (C), 47.8 (2CH₂), 39.3 (CH), 39.2 (CH), 38.9

(CH), 38.7 (CH), 35.0 (2CH₃), 34.0 (2CH₂), 32.9 (CH₂), 31.8 (CH₂), 30.4 (CH₂), 29.6 (CH₂), 28.5 (2CH₃), 27.8 (CH₂), 27.7 (CH₂), 24.6 (CH₂), 24.4 (CH₂);
HRMS (ESI+) 722.2701 (calcd for C₃₅H₄₅N₃NaO₁₀S 722.2723).

(2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*R*)-*tert*-Butyl 8-hydroxy-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (116**)**



To a solution of **113** (30.0 mg, 0.0429 mmol) in THF (3.0 mL) was added DBU (30.0 μL , 0.201 mmol) at 0 °C and the solution was stirred for 15 min at room temperature. To this solution was added CH_2Cl_2 and aqueous NH_4Cl at 0 °C and then the resulting solution was extracted three times with CH_2Cl_2 . The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by PTLC (SiO_2 ; *n*-hexane:EtOAc = 1:3) to afford **115** (20.2 mg, 67 %) as white amorphous and **116** (8.1 mg 27%) as a pale yellow gum.

$[\alpha]_{\text{D}}^{27} 27.6^\circ$ ($c = 1.25$, CHCl_3);

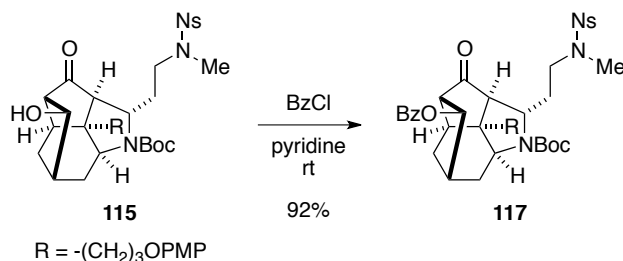
IR (film) 3479, 2938, 1730, 1682, 1544, 1508, 1456, 1369, 1231, 1167, 1127, 1102, 1036, 826, 760 cm^{-1}

^1H NMR (400 MHz, CDCl_3 ; this material was observed as a mixture of rotamers) δ 8.00-7.92 (m, 1H), 7.71-7.62 (m, 2H), 7.60-7.52 (m, 1H), 6.83 (s, 4H), 4.18 (d, $J=10.5$ Hz, 1H), 4.10-3.92 (m, 2H), 3.90-3.60 (m, 4.6H), 3.51 (t, $J=8.7$ Hz, 0.7H), 3.45-3.25 (m, 1.7H), 3.25-3.10 (m, 1.4H), 3.00-2.85 (m, 3H), 2.80 (dd, $J=10.5$, 8.3 Hz, 1H), 2.70 (dd, $J=8.2$, 5.5, 1.6 Hz, 1.6H), 2.60-2.50 (m, 1.7H), 2.44-2.30 (m, 0.7H), 2.25-2.15 (m, 1H), 2.00-1.70 (m, 4.5H), 1.55-1.50 (m, 3H), 1.50-1.35 (m, 10H), 1.15-1.10 (m, 1H);

^{13}C NMR (100 MHz, CDCl_3 ; this material was observed as a mixture of rotamers) δ 220.4 (C), 154.7 (C), 153.9 (C), 153.0 (C), 148.2 (C), 133.5 (CH), 133.4 (CH), 132.1 (C), 131.6 (CH), 130.7 (CH), 130.6 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 80.3 (C), 79.9 (C), 77.3 (CH), 77.2 (CH), 68.4 (CH_2), 59.0 (CH), 57.8 (CH), 56.3 (CH), 55.7 (CH_3), 55.0 (C), 50.3 (CH), 50.2 (CH), 47.8 (CH_2), 40.7 (CH), 40.6 (CH), 35.2 (CH), 35.1 (CH), 33.8 (CH_2), 32.9 (CH_2), 31.8 (CH_2), 29.7 (CH_2), 28.5 (CH_3), 25.9 (CH_2), 25.8 (CH_2), 25.4 (CH_2), 24.5 (CH_2), 24.4 (CH_2), 24.3 (CH_2);

HRMS (ESI+) 722.2742 (calcd for $\text{C}_{35}\text{H}_{45}\text{N}_3\text{NaO}_{10}\text{S}$ 722.2723)

(2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*S*)-tert-Butyl 8-(benzoyloxy)-2*a*¹-(3-(4-methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (117**)**



To a solution of **115** (460 mg, 0.657 mmol) in pyridine (8.0 mL) was added benzoyl chloride (152 μ L, 1.31 mmol) at 0 °C and the solution was stirred for 1 h at room temperature. To this solution was added CH₂Cl₂ and aqueous NaHCO₃ at 0 °C and then the resulting solution was extracted three times with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 4:1~1:2) to afford **117** (486 mg, 92%) as a white amorphous solid.

$[\alpha]_D^{26}$ 88.1° (*c* = 1.50, CHCl₃);

IR (film) 3471, 2952, 1736, 1716, 1687, 1545, 1508, 1453, 1369, 1273, 1231, 1168, 1110, 1069, 1026, 953, 826, 760 cm⁻¹;

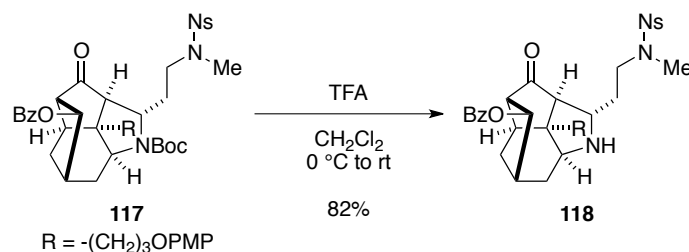
¹H NMR (400 MHz, CDCl₃; this material was observed as a 3:2 mixture of rotamers) δ 8.10-7.92 (m, 3H), 7.70-7.52 (m, 4H), 7.50-7.27 (m, 2H), 6.92-6.80 (m, 4H), 5.10-5.00 (m, 1H), 4.20-3.70 (m, 3H), 3.75 (s, 3H), 3.67 (t, *J*=9.2 Hz, (2/5)1H), 3.50 (t, *J*=9.2 Hz, (3/5)1H), 3.45-3.25 (m, 1H), 3.22-2.84 (m, 3H), 2.94 (s, (3/5)3H), 2.92 (s, (2/5)3H), 2.78-2.55 (m, 1+(3/5)2H), 2.55-2.40 (m, 1+(2/5)1H), 2.15-1.35 (m, 7+(2/5)1H), 1.45 (s, 3.8H), 1.43 (s, 5.2H), 0.60 (m, 1H);

¹³C NMR (100 MHz, CDCl₃; this material was observed as a mixture of rotamers) δ 216.5 (C), 216.2 (C), 165.5 (2C), 154.3 (C), 154.0 (C), 153.8 (2C), 153.0 (2C), 148.3 (2C), 133.5 (CH), 133.4 (CH), 133.1 (2CH), 132.1 (2C), 131.6 (2CH), 130.6 (CH), 130.5 (CH), 130.1 (2C), 130.0 (2CH), 128.4 (2CH), 124.1 (CH), 124.0 (CH), 115.5 (2CH), 114.7 (2CH), 85.8 (2CH), 80.3 (C), 80.0 (C), 68.4 (2CH₂), 60.4 (CH), 59.2 (CH), 57.9 (CH), 57.8 (CH), 57.6 (2CH), 57.3 (CH), 57.1 (CH), 55.7 (2CH₃), 54.2 (C), 53.1 (C), 47.9 (2CH₂), 39.4 (CH), 39.3 (CH), 36.7 (CH), 36.5 (CH), 35.2 (CH₃), 35.1 (CH₃),

33.9 (2CH₂), 33.1 (CH₂), 32.1 (CH₂), 30.3 (CH₂), 29.4 (CH₂), 28.4 (2CH₃), 28.3 (CH₂),
28.0 (CH₂), 24.5 (CH₂), 24.3 (CH₂);

HRMS (ESI+) 826.2996 (calcd for C₄₂H₄₉N₃NaO₁₁S 826.2986).

(2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*S*)-2*a*¹-(3-(4-Methoxyphenoxy)propyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indol-8-yl benzoate (118**)**



To a solution of **117** (70.0 mg, 0.0871 mmol) in CH_2Cl_2 (2.0 mL) was added TFA (2.0 mL) at 0 °C and the solution was stirred for 30 min at room temperature. The solution was evaporated and the residue partitioned between CH_2Cl_2 and aqueous NaHCO_3 . The resulting solution was extracted three times with CH_2Cl_2 . The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO_2 ; *n*-hexane:EtOAc = 1:4~0:1) to afford **118** (50.3 mg, 82%) as a white amorphous.

$[\alpha]_{\text{D}}^{26}$ 38.3° ($c = 1.00$, CHCl_3);

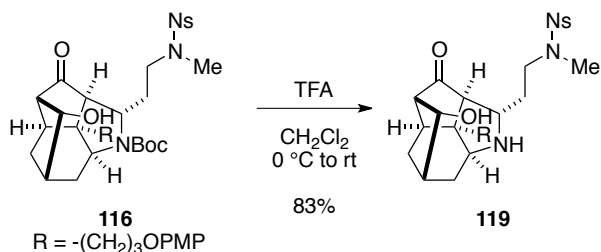
IR (film) 3448, 3019, 2947, 1727, 1601, 1544, 1508, 1452, 1373, 1349, 1273, 1231, 1164, 1111, 1026, 958, 826, 761 cm^{-1}

^1H NMR (400 MHz, CDCl_3) δ 8.05-7.95 (m, 3H), 7.70-7.64 (m, 2H), 7.64-7.50 (m, 2H), 7.50-7.41 (m, 2H), 6.84 (s, 4H), 5.08 (s, 1H), 4.01-3.90 (m, 2H), 3.77 (s, 3H), 3.48-3.31 (m, 2H), 3.20 (ddd, $J=14.2, 9.6, 4.6$ Hz, 1H), 3.11 (dd, $J=9.2, 9.2$ Hz, 1H), 2.97 (d, $J=7.8$ Hz, 1H), 2.93 (s, 3H), 2.82 (ddd, $J=7.8, 2.5, 2.5$ Hz, 1H), 2.46 (dd, $J=9.2, 3.7$ Hz, 1H), 2.30 (s, 1H), 2.23, (ddd, $J=15.6, 9.2, 9.2$ Hz, 1H), 2.00-1.60 (m, 9H), 0.89 (dd, $J=16.0, 8.7$ Hz, 1H);

^{13}C NMR (100 MHz, CDCl_3) δ 219.5 (C), 165.4 (C), 153.8 (C), 152.9 (C), 148.1 (C), 133.5 (CH), 133.0 (CH), 132.1 (C), 131.5 (CH), 130.7 (CH), 130.1 (C), 129.5 (CH), 128.3 (CH), 124.0 (CH), 115.4 (C), 114.6 (C), 85.9 (CH), 68.6 (CH_2), 63.9 (CH), 59.7 (CH), 59.3 (CH), 57.3 (CH), 55.7 (CH_3), 55.5 (C), 47.9 (CH_2), 41.1 (CH), 38.0 (CH), 35.4 (CH_2), 34.8 (CH_3), 30.4 (CH_2), 29.2 (CH_2), 25.1 (CH_2);

HRMS (ESI+) 726.2460 (calcd for $\text{C}_{37}\text{H}_{41}\text{N}_3\text{NaO}_9\text{S}$ 726.2461).

***N*-(2-((2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*R*)-8-Hydroxy-2*a*¹-(3-(4-methoxyphenoxy)propyl)-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indol-2-yl)ethyl)-*N*-methyl-2-nitrobenzenesulfonamide (**119**)**



To a solution of **116** (20.0 mg, 0.0286 mmol) in CH₂Cl₂ (700 μL) was added TFA (700 μL) at 0 °C and the solution was stirred for 20 min at room temperature. To this solution was added CH₂Cl₂ and aqueous NH₄Cl at 0 °C and then the resulting solution was extracted three times with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:0~7:1) to afford **119** (16.3 mg, 95%) as a white amorphous.

$[\alpha]_D^{27} -19.5^\circ$ ($c = 0.75$, CHCl₃);

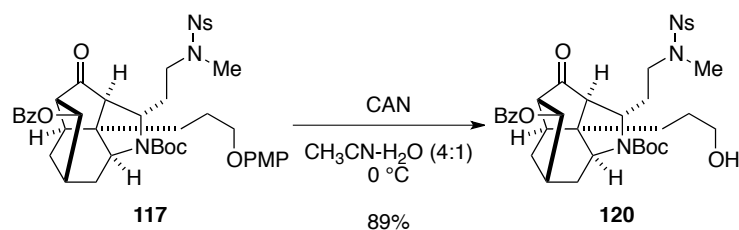
IR (film) 3437, 2951, 1729, 1674, 1545, 1508, 1467, 1372, 1348, 1230, 1203, 1164, 1140, 1036, 829, 760 cm⁻¹

¹H NMR (400 MHz, CDCl₃) δ 8.02-7.95 (m, 1H), 7.70-7.64 (m, 2H), 7.60-7.55 (m, 1H), 6.82 (s, 4H), 4.54 (dd, $J=11.0, 5.5$ Hz, 1H), 4.00-3.85 (m, 3H), 3.83-3.77 (m, 1H), 3.76 (s, 3H), 3.55 (ddd, $J=14.2, 6.9, 6.8$ Hz, 1H), 3.30 (ddd, $J=14.2, 7.8, 6.0$ Hz, 1H), 3.00-2.87 (m, 4H), 2.71-2.65 (m, 1H), 2.61 (s, 1H), 2.50-2.38 (m, 1H), 2.33-2.21 (m, 1H), 2.20-1.74 (m, 8H), 1.71-1.64 (m, 2H);

¹³C NMR (100 MHz, CDCl₃) δ 216.8 (C), 154.0 (C), 152.8 (C), 148.2 (C), 133.8 (CH), 132.0 (CH), 131.5 (C), 130.9 (CH), 124.1 (CH), 115.5 (CH), 114.7 (CH), 74.3 (CH), 68.1 (CH₂), 63.5 (CH), 58.2 (CH), 57.6 (CH), 56.4 (CH), 55.7 (CH₃), 53.1 (C), 47.1 (CH₂), 44.0 (CH), 36.3 (CH₂), 35.8 (CH), 34.8 (CH₃), 30.2 (CH₂), 30.0 (CH₂), 27.0 (CH₂), 25.5 (CH₂);

HRMS (ESI+) 600.2386 (calcd for C₃₀H₃₈N₃O₈S 600.2380).

(2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*S*)-tert-Butyl 8-(benzoyloxy)-2*a*¹-(3-hydroxypropyl)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxodecahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (120**)**



To a solution of **117** (760 mg, 0.946 mmol) in CH₃CN (20.0 mL) and H₂O (5.0 mL) was added cerium(IV) ammonium nitrate (570 mg, 1.04 mmol) at 0 °C and the solution was stirred for 2.5 h at the same temperature. To this solution was added CH₂Cl₂ and aqueous NaHCO₃ at 0 °C and then the resulting solution was extracted three times with CH₂Cl₂. The organic phase was washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:1~1:3) to afford **120** (590 mg, 89%) as a white amorphous solid.

[α]_D²⁷ 67.7° (*c* = 1.00, CHCl₃);

IR (film) 3503, 2944, 1735, 1716, 1683, 1543, 1454, 1369, 1274, 1166, 1112, 1068, 985, 852, 760 cm⁻¹;

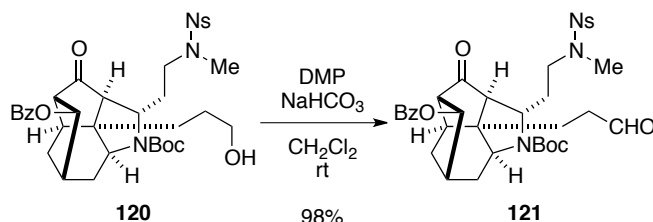
¹H NMR (400 MHz, CDCl₃; this material was observed as a 2:1 mixture of rotamers) δ 8.00-7.91 (m, 3H), 7.74-7.52 (m, 4H), 7.47-7.40 (m, 2H), 5.08-5.02 (m, 1H), 3.92 (d, *J*=9.2 Hz, (2/3)1H), 3.84-3.75 (m, 1H+(1/3)1H), 3.73-3.60 (m, 1H+(1/3)1H), 3.50-3.30 (m, 1H+(2/3)1H), 3.15-2.84 (m, 3H), 2.95 (s, (2/3)3H), 2.94 (s, (1/3)3H), 2.75-2.62 (m, 2H+(2/3)1H), 2.55-2.38 (m, 1H+(1/3)1H), 1.98-1.55 (m, 7H), 1.46 (s, (1/3)9H), 1.43 (s, (2/3)9H), 0.66-0.53 (m, 1H);

¹³C NMR (100 MHz, CDCl₃; this material was observed as a mixture of rotamers) δ 216.7 (C), 216.4 (C), 165.5 (2C), 154.2 (C), 153.9 (C), 148.2 (2C), 133.7 (CH), 133.6 (CH), 133.1 (2CH), 131.9 (C), 131.8 (C), 131.7 (2CH), 130.6 (CH), 130.4 (CH), 130.1 (C), 129.5 (2CH), 128.4 (2CH), 124.1 (CH), 124.1 (CH), 85.8 (CH), 85.7 (CH), 80.2 (C), 80.0 (C), 62.6 (2CH₂), 59.4 (CH), 58.4 (CH), 58.2 (CH), 58.0 (CH), 57.5 (CH), 57.5 (CH), 57.3 (CH), 57.0 (CH), 54.4 (C), 53.3 (C), 48.0 (2CH₂), 39.2 (CH), 39.0 (CH), 36.7 (CH), 36.5 (CH), 35.5 (CH₃), 35.3 (CH₃), 33.1 (CH₂), 33.0 (CH₂), 32.9 (CH₂), 31.9

(CH₂), 30.5 (CH₂), 29.6 (CH₂), 28.4 (2CH₃), 28.1 (CH₂), 27.8 (CH₂), 27.5 (CH₂), 27.3 (CH₂);

HRMS (ESI+) 720.2587 (calcd for C₃₅H₄₃N₃NaO₁₀S 720.2567).

(2*S*,2*aR*,2*a*¹*S*,4*S*,4*aS*,6*S*,7*aS*,8*S*)-*tert*-Butyl 8-(benzoyloxy)-2-(2-(*N*-methyl-2-nitrophenylsulfonamido)ethyl)-3-oxo-2*a*¹-(3-oxopropyl)decahydro-1*H*-4,6-methanocyclopenta[*cd*]indole-1-carboxylate (**121**)



To a solution of **120** (550 mg, 0.788 mmol) in CH₂Cl₂ (600 mL) was added sodium hydrogen carbonate (1.10 g, 13.1 mmol), Dess-Martine periodinane (401 mg, 0.946 mmol) at 0 °C. After stirring for 1 h at room temperature, water was added at the same temperature. The resulting solution was extracted three times with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; *n*-hexane:EtOAc = 1:2) to give **121** (540 mg, 98%) as a colorless oil.

[α]_D²⁷ 76.7° (*c* = 1.75, CHCl₃);

IR (film) 3854, 2968, 1718, 1685, 1544, 1453, 1369, 1273, 1167, 1111, 1069, 985, 852, 759 cm⁻¹;

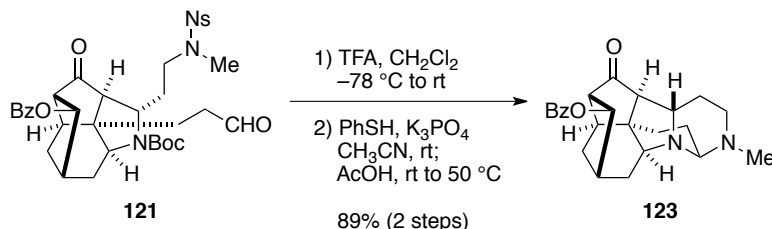
¹H NMR (400 MHz, CDCl₃; this material was observed as a 2:1 mixture of rotamers) δ 9.90 (s, (2/3)1H), 9.88 (s, (1/3)1H), 8.00-7.88 (m, 3H), 7.75-7.65 (m, 2H), 7.65-7.52 (m, 2H), 7.47-7.40 (m, 2H), 5.04 (s, 1H), 3.91 (d, *J*=10.0 Hz, (2/3)1H), 3.81 (d, *J*=10.0 Hz, (1/3)1H), 3.67 (dd, *J*=8.6, 8.6 Hz, (1/3)1H), 3.50 (dd, *J*=9.2, 9.2 Hz, (2/3)1H), 3.46-3.30 (m, 1H), 3.15-3.00 (m, 2H), 2.95 (s, (2/3)3H), 2.94 (s, (1/3)3H), 2.90-2.58 (m, 5H+(2/3)1H), 2.55-2.41 (m, 1H+(1/3)1H), 2.22-2.17 (m, 1H), 2.02-1.92 (m, 2H), 1.75-1.49 (m, 3H), 1.45 (s, (1/3)9H), 1.43 (s, (2/3)9H), 0.65-0.50 (m, 1H);

¹³C NMR (100 MHz, CDCl₃; this material was observed as a mixture of rotamers) δ 216.1 (C), 215.7 (C), 201.2 (CH), 200.9 (CH), 165.5 (2C), 154.2 (C), 153.9 (C), 148.3 (C), 148.2 (C), 133.7 (CH), 133.6 (CH), 133.2 (2CH), 132.0 (2C), 131.7 (2CH), 130.6 (CH), 130.4 (CH), 130.0 (2C), 129.6 (2CH), 128.4 (2CH), 124.2 (CH), 124.1 (CH), 85.7 (CH), 85.6 (CH), 80.5 (C), 80.2 (C), 60.3 (CH), 58.6 (CH), 58.3 (CH), 57.9 (CH), 57.7 (CH), 57.5 (CH), 57.3 (CH), 57.1 (CH), 53.7 (C), 52.7 (C), 47.9 (2CH₂), 39.4 (CH),

39.2 (CH), 39.0 (CH₂), 38.8 (CH₂), 36.7 (CH), 36.5 (CH), 35.6 (CH₃), 35.4 (CH₃), 33.3 (CH₂), 32.3 (CH₂), 30.1 (CH₂), 29.3 (CH₂), 28.7 (CH₂), 28.5 (2CH₃), 28.3 (CH₂), 28.2 (CH₂), 27.8 (CH₂);

HRMS (ESI+) 718.2388 (calcd for C₃₅H₄₁N₃NaO₁₀S 718.2410).

(2*S*,2*aS*,2*a*¹*S*,4*S*,5*aS*,6*S*,7*S*,10*aS*,10*bR*,13*S*)-8-Methyl-1-oxododecahydro-1*H*-2*a*¹,7-ethano-2,4-methanocyclopenta[*cd*]pyrimido[1,6-*a*]indol-13-yl benzoate (**123**)



To a solution of **121** (67.0 mg, 0.144 mmol) in CH₂Cl₂ (3.0 mL) was added TFA (2.0 mL) at -78°C . After stirring for 15 min at room temperature, CH₂Cl₂ and aqueous NaHCO₃ were added at the 0°C . The resulting solution was extracted twice with CH₂Cl₂. The combined organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo*. The residual oil was dissolved in CH₃CN (40.0 mL) and potassium phosphate (200 mg, 0.941 mmol), thiophenol (230 μL , 2.26 mmol) was added at room temperature. After stirring for 2 h at room temperature, acetic acid (320 μL) was added and then the reaction mixture was heated at 50°C for 18 h. After cooling to room temperature, the solution was concentrated *in vacuo* and the residue was purified by flash column chromatography (SiO₂; CHCl₃:MeOH = 5:1) to give **123** (49.0 mg, 89% for 2 steps) as a white solid.

m.p. 212.2-213.0 $^\circ\text{C}$;

$[\alpha]_{\text{D}}^{27} 156^\circ$ ($c = 1.75$, CHCl₃);

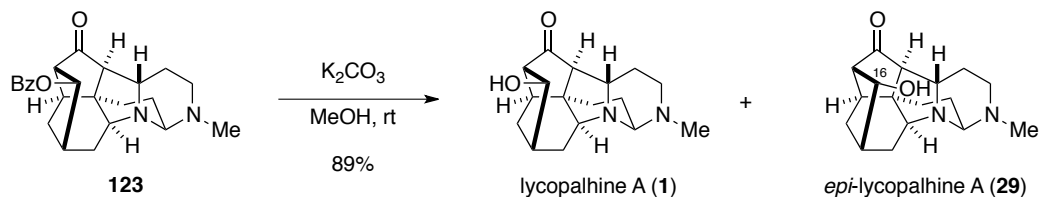
IR (film) 3421, 2943, 1722, 1451, 1274, 1177, 1110, 1068, 984, 855 cm^{-1} ;

¹H NMR (400 MHz, CDCl₃) δ 7.98 (dd, $J=7.6, 1.4$ Hz, 2H), 7.55 (dd, $J=7.6, 7.6$ Hz, 1H), 7.42 (dd, $J=7.6, 7.6$ Hz, 2H), 5.02 (s, 1H), 3.70 (t, $J=8.2$ Hz, 1H), 3.51-3.43 (m, 1H), 3.00-2.90 (m, 2H), 2.71-2.57 (m, 2H), 2.56-2.46 (m, 2H), 2.45 (s, 3H), 2.41 (d, $J=6.4$ Hz, 1H), 2.38-2.30 (m, 1H), 2.22 (ddd, $J=15.6, 9.9, 9.9$ Hz, 1H), 2.10-1.93 (m, 2H), 1.80-1.70 (m, 3H), 0.99 (dd, $J=15.6, 10.1$ Hz, 1H);

¹³C NMR (100 MHz, CDCl₃) δ 219.9 (C), 165.5 (C), 133.0 (CH), 130.2 (C), 129.6 (CH), 128.4 (CH), 86.4 (CH), 76.5 (CH), 65.1 (CH), 63.2 (CH), 61.2 (CH), 60.8 (CH), 54.4 (C), 42.7 (CH₃), 42.6 (CH₂), 42.0 (CH), 38.5 (CH), 35.8 (CH₂), 28.1 (CH₂), 26.6 (CH₂), 24.5 (CH₂), 23.4 (CH₂);

HRMS (ESI+) 393.2180 (calcd for C₂₄H₂₉N₂O₃ 393.2178).

(+)-Lycopalhine A (1)



To a solution of **123** (20.0 mg, 0.0509 mmol) in MeOH (1.0 mL) was added potassium carbonate (20 mg 0.145 mmol) at 0 °C. After stirring for 3 h at room temperature, the solution was concentrated *in vacuo* and the residue was purified by PTLC (NH₂ silica gel; CHCl₃:MeOH = 10:1) to give (+)-lycopalhine A (**1**) and *epi*-lycopalhine A (**29**) (13.0 mg, 89%) as a colorless gum.

$[\alpha]_{\text{D}}^{25}$ 105° (c = 0.200, MeOH); lit.¹ $[\alpha]_{\text{D}}^{15}$ 89.1° (c = 0.17, MeOH);

IR (film) 3411, 2940, 1714, 1659, 1454, 1367, 1300, 1177, 1048, 1026, 854 cm⁻¹;

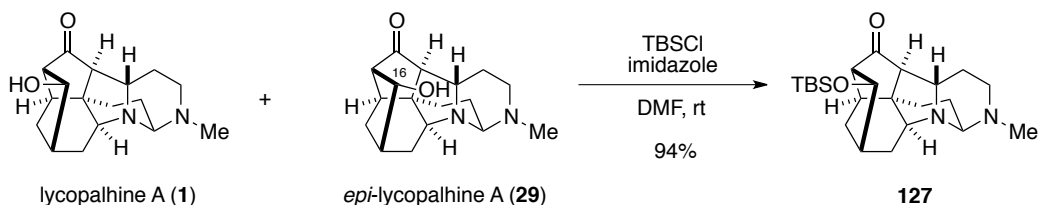
¹H NMR (400 MHz, pyridine-*d*₅) δ 4.46 (dd, J =11.0, 5.5 Hz, 0.2H, minor isomer), 4.29 (s, 1H), 3.95-3.89 (m, 0.2H, minor isomer), 3.81 (dd, J =10.1, 7.4 Hz, 0.2H, minor isomer), 3.65 (dd, J =10.1, 6.4 Hz, 1H), 3.59-3.54 (m, 1H), 3.05 (d, J =8.2 Hz, 1H), 2.98 (ddd, J =12.8, 9.2, 3.2 Hz, 1H), 2.84 (ddd, J =10.6, 7.8, 2.5 Hz, 0.2H, minor isomer), 2.63-2.55 (m, 0.2H, minor isomer), 2.57 (dd, J =9.9, 9.9 Hz, 1H), 2.47-2.22 (m, 6H), 2.45 (s, 3H), 2.16 (ddd, J =11.5, 4.6, 4.6 Hz, 1H), 2.07 (ddd, J =15.6, 9.6, 9.6 Hz, 1H), 1.87 (ddd, J =11.9, 11.9, 7.4 Hz, 1H), 1.75-1.60 (m, 4H), 1.55 (dd, J =12.5, 7.8 Hz, 1H), 1.35-1.25 (m, 0.2H, minor isomer), 0.93 (dd, J =15.1, 10.3 Hz, 1H);

¹³C NMR (100 MHz, pyridine-*d*₅) major isomer: δ 221.6 (C), 85.6 (CH), 77.0 (CH), 65.6 (CH), 65.3 (CH), 63.4 (CH), 61.1 (CH), 54.3 (C), 43.0 (CH₂), 42.8 (CH₃), 42.3 (CH), 41.4 (CH), 36.0 (CH₂), 27.9 (CH₂), 27.3 (CH₂), 25.4 (CH₂), 24.2 (CH₂); minor isomer: δ 219.1 (C), 76.3 (CH), 75.5 (CH), 64.3 (CH), 62.1 (CH), 58.7 (CH), 58.2 (CH), 55.6 (C), 43.8 (CH), 42.1 (CH₃), 41.0 (CH₂), 37.6 (CH), 36.7 (CH₂), 27.0 (CH₂), 23.5 (CH₂), 23.0 (CH₂), 22.8 (CH₂);

HRMS (ESI+) 289.1902 (calcd for C₁₇H₂₅N₂O₂ 289.1916).

¹ Dong, L.-B.; Yang, J.; He, J.; Luo, H.-R.; Wu, X.-D.; Deng, X.; Peng, L.-Y.; Cheng, X.; Zhao, Q.-S. *Chem. Commun.* **2012**, 48, 9038.

(2*S*,2*aS*,2*a*¹*S*,4*S*,5*aS*,6*S*,7*S*,10*aS*,10*bR*,13*S*)-13-((*tert*-Butyldimethylsilyl)oxy)-8-methyldodecahydro-1*H*-2*a*¹,7-ethano-2,4-methanocyclopenta[*cd*]pyrimido[1,6-*a*]indol-1-one (127**)**



To a solution of **1** containing **29** (16.6 mg, 0.0574 mmol) in *N,N*-dimethylformamide (250 μ L) was added imidazole (28.0 mg, 0.411 mmol) and *tert*-butyldimethylchlorosilane (38.0 mg, 0.252 mmol) at room temperature. After stirring for 11 h at room temperature, CH_2Cl_2 and aqueous NaHCO_3 was added at the 0 $^\circ\text{C}$. The resulting solution was extracted with CH_2Cl_2 . The organic phases were washed with brine, dried over sodium sulfate and filtered. The filtrate was concentrated *in vacuo* and the residue was purified by PTLC (NH; *n*-hexane:EtOAc = 3:1) to give **127** (19.2 mg, 94%) as a white solid.

m.p. 132.2-132.6 $^\circ\text{C}$;

$[\alpha]_{\text{D}}^{27}$ 99.8 $^\circ$ ($c = 1.10$, CHCl_3);

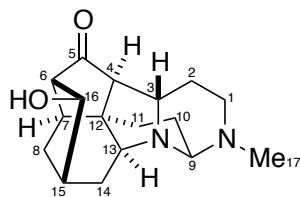
IR (film) 3375, 2930, 2856, 1717, 1470, 1361, 1252, 1176, 1052, 836, 776 cm^{-1}

^1H NMR (400 MHz, CDCl_3) δ 3.82 (s, 1H), 3.66 (t, $J=8.2$ Hz, 1H), 3.43-3.30 (m, 1H), 2.93 (ddd, $J=14.2, 10.1, 4.6$ Hz, 1H), 2.64 (dd, $J=8.2, 1.8$ Hz, 1H), 2.58 (dd, $J=9.6, 9.6$ Hz, 1H), 2.47-2.30 (m, 5H), 2.28-2.25 (m, 2H), 2.15-2.03 (m, 2H), 2.00-1.92 (m, 1H), 1.88 (dd, $J=11.9, 4.6, 4.6$ Hz, 1H), 1.82 (dddd, $J=14.2, 4.6, 4.6, 4.6$ Hz, 1H), 1.73-1.63 (m, 6H), 0.86 (s, 9H), 0.72 (dd, $J=15.1, 10.5$ Hz, 1H), 0.09 (s, 3H), 0.07 (s, 3H)

^{13}C NMR (100 MHz, CDCl_3) δ 221.6 (C), 86.2 (CH), 76.6 (CH), 65.3 (CH), 65.2 (CH), 64.1 (CH), 60.5 (CH), 54.1 (C), 43.2 (CH_2), 42.8 (CH_3), 41.7 (CH), 41.2 (CH), 35.8 (CH_2), 27.5 (CH_2), 26.6 (CH_2), 25.8 (CH_3), 24.7 (CH_2), 23.4 (CH_2), 18.0 (C), -4.8 (CH_3);

HRMS (ESI+) 403.2783 (calcd for $\text{C}_{23}\text{H}_{39}\text{N}_2\text{O}_2\text{Si}$ 403.2781).

Table S1. ^1H and ^{13}C NMR data for (+)-lycopalhine A (1) in pyridine- d_5



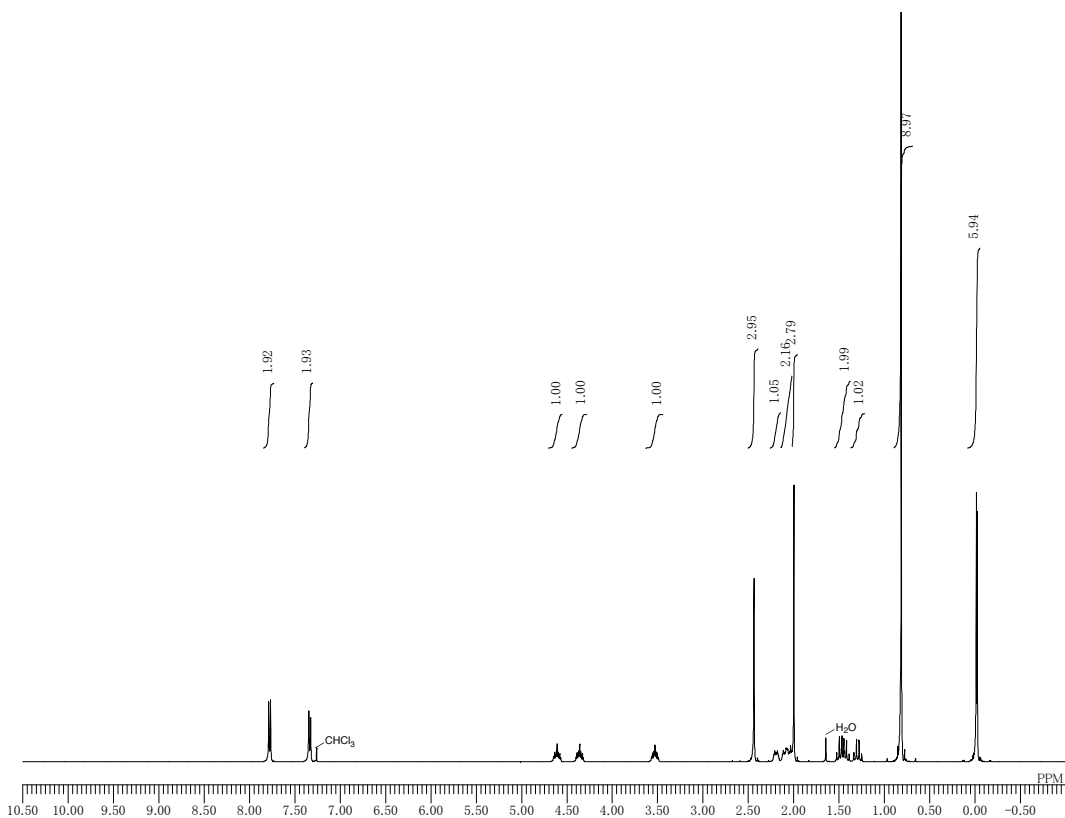
(+)-lycopalhine A (1)

Synthetic			Natural ^a	
no.	δ_{C} (100 MHz)	δ_{H} (400 MHz)	δ_{C} (125 MHz)	δ_{H} (500 MHz)
1a	42.95	2.98 (ddd, 12.8, 9.2, 3.2 Hz, 1H)	43.06	2.98 (ddd, 13.5, 10.5, 4.5 Hz, 1H)
1b		2.34-2.31 (m, 1H)		2.34 (m, 1H)
2a	24.19	2.29-2.21 (m, 1H)	24.32	2.27 (m, 1H)
2b		1.75-1.73 (m, 1H)		1.74 (m, 1H)
3	61.04	3.58-3.54 (m, 1H)	61.17	3.56 (m, 1H)
4	63.39	2.37-2.35 (m, 1H)	63.57	2.36 (m, 1H)
5	221.53		221.56	
6	65.49	3.05 (d, 8.2 Hz, 1H)	65.58	3.05 (d, 7.5 Hz, 1H)
7	42.21	2.43-2.40 (m, 1H)	42.31	2.43 (m, 1H)
8a	27.89	2.16 (ddd, 11.5, 4.6, 4.6 Hz)	27.95	2.16 (dt, 12.0, 4.5 Hz, 1H)
8b		1.72-1.70 (m, 1H)		1.70 (overlap, 1H)
9	76.94	3.65 (dd, 10.1, 6.4 Hz)	77.12	3.64 (dd, 10.5, 7.5 Hz, 1H)
10a	25.37	1.75-1.73 (m, 1H)	25.48	1.70 (overlap, 1H)
10b		1.65-1.60 (m, 1H)		1.63 (m, 1H)
11a	35.94	1.87 (ddd, 11.9, 11.9, 7.4 Hz)	36.07	1.85 (td, 12.0, 7.5 Hz, 1H)
11b		1.55 (dd, 12.5, 7.8 Hz)		1.55 (dd, 12.0, 7.5 Hz, 1H)
12	54.28		54.38	
13	65.21	2.57 (dd, 9.9, 9.9 Hz, 1H)	65.35	2.56 (t, 10.0, 1H)
14a	27.24	2.07 (ddd, 15.6, 9.6, 9.6 Hz, 1H)	27.34	2.07 (dt, 15.5, 10.0, 1H)
14b		0.93 (dd, 15.1, 10.3 Hz, 1H)		0.92 (dd, 15.5, 10.0 Hz, 1H)
15	41.31	2.42-2.40 (m, 1H)	41.41	2.40 (m, 1H)
16	85.56	4.29 (s, 1H)	85.68	4.29 (brs, 1H)
17	42.78	2.45 (s, 3H)	42.86	2.45 (s, 3H)

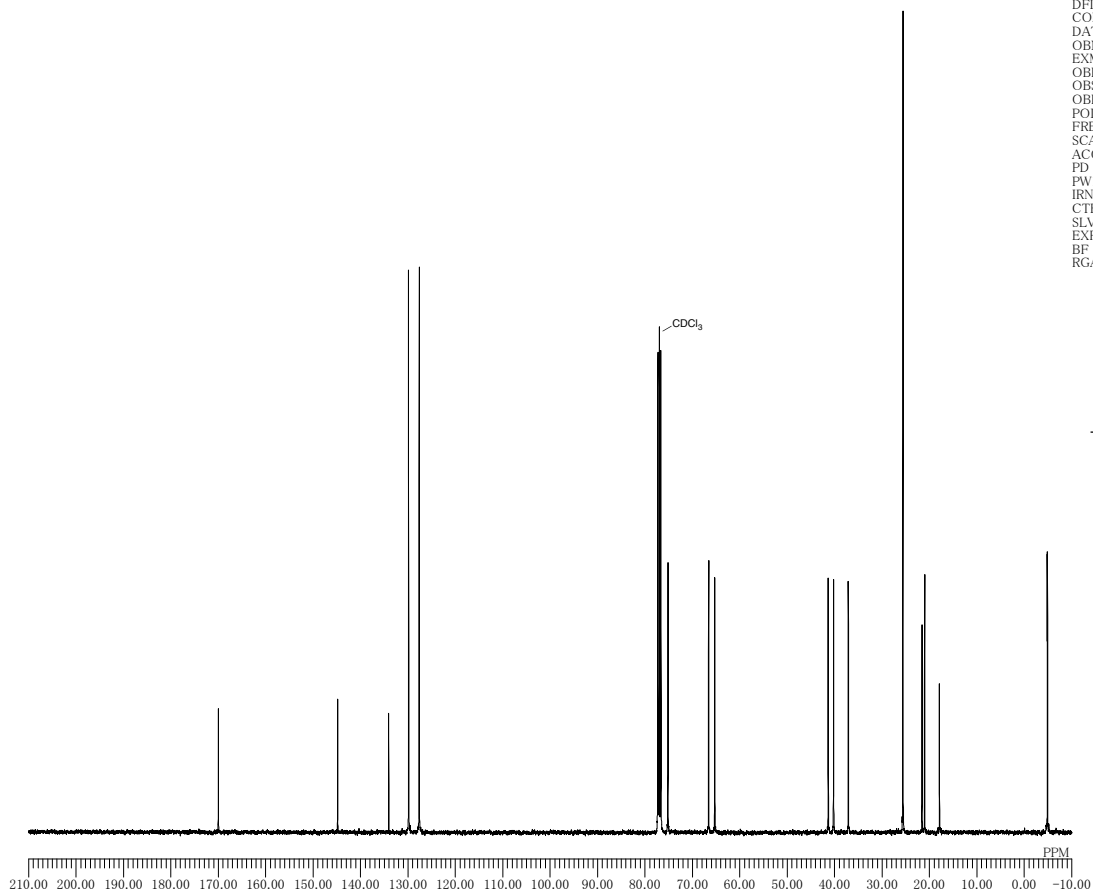
^a Dong, L.-B.; Yang, J.; He, J.; Luo, H.-R.; Wu, X.-D.; Deng, X.; Peng, L.-Y.; Cheng, X.; Zhao, Q.-S. *Chem. Commun.* **2012**, 48, 9038.

