遷移状態構造のエネルギーの評価

第2章に示したように、ジベンゾビシクロ[2.2.2]オクタトリエン骨格を有するマレイン酸誘導体**1**は、Diels-Alder反応において反応面選択性を示した。そこで、無置換体**1a**および反応に偏りの見られた**1c, 1d, 1e**について1,3-ブタジエンおよびシクロペンタジエンとの反応の計算を半経験的手法であるPM3法と*ab initio*法（HF/STO-3Gおよび一部のものについてはHF/6-31G*）を用いて行った。[193-195]また同時に反応中心である無水マレイン酸自体（**MA**）を基質とした計算も行った。反応は全てRHF計算で行い、**MA, 1a, 1d**についてはCs対称を導入した。**1d**のPM3による計算ではCartesian座標系を用いているので厳密にはC_1対称であるが、得られた構造はほぼCS対称となっている。**1c**および**1e**は分子自体に対称性がないのでCs対称は導入できない。これらの遷移状態構造のエネルギー値、活性化エネルギー（$\Delta E^{\ddagger}$）および*anti/syn*、*endo/exo*によるその活性化エネルギーの相対的な差（$\Delta\Delta E^{\ddagger}$）を**Table 17**から**Table 19**に示した。

各計算における活性化エネルギーの相対的な差（$\Delta\Delta E^{\ddagger}$）は、Table中で斜体にて*0.0*としたものに対する相対的な数値である。遷移状態構造はエネルギーの値の位置のカッコ内に示したとおり、ただ1つの負の振動モードとなっており、また全てのTSについてIRC計算を行い、的確な反応経路であることを確認している。

このエネルギー値からわかるように、分子軌道計算による活性化エネルギーの値は実験における反応の選択性の傾向を再現していない。実験による選択性の比から考えるとそのエネルギー差というのは0.4から0.6 kcal/molほどと考えられ、ここで行ったような計算によってはこのようなエネルギー差は再現するのは非常に困難であると考えられる。

structure [a]	mode	symm	Hf (PM3) [b,c]	$\Delta E^{\ddagger}$ [d]	$\Delta\Delta E^{\ddagger}$ [d,e]
MA	-	C_{2v}	-90.1 (0)		
BD	-	C_{2v}	31.8 (0)		
CPD	-	C_{2v}	31.8 (0)		
1a	-	C_{2v}	-21.2 (0)		
1c	-	C_1	-28.6 (0)		
1d	-	C_1	-188.2 (0)		
1e	-	C_1	-332.8 (0)		
TS(**MA**+**BD**)	*endo*	C_s	-32.9 (1)	25.4	*0.0*
TS(**MA**+**BD**)	*exo*	C_s	-33.8 (1)	24.5	-0.9
TS(**MA**+**CPD**)	*endo*	C_s	-27.6 (1)	30.7	*0.0*
TS(**MA**+**CPD**)	*exo*	C_s	-27.6 (1)	30.7	0.0
TS(**1a**+**BD**)	*endo*	C_s	39.6 (1)	29.0	*0.0*
TS(**1a**+**BD**)	*exo*	C_s	43.2 (1)	32.6	3.6
TS(**1c**+**BD**)	*endo-anti*	C_1	31.9 (1)	28.7	*0.0*
TS(**1c**+**BD**)	*endo-syn*	C_1	32.1 (1)	28.9	0.2
TS(**1d**+**BD**)	*endo-anti*	C_1	-127.7 (1)	28.8	*0.0*
TS(**1d**+**BD**)	*endo-syn*	C_1	-127.6 (1)	28.9	0.1
TS(**1e**+**BD**)	*endo-anti*	C_1	-272.3 (1)	28.7	*0.0*
TS(**1e**+**BD**)	*endo-syn*	C_1	-272.3 (1)	28.7	0.0
TS(**1a**+**CPD**)	*endo*	C_s	53.2 (1)	30.7	*0.0*
TS(**1a**+**CPD**)	*exo*	C_s	53.4 (1)	30.7	0.0
TS(**1c**+**CPD**)	*endo-anti*	C_1	45.4 (1)	42.2	*0.0*
TS(**1c**+**CPD**)	*exo-anti*	C_1	45.5 (1)	42.3	0.1
TS(**1c**+**CPD**)	*endo-syn*	C_1	45.4 (1)	42.3	0.1
TS(**1c**+**CPD**)	*exo-syn*	C_1	45.4 (1)	42.2	0.0
TS(**1d**+**CPD**)	*endo-anti*	C_1	-114.2 (1)	42.3	*0.0*
TS(**1d**+**CPD**)	*exo-anti*	C_1	-114.1 (1)	42.4	0.1
TS(**1d**+**CPD**)	*endo-syn*	C_1	-114.4 (1)	42.1	-0.2
TS(**1d**+**CPD**)	*exo-syn*	C_1	-114.5 (1)	42.0	-0.3
TS(**1e**+**CPD**)	*endo-anti*	C_1	-258.9 (1)	42.2	*0.0*
TS(**1e**+**CPD**)	*exo-anti*	C_1	-258.7 (1)	42.3	0.1
TS(**1e**+**CPD**)	*endo-syn*	C_1	-259.0 (1)	42.0	-0.2
TS(**1e**+**CPD**)	*exo-syn*	C_1	-259.2 (1)	41.8	-0.4

単位：kcal/mol, a) MA = maleic anhydride, BD = 1,3-butadiene, CPD = cyclopentadiene. b) Heat of formation at 298K, c) ()内は負の振動モードの数, d) Activation enthalpy at 298K, e) 斜字体をのものを基準とした相対値

Table 17: PM3 法による計算

structure [a]	mode	symm	HF/STO-3G [b]	HF/6-31G*(SP) [c]	HF/6-31G*(OPT)	scaled ZPE [d,e]	
MA	–	C_{2v}	-372.27461 (0)	-377.21791	-377.23017 (0)	37.96	(36.49)
BD	–	C_{2v}	-153.01744 (0)	-154.91291	-154.91346 (1)	59.44	(54.39)
CPD	–	C_{2v}	-190.45711 (0)	-192.79094	-192.79172 (0)	65.29	(59.46)
1a	–	C_{2v}	-900.64465 (0)	-912.04681	–	160.23	
1d	–	C_s	-1290.46590 (0)	-1307.41240	–	136.78	
TS(MA+BD)	*endo*	C_s	-525.24093 (1)	-532.07867	-532.09104 (1)	99.53	(93.08)
TS(MA+BD)	*exo*	C_s	-525.23904 (1)	-532.07568	-532.08798 (1)	99.50	(93.03)
TS(MA+CPD)	*endo*	C_s	-562.68076 (1)	-569.96119	-569.97349 (1)	104.73	(97.76)
TS(MA+CPD)	*exo*	C_s	-562.67865 (1)	-569.95783	-569.97016 (1)	104.75	(97.81)
TS(1a+BD)	*endo*	C_s	-1053.60525 (1)	-1066.90411	–	221.23	
TS(1a+BD)	*exo*	C_s	-1053.60048 (1)	-1066.89789	–	221.31	
TS(1a+CPD)	*endo*	C_s	-1091.02994 (1)	-1104.77316	–	226.62	
TS(1a+CPD)	*exo*	C_s	-1091.03380 (1)	-1104.77264	–	226.62	
TS(1d+CPD)	*endo-anti*	C_s	-1480.85161 (1)	-1500.14036	–	202.91	
TS(1d+CPD)	*endo-syn*	C_s	-1480.85151 (1)	-1500.14040	–	202.90	
TS(1d+CPD)	*exo-anti*	C_s	-1480.85597 (1)	-1500.14094	–	203.14	
TS(1d+CPD)	*exo-syn*	C_s	-1480.85562 (1)	-1500.14014	–	203.16	

単位：a.u. a) MA = maleic anhydride, BD = 1,3-butadiene, CPD = cyclopentadiene. b) ()内は負の振動モードの数, c) Single-point calculations on HF/STO-3G geometries d) ZPE (HF/STO-3G zero-point energy) scaled by 0.95. e) In parethese, ZPE (HF/6-31G*) scaled by 0.95 was shown.

Table 18: *ab initio*計算による total energy

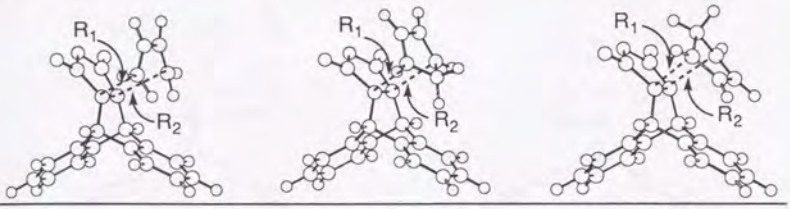
structure [a]	mode	$\Delta E^{\ddagger}$ HF/STO-3G [b,c]	$\Delta E^{\ddagger}$ HF/6-31G*(SP)	$\Delta E^{\ddagger}$ HF/6-31G*(OPT)	$\Delta\Delta E^{\ddagger}$ HF/STO-3G [b,c]	$\Delta\Delta E^{\ddagger}$ HF/6-31G* [d,e,f]	
TS(MA+BD)	*endo*	32.08 (34.21)	32.72	33.00 (35.20)	*0.00 (0.00)*	*0.00 (0.00)*	*[0.00]*
TS(MA+BD)	*exo*	33.27 (35.37)	34.60	34.94 (37.08)	1.19 (1.16)	1.88 (1.92)	[1.88]
TS(MA+CPD)	*endo*	31.97 (33.46)	29.91	30.37 (32.18)	*0.00 (0.00)*	*0.00 (0.00)*	*[0.00]*
TS(MA+CPD)	*exo*	33.30 (34.80)	32.02	32.46 (34.32)	1.33 (1.34)	2.11 (2.09)	[2.14]
TS(1a+BD)	*endo*	35.67 (37.23)	34.90	–	*0.00 (0.00)*	*0.00*	
TS(1a+BD)	*exo*	38.66 (40.30)	38.80	–	2.99 (3.07)	3.90	
TS(1a+CPD)	*endo*	45.06 (46.16)	40.53	–	*0.00 (0.00)*	*0.00*	
TS(1a+CPD)	*exo*	42.64 (43.74)	40.86	–	-2.43 (-2.42)	0.33	
TS(1d+CPD)	*endo-anti*	44.80 (45.65)	39.52	–	*0.00 (0.00)*	*0.00*	
TS(1d+CPD)	*endo-syn*	44.87 (45.70)	39.50	–	0.04 (0.04)	-0.02	
TS(1d+CPD)	*exo-anti*	42.07 (43.14)	39.16	–	-2.74 (-2.51)	-0.36	
TS(1d+CPD)	*exo-syn*	42.29 (43.37)	39.66	–	-2.52 (-2.27)	0.14	

単位：kcal/mol, a) MA = maleic anhydride, BD = 1,3-butadiene, CPD = cyclopentadiene. b) Values uncorrected with ZPE. c) Values corrected with ZPE (scaled by 0.95) in parentheses. d) Energy differences based on HF/6-31G*//STO-3G (SP). e) In parentheses, HF/6-31G*//HF/6-31G* without ZPE correction. f) In blankets, HF/6-31G*//HF/6-31G* + scaled ZPE. それぞれ斜字体をのものを基準とした相対値

Table 19: *ab initio*計算による活性化エネルギー

TSにおける構造の評価

一方得られた遷移状態構造における結合長と角度であるが、**Table 20**には**1a,c-e**の各ジエンとの反応での生成するC-C結合の長さを記してある。置換基によらずにほぼ一定の値（2.25-2.27 Å）をとっていることがわかる。またこれらはほとんどR_1=R_2であるといって良い値である。*anti*付加と*syn*付加における結合長の違いは見られない。また、置換基による効果も議論すべき違いは見られない。

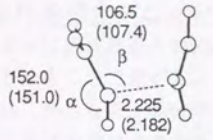


		1 + **BD** (*endo*)		1 + **CPD** (*endo*)		1 + **CPD** (*exo*)	
dienophile	mode	R_1	R_2	R_1	R_2	R_1	R_2
1a	-	2.245	2.245	2.260	2.260	2.258	2.258
1c	*anti*	2.251	2.247	2.269	2.260	2.266	2.258
1c	*syn*	2.247	2.250	2.259	2.269	2.256	2.265
1d	*anti*	2.249	2.249	2.265	2.265	2.262	2.262
1d	*syn*	2.250	2.250	2.265	2.265	2.262	2.262
1e	*anti*	2.250	2.250	2.266	2.266	2.263	2.263
1e	*syn*	2.250	2.250	2.266	2.266	2.263	2.262

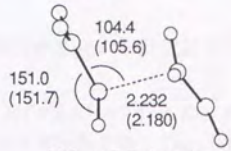
C-C結合長（Å）

Table 20: 遷移状態構造における生成する結合長

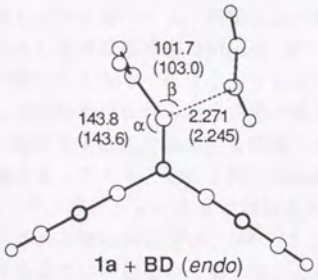
そこで、構造的な特徴を考える上では無置換体**1a**を取り上げれば十分であると考え、また反応中心である無水マレイン酸（**MA**）との比較は重要であると考えた。これらの遷移状態構造における結合長および反応中心周辺の二面角を**Figure 86**に示した。これらの構造は試薬であるジエンとその*endo/exo*の付加形式によらずに共通した傾向がある。即ち、**1a**に対する反応においてはその反応中心の屈曲（α）が**MA**の場合に比べて大きくなっている。これは一つにはβの角度が**MA**の場合に比べて小さくなっていることからもわかるように、ジエンが上側に位置が移っていることが要因と考えられる。これはアロマティック部分とジエンとのおそらく立体的な反発を表現しているためであり、環状ジエンとの反応の*endo/exo*比について以前に述べたジベンゾビシクロ[2.2.2]オクタトリエン骨格に基づく立体反発はやはり存在するといえる。またもう一つにはビシクロ骨格による反応中心の歪みは屈曲（α）によって解放されるため、**MA**の場合よりもこの度合いが強くなることも考えられる。



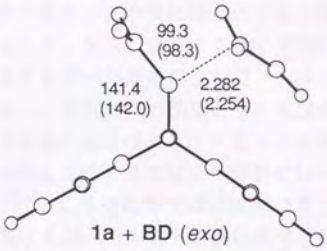
MA + BD (*endo*)



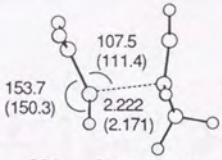
MA + BD (*exo*)



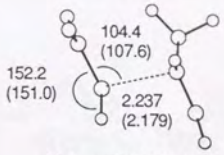
1a + BD (*endo*)



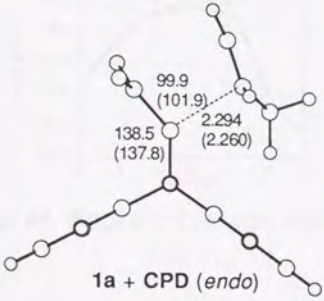
1a + BD (*exo*)



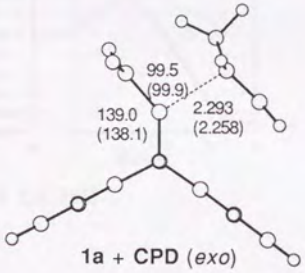
MA + CPD (*endo*)



MA + CPD (*exo*)



1a + CPD (*endo*)



1a + CPD (*exo*)

Figure 86: HF/STO-3G 計算による遷移状態構造の構造：二面角および結合長（カッコ内は PM3 計算による）

IRC上における結合ポピュレーションの変化

第3章において求核反応とDiels-Alder反応での結合性性の度合いを計算結果として示した。その方法をここで述べる。

計算方法は、小さなモデル分子を取り上げて、HF/6-31G*を用いて行った。求核反応としてはホルムアルデヒドの水素化ホウ素リチウムによる還元反応を、Diels-Alder反応は無水マレイン酸とブタジエンの反応を取り上げた。Diels-Alder反応はもちろんであるが、還元反応においても一段階反応の遷移状態が得られた。[196, 197]

得られた遷移状態構造は**Figure 87**の様なものである。この図にはここから出発したIRC計算のエネルギー変化をも合わせてプロットした。反応が進行する様子が見られる。しかし反応の進行に伴う結合状態の変化は、全エネルギーや構造の変化だけを追っていても、極めて主観的で抽象的な情報しか得られない。そこで何か指標となる変数の導入が必要となってくる。そこで新たに生成してくる結合の結合ポピュレーションを取り上げた。[198] ポピュレーション解析自体は種類の異なる原子間の結合の評価には問題があるとされる場合があるが、[199] ここで取り上げるような結合生成の変化の度合いを評価する上では問題ないと考えた。これはまた先にも述べたとおり、反応の進行度の状況を数字として表すことが必要であるため導入した変数である。

横軸に反応座標をあらわす標準座標を、縦軸に還元反応においてはC-H結合の、Diels-Alder反応においてはC-C結合のポピュレーションをプロットしたものが**Figure 88**である。

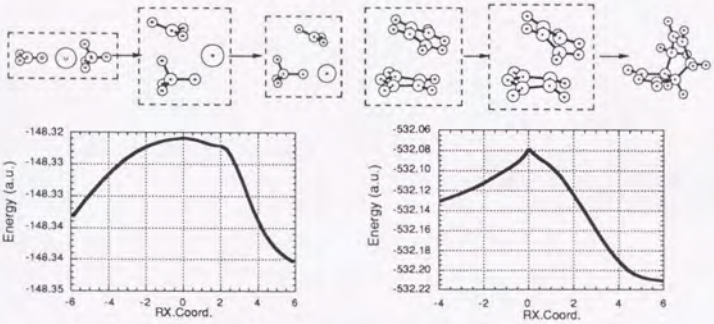


Figure 87: 求核反応とDiels-Alder反応とにおけるIRC計算

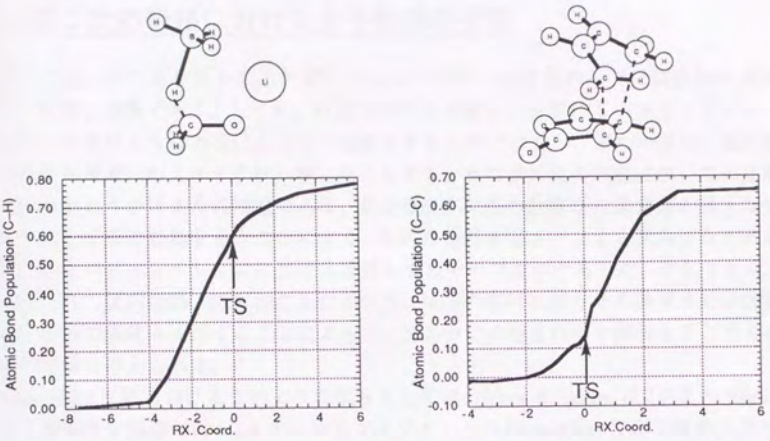


Figure 88: 新たに生成する結合のポピュレーション

これを用いて、第3章・第3節においては反応の進行に伴う相互作用の発現についての議論を行った。これについては重複するのでここでは省略する。

第2節：反応経路における分子軌道の考察

前節で示したとおり分子軌道計算によるエネルギーの評価のみでは選択性を説明する上で非常に困難である。とくに、計算では再現が難しいとされる小さなエネルギー差の場合にはそのような方法はとうてい信頼できるものではない。またかりに、選択性と活性化エネルギーの大小・差が一致したとしても、その選択性の起源についての見解を得られるかどうかはまた別問題である。そこで反応経路の計算から通常何か適当な変数を取り出してその変動を追うことにより、反応の情報を得ようとする試みがなされる。前述の結合ポピュレーションにおける考察もまたそのひとつであった。そしてまた、計算で得られた反応経路、即ちIRC上において、反応の進行に伴うその基質または基質系の分子軌道の変化を追跡することによって、反応中での相互作用を解明することもまた可能であると考えられる。

Diels-Alder反応におけるこのような試みとしては、Hehre と Salem、[187] および Bach [200] による興味深い報告がある。エチレンとブタジエンとの Diels-Alder 反応の遷移状態を *ab initio* 計算によって求め、反応体系・遷移状態・生成物における分子軌道のエネルギーを比較すると、この反応におけるエネルギー障壁というのは大部分は被占軌道同士の closed-shell repulsion によっているという考え方である。この作用が求核・求電子・周辺環状反応という様々な反応における HOMO-HOMO 相互作用として存在することが Bach らにより報告されている。[201-203]

対称性により対称な軌道（**S**）と反対称な軌道（𝔸）とに分けて考えると、Diels-Alder 反応では対称性の要請により HOMO と HOMO との相互作用ではない。対称性の合う **S** と **S** との被占軌道同士の不安定化相互作用（closed-shell repulsion）として存在し、全体としてはエネルギーの上昇を伴う相互作用を行う（**Figure 89**）。対称性の合わない **S** と 𝔸 とは相互作用せず、エネルギーが交差することもある。この原型はもちろん Woodward-Hoffmann の相関図であるが、[204] 分子軌道計算を行うとこれをより定量的な方法で評価することができる。実際に Bach らが加えている考察は、空軌道をも考慮して π 軌道全体によるエネルギーの定量的変化を追っており、相互作用の有無や大きさを論じるのは、空軌道も合わせて考えなければならないのであるが、結論として定性的に重要なのは被占軌道の挙動である。

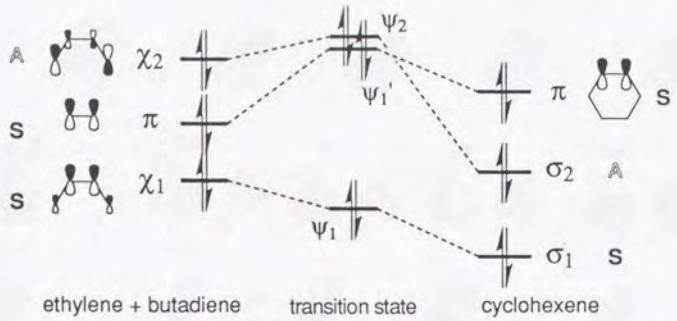


Figure 89: エチレンとブタジエンとのDiels-Alder反応におけるπ軌道のエネルギー変化

エチレンのHOMO（π）とブタジエンのNXHOMO（χ_1）は共に対称的（**S**）であり、遷移状態に近づくにつれて相互作用をしてエネルギーの分裂を生じる。この結果が、ψ_1とψ_1'とである。これによって全エネルギーとしての上昇がおこり、エネルギー障壁となっている。一方この作用のあとに反対称（**A**）の軌道であるブタジエンのHOMO（χ_2）とエチレンのLUMO（π^*：**Figure 89**には示していない）との相互作用が現れ、安定化がおこることによって反応が進行するというのがBachらの考えである。