Spectral Data

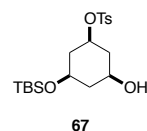
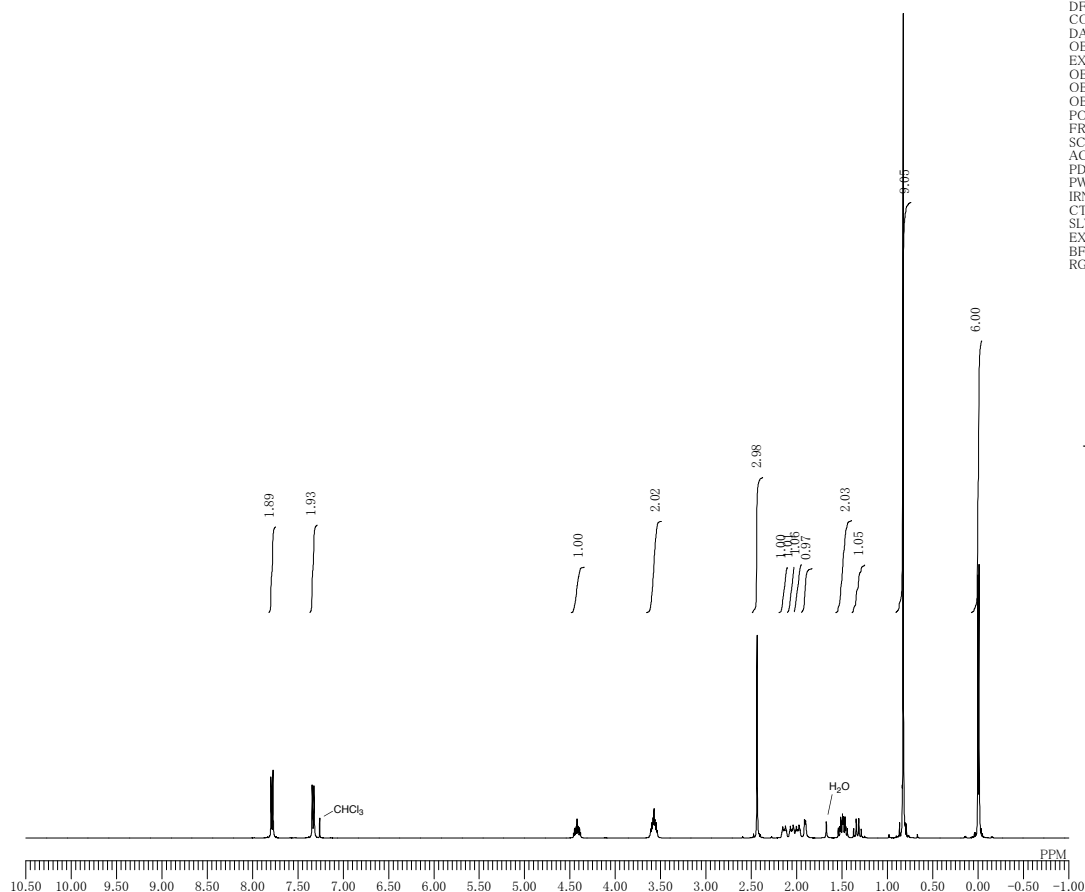
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 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.3 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 28



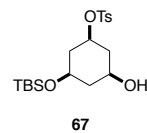
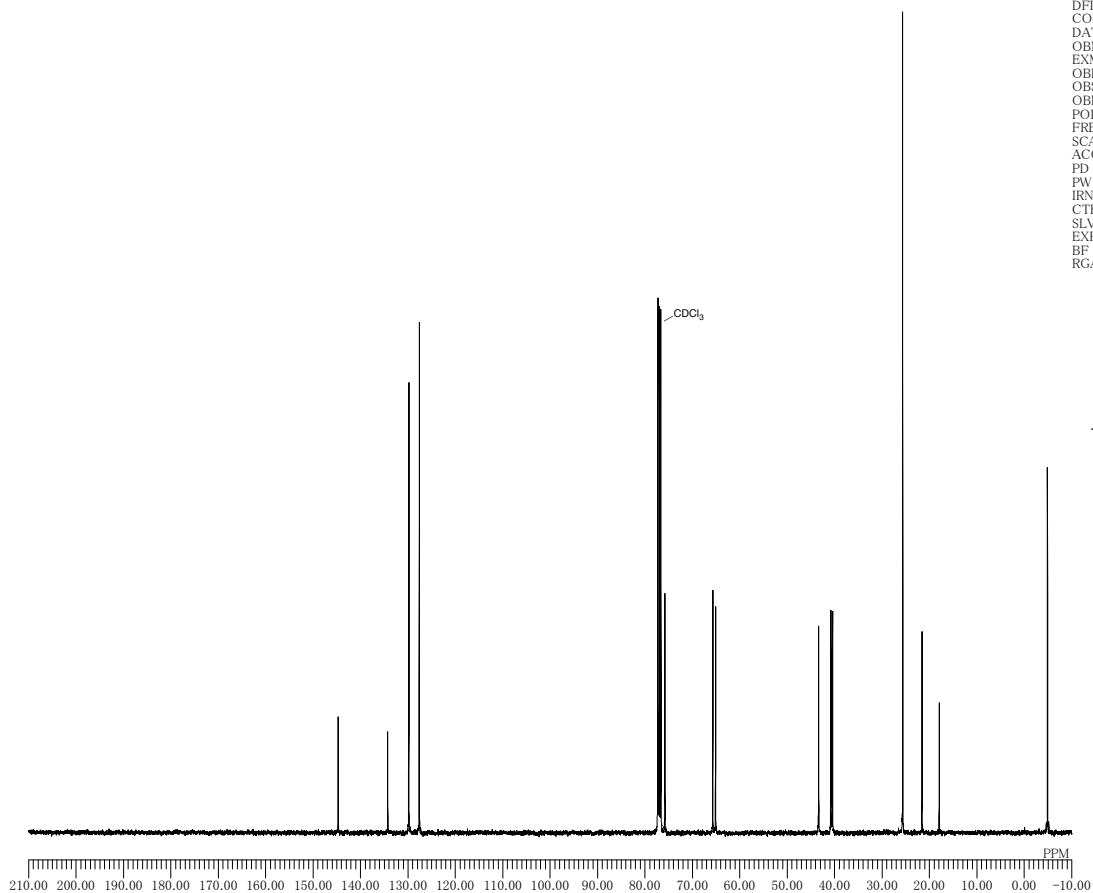
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 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



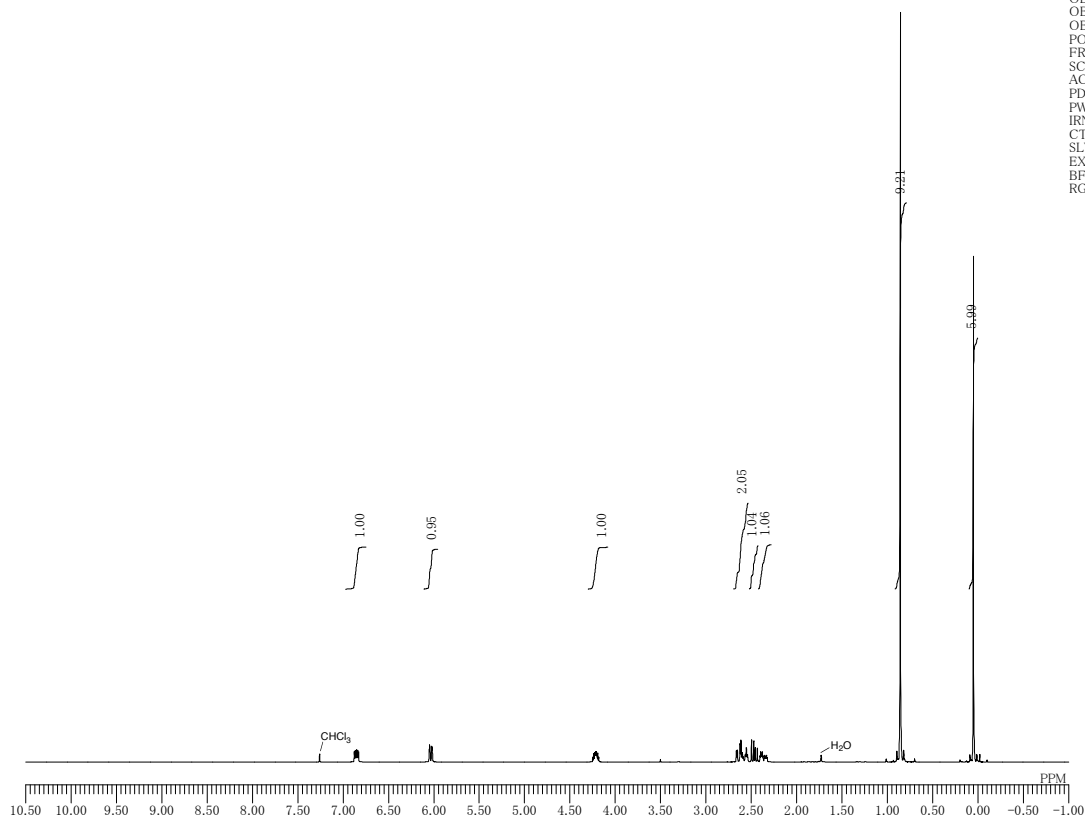
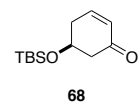
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 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 30



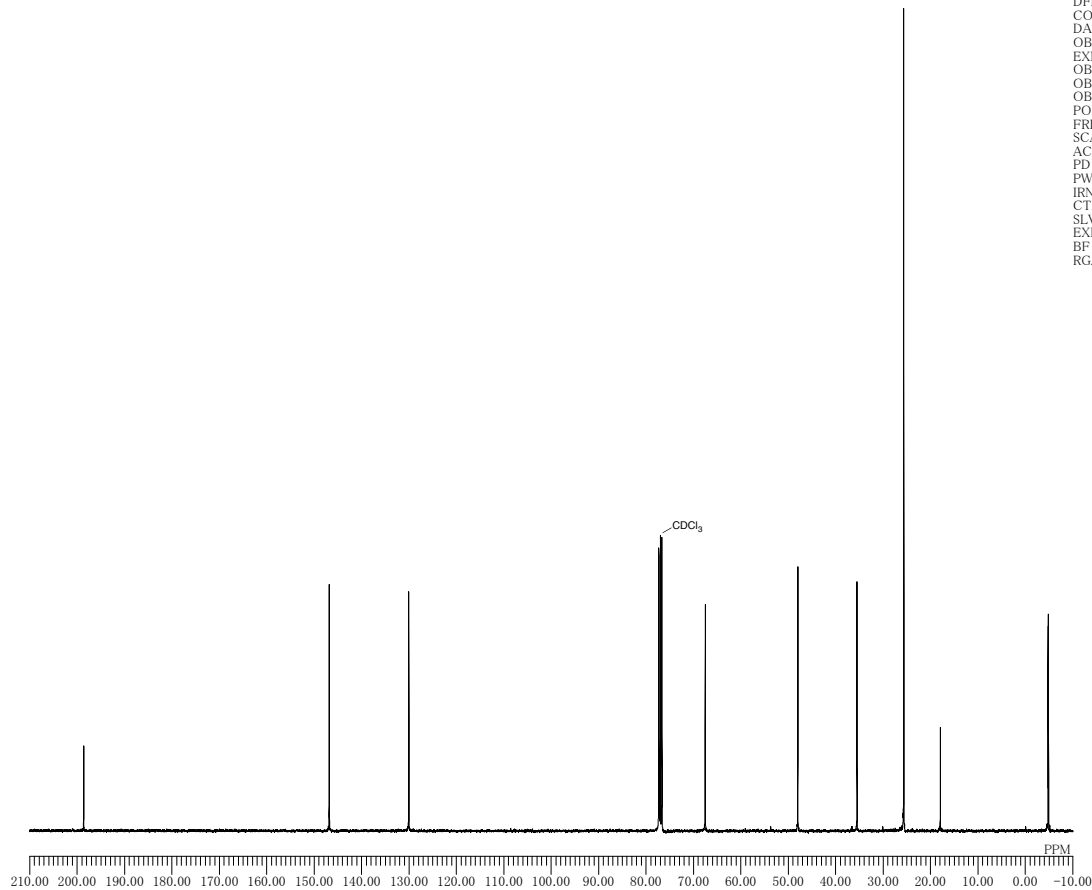
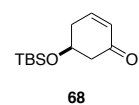
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 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



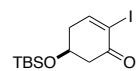
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 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
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 IRNUC 1H
 CTEMP 25.3 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 26



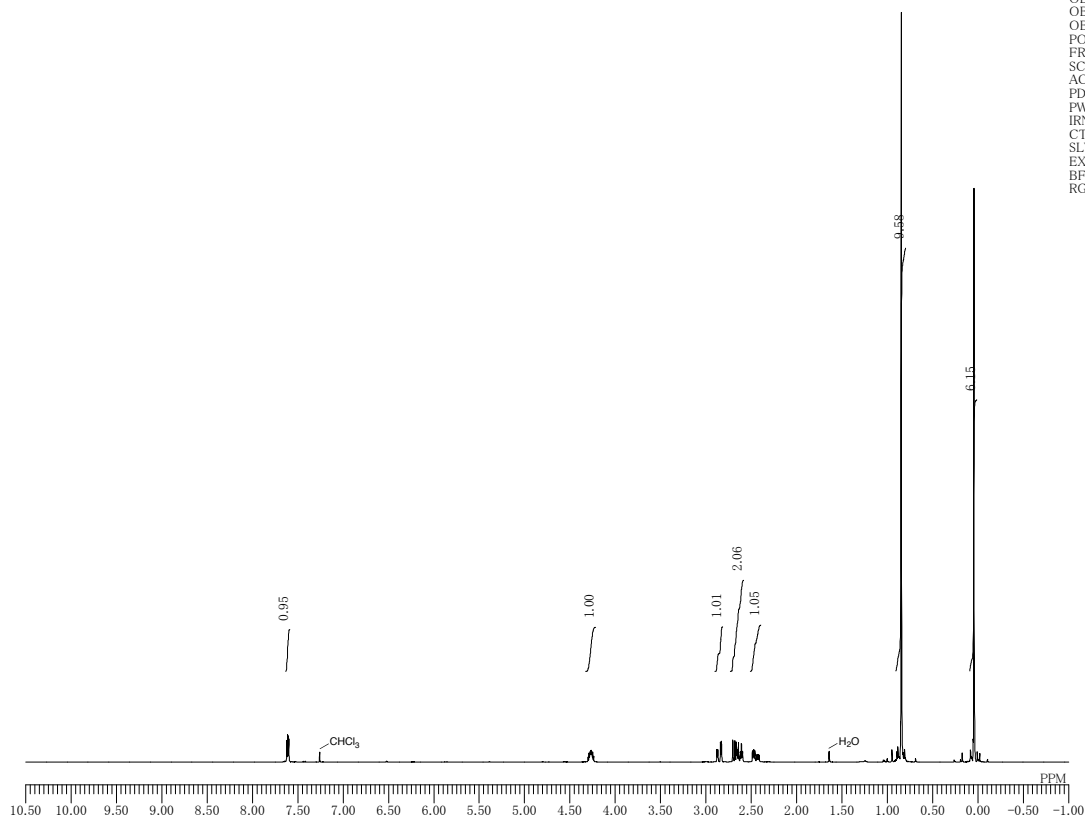
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 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
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 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



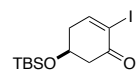
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 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 24.9 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 26



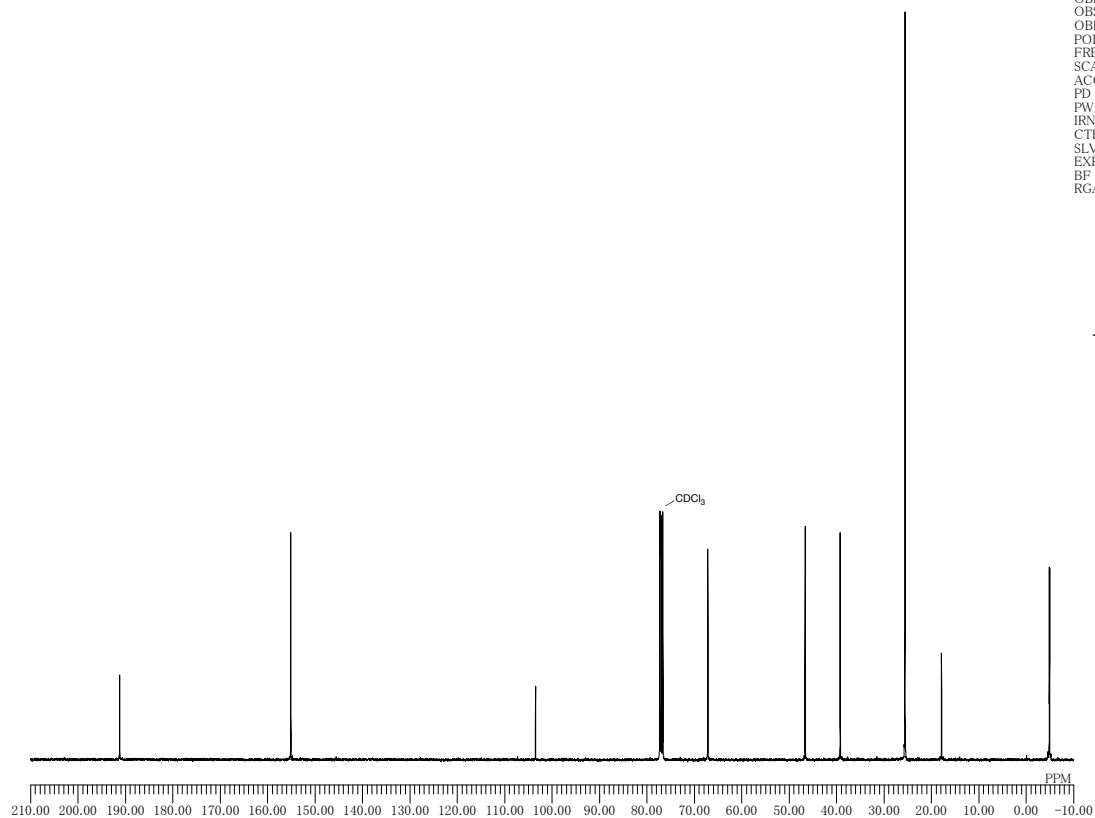
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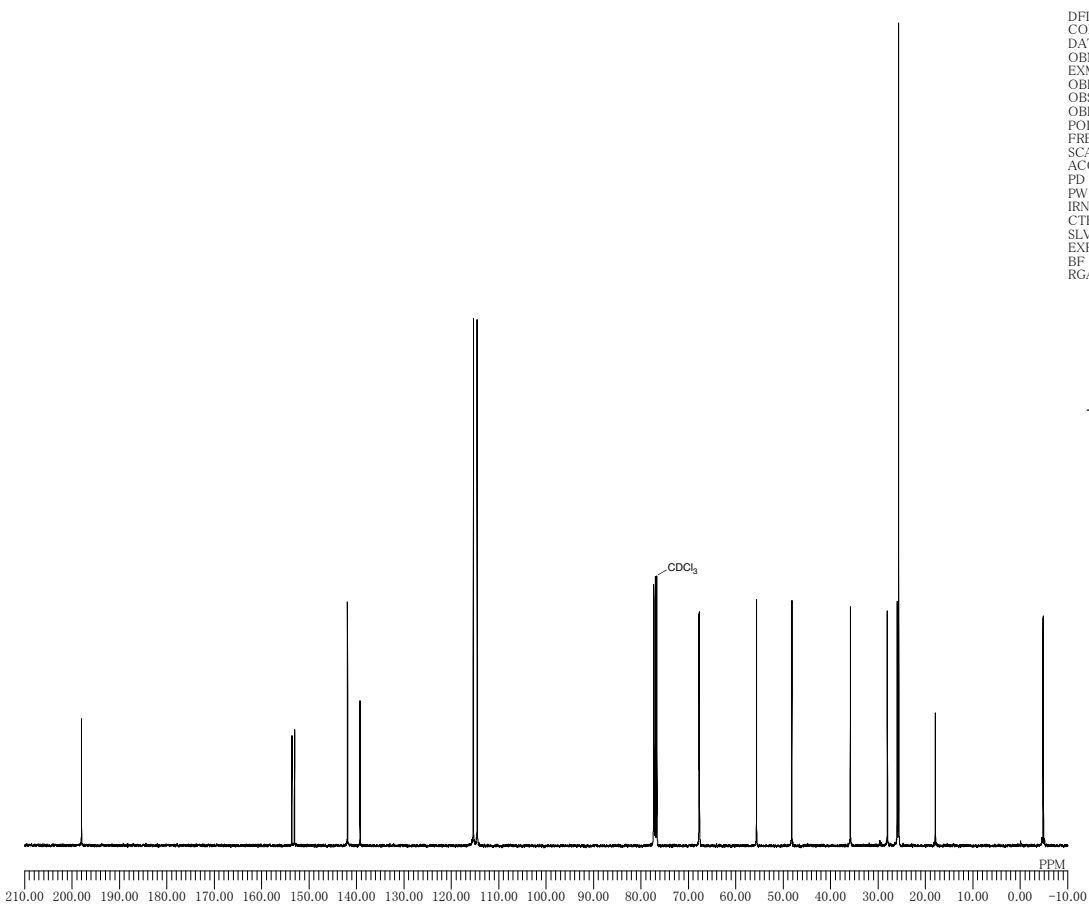
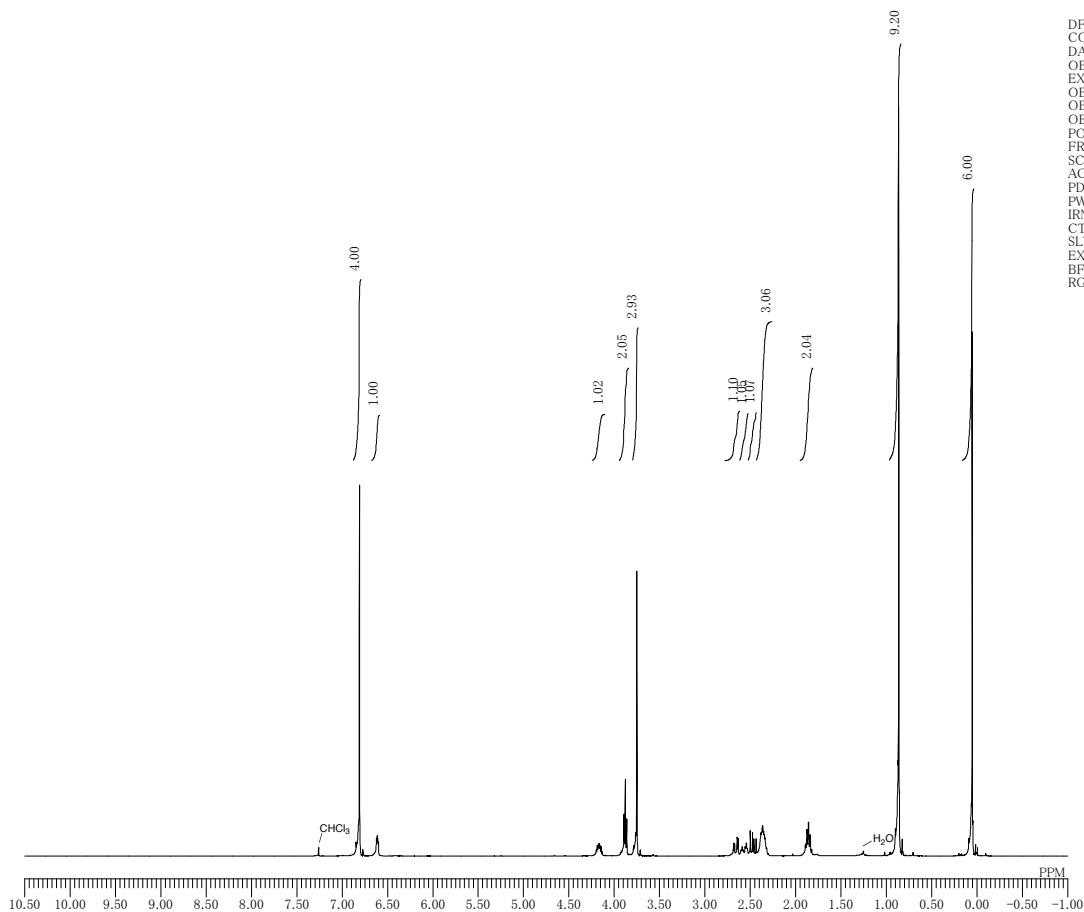


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 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
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 IRNUC 1H
 CTEMP 24.9 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

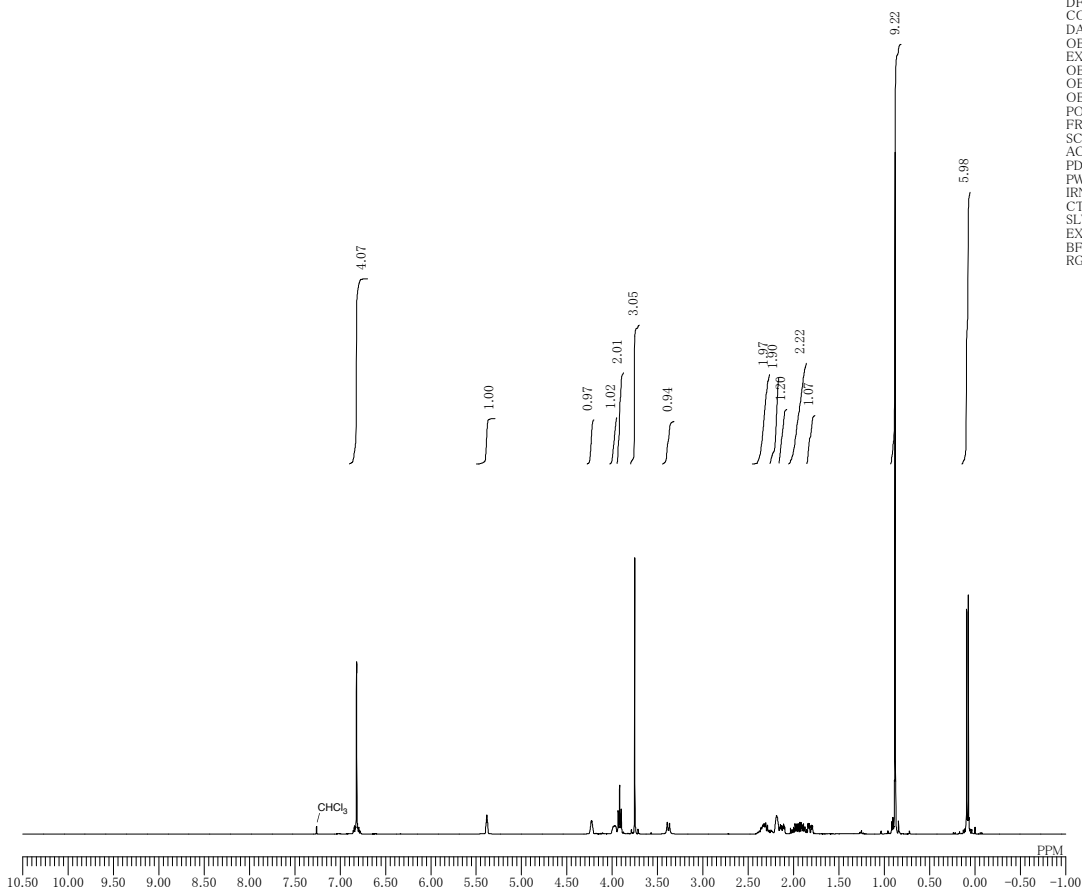


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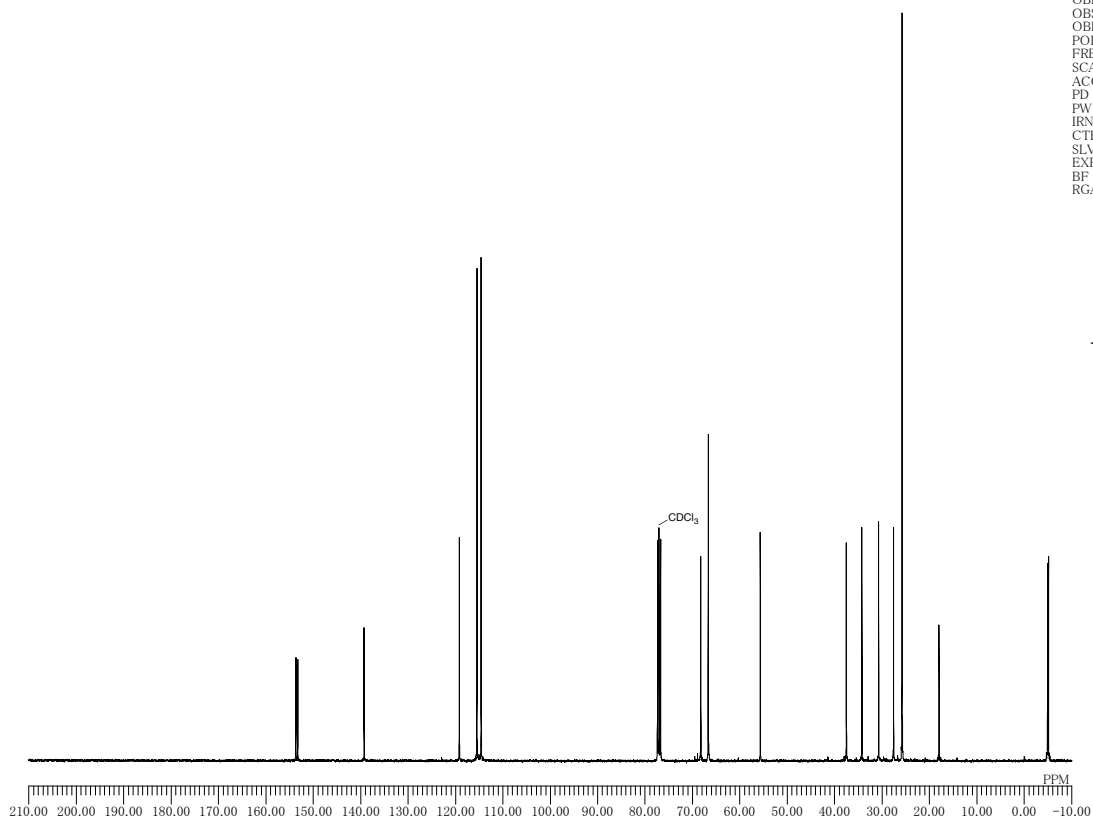




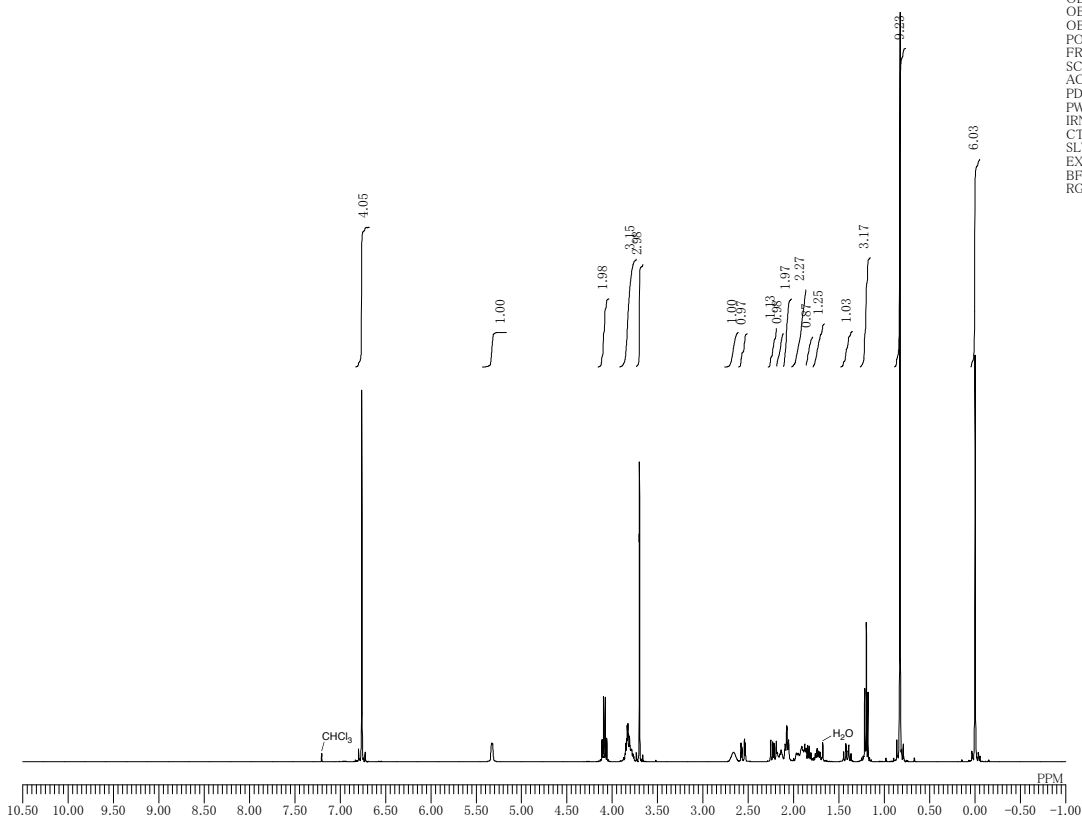
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 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
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 IRNUC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 22



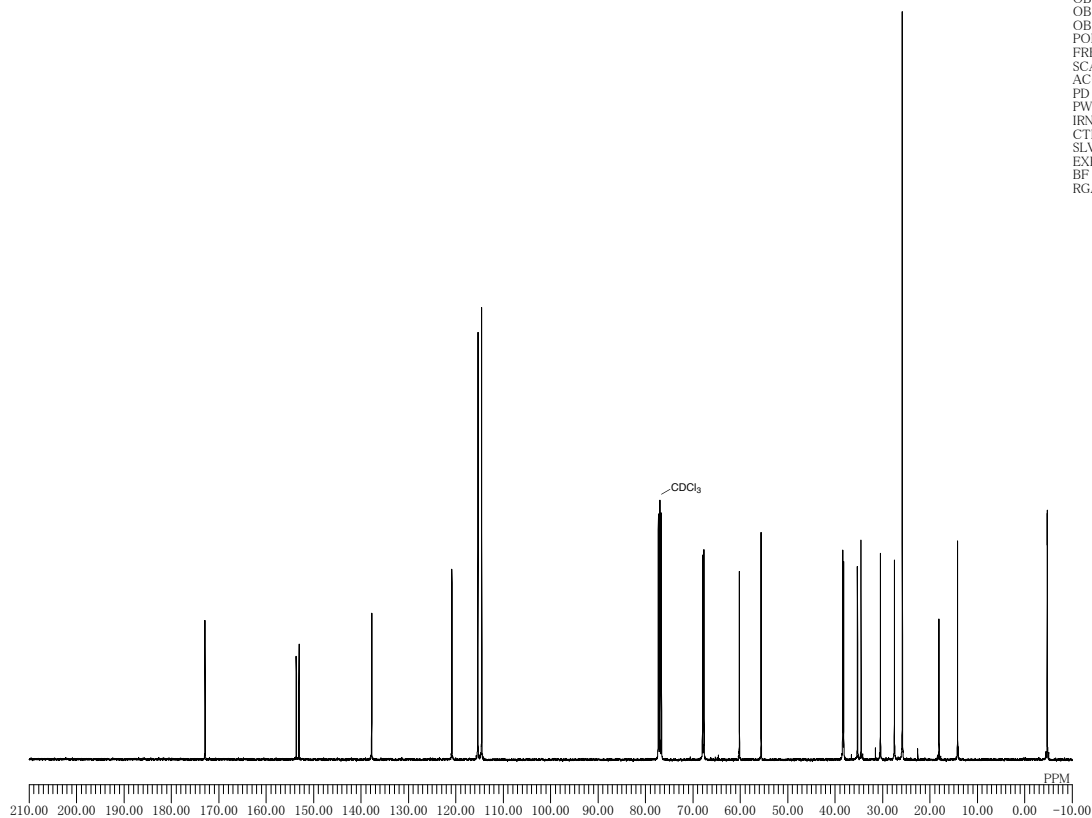
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 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 13C
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 2.02 Hz
 RGAIN 50



DFILE YO-5-089_non-data-1-1.als
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 OBFIN 7.29 Hz
 POINT 13107
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 SCANS 8
 ACQTM 2.1837 sec
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 IRNUC 1H
 CTEMP 25.3 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 22

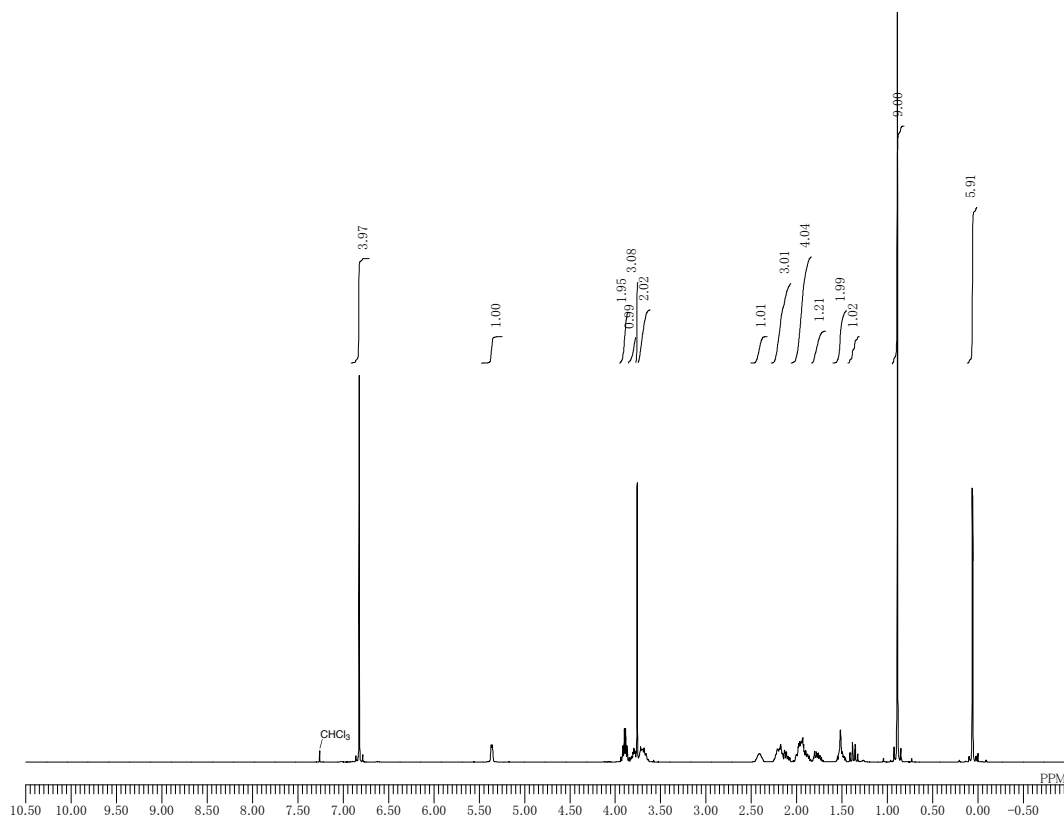


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 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
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 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

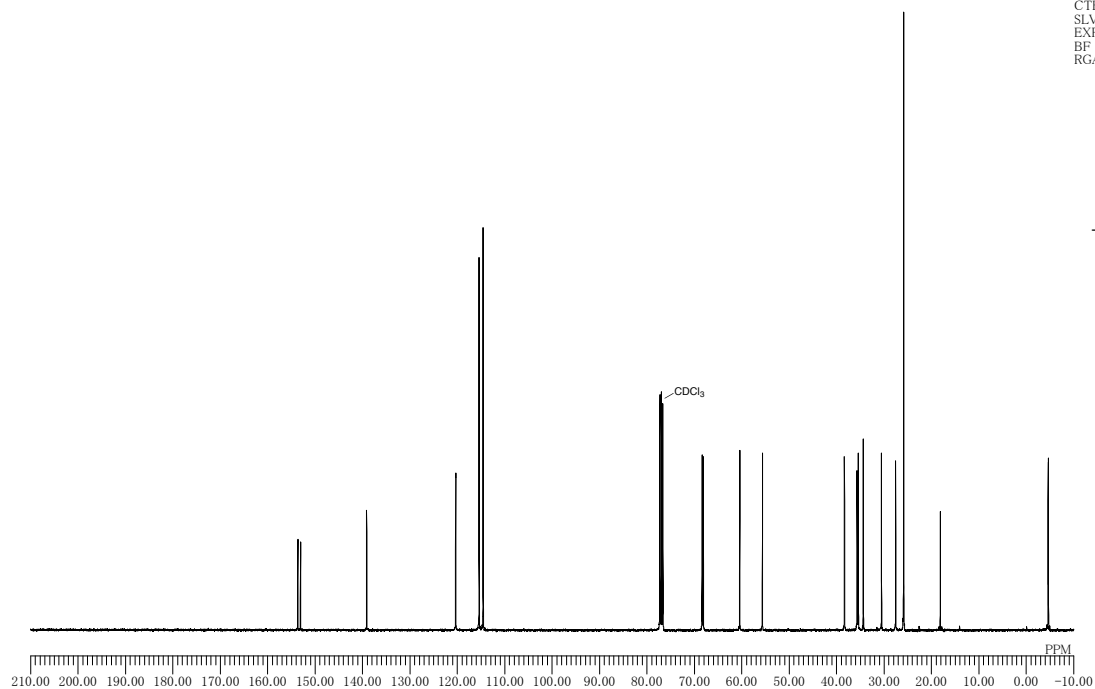


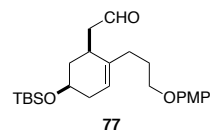
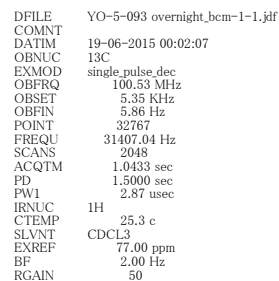
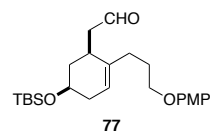
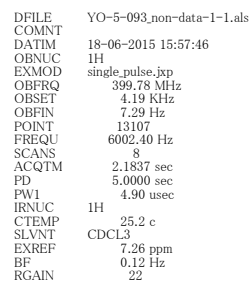
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76

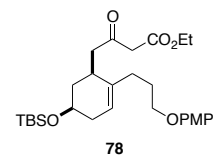
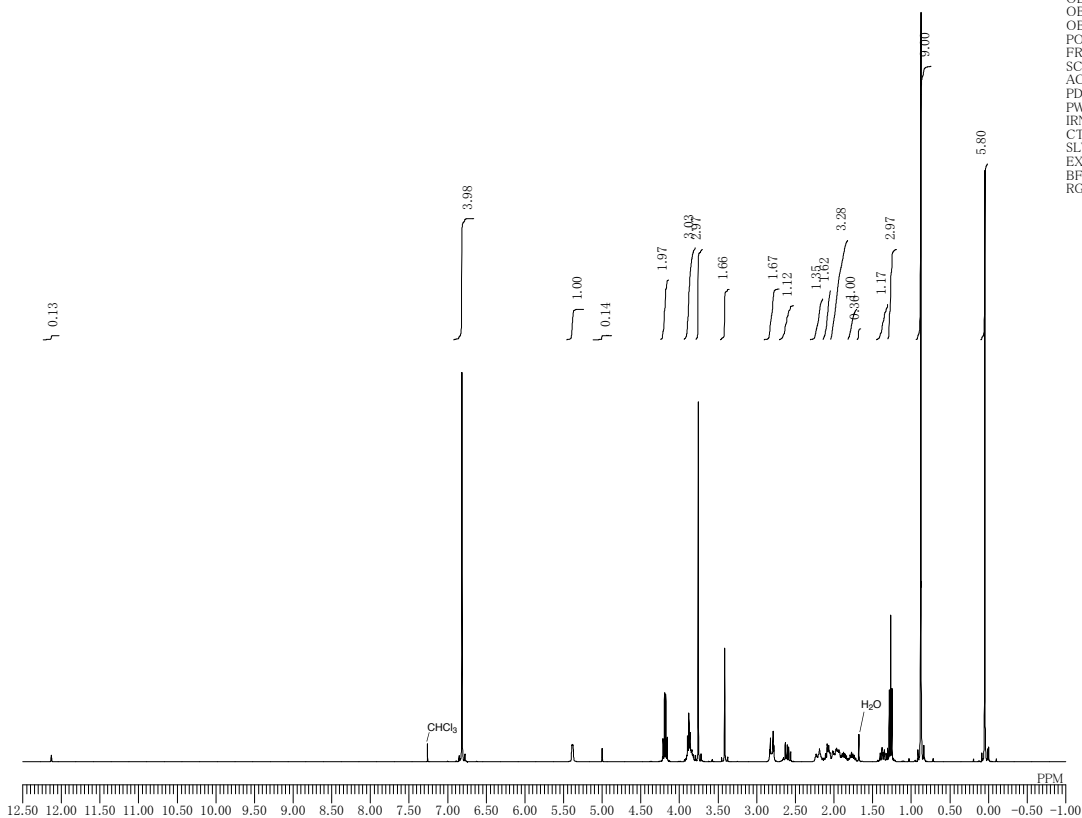


76

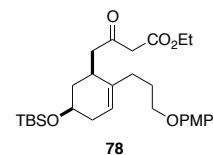
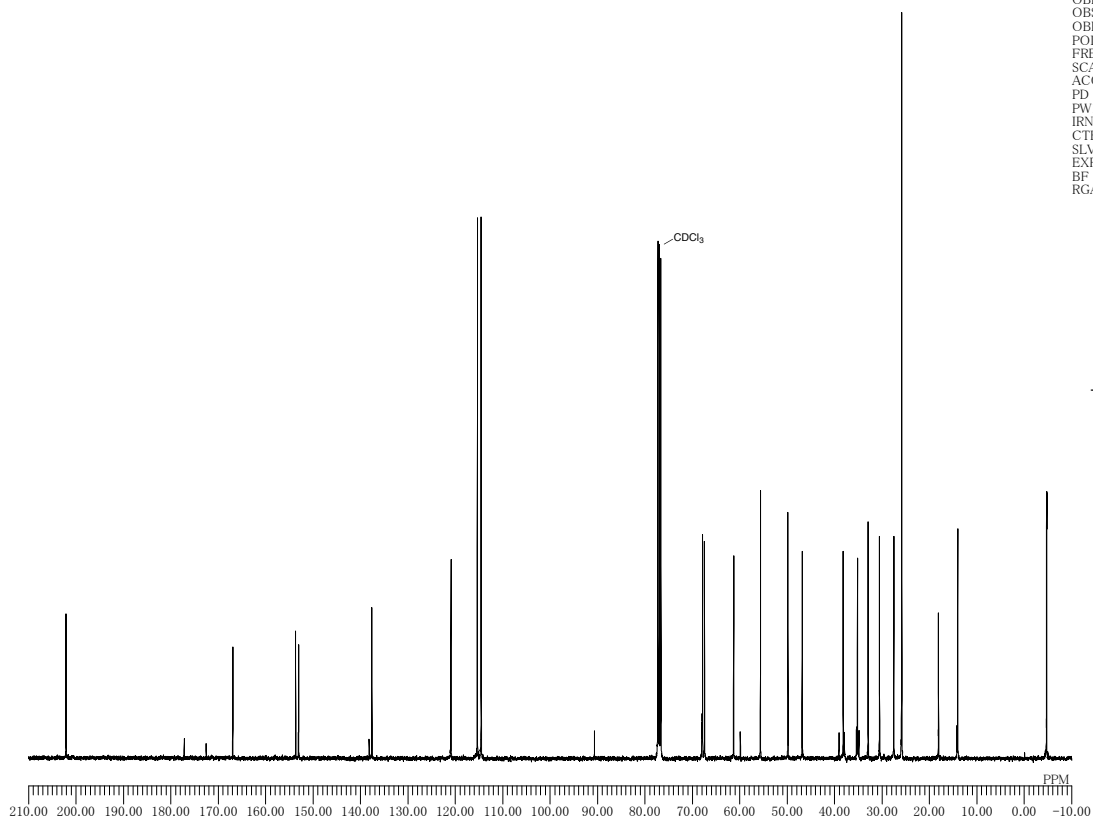




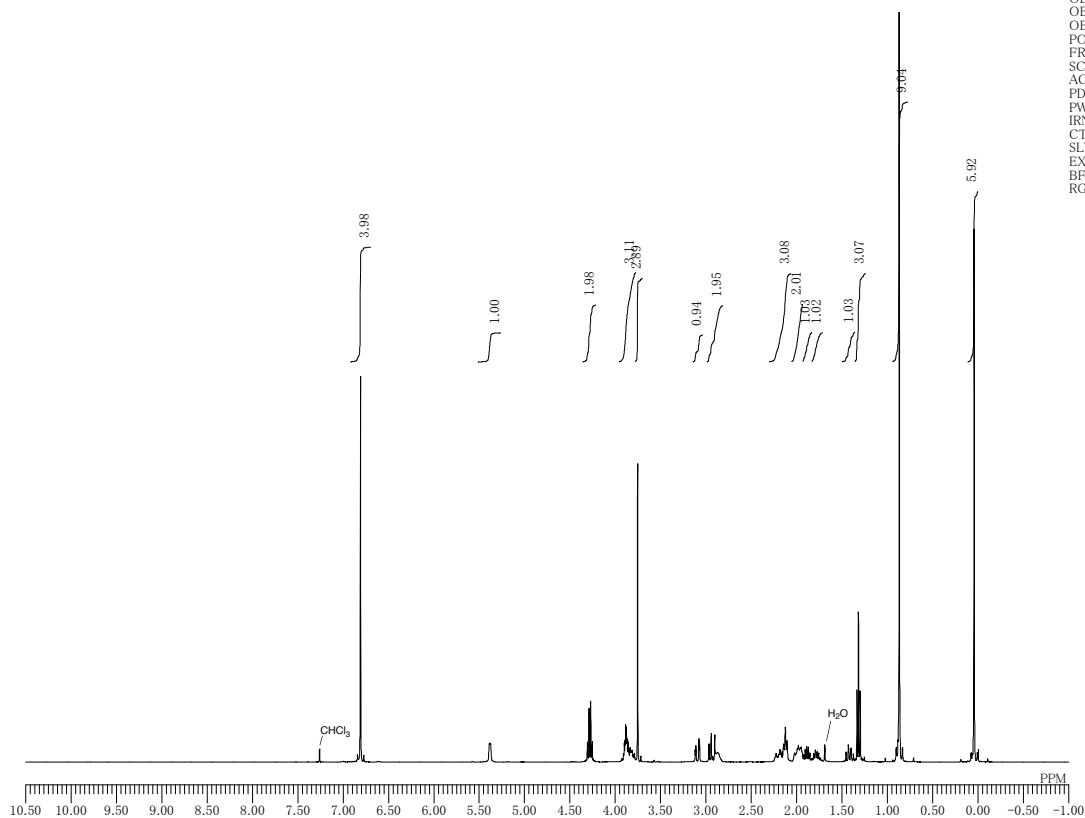
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 ACQTM 2.1837 sec
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 IRNUC 1H
 CTEMP 25.2 c
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 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 24



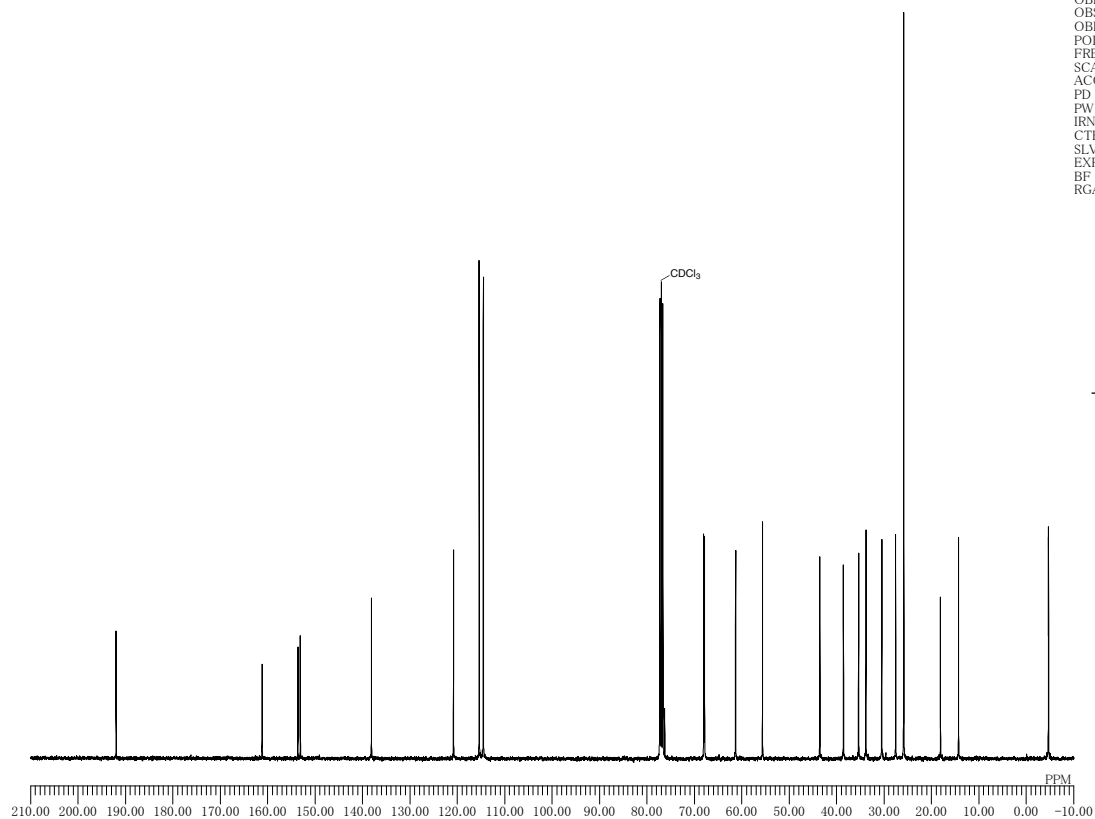
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 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



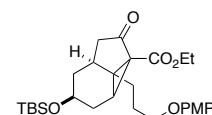
Chemical structure of compound **79** is shown. It features a bicyclic system with a TBSO group, a diazomethyl group, and an ethyl ester group.



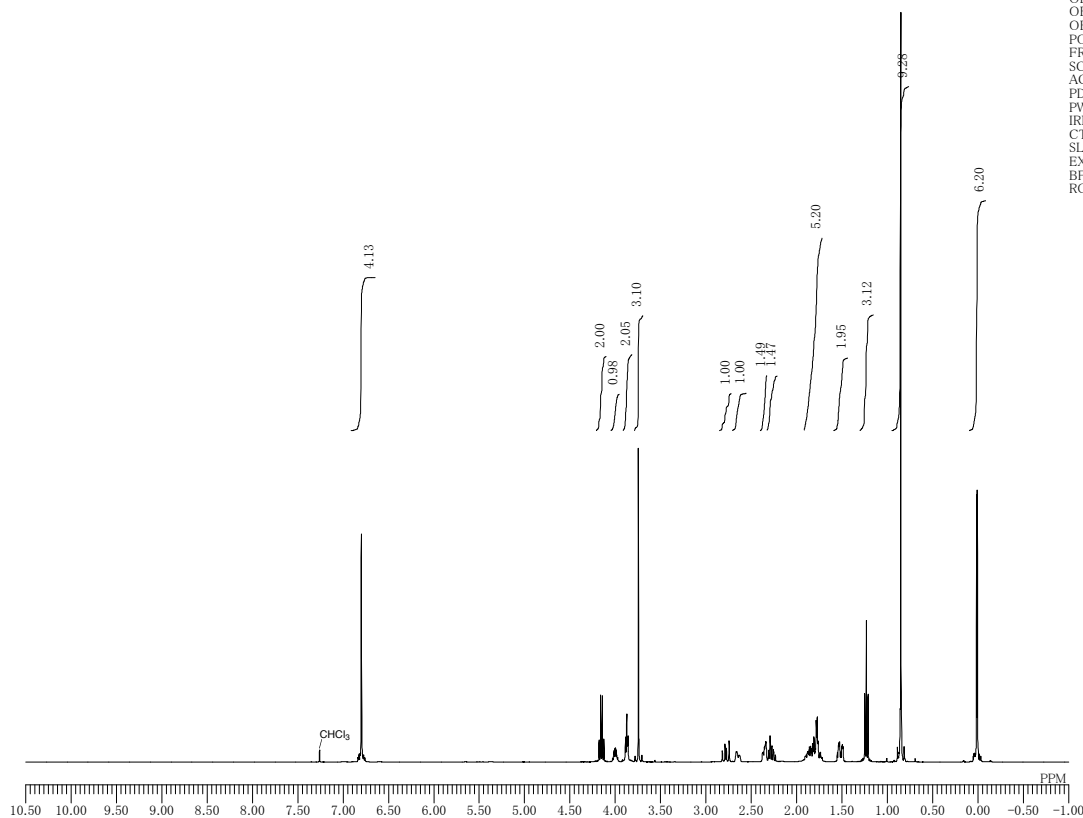
Chemical structure of compound **79** is shown. It features a bicyclic system with a TBSO group, a diazomethyl group (N_2), and an ethyl ester group (CO_2Et).



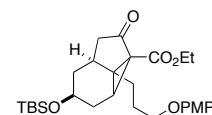
DFILE YO-5-097_non-data-1-1.als
 COMNT
 DATIM 22-06-2015 22:02:37
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 22



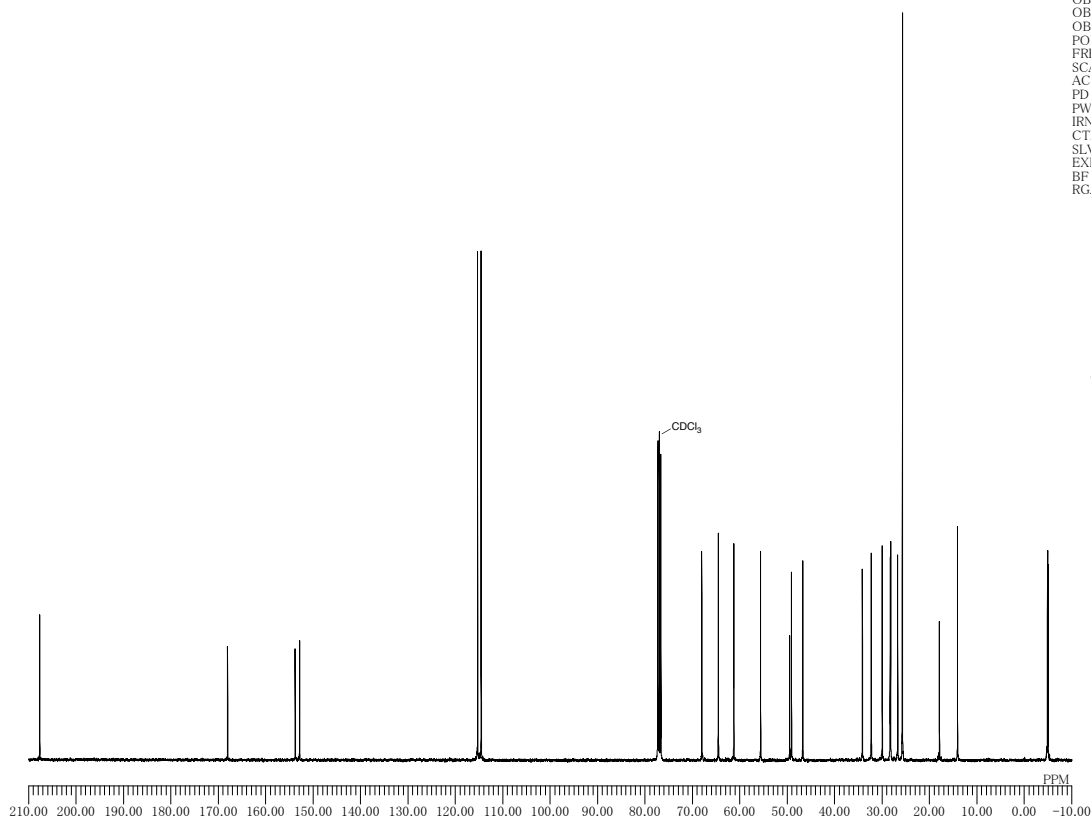
80

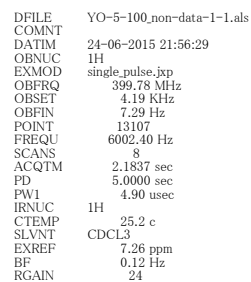


DFILE YO-5-097_overnight_bcm-1-1.als
 COMNT
 DATIM 24-06-2015 00:02:26
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

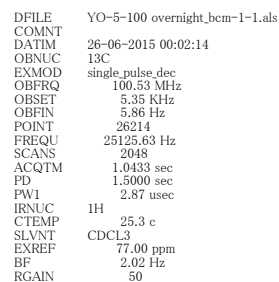


80

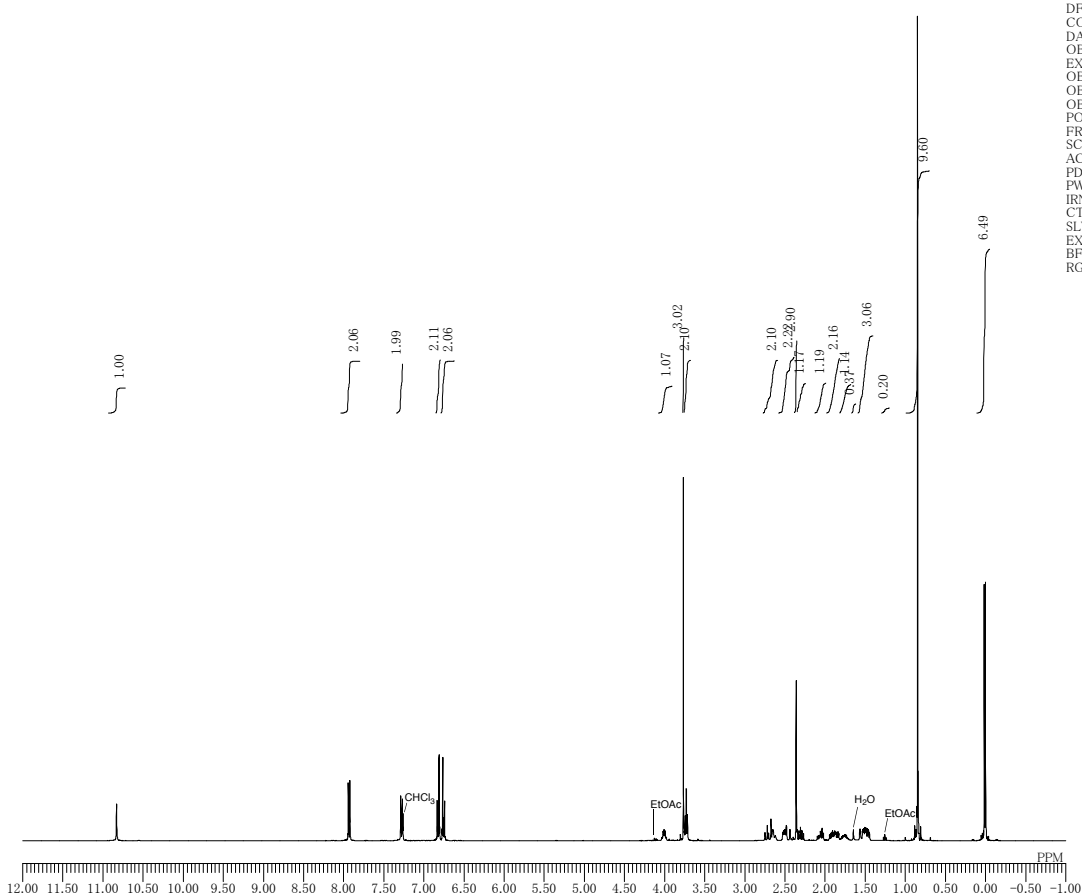




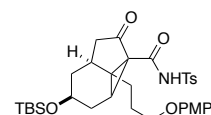
81



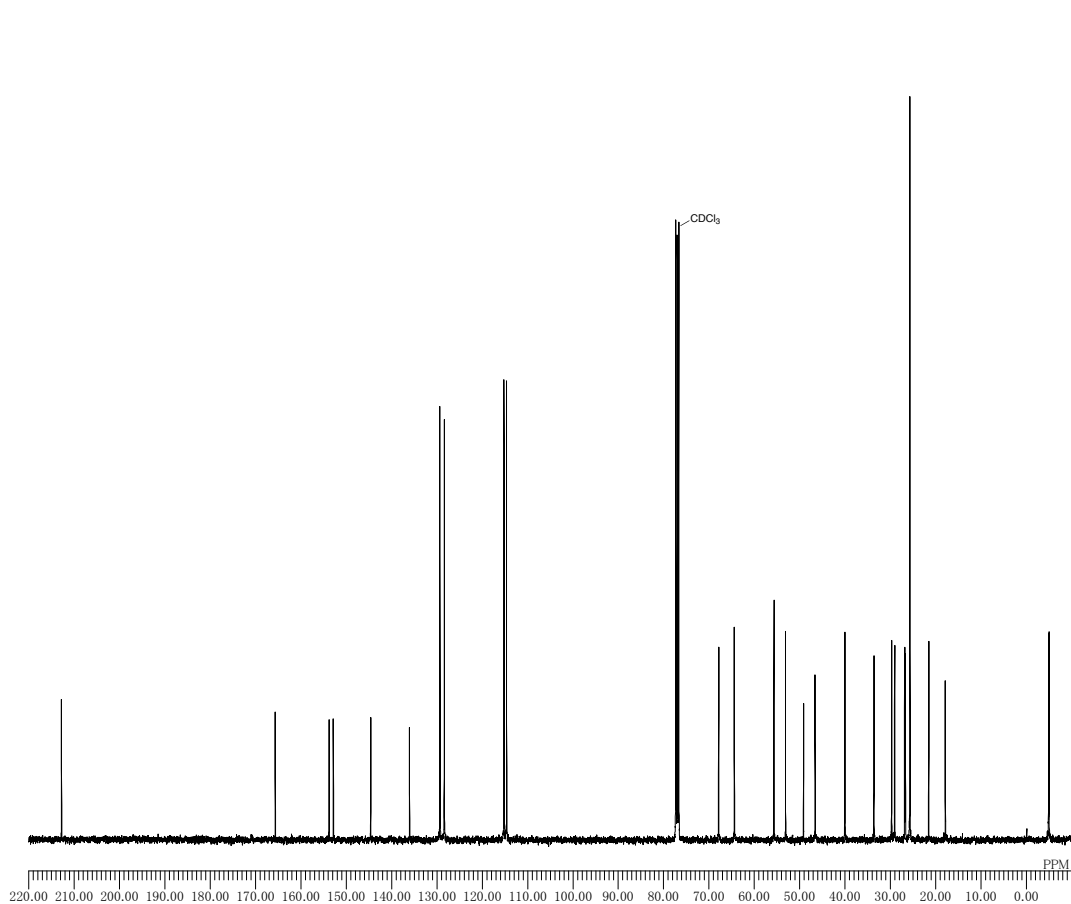
81



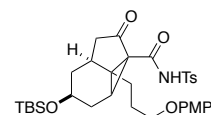
DFILE YO-5-101_non-data-1-1.als
COMNT
DATIM 27-06-2015 16:33:38
OBNUC 1H
EXMOD single_pulse.jpg
OBFRQ 399.78 MHz
OBSET 4.19 KHz
OBFIN 7.29 Hz
POINT 13107
FREQU 6002.40 Hz
SCANS 8
ACQTM 2.1837 sec
PD 5.0000 sec
PW1 4.90 usec
IRNUC 1H
CTEMP 25.1 c
SLVNT CDCL3
EXREF 7.26 ppm
BF 0.12 Hz
RGAIN 28



82

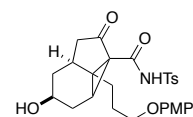
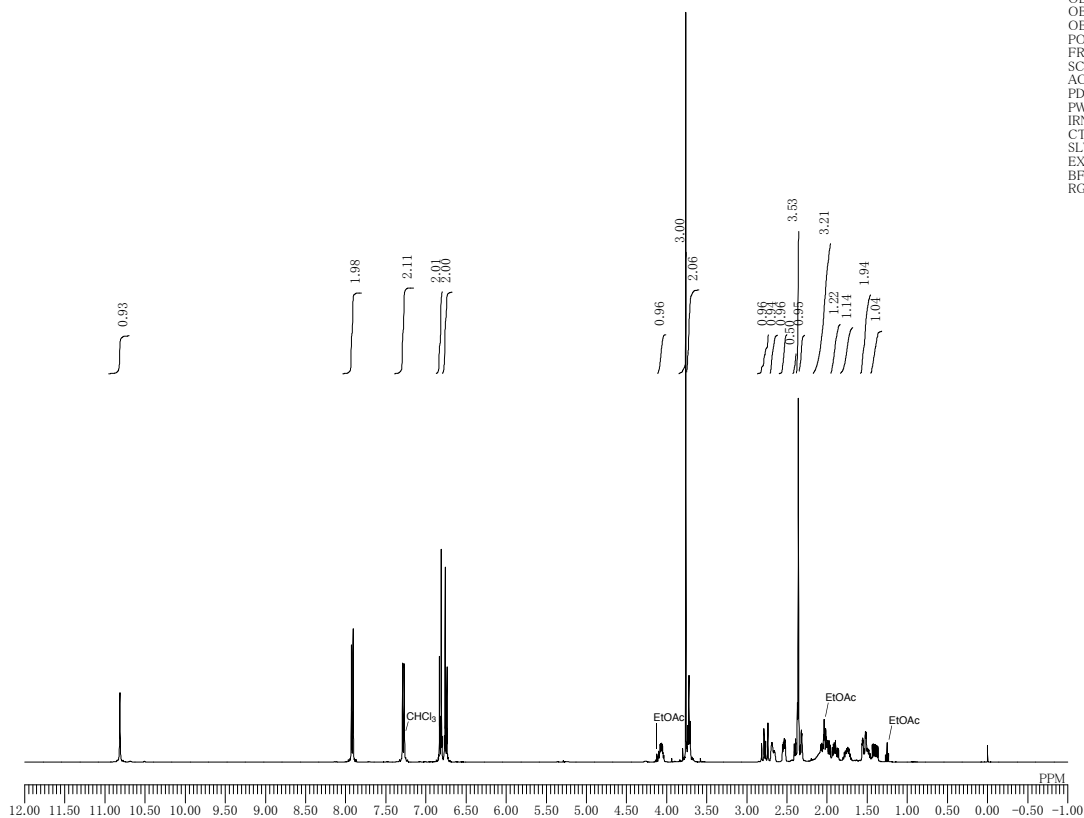


DFILE YO-5-101_overnight_bcm-1-1.als
COMNT
DATIM 27-06-2015 22:02:16
OBNUC 13C
EXMOD single_pulse.dec
OBFRQ 100.53 MHz
OBSET 5.35 KHz
OBFIN 5.86 Hz
POINT 26214
FREQU 25125.63 Hz
SCANS 1024
ACQTM 1.0433 sec
PD 1.5000 sec
PW1 2.87 usec
IRNUC 1H
CTEMP 25.1 c
SLVNT CDCL3
EXREF 77.00 ppm
BF 2.02 Hz
RGAIN 50



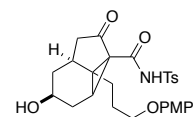
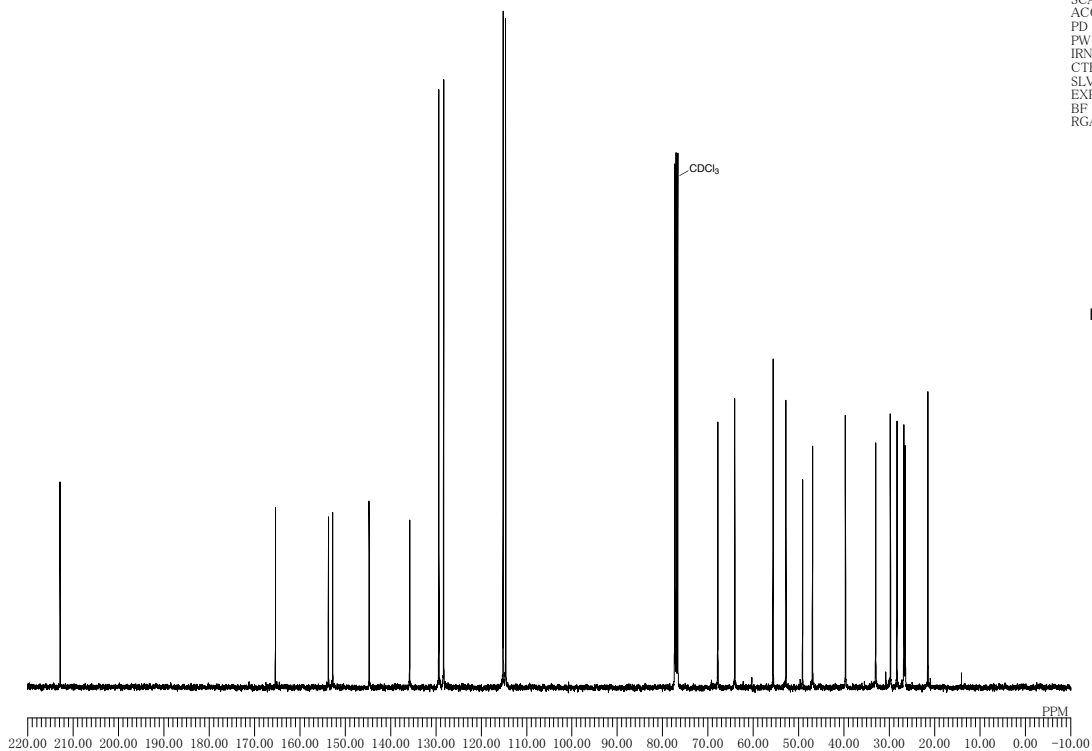
82

DFILE YO-5-104.non-data-1-1.als
 COMNT
 DATIM 27-06-2015 16:47:59
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 26



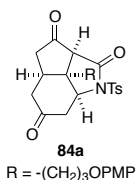
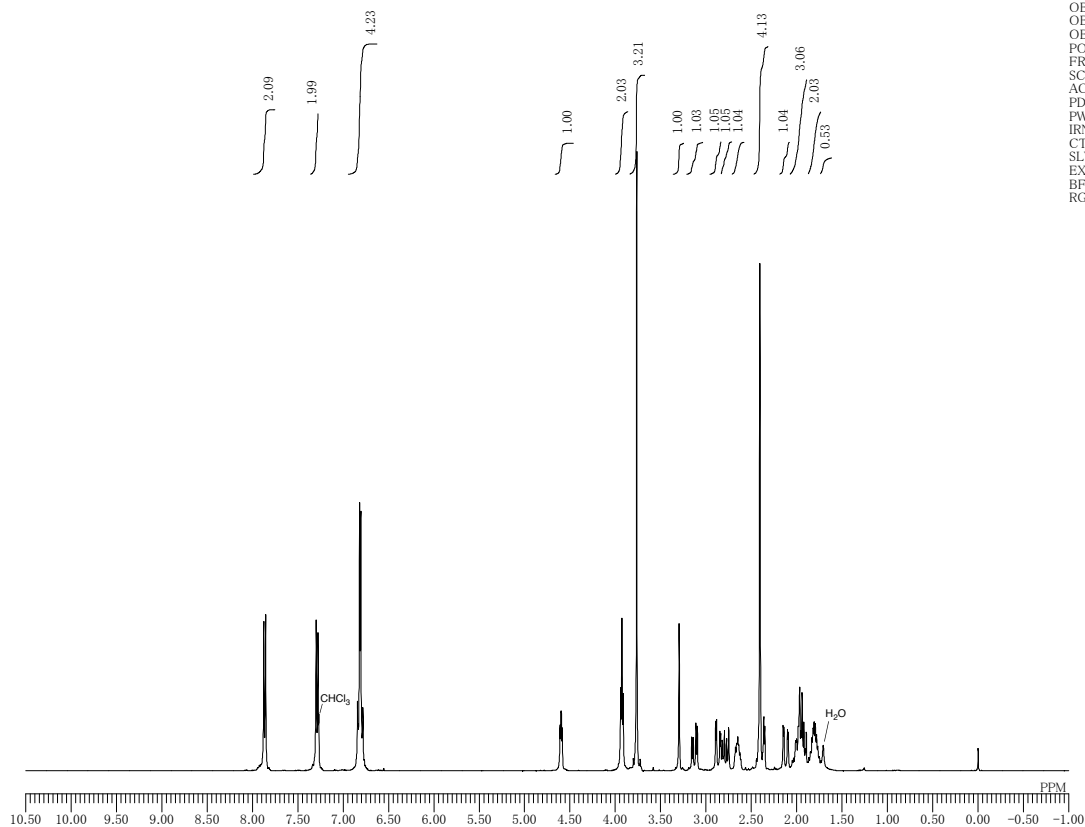
83

DFILE YO-5-104 overnight_bcm-1-1.als
 COMNT
 DATIM 28-06-2015 11:33:41
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 1024
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

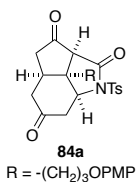
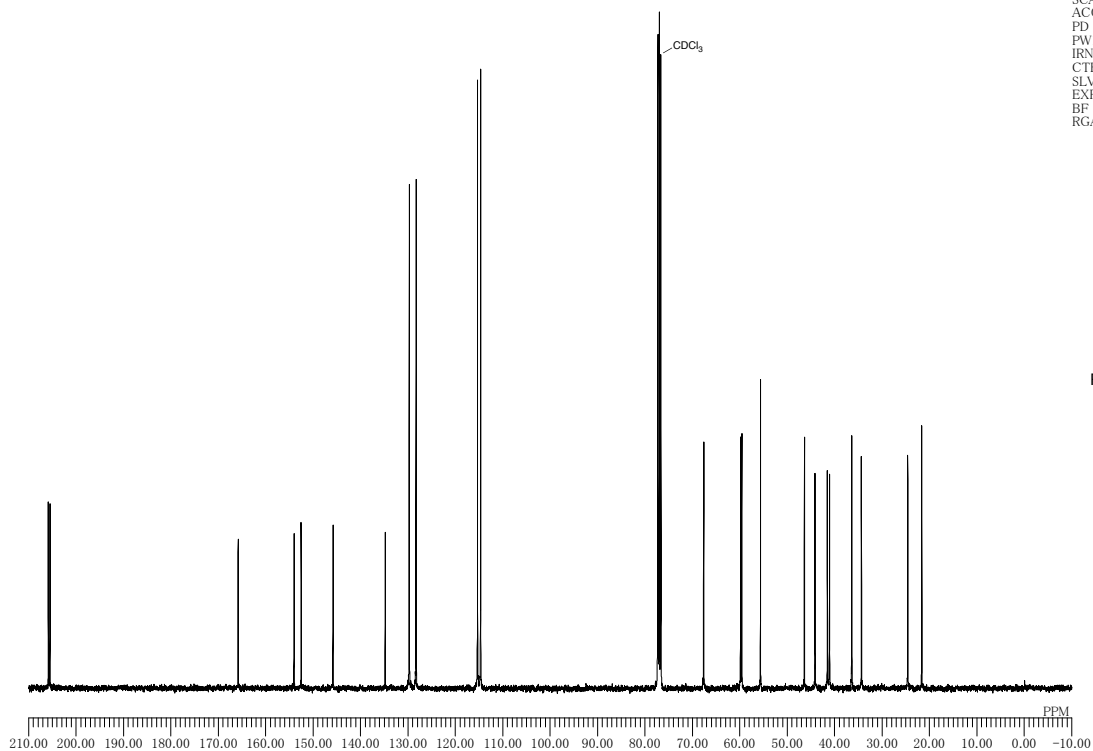


83

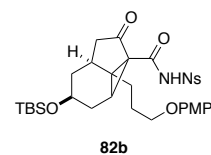
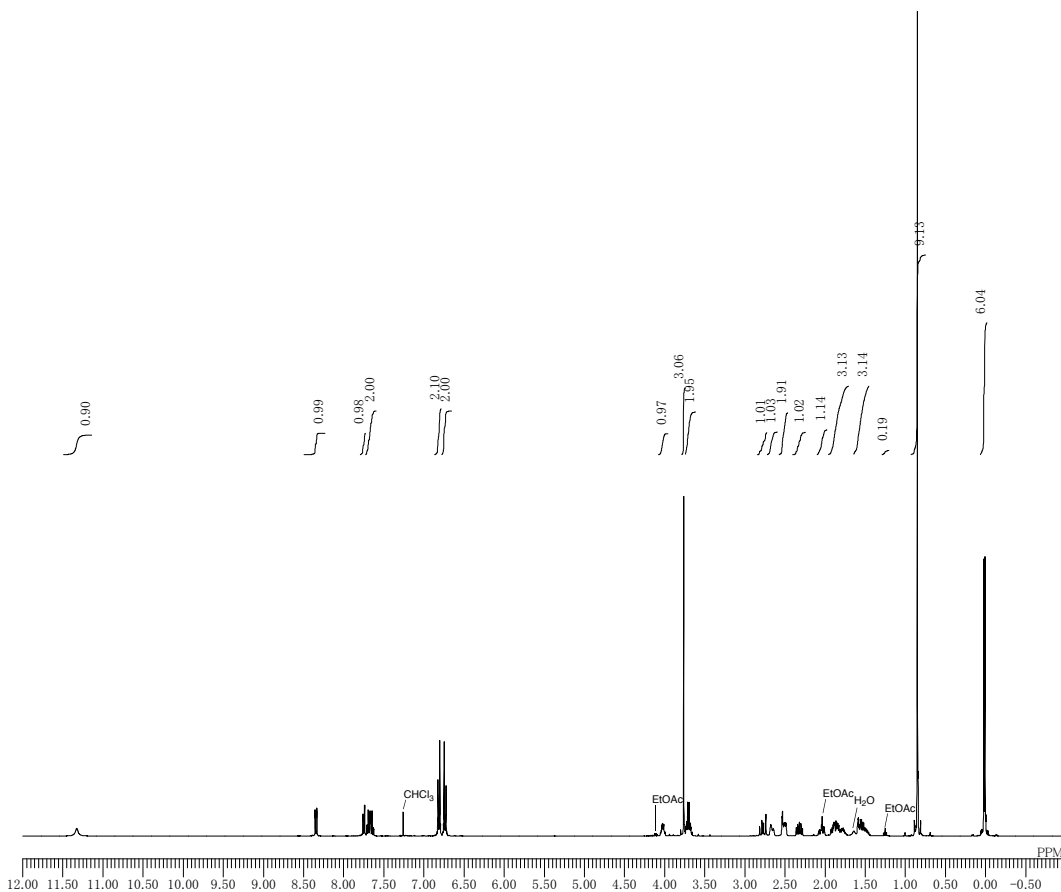
DFILE YO-5-106-2.non-data-1-1.als
 COMNT
 DATIM 29-06-2015 20:25:15
 OBNUC ¹H
 EXMOD single_pulse.jpg
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.0 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



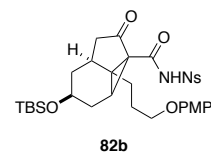
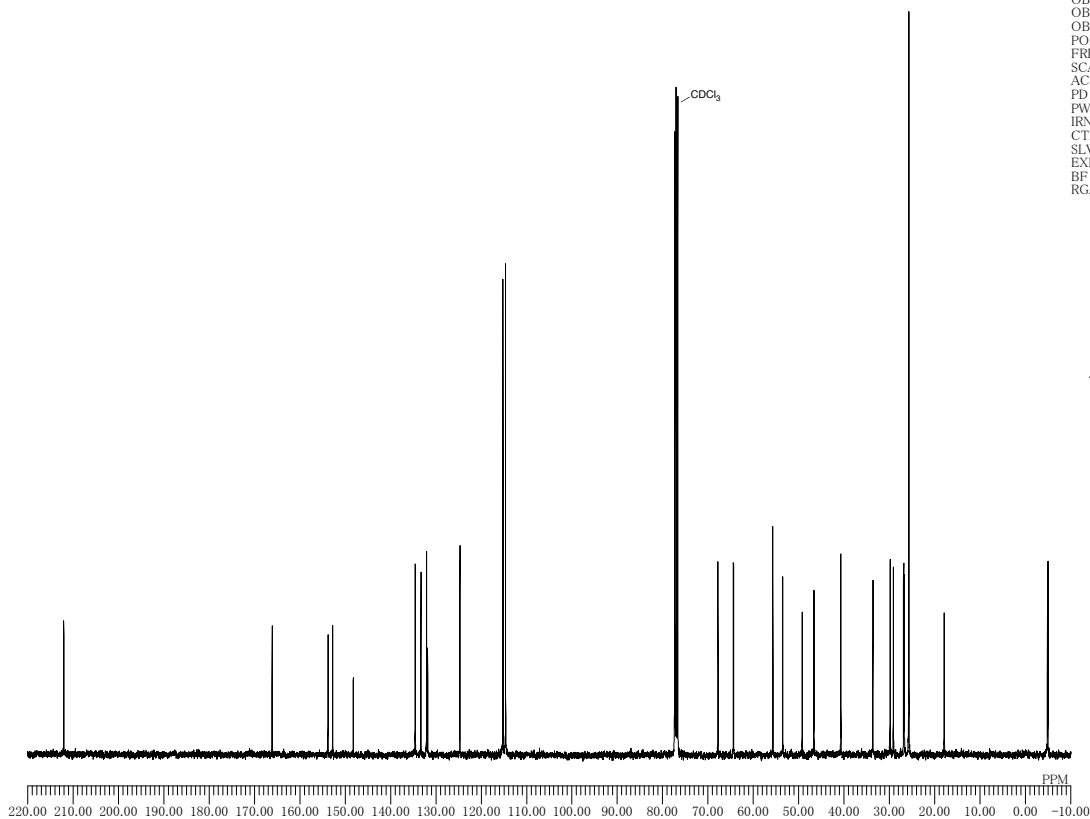
DFILE YO-5-106 overnight_bcm-1-1.als
 COMNT
 DATIM 02-07-2015 00:03:39
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹³C
 CTEMP 25.0 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



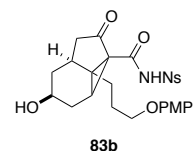
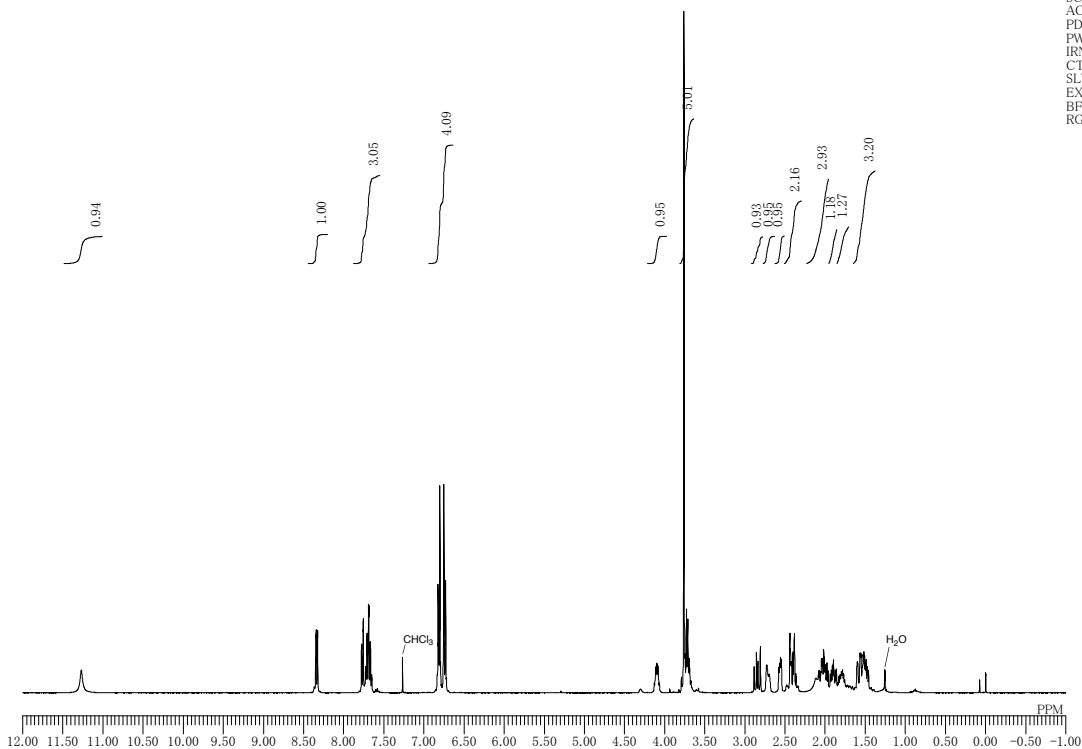
DFILE YO-5-102.non-data-1-1.als
 COMNT 27-06-2015 16:38:19
 DATIM 1H
 OBNUC single_pulse.jpg
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT 6002.40 Hz
 FREQU 8
 SCANS 2.1837 sec
 ACQTM 5.0000 sec
 PD 4.90 usec
 PW1 1H
 IRNUC 25.1 c
 CTEMP CDCL3
 SLVNT 7.26 ppm
 EXREF BF
 0.12 Hz
 RGAIN 28



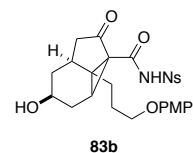
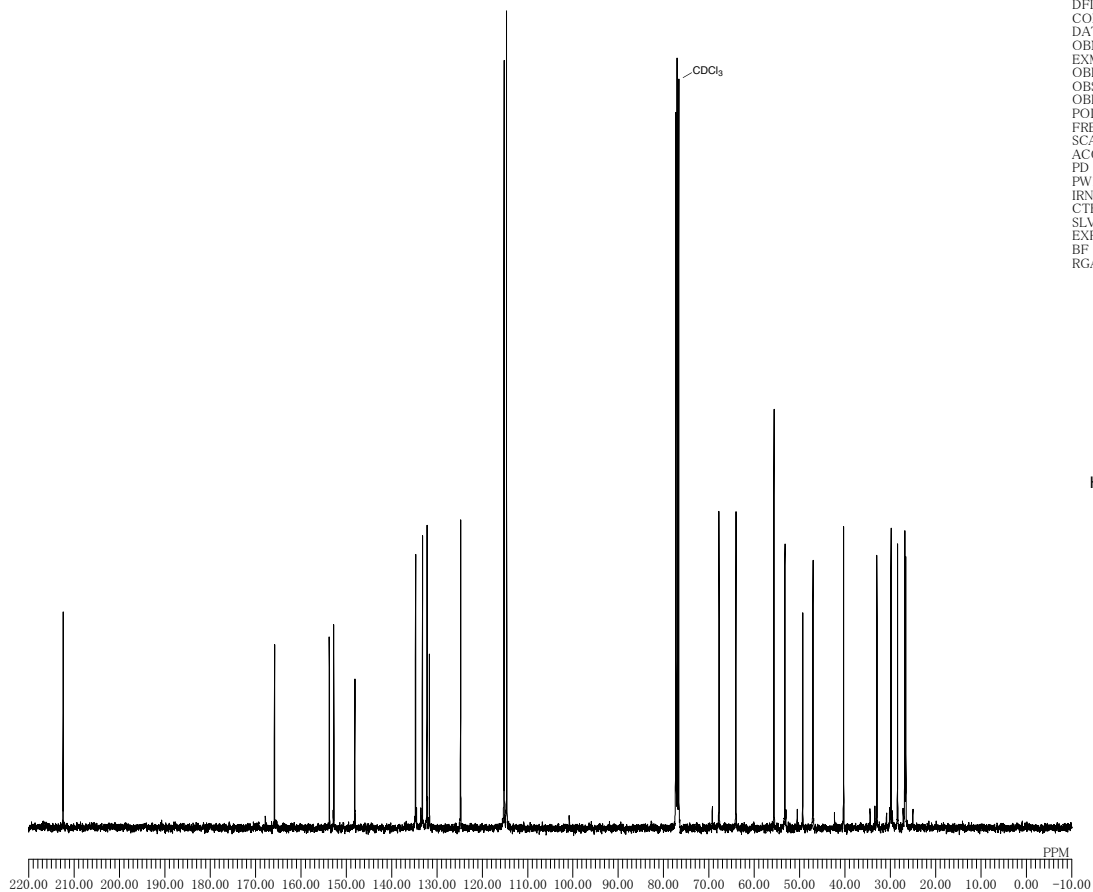
DFILE YO-5-102 overnight_bcm-1-1.als
 COMNT 28-06-2015 02:32:26
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26214
 POINT 25125.63 Hz
 FREQU 1024
 SCANS 1.0433 sec
 ACQTM 1.5000 sec
 PD 2.87 usec
 PW1 1H
 IRNUC 25.1 c
 CTEMP CDCL3
 SLVNT 77.00 ppm
 EXREF BF
 2.02 Hz
 RGAIN 50



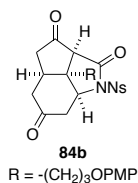
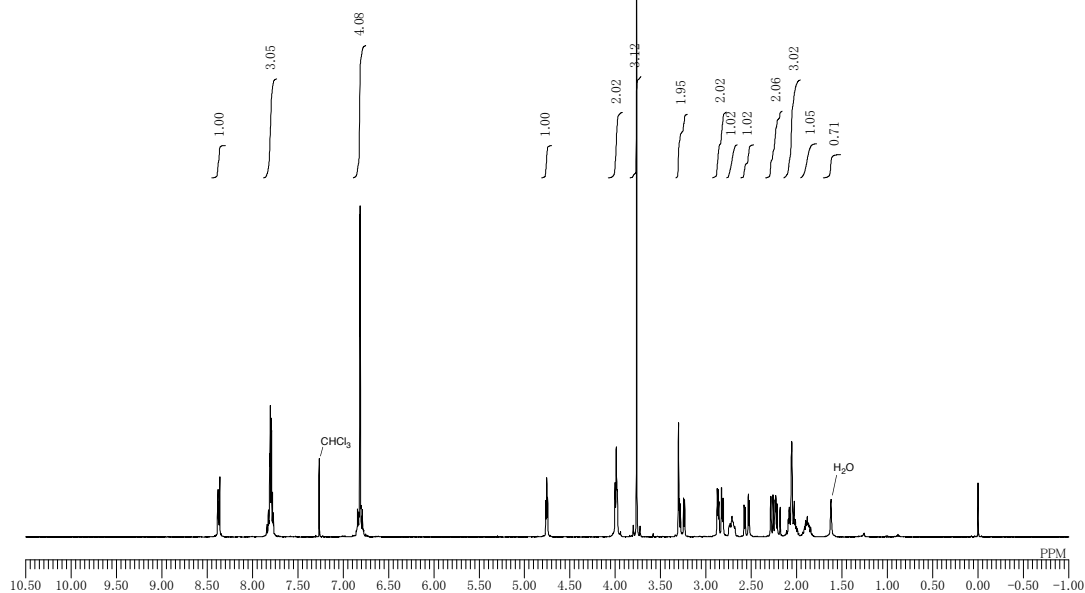
DFILE YO-5-105.non-data-1-1.als
 COMNT 27-06-2015 16:53:54
 DATIM 1H
 OBNUC single_pulse.jxp
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT 6002.40 Hz
 FREQU 8
 SCANS 2.1837 sec
 ACQTM 5.0000 sec
 PD 4.90 usec
 PW1 1H
 IRNLC 25.1 c
 CTEMP CDCL3
 SLVNT 0.00 ppm
 EXREF 0.12 Hz
 BF 28
 RGAIN