遷移状態ではエネルギーの勾配はゼロであるので、既に安定化相互作用は発現し始めていて、それとエネルギー障壁を作る不安定化相互作用とが釣り合って遷移状態となっていると考えるべきであろう。それ故、活性化エネルギーの大きさを左右する要因は、この遷移状態に至る障壁の相互作用だけというわけではないが、この考え方は興味深く、本研究における選択性に対して影響を及ぼしている可能性もあると考えた。

後に置換基を導入したいくつかのジエノファイル分子そのものの計算をすることを考え、また空軌道の信頼性のためにsplit valenceを避けてPM3法を計算方法として選択した。まず最初に無水マレイン酸（**MA**）および無置換体（**1a**）と1,3-ブタジエン（**BD**）のDiels-Alder反応におけるIRC上の分子軌道を**Figure 90**から**Figure 93**に、そのエネルギー変化を**Figure 94**に示す。また、エネルギーのグラフにおける番号は、反応体系・TS系・生成物における何番目の軌道かを表している。

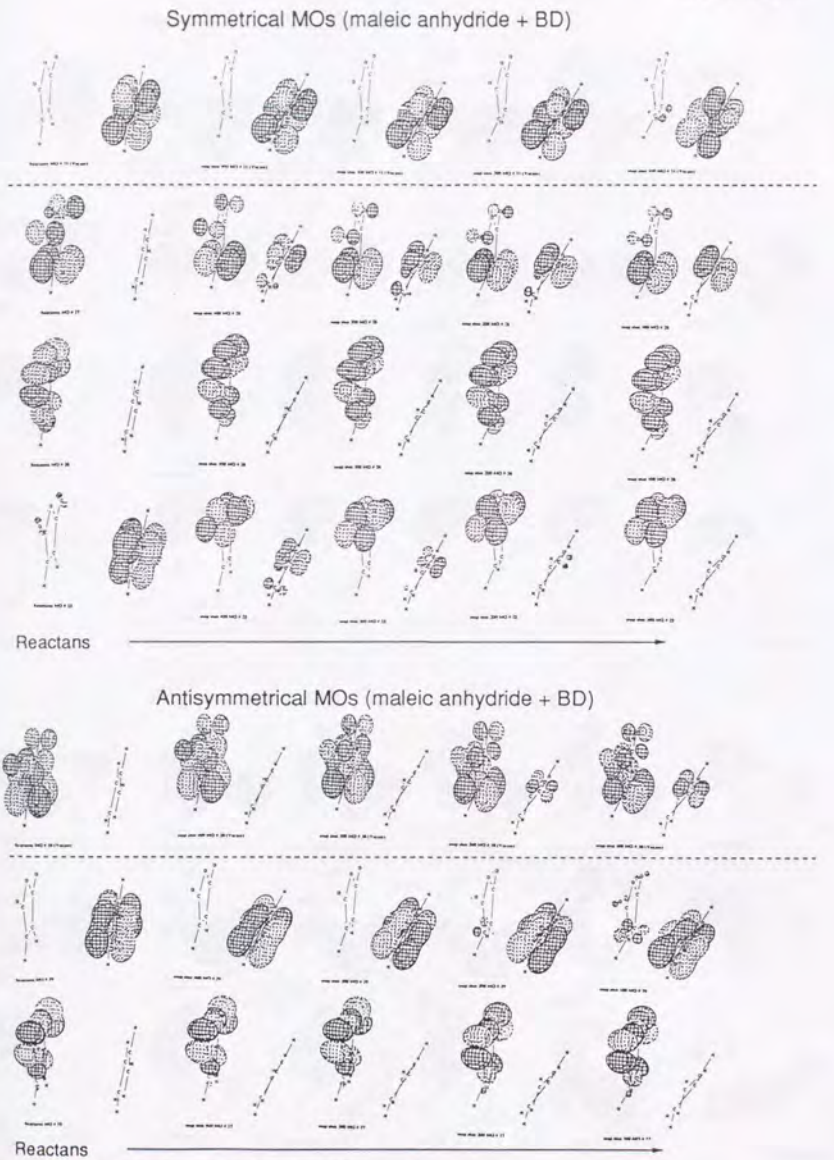


Figure 90: IRC における分子軌道（**MA + BD → TS**）

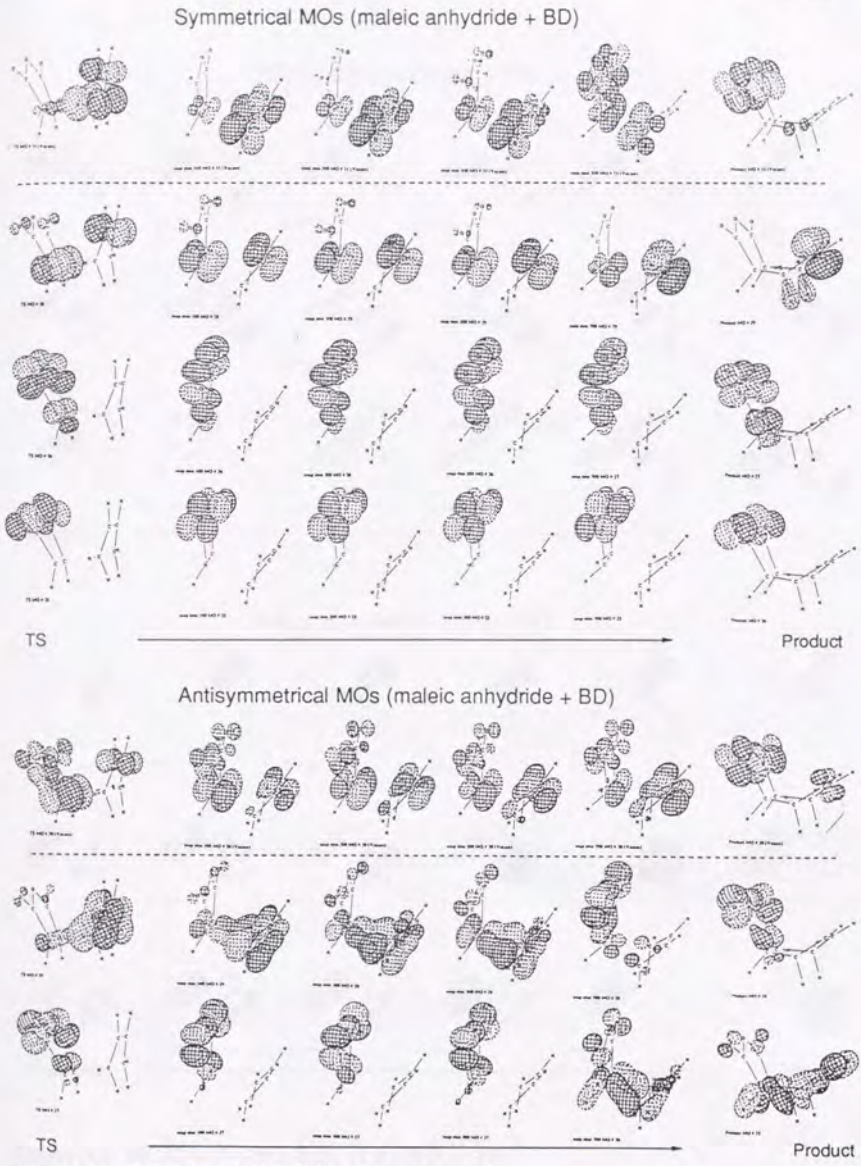


Figure 91: IRC における分子軌道（**TS → Adduct**）

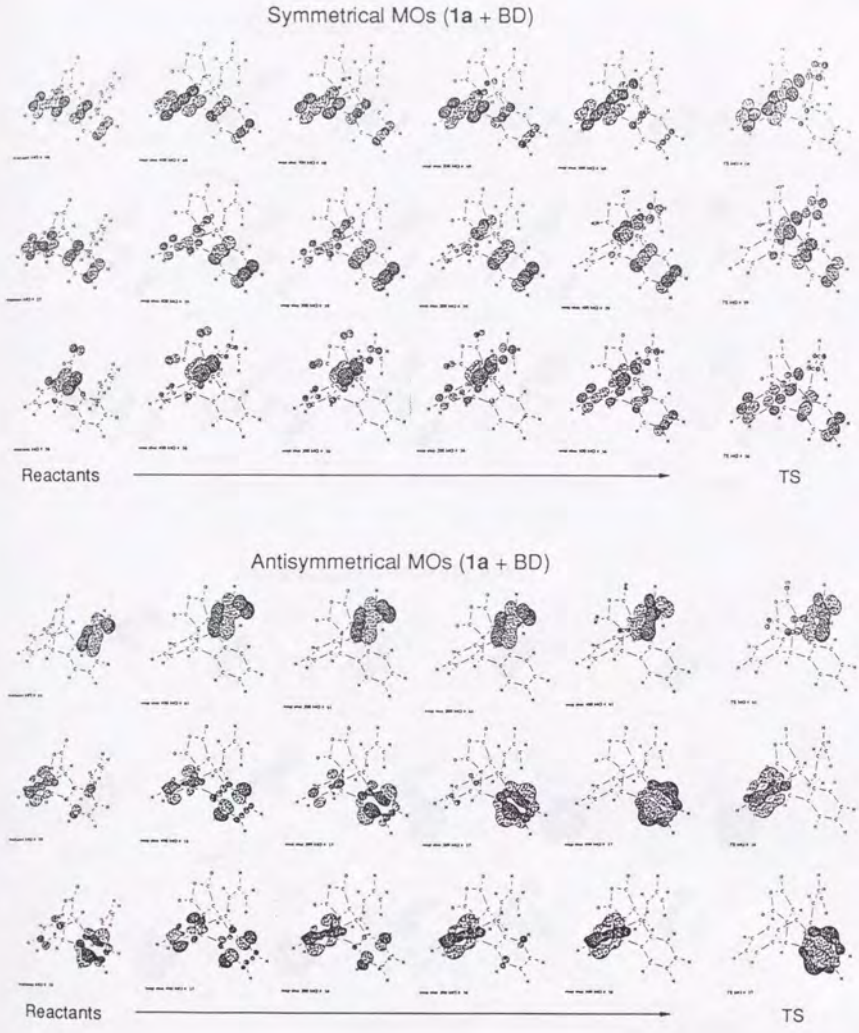


Figure 92: IRC における分子軌道（**1a** + **BD** → **TS**）

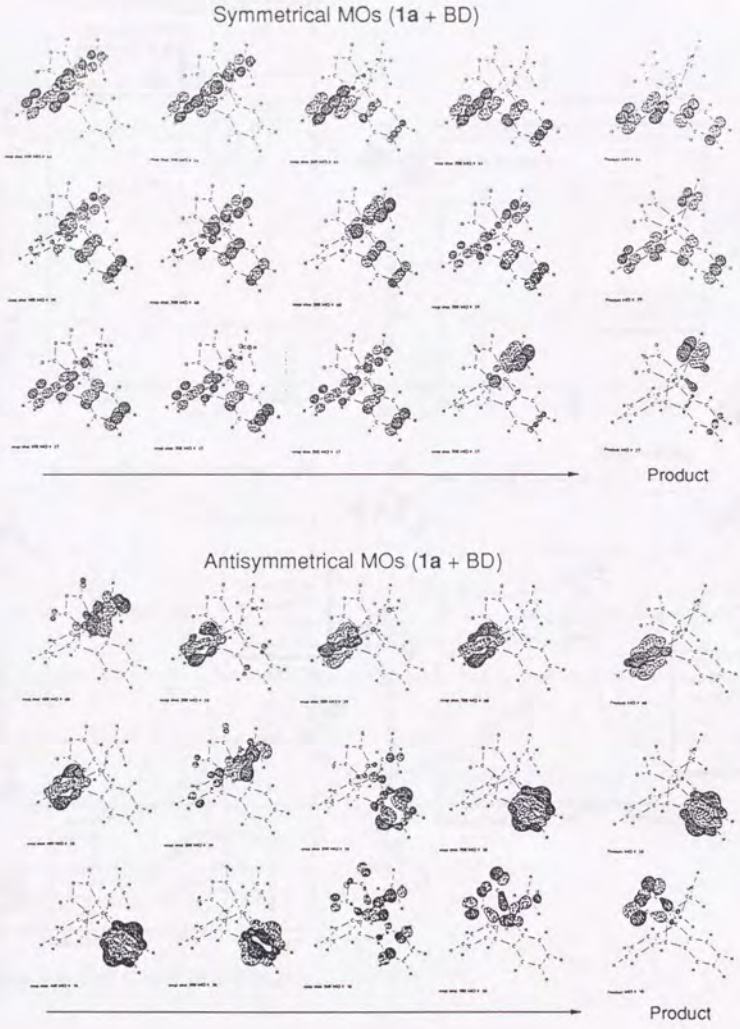


Figure 93: IRC における分子軌道（TS → **34a**）

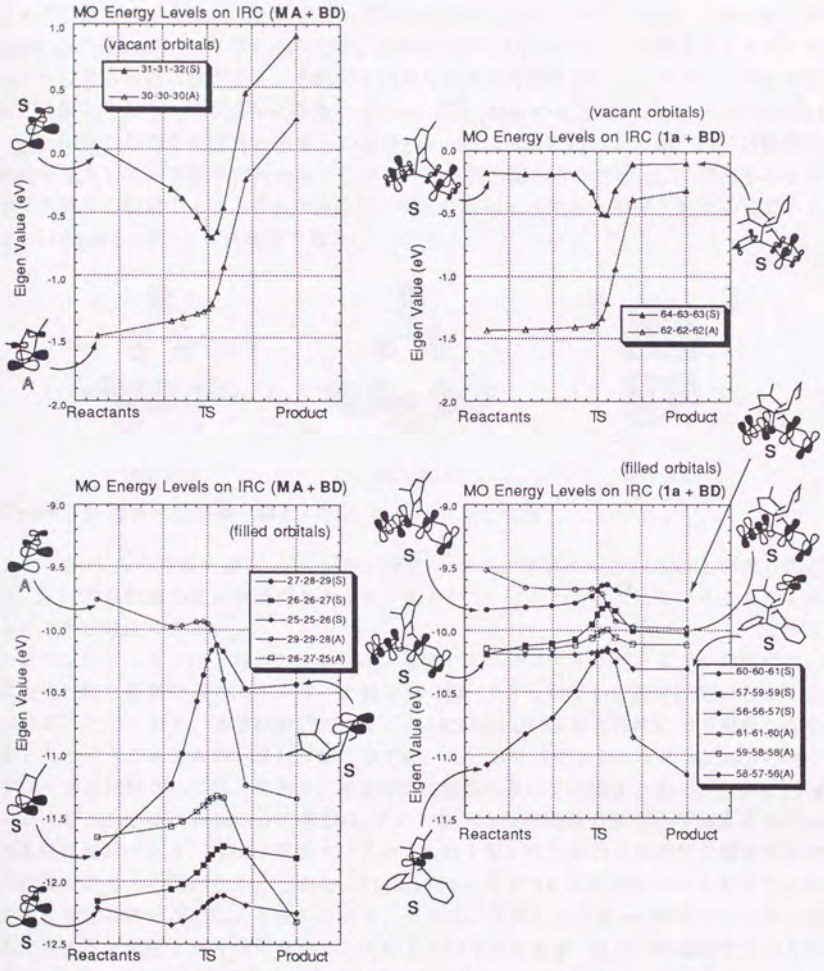
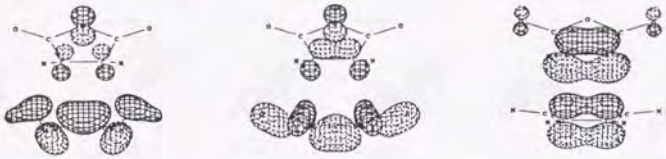


Figure 94 IRC における分子軌道のエネルギー

まずは反応中心である **MA** についてであるが、これについて Bach らの指摘する closed-shell repulsion の考察を試みたが、当然のことながらエチレンの場合よりも高エネルギーにある軌道は数が多く、それらとの更なる相互作用によりエネルギー・分布がさらに分裂しており、その解析は容易ではない。実際、**MA** のπとブタジエンの NXHOMO（χ_1）由来のものを主成分とするものは**Figure 95**に示す軌道であるが、同じ対称性の軌道が混入している様子がわかる。しかし、逆位相の組み合わせの ψ_1'に相当するものが２８番目の軌道であり、これが逆位相の相互作用によってエネルギーが上昇していることは**Figure 94**から一目瞭然である。



MO #22　　MO #24　　MO #28

Figure 95: 遷移状態構造（**MA**＋**BD**）における分子軌道

また Bach らの指摘の通り、ジエンの HOMO とジエノファイルの LUMO との相互作用は、反対称な軌道の最高軌道のエネルギー低下が TS 付近からおこっていることからも遅いことが確認できる。

ジベンゾビシクロ[2.2.2]オクタトリエン骨格のジエノファイルである **1a** の場合は、この反対称な最高軌道のエネルギーの低下は **MA** よりもわずかに速い段階からおこっていることがわかる。遷移状態においてこの HOMO-LUMO 相互作用はより重要となっているということである。また、第３章で述べたとおり、ブタジエンの HOMO のバックローブは依然として残っており、相互作用に影響を及ぼすと考えられる。しかし、**1a** における closed-shell repulsion の考察は、その対称的な軌道の数の多さから **MA** の場合よりも更に複雑であり、もはや明瞭ではない。これを用いて反応面の選択性を議論するのは困難であると考えられる。しかし、**Figure 95**に示す **1a** の反応における軌道のエネルギー変化は興味深いことを表している。それは、上昇してくる ψ_1'軌道がベンゼン環に分布するπ軌道と相互作用をおこしているという点であり、反応に面選択性を示した **1c-e** においては２つの異なるベンゼン環と相互作用しているはずである。。

そこで次に電子吸引性基を導入した基質のうちテトラフルオロ体 **1d** の反応についての計算を行った。**1d** は分子とその反応の対称性が Cs 対称であり、ここでの考察に適していると考えられる。反応体系から遷移状態構造までで十分と考え、同様に *anti* 付加と *syn* 付加それぞれにおける各分子軌道を**Figure 96**と**Figure 97**に、エネルギーを**Figure 98**に示す。

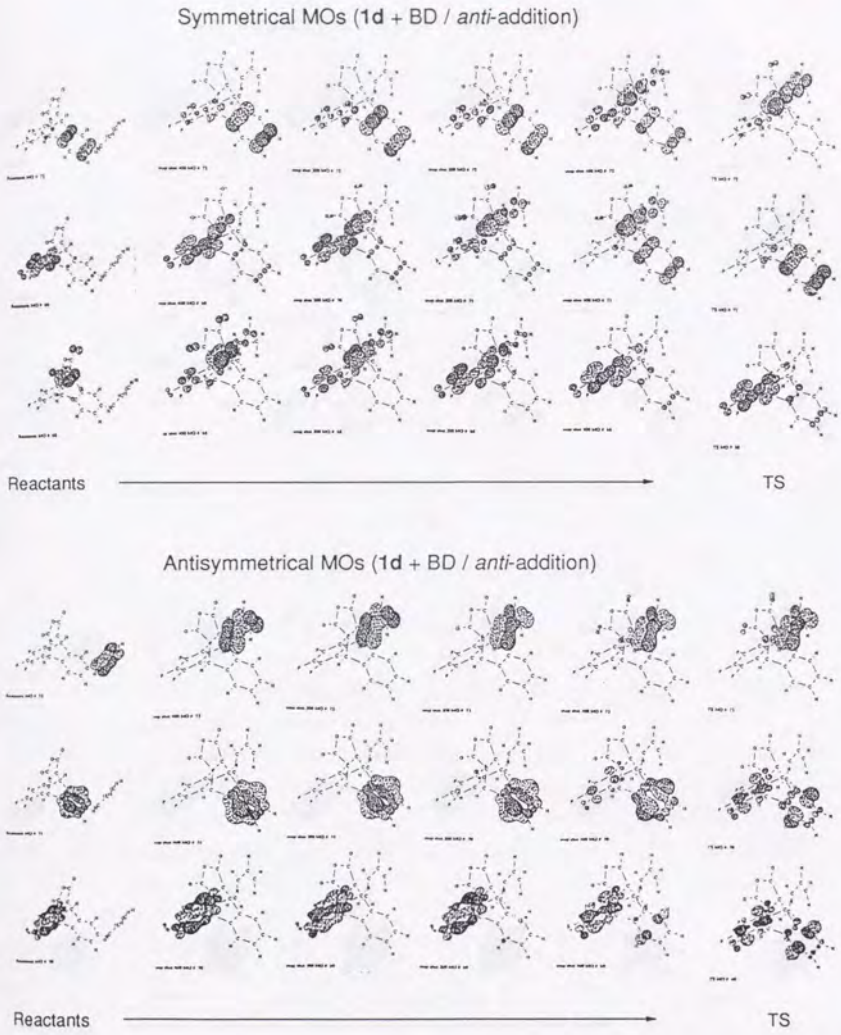


Figure 96: IRC における分子軌道（**1d** + **BD** → **TS** / *anti*-付加）

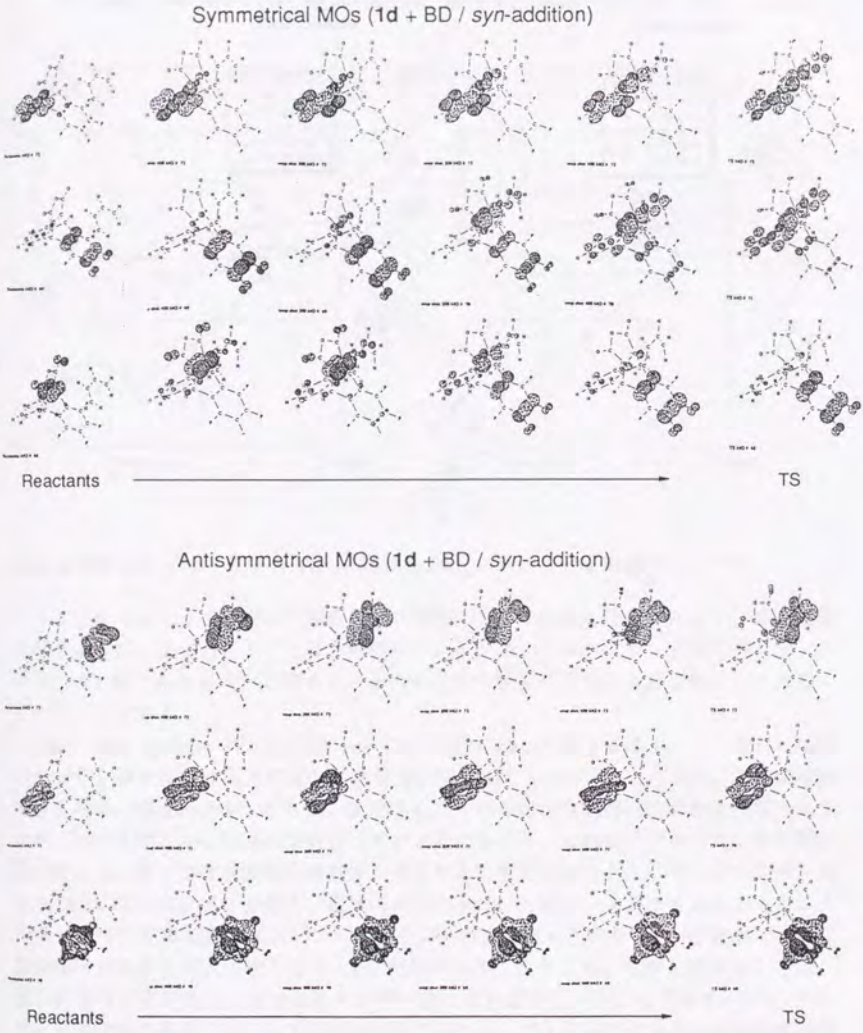


Figure 97: IRC における分子軌道（**1d** + **BD** → **TS** / *syn*-付加）

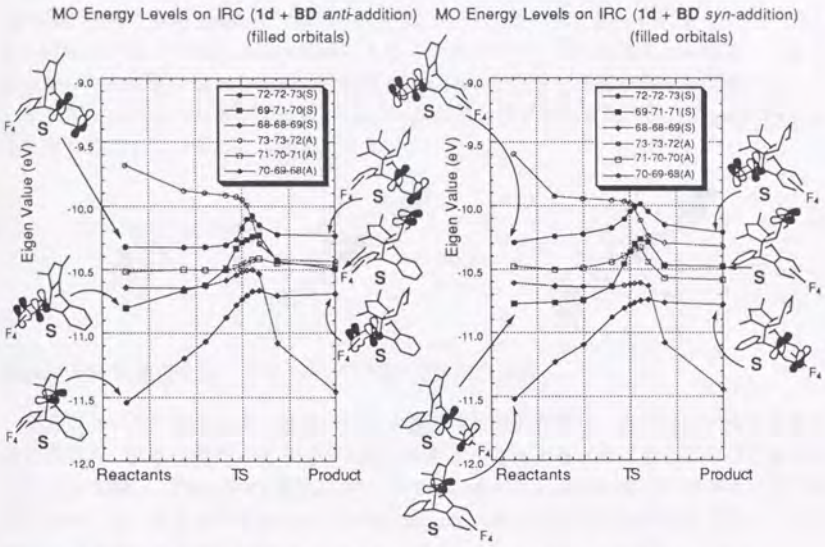


Figure 98: IRC（**1d**＋**BD** → **TS** → **34d, 35d**）における分子軌道のエネルギー

ここではもはやπおよびπ*軌道全体の考察は困難であると思われたので、被占軌道のみを示した。まずわかることは、両側のベンゼン環つまりベンゼンと置換ベンゼンとのHOMOは、エネルギーが離れているために分子軌道においてもほぼ独立して分布していることである。

closed-shell repulsion相互作用が*anti*付加と*syn*付加とで異なるとすると、それは両側のベンゼン環が相互作用系に混合されて違いが出てくるということである。これが確認できるのは、**Figure 98**のグラフに**S**で示した3個の対称な軌道同士の相互作用の大きさが、*anti*付加と*syn*付加とで異なっている点であろう。これは、ブタジエンから見て*anti*側と*syn*側とでは空間的な重なりが違うために生じる差である。そしてベンゼン環のHOMOは、ベンゼンが高く、置換ベンゼンが低いために、上昇する反応中心のエネルギーに対して順次置換ベンゼン・ベンゼンと相互作用していくが、*anti*付加ではその相互作用の大きさが大・小となり、*syn*付加では小・大となる。しかし重要なことは、差し引きの不安定化の大きさはエネルギー差によらないということである。[156] つまり、*anti*付加の過程において大小の差が生じるのは、ブタジエンから見た位置関係の違いにより、空間的な軌道の重なり方が異なるからであるが、その大・小という順番はエネルギー差によっており、これには不安定化上は意味はない。*syn*付加においても同様である。そのため、これらのことは*anti*/*syn*での違いということにはならず、closed-shell

repulsion 相互作用が *anti*/*syn* で異なっているということは考えにくい。もちろん、ベンゼン環の空軌道との相互作用は考慮に入れていないので、*anti* 付加と *syn* 付加とで全く差異がないとは言い切れないが、同位相の安定化相互作用が存在するならば混合されてくると考えられるベンゼン環の軌道は、[33] 反応系の分子軌道を見る限り**Figure 99**のような形で存在していることは確認できない。

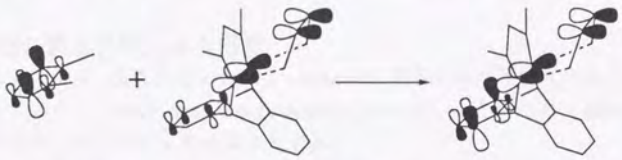


Figure 99: 軌道混合則によるベンゼン環の空軌道の混合

反応において、エネルギー障壁の後にある遷移状態の存在は、反応に対する不安定化相互作用と、反応を進行させる安定化相互作用とが存在するために生じるものであるが（**Figure 100**）、Diels-Alder 反応においては closed-shell repulsion 相互作用が不安定化相互作用として、また HOMO(diene)-LUMO(dienophile)相互作用が安定化相互作用としての主たる要因であると考えられる。

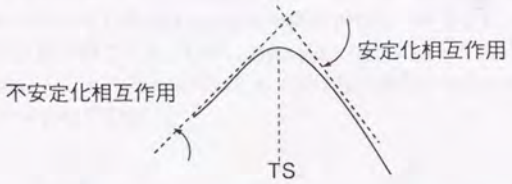


Figure 100

本節で示してきたとおり、その不安定化相互作用には反応面選択性の起源となる有力な差異は見られなかった。また、前章においてはこの安定化相互作用が *anti*/*syn* で違いを生じることを示してきた。このような考察からも、このジベンゾビシクロ[2.2.2]オクタトリエン骨格における反応面選択性についてはフロンティア軌道の非対称化によっているのであることが強く示唆されるものである。

第5章：他の理論による反応面の予測

本章においては、第2章で示したπ面選択性をいくつかの理論・モデルによる説明を行うことを試みる。詳細な計算や追加実験等は行っていないので、それぞれ簡単な考察にとどめる。各理論・モデルの説明については序章を参照されたい。

Electrostatic 相互作用による考察

本研究においては、基質分子における electrostatic 効果の非対称性を計算により求めることは行っていない（MEP: molecular electrostatic potential）。そのため、electrostatic 効果の考察も定性的なものにとどめることとする。

まず最も単純に、ジベンゾビシクロ[2.2.2]オクタトリエン骨格の基質 **1**,**2** に対し、試薬が攻撃する際に、electrostatic 効果を *anti* と *syn* とで異なるように受けて選択性が現れると考える。求核試薬、およびジエンは共に静電的に正の部分と有利な相互作用をすることが考えられる。実際、求核試薬は陰イオンであり、Houk らによりそのような考察がなされている。[68,73] またジエンについても Hehre らによると求核的な性質が重要であり、同時にジエノファイル分子はより求電子的な面が反応性が高いと考えるべきである。[75] これらに習ってジベンゾビシクロ[2.2.2]オクタトリエン骨格の基質における反応性を考えると、求核付加反応では不飽和ラクトン **2** の電子吸引性置換基をもつベンゼン環と求核試薬との間の相互作用は *syn* 付加を優先させると考えられ、求核的共役付加反応における選択性は予測できる。しかし Diels-Alder 反応においてもこれらのことは全く同様であり、ジエノファイル **1** に対しても *syn* 付加が優先されると考えられ、*anti* 付加が優先することは予測できない。

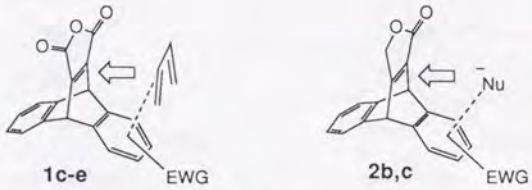


Figure 101: electrostatic 効果による面選択性

第2章・第2節でも示したとおり、Diels-Alder 反応における *anti* 付加優先性と求核反応における *syn* 付加優先性とは基質分子の違いではなく、反応もしくは試薬の違いによるものである。そのため、無水マレイン酸部分とフラノン部分との違いは問題にならず、アロマティック部分の両側での差異だけが問題となる。そのため、これら一連の反応系におけるπ面選択性をこのような単純な electrostatic 効果によって説明することは困難

である。

この効果のもう一つの見方であるが、反応中心部分は静電的な分極が強く、これと両ベンゼン環との相互作用は *anti*付加と *syn*付加との間で異なると考えられる。

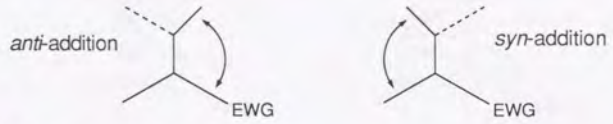


Figure 102: 分子内での electrostatic 効果

しかしこの作用も Diels-Alder 反応と求核反応との両方を説明しようとすると、修正が必要となることは同様のことである。

遷移状態における超共役効果

Anh と Cieplak に代表される遷移状態における超共役効果によって、これらの反応面を予測するとどうなるであろうか。Anh のモデルでは、生成する C-C, C-H または C-S 結合の $\sigma^{\ddagger}$軌道が隣接の σ^{*}軌道に非局在化して安定化相互作用をすると考えるので、**Figure 103**のような相互作用を考える。この時、電子受容体である σ^{*}(C-C)軌道のその受容能が問題となるわけであるが、電子吸引性の置換基をもつ置換ベンゼンからの結合、つまり $\sigma^{*}(syn)$の方が $\sigma^{*}(anti)$よりも影響が強いことが考えられる。そのため *anti*付加が優先することを予測する。これは Diels-Alder 反応の選択性を正しく予測するが、求核反応は反対の方向である。

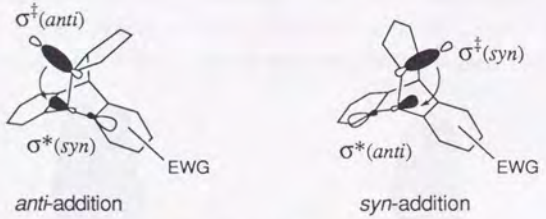


Figure 103: Anh モデルによる遷移状態安定化

一方 Cieplak モデルは生成する結合の $\sigma^{*\ddagger}$軌道と隣接の σ 軌道との相互作用であるので、これらを考える（**Figure 104**）。やはり問題となるのは置換ベンゼン側の $\sigma(syn)$ と無置換ベンゼン側の $\sigma(anti)$との電子供与能力の差であるが、$\sigma(anti)$の方がより供与性が高いことが予想され、また Halterman もそれを支持している。[100, 101] そのため、Cieplak モデルによる予測では *syn*付加が *anti*付加よりも優先されることが考えられる。

これは求核反応は正しく予測するが、Diels-Alder 反応は反対の方向である。

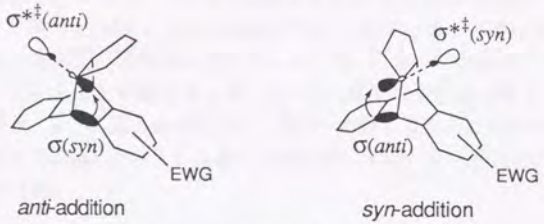


Figure 104: Cieplak モデルによる遷移状態安定化

このように、Anh モデルと Cieplak モデルとはお互いに反対の方向を予測するため、これらは一方の反応で正しい予測が成り立てばもう一方は成り立たないということになる。どちらの反応の場合にどちらのモデルを適用するのが適当かということが明確であれば、あるいはこれらの反応の選択性を、うまく説明できる可能性もある。しかし、先にも述べたように反応中心部分の構造は面選択性には関係がなく、アロマティック部分からの C-C 結合が電子受容性と供与性のどちらをもつかということが重要である。le Noble が示したような大きく異なる置換基の間ならまだしも、[92] このように全く同じ部分構造の役割が簡単に入れ替わることは考えにくい。これら Anh および Cieplak モデルの遷移状態安定化の考え方では、この系の反応面選択性は説明できない。

軌道の2次混合

軌道混合則に基づいて考えると、π 面が他のエネルギーの軌道を混合することにより非対称化することが考えられる。[32, 33, 49, 50] PM3 方により計算したマレイン酸誘導体の無置換体 **1a** とビストリフルオロメチル体 **1e** との LUMO を **Figure 105** に示す。

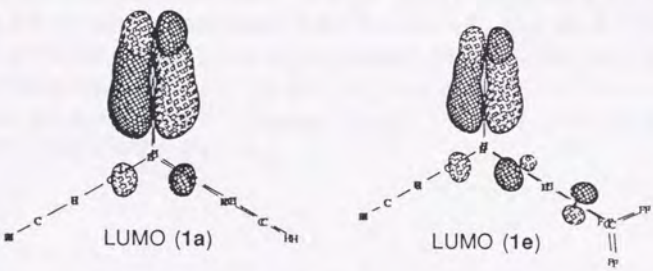


Figure 105: PM3 計算によるマレイン酸誘導体 **1a**, **1e** の LUMO

この図を見る限り、反応中心π面における hybrid や tilting などの2次軌道混合は大きな影響としては現れてはいない。かわりに顕著な効果が見られるのはアロマティック部分である。ベンゼン環の LUMO にσ(C-C)軌道が混合されていることがわかる。**1a** においてはこの効果は当然両側で同程度に現れている。**1e** においては置換ベンゼン側でこの効果が弱くなっていることが確認される。これは、電子求引性基の導入によるσ軌道のエネルギー低下が、π*軌道との相互作用（混合）を弱くするためであると考えられる。この結果得られた LUMO というのはまさに第3章にて示した「非対称化した LUMO」である（**Figure 106**）。

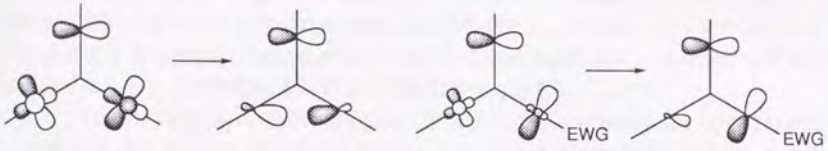


Figure 106: 軌道の2次混合による hybrid と tilting

また同時に、電子吸引性置換基はσ(C-C)軌道に大きな影響を与えるようであるが、Halterman らが指摘したような効果[100, 101]がこの系にも存在するとすれば、軌道相互作用によるπ面非対称化は、反応面の決定に関して更に強い効果を及ぼしていると考えるべきではないだろうか。

三体相互作用

福井らによる三体相互作用は、[205] この反応系での面選択性に良好な予測を与える。*syn*側での反応中心・置換ベンゼン・反応試薬の相互作用を考えると三体問題となるが、これらは Diels-Alder 反応、求核反応どちらにおいてもそれぞれ電子受容体・受容体・供与体であるので、LUMO-LUMO-HOMO の相互作用系となる。D と A、A と A であるので、どの場合も同位相の組み合わせとなる。求核反応では**Figure 107,(A)**に示すように同位相の相互作用系を作ることができる。しかし Diels-Alder 反応ではジエンのπ型軌道により同位相の系は形成できない（**Figure 107,(B)**）。これによって本反応系におけるπ面選択性を予測できると考えられる。

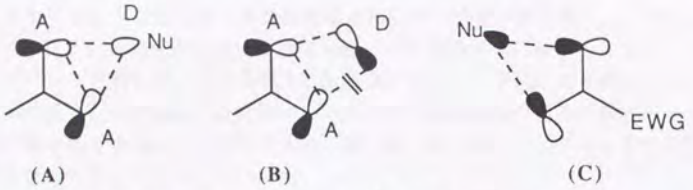


Figure 107: 電子供与体（D）と電子受容体（A）の三体相互作用

ただし、軌道混合則の出発点である基質分子のフロンティア軌道の考え方は、反応中心部分が主成分となるものを選ぶためNXLUMOを問題とし、不飽和ラクトンであるフラノン誘導体**2**では**Figure 107,(C)**のようになり、これは本反応系のπ面選択性を予測するものではない。三体問題はまた異なった説明の仕方である。

また、**Figure 107,(B)**の形式の相互作用系を考えることは、Diels-Alder反応において*syn*付加が不利となることは説明できるが、*anti*付加での反応の加速が存在することを説明するにはやはり基質分子のLUMOを問題とする必要があると考えられる。

構造の歪み

ジベンゾビシクロ[2.2.2]オクタトリエン骨格の基質においては、その構造の面等価性から考えて、Houkらがノルボルネンおよびイソジシクロペンタジエンの反応面選択性において指摘したような構造の歪み効果は問題とならないと考えられる。[19, 30] ここで問題となる構造の歪みがあるとすれば、それは反応中心のピラミッド化であろう。これらの基質の構造的な情報が望まれるところであるが、マレイン酸誘導体はその結晶性の問題からX線結晶構造解析による構造は得られていない。**Figure 108**に2-ニトロ体のフラノン誘導体**2b**のX線による構造を示す。

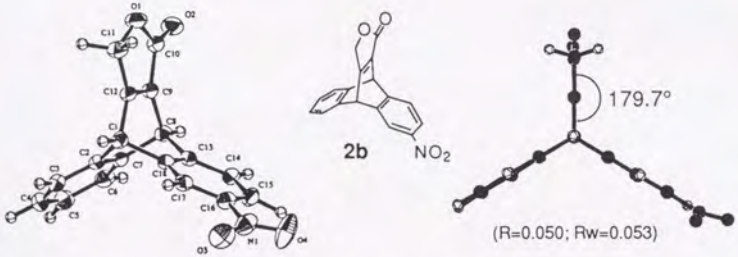


Figure 108: X線結晶構造解析によるフラノン誘導体**2b**の構造

この基質の反応中心オレフィンの二面角は平面からずれることわずかに0.3度であり、

ノルボルネンのようなピラミッド化は確認されない（序章・第2節）。この結晶状態における0.3度という角度が大きいか小さいかという議論は他にゆずるとして、少なくともニトロベンゼン側に傾いている以上、反応面がピラミッド化により決定されているとは考えられない。また*ab initio*計算によるマレイン酸誘導体の構造の振動モードも、平面構造が極小値であることを示しており（第4章・第1節）、ピラミッド化は問題となってはいないと考えられる。

以上本章では、反応面選択性の問題において取り上げられることの多いいくつかの理論・モデルの視点に立ち、本反応系の反応面の選択性を議論した。このジベンゾビシクロ[2.2.2]オクタトリエン骨格を有する基質に対するDiels-Alder反応と求核反応との反応面選択性を、統一的に予測できる理論は無いことがわかる。特に、盲目的に取り上げられることの多い遷移状態での超共役相互作用による安定化機構は、その適用には注意を要するべきである。

第6章：結論

以上述べてきたとおり、オレフィンπ面が立体効果ではなく周辺の軌道位相環境の差異により非対称化することを示した。

本研究において示した手法に基づいて考える以上、その非対称化の予測は容易であり、他の反応系においても指針となり得るものであると考えられる。

本反応系において問題となった非対称化は、反応を支配するフロンティア軌道を考える際に取り入れられたもので、その必然性は明確である。

これらのπ面非対称化は、相互作用の適切な評価法により、定量的な扱いも可能であると考えられる。

実験の部

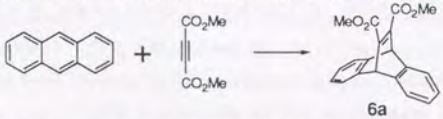
General Methods

All the melting points were measured with a Yanagimoto hot-stage melting point apparatus (MP-500) and are uncorrected. Proton NMR spectra were measured on a JEOL GX 400-MHz NMR spectrometer with TMS as an internal reference in $CDCl_3$ as the solvent. All coupling constants (J) are given in hertz in parentheses, and chemical shifts are reported in ppm. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; m, multiplet; and br, broad. High-resolution mass spectra (HRMS) were recorded on a JEOL SX-102 instrument. Infrared spectra (IR) were recorded on a Shimadzu IR-408 instrument. High-performance liquid chromatography (HPLC) was run on a Shimadzu LC-6A system on silica gel SIL S-5 (SH-043-5, YMC, Japan) packing (20 mm x 25 cm) with the specified eluent. Flash column chromatography was performed on silica gel (Kieselgel 60, 230-400 mesh, Merck) with the specified solvent. Thin layer chromatography was performed on precoated TLC plates (Kieselgel 60, F-254, Merck). 2,3-Dimethyl-1,3-butadiene (DMBD), 1,3-cyclohexadiene (CHD), ethanethiol, potassium cyanide, 18-crown-6 and sodium hydride were commercially available (Aldrich) and were used without further purification. 1,3-Butadiene (BD) was distilled to the flask which was cooled at -78 ℃. Cyclopentadiene (CPD) was freshly distilled,[206] and the purity was checked by ^1H NMR. The combustion analyses were carried out in the microanalytical laboratory of this faculty.

In this section, dibenzobicyclo[2.2.2]octatriene is renamed to 9,10-dihydro-9,10-ethenoanthracene.

Syntheses of the anhydride **1a-e**.