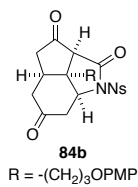
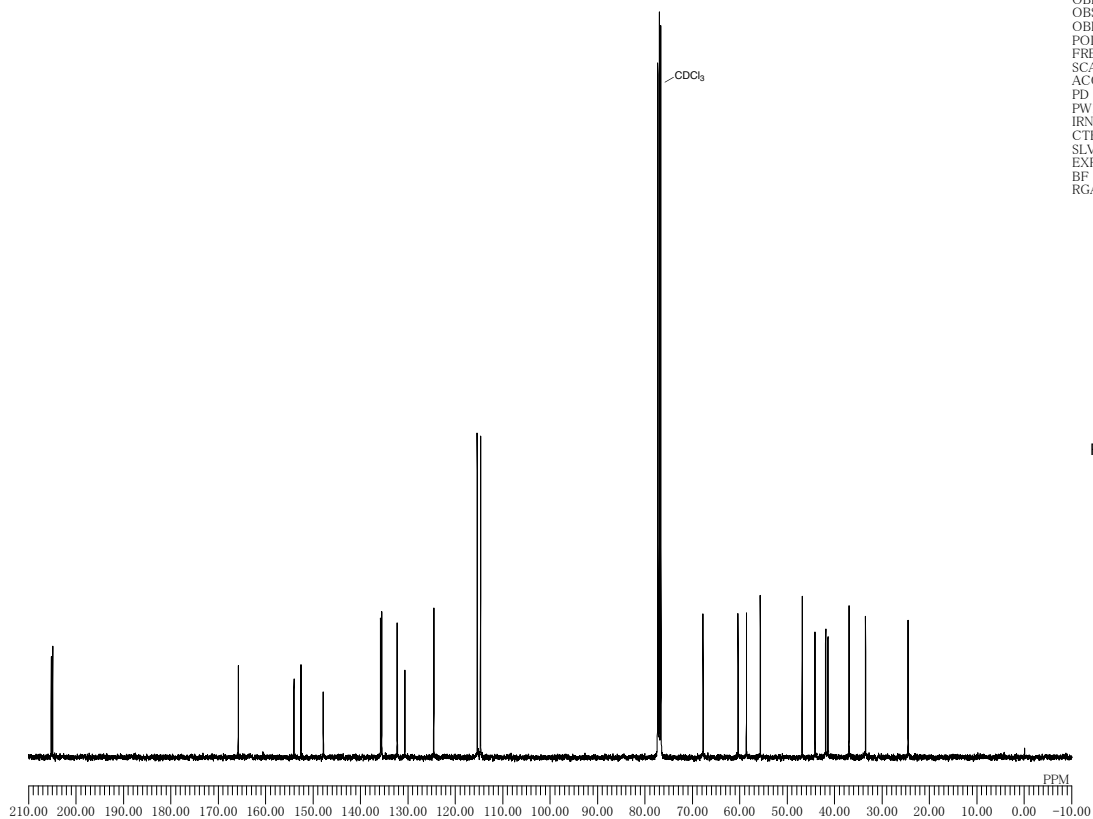
DFILE YO-5-105 overnight_bcm-1-1.als
 COMNT 28-06-2015 16:03:35
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26214
 POINT 25125.63 Hz
 FREQU 1024
 SCANS 1.0433 sec
 ACQTM 1.5000 sec
 PD 2.87 usec
 PW1 1H
 IRNLC 25.1 c
 CTEMP CDCL3
 SLVNT 77.00 ppm
 EXREF 2.02 Hz
 BF 50
 RGAIN



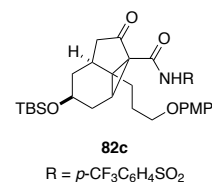
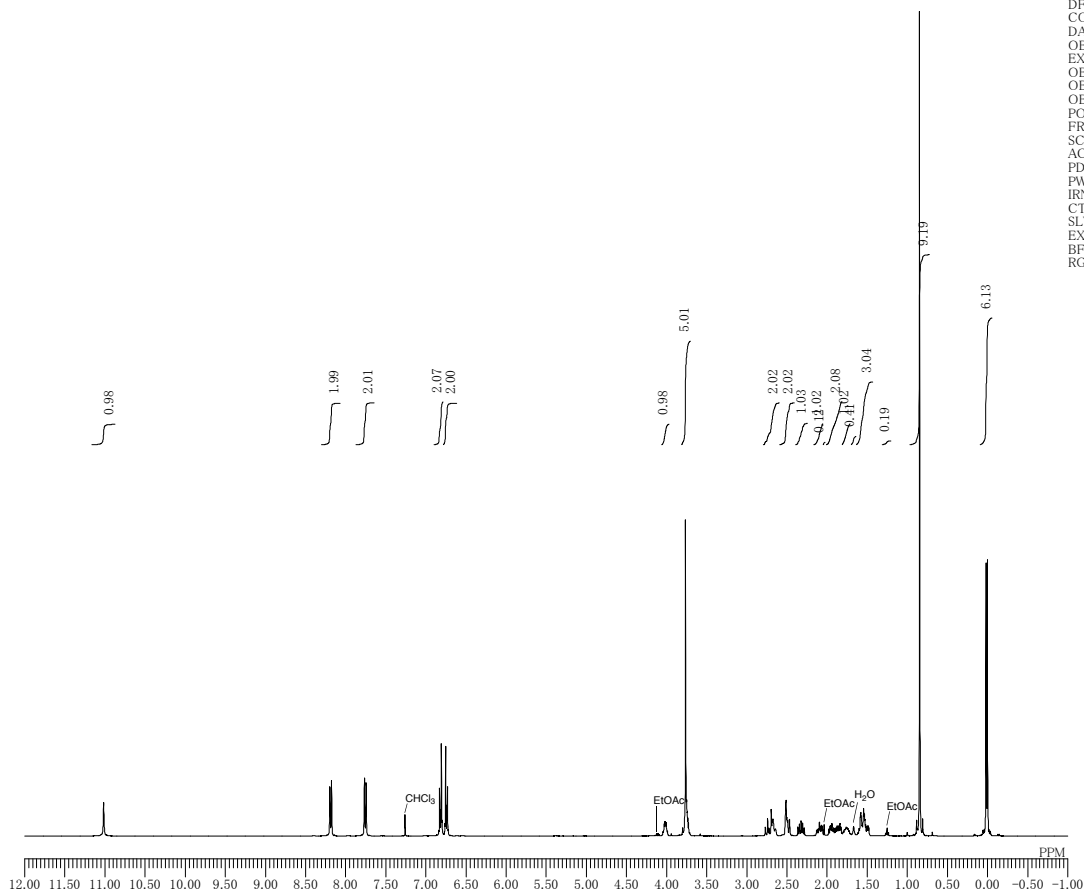
DFILE YO-5-107-2.non-data-1-1.als
 COMNT
 DATIM 29-06-2015 21:46:31
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 36



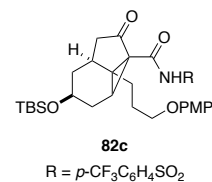
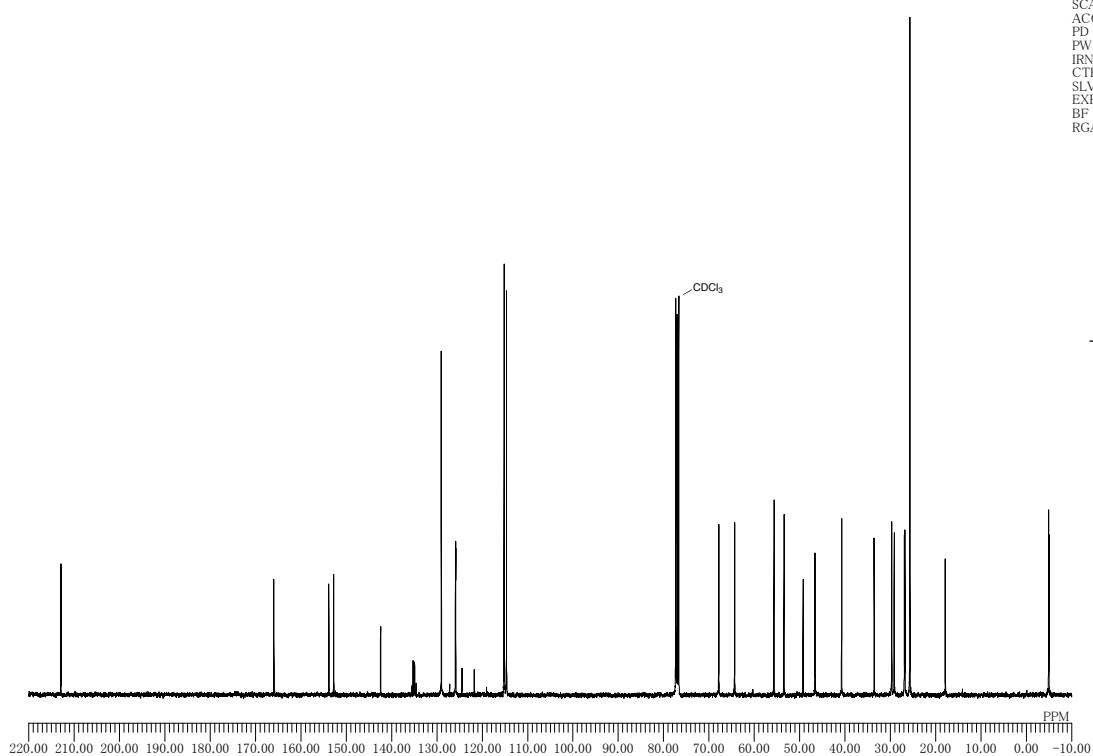
DFILE YO-5-107 overnight_bcm-3-1.als
 COMNT
 DATIM 01-07-2015 00:02:50
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



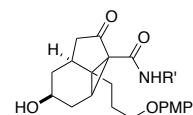
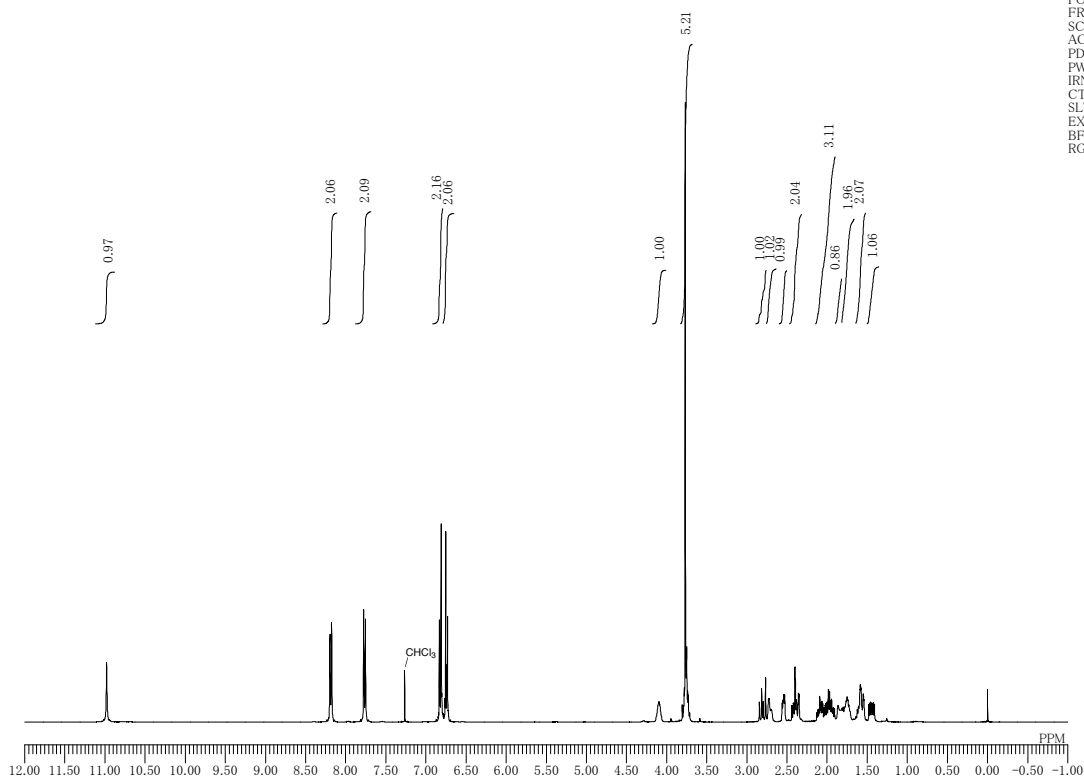
DFILE YO-5-103.non-data-1-1.als
 COMNT 27-06-2015 16:42:47
 DATIM 1H
 OBNUC single_pulse.jxp
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT 6002.40 Hz
 FREQU 8
 SCANS 2.1837 sec
 ACQTM 5.0000 sec
 PD 4.90 usec
 PW1 1H
 IRNLC 25.1 c
 CTEMP CDCL3
 SLVNT 7.26 ppm
 EXREF BF
 0.12 Hz
 RGAIN 26



DFILE YO-5-103 overnight_bcm-1-1.als
 COMNT 28-06-2015 07:02:42
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26214
 POINT 25125.63 Hz
 FREQU 1024
 SCANS 1.0433 sec
 ACQTM 1.5000 sec
 PD 2.87 usec
 PW1 1H
 IRNLC 25.2 c
 CTEMP CDCL3
 SLVNT 77.00 ppm
 EXREF BF
 2.02 Hz
 RGAIN 50

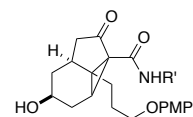
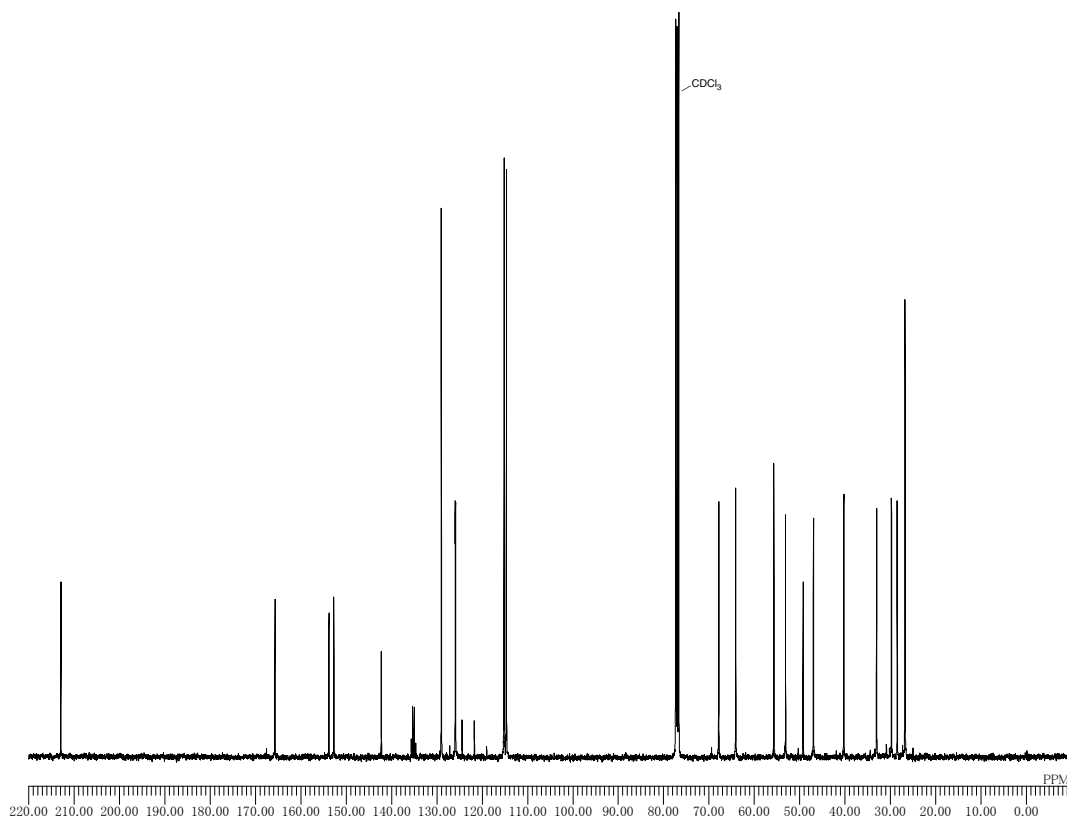


DFILE YO-5-108.non-data-2-1.als
 COMNT
 DATIM 30-06-2015 21:05:56
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNLC ¹H
 CTEMP 25.0 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



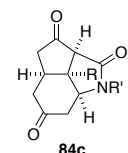
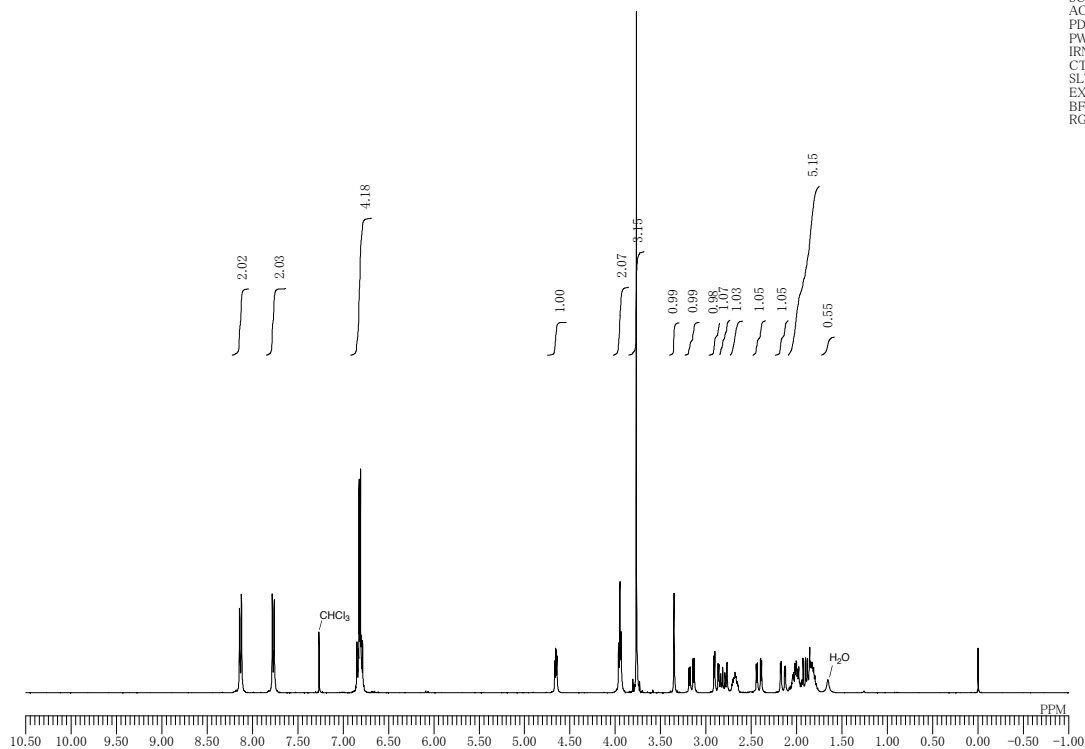
83c
 $R' = p\text{-CF}_3\text{C}_6\text{H}_4\text{SO}_2$

DFILE YO-5-108 overnight_bcm-1-1.als
 COMNT
 DATIM 03-07-2015 00:03:15
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNLC ¹H
 CTEMP 25.2 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 2.52 Hz
 RGAIN 50



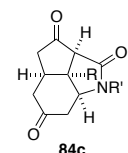
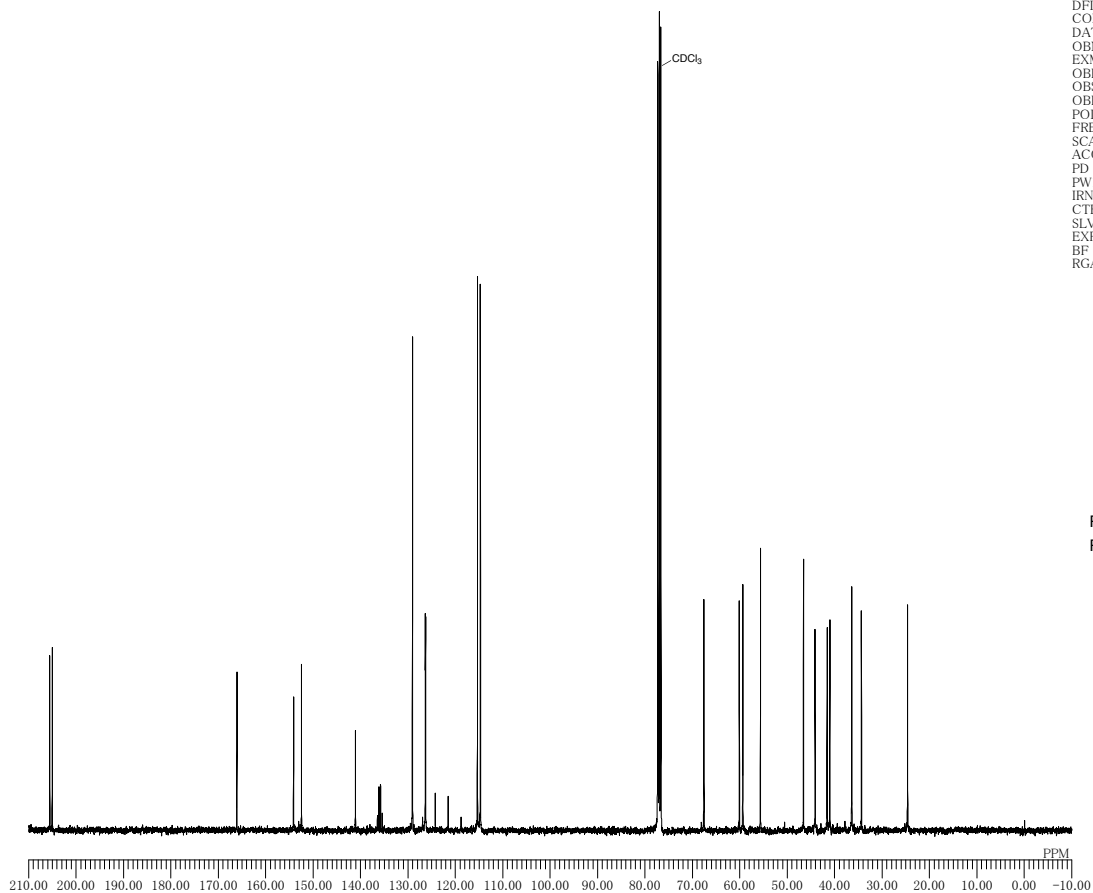
83c
 $R' = p\text{-CF}_3\text{C}_6\text{H}_4\text{SO}_2$

DFILE YO-5-109.non-data-1-1.als
 COMNT
 DATIM 01-07-2015 21:31:11
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 34



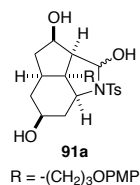
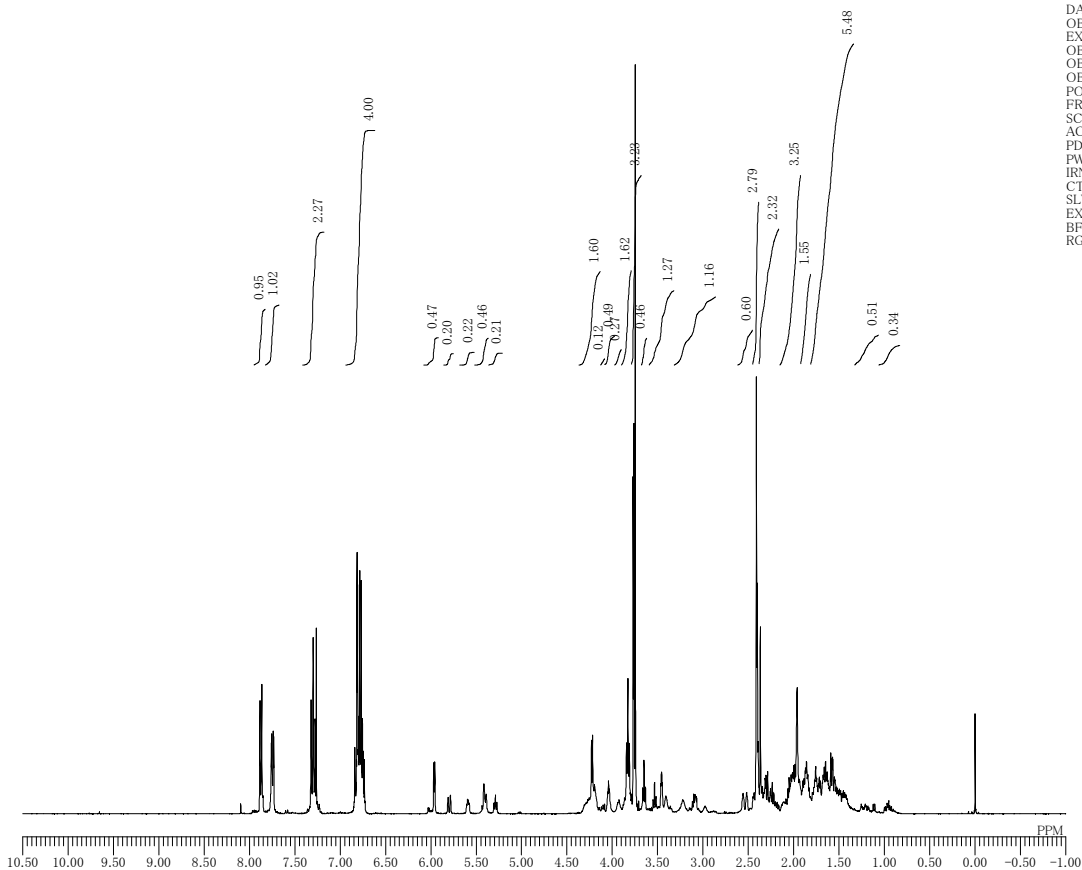
R = $-(\text{CH}_2)_3\text{OPMP}$
 R' = $p\text{-CF}_3\text{C}_6\text{H}_4\text{SO}_2$

DFILE YO-5-109 overnight_bcm-1-1.als
 COMNT
 DATIM 05-07-2015 00:03:16
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

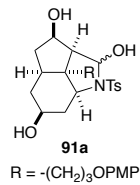
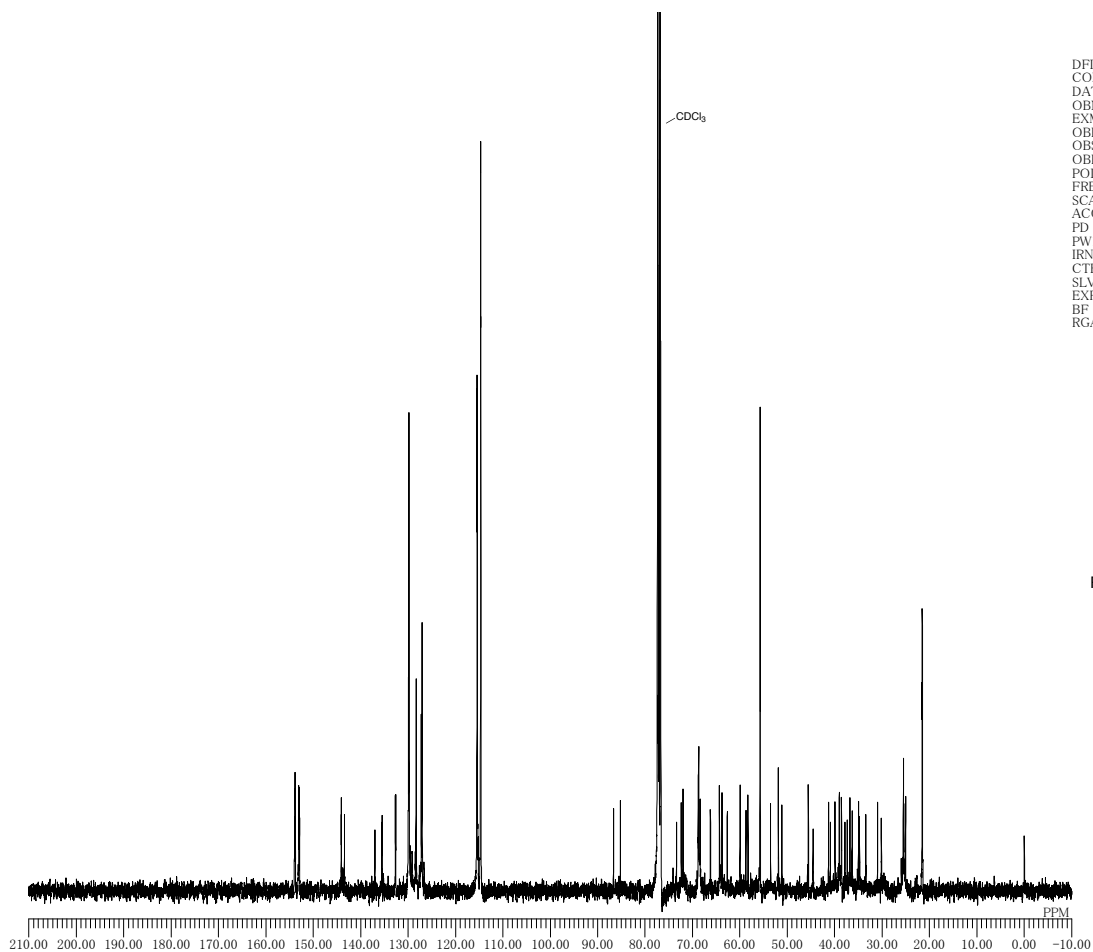


R = $-(\text{CH}_2)_3\text{OPMP}$
 R' = $p\text{-CF}_3\text{C}_6\text{H}_4\text{SO}_2$

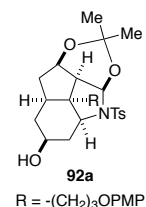
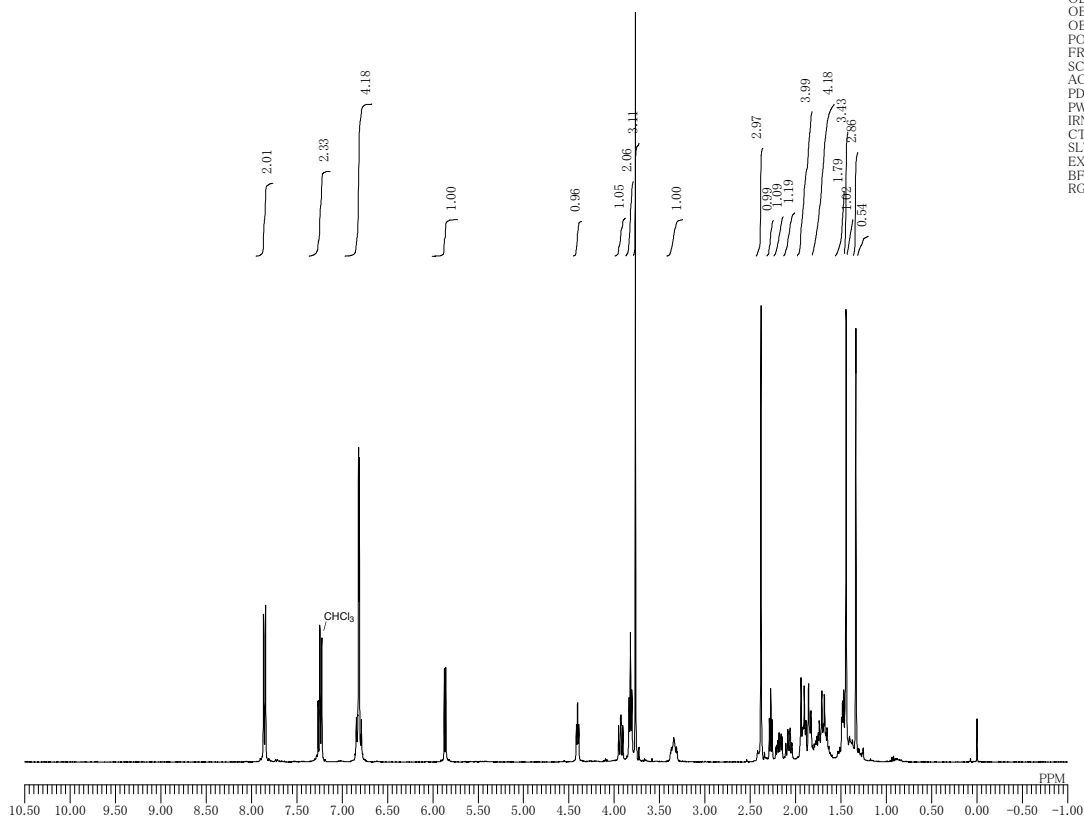
DFILE YO-5-113.non-data-2-1.als
 COMNT 04-07-2015 13:29:19
 DATIM 1H
 OBNUC single_pulse.jxp
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT 6002.40 Hz
 FREQU 8
 SCANS 2.1837 sec
 ACQTM 5.0000 sec
 PD 4.90 usec
 PW1 1H
 IRNUC 25.1 c
 CTEMP CDCL3
 SLVNT 0.00 ppm
 EXREF BF 0.12 Hz
 RGAIN 30



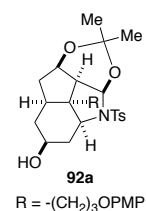
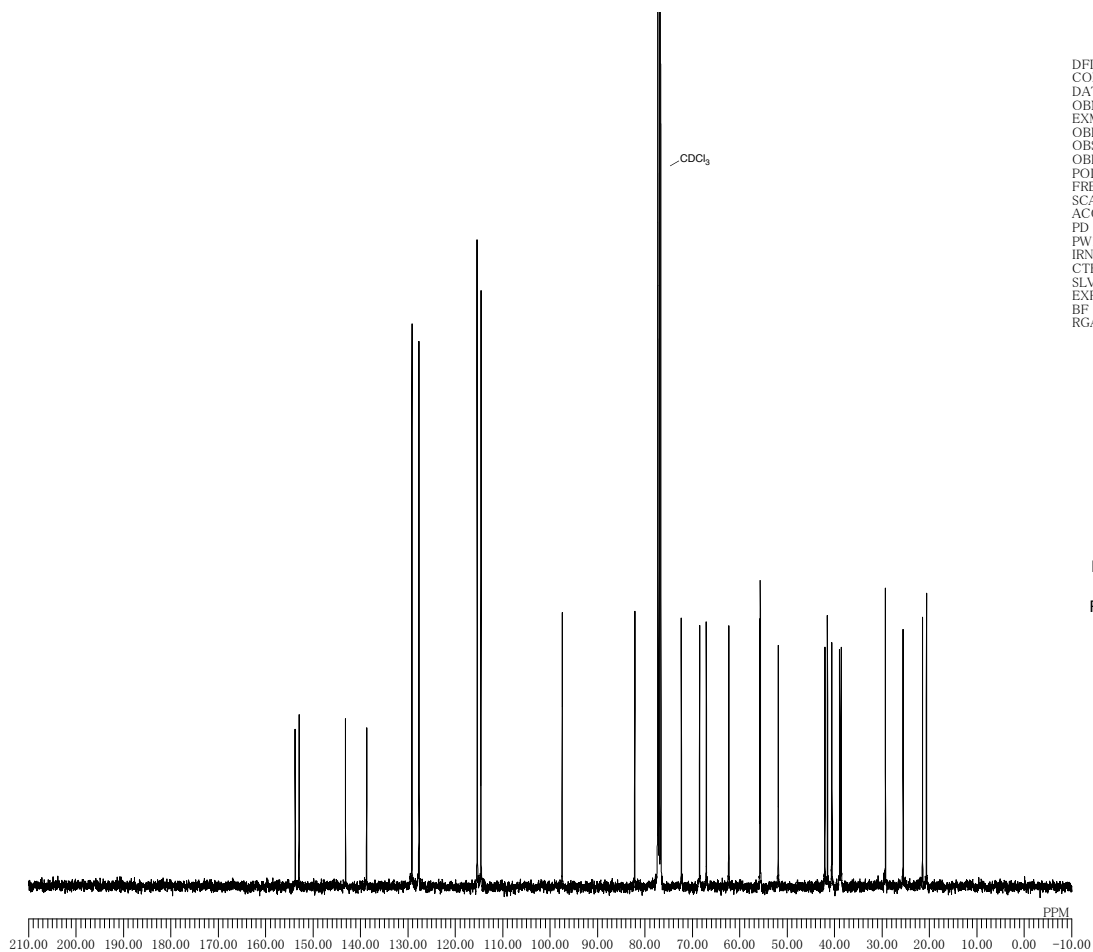
DFILE YO-5-113 2 overnight_bcm-1-1.als
 COMNT 30-08-2015 18:02:22
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26214
 POINT 25125.63 Hz
 FREQU 4096
 SCANS 1.0433 sec
 ACQTM 1.5000 sec
 PD 2.87 usec
 PW1 1H
 IRNUC 25.3 c
 CTEMP CDCL3
 SLVNT 0.00 ppm
 EXREF BF 2.02 Hz
 RGAIN 50



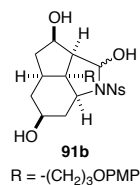
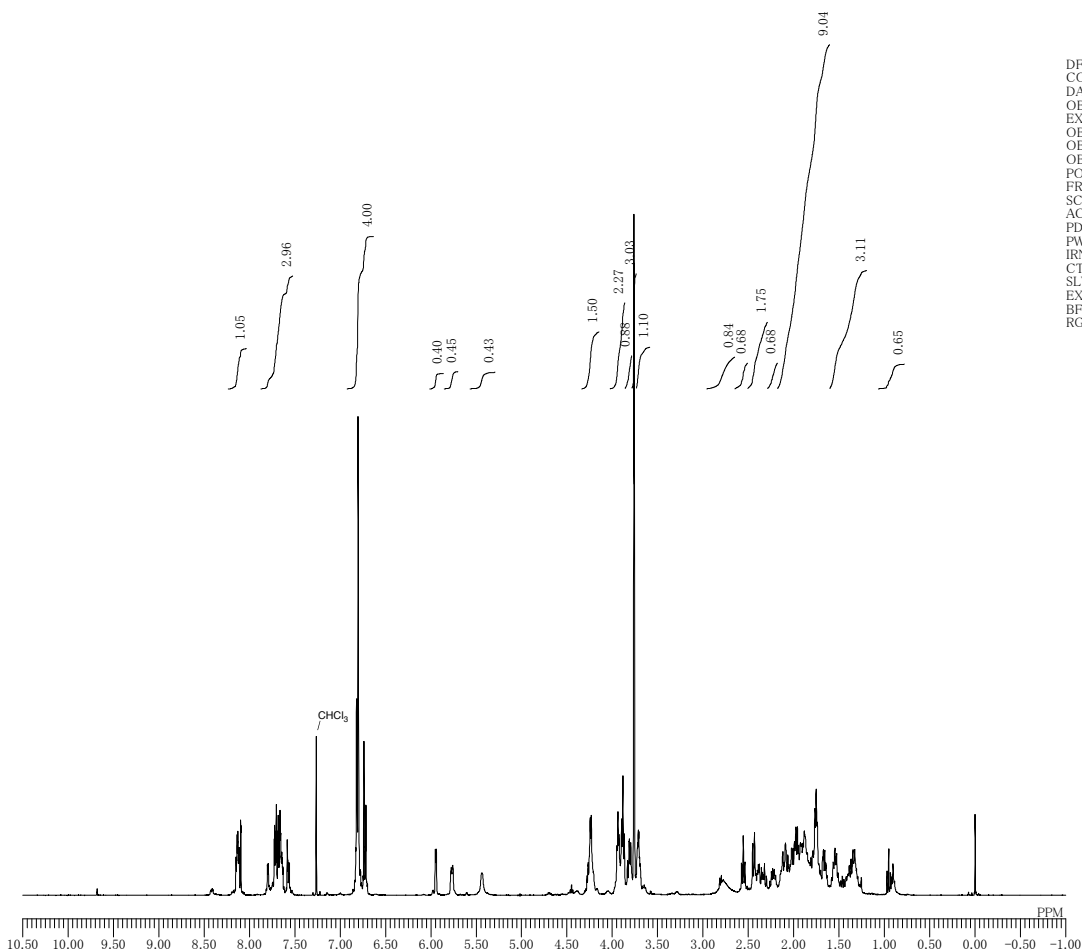
DFILE YO-5-114.non-data-2-1.als
 COMNT
 DATIM 04-07-2015 13:34:10
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSEF 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.1 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



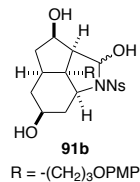
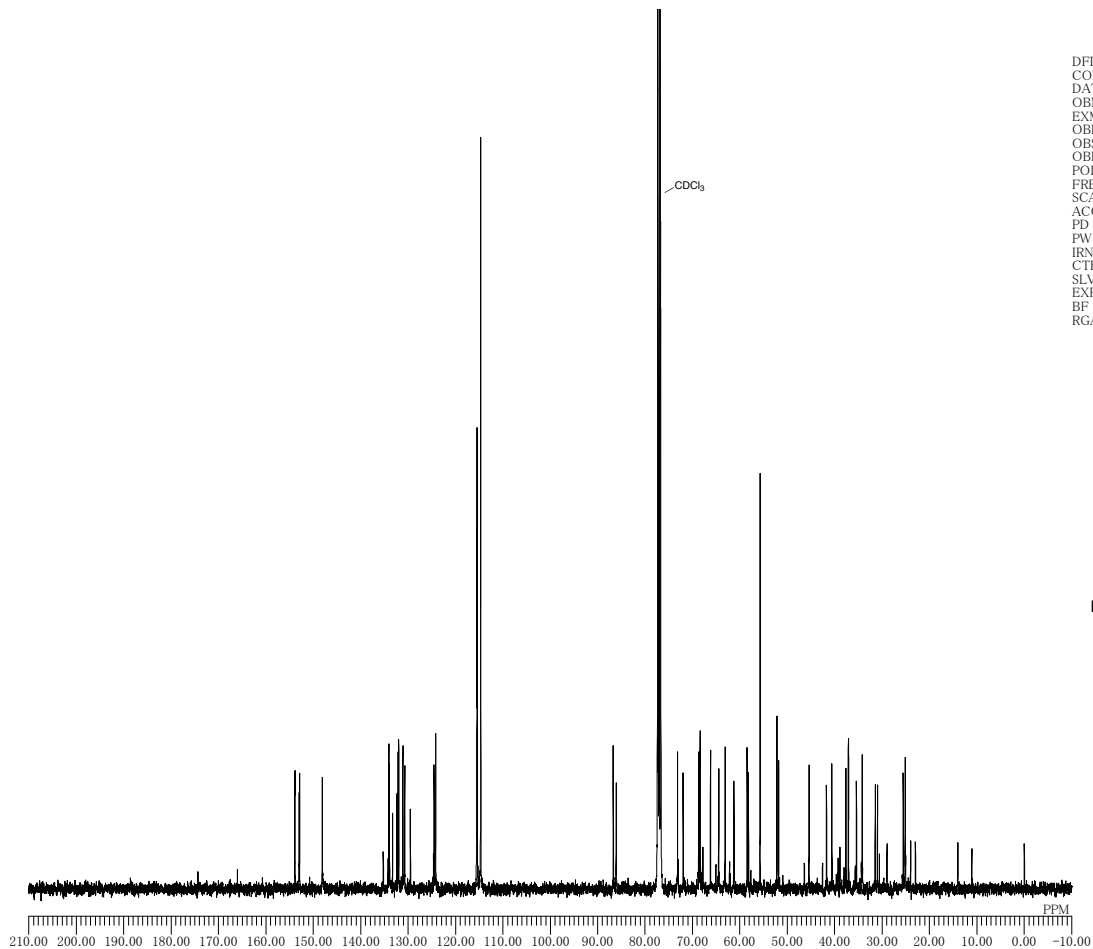
DFILE YO-5-114 overnight_bcm-1-1.als
 COMNT
 DATIM 05-07-2015 12:03:58
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSEF 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 1024
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹H
 CTEMP 25.0 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



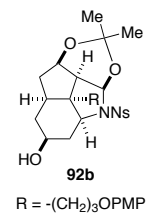
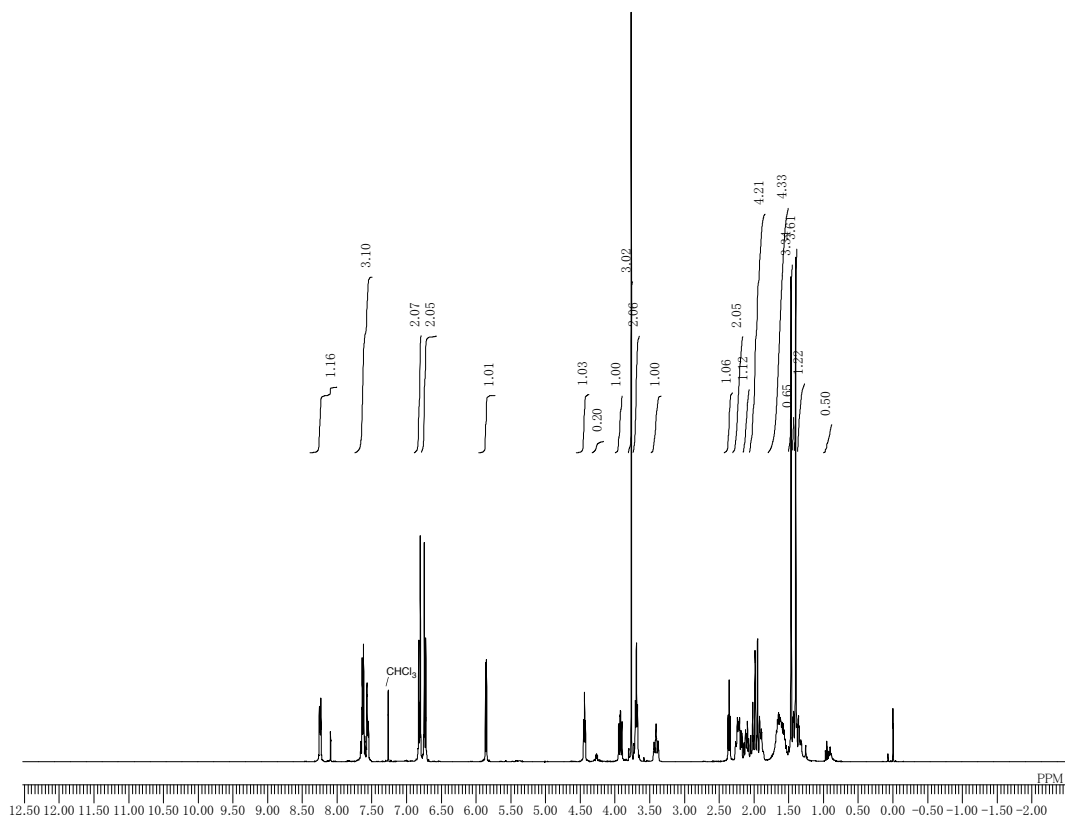
DFILE YO-5-115.non-data-2-1.als
 COMNT
 DATIM 04-07-2015 13:39:13
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNLC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 32