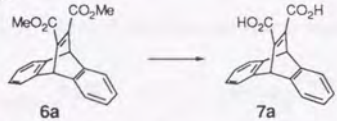
Dimethyl 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate (6a).



6a

A mixture of 10.2 g (562 mmol) of anthracene and 250 mL (2.03 mol, 3.6 equiv.) of dimethyl acetylenedicarboxylate was heated at 110 ℃ for 22 hrs, then poured into cold methanol (800 mL) and washed with more 600 mL of cold methanol to give 116.0 g (64 %) of **6a**. **6a**: mp 160.5-161.5 ℃ (colorless prisms, recrystallized from methanol). ^{1}H NMR: 7.38 (4H, $H_{1,4,5,8}$, d,d, J=5.5, 3.5), 7.02 (4H, $H_{2,3,6,7}$, d,d, J=5.5, 3.3), 5.47 (2H, $H_{9,10}$, s), 3.78 (6H, OCH_3, s). Anal. Calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 74.90; H, 4.96.

Hydrolysis of the diester to 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid (7a).



6a 7a

To a solution of **6a** (10.02 g, 31.3 mmol, obtained as above) in methanol (120 mL), aqueous NaOH (2N) (180 mL) was added, and the mixture was heated at 60 ℃ for 6 hrs, followed by acidification with aqueous HCl (2N). The whole mixture was extracted with ether (900 mL), and the organic phase was washed by brine, dried over $MgSO_4$ and then evaporated to give 8.90 g (97 %) of the diacid **7a**. Mp 247.5-248.5 ℃ (colorless needles, recrystallized from water). ^{1}H NMR (CD_3OD): 7.40 (4H, $H_{1,4,5,8}$, d,d, J=5.5, 3.3), 7.02 (4H, $H_{2,3,6,7}$, d,d, J=5.5, 3.3), 5.62 (2H, $H_{9,10}$, s). IR (KBr, cm^{-1}): 3400, O-H; 1695, C=O. Anal. Calcd. for $C_{18}H_{12}O_4$: C, 73.97; H, 4.14. Found: C, 73.67; H, 3.93.

9,10-Dihydro-9,10-ethenoanthracene-11,12-dicarboxylic anhydride (1a).

7a 1a

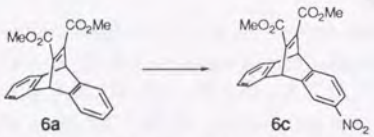
(Method A) A mixture of 2.766 g (9.46 mmol) of the diacid (obtained as above), 16.38 g (138 mmol, 7.3 equiv.) of thionyl chloride and a catalytic amount of DMF (*N*,*N*-dimethylformamide)

was refluxed for 2 hrs. Remaining thionyl chloride was removed under reduced pressure to give the crude acid chloride. The resultant acid chloride was dissolved in pyridine (8 mL) and was treated with 165 mg of water (9.17 mmol, 1 equiv. with respect to the acid chloride), and the mixture was allowed to stir at 18 ℃ for 10 min. The reaction mixture was poured into a vigorously stirred mixture of aqueous HCl (2N, 200 mL) and 200 mL of dichloromethane. The organic layer was separated, washed with 2N-aqueous HCl, saturated aqueous sodium bicarbonate and brine, and was dried over sodium sulfate. Evaporation of the solvent gave 1.873 g (72 %) of the anhydride **1 a**.

(Method B) A mixture of the diacid (195 mg, 0.677 mmol) and 8 mL of acetic anhydride was heated at 70 ℃ for 5 hrs. Unreacted acetic anhydride was removed under reduced pressure to give the anhydride **1 a** (158 mg, 85 %), after washing with *n*-hexane.

1 a: mp 258.0-260.0 ℃ (colorless prisms, recrystallized from benzene). ^{1}H NMR: 7.44 (4H, $H_{1,4,5,8}$, d,d, J=5.5, 3.3), 7.08 (4H, $H_{2,3,6,7}$, d,d, J=5.5, 3.3), 5.54 (2H, $H_{9,10}$, s). IR (KBr, cm^{-1}): 1840, 1765, C=O. Anal. Calcd. for $C_{18}H_{10}O_3$: C, 78.83; H, 3.68. Found: C, 79.13; H, 3.56.

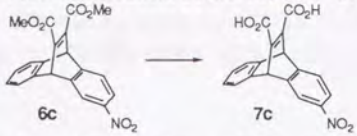
Dimethyl 2-nitro-9,10-Dihydro-9,10-ethenoanthracene-11,12-dicarboxylate (6 c).



6a 6c

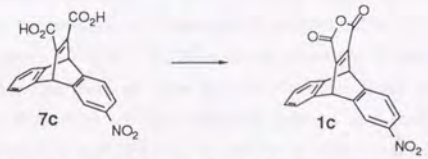
Acetic anhydride (80 mL) was added in one portion to a weighted amount of fuming HNO_3 (6.1 g, 93 %) at -43 ℃ (acetonitrile-dry ice). The mixture was stirred at -43 ℃ for 3 min, and then the solution of **6 a** (20.0 g, 62.5 mmol) in dichloromethane (methanol-free, 100 mL) was added dropwise. After being stirred at -43 ℃ for 12 hrs, the whole mixture was added to 500 mL of ice and water and extracted with methylene chloride. The extract was washed with brine and dried over sodium sulfate. Evaporation of the solvent gave a residue (20.6 g), which was flash-chromatographed (ethyl acetate: *n*-hexane 1:4) to give 13.1 g (57 %) of dimethyl 2-nitro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate (**6 c**). **6 c**: mp 166.5-168.0 ℃ (pale yellow prisms, recrystallized from methanol). ^{1}H NMR: 8.22 (1H, H_1, d, J=2.2), 7.98 (1H, H_3, d,d, J=8.1, 2.2), 7.51 (1H, H_4, d, J=8.1), 7.43 (2H, $H_{5,8}$, m), 7,09 (2H, $H_{6,7}$, m), 5.604 (1H, $H_{9/10}$, s), 5.598 (1H, $H_{10/9}$, s), 3.82 (3H, OCH_3, s), 3.81 (3H, OCH_3, s). Anal. Calcd. for $C_{20}H_{15}NO_6$: C, 65.75; H, 4.14; N, 3.83. Found: C, 65.89; H, 4.10; N, 3.87.

2-Nitro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid (7c).



Hydrolysis of the above diester **6c** gave 2-nitro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid **7c** in qu*anti*tative yield. ^{1}H NMR (CD_3OD): 8.32 (1H, H_1, d, J=2.2), 8.04 (1H, H_3, d,d, J=8.4, 2.2), 7.67 (1H, H_4, d, J=8.4), 7.53 (2H, $H_{5,8}$, m), 7.13 (2H, $H_{6,7}$, m), 5.86 (1H, $H_{9/10}$, s), 5.85 (1H, $H_{10/9}$, s). IR (KBr, cm^{-1}): 3400, O-H; 1705, C=O; 1515, 1340, NO_2.

2-Nitro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic anhydride (1c).



Dehydroxylation of the above diacid gave **1c** in 38 % yield (Method A), and 87 % yield (Method B), respectively. **1c**: mp 130 ℃ (pale brown powder, recrystallized from benzene). ^{1}H NMR: 8.27 (1H, H_1, d, J=2.2), 8.02 (1H, H_3, d,d, J=8.1, 2.2), 7.59 (1H, H_4, d, J=8.4), 7.49 (2H, $H_{5,8}$, m), 7.14 (2H, $H_{6,7}$, m), 5.67 (1H, H_9, s), 5.66 (1H, H_{10}, s). IR (KBr, cm^{-1}): 1840, 1770, C=O; 1515, 1345, NO_2. Anal. Calcd. for $C_{18}H_9NO_5 \cdot 4/5H_2O$: C, 64.79; H, 3.20; N, 4.20. Found: C, 64.63; H, 3.23; N, 4.30.

Reduction of dimethyl 2-nitro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate to 2-amino-diester (11).

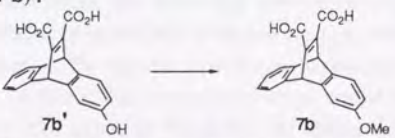
A solution of the nitro diester **6c** (5.41 g, 14.8 mmol) in 500 mL of ethanol was heated under gentle reflux in the presence of diluted aqueous HCl (2N, 20 mL) and iron powder (20 g) with vigorous stirring. After 1 hr, the cold mixture was poured into saturated aqueous sodium bicarbonate, and extracted with methylene chloride. The residue was flash-chromatographed (dichloromethane) to give 4.60 g (93 %) of dimethyl 2-amino-9,10-dihydro-9,10-

ethenoanthracene-11,12-dicarboxylate **11**. ^{1}H NMR: 7.34 (2H, $H_{5,8}$, m), 7.12 (1H, H_4, d, J=8.1), 7.00 (2H, $H_{6,7}$, m), 6.78 (1H, H_1, d, J=2.2), 6.29 (1H, H_3, d,d, J=8.1, 2.2), 5.34 (1H, $H_{9/10}$, s), 5.33 (1H, $H_{10/9}$, s), 3.78 (3H, OCH_3, s), 3.77 (3H, OCH_3, s), 3.56 (2H, NH_2, br-s).

Diazotization and hydrolysis to 2-hydroxy-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid.

To a solution of dimethyl 2-amino-9,10-dihydro-9,19-ethenoanthracene-11,12-dicarboxylate (4.21 g, 12.5 mmol) in acetic anhydride (40 mL), 11 mL of concentrated sulfuric acid was added slowly, and followed by the addition of a solution of sodium nitrite (1.27 g, 18.5 mmol, 1.47 equiv) in water (10 mL) over 5 min at 0 ℃. After being stirred for 15 min at 0 ℃, urea (0.444 g, 7.39 mmol) was added in one portion. After the mixture was stirred at 0 ℃ for 15 min, the resultant solution of the diazonium ion was added in portions to a preheated (to gentle reflux) solution of concentrated sulfuric acid (12 mL) in 100 mL of water over 40 min. After heating for another 10 min, the mixture was extracted with methylene chloride and evaporated to give black-brown viscous oil (3.91 g). This residue was dissolved in aqueous sodium hydroxide (2N, 100 mL) and the mixture was heated at 60 ℃ for 4.8 hrs. The cold mixture was acidified with aqueous hydrochloric acid (2N), and then extracted with ethyl acetate, followed by evaporation to give 3.50 g (91 % from the 2-amino diester) of 2-hydroxy-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid. ^{1}H NMR (DMSO-d_6): 7.40 (1H, $H_{5/8}$, d,d, J=8.4, 2.2), 7.38 (1H, H8/5, d,d, J=8.4, 2.2), 7.17 (1H, H_4, d, J=7.7), 6.99 (2H, $H_{6,7}$, m), 6.87 (1H, H_1, d, J=2.2), 6.35 (1H, H_3, d,d, J=8.1, 2.2), 5.45 (1H, $H_{9/10}$, s), 5.44 (1H, $H_{10/9}$, s).

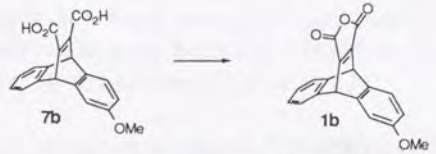
Methylation to 2-methoxy-9,10-dihydro-9,10-etheno-anthracene-11,12-dicarboxylic acid (7b).



The above 2-hydroxy diacid (3.17 g) was dissolved in aqueous 3N NaOH (100 mL), and dimethyl sulfate (27 mL, 286 mmol) was added at ambient temperature. The reaction mixture was heated at 60 ℃ for one night. The cold mixture was acidified (pH=1) with aqueous hydrochloric

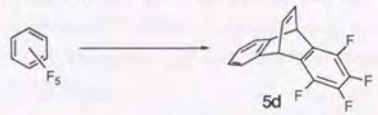
acid and the whole was extracted with ethyl acetate. The residue was flash-chromatographed (chloroform: methanol 9:1) to give 2.69 g (81 %) of 2-methoxy-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid **7b**. ^{1}H NMR (DMSO-d_6): 7.40 (2H, $H_{5,8}$, m), 7.30 (1H, H_4, d, J=8.1), 7.08 (1H, H_1, d, J=2.2), 7.01 (2H, $H_{6,7}$, m), 6.53 (1H, H3, d,d, J=8.1, 2.6), 5.54 (1H, $H_{9/10}$, s), 5.51 (1H, $H_{10/9}$, s), 3.69 (3H, OCH_3, s). IR (KBr, cm^{-1}): 3400, O-H; 1700, C=O.

2-Methoxy-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic anhydride (1b).



Dehydroxylation of the above diacid gave the anhydride **1b** in 79 % yield (Method A), and 98 % yield (Method B), respectively. **1b**: mp 176.0-178.0 ℃ (pale yellow powder, recrystallized from toluene). ^{1}H NMR: 7.42 (2H, $H_{5,8}$, m), 7.31 (1H, H_4, d, J=8.1), 7.07 (2H, $H_{6,7}$, m), 7.04 (1H, H_1, d, J=2.6), 6.54 (1H, H_3, d,d, J=8.1, 2.6), 5.47 (1H, $H_{9/10}$, s), 5.46 (1H, $H_{10/9}$, s), 3.76 (3H, OCH_3, s). IR (KBr, cm^{-1}): 1840, 1770, C=O. Anal. Calcd. for $C_{19}H_{12}O_4 \cdot 6/5H_2O$: C, 70.02; H, 4.45. Found: C, 69.98; H, 4.45.

1,2,3,4-Tetrafluoro-9,10-dihydro-9,10-ethenoanthracene (5d).

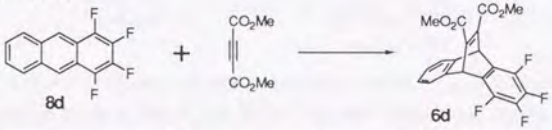


To the solution of 24.64 g (192 mmol) of naphthalene and 19.94 g (119 mmol) of pentafluorobenzene in 200 mL of *n*-hexane, 140 mL of 1.0 M *n*-butyllithium in hexanes (140 mmol) was added at 0 ℃. [207] The reaction mixture was stirred at ambient temperature for 21 hrs, then poured into 300 mL of 2N-aqueous hydrochloric acid. The organic layer was washed with brine, and dried over sodium sulfate. The solvent was removed by evaporation, and the solution was concentrated by distillation of naphthalene at reduced pressure, followed by cooling to room temperature for recrystallization. The colorless crystals were filtrated and washed with *n*-hexane to give 5.55 g of product. The filtrate was chromatographed on neutral alumina to give 2.53 g of product, and thus 8.08 g (29.3 mmol, 25 %) of **5d** was obtained in total. **5d**: mp 111.0 ℃ (colorless prisms, recrystallized from *n*-hexane). ^{1}H NMR: 7.33 (2H, $H_{5,8}$, d,d, J=3.3, 5.5), 7.03 (4H, $H_{6,7,11,12}$, m), 5.52 (2H, $H_{9,10}$, t, J=3.7). Anal. Calcd. for $C_{16}H_8F_4$: C, 69.57; H, 2.92. Found: C, 69.42; H, 2.62.

1,2,3,4-Tetrafluoroanthracene (8d).[130]

A mixture of 5.01 g (18.1 mmol) of foregoing tetrafluoroethenoanthracene **5d** and 7.67 g (20.0 mmol, 1.10 equiv.) of tetraphenylcyclopentadienone was heated in a sealed bottle at 190 ℃ for 26 hrs, and then flash-chromatographed to give 3.99 g (15.9 mmol, 88 %) of **8d** as pale yellow solid. **8d**: mp 182.0-184.5 ℃ (pale yellow rods, recrystallized from *n*-hexane). ^{1}H NMR: 8.62 (2H, $H_{9,10}$, s), 8.05 (2H, $H_{5,8}$, d,d, J=3.3, 6.2), 7.58 (2H, $H_{6,7}$, d,d, J=3.3, 6.6). Anal. Calcd. for $C_{14}H_6F_4$: C, 67.21; H, 2.42. Found: C, 67.23; H, 2.24.

Dimethyl 1,2,3,4-tetrafluoro-9,10-dihydro-9,10-etheno-anthracene-11,12-dicarboxylate (6d).

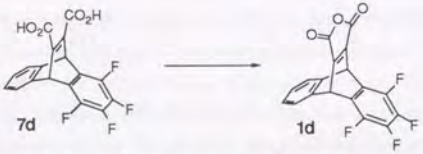


The 1,2,3,4-tetrafluoro diester **6d** was prepared by the Diels-Alder cyclization of 1,2,3,4-tetrafluoroanthracene (3.61 g, 14.42 mmol) and 7 mL of dimethyl acetylenedicarboxylate (57 mmol, 4.0 equiv.) in 88 % yield (4.976 g, 12.68 mmol). **6d**: mp 112.0-113.0 ℃ (colorless prisms, recrystallized from methanol). ^{1}H NMR: 7.43 (2H, $H_{5,8}$, d,d, J=5.5, 3.3), 7.10 (2H, $H_{6,7}$, d,d, J=5.5, 3.3), 5.84 (2H, $H_{9,10}$, s), 3.82 (6H, OCH_3, s). Anal. Calcd. for $C_{20}H_{12}O_4F_4$: C, 61.23; H, 3.08. Found: C, 61.07; H, 2.79.

1,2,3,4-Tetrafluoro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid (7d).

Hydrolysis of the above diester **6d** gave 1,2,3,4-tetrafluoro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid **7d** in 96 % yield. Dp 253 ℃. ^{1}H NMR (DMSO-d_6): 7.59 (2H, $H_{5,8}$, d,d, J=5.5, 3.3), 7.10 (2H, $H_{6,7}$, d,d, J=5.5, 3.3), 6.05 (2H, $H_{9,10}$, s). IR (KBr, cm^{-1}): 3400, O-H; 1695, C=O. Anal. Calcd. for $C_{18}H_8O_4F_4 \cdot 1/3H_2O$: C, 58.39; H, 2.27. Found: C, 58.13; H, 2.03.

1,2,3,4-Tetrafluoro-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic anhydride (1d).

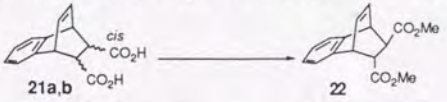


Dehydroxylation of diacid obtained as above gave **1d** in 55 % yield (Method A), and 52 % yield (Method B). ^{1}H NMR: 7.51 (2H, $H_{5,8}$, d,d, J=5.5, 3.3), 7.16 (2H, $H_{6,7}$, d,d, J=5.5, 2.9), 5.92 (2H, $H_{9,10}$, s). IR (KBr, cm^{-1}): 1845, 1780, C=O. HRMS (M^+) Calcd. for $C_{18}H_6O_3F_4$: 346.0253, Found: 346.0271.

1,4-Dihydro-1,4-ethenonaphthalene-*cis*-2,3-dicarboxylic acid (21).[138]

A mixture of 479.9 g (5.00 mol) of maleic anhydride and 413.0 g (3.22 mol) of naphthalene was heated in a sealed bottle at 100 ℃ for 24 hrs. The hot mixture was poured into 3 L of ice-water, the solid was washed with 5 L of water and extracted with 2 L of 1N-aqueous potassium hydroxide at ambient temperature for 2 days. The mixture was filtered and the solid was washed with 500 mL of water. Aqueous layer was acidified with hydrochloric acid, and color less powder was assembled by filtration and the filtrate was extracted with ether, which was washed with brine and dried over magnesium sulfate, followed by evaporation to remove the solvent. The mixture of *endo-cis* **21a** and *exo-cis* **21b** products (13.5 g, 55.7 mmol, 1.7 %) and maleic acid (4.4 g, 37,9 mmol) was obtained as colorless oil. ^{1}H NMR (DMSO-d_6) (major isomer): 7.14 (2H, $H_{5,8}$, d,d, J=3.3, 5.5), 7.00 (2H, $H_{6,7}$, d,d, J=3.3, 5.5), 6.61 (2H, $H_{9,10}$, d,d, J=2.9, 4.4), 4.10 (2H, $H_{1,4}$, br-t, J=3.3), 2.94 (2H, $H_{2,3}$, s). (minor isomer): 7.25 (2H, $H_{5,8}$, d,d, J=3.3, 5.5), 7.06 (2H, $H_{6,7}$, d,d, J=3.3, 5.5), 6.49 (2H, $H_{9,10}$, d,d, J=3.3, 4.4), 4.16 (2H, $H_{1,4}$, br-t, J=3.3), 2.80 (2H, $H_{2,3}$, s).

Dimethyl 1,4-dihydro-1,4-ethenonaphthalene-*trans*-2,3-dicarboxylate (22).



The foregoing diacid **21a,b** mixture was dissolved in 200 mL of methanol, and 0.5 mL of concentrated sulfuric acid was added. This solution was refluxed for 20 hrs, cooled, evaporated

for concentration, and poured into saturated aqueous sodium bicarbonate (250 mL) and extracted with 300 mL of dichloromethane. The organic layer was washed with brine and dried over sodium sulfate, then the solvent was evaporated to give a mixture of related diesters and dimethyl maleate.

This mixture was refluxed in 200 mL of methanol containing 4 % of sodium methoxide for 2 hrs, followed by evaporation for concentration. The solution was acidified with 2N-aqueous hydrochloric acid (250 mL) and extracted with 500 mL of dichloromethane. The organic layer was washed with saturated aqueous sodium bicarbonate, brine and dried over sodium sulfate, and the solvent was evaporated and then flash-chromatographed (dichloromethane) to give 12.6 g (46.6 mmol, 84 %) of *trans*-diester **22** as colorless oil. ^{1}H NMR 7.24 (1H, $H_{5/8}$, d,d, J=1.8, 6.6), 7.14-7.05 (3H, $H_{6,7,8/5}$, m), 6.65 (1H, $H_{9/10}$, d,d,d, J=1.5, 6.2, 7.7), 6.52 (1H, $H_{10/9}$, d,d,d, J=1.5, 5.9, 7.7), 4.38 (1H, $H_{4/1}$, d,t, J=5.9, 1.8), 4.33 (1H, $H_{1/4}$, d,d,d, J=1.1, 2.6, 6.2), 3.73 (3H, -CH_3, s), 3.57 (3H, -CH_3, s), 3.27 (1H, $H_{2/3}$, d,d, J=2.6, 4.8), 3.16 (1H, $H_{3/2}$, d,d, J=2.6, 4.8).