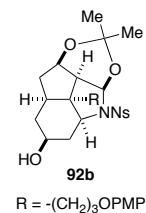
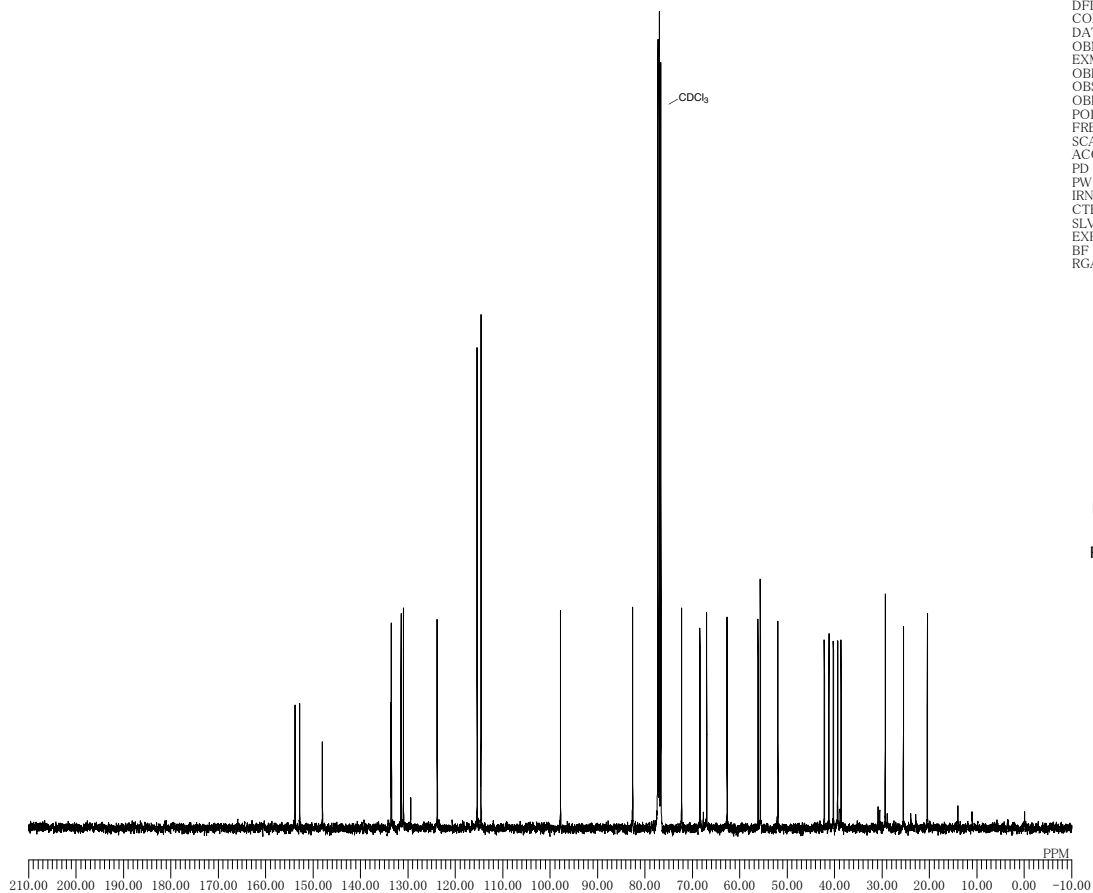
DFILE YO-5-115 2 overnight_bcm-1-1.als
 COMNT
 DATIM 01-09-2015 00:02:14
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNLC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 2.02 Hz
 RGAIN 50



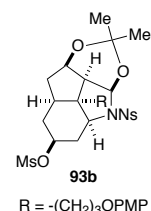
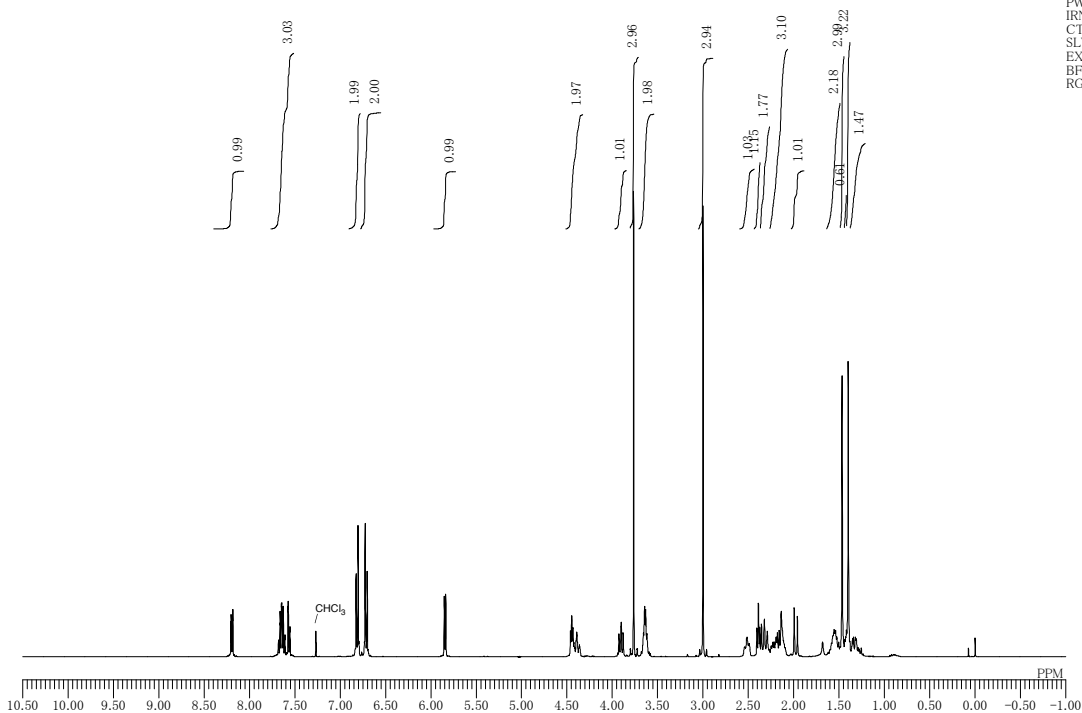
DFILE YO-5-116.non-data-1-1.als
 COMNT
 DATIM 03-07-2015 20:28:12
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



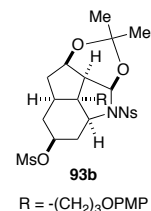
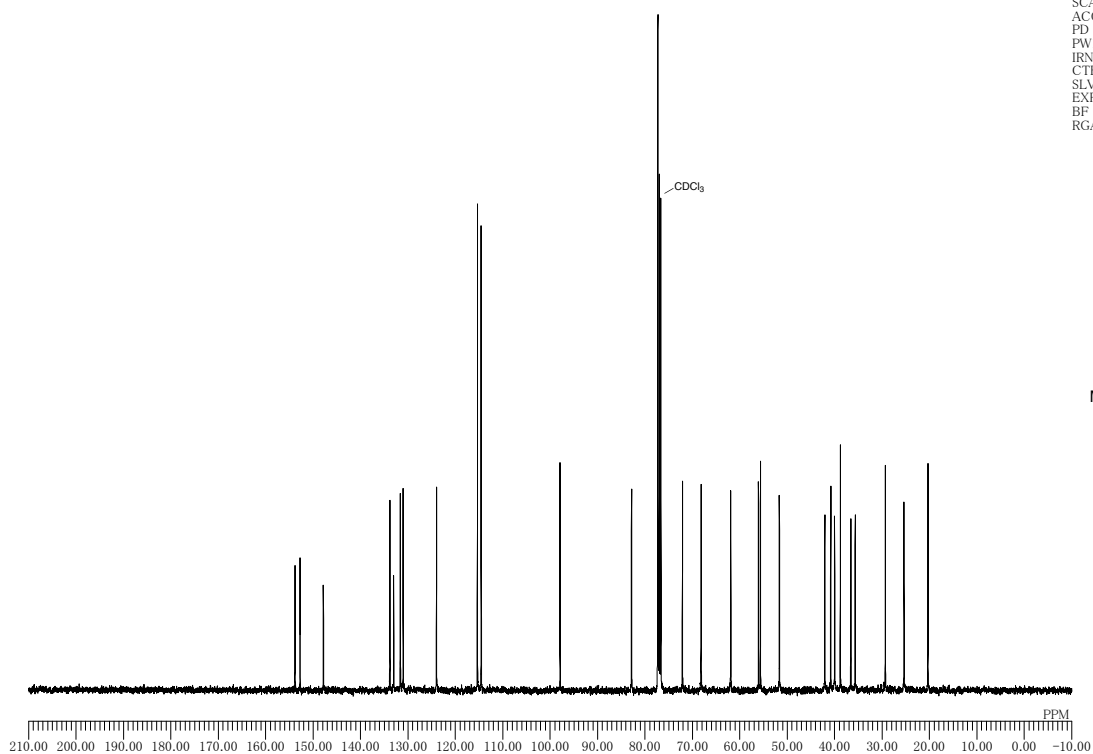
DFILE YO-5-116 overnight_bcm-1-1.als
 COMNT
 DATIM 05-07-2015 07:33:27
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 1024
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



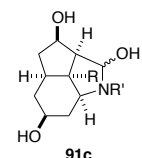
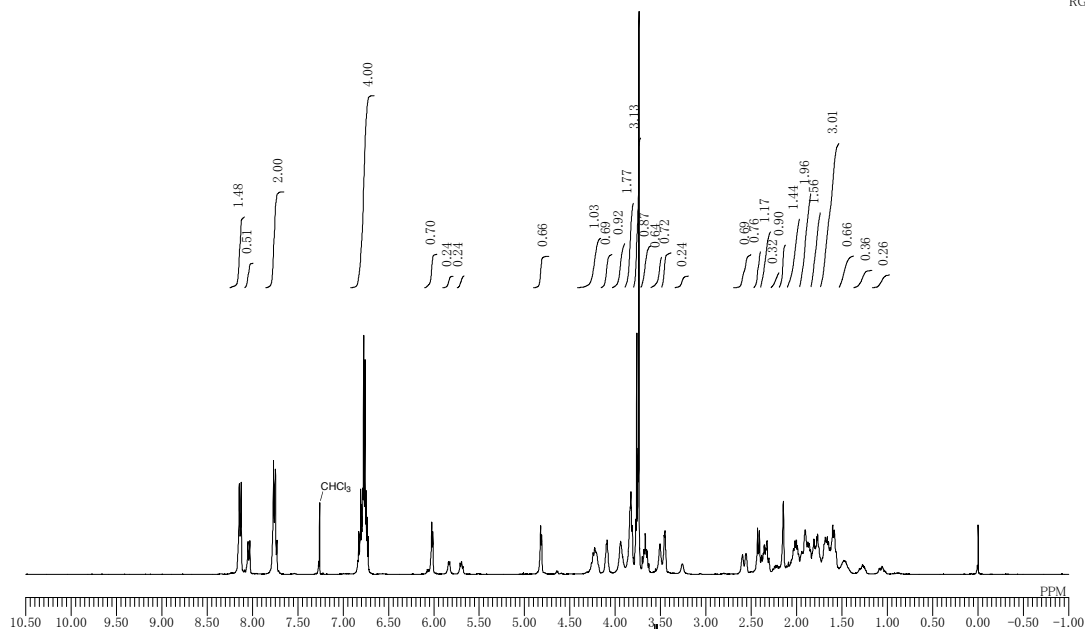
DFILE YO-5-117.non-data-1-1.als
 COMNT
 DATIM 03-07-2015 20:32:45
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNLC 1H
 CTEMP 25.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 26



DFILE YO-5-117 overnight_bcm-1-1.als
 COMNT
 DATIM 04-07-2015 19:02:32
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 1024
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNLC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

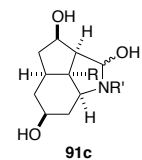
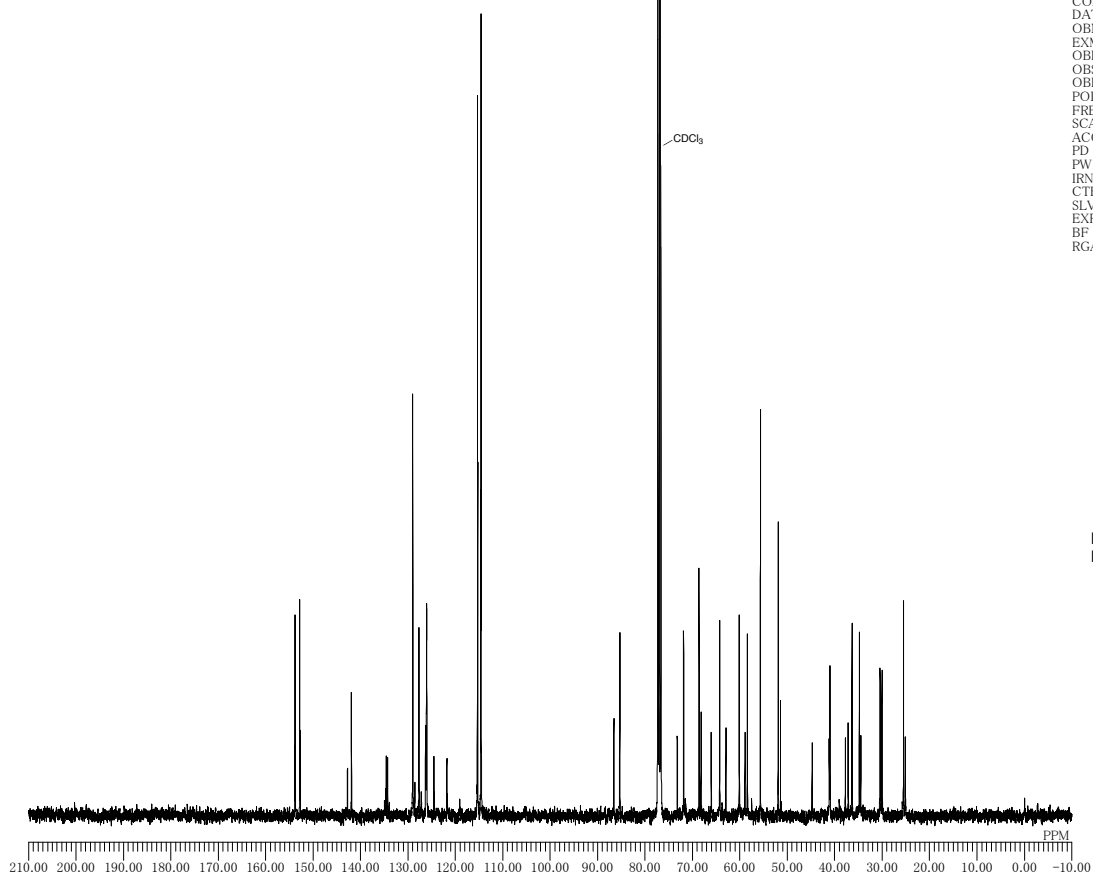


DFILE YO-5-118_non-data-2-1.als
 COMNT
 DATIM 06-07-2015 18:56:11
 OBNUC 1H
 EXMOD single_pulse.jsp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 30



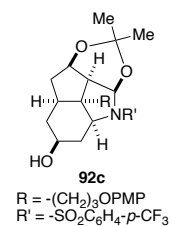
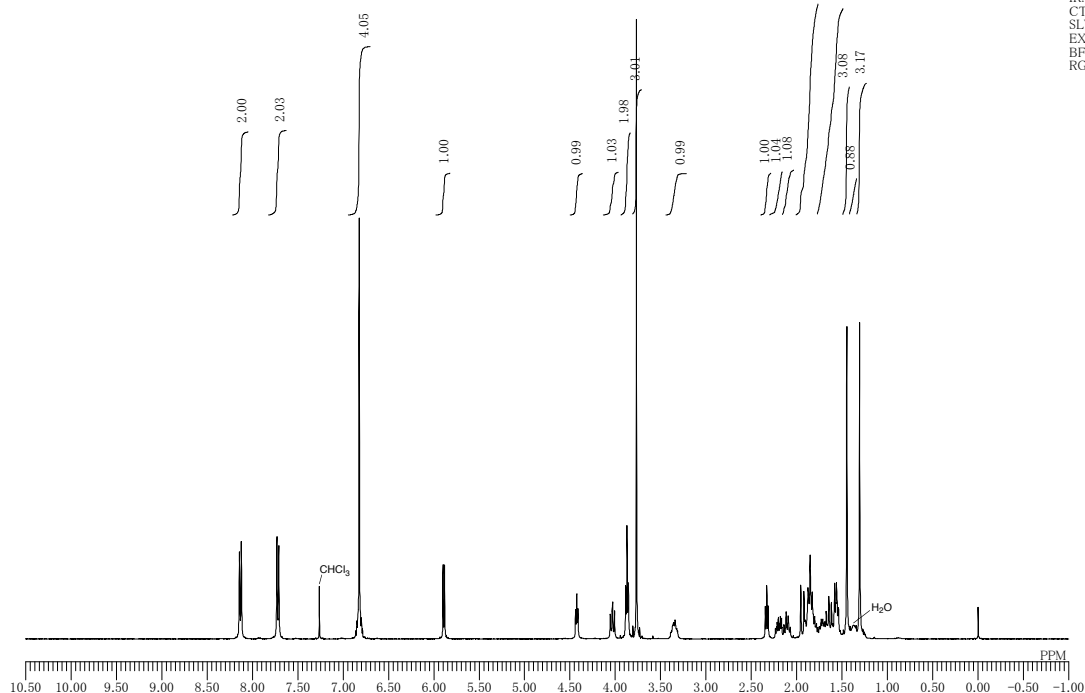
R = $-(CH_2)_3OPMP$
 R' = $-SO_2C_6H_4-p-CF_3$

DFILE YO-5-118 overnight_bcm-1-11-1.als
 COMNT
 DATIM 07-07-2015 00:02:08
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26224
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 50

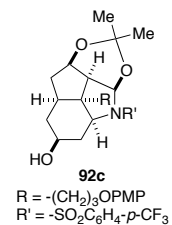
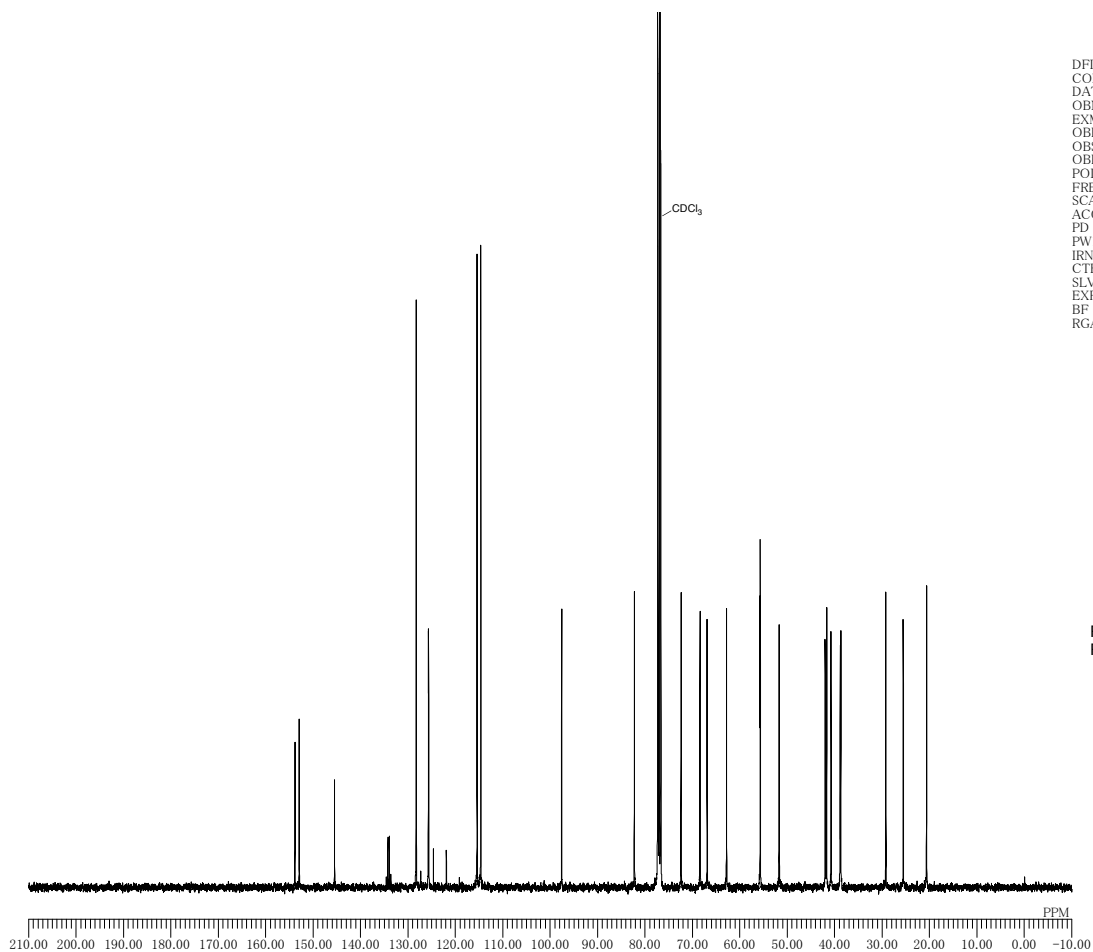


R = $-(CH_2)_3OPMP$
 R' = $-SO_2C_6H_4-p-CF_3$

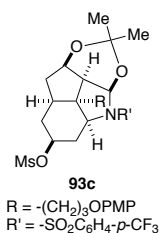
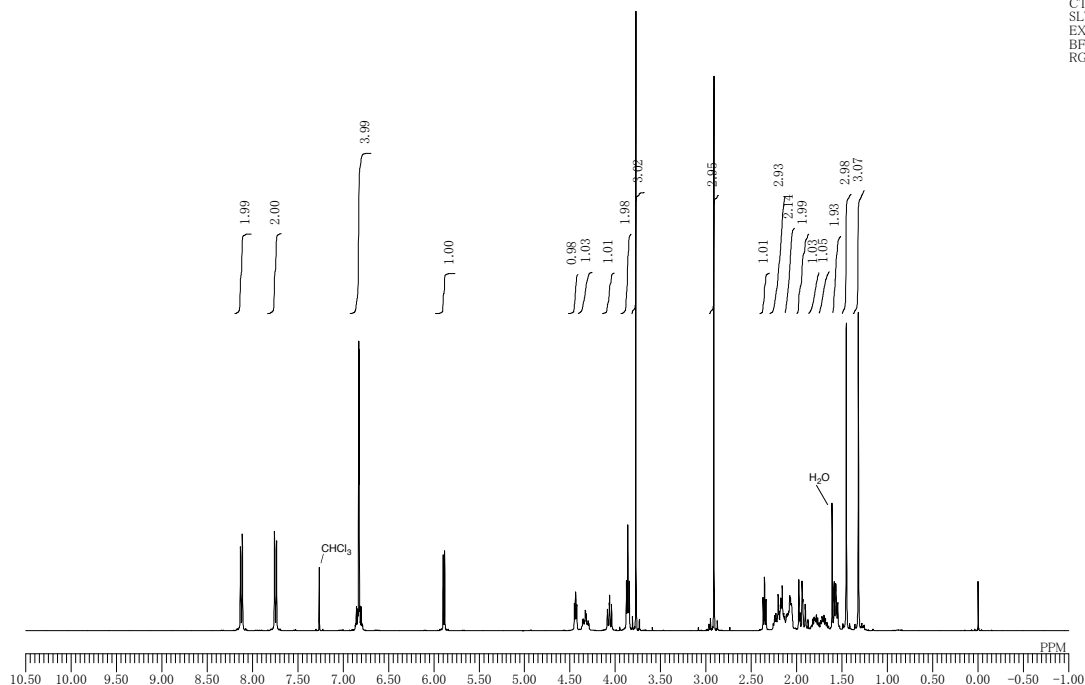
DFILE YO-5-119_non-data-1-1.als
 COMNT
 DATIM 07-07-2015 21:16:13
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.10 Hz
 RGAIN 30



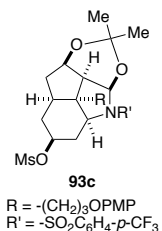
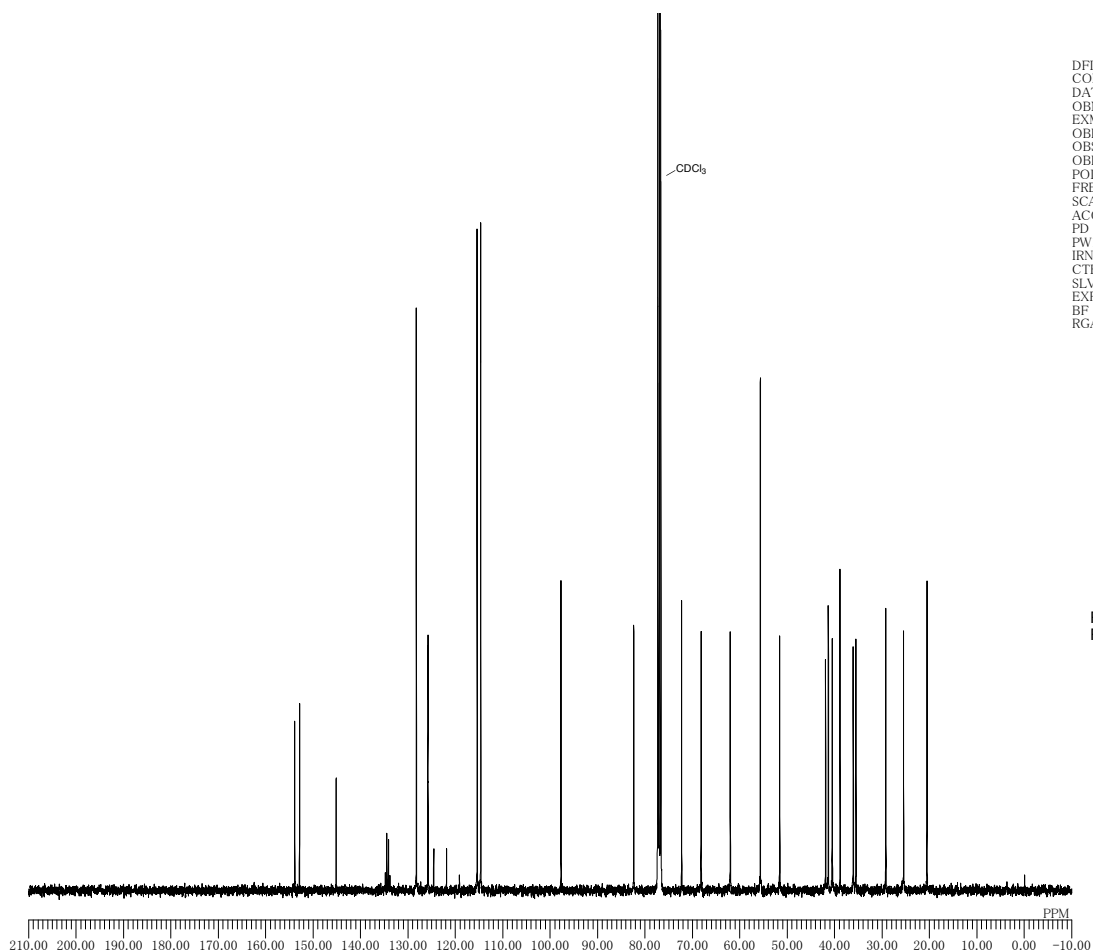
DFILE YO-5-119 overnight_bcm-1-1.als
 COMNT
 DATIM 08-07-2015 00:02:58
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



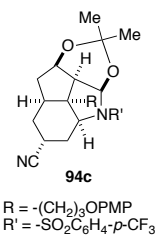
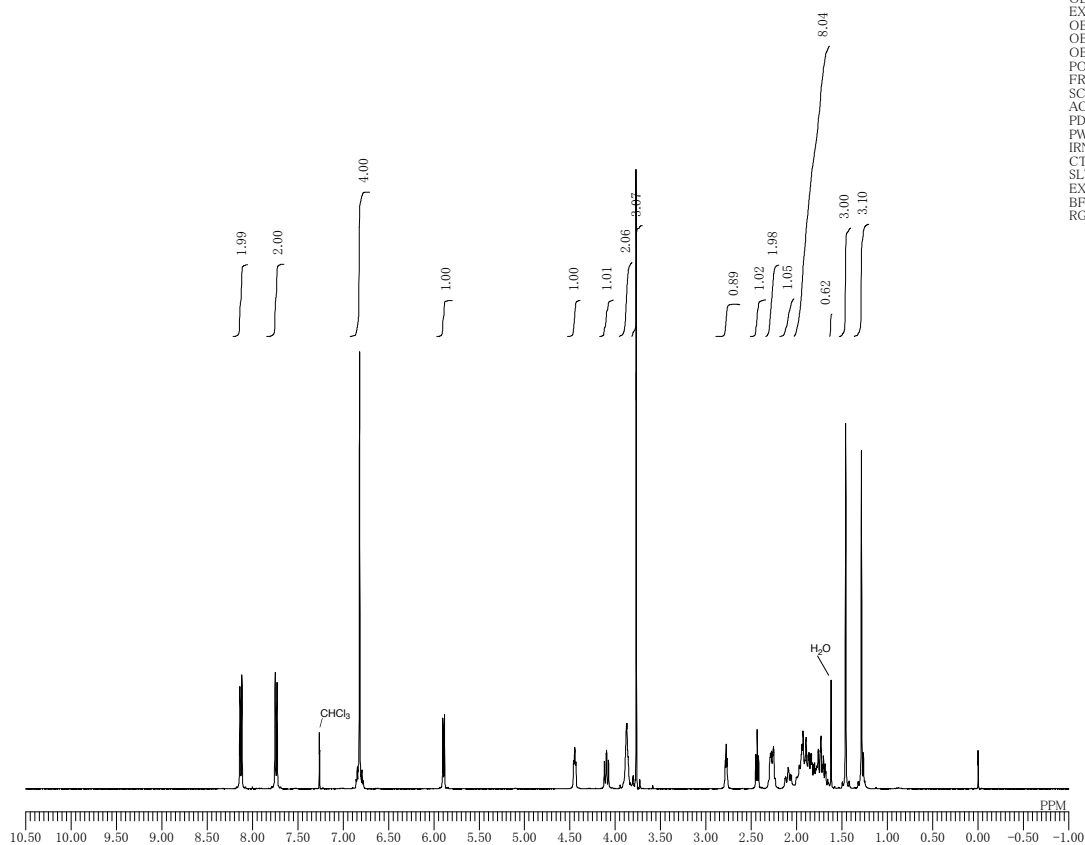
DFILE YO-5-124_non-data-1-1.als
 COMNT
 DATIM 09-07-2015 16:45:29
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.0 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 32



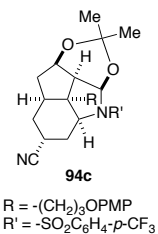
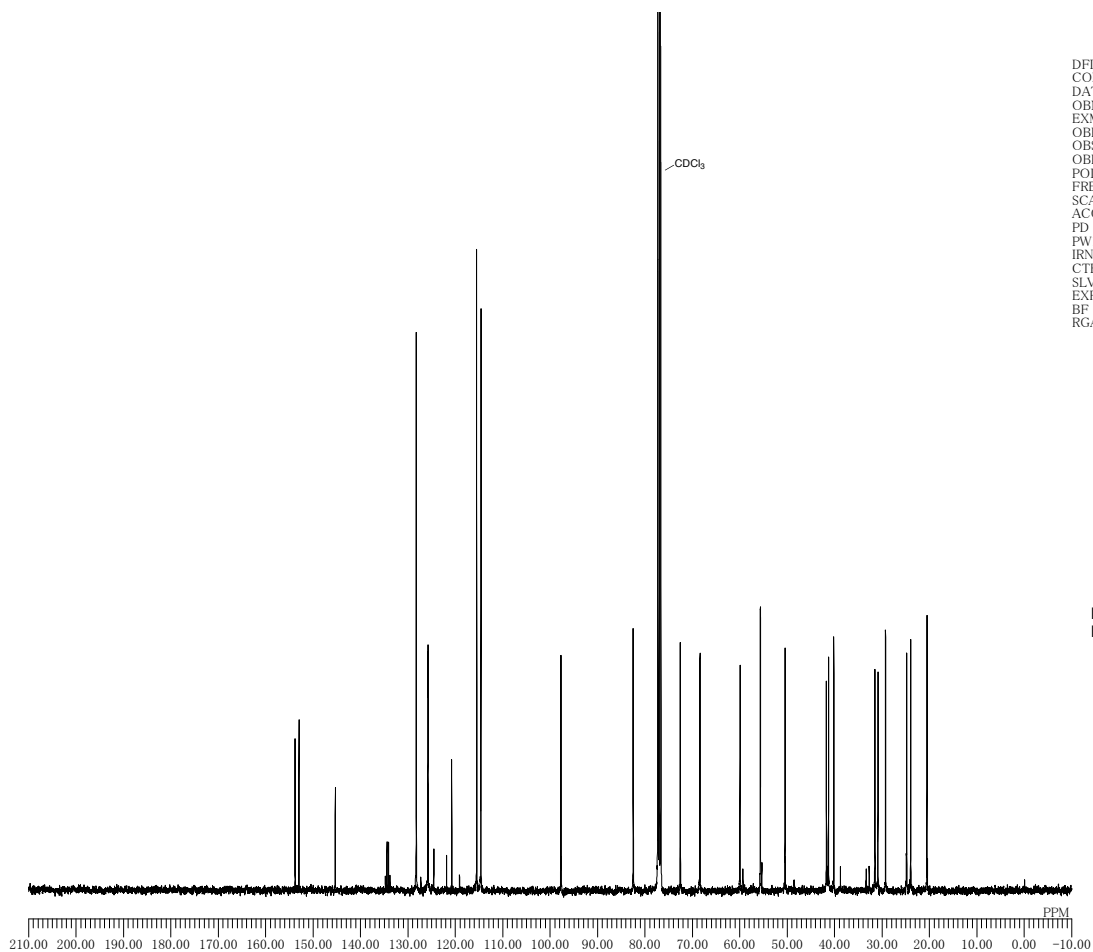
DFILE YO-5-124_overnight_bcm-1-1.als
 COMNT
 DATIM 10-07-2015 00:02:32
 OBNUC 13C
 EXMOD single_pulse_dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



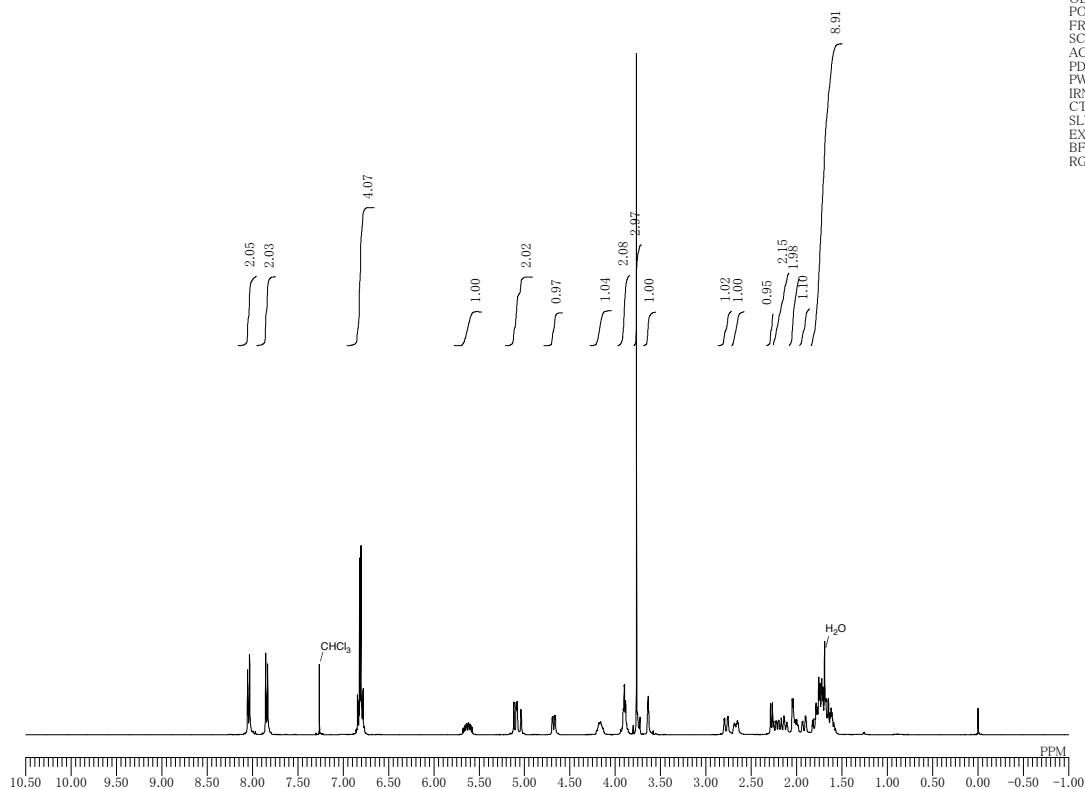
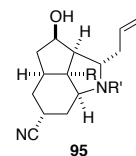
DFILE YO-5-126.non-data-1-1.als
 COMNT
 DATIM 09-07-2015 20:54:39
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.1 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



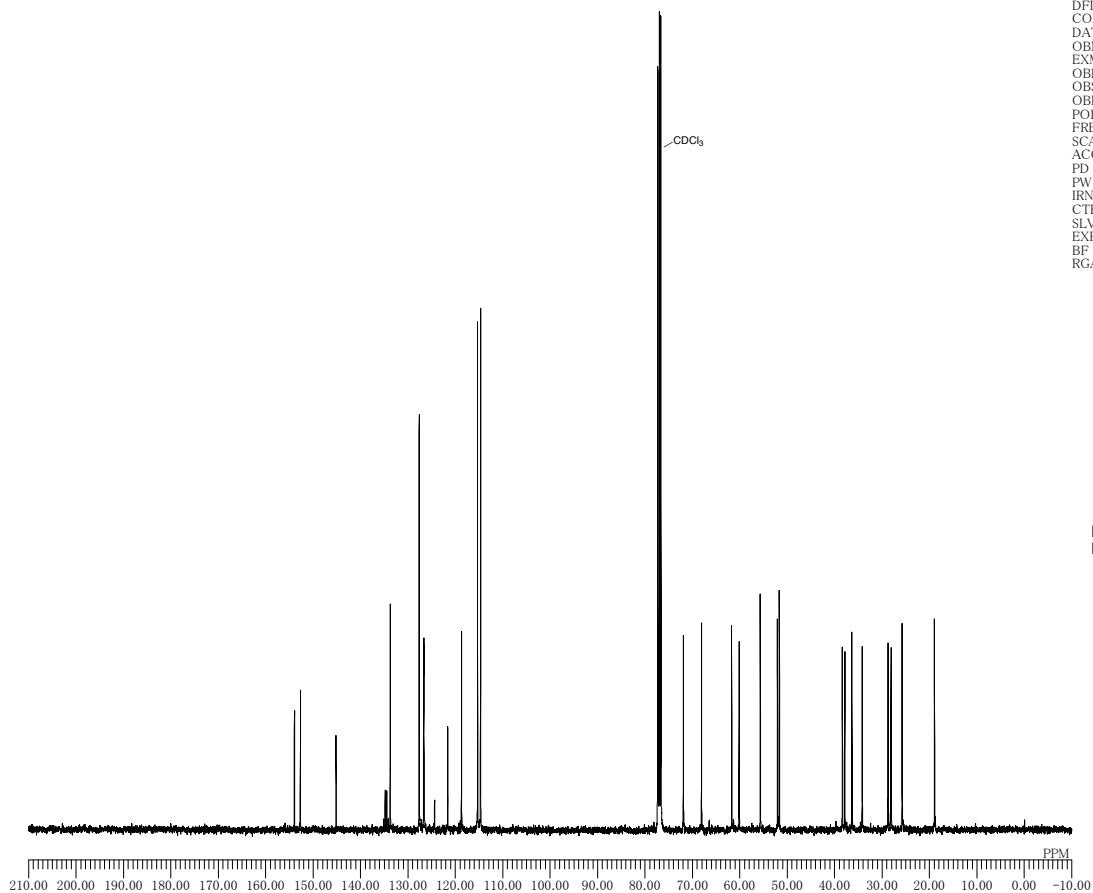
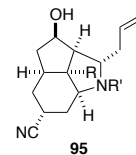
DFILE YO-5-126 overnight_bcm-1-1.als
 COMNT
 DATIM 11-07-2015 00:03:19
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹³C
 CTEMP 25.2 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



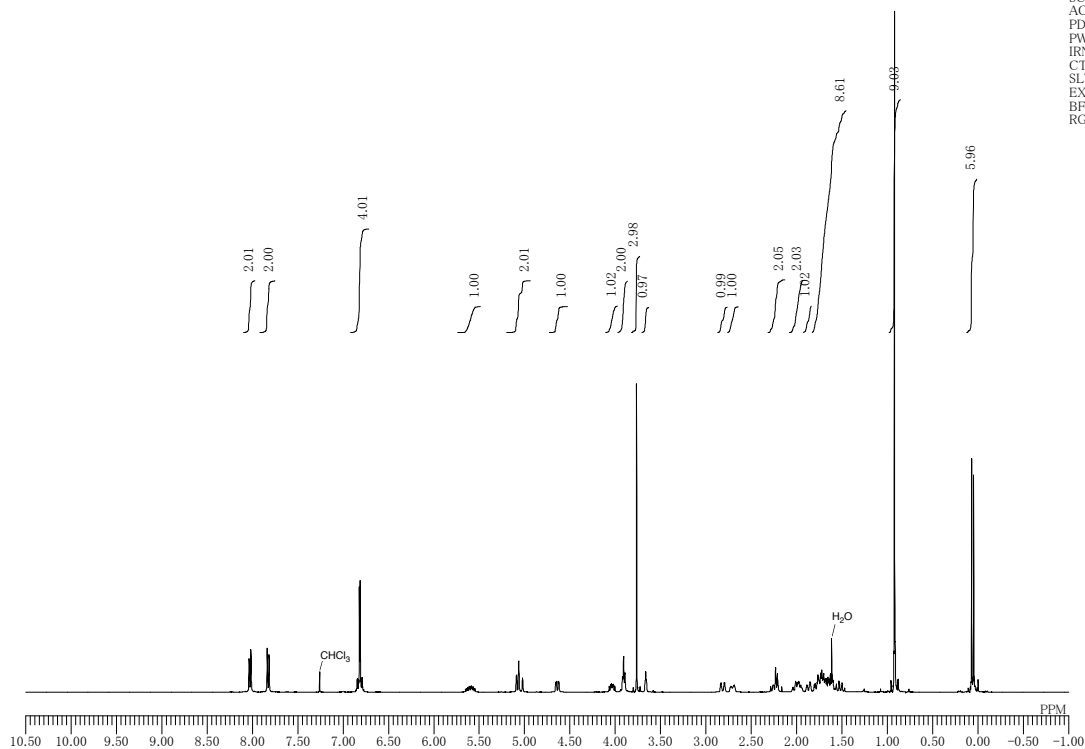
DFILE YO-5-130_non-data-1-1.als
 COMNT
 DATIM 13-07-2015 22:23:14
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.5 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



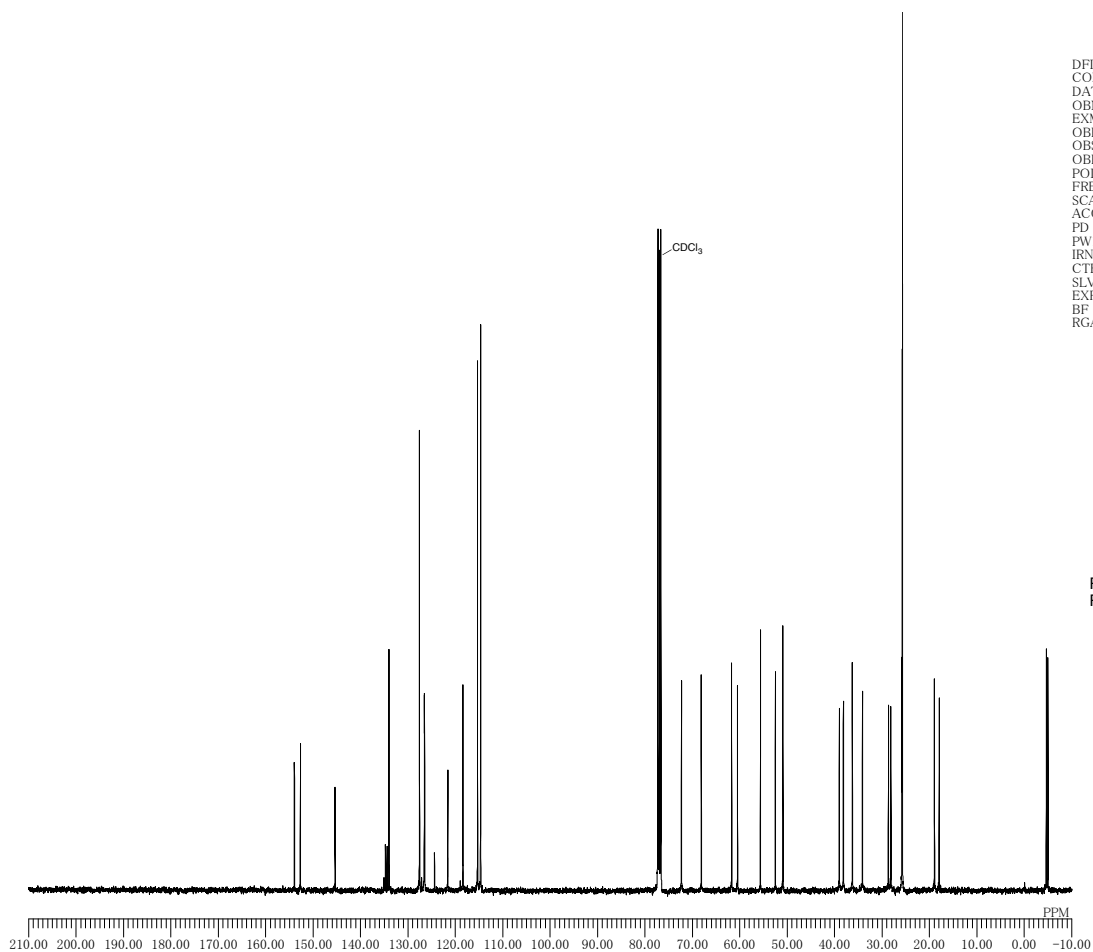
DFILE YO-5-130 overnight_bcm-1-1.als
 COMNT
 DATIM 14-07-2015 00:01:57
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.5 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