1,4-Dihydro-*trans*-2,3-bis(hydroxymethyl)-1,4-ethenonaphthalene (23).

22 23

To the mixture of 3.98 g (104.87 mmol) of lithium aluminum hydride and 150 mL of tetrahydrofuran, the above *trans*-diester **22** dissolved in 100 mL of tetrahydrofuran was added for 15 min. The mixture was refluxed for 1.5 hrs, and cooled to room temperature. Methanol (30 mL) and 15 mL of 2N-aqueous sodium hydroxide were added, and then 300 mL of dichloromethane was added and stirred. The mixture was filtered and 500 mL of dichloromethane was added, and the organic layer was washed with brine and dried over sodium sulfate and evaporated to give 8.36 g (38.65 mmol, 83 %) of *trans*-bis(hydroxymethyl) derivative **23** as colorless solid. **23**: mp 144.5-145.0 ℃ (colorless plates, recrystallized from chloroform). ^{1}H NMR: 7.19-7.07 (4H, $H_{5,6,7,8}$, m), 6.65 (1H, H_9, m), 6.41 (1H, H_{10}, t, J=7.0), 3.86 (1H, H_4, d, J=5.9), 3.82 (1H, H_1, d, J=6.2), 3.71 (1H, H_3, m), 3.38 (2H, H_2,C_3-CH_2-, m), 2.90 (1H, C_2-CH_2-, t, J=9.9), 2.27 (1H, -OH, br-s), 2.07 (1H, -OH, br-s), 1.68 (1H, C_2-CH_2-, m), 1.52 (1H, C_3-CH_2-, m). Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.45; H, 7.49.

Di-*O*-tosylate (24). [137]

To the solution of 8.34 g (38.6 mmol) of foregoing diol **23** in dry pyridine (150 mL), 22.34 g (117 mmol) of *p*-toluenesulphonyl chloride was added and stirred at ambient temperature for 19 hrs. The mixture was concentrated at reduced pressure, and poured into 2N-aqueous hydrochloric acid (800 mL) and extracted with 1.3 L of dichloromethane. The organic layer was washed with 2N-aqueous hydrochloric acid and brine, dried over sodium sulfate, and then the solvent was evaporated. The residue was chromatographed (dichloromethane) to give 18.5 g (35.3 mmol, 91 %) of **24** as colorless powder. **24**: mp 132.0-133.0 ℃ (colorless rods, recrystallized from methanol). ^{1}H NMR: 7.79 (2H, Ts, d, J=8.4), 7.70 (2H, Ts, d, J=8.4), 7.37 (2H, Ts, d, J=8.1), 7.32 (2H, Ts, d, J=8.1), 7.10-7.03 (2H, $H_{5,8}$, m), 6.96 (1H, d,t, J=1.5, 7.3), 6.86 (1H, br-d, J=7.0), 6.54 (1H, br-t, J=6.2), 6.22 (1H, br-t, J=7.0), 3.88-3.82 (3H, $H_{1,4}$,-CH_2-, m), 3.76 (1H, -CH_2-, t, J=9.5), 3.59 (1H, -CH_2-, d,d, J=5.5, 9.5), 3.17 (1H, -CH_2-, t, J=9.5), 2.46 (6H, Ts, s), 1.54 (1H, $H_{2/3}$, m), 1.34 (1H, $H_{3/2}$, m). Anal. Calcd. for $C_{28}H_{28}O_6S_2$: C, 64.10; H, 5.38. Found: C, 63.90; H, 5.43.

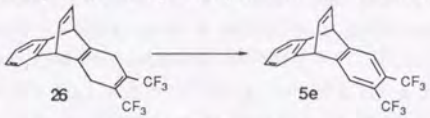
1,4-Dihydro-2,3-dimethylene-1,4-ethenonaphthalene (25). [137]

To the solution of 16.355 g (31.2 mmol) of ditosylate **24** in 200 mL of dimethylsulfoxide, 8.73 g (77.8 mmol) of potassium *tert*-butoxide was added and the mixture was stirred at ambient temperature for 5.5 hrs, then it was poured into 1 L of ice-water and extracted with 1.8 L of *n*-hexane. The organic layer was washed with brine and dried over sodium sulfate, and the solvent was evaporated to give 5.693 g (97 %) of bis(*exo*-methylene) derivative **25** as colorless solid. It was used without further purification because it polymerized easily to form the insoluble gum, and thus it should be stored refrigerated. **25**: ^{1}H NMR: 7.22 (2H, $H_{5,8}$, d,d, J=3.3, 5.5), 7.11 (2H, $H_{6,7}$, d,d, J=3.3, 5.5), 6.62 (2H, $H_{9,10}$, d,d, J=3.3, 4.4), 5.22 (2H, =CH_2, s), 5.00 (2H, =CH_2, s), 4.51 (2H, $H_{1,4}$, br-t, J=4.0). Anal. Calcd. for $C_{14}H_{12}\cdot 1/2H_2O$: C, 88.85; H, 6.92. Found: C, 88.89; H, 6.98.

2,3-Bis(trifluoromethyl)-1,4,9,10-tetrahydro-9,10-ethenoanthracene (26).

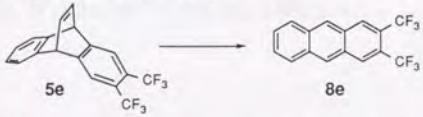
A mixture of 9,10-dimethylene-1,4-dihydro-1,4-ethanonaphthalene **25** (5.490 g, 30.46 mmol), hexafluoro-2-butyne (15.2 g, 93.83 mmol, 3.1 equiv.) and 30 mL of dichloromethane was stirred at ambient temperature for 15.5 hrs, in a sealed bottle. The residue was flash-chromatographed (*n*-hexane) to give 7.79 g of 2,3-bis(trifluoromethyl)-1,4,9,10-tetrahydro-9,10-ethenoanthracene (22.8 mmol, 75 %). Mp 149.5-150.0 ℃ (colorless prisms, recrystallized from methanol). ^{1}H NMR: 7.18 (2H, $H_{5,8}$, d,d, J=5.1, 2.9), 6.93 (2H, $H_{6,7}$, d,d, J=5.1, 2.9), 6.89 (2H, $H_{11,12}$, d,d, J=4.0, 3.3), 4.61 (2H, $H_{9,10}$, d,d, J=4.0, 3.3), 3.24 (4H, $H_{1,4}$, m). Anal. Calcd. for $C_{18}H_{12}F_6$: C, 63.16; H, 3.53. Found: C, 63.00; H, 3.40.

2,3-Bis(trifluoromethyl)-9,10-dihydro-9,10-ethenoanthracene (5e).



A mixture of 2,3-bis(trifluoromethyl)-1,4,9,10-tetrahydro-9,10-ethenoanthracene (obtained as above, 7.79 g, 22.8 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (6.24 g, 27.5 mmol, 1.2 equiv.) in 200 mL of benzene was refluxed for 20 hrs. The solvent was evaporated, and 500 mL of dichloromethane was added and filtered to remove insoluble materials. The organic layer was washed with aqueous 2N-NaOH, brine, and dried over sodium sulfate. Evaporation of the solvent gave 7.38 g of **5e** (21.7 mmol, 95 %). Mp 169.0-169.5 ℃ (colorless cubes, recrystallized from methanol). ^{1}H NMR: 7.72 (2H, $H_{1,4}$, s), 7.34 (2H, $H_{5,8}$, d,d, J=5.5, 3.3), 7.04 (2H, $H_{11,12}$, d,d, J=4.0, 3.3), 7.02 (2H, $H_{6,7}$, d,d, J=5.5, 3.3), 5.29 (2H, $H_{9,10}$, d,d, J=4.0, 3.3). Anal. Calcd. for $C_{18}H_{10}F_6$: C, 63.54; H, 2.96. Found: C, 63.31; H, 2.69.

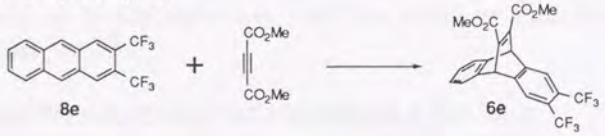
2,3-Bis(trifluoromethyl)anthracene (8e).



2,3-Bis(trifluoromethyl)-anthracene was prepared in the similar method as 1,2,3,4-tetrafluoroanthracene with the following modification: 2,3-Bis(trifluoromethyl)-9,10-dihydro-9,10-ethenoanthracene (**5e**) (obtained as above, 4.34 g, 12.8 mmol) and tetraphenyl-1,3-

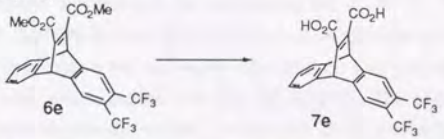
cyclopentadienone (5.40 g, 1.1 equiv.) were placed in a 100-mL bottle and sealed . The bottle was heated at 200 ℃ for 20 hrs. The residue was flash-chromatographed (*n*-hexane) to give 3.43 g of 2,3-bis(trifluoromethyl)-anthracene (86 %): mp 138.5-139.0 ℃ (yellow rod-like plates, recrystallized from *n*-hexane). ^{1}H NMR: 8.59 (2H, $H_{9,10}$, s), 8.53 (2H, $H_{1,4}$, s), 8.10 (2H, $H_{5,8}$, d,d, J=6.6, 3.3), 7.63 (2H, $H_{6,7}$, d,d, J=6.6, 2.9). Anal Calcd. for $C_{16}H_8F_6$: C, 61.16; H, 2.57. Found: C, 60.94; H, 2.54.

Dimethyl 2,3-bis(trifluoromethyl)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate (6e).



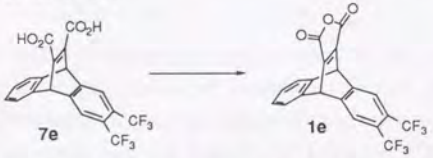
The 2,3-bis(trifluoromethyl) diester **6e** was prepared by the Diels-Alder cyclization of 2,3-bis(trifluoromethyl)anthracene **8e** (3.01 g, 9.59 mmol) and 10.2 g of dimethyl acetylene-dicarboxylate (72.4 mmol, 7.5 equiv.) in 91 % yield (3.96 g, 8.69 mmol). Mp 136.0-136.5 ℃ (colorless prisms, recrystallized from methanol). ^{1}H NMR: 7.84 (2H, $H_{1,4}$, s), 7.44 (2H, $H_{5,8}$, d,d, J=5.5, 3.3), 7.09 (2H, $H_{6,7}$, d,d, J=5.5, 2.9), 5.63 (2H, $H_{9,10}$, s),3.82 (6H, OCH_3, s). Anal. Calcd. for $C_{22}H_{14}O_4F_6$: C, 57.90; H, 3.09. Found: C, 57.80; H, 3.11.

2,3-Bis(trifluoromethyl)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid (7e).



Hydrolysis of the above diester **6e** gave the corresponding diacid, 2,3-bis(trifluoromethyl)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid **7e** in 96 % yield. ^{1}H NMR (DMSO-d_6): 8.17 (2H, $H_{1,4}$, s), 7.50 (2H, $H_{5,8}$, d,d, J=5.5, 3.3), 7.09 (2H, $H_{6,7}$, d,d, J=5.5, 3.3), 6.01 (2H, $H_{9,10}$, s). IR (KBr, cm^{-1}): 3350, OH; 1700, C=O.

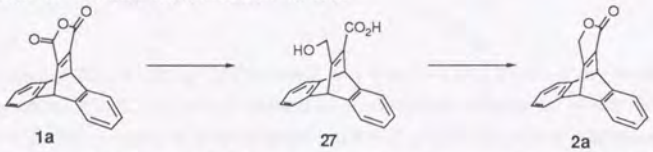
2,3-Bis(trifluoromethyl)-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic anhydride (1e).



Dehydroxylation of the above diacid gave the anhydride **1e** in 93 % yield (Method B). ^{1}H NMR: 7.92 (2H, $H_{1,4}$, s), 7.52 (2H, $H_{5,8}$, d,d, J=5.5, 2.9), 7.16 (2H, $H_{6,7}$, d,d, J=5.5, 2.9), 5.71 (2H, $H_{9,10}$, s). IR (KBr, cm^{-1}): 1845, 1770, C=O. HRMS (M^+) Calcd. for $C_{20}H_8O_3F_6$: 410.0378, Found: 410.0359.

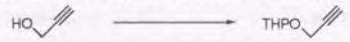
Syntheses of the α,β-unsaturated lactones **2a-c** and **3a-c**.

Reduction of 1a and lactonization to 2a.



To a mixture of 401 mg (10.57 mmol) of lithium aluminum hydride and 50 mL of tetrahydrofuran, 9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic anhydride **1a** dissolved in 50 mL of tetrahydrofuran was added at the temperature below -65 ℃. The temperature slowly raised to 0 ℃ for 5 hrs, then 6N-aqueous hydrochloric acid (8 mL) was added at -20 ℃, followed by stirring at ambient temperature for one night. The mixture was poured into 200 mL of 2N-aqueous hydrochloric acid, and extracted with 250 mL of ether. The organic layer was washed with brine, and dried over magnesium sulfate. Evaporation of the solvent gave related γ-hydroxy carboxylic acid **27**, which was washed with 20 mL of dichloromethane. This carboxylic acid **27** was refluxed in 150 mL of toluene containing a catalytic amount of *p*-toluenesulphonic acid monohydrate for 30 hrs. The toluene was evaporated, and the residue was flash-chromatographed (dichloromethane) to give 1.13 g (4.34 mmol, 41 %) of lactone **2a** as colorless solid. **2a**: mp 277.0-278.0 ℃ (colorless rods, recrystallized from ethyl acetate). ^{1}H NMR: 7.38 (4H, $H_{1,4,5,8}$, m), 7.03 (2H, $H_{(1,8)/(4,5)}$, d,t, J=1.5, 7.7), 7.01 (2H, $H_{(4,5)/(1,8)}$, d,t, J=1.5, 7.7), 5.44 (1H, $H_{9/10}$, s), 5.30 (1H, $H_{10/9}$, s), 4.96 (2H, -CH_2-, s). Anal. Calcd. for $C_{18}H_{12}O_2$: C, 83.06; H, 4.65. Found: C, 83.25; H, 4.43.

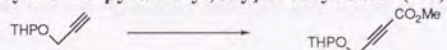
3-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-1-pronine (28).[144]



28

A mixture of 24.009 g (428.27 mmol) of propargyl alcohol, 36.260 g (431.05 mmol) of 3,4-dihydro-2*H*-pyran and a catalytic amount of phosphoryl chloride was stirred at ambient temperature for 2 hrs. 200 mL of 0.5N-aqueous sodium hydroxide was added to the mixture, and extracted with ether. The organic layer was washed with brine, and dried over sodium sulfate. Evaporation of the solvent and distillation at reduced pressure gave 50.132 g of **28** (357.63 mmol, 84 %) as colorless liquid, bp_{23}: 80.0 ℃ (lit. bp_{25}: 78 ℃,[144] $bp_{0.25}$: 34-36 ℃[145]). ^{1}H NMR: 4.83 (1H, THP, t, J=3.7), 4.29 (1H, -CH_2-, d,d, J=2.6, 15.8), 4.24 (1H, -CH_2-, d,d, J=2.6, 15.8), 3.81-3.87 (1H, THP, m), 3.52-3.57 (1H, THP, m), 2.42 (1H, -C≡CH, t, J=2.6), 1.71-1.85 (2H, THP, m), 1.53-1.67 (4H, THP, m).

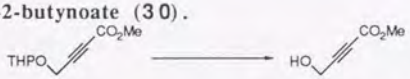
Methyl 3-[(tetrahydro-2*H*-pyran-2-yl)oxy]-2-butynoate (29).



28 29

The foregoing **28** (50.131 g, 357.6 mmol) was dissolved in 150 mL of dry tetrahydrofuran and slowly added at 4 ℃ to a stirred solution of ethylmagnesium bromide, which was prepared from 39.971 g (366.8 mmol) of ethyl bromide and 8.927 g (367.2 mmol) of magnesium turnings in 150 mL of dry tetrahydrofuran. After the evolution of the gas was stopped, 34.713 g (367.3 mmol) of methyl chloroformate was added to this solution for 1.5 hrs at 4 ℃, and stirred for additional 1 hr. Water (400 mL) was added and extracted with 600 mL of ether. The organic layer was washed with brine, and dried over sodium sulfate. Evaporation of the solvent and distillation at reduced pressure gave 25.130 g of **29** (126.78 mmol, 35 %) as colorless liquid,[145] bp_8: 121.5 ℃ (lit. bp_{32}: 145-148 ℃[208]). ^{1}H NMR: 4.81 (1H, THP, t, J=3.3), 4.39 (2H, -CH_2-, s), 3.80-3.85 (1H, THP, m), 3.79 (3H, -CO_2CH_3, s), 3.53-3.58 (1H, THP, m), 1.71-1.85 (2H, THP, m), 1.54-1.65 (4H, THP, m).

Methyl 3-hydroxy-2-butynoate (30).

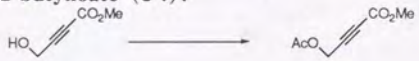


29 30

A mixture of 25.130 g (126.78 mmol) of methyl butynoate derivative **29** and 150 mL of methanol containing 350 mg (1.84 mmol) of *p*-toluenesulphonic acid mono-hydrate was refluxed for 4.5 hrs. Saturated aqueous sodium bicarbonate solution (40 mL) was added to the cooled solution, which was evaporated to dryness in vacuum. Water (100 mL) was added and extracted

with 250 mL of dichloromethane, and was dried over sodium sulfate. Evaporation of the solvent and distillation at reduced pressure gave 10.869 g of **30** (95.25 mmol, 75 %) as colorless liquid, bp_1: 90.5 ℃ (lit. bp_3: 114-118 ℃[209]). ^{1}H NMR: 4.40 (2H, -CH_2-, s), 3.79 (3H, -CO_2CH_3, s).

Methyl 3-acetoxy-2-butynoate (31).



30 **31**

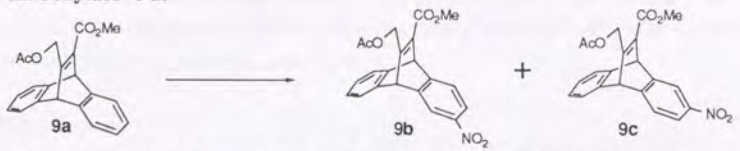
A mixture of foregoing 3-hydroxybutynoate **30** and 48 mL of acetic anhydride was heated at 80 ℃ for 20 hrs. Excess acetic anhydride and acetic acid was removed at reduced pressure, and distillation at reduced pressure gave 12.069 g of **31** (77.29 mmol, 81 %) as colorless liquid, bp_2: 93.5℃ (lit. $bp_{0.3}$: 67-69 ℃[210]). ^{1}H NMR: 4.79 (2H, -CH_2-, s), 3.80 (3H, CO_2CH_3, s), 2.12 (3H, AcO-, s).

Methyl 12-acetoxymethyl-9,10-dihydro-9,10-ethenoanthracene-11-carboxylate (9a).

31 **9a**

A mixture of 10.366 g (66.390 mmol) of methyl 3-acetoxy-2-butynoate **31** and 11.828 g (66.36 mmol) of anthracene was heated at 200 ℃ for 21 hrs. The cooled mixture was flash-chromatographed (dichloromethane: *n*-hexane 1:1) and recrystallized from methanol to give 13.567 g (40.57 mmol, 61 %) of bicyclo diester **9a**. **9a**: mp 117.0-118.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.37 (2H, $H_{4,5}$, d,d, J=2.2, 5.1), 7.31 (2H, $H_{1,8}$, d,d, J=2.2, 5.1), 7.01 (4H, $H_{2,3,6,7}$, m), 5.70 (1H, H_{10}, s), 5.29 (1H, H_9, s), 5.25 (2H, H_{13}, s), 3.78 (3H, -CO_2CH_3, s), 2.16 (3H, -OAc, s). Anal. Calcd. for $C_{21}H_{18}O_4$: C, 75.43; H, 5.43. Found: C, 75.35; H, 5.20.

Nitration of Methyl 12-acetoxymethyl-9,10-dihydro-9,10-ethenoanthracene-11-carboxylate 9a.



Nitration of **9a** (13.046 g, 39.017 mmol) was carried out in the similar procedure of the nitration of **6a** to give 5.435 g (14,33 mmol, 37 %) of 2-nitro compound **9b** and 4.866 g (12.83 mmol, 33 %) of 3-nitro compound **9c**, respectively. Two isomers were separated by flash column chromatography (ethyl acetate: *n*-hexane 1:4).

Methyl 12-acetoxymethyl-2-nitro-9,10-dihydro-9,10-ethenoanthracene-11-carboxylate (9b): mp 157.0-158.0 ℃ (pale yellow prisms, recrystallized from ethyl acetate/*n*-hexane). ^{1}H NMR: 8.14 (1H, H_1, d, J=2.2), 7.97 (1H, H_3, d,d, J=2.2, 8.1), 7.49 (1H, H_4, d, J=8.1), 7.41 (1H, $H_{5/8}$, m), 7.37 (1H, $H_{8/5}$, m), 7.07 (2H, $H_{6,7}$, m), 5.82 (1H, H_{10}, s), 5.43 (1H, H_9, s), 5.28 (1H, -CH_2-, d, J=14.7), 5.23 (1H, -CH_2-, d, J=14.3), 3.81 (3H, -CO_2CH_3, s), 2.18 (3H, AcO-, s). Anal. Calcd. for $C_{21}H_{17}NO_6 \cdot 1/6H_2O$: C, 65.97; H, 4.57; N, 3.66. Found: C, 65.94; H, 4.46; N, 3.39.

Methyl 12-acetoxymethyl-3-nitro-9,10-dihydro-9,10-ethenoanthracene-11-carboxylate (9c): it was failed to be crystallized. ^{1}H NMR: 8.19 (1H, H_4, d, J=2.2), 7.94 (1H, H_2, d,d, J=2.2, 8.1), 7.41 (2H, $H_{1,5/8}$, br-d, J=7.7), 7.34 (1H, $H_{8/5}$, d,d, J=1.8, 6.6), 7.06 (2H, $H_{6,7}$, m), 5.81 (1H, H_{10}, s), 5.40 (1H, H_9, s), 5.28 (1H, -CH_2-, d, J=14.7), 5.22 (1H, -CH_2-, d, J=14.3), 3.81 (3H, -CO_2CH_3, s), 2.14 (3H, AcO-, s).

2-Nitro-lactone (2b).

A mixture of 4.756 g (12.54 mmol) of 2-nitro diester **9b** and 300 mL of methanol containing 150 mg (0.789 mmol) of *p*-toluenesulphonic acid mono-hydrate was heated at 60 ℃ for 22 hrs, and then the methanol was evaporated and the residue was flash-chromatographed (dichloromethane) to give 2.30 g the related alcohol (54 %). This alcohol was heated in 300 mL of toluene containing 120 mg (0.63 mmol) of *p*-toluenesulphonic acid mono-hydrate at 100 ℃ for 3.5 hrs, and then the toluene was evaporated and the residue was flash-chromatographed (dichloromethane) to give 1.87 g (6.13 mmol, 93 %) of the lactone **2b**. **2b**: dp 270.0-271.0 ℃.

(pale yellow rods, recrystallized from ethyl acetate). ^{1}H NMR: 8.20 (1H, H_1, d, J=2.2), 7.99 (1H, H_3, d,d, J=2.2, 8.1), 7.52 (1H, H_4, d, J=8.1), 7.43 (2H, $H_{5,8}$, m), 7.09 (2H, $H_{6,7}$, m), 5.55 (1H, H_{10}, s), 5.44 (1H, H_9, s), 5.02 (2H, -CH_2-, s). Anal. Calcd. for $C_{18}H_{11}NO_4$: C, 70.82; H, 3.63; N, 4.59. Found: C, 70.94; H, 3.48; N, 4.38.

3-Nitro-lactone (2c).

9c 2c

2c was obtained in the similar method as above from 3.243 g (8.548 mmol) of 3-nitro diester **9c**, in 67 % yield (1.53 g, 5.01 mmol). **2c**: dp 276.0-278.5 ℃. (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.21 (1H, H_4, d, J=2.2), 7.96 (1H, H_2, d,d, J=2.2, 8.1), 7.49 (1H, H_1, d, J=8.1), 7.45 (1H, H_5, d,d, J=1.5, 7.0), 7.41 (1H, H_8, d,d, J=1.8, 6.6), 7.10 (1H, $H_{6/7}$, d,t, J=1.5, 6.6), 7.07 (1H, $H_{7/6}$, d,t, J=1.5, 7.0), 5.56 (1H, H_{10}, s), 5.43 (1H, H_9, s), 5.00 (1H, -CH_2-, d, J=18.0), 4.99 (1H, -CH_2-, d, J=18.0). Anal. Calcd. for $C_{18}H_{11}NO_4$: C, 70.82; H, 3.63; N, 4.59. Found: C, 70.53; H, 3.49; N, 4.30.

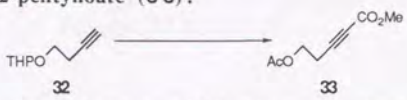
The lactones **3a**, **3b** and **3c** was obtained from 1-butyn-4-ol in the similar method as **2b** or **2c**.

4-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-1-butyne (32).

32

The protection of 23.3 g (332 mmol) of 1-butyn-4-ol with 30.0 g (357 mmol) of 3,4-dihydro-2*H*-pyran and a catalytic amount of phosphoryl chloride gave 47.424 g (307 mmol, 93 %) of **32**, as colorless liquid, bp_2: 50 ℃ (lit. bp_2: 60-63 ℃[146]). ^{1}H NMR: 4.66 (1H, THP, t, J=4.0), 3.81-3.92 (2H, THP, THPO-CH_2-, m), 3.49-3.61 (2H, THP, THPO-CH_2-, m), 2.50 (2H, -CH_2-C≡C, d,t, J=2.6, 7.0), 1.98 (1H, C≡CH, t, J=2.6), 1.79-1.87 (1H, THP, m), 1.69-1.76 (1H, THP, m), 1.51-1.64 (4H, THP, m).

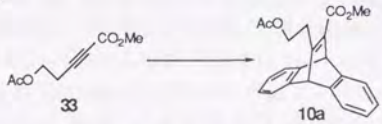
Methyl 5-acetoxy-2-pentynoate (33).



32 33

From the foregoing **32**, The reaction of **32** with methyl chloroformate and distillation, followed by heating in 100 mL of acetic anhydride containing 10 mL of acetic acid at 80 ℃ for 19 hrs, removal of volatile and distillation gave 32.869 g (193 mmol, 65 %) of methyl 5-acetosy-2-pentynoate **33** as colorless liquid, bp_3: 97 ℃. ^{1}H NMR: 4.21 (2H, -OCH_2-, t, J=6.6), 3.77 (3H, -CO_2CH_3, s), 2.69 (2H, -CH_2-C≡C, t, J=6.6), 2.08 (3H, AcO-, s). HRMS (M^+) Calcd. for $C_8H_{10}O_4$: 170.0579, Found: 170.0577.

Methyl 12-(2-acetoxyethyl)-9,10-dihydro-9,10-ethenoanthracene-11-carboxylate (10a).



33 10a

From the foregoing methyl 5-acetosy-2-pentynoate **33** (20.84 g, 122 mmol) and anthracene (19.74 g, 111 mmol), 12.247 g (35.15 mmol, 32 %) of bicyclo diester **10a** was obtained. **10a**: mp 120.0-121.0 ℃ (pale yellow rods, recrystallized from methanol). ^{1}H NMR: 7.35 (2H, $H_{4,5}$, d,d, J=1.8, 5.5), 7.30 (2H, $H_{1,8}$, d,d, J=1.8, 5.5), 6.98 (4H, $H_{2,3,6,7}$, m), 5.67 (1H, H_{10}, s), 5.09 (1H, H_9, s), 4.18 (2H, H_{14}, t, J=6.6), 3.76 (3H, -CO_2CH_3, s), 3.13 (2H, H_{13}, t, J=6.6), 1.94 (3H, -OAc, s). Anal. Calcd. for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: C, 76.00; H, 5.71.

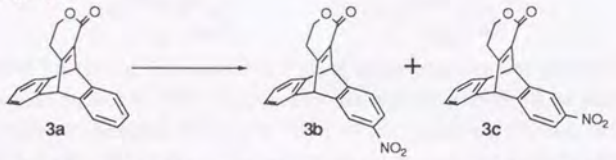
Lactone 3a.

10a 3a

A mixture of 9.70 g (27.8 mmol) of foregoing diester **10a**, 115 mg (0.60 mmol) of *p*-toluenesulphonic acid mono-hydrate, 300 mL of methanol and 60 mL of dichloromethane was reflux for 55 hrs, followed by evaporation. The residue was flash-chromatographed (ethyl acetate: *n*-hexane 1:2 , then dichloromethane) to give 6.784 g (24.7 mmol, 89 %) of lactone **3a**. **3a**: dp 288.0-290.0 ℃ (colorless prisms, recrystallized from ethyl acetate). ^{1}H NMR: 7.39 (2H, $H_{4,5}$, d,d, J=1.8, 6.6), 7.33 (2H, $H_{1,8}$, d,d, J=1.8, 6.6), 7.01 (4H, $H_{2,3,6,7}$, m), 5.66 (1H, H_{10}, s),

5.06 (1H, H_9, s), 4.30 (2H, H_{14}, t, J=6.6), 2.73 (2H, H_{13}, t, J=6.6). Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 83.30; H, 5.17.

Nitration of 3a.



Nitration of 3.01 g (10.97 mmol) of foregoing unsubstituted lactone **3a** and flash-chromatography (ethyl acetate: *n*-hexane 1:2) gave 1.014 g (3.18 mmol, 29 %) of 2-nitro lactone **3b** and 0.814 g (2.55 mmol, 23 %) of 3-nitro lactone **3c**.

2-Nitro-lactone (3b): mp 229.0-231.5 ℃ (colorless powder, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.17 (1H, H_1, d, J=2.2), 7.99 (1H, H_3, d,d, J=2.2, 8.1), 7.51 (1H, H_4, d, J=8.1), 7.43 (1H, H_5, d,d, J=2.2, 6.2), 7.39 (1H, H_8, d,d, J=2.2, 6.2), 7.09 (2H, $H_{6,7}$, m), 5.78 (1H, H_{10}, s), 5.21 (1H, H_9, s), 4.34 (2H, H_{14}, t, J=6.2), 2.78 (2H, H_{13}, t, J=6.2). Anal. Calcd. for $C_{19}H_{13}NO_4$: C, 71.47; H, 4.10; N, 4.39. Found: C, 71.19; H, 3.91; N, 4.26.

3-Nitro-lactone (3c): mp 240.0-241.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.20 (1H, H_4, d, J=2.2), 7.95 (1H, H_2, d,d, J=2.2, 8.1), 7.60 (2H, $H_{1,5}$, m), 7.37 (1H, H_8, br-d, J=7.7), 7.08 (2H, $H_{6,7}$, m), 5.79 (1H, H_{10}, s), 5.20 (1H, H_9, s), 4.33 (2H, H_{14}, t, J=6.2), 2.76 (2H, H_{13}, t, J=6.2). Anal. Calcd. for $C_{19}H_{13}NO_4$: C, 71.47; H, 4.10; N, 4.39. Found: C, 71.20; H, 3.89; N, 4.26.

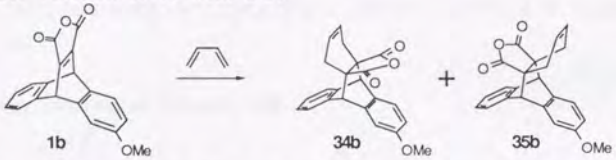
Diels-Alder reactions of the anhydride 1a-e.

Diels-Alder reactions of the anhydrides **1a-e** were carried out under the similar conditions as unsubstituted **1a**. The adducts were separated as a mixture by flash column chromatography, and the stereoisomers were separated by the specified methods (HPLC, repeated flash column chromatography and preparative thin layer chromatography). Ratios of the diastereomers were determined from signal integration values in the ^{1}H NMR spectra. The assignments of the ^{1}H NMR signals of pure diastereomers were based on NOE and INDOR (internuclear double resonance) measurements.

Diels-Alder reaction of 1a with 1,3-butadiene (BD).

A solution of **1a** (28 mg, 0.10 mmol) in 3 mL of dichloromethane was treated with BD (460 mg, 8.5 mmol, 85 equiv.) at -78 ℃ (dry ice-acetone), and the reaction vessel was sealed. The mixture was stirred in the sealed bottle at 23 ℃ for 15 hrs. Remaining BD and dichloromethane was removed under reduced pressure. The residue was flash-chromatographed (dichloromethane) to give 33 mg (98 %) of the adduct **34a**: mp 222.5-223.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.39 (2H, d,d, J=5.5, 3.3), 7.28 (2H, d,d, J=5.1, 3.3), 7.22 (2H, d,d, J=5.5, 3.3), 7.17 (2H, d,d, J=5.1, 3.3), 5.80 (2H, olefin, m), 4.38 (2H, bridge head, s), 2.80 (2H, -CH_2-, d,d,d, J=14.7, 4.8, 2.6), 1.73 (2H, -CH_2-, br-d, J=14.7). Anal. Calcd. for $C_{22}H_{16}O_3$: C, 80.47; H, 4.91. Found: C, 80.75; H, 4.93.

Diels-Alder reaction of 1b with BD.

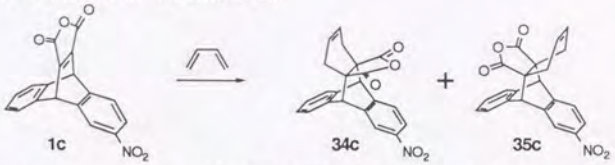


Two diastereomers were separated by preparative TLC (dichloromethane: *n*-hexane 2:3).

***Anti*-adduct (34b)**: mp 230.0-231.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.37 (2H, m), 7.21 (2H, m), 7.18 (1H, d, J=8.4), 6.86 (1H, d, J=2.6), 6.67 (1H, d,d, J=8.4, 2.6), 5.79 (2H, olefin, br-t, J=4.0), 4.32 (1H, bridge head, s), 4.31 (1H, bridge head, s), 3.74 (3H, OCH_3, s), 2.79 (2H, -CH_2-, br-d, J=15.0), 1.71 (2H, -CH_2-, br-d, J=16.9). Anal. Calcd. for $C_{23}H_{18}O_4 \cdot 1/5H_2O$: C, 76.31; H, 5.12. Found: C, 76.42; H, 4.87.

***Syn*-adduct (35b)**: mp 223.0-223.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.27 (3H, m), 7,17 (2H, m), 6.98 (1H, d, J=2.6), 6.72 (1H, d,d, J=8.4, 2.6), 5.81 (2H, olefin, br-t, J=4.0), 4.31 (2H, bridge head, s), 3.79 (3H, OCH_3, s), 2.79 (2H, -CH_2-, d,d, J=15.0, 6.6), 1.77 (2H, -CH_2-, J=14.7, 4.4). Anal. Calcd. for $C_{23}H_{18}O_4$: C, 77.08; H, 5.06. Found: C, 77.00; H, 4.99.

Diels-Alder reaction of 1c with BD.

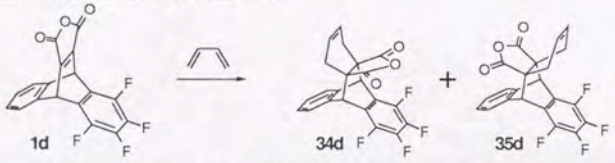


Two diastereomers were separated by HPLC (15 % ethyl acetate / *n*-hexane).

***Anti*-adduct (34c)**: mp 254.5-255.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.16 (1H, d, J=2.2), 8.10 (1H, d,d, J=8.1, 2.2), 7.46 (1H, d, J=8.1), 7.43 (2H, m), 7.28 (2H, m), 5.83 (2H, olefin, t, J=1.8), 4.53 (1H, bridge head, s), 4.52 (1H, bridge head, s), 2.84 (2H, -CH_2-, m), 1.75 (2H, -CH_2-, br-d, J=16.9). Anal. Calcd. for $C_{22}H_{15}NO_5$: C, 70.77; H, 4.05; N, 3.75. Found: C, 70.90; H, 4.09; N, 3.75.

***Syn*-adduct (35c)**: mp 194.5-196.0 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.26 (1H, d, J=2.2), 8.16 (1H, d,d, J=8.1, 2.2), 7.57 (1H, d, J=8.1), 7.32 (2H, m), 7.24 (2H, m), 5.83 (2H, olefin, t, J=3.7), 4.55 (1H, bridge head, s), 4.54 (1H, bridge head, s), 2.88 (2H, -CH_2-, m), 1.73 (1H, -CH_2-, d,d, J=15.4, 2.9), 1.68 (1H, -CH_2-, d,d, J=15.4, 2.9). Anal. Calcd. for $C_{22}H_{15}NO_5$: C, 70.77; H, 4.05; N, 3.75. Found: C, 71.05; H, 3.85; N, 4.03.

Diels-Alder reaction of 1d with BD.

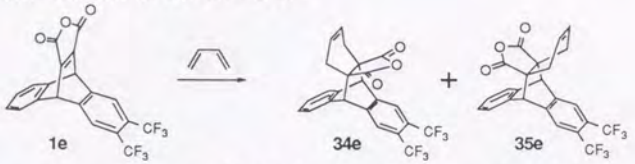


Two diastereomers were separated by flash column chromatography (ethyl acetate: *n*-hexane 1:10).

***Anti*-adduct (34d)**: mp 272.0-273.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.45 (2H, d,d, J=5.5, 3.3), 7.31 (2H, d,d, J=5.5, 3.3), 5.82 (2H, olefin, t, J=4.0), 4.80 (2H, bridge head, s), 2.84 (2H, -CH_2-, d,d,d, J=14.3, 4.8, 2.6), 1.70 (2H, -CH_2-, br-d, J=14.7). Anal. Calcd. for $C_{22}H_{12}O_3F_4$: C, 66.01; H, 3.02. Found: C, 65.71; H, 2.74.

***Syn*-adduct (35d)**: mp 242.0-242.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.34 (2H, d,d, J=5.5, 3.3), 7.27 (2H, d,d, J=5.5, 3.3), 5.86 (2H, olefin, t, J=3.3), 4.84 (2H, bridge head, s), 2.92 (2H, -CH_2-, m(br-d-like)), 1.74 (2H, -CH_2-, d, J=14.7). Anal. Calcd. for $C_{22}H_{12}O_3F_4$: C, 66.01; H, 3.02. Found: C, 65.80; H, 2.96.

Diels-Alder reaction of 1e with BD.

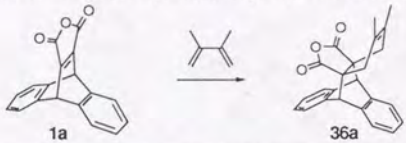


Two diastereomers were separated by flash column chromatography (ethyl acetate: *n*-hexane 1:10).

***Anti*-adduct (34e)**: mp 290.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.77 (2H, s), 7.44 (2H, d,d, J=5.5, 3.3), 7.29 (2H, d,d, J=5.5, 3.3), 5.84 (2H, olefin, t, J=3.7), 4.54 (2H, bridge head, s), 2.85 (2H, -CH_2-, d,d,d, J=14.3, 4.8, 2.6), 1.76 (2H, -CH_2-, d, J=14.7). Anal. Calcd. for $C_{24}H_{14}O_3F_6$: C, 62.08; H, 3.04. Found: C, 61.98; H, 2.98.

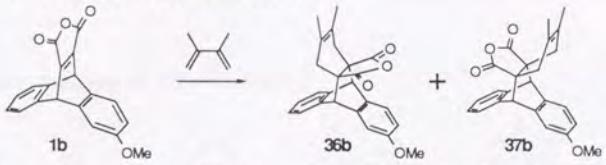
***Syn*-adduct (35e)**: mp 224.0-224.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.87 (2H, s), 7.33 (2H, d,d, J=5.6, 3.4), 7.25 (2H, d,d, J=5.6, 3.4), 5.84 (2H, olefin, t, J=3.4), 4.57 (2H, bridge head, s), 2.89 (2H, -CH_2-, d,d,d, J=14.5, 5.1, 2.6), 1.67 (2H, -CH_2-, d, J=14.5). Anal. Calcd. for $C_{24}H_{14}O_3F_6$: C, 62.08; H, 3.04. Found: C, 62.32; H, 2.83.

Diels-Alder reaction of 1a with 2,3-dimethyl-1,3-butadiene (DMBD).



A solution of **1a** (28 mg, 0.10 mmol) in 3 mL of dichloromethane was treated with DMBD (34 mg, 0.41 mmol, 4.1 equiv.). The mixture was stirred at 23 ℃ for 15 hrs, then DMBD and dichloromethane was removed at reduced pressure. The residue was flash-chromatographed (dichloromethane) to give 36 mg (100 %) of **36a**: mp 256.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.37 (2H, d,d, J=5.1, 3.3), 7.29 (2H, d,d, J=5.5, 3.3), 7.21 (2H, d,d, J=5.1, 3.3), 7.17 (2H, d,d, J=5.5, 2.9), 4.36 (2H, bridge head, s), 2.53 (2H, -CH_2-, d, J=14.7), 1.79 (2H, -CH_2-, br-d, J=15.0), 1.57 (6H, CH_3, s). Anal. Calcd. for $C_{24}H_{20}O_3$: C, 80.88; H, 5.66. Found: C, 80.75; H, 5.67.

Diels-Alder reaction of 1b with DMBD.

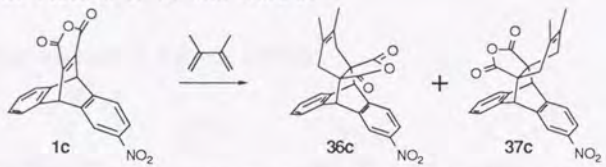


Two diastereomers were separated by preparative TLC (dichloromethane: *n*-hexane 2:3).

***Anti*-adduct (36b)**: mp 244.0-245.0 ℃ (colorless prisms, recrystallized from ethyl acetate/*n*-hexane). ^{1}H NMR: 7.34 (2H, m), 7.18 (3H, m), 6.85 (1H, d, J=2.2), 6.66 (1H, d,d, J=8.1, 2.6), 4.30 (1H, bridge head, s), 4.29 (1H, bridge head, s), 3.74 (3H, OCH_3, s), 2.52 (2H, $-CH_2-$, d, J=14.7), 1.77 (2H, $-CH_2-$, br-d, J=13.9), 1.568 (3H, CH_3, s), 1.565 (3H, CH_3, s). Anal. Calcd. for $C_{25}H_{22}O_4$: C,77.70; H, 5.74. Found: C, 77.47; H5.51.

***Syn*-adduct (37b)**: mp 214.0-215.0 ℃ (colorless flakes, recrystallized from *n*-hexane). ^{1}H NMR: 7.26 (3H, m), 7.16 (2H, m), 6.96 (1H, d, J=2.6), 6.70 (1H, d,d, J=8.1, 2.6), 4.29 (2H, bridge head, s), 3.78 (3H, OCH_3, s), 2.52 (2H, $-CH_2-$, d, J=14.7), 1.83 (2H, $-CH_2-$, br-d, J=16.5), 1.58 (3H, CH_3, s), 1.57 (3H, CH_3, s). HRMS (M^+) Calcd. for $C_{25}H_{22}O_4$: 386.1518, Found: 386.1526.

Diels-Alder reaction of 1c with DMBD.



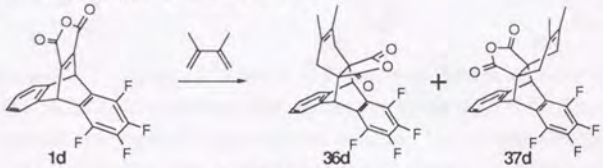
Two diastereomers were separated by preparative TLC (dichloromethane: *n*-hexane 1:2).

***Anti*-adduct (36c)**: mp 245.0-248.0 ℃ (colorless powder, recrystallized from ethyl acetate/*n*-hexane). ^{1}H NMR: 8.16 (1H, d, J=1.8), 8.10 (1H, d,d, J=8.1, 2.2), 7.47 (1H, d, J=8.1), 7.42 (2H, m), 7.27 (2H, m), 4.51 (1H, bridge head, s), 4.50 (1H, bridge head, s), 2.57 (1H, $-CH_2-$, d, J=14.7), 2.56 (1H, $-CH_2-$, d, J=14.7), 1.82 (2H, $-CH_2-$, br-d, J=15.8), 1.590 (3H, CH_3, s), 1.587 (3H, CH_3, s). Anal. Calcd. for $C_{24}H_{19}NO_5$: C, 71.81; H, 4.77; N, 3.49. Found: C, 71.65; H, 4.88; N, 3.76.