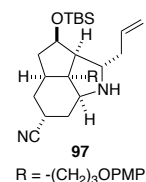
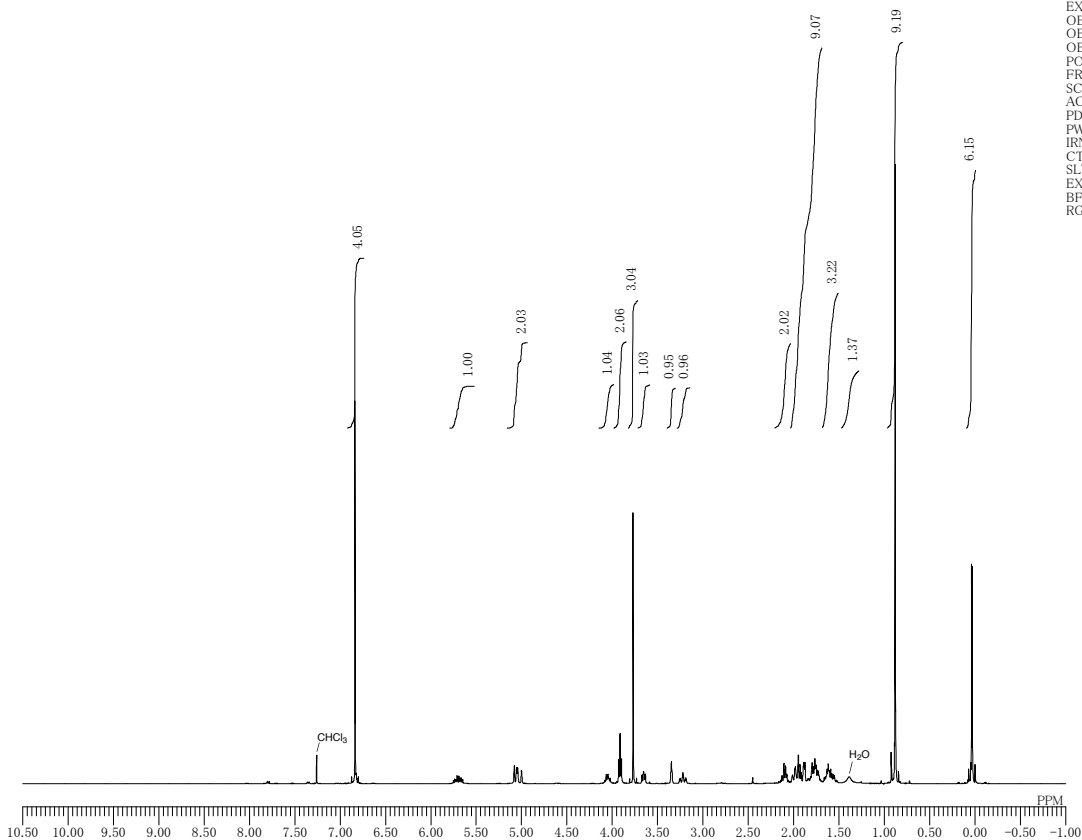
DFILE YO-5-133.non-data-1-1.als
 COMNT
 DATIM 14-07-2015 22:13:54
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.5 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 26



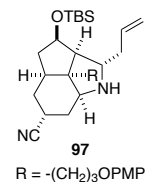
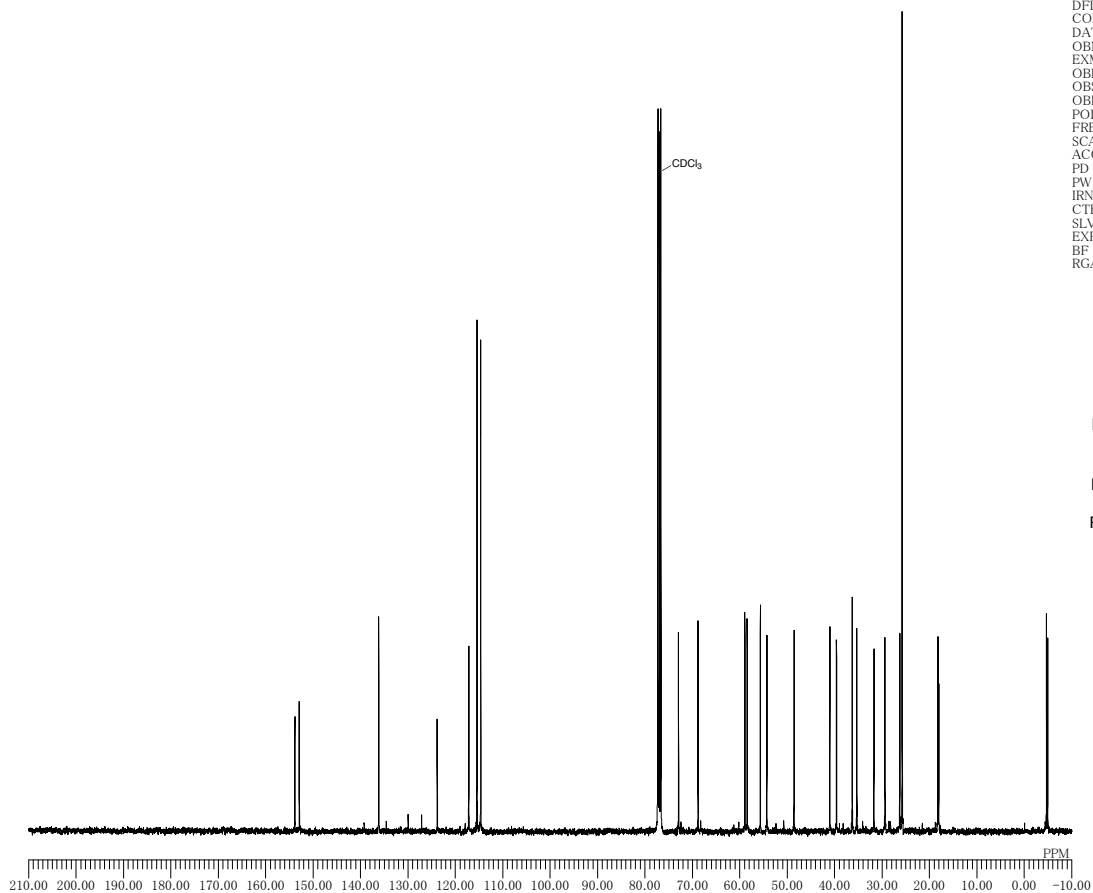
DFILE YO-5-133 overnight_bcm-1-1.als
 COMNT
 DATIM 15-07-2015 00:02:26
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.6 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



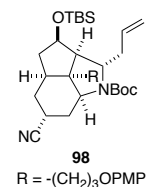
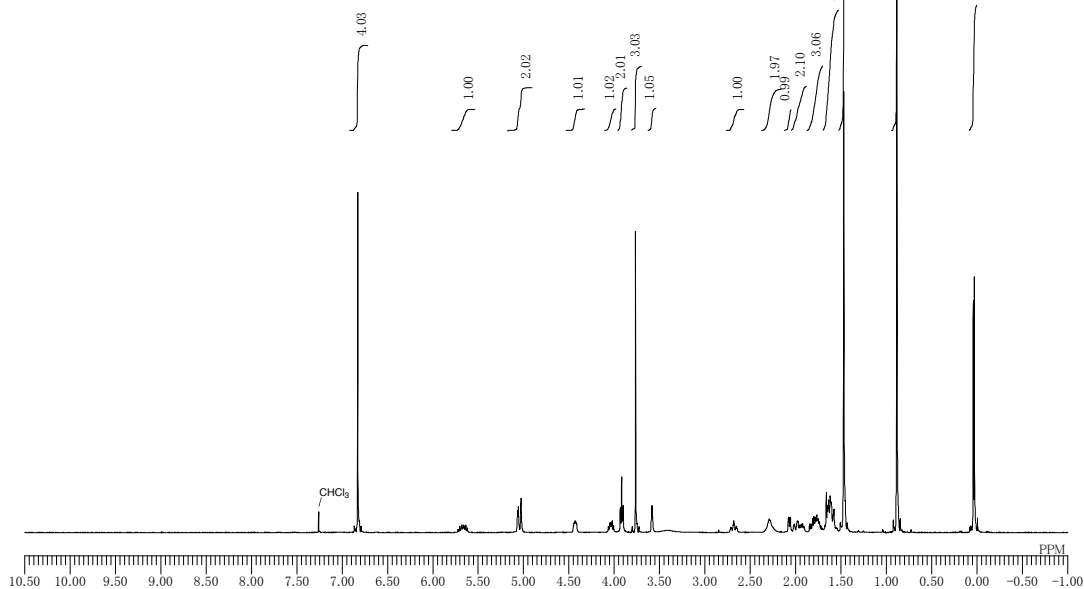
DFILE YO-5-135.non-data-1-1.als
 COMNT
 DATIM 15-07-2015 21:22:14
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.6 c
 SLVNT CDCL₃
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 30



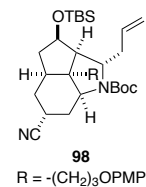
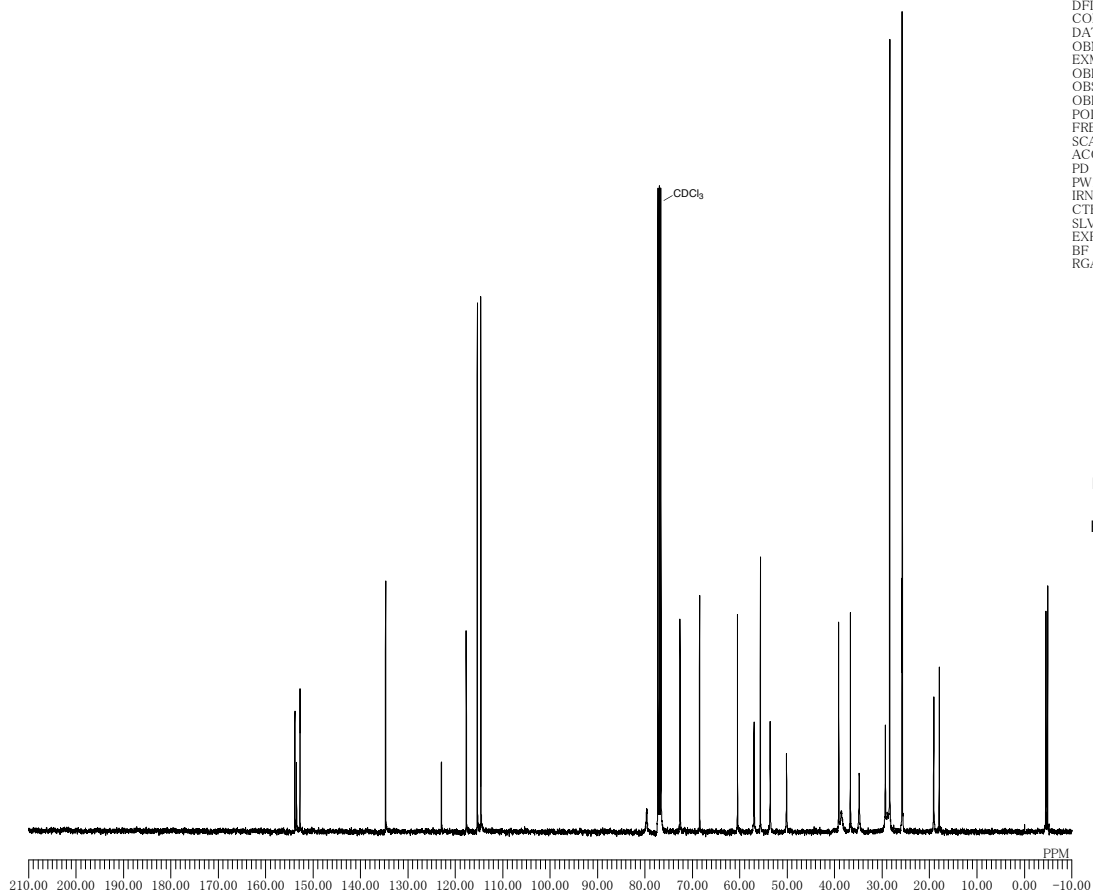
DFILE YO-5-135 overnight_bcm-1-1.als
 COMNT
 DATIM 16-07-2015 00:03:01
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹H
 CTEMP 25.6 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



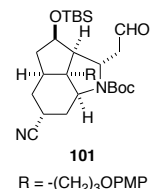
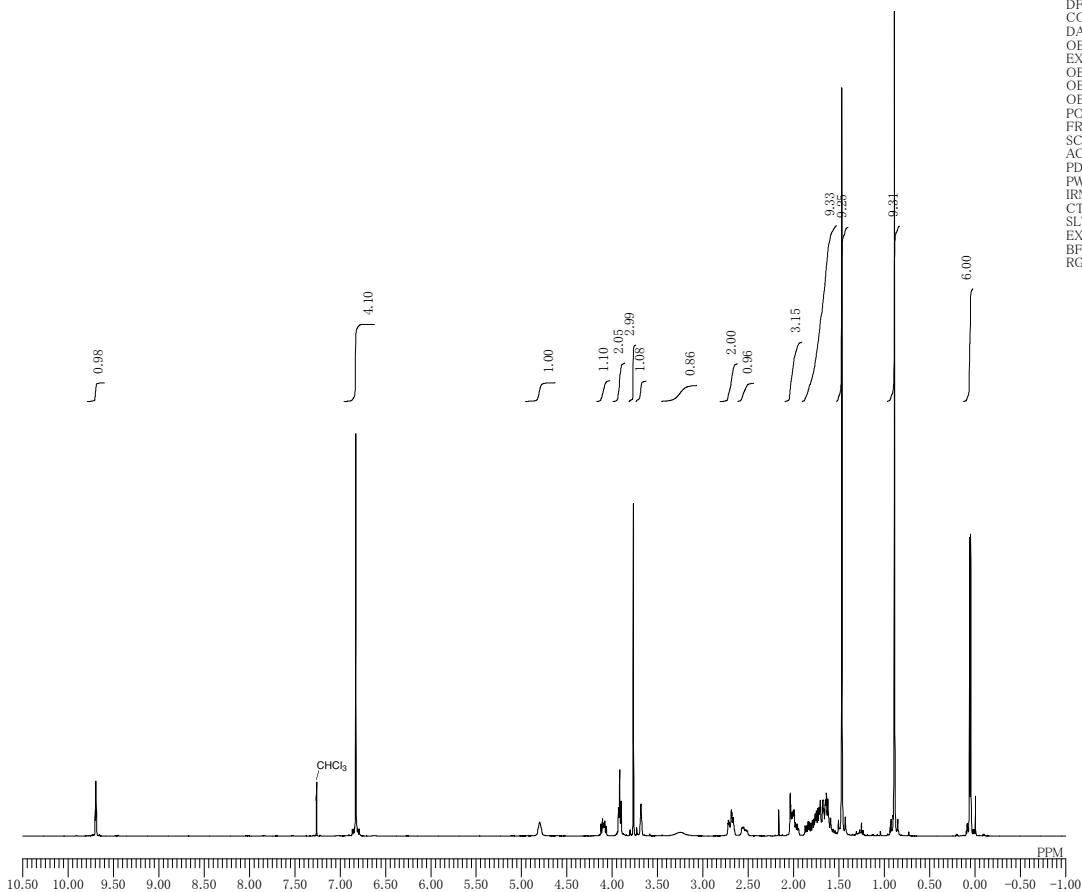
DFILE YO-5-138_non-data-1-1.als
 COMNT
 DATIM 17-07-2015 17:43:39
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.5 c
 SLVNT CDCL₃
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 26



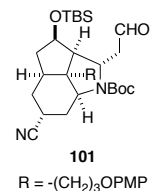
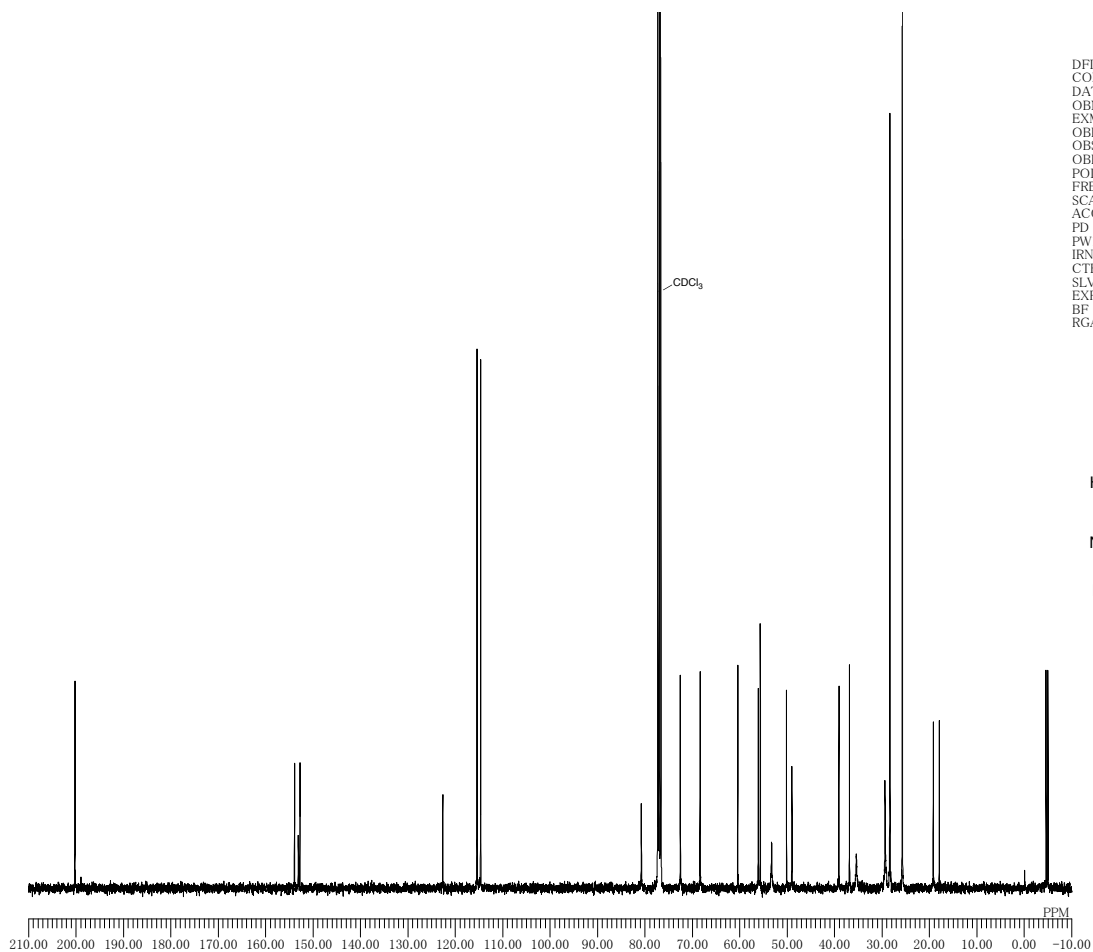
DFILE YO-5-138_overnight_bcm-12-1.als
 COMNT
 DATIM 19-07-2015 00:02:49
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26224
 FREQU 25125.63 Hz
 SCANS 2048
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹³C
 CTEMP 25.4 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 50

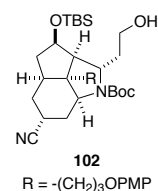
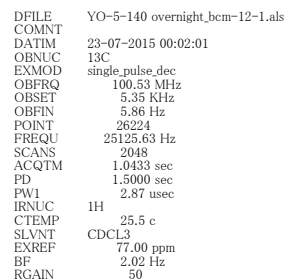
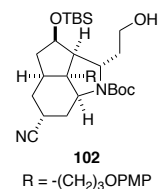
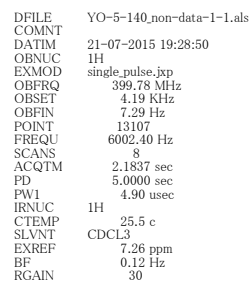


DFILE YO-5-139.non-data-1-1.als
 COMNT 21-07-2015 19:23:52
 DATIM 1H
 OBNUC single_pulse.jpg
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT 6002.40 Hz
 FREQU 8
 SCANS 2.1837 sec
 ACQTM 5.0000 sec
 PD 4.90 usec
 PW1 1H
 IRNUC 25.5 c
 CTEMP CDCL3
 SLVNT 7.26 ppm
 EXREF BF 0.12 Hz
 RGAIN 30

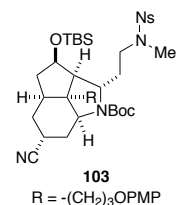
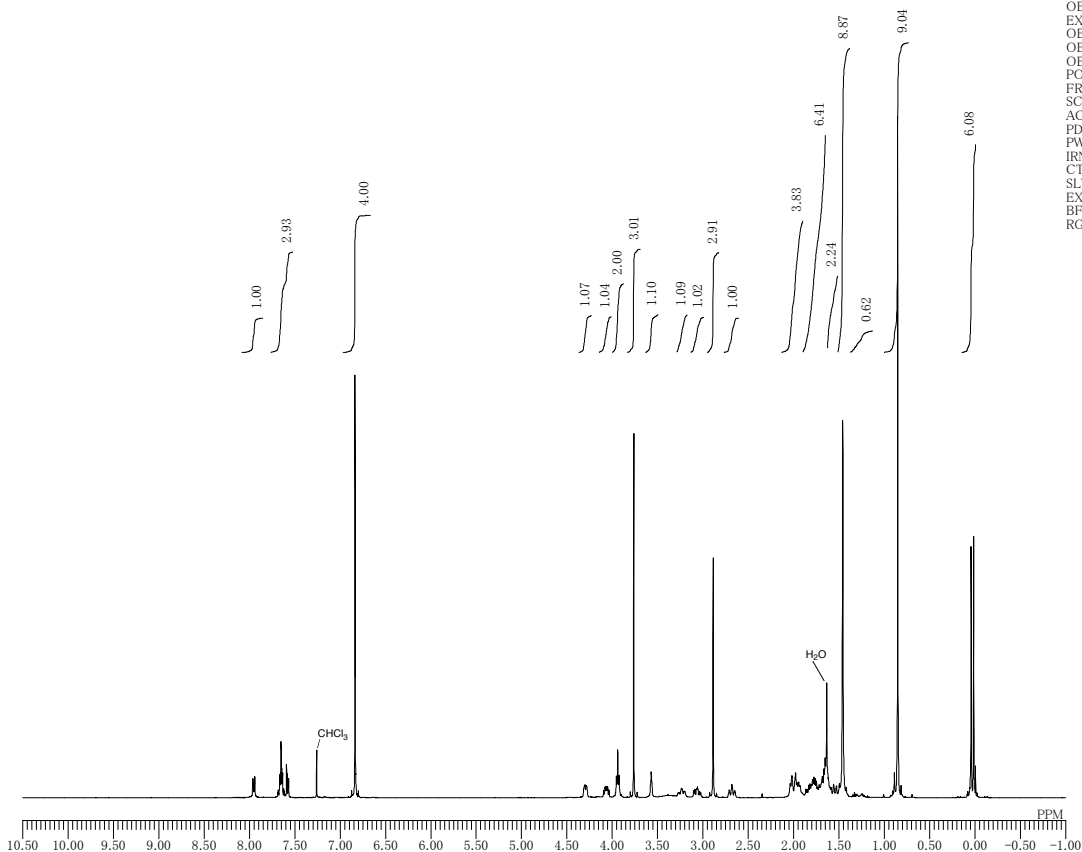


DFILE YO-5-139 overnight_bcm-1-1.als
 COMNT 22-07-2015 00:02:54
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26214
 POINT 25125.63 Hz
 FREQU 2048
 SCANS 1.0433 sec
 ACQTM 1.5000 sec
 PD 2.87 usec
 PW1 1H
 IRNUC 25.6 c
 CTEMP CDCL3
 SLVNT 77.00 ppm
 EXREF BF 2.02 Hz
 RGAIN 50

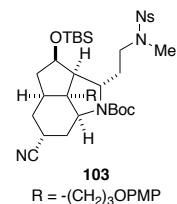
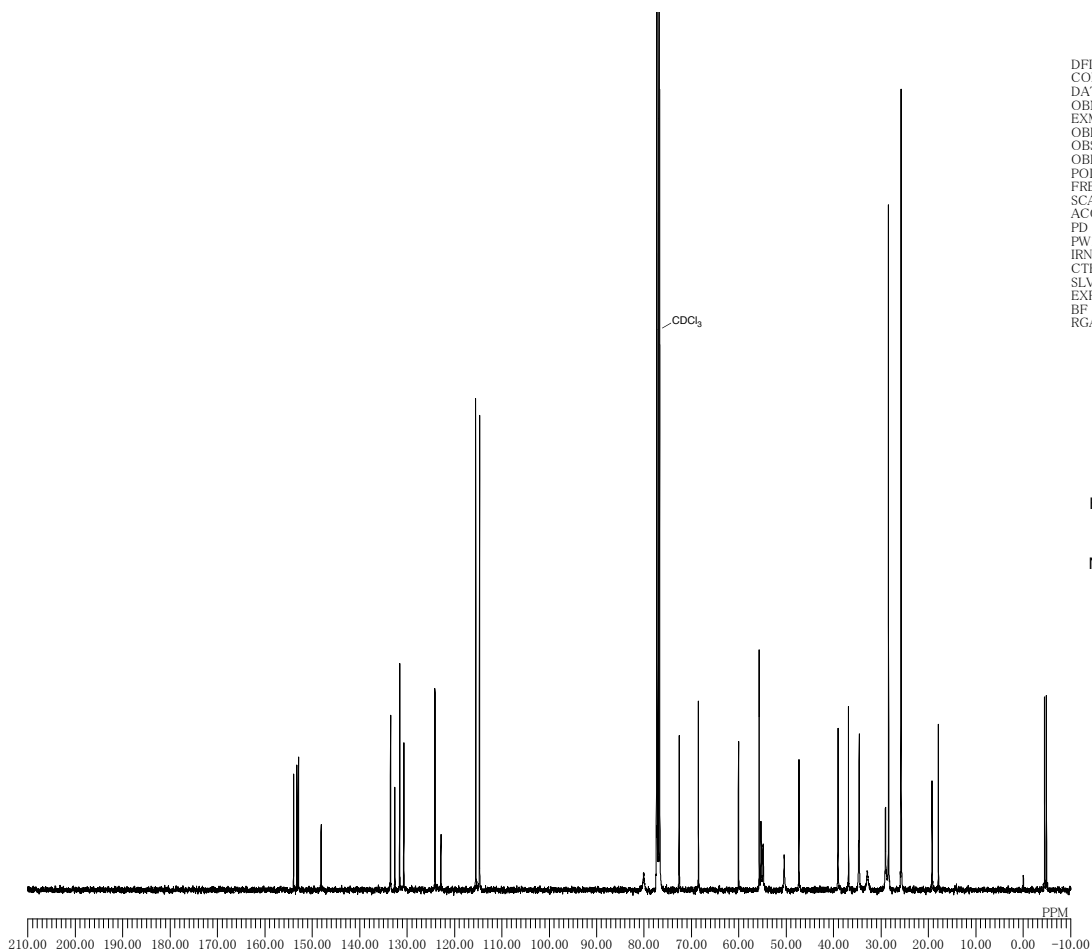




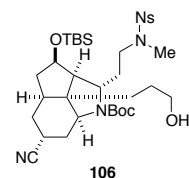
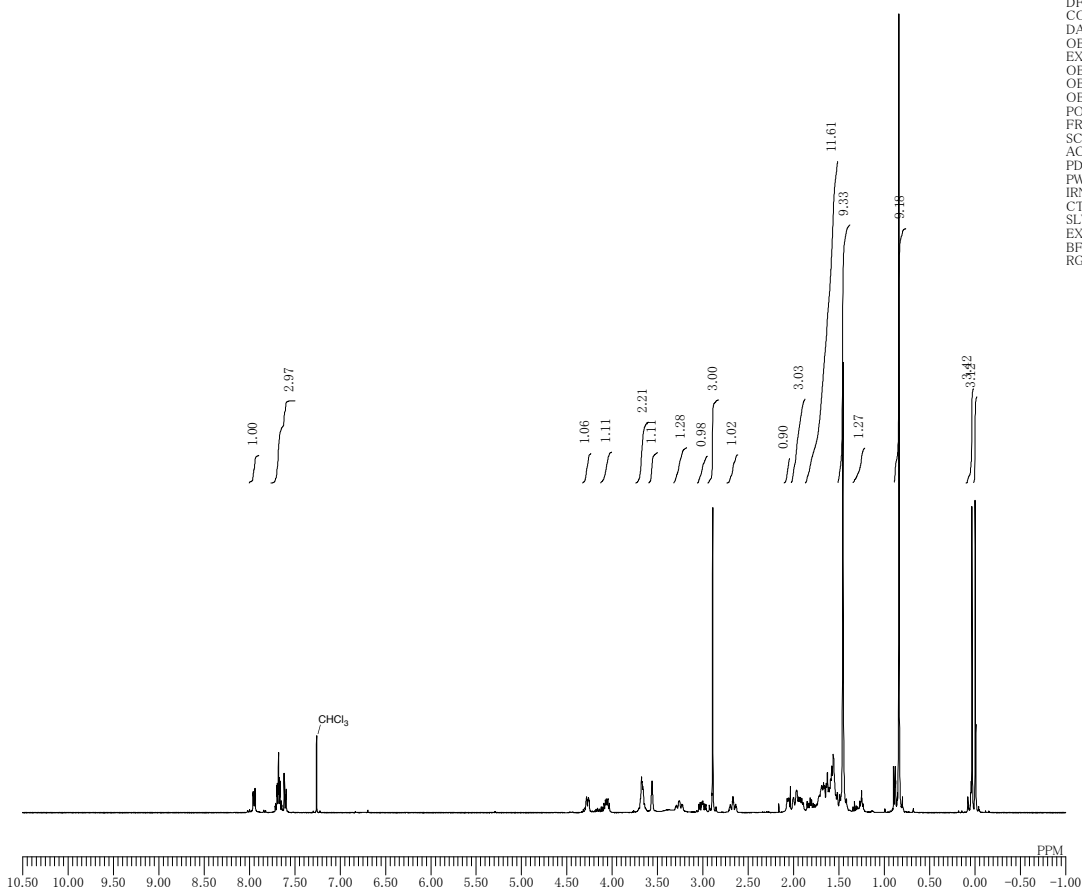
DFILE YO-5-141_non-data-1-1.als
 COMNT
 DATIM 22-07-2015 21:35:45
 OBNUC 1H
 EXMOD single_pulse.jpg
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.3 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.22 Hz
 RGAIN 30



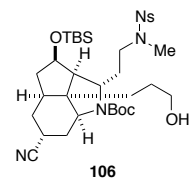
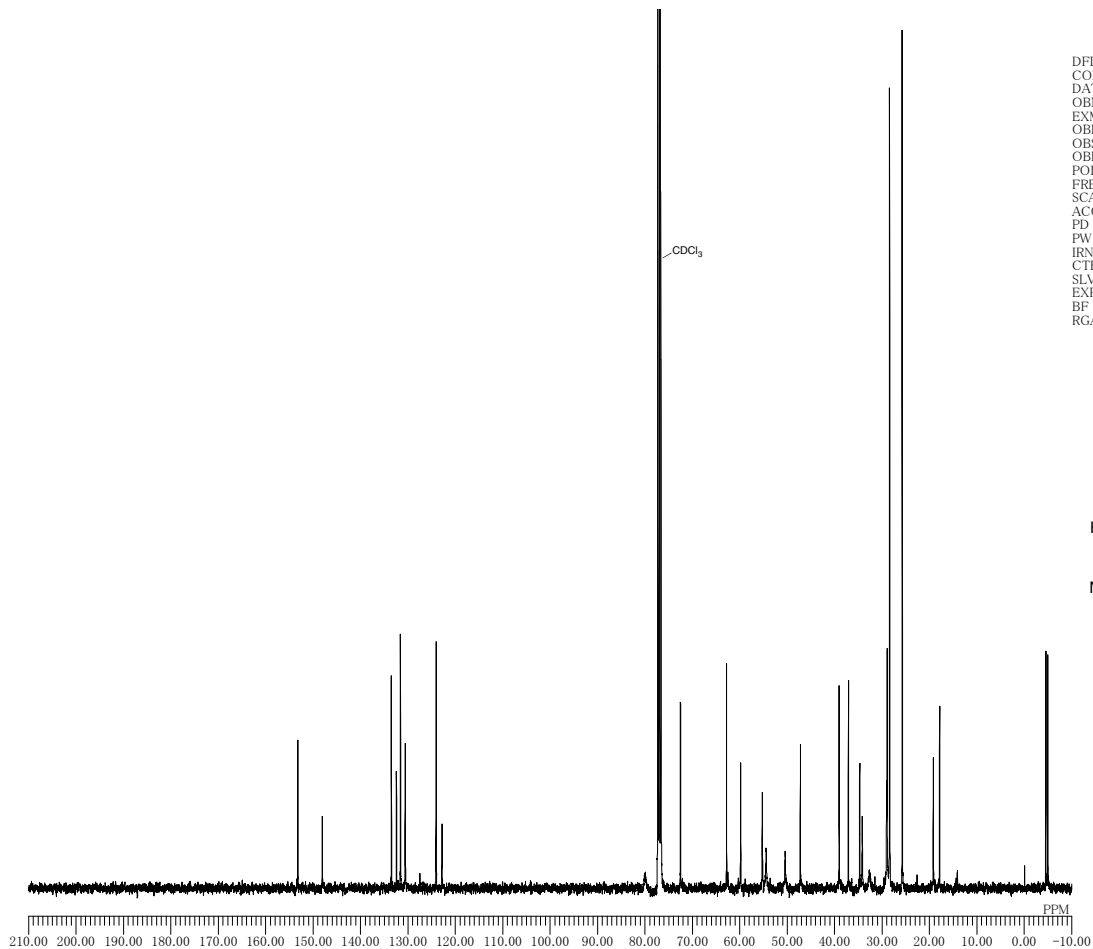
DFILE YO-5-141_overnight_bcm-1-1.als
 COMNT
 DATIM 24-07-2015 00:02:20
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.4 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 2.02 Hz
 RGAIN 50



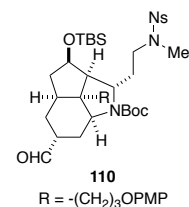
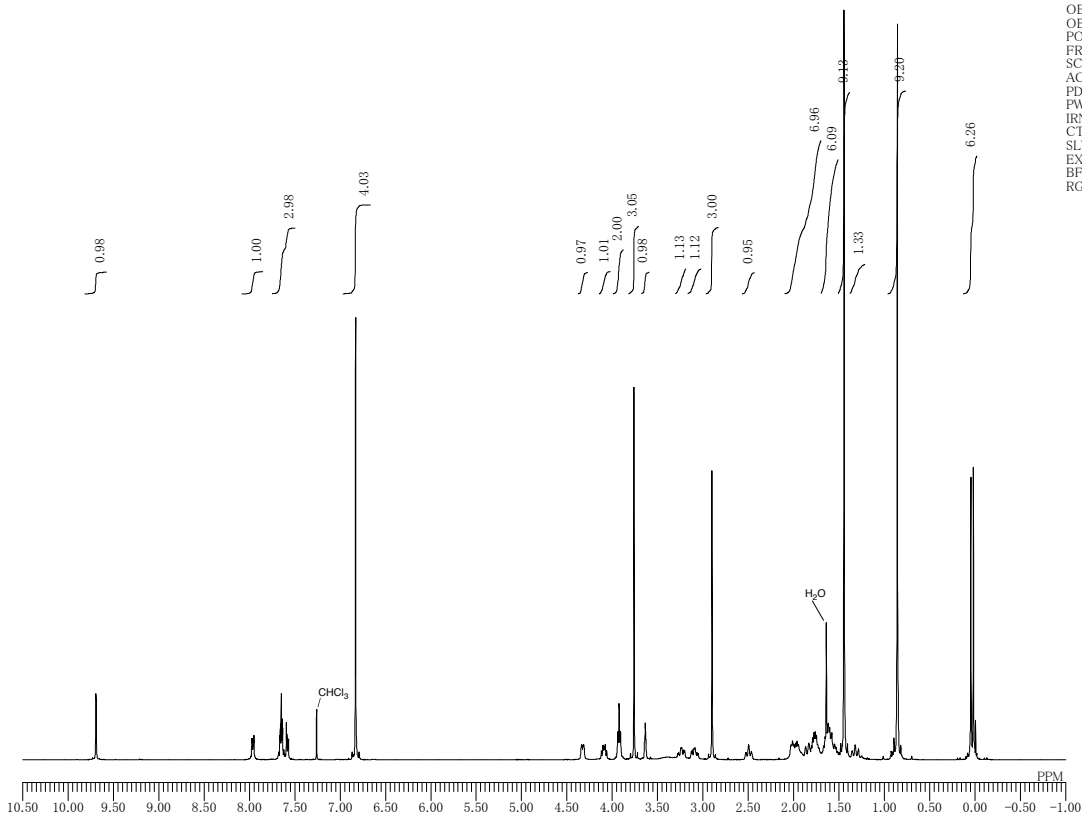
DFILE YO-5-164.non-data-1-1.als
 COMNT
 DATIM 17-08-2015 21:07:28
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNLC ¹H
 CTEMP 25.6 c
 SLVNT CDCL₃
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 32



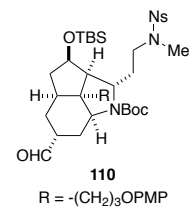
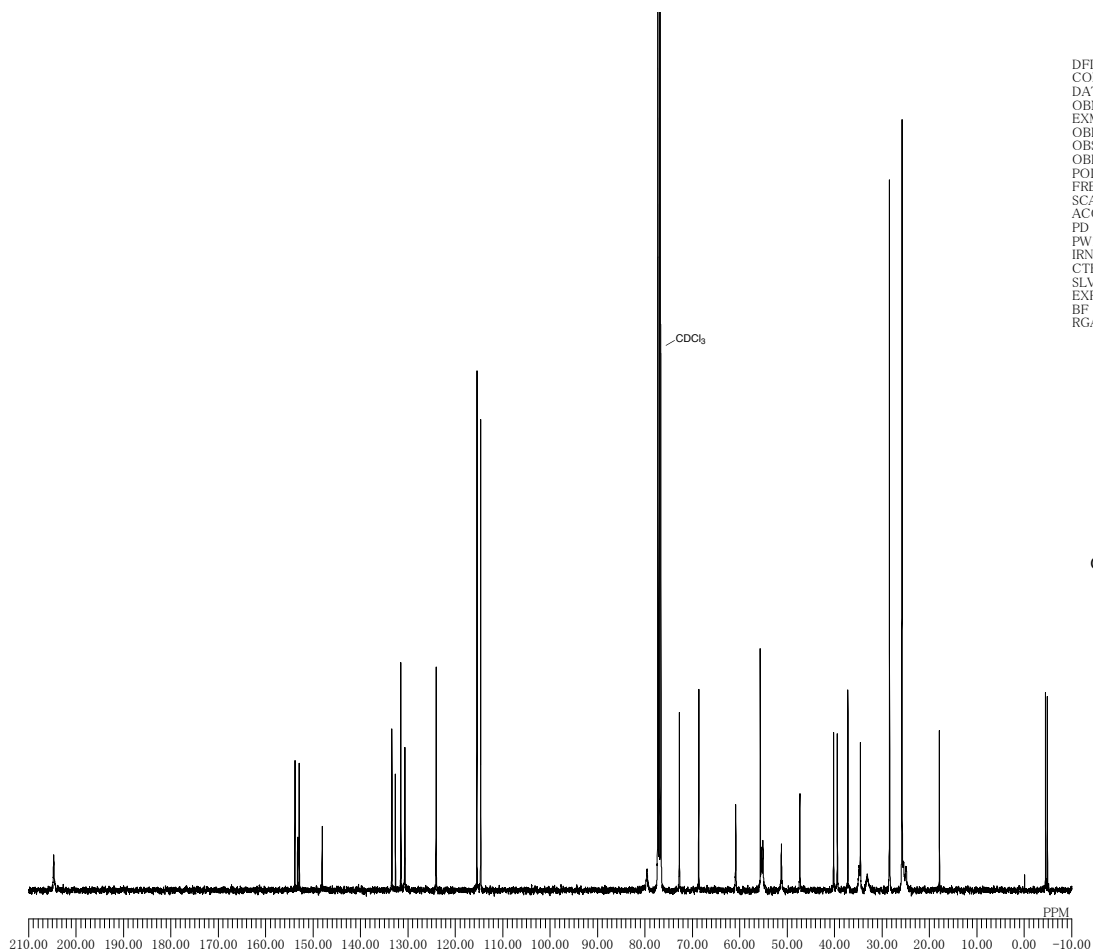
DFILE YO-5-164 overnight_bcm-1-1.als
 COMNT
 DATIM 18-08-2015 00:01:53
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNLC ¹H
 CTEMP 25.5 c
 SLVNT CDCL₃
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

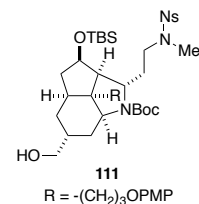
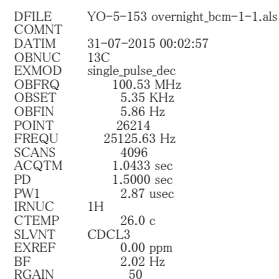
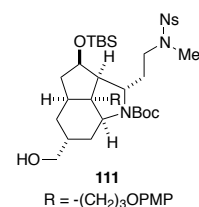
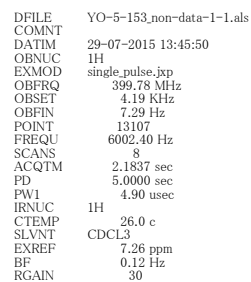


DFILE YO-5-142_non-data-1-1.als
 COMNT 22-07-2015 21:40:44
 DATIM 1H
 OBNUC single_pulse.jxp
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNLC 1H
 CTEMP 25.3 c
 SLVNT CDCL3
 EXREF 7.26 ppm
 BF 0.22 Hz
 RGAIN 30

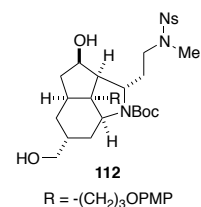
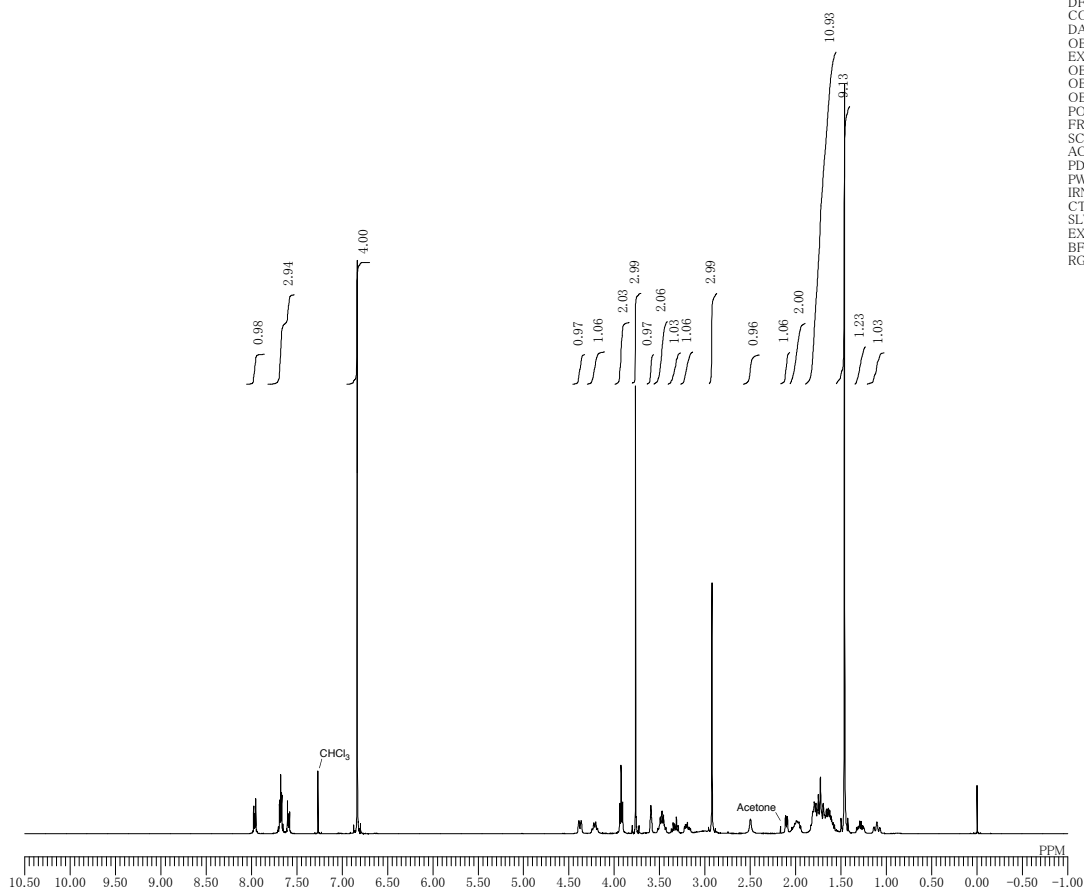


DFILE YO-5-142_overnight_bcm-1-1.als
 COMNT 25-07-2015 00:03:19
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26214
 POINT FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNLC 1H
 CTEMP 25.4 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