***Syn*-adduct (37c)**: mp 243.0-245.0 ℃ (colorless prisms, recrystallized from ethyl acetate/*n*-hexane). The structure was confirmed by X-ray crystallographic analysis. ^{1}H NMR: 8.25 (1H, d, J=2.2), 8.15 (1H, d,d, J=8.1, 2.2), 7.55 (1H, d, J=8.4), 7.32 (2H, m), 7.23 (2H, m), 4.53 (1H, bridge head, s), 4.52 (1H, bridge head, s), 2.61 (1H, $-CH_2-$, d, J=14.7), 2.58 (1H, $-CH_2-$, d, J=14.3), 1.79 (1H, $-CH_2-$, br-d, J=14.7), 1.75 (1H, $-CH_2-$, br-d, J=14.3), 1.58 (6H, CH_3,

s). Anal. Calcd. for $C_{24}H_{19}NO_5$: C, 71.81; H, 4.77; N, 3.49. Found: C, 71.68; H, 4.66; N, 3.74.

Diels-Alder reaction of 1d with DMBD.

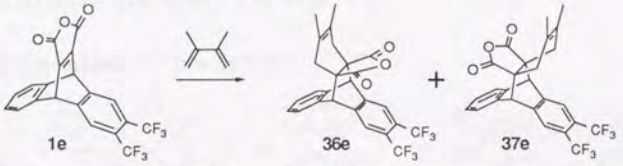


Two diastereomers were separated by flash column chromatography (ethyl acetate: *n*-hexane 1:20).

***Anti*-adduct (36d)**: mp 267.5-268.0 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.43 (2H, d,d, J=5.5, 2.9), 7.29 (2H, d,d, J=5.5, 2.9), 4.78 (2H, bridge head, s), 2.56 (2H, -CH_2-, d, J=14.3), 1.76 (2H, -CH_2-, br-d, J=15.0), 1.58 (6H, CH_3, br-d, J=1.1). HRMS Calcd. for $C_{24}H_{16}O_3F_4$: 428.1036, Found: 428.1064.

***Syn*-adduct (37d)**: mp 230.5-231.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.33 (2H, d,d, J=5.5, 3.3), 7.25 (2H, d,d, J=5.5, 3.3), 4.81 (2H, bridge head, s), 2.64 (2H, -CH_2-, d, J=14.6), 1.81 (2H, -CH_2-, br-d, J=15.0), 1.61 (6H, CH_3, br-d, J=1.1). HRMS Calcd. for $C_{24}H_{16}O_3F_4$: 428.1036, Found: 428.1053.

Diels-Alder reaction of 1e with DMBD.

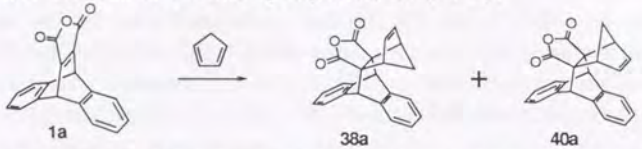


Two diastereomers were separated by flash column chromatography (ethyl acetate: *n*-hexane 2:25).

***Anti*-adduct (36e)**: mp 278.5-279.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.77 (2H, s), 7.42 (2H, d,d, J=5.5, 3.3), 7.27 (2H, d,d, J=5.5, 3.3), 4.52 (2H, bridge head, s), 2.57 (2H, -CH_2-, d, J=14.3), 1.82 (2H, -CH_2-, br-d, J=15.0), 1.60 (6H, CH_3, br-d, J=1.1). Anal. Calcd. for $C_{26}H_{18}O_3F_6$: C, 63.42; H, 3.68. Found: C, 63.25; H, 3.31.

***Syn*-adduct (37e)**: mp 246.0-246.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.85 (2H, s), 7.33 (2H, d,d, J=5.5, 3.3), 7.24 (2H, d,d, J=5.5, 3.3), 4.55 (2H, bridge head, s), 2.61 (2H, -CH_2-, d, J=14.7), 1.74 (2H, -CH_2-, br-d, J=15.0), 1.59 (6H, CH_3, br-d, J=1.1). Anal. Calcd. for $C_{26}H_{18}O_3F_6$: C, 63.42; H, 3.68. Found: C, 63.51; H, 3.59.

Diels-Alder reaction of 1a with cyclopentadiene (CPD).

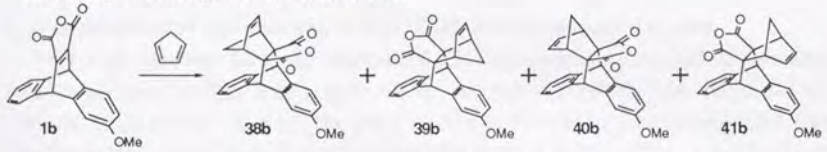


Freshly distilled CPD (222 mg, 3.36 mmol, 34 equiv.) was added to a solution of **1a** (27 mg, 0.099 mmol) in 3 mL of dichloromethane. The mixture was stirred at 23 ℃ for 15 hrs, then CPD and dichloromethane was removed under reduced pressure. The residue was flash-chromatographed (*n*-hexane, followed by dichloromethane) to give 21 mg (63 %) of a mixture of the *endo*-adduct **38a** and the *exo*-adduct **40a**, which was separated by flash column chromatography (ethyl acetate: *n*-hexane 1:20).

***Endo*-Adduct (38a)**: mp >300 ℃ (colorless prisms, recrystallized from *n*-hexane). ^{1}H NMR: 7.34 (2H, d,d, J=5.1, 3.3), 7.28 (2H, d,d, J=5.5, 3.3), 7.22 (2H, d,d, J=5.1, 3.3), 7.12 (2H, d,d, J=5.5, 3.3), 6.41 (2H, olefin, br-t, J=1.8), 4.64 (2H, bridge head (dibenzyl), s), 3.01 (2H, bridge head, m), 1.19 (1H, -CH_2-, br-d, J=9.9), 0.19 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{23}H_{16}O_3$: C, 81.16; H, 4.74. Found: C, 81.03; H, 4.61.

***Exo*-adduct (40a)**: mp 241.0-242.5 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.26 (2H, d,d, J=5.1, 3.3), 7.15 (4H, s), 7.12 (2H, d,d, J=5.5, 3.3), 5.18 (2H, olefin, t, J=1.5), 4.51 (2H, bridge head (dibenzyl), s), 3.20 (2H, bridge head, t, J=1.5), 1.67 (1H, -CH_2-, br-d, J=10.3), 1.53 (1H, -CH_2-, t,d, J=1.5, 10.3). Anal. Calcd. for $C_{23}H_{16}O_3$: C, 81.16; H, 4.74. Found: C, 80.95; H, 4.62.

Diels-Alder reaction of 1b with CPD.



Four diastereomers were separated by HPLC (10 % ethyl acetate / *n*-hexane), and then preparative TLC (dichloromethane: *n*-hexane 2:3).

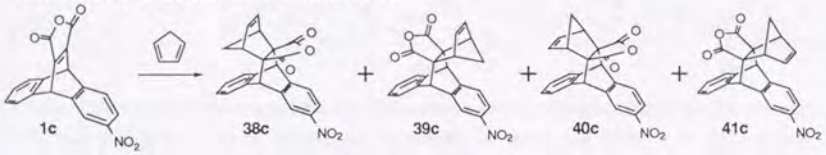
***Anti-endo*-adduct (38b)**: mp 265.0-266.0 ℃ (colorless plates, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.33 (2H, m), 7.21 (2H, m), 7.17 (1H, d, J=8.1), 6.86 (1H, d, J=2.2), 6.62 (1H, d,d, J=8.4, 2.6), 6.41 (2H, olefin, br-s), 4.59 (1H, bridge head (dibenzyl), s), 4.58 (1H, bridge head (dibenzyl), s), 3.73 (3H, OCH_3, s), 3.00 (2H, bridge head, br-s), 1.18 (1H, -CH_2-, br-d, J=10.3), 0.17 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.95; H, 4.73.

***Syn-endo*-adduct (39b)**: mp 244.5-245.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.26 (2H, m), 7.23 (1H, d, J=8.1), 7.12 (2H, m), 6.95 (1H, d, J=2.6), 6.71 (1H, d,d, J=8.1, 2.6), 6.41 (2H, olefin, br-s), 4.59 (1H, bridge head (dibenzyl), s), 4.58 (1H, bridge head (dibenzyl), s), 3.80 (3H, OCH_3, s), 3.01 (2H, bridge head, br-d, J=1.5), 1.23 (1H, -CH_2-, br-d, J=9.9), 0.31 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.65; H, 4.82.

***Anti-exo*-adduct (40b)**: mp 179.5-180.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.15 (1H, d, J=8.1), 7.13 (4H, m), 6.83 (1H, d, J=2.2), 6.70 (1H, d,d, J=8.1, 2.2), 5.16 (2H, olefin, br-s), 4.45 (2H, bridge head (dibenzyl), s), 3.74 (3H, OCH_3, s), 3.18 (2H, bridge head, br-s), 1.66 (1H, -CH_2-, br-d, J=10.3), 1.53 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.76; H, 4.94.

***Syn-exo*-adduct (41b)**: mp 250.0-250.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.24 (2H, d,d, J=8.4, 3.7), 7.11 (2H, m), 7.03 (1H, d, J=8.1), 6.77 (1H, d, J=2.2), 6.63 (1H, d,d, J=8.1, 2.6), 5.28 (1H, olefin, m), 5.23 (1H, olefin, m), 4.46 (1H, bridge head (dibenzyl), s), 4.43 (1H, bridge head (dibenzyl), s), 3.77 (3H, OCH_3, s), 3.19 (2H, bridge head, br-t, J=1.5), 1.66 (1H, -CH_2-, br-d, J=10.3), 1.54 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{18}O_4$: C, 77.82; H, 4.90. Found: C, 77.54; H, 4.85.

Diels-Alder reaction of 1c with CPD.



Four diastereomers were separated by HPLC (20 % dichloromethane / *n*-hexane).

***Anti-endo*-adduct (38c)**: mp 296.0-300.0 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.15 (1H, d, J=2.2), 8.06 (1H, d,d, J=8.1), 7.46 (1H, d, J=8.1), 7.40 (2H, m), 7.29 (2H, m), 6.45 (2H, olefin, br-s), 4.81 (1H, bridge head (dibenzyl), s), 4.80 (1H, bridge head (dibenzyl), s), 3.08 (2H, bridge head, br-s), 1.24 (1H, -CH_2-, d, J=10.3), 0.16 (1H, -CH_2-, d, J=10.6). Anal. Calcd. for $C_{23}H_{15}NO_5$: C, 71.68; H, 3.92; N, 3.63. Found: C, 71.46; H, 3.85; N, 3.79.

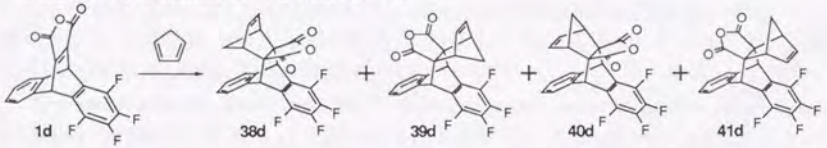
***Syn-endo*-adduct (39c)**: mp 279.5-281.5 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). The structure was confirmed by X-ray crystallographic analysis. ^{1}H NMR: 8.22 (1H, d, J=2.2), 8.17 (1H, d,d, J=8.1, 2.2), 7.54 (1H, d, J=8.1), 7.32 (2H, m), 7.18 (2H, m), 6.44 (2H, olefin, br-s), 4.81 (1H, bridge head (dibenzyl), s), 4.80 (1H, bridge head (dibenzyl), s), 3.12 (1H, bridge head, br-s), 3.09 (1H, bridge head, br-s), 1.30 (1H, -CH_2-, br-d,

J=10.3), 0.30 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{23}H_{15}NO_5$: C, 71.68; H, 3.92; N, 3.63. Found: C, 71.45; H, 3.79; N, 3.90.

***Anti-exo*-adduct (40c)**: mp 210.0-211.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.12 (1H, d, J=2.2), 8.05 (1H, d,d, J=8.1, 2.2), 7.43 (1H, d, J=8.1), 7.20 (4H, m), 5.20 (2H, olefin, br-t, J=1.5), 4.670 (1H, bridge head (dibenzyl), s), 4.665 (1H, bridge head (dibenzyl), s), 3.26 (2H, bridge head, m), 1.69 (1H, -CH_2-, br-d, J=10.3), 1.57 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{23}H_{15}NO_5$: C, 71.68; H, 3.92; N, 3.63. Found: C, 71.85; H, 3.82; N, 3.89.

***Syn-exo*-adduct (41c)**: mp 267.0-267.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.10 (1H, d,d, J=8.4, 2.2), 8.02 (1H, d, J=2.2), 7.33 (1H, d, J=8.4), 7.29 (2H, m), 7.18 (2H, m), 5.25 (2H, olefin, br-t, J=1.8), 4.68 (1H, bridge head (dibenzyl), s), 4.66 (1H, bridge head (dibenzyl), s), 3.29 (1H, bridge head, br-s), 3.26 (1H, bridge head, br-s), 1.72 (1H, -CH_2-, br-d, J=10.3), 1.62 (1H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{23}H_{15}NO_5 \cdot 1/2H_2O$: C, 70.05; H, 4.09; N, 3.55. Found: C, 70.24; H, 3.75; N, 3.90.

Diels-Alder reaction of 1d with CPD.



Four diastereomers were separated by flash column chromatography (ethyl acetate: *n*-hexane 1:10), and then HPLC (10 % chloroform / *n*-hexane for **38d** and **40d**, 2 % ethyl acetate / *n*-hexane for **39d** and **41d**).

***Anti-endo*-adduct (38d)**: mp >300 ℃. ^{1}H NMR: 7.41 (2H, d,d, J=5.5, 3.3), 7.30 (2H, d,d, J=5.5, 3.3), 6.44 (2H, olefin, br-s), 5.09 (2H, bridge head (dibenzyl), s), 3.05 (2H, bridge head, br-t, J=1.8), 1.22 (1H, -CH_2-, d, J=10.6), 0.08 (1H, -CH_2-, d, J=10.6). HRMS (M^+) Calcd. for $C_{23}H_{12}O_3F_4$: 412.0723, Found: 412.0716.

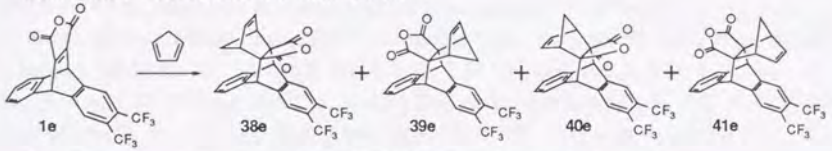
***Syn-endo*-adduct (39d)**: mp 281.5-283.0 ℃ (colorless rods, recrystallized from *n*-hexane). ^{1}H NMR: 7.33 (2H, d,d, J=5.5, 3.3), 7.21 (2H, d,d, J=5.5, 3.3), 6.45 (2H, olefin, br-t, J=1.8), 5.09 (2H, bridge head (dibenzyl), s), 3.14 (2H, bridge head, br-t, J=1.8), 1.46 (1H, -CH_2-, d, J=10.3), 0.43 (1H, -CH_2-, d, J=10.3). Anal. Calcd. for $C_{23}H_{12}O_3F_4$: C, 67.00; H, 2.93. Found: C, 66.71; H, 2.71.

***Anti-exo*-adduct (40d)**: mp 261.5-262.5 ℃ (colorless rods, recrystallized from *n*-hexane). ^{1}H NMR: 7.22 (4H, m), 5.16 (2H, olefin, br-t, J=1.8), 4.97 (2H, bridge head (dibenzyl), s),

3.25 (2H, bridge head, br-t, J=1.8), 1.69 (1H, -CH_2-, d, J=10.3), 1.57 (1H, -CH_2-, d, J=10.3). Anal. Calcd. for $C_{23}H_{12}O_3F_4$: C, 67.00; H, 2.93. Found: C, 66.92; H, 2.72.

***Syn-exo*-adduct (41d)**: mp 254.5-255.0 ℃ (colorless rods, recrystallized from *n*-hexane). ^{1}H NMR: 7.31 (2H, d,d, J=5.1, 3.3), 7.21 (2H, d,d, J=5.5, 3.3), 5.52 (2H, olefin, br-t, J=1.8), 4.92 (2H, bridge head (dibenzyl), s), 3.28 (2H, bridge head, br-s), 1.71 (1H, -CH_2-, d, J=10.6), 1.68 (1H, -CH_2-, d,t, J=10.6, 1.8). Anal. Calcd. for $C_{23}H_{12}O_3F_4$: C, 67.00; H, 2.93. Found: C, 67.23; H, 2.94.

Diels-Alder reaction of 1e with CPD.



Four diastereomers were separated by HPLC (5 % ethyl acetate / *n*-hexane).

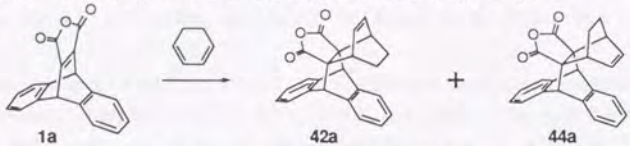
***Anti-endo*-adduct (38e)**: mp 239.5-240.5 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.76 (2H, s), 7.40 (2H, d,d, J=5.6, 3.4), 7.29 (2H, d,d, J=5.6, 3.4), 6.45 (2H, olefin, br-t, J=1.7), 4.81 (2H, bridge head (dibenzyl), s), 3.08 (2H, bridge head, br-t, J=1.7), 1.25 (1H, -CH_2-, d, J=10.3), 0.15 (1H, -CH_2-, d, J=10.3). Anal. Calcd. for $C_{25}H_{14}O_3F_6$: C, 63.03; H, 2.96. Found: C, 62.92; H, 2.85.

***Syn-endo*-adduct (39e)**: mp >300 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.83 (2H, s), 7.32 (2H, d,d, J=5.5, 3.3), 7.18 (2H, d,d, J=5.5, 3.3), 6.44 (2H, olefin, br-s), 4.81 (2H, bridge head (dibenzyl), s), 3.11 (2H, bridge head, br-t, J=1.8), 1.33 (1H, -CH_2-, d, J=10.6), 0.24 (1H, -CH_2-, d, J=10.6). Anal. Calcd. for $C_{25}H_{14}O_3F_6$: C, 63.03; H, 2.96. Found: C, 62.75; H, 2.66.

***Anti-exo*-adduct (40e)**: mp 238.0-238.5 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.73 (2H, s), 7.20 (4H, br-s), 5.20 (2H, olefin, br-t, J=1.8), 4.67 (2H, bridge head (dibenzyl), s), 3.27 (2H, bridge head, br-t, J=1.8), 1.71 (1H, -CH_2-, d, J=10.6), 1.58 (1H, d,t, J=10.6, 1.5). Anal. Calcd. for $C_{25}H_{14}O_3F_6$: C, 63.03; H, 2.96. Found: C, 62.83; H, 2.72.

***Syn-exo*-adduct (41e)**: mp >300 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.62 (2H, s), 7.31 (2H, d,d, J=5.5, 2.9), 7.19 (2H, d,d, J=5.5, 2.9), 5.22 (2H, olefin, br-t, J=1.8), 4.69 (2H, bridge head (dibenzyl), s), 3.28 (2H, bridge head, br-t, J=1.8), 1.72 (1H, -CH_2-, d, J=10.3), 1.63 (1H, -CH_2-, d, J=10.3). Anal. Calcd. for $C_{25}H_{14}O_3F_6$: C, 63.03; H, 2.96. Found: C, 62.81; H, 2.74.

Diels-Alder reaction of 1a with 1,3-cyclohexadiene (CHD).

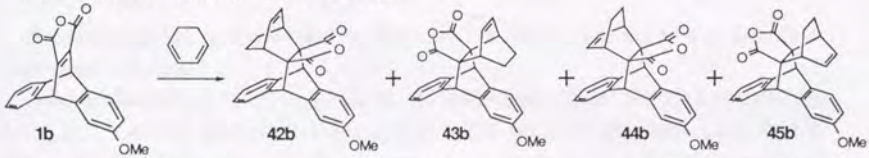


A mixture of **1a** (74 mg, 0.27 mmol) and CHD (2.64 g, 33 mmol, 122 equiv.) was heated in a sealed bottle at 100 ℃ for 15 hrs, and then the volatile was evaporated and the residue was flash-chromatographed (dichloromethane: *n*-hexane 1:1) to give 55 mg of a mixture of the products (**42a** and **44a**), which was separated by HPLC (ethyl acetate 5 %/ *n*-hexane).

***Endo*-adduct (42a)**: mp >300 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.41 (2H, d,d, J=5.5, 3.3), 7.22 (2H, d,d, J=5.5, 3.3), 7.18 (2H, d,d, J=5.5, 3.3), 7.08 (2H, d,d, J=5.5, 3.3), 6.33 (2H, olefin, d,d, J=4.4, 2.9), 4.57 (2H, bridge head (dibenzyl), s), 3.16 (2H, bridge head, br-s), 1.03 (2H, -CH_2-, br-d, J=9.9), 0.79 (2H, -CH_2-, br-d, J=9.9). Anal. Calcd. for $C_{24}H_{18}O_3 \cdot 1/2H_2O$: C, 79.32; H, 5.27. Found: C, 79.15; H, 5.01.

***Exo*-adduct (44a)**: mp 267.0-268.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.26 (2H, d,d, J=4.8, 3.3), 7.16 (6H, m), 5.17 (2H, olefin, d,d, J=4.8, 2.9), 4.43 (2H, bridge head (dibenzyl), s), 3.00 (2H, bridge head, br-s), 1.61 (2H, -CH_2-, br-d, J=9.5), 1.16 (2H, -CH_2-, br-d, J=9.9). Anal. Calcd. for $C_{24}H_{18}O_3$: C, 81.34; H, 5.12. Found: C, 81.05; H, 5.04.

Diels-Alder reaction of 1b with CHD.



Four diastereomers were separated by HPLC (7 % ethyl acetate / *n*-hexane, then 15 % dichloromethane / *n*-hexane).