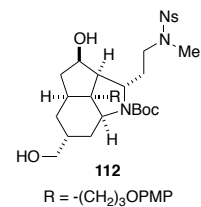
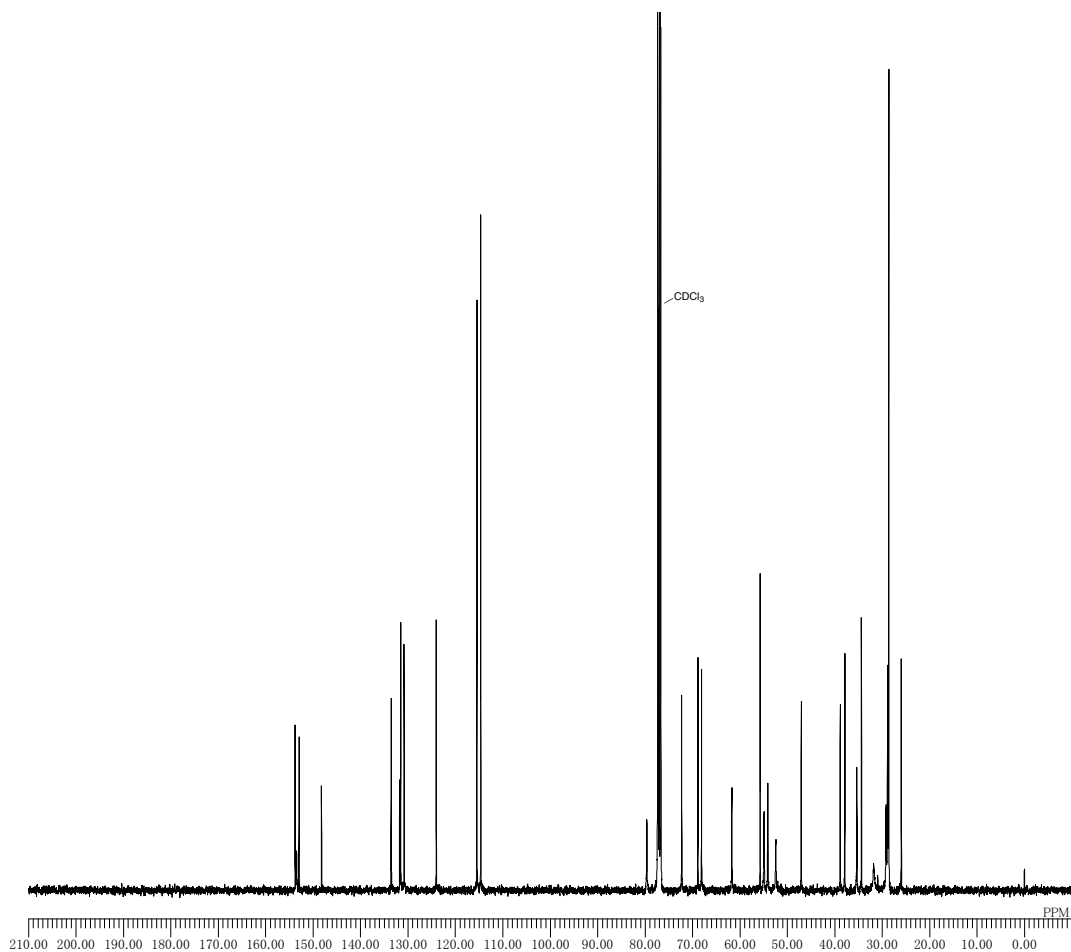




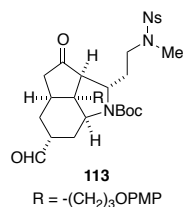
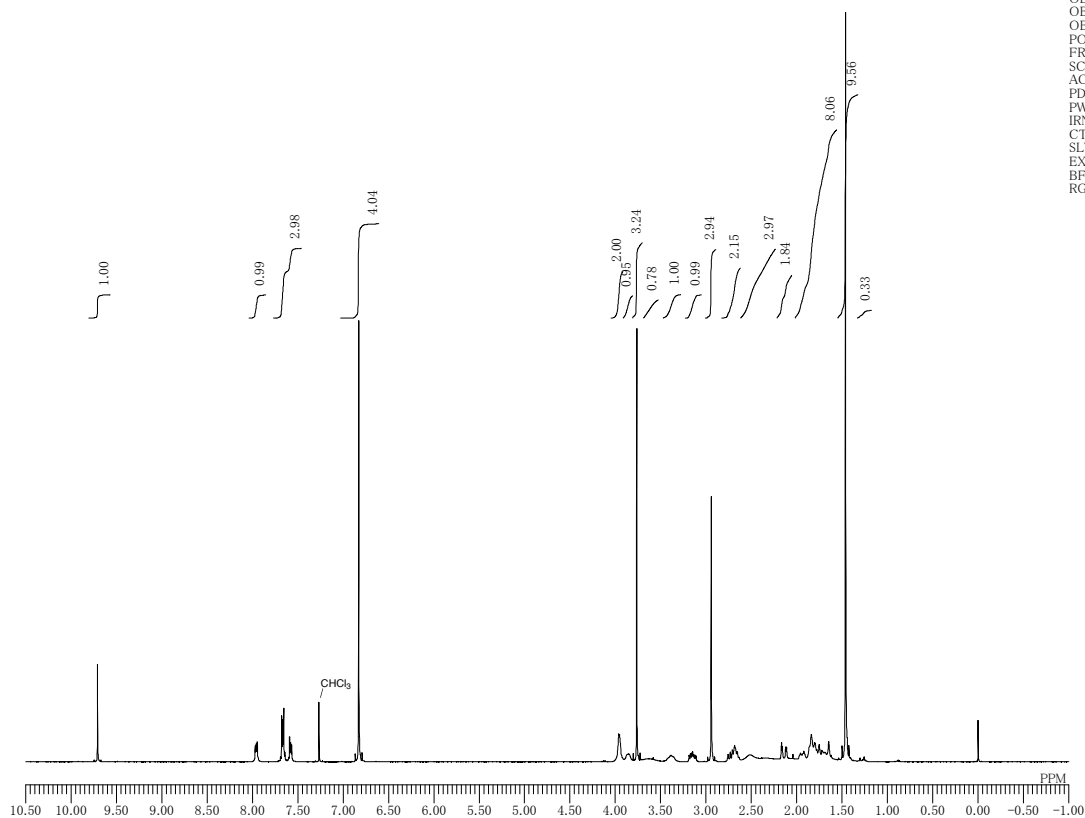
DFILE YO-5-154.non-data-1-1.als
 COMNT 30-07-2015 20:19:45
 DATIM 1H
 OBNUC single_pulse.jxp
 EXMOD 399.78 MHz
 OBFRQ 4.19 KHz
 OBSET 7.29 Hz
 OBFIN 13107
 POINT 6002.40 Hz
 FREQU 8
 SCANS 2.1837 sec
 ACQTM 5.0000 sec
 PD 4.90 usec
 PW1 1H
 IRNUC 25.9 c
 CTEMP CDCL3
 SLVNT 0.00 ppm
 EXREF 0.12 Hz
 BF 30
 RGAIN



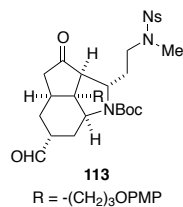
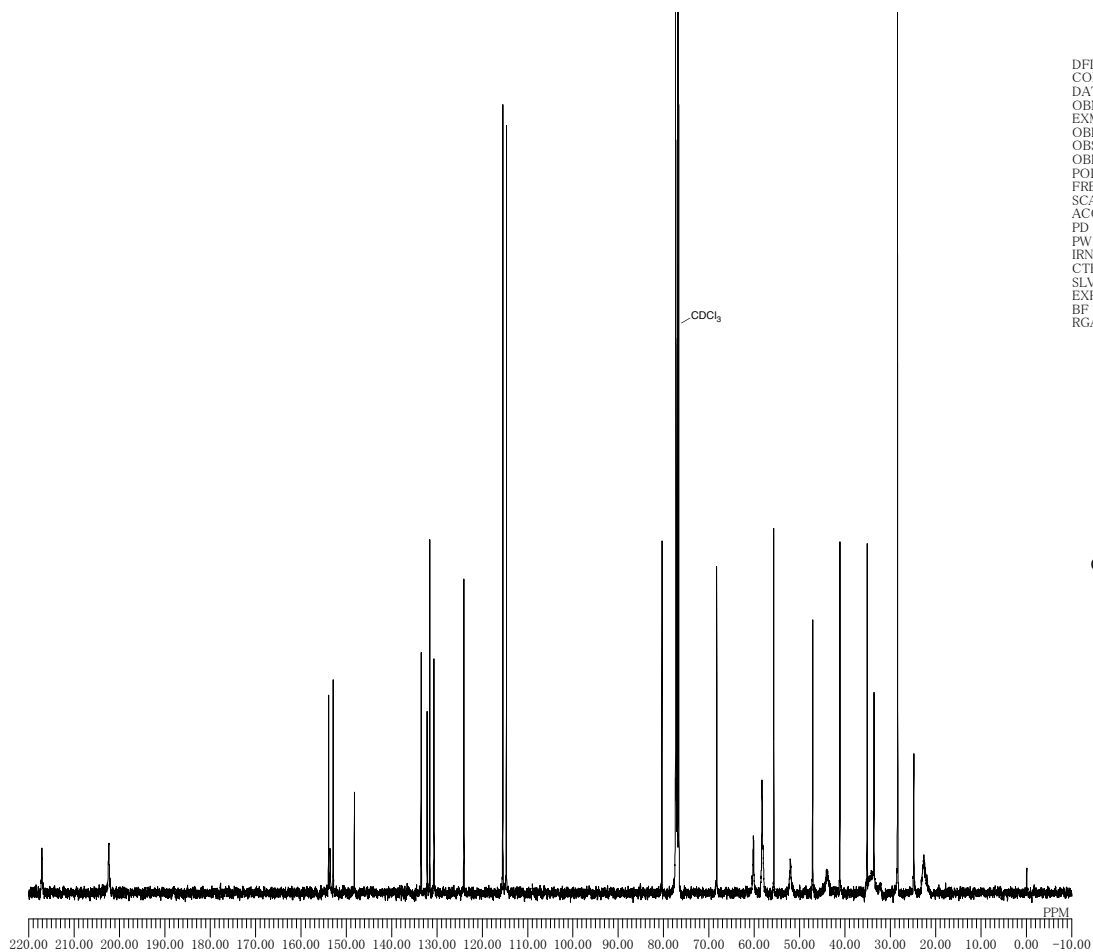
DFILE YO-5-154 overnight_bcm-12-1.als
 COMNT 01-08-2015 00:03:38
 DATIM 13C
 OBNUC single_pulse.dec
 EXMOD 100.53 MHz
 OBFRQ 5.35 KHz
 OBSET 5.86 Hz
 OBFIN 26224
 POINT 25125.63 Hz
 FREQU 4096
 SCANS 1.0433 sec
 ACQTM 1.5000 sec
 PD 2.87 usec
 PW1 1H
 IRNUC 26.0 c
 CTEMP CDCL3
 SLVNT 0.00 ppm
 EXREF 0.12 Hz
 BF 50
 RGAIN



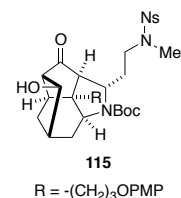
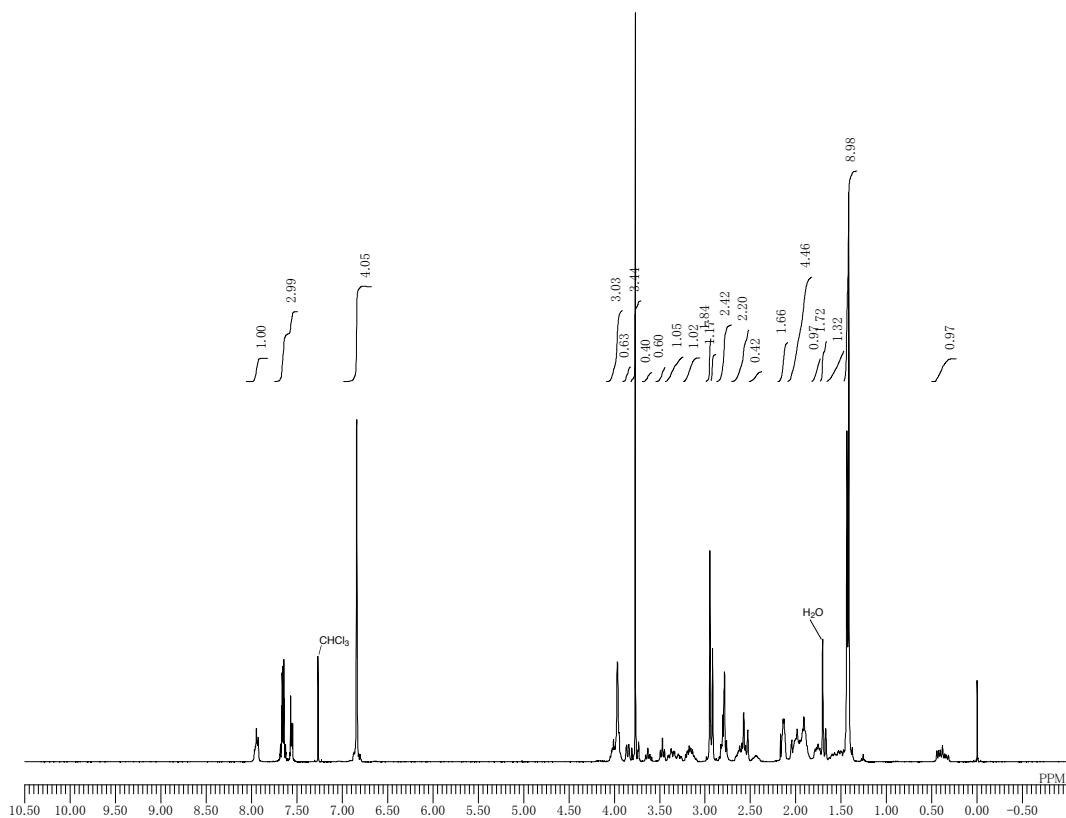
DFILE YO-5-156.non-data-1-1.als
 COMNT
 DATIM 31-07-2015 16:42:26
 OBNUC 1H
 EXMOD single_pulse.jsp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 26.2 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 32



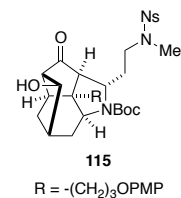
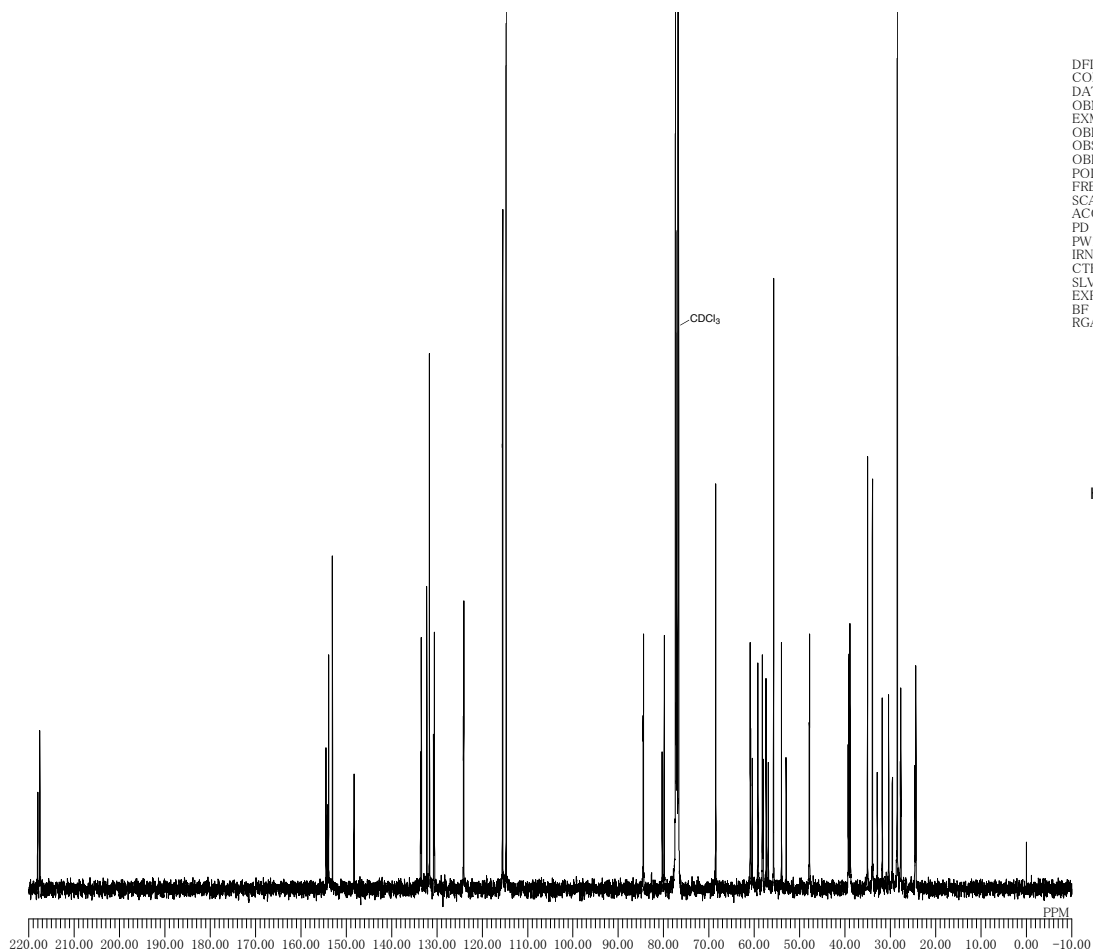
DFILE YO-5-156 overnight_bcm-1-1.als
 COMNT
 DATIM 02-08-2015 00:02:58
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



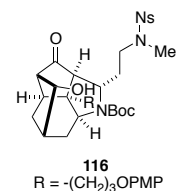
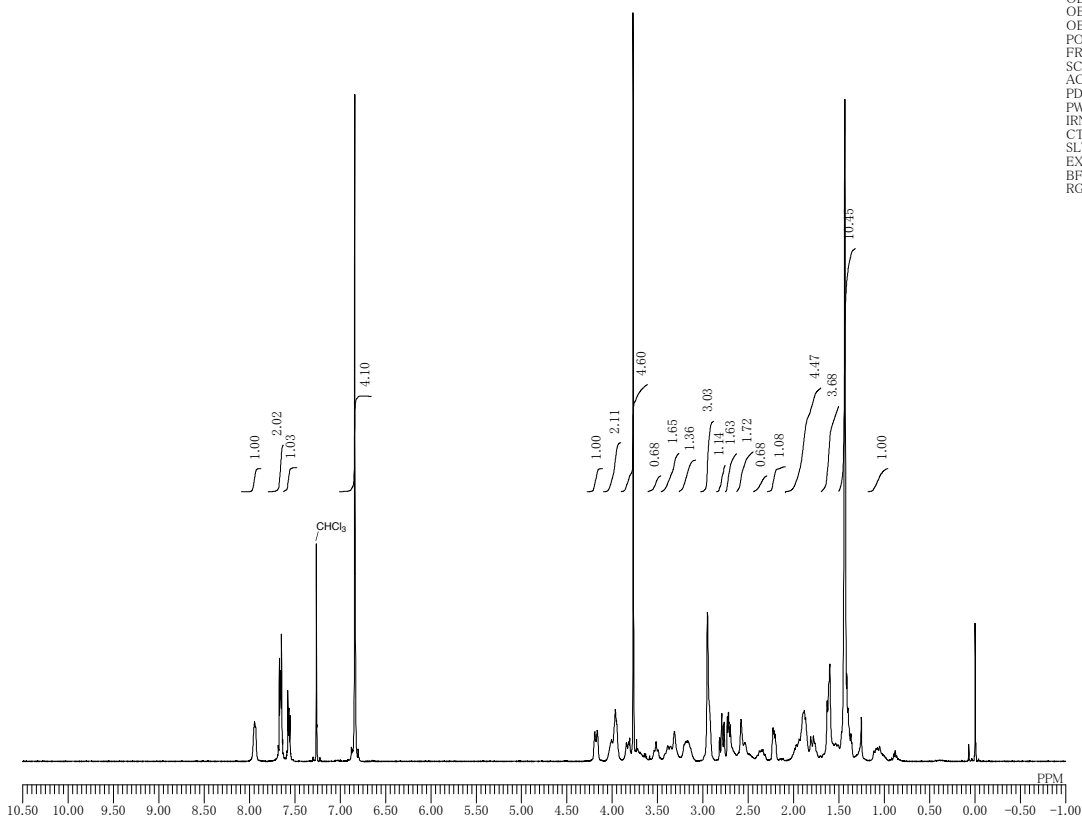
DFILE YO-5-158_non-data-1-1.als
 COMNT
 DATIM 01-08-2015 14:16:12
 OBNUC 1H
 EXMOD single_pulse.jsp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 32



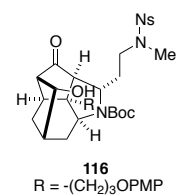
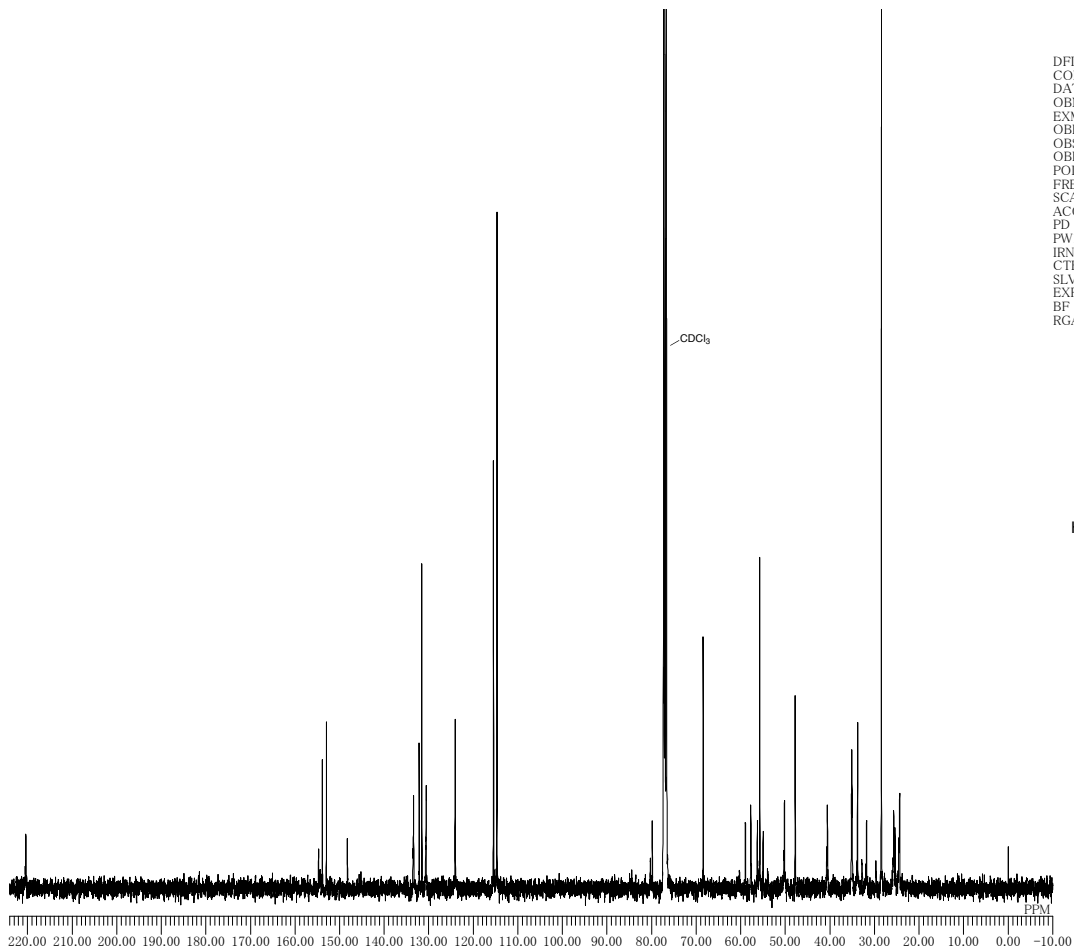
DFILE YO-5-158_overnight_bcm-1-1.als
 COMNT
 DATIM 02-08-2015 09:03:21
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 26.3 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 2.02 Hz
 RGAIN 50



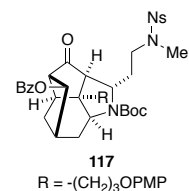
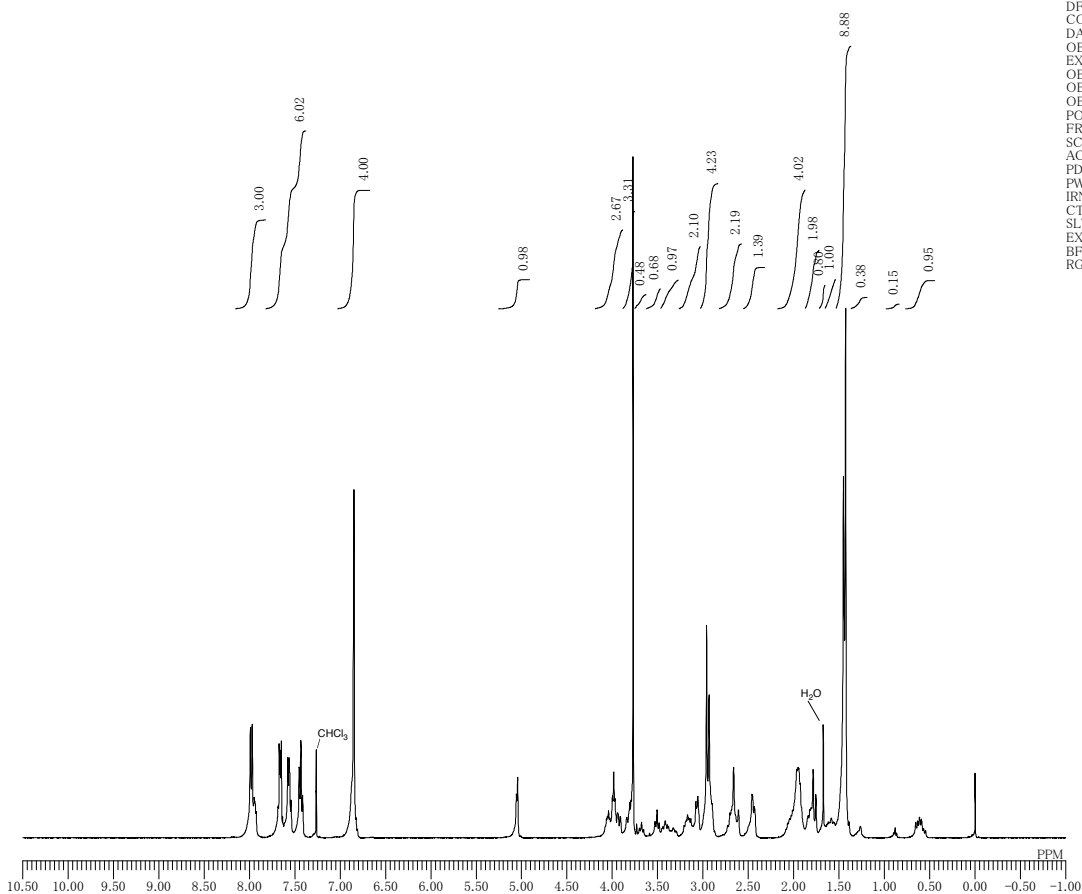
DFILE YO-5-166.non-data-2-1.als
 COMNT
 DATIM 18-08-2015 13:17:23
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNLC 1H
 CTEMP 25.5 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 38



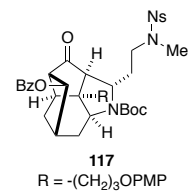
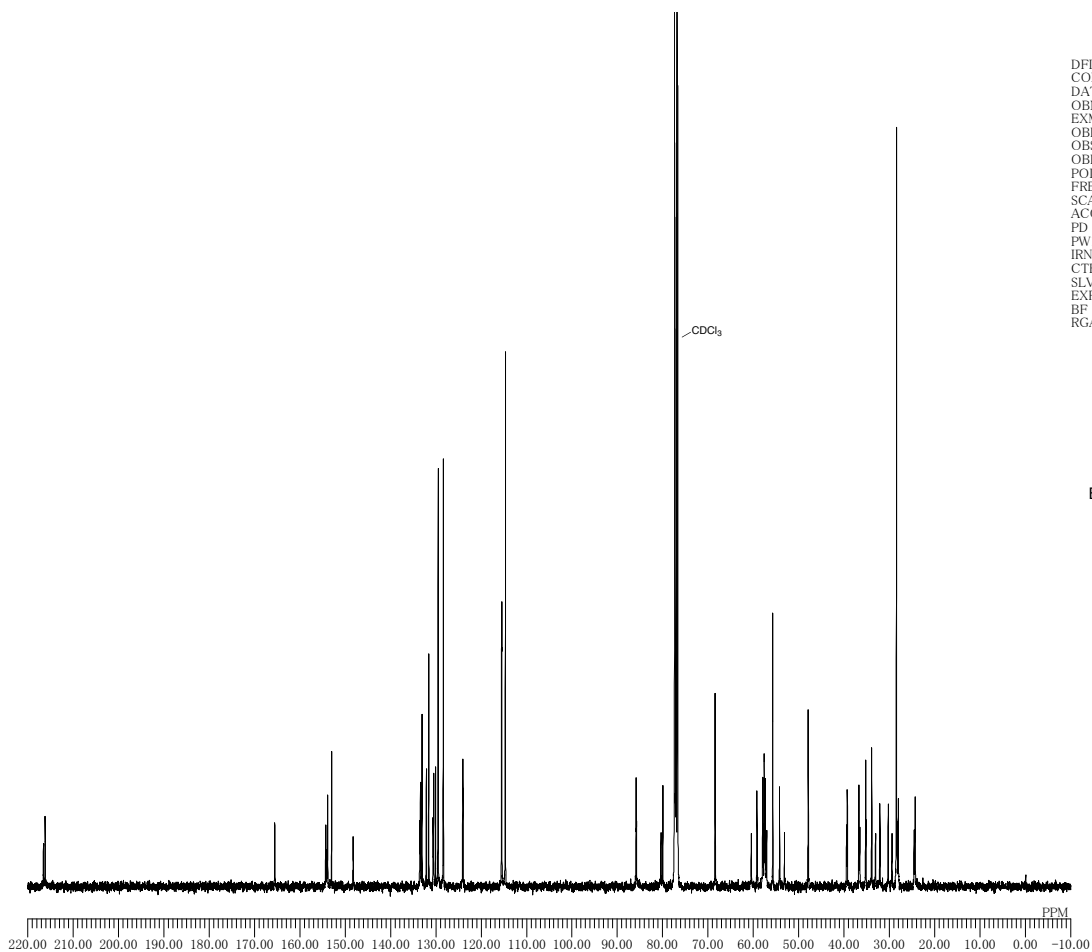
DFILE YO-5-166 overnight_bcm-1-1.als
 COMNT
 DATIM 19-08-2015 00:03:02
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNLC 1H
 CTEMP 25.6 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



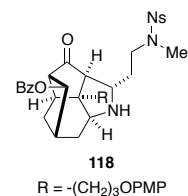
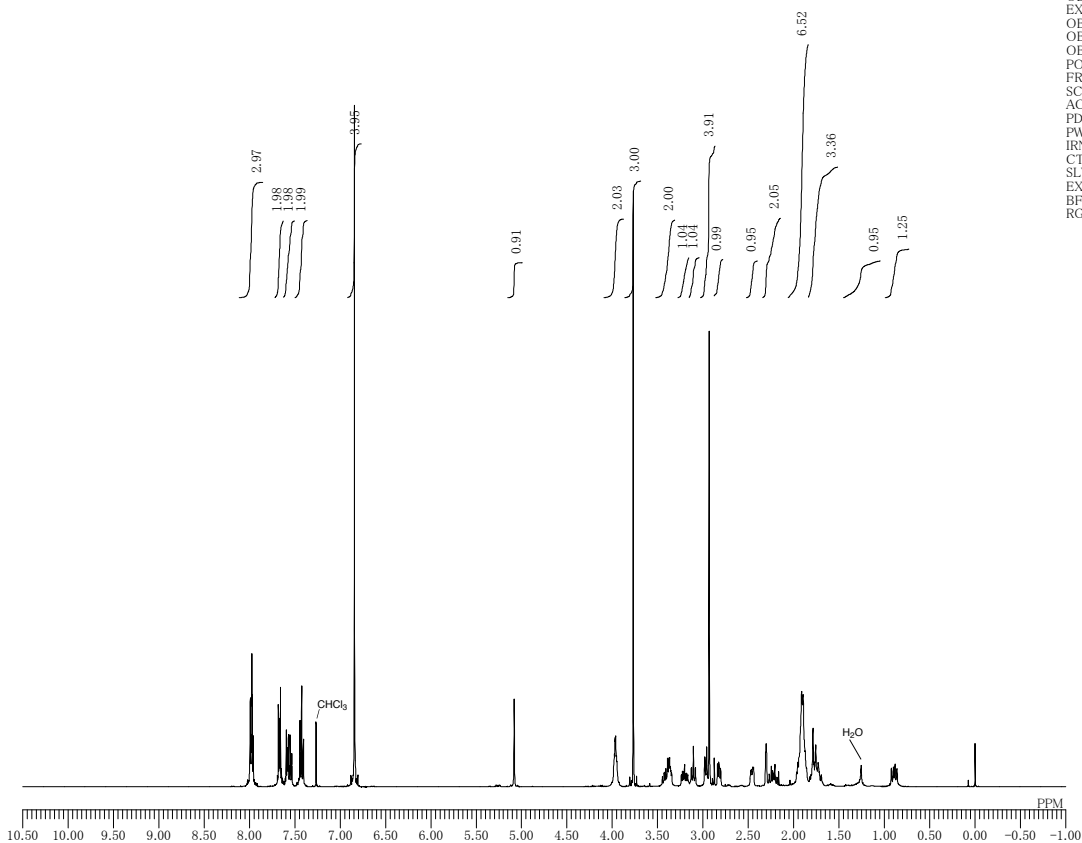
DFILE YO-5-160.non-data-1-1.als
 COMNT
 DATIM 03-08-2015 19:12:45
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



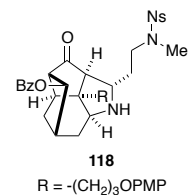
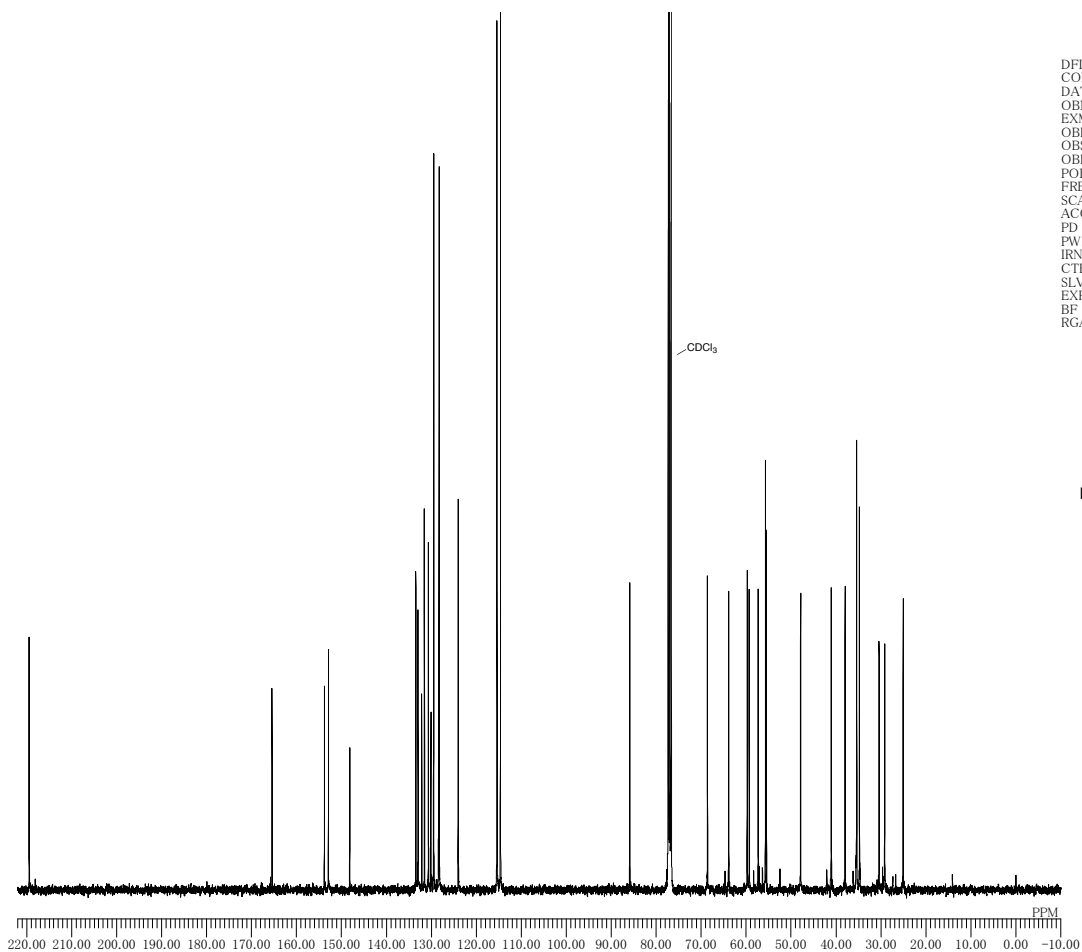
DFILE YO-5-160 overnight_bcm-1-1.als
 COMNT
 DATIM 06-08-2015 00:04:10
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50



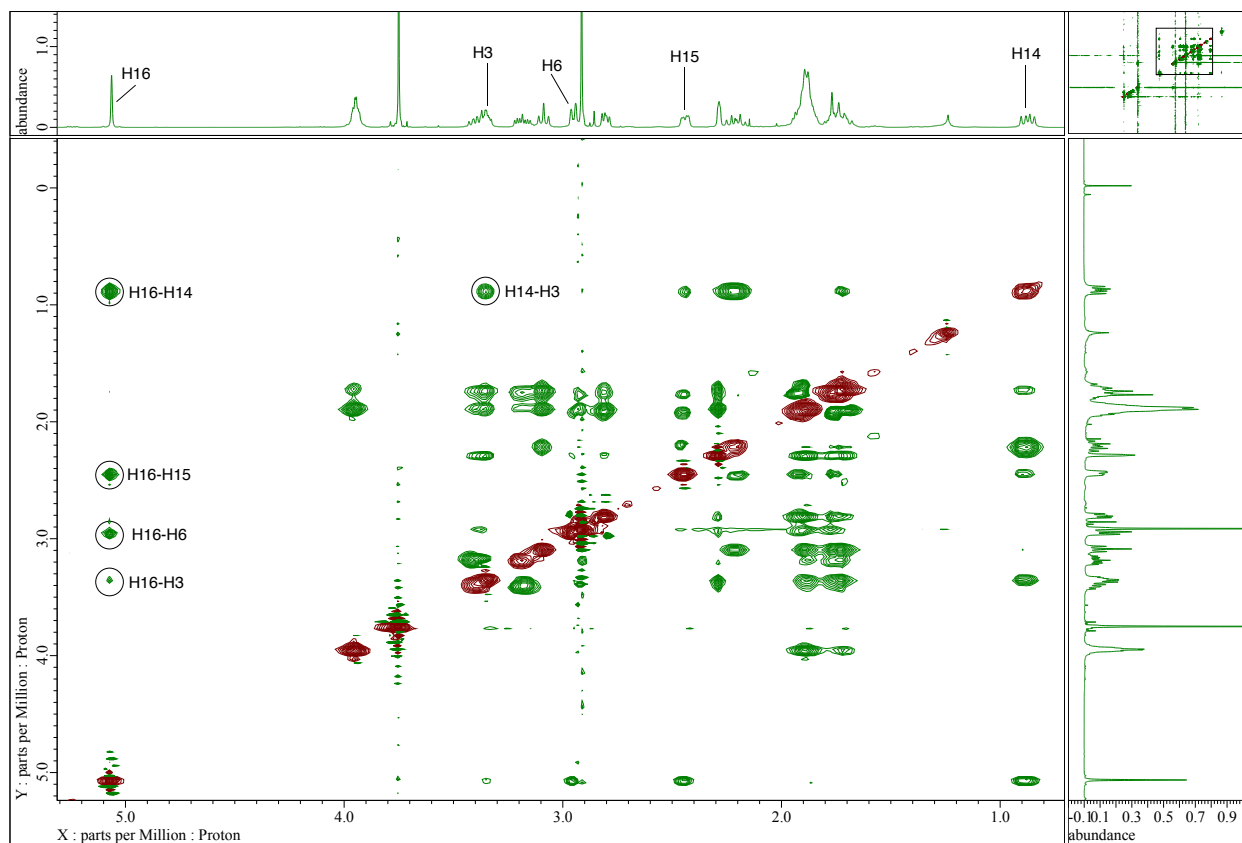
DFILE YO-5-162.non-data-1-1.als
 COMNT
 DATIM 03-08-2015 19:17:30
 OBNUC 1H
 EXMOD single_pulse.jsp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 30



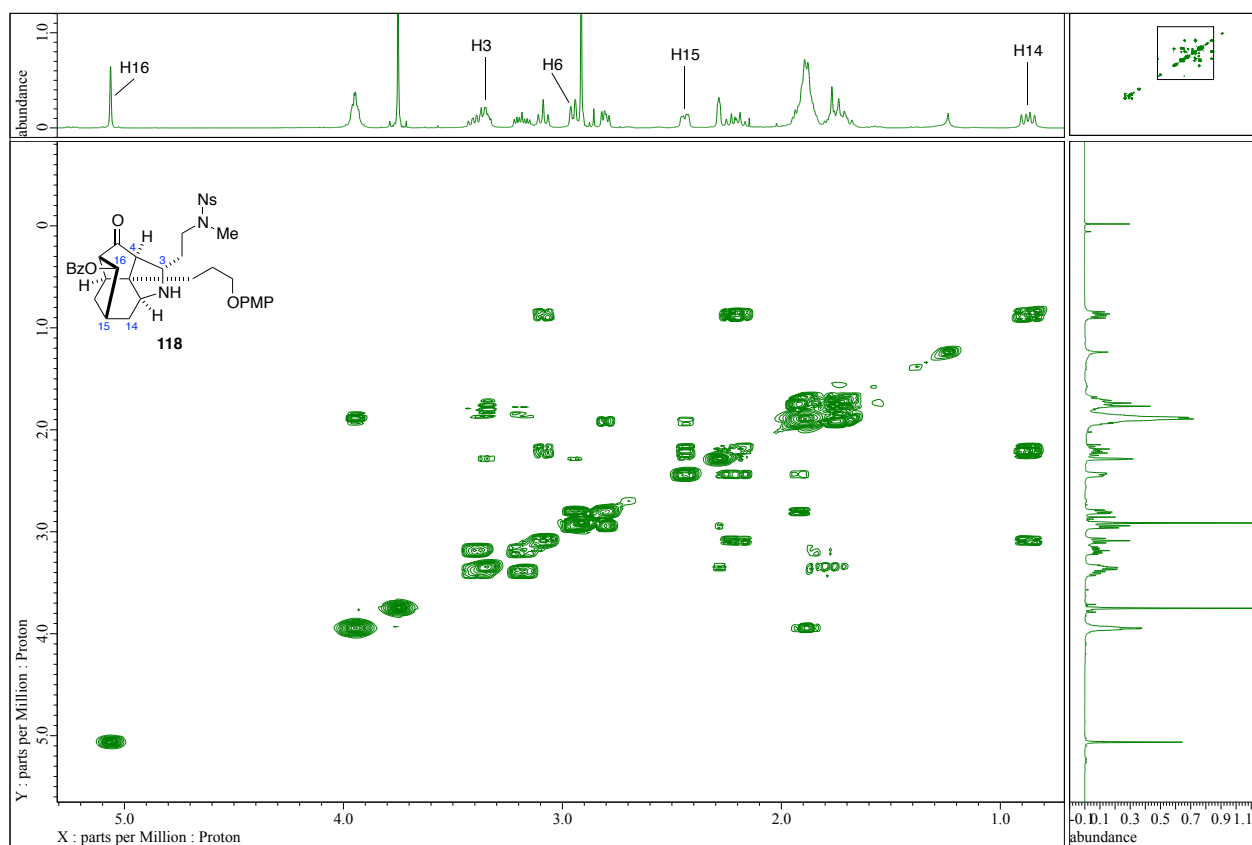
DFILE YO-5-162 overnight_bcm-12-1.als
 COMNT
 DATIM 05-08-2015 00:02:32
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26224
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 0.12 Hz
 RGAIN 50



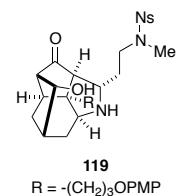
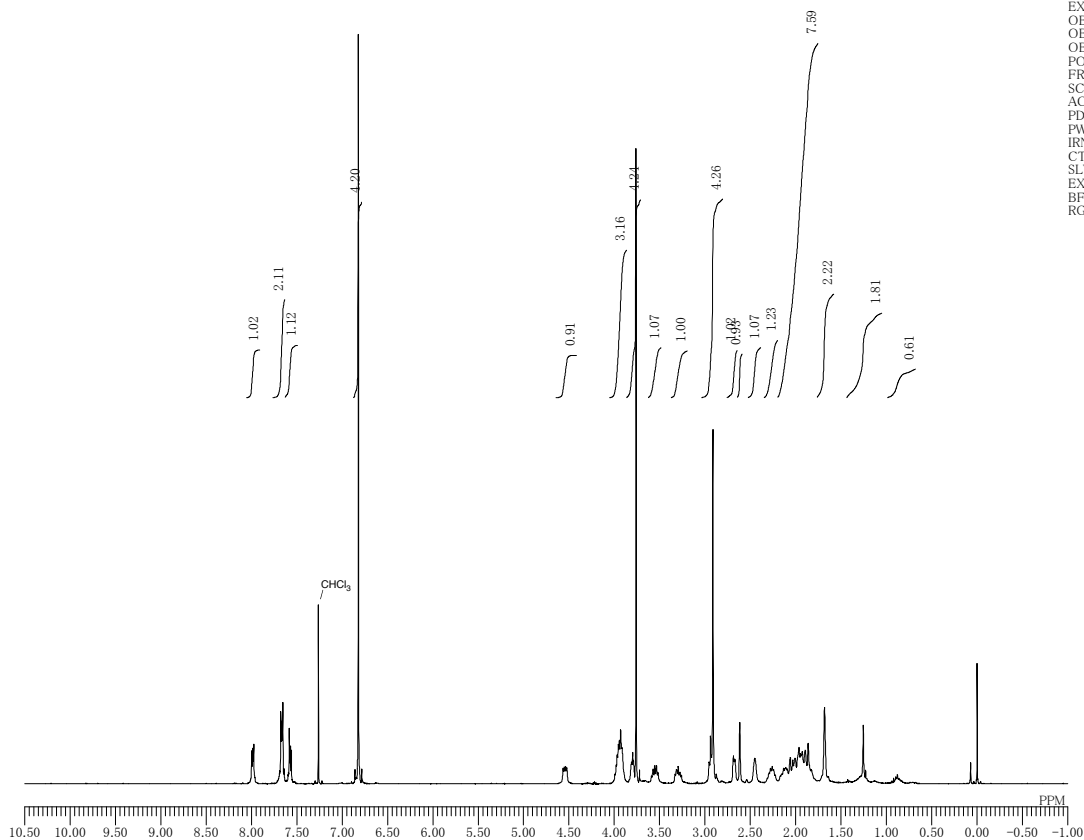
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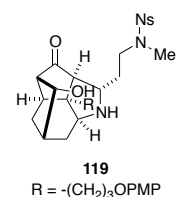
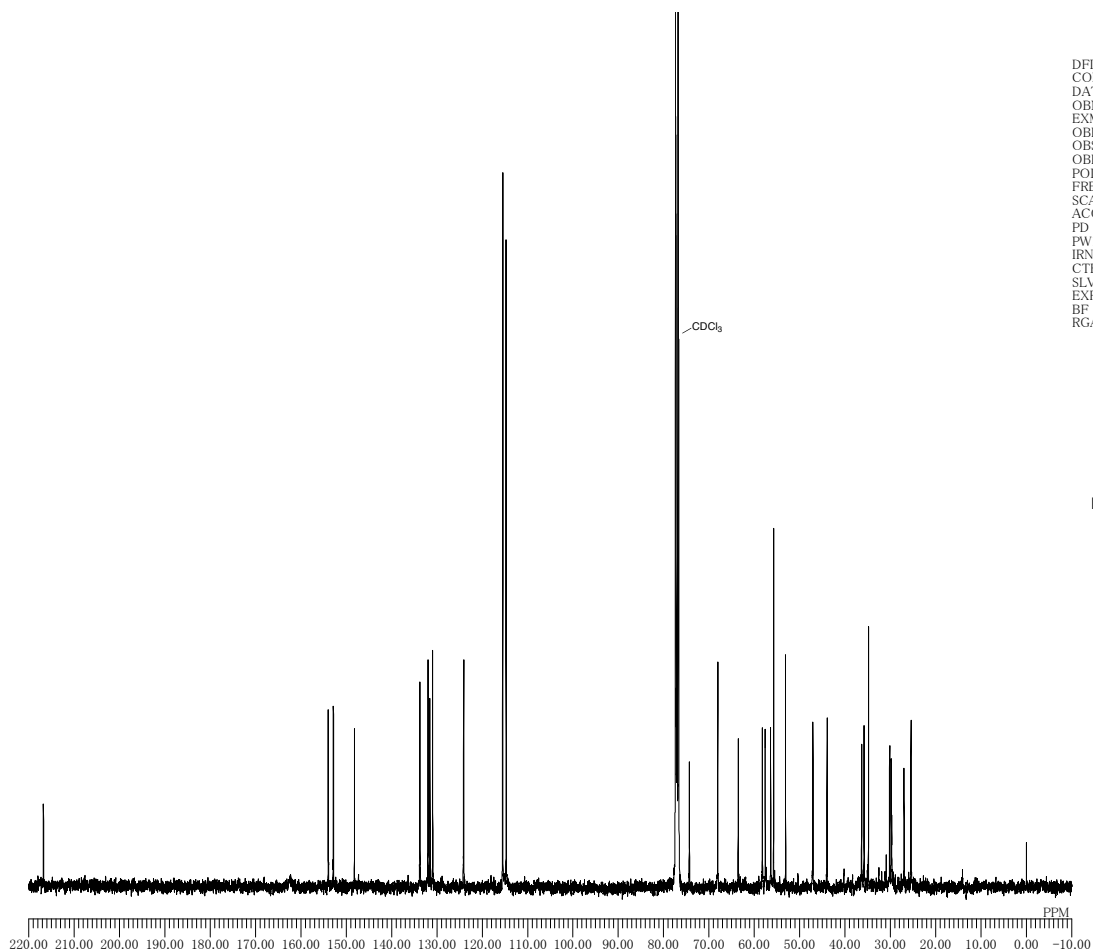
^1H - ^1H COSY



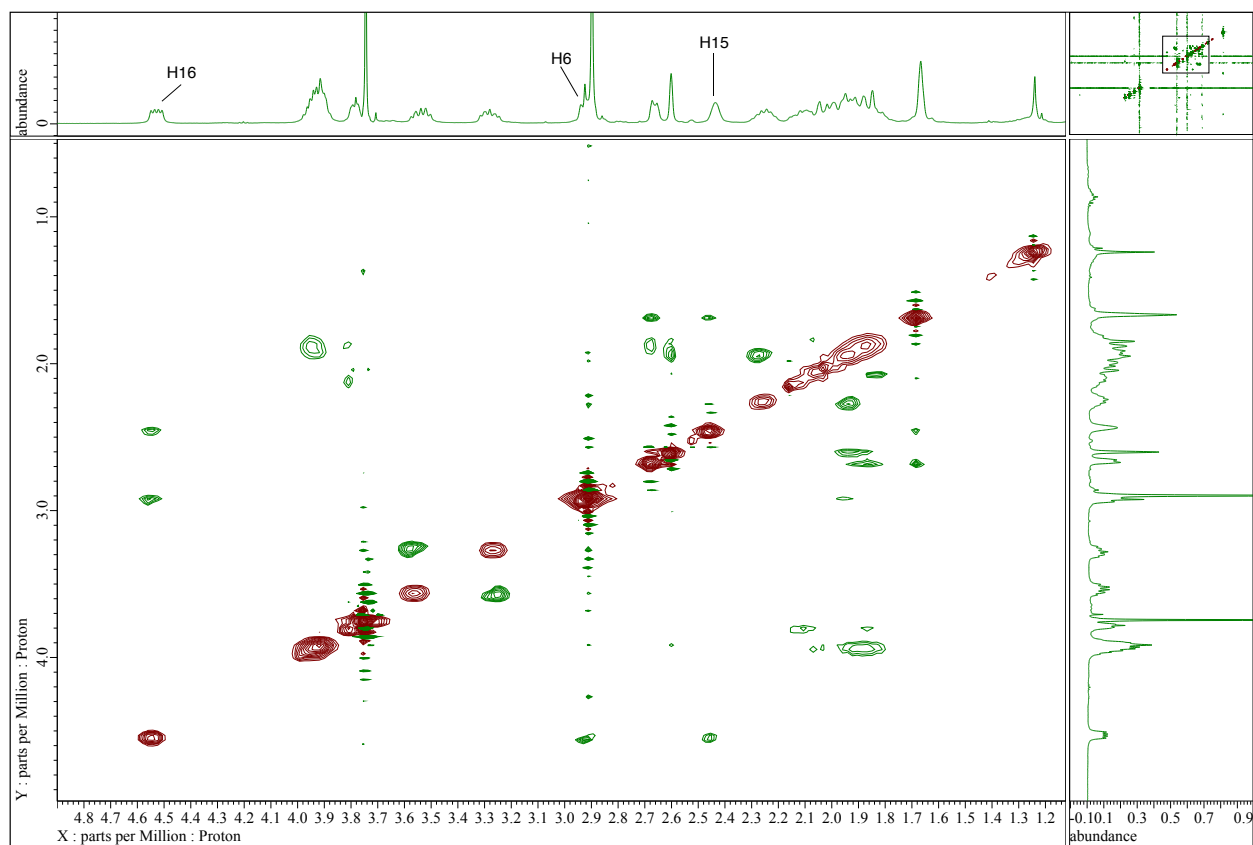
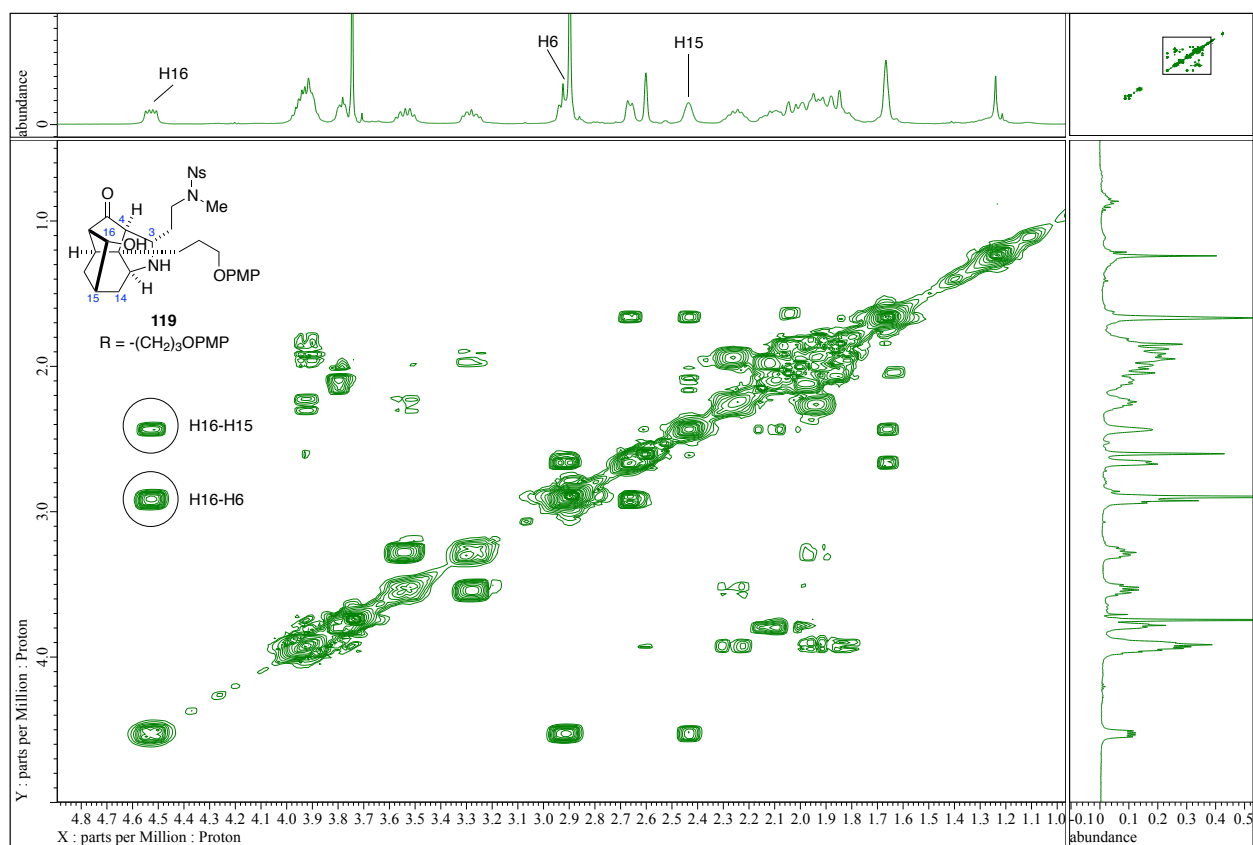
DFILE YO-5-170.non-data-2-1.als
 COMNT
 DATIM 20-08-2015 12:43:14
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.6 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 38



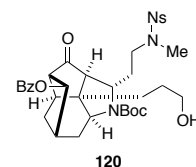
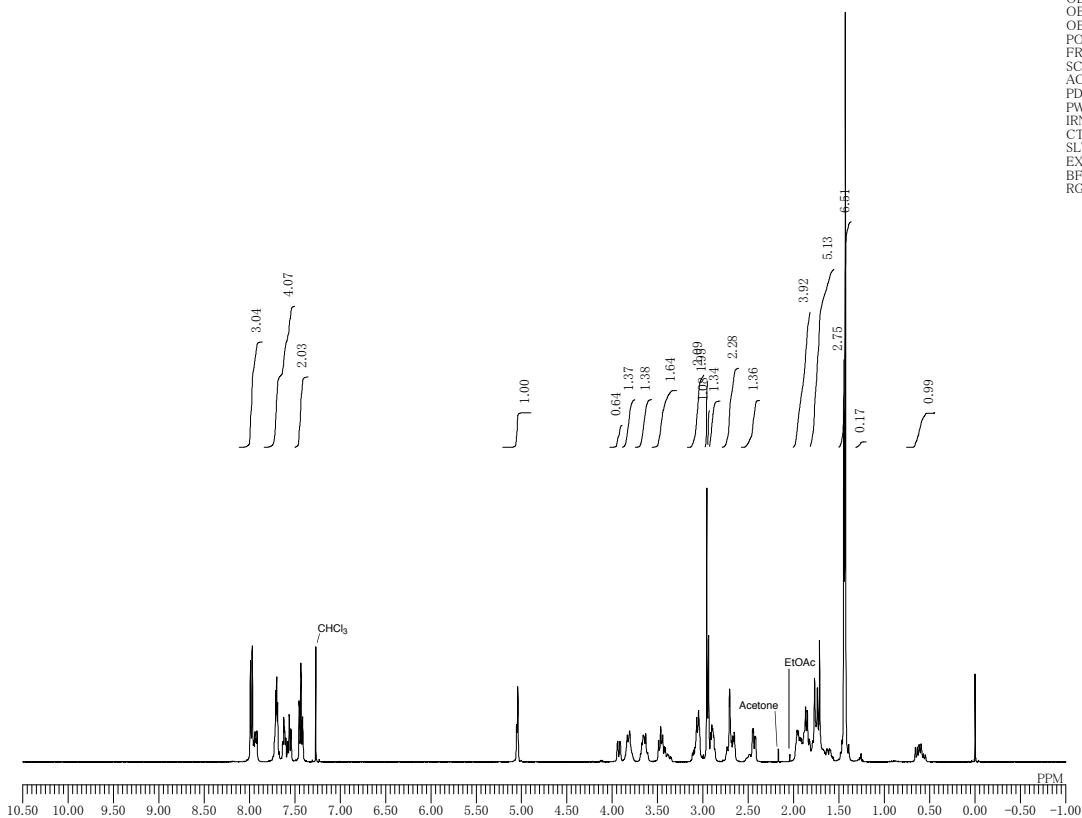
DFILE YO-5-170 overnight_bcm-1-1.als
 COMNT
 DATIM 21-08-2015 22:15:03
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 8192
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹³C
 CTEMP 25.4 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 2.02 Hz
 RGAIN 50



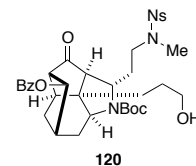
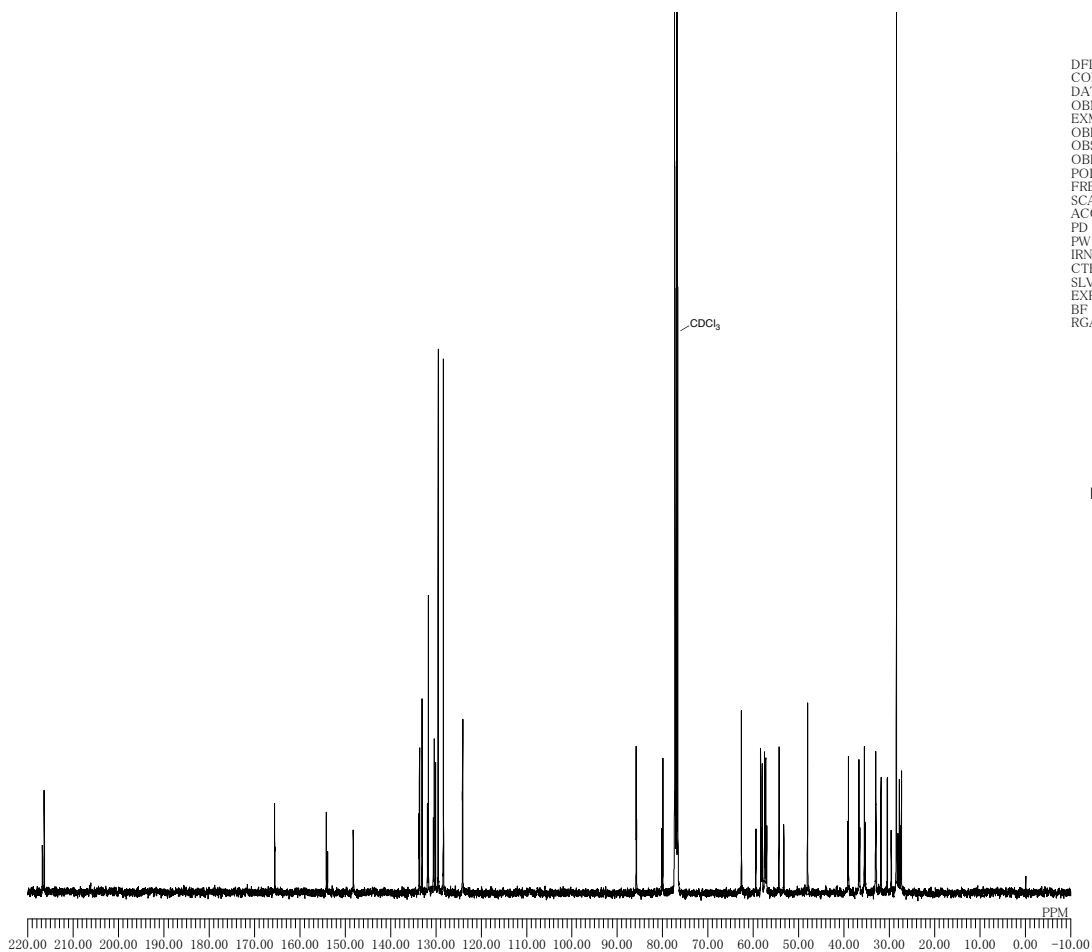
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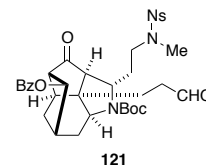
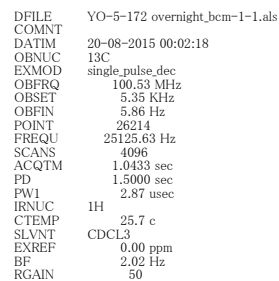
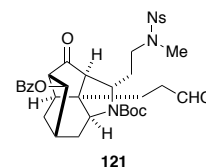
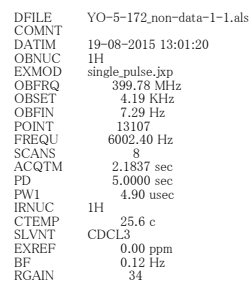
 ^1H - ^1H COSY

DFILE YO-5-163.non-data-1-1.als
 COMNT
 DATIM 04-08-2015 16:22:35
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 26.5 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 34

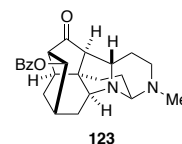
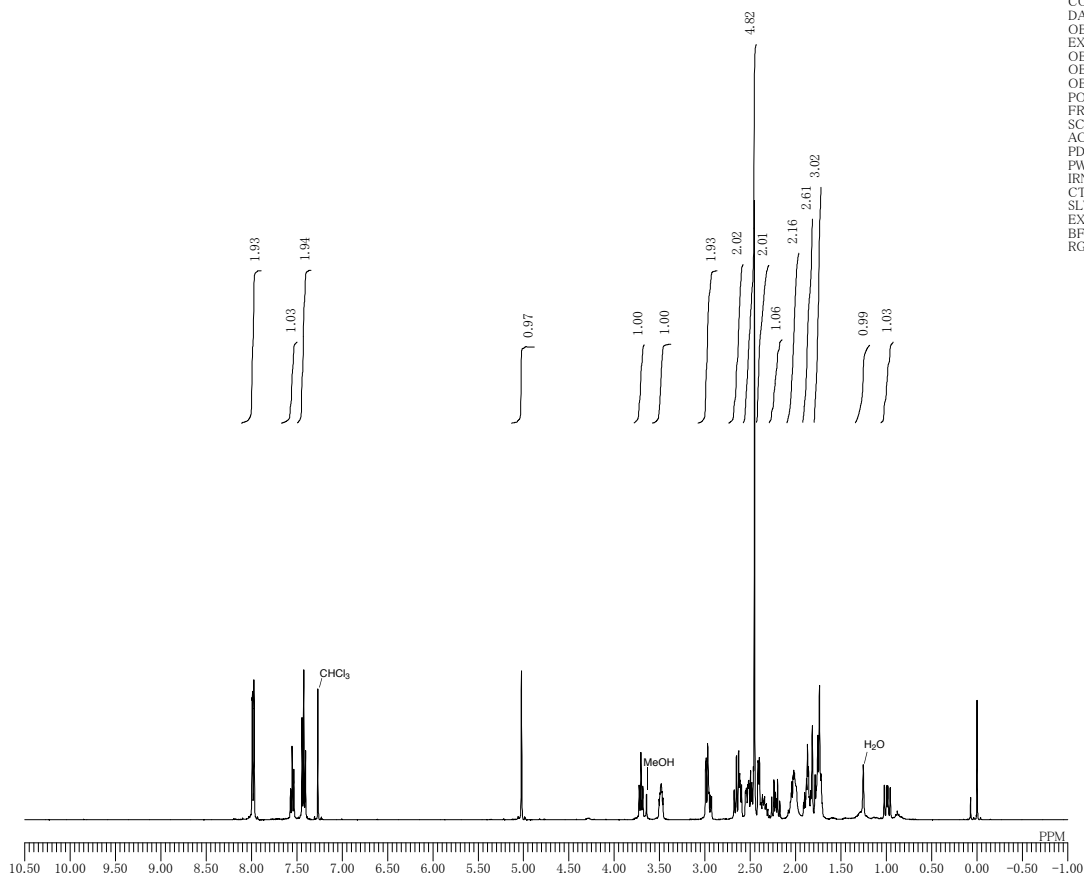


DFILE YO-5-163 overnight_bcm-1-1.als
 COMNT
 DATIM 07-08-2015 03:17:49
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 26.1 c
 SLVNT CDCL3
 EXREF 77.00 ppm
 BF 2.02 Hz
 RGAIN 50

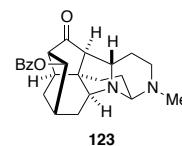
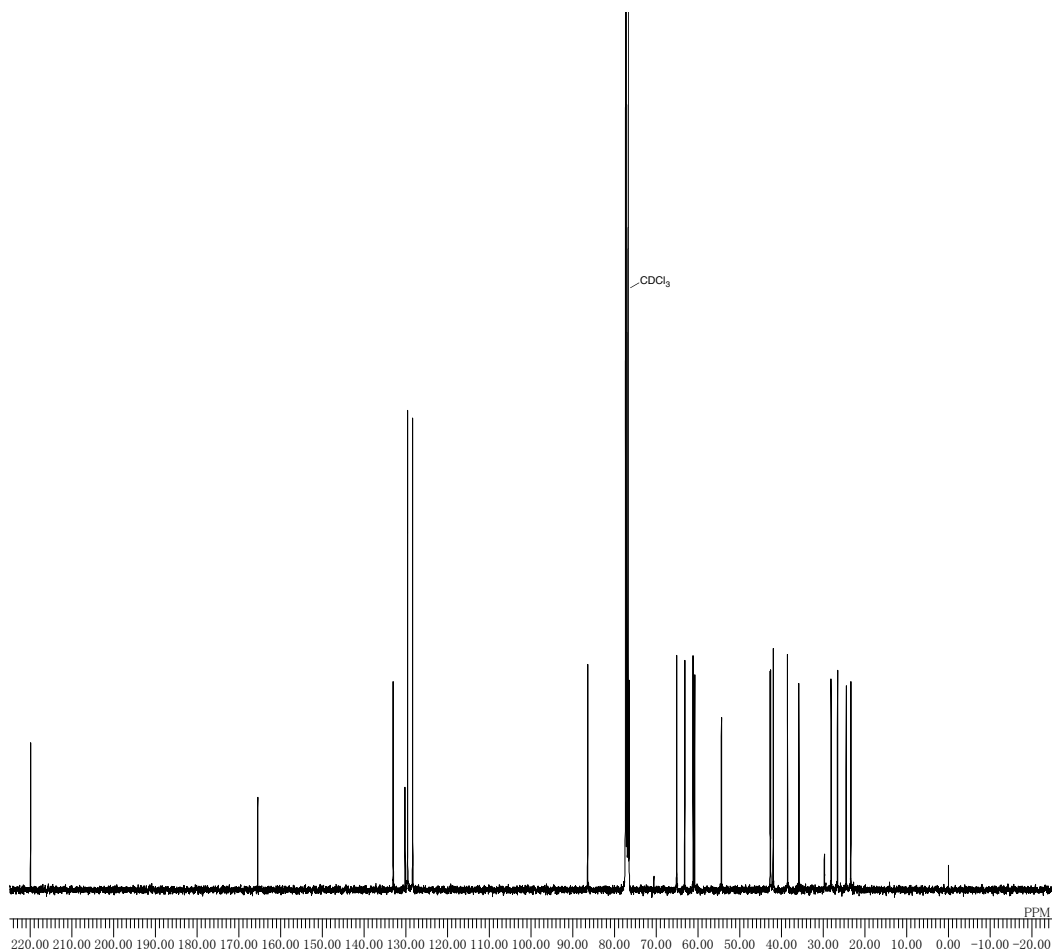


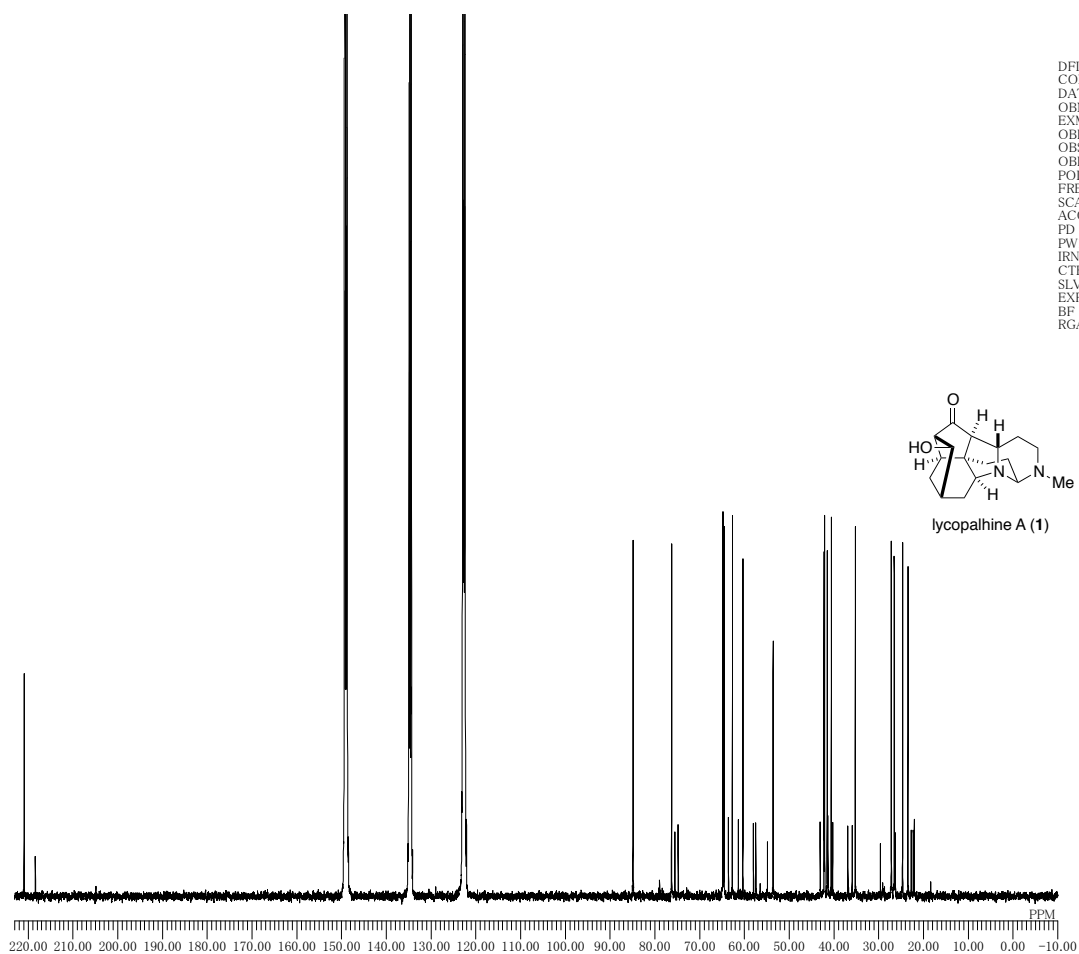
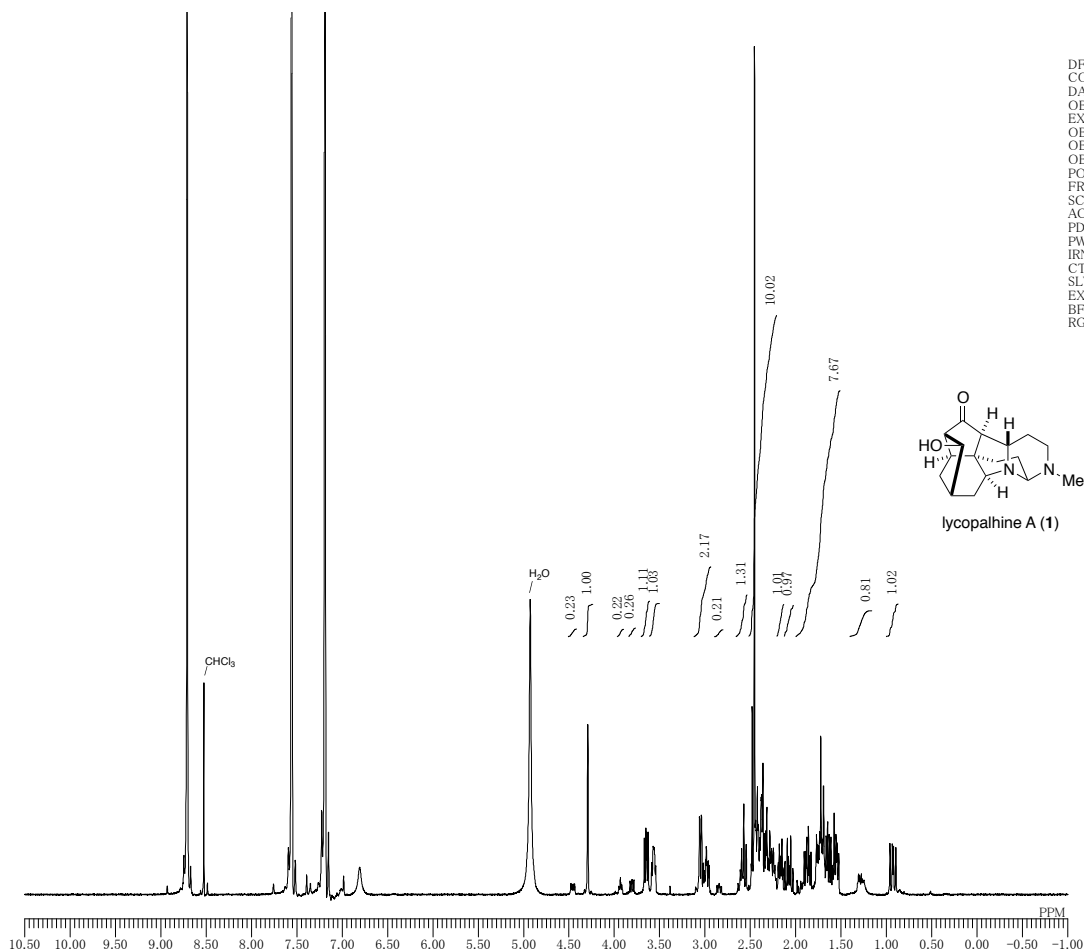


DFILE YO-5-189.non-data-1-1.als
 COMNT
 DATIM 24-08-2015 19:02:00
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.6 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 36



DFILE YO-5-189 overnight_bcm-1-1.als
 COMNT
 DATIM 25-08-2015 00:03:02
 OBNUC 13C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 4096
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC 1H
 CTEMP 25.5 c
 SLVNT CDCL3
 EXREF 0.00 ppm
 BF 2.02 Hz
 RGAIN 50





Synthetic lycopalhine A

DFILE YO-5-196 py_non-data-1-1.als
 COMNT
 DATIM 25-08-2015 16:36:50
 OBNUC 1H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC 1H
 CTEMP 25.3 c
 SLVNT C5D5N
 EXREF 7.19 ppm
 BF 0.12 Hz
 RGAIN 38

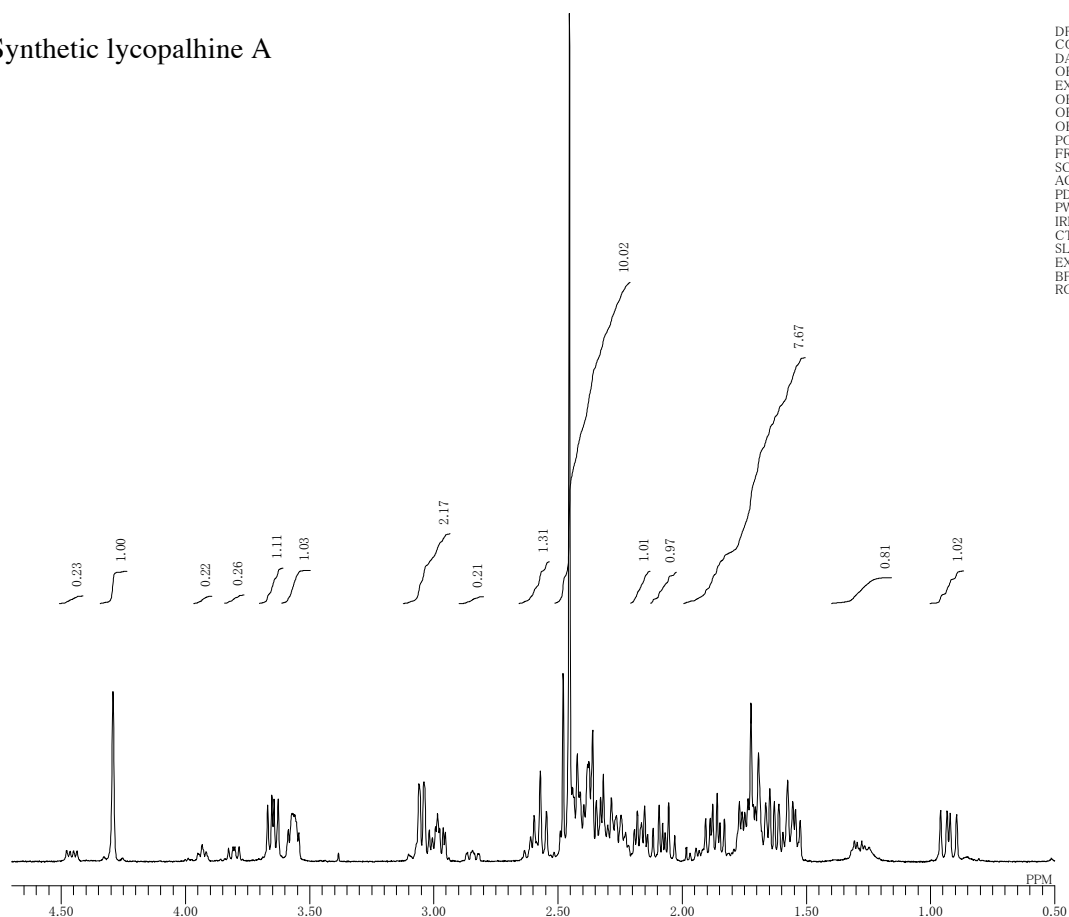
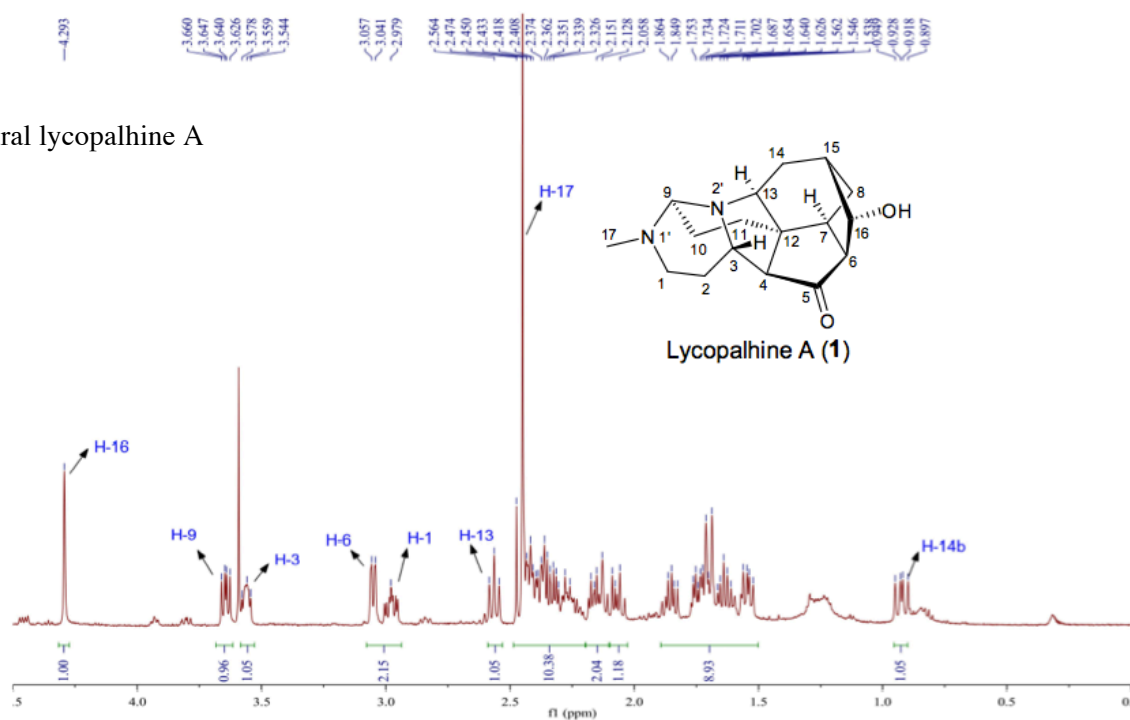
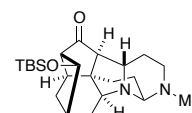
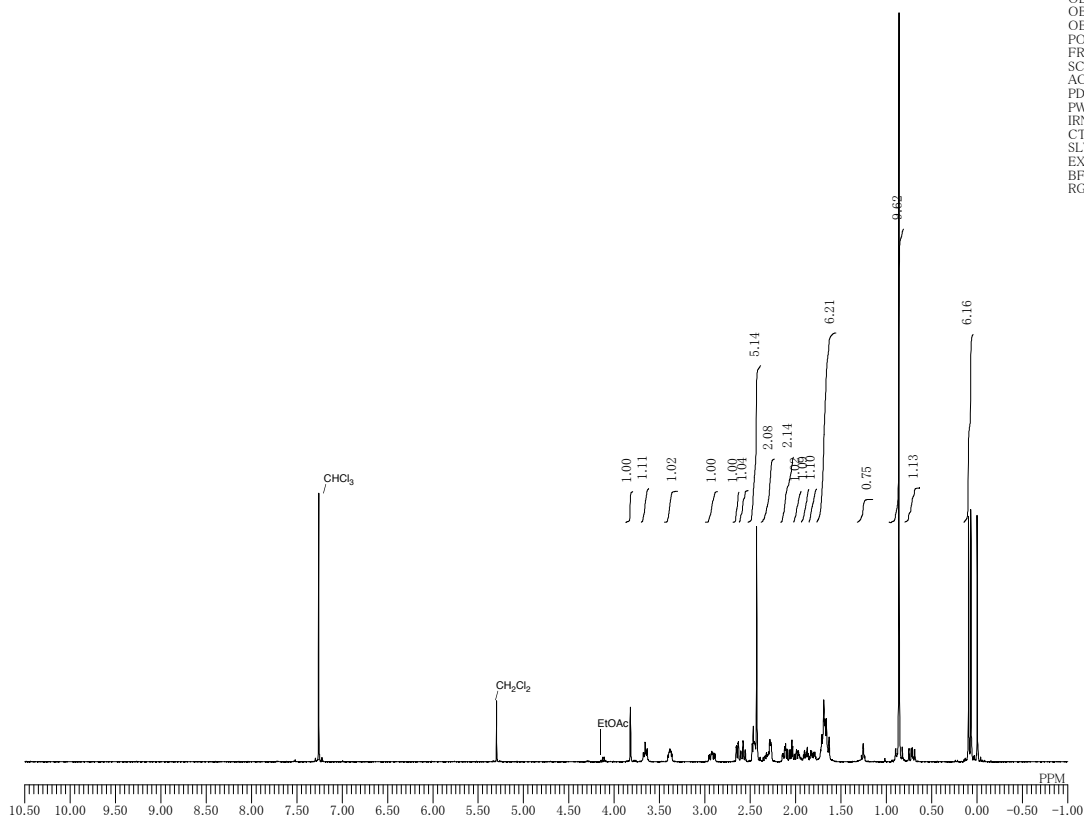


Figure S1. ¹H NMR spectrum of lycopalhine A (1) in pyridine-d₅ (500 MHz) from Zhao, Q.-S. et al. (*Chem. Commun.* **2012**, 48, 9038., Supporting Information).

Natural lycopalhine A

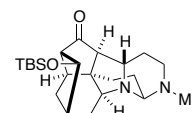
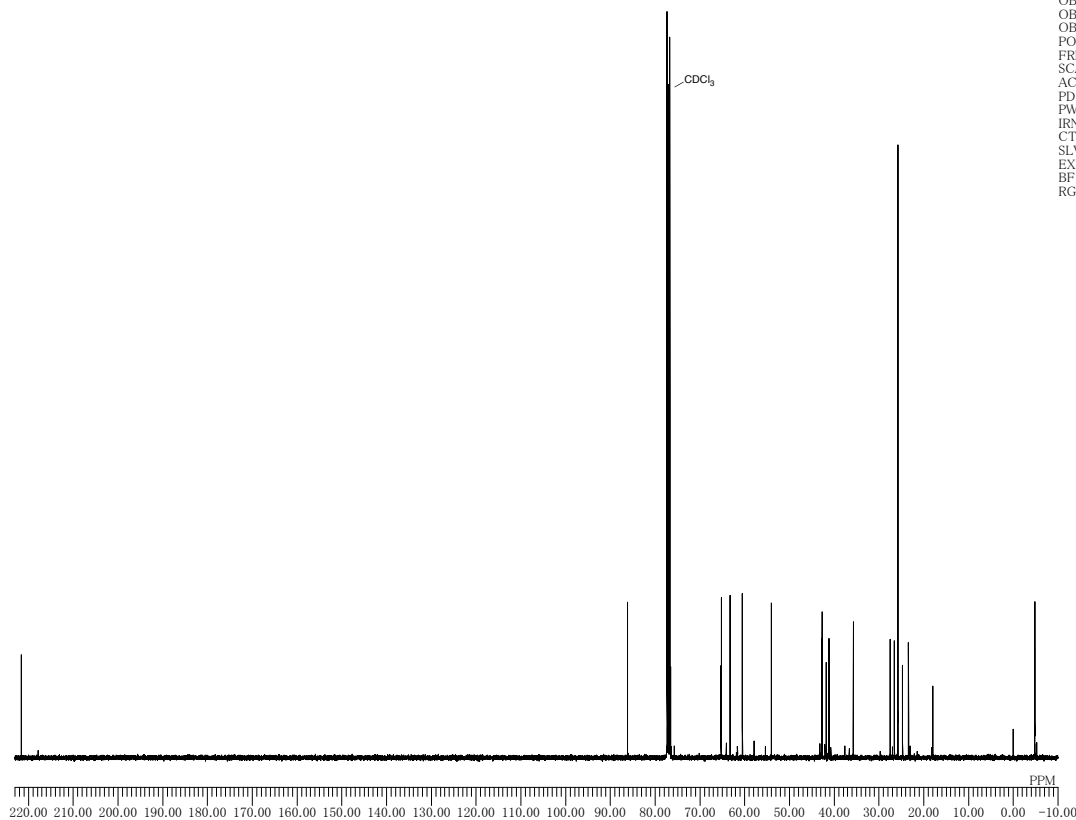


DFILE YO-5-197_non-data-1-1.als
 COMNT
 DATIM 29-08-2015 14:24:54
 OBNUC ¹H
 EXMOD single_pulse.jxp
 OBFRQ 399.78 MHz
 OBSET 4.19 KHz
 OBFIN 7.29 Hz
 POINT 13107
 FREQU 6002.40 Hz
 SCANS 8
 ACQTM 2.1837 sec
 PD 5.0000 sec
 PW1 4.90 usec
 IRNUC ¹H
 CTEMP 25.2 c
 SLVNT CDCL₃
 EXREF 7.26 ppm
 BF 0.12 Hz
 RGAIN 46



127

DFILE YO-5-197_overnight_bcm-1-1.als
 COMNT
 DATIM 30-08-2015 06:03:30
 OBNUC ¹³C
 EXMOD single_pulse.dec
 OBFRQ 100.53 MHz
 OBSET 5.35 KHz
 OBFIN 5.86 Hz
 POINT 26214
 FREQU 25125.63 Hz
 SCANS 8192
 ACQTM 1.0433 sec
 PD 1.5000 sec
 PW1 2.87 usec
 IRNUC ¹H
 CTEMP 25.4 c
 SLVNT CDCL₃
 EXREF 0.00 ppm
 BF 0.12 Hz
 RGAIN 50



127

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