***Anti-endo*-adduct (42b)**: mp 220.0-222.0 ℃. ^{1}H NMR: 7.39 (2H, m), 7.17 (2H, m), 7.11 (1H, d, J=8.1), 6.80 (1H, d, J=2.6), 6.57 (1H, d,d, J=8.1, 2.6), 6.33 (2H, olefin, d,d, J=4.4, 2.9), 4.51 (1H, bridge head (dibenzyl), s), 4.50 (1H, bridge head (dibenzyl), s), 3.71 (3H, OCH_3, s), 3.14 (2H, bridge head, br-s), 1.02 (2H, -CH_2-, br-d, J=8.8), 0.78 (2H, -CH_2-, br-d, J=8.8). HRMS (M^+) Calcd. for $C_{25}H_{20}O_4$: 384.1362, Found: 384.1315.

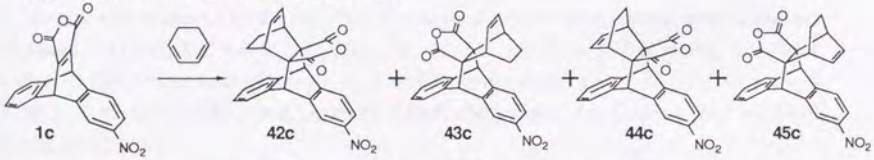
***Syn-endo*-adduct (43b)**: mp 280.5-281.0 ℃. ^{1}H NMR: 7.29 (1H, d, J=8.4), 7.21 (2H, m), 7.08 (2H, m), 6.98 (1H, d, J=2.6), 6.71 (1H, d,d, J=8.1, 2.6), 6.33 (2H, olefin, t, J=3.7),

4.51 (2H, bridge head (dibenzyl), s), 3.80 (3H, OCH_3, s), 3.15 (2H, bridge head, br-s), 1.13 (2H, $-CH_2-$, m), 0.81 (2H, $-CH_2-$, m). HRMS (M^+) Calcd. for $C_{25}H_{20}O_4$: 384.1362, Found: 384.1355.

***Anti-exo*-adduct (44b)**: mp 216.0-218.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^1H NMR: 7.14 (5H, m), 6.83 (1H, d,d, J=8.4, 2.6), 6.65 (1H, d,d, J=8.4, 2.6), 5.16 (2H, olefin, m), 4.37 (1H, bridge head (dibenzyl), s), 4.36 (1H, bridge head (dibenzyl), s), 3.74 (3H, OCH_3, s), 2.98 (2H, bridge head, br-s), 1.61 (2H, $-CH_2-$, br-d, J=8.8), 1.15 (2H, $-CH_2-$, br-d, J=9.9). Anal. Calcd. for $C_{25}H_{20}O_4$: C, 78.11; H, 5.24. Found: C, 77.83; H, 5.24.

***Syn-exo*-adduct (45b)**: mp 266.5-268.5 ℃ (colorless powder, recrystallized from ethyl acetate/ *n*-hexane). ^1H NMR: 7.23 (2H, m), 7.13 (2H, m), 7.06 (1H, d, J=8.1), 6.81 (1H, d, J=2.6), 6.63 (1H, d,d, J=8.1, 2.6), 5.27 (1H, olefin, d,t, J=1.5, 6.6), 5.22 (1H, olefin, d,t, J=1.5, 6.6), 4.37 (1H, bridge head (dibenzyl), s), 4.34 (1H, bridge head (dibenzyl), s), 3.77 (3H, OCH_3, s), 2.99 (2H, bridge head, br-d, J=6.6), 1.61 (2H, $-CH_2-$, br-d, J=10.6), 1.16 (2H, $-CH_2-$, br-d, J=11.0). Anal. Calcd. for $C_{25}H_{20}O_4$: C, 78.11; H, 5.24. Found: C, 77.90; H, 5.40.

Diels-Alder reaction of 1c with CHD.



Four diastereomers were separated by HPLC (10 % ethyl acetate / *n*-hexane, then 25 % chloroform / *n*-hexane).

***Anti-endo*-adduct (42c)**: mp >300 ℃. ^1H NMR: 8.08 (1H, d, J=2.2), 8.01 (1H, d,d, J=8.1, 2.2), 7.45 (2H, m), 7.39 (1H, d, J=8.1), 7.24 (2H, m), 6.36 (2H, olefin, t, J=1.5), 4.72 (1H, bridge head (dibenzyl), s), 4.71 (1H, bridge head (dibenzyl), s), 3.20 (2H, bridge head, br-s), 1.01 (2H, $-CH_2-$, br-d, J=9.9), 0.83 (2H, $-CH_2-$, br-d, J=10.3). HRMS (M^+) Calcd. for $C_{24}H_{17}NO_5$: 399.1107, Found: 399.1138.

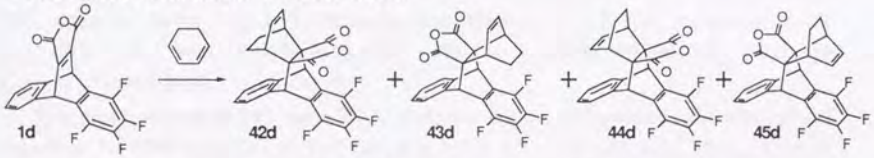
***Syn-endo*-adduct (43c)**: mp >300 ℃. ^1H NMR: 8.31 (1H, d, J=2.2), 8.11 (1H, d,d, J=8.4, 2.2), 7.61 (1H, d, J=8.4), 7.27 (2H, m), 7.14 (2H, m), 6.37 (2H, olefin, m), 4.71 (2H, bridge head (dibenzyl), s), 3.21 (2H, bridge head, br-s), 0.90 (4H, $-CH_2-$, m). HRMS (M^+) Calcd. for $C_{24}H_{17}NO_5$: 399.1107, Found: 399.1135.

***Anti-exo*-adduct (44c)**: mp 294.0-295.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^1H NMR: 8.13 (1H, d, J=2.2), 8.07 (1H, d,d, J=8.4, 2.2), 7.43 (1H, d,

J=8.4), 7.21 (4H, m), 5.19 (2H, olefin, d,d, J=4.8, 2.9), 4.583 (1H, bridge head (dibenzyl), s), 4.576 (1H, bridge head (dibenzyl), s), 3.05 (2H, bridge head, br-s), 1.62 (2H, -CH_2-, br-d, J=9.9), 1.19 (2H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{17}NO_5$: C, 72.17; H, 4.29; N, 3.51. Found: C, 72.04; H, 4.19; N, 3.70.

***Syn-exo*-adduct (45c)**: mp 276.0-277.5 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.10 (1H, d,d, J=8.1, 2.2), 8.05 (1H, d, J=2.2), 7.36 (1H, d, J=8.1), 7.30 (2H, m), 7.21 (2H, m), 5.26 (2H, olefin, t, J=1.8), 4.60 (1H, bridge head (dibenzyl), s), 4.58 (1H, bridge head (dibenzyl), s), 3.08 (1H, bridge head, br-s), 3.06 (1H, bridge head, br-s), 1.64 (2H, -CH_2-, br-d, J=9.9), 1.20 (2H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{17}NO_5$: C, 72.17; H, 4.29; N, 3.51. Found: C, 72.37; H, 4.36; N, 3.76.

Diels-Alder reaction of 1d with CHD.



Four diastereomers were separated by HPLC (5 % ethyl acetate / *n*-hexane).

***Anti-endo*-adduct (42d)**: mp >300 ℃ (colorless needles, recrystallized from *n*-hexane). ^{1}H NMR: 7.47 (2H, d,d, J=5.5, 3.3), 7.27 (2H, d,d, J=5.5, 3.3), 6.36 (2H, olefin, d,d, J=4.8, 2.9), 5.01 (2H, bridge head (dibenzyl), s), 3.19 (2H, bridge head, br-s), 0.95 (2H, -CH_2-, br-d, J=10.3), 0.82 (2H, -CH_2-, br-d, J=10.3). HRMS (M^+) Calcd. for $C_{24}H_{14}O_3F_4$: 426.0879, Found: 426.0873.

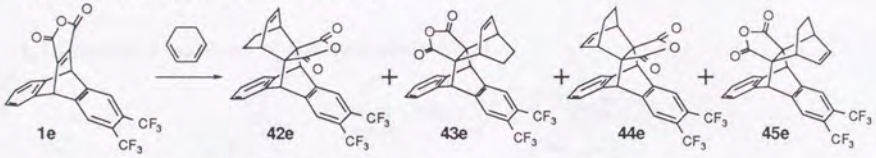
***Syn-endo*-adduct (43d)**: mp >300 ℃ (colorless needles, recrystallized from *n*-hexane). ^{1}H NMR: 7.28 (2H, d,d, J=5.1, 3.3), 7.17 (2H, d,d, J=5.5, 3.3), 6.37 (2H, olefin, d,d, J=4.4, 2.9), 4.94 (2H, bridge head (dibenzyl), s), 3.20 (2H, bridge head, br-s), 1.04 (2H, -CH_2-, br-d, J=10.6), 0.97 (2H, -CH_2-, br-d, J=9.9). HRMS (M^+) Calcd. for $C_{24}H_{14}O_3F_4$: 426.0879, Found: 426.0866.

***Anti-exo*-adduct (44d)**: mp >300 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.23 (4H, m), 5.16 (2H, olefin, d,d, J=4.4, 2.9), 4.85 (2H, bridge head (dibenzyl), s), 3.02 (2H, bridge head, br-s), 1.63 (2H, -CH_2-, br-d, J=9.5), 1.19 (2H, -CH_2-, br-d, J=10.3). Anal. Calcd. for $C_{24}H_{14}O_3F_4$: C, 67.61; H, 3.31. Found: C, 67.67; H, 3.05.

***Syn-exo*-adduct (45d)**: mp 288.5-289.5 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.31 (2H, d,d, J=5.5, 3.3), 7.23 (2H, d,d, J=5.5, 3.3), 5.51 (2H, olefin, d,d, J=4.8, 3.3), 4.86 (2H, bridge head (dibenzyl), s), 3.09 (2H, bridge head, br-s), 1.63

(2H, -CH_2-, br-d, J=9.5), 1.22 (2H, -CH_2-, br-d, J=9.9). Anal. Calcd. for $C_{24}H_{14}O_3F_4$: C, 67.61; H, 3.31. Found: C, 67.63; H, 3.01.

Diels-Alder reaction of 1e with CHD.



Four diastereomers were separated by HPLC (10 % ethyl acetate / *n*-hexane).

***Anti-endo*-adduct (42e)**: mp 263.0-264.0 ℃ (colorless prisms, recrystallized from *n*-hexane). ^{1}H NMR: 7.69 (2H, s), 7.46 (2H, d,d, J=5.5, 3.3), 7.25 (2H, d,d, J=5.5, 3.3), 6.37 (2H, olefin, d,d, J=4.4, 2.9), 4.73 (2H, bridge head (dibenzyl), s), 3.21 (2H, bridge head, br-s), 1.01 (2H, -CH_2-, br-d, J=10.3), 0.83 (2H, -CH_2-, br-d, J=8.8). HRMS (M^+) Calcd. for $C_{26}H_{16}O_3F_6$: 490.1004, Found: 490.1013.

***Syn-endo*-adduct (43e)**: mp >300 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.92 (2H, s), 7.27 (2H, d,d, J=5.1, 2.9), 7.15 (2H, d,d, J=5.1, 2.9), 6.37 (2H, olefin, d,d, J=4.4, 2.9), 4.71 (2H, bridge head (dibenzyl), s), 3.20 (2H, bridge head, br-s), 0.93 (2H, -CH_2-, br-d, J=10.6), 0.78 (2H, -CH_2-, br-d, J=10.6). HRMS (M^+) Calcd. for $C_{26}H_{16}O_3F_6$: 490.1004, Found: 490.0998.

***Anti-exo*-adduct (44e)**: mp 242.0-242.5 ℃ (colorless needles, recrystallized from *n*-hexane). ^{1}H NMR: 7.73 (2H, s), 7.22 (4H, m), 5.19 (2H, olefin, d,d, J=4.8, 2.9), 4.58 (2H, bridge head (dibenzyl), s), 3.05 (2H, bridge head, br-s), 1.64 (2H, -CH_2-, br-d, J=9.9), 1.20 (2H, -CH_2-, br-d, J=9.9). Anal. Calcd. for $C_{26}H_{16}O_3F_6$: C, 63.68; H, 3.29. Found: C, 63.50; H, 3.16.

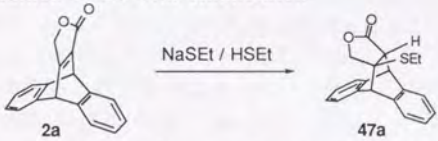
***Syn-exo*-adduct (45e)**: mp >300 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.65 (2H, s), 7.30 (2H, d,d, J=5.5, 3.3), 7.21 (2H, d,d, J=5.5, 3.3), 5.23 (2H, olefin, d,d, J=4.4, 2.9), 4.60 (2H, bridge head (dibenzyl), s), 3.07 (2H, bridge head, br-s), 1.65 (2H, -CH_2-, br-d, J=9.5), 1.19 (2H, -CH_2-, br-d, J=10.3). HRMS (M^+) Calcd. for $C_{26}H_{16}O_3F_6$: 490.1004, Found: 490.1009.

1,4-Conjugate addition to the α,β-unsaturated lactones.

1,4-Conjugate additions were carried out under the similar conditions as unsubstituted furanone derivative **2a**. The adducts were separated as a mixture (in the case of the reactions of nitro substituted compounds) by flash column chromatography, and the stereoisomers were

separated by preparative thin layer chromatography. The ratios of the diastereomers were determined from signal integration values in the ^{1}H NMR spectra. The assignments of the ^{1}H NMR signals of pure diastereomers and the structual confirmation were based on NOE measurements.

1,4-Conjugate addition of 2a with ethanethiol.



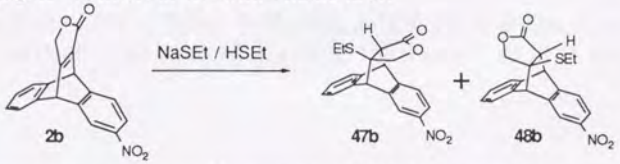
2a 47a

(Method A: in the neat condition or *n*-hexane, carbon tetrachloride, benzene, or ether was used as the solvent.) A mixture of 40.2 mg (0.154 mmol) of **2a**, 3.5 mL (47 mmol, 3.7 equiv.) of thanethiol and 1.7 mg (60 %, 0.043 mmol, 0.28 equiv.) of sodium hydride was stirred at 23 ℃ in a sealed bottle for 75 hrs. Then the volatile solvent and thanethiol were distilled off with an argon flow, and the residue was flash-chromatographed (dichloromethane) to give 41.8 mg (0.130 mmol, 84 %) of the product **47a** (or the product mixture, in the nitro compound case).

(Method B: DMF (*N*,*N*-dimethylformamide) or DMSO (dimethylsulfoxide) was used as the solvent.) The reaction was carried out in the similar method as above, however after the specified time of the reaction, the reaction mixture was poured into ether. The organic layer was washed with dilute aqueous hydrochloric acid, dried over magnesium sulfate, and the solvent was evaporated and then the residue was flash-chromatographed to give the product mixture.

47a: mp 85.5-87.5 ℃ (colorless amorphous). ^{1}H NMR: 7.34 (4H, $H_{1,4,5,8}$, m), 7.18 (4H, $H_{2,3,6,7}$, m), 4.69 (1H, H_{10}, d, J=3.3), 4.45 (1H, H_{13exo}, d, J=9.9), 4.34 (1H, H_9, s), 4.05 (1H, H_{13endo}, d, J=9.9), 2.93 (1H, H_{11}, d, J=3.3), 2.60 (1H, -SCH_2-, d,q, J=11.4, 7.3), 2.48 (1H, -SCH_2-, d,q, J=11.4, 7.3), 1.20 (3H, -CH_3, t, J=7.3). Anal. Calcd. for $C_{20}H_{18}O_2S$: C, 74.50; H, 5.63. Found: C, 74.58; H, 5.51.

1,4-Conjugate addition of 2b with ethanethiol.



2b 47b 48b

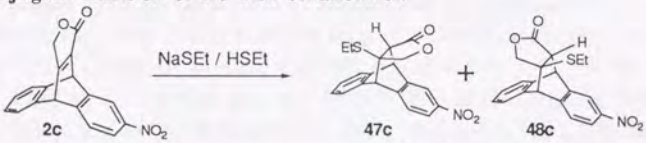
Two diastereomers were separated by preparative TLC (ethyl acetate: *n*-hexane 1:6).

***Anti*-adduct (47b)**: mp 185.0-187.0 ℃ (colorless rods, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.21 (1H, H_1, d, J=2.2), 8.09 (1H, H_3, d,d, J=2.2, 8.1), 7.49 (1H, H_4, d,

J=8.1), 7.38 (2H, $H_{5,8}$, m), 7.25 (2H, $H_{6,7}$, m), 4.83 (1H, H_{10}, d, J=3.3), 4.53 (1H, H_{13exo}, d, J=10.3), 4.50 (1H, H_9, s), 4.07 (1H, H_{13endo}, d, J=9.9), 2.99 (1H, H_{11}, d, J=3.7), 2.63 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 2.50 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 1.22 (3H, $-CH_3$, t, J=7.3). Anal. Calcd. for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81. Found: C, 65.30; H, 4.50; N, 3.51.

***Syn*-adduct (48b)**: mp 210.0-211.0 ℃ (colorless plates, recrystallized from ethyl acetate/*n*-hexane). The structure was confirmed by X-ray crystallographic analysis. ^1H NMR: 8.19 (1H, H_1, d, J=2.2), 8.11 (1H, H_3, d,d, J=2.2, 8.4), 7.50 (1H, H_4, d, J=8.1), 7.36 (2H, $H_{5,8}$, m), 7.23 (2H, $H_{6,7}$, m), 4.82 (1H, H_{10}, d, J=3.3), 4.50 (1H, H_{13exo}, d, J=10.3), 4.48 (1H, H_9, s), 4.07 (1H, H_{13endo}, d, J=9.9), 2.89 (1H, H_{11}, d, J=3.7), 2.69 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 2.57 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 1.24 (3H, $-CH_3$, t, J=7.3). Anal. Calcd. for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81. Found: C, 65.44; H, 4.41; N, 3.63.

1,4-Conjugate addition of 2c with ethanethiol.

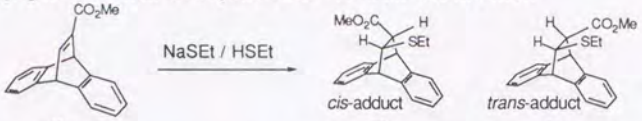


Two diastereomers were separated by preparative TLC (dichloromethane: *n*-hexane 10:16).

***Anti*-adduct (47c)**: mp 223.0-224.5 ℃ (colorless flakes, recrystallized from ethyl acetate/*n*-hexane). ^1H NMR: 8.19 (1H, H_4, d, J=2.2), 8.11 (1H, H_2, d,d, J=2.2, 8.1), 7.49 (1H, H_1, d, J=8.1), 7.38 (2H, $H_{5,8}$, m), 7.24 (2H, $H_{6,7}$, m), 4.84 (1H, H_{10}, d, J=3.7), 4.51 (1H, H_{13exo}, d, J=9.9), 4.48 (1H, H_9, s), 4.02 (1H, H_{13endo}, d, J=9.9), 2.99 (1H, H_{11}, d, J=3.3), 2.61 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 2.48 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 1.21 (3H, $-CH_3$, t, J=7.3). Anal. Calcd. for $C_{20}H_{16}O_4$: C, 74.99; H, 5.03. Found: C, 65.11; H, 4.43; N, 3.88.

***Syn*-adduct (48c)**: mp 237.0 ℃ (colorless needles, recrystallized from ethyl acetate/*n*-hexane). ^1H NMR: 8.21 (1H, H_4, d, J=2.2), 8.10 (1H, H_2, d,d, J=2.2, 8.1), 7.49 (1H, H_1, d, J=8.1), 7.36 (2H, $H_{5,8}$, m), 7.24 (2H, $H_{6,7}$, m), 4.83 (1H, H_{10}, d, J=3.3), 4.49 (1H, H_{13exo}, d, J=9.9), 4.47 (1H, H_9, s), 4.07 (1H, H_{13endo}, d, J=9.9), 2.95 (1H, H_{11}, d, J=3.7), 2.66 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 2.55 (1H, $-SCH_2-$, d,q, J=11.4, 7.3), 1.23 (3H, $-CH_3$, t, J=7.3). Anal. Calcd. for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81. Found: C, 65.55; H, 4.87; N, 3.60.

1,4-Conjugate addition of acyclic ester 49 with ethanethiol.



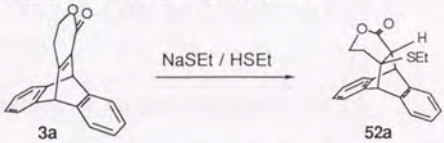
49 50 51

Two diastereomers were separated by flash column chromatography (ether: *n*-hexane 1:10).

***Cis*-adduct (50)**: failed to recrystallization. ^{1}H NMR: 7.33 (2H, $H_{(5,8)/(1,4)}$, m), 7.28 (1H, $H_{1/8}$, d,d, J=1.5, 7.0), 7.21 (1H, $H_{4/5}$, d,d, J=1.8, 6.6), 7.16 (2H, $H_{(6,7)/(2,3)}$, m), 7.12 (1H, $H_{2/7}$, d,t, J=1.5, 7.0), 7.09 (1H, $H_{3/6}$, d,t, J=1.5, 7.0), 4.63 (1H, H_{10}, d, J=2.6), 4.35 (1H, H_9, d, J=2.6), 3.64 (3H, -CO_2CH_3, s), 3.54 (1H, H_{12}, d,d, J=2.6, 5.1), 2.71 (1H, H_{11}, d,d, J=2.6, 4.8), 2.62 (1H, -SCH_2-, d,q, J=12.5, 7.3), 2.60 (1H, -SCH_2-, d,q, J=12.5, 7.3), 1.25 (3H, -CH_3, t, J=7.3).

***Trans*-adduct (51)**: mp 148.0-149.0 ℃ (colorless rods, recrystallized from *n*-hexane). ^{1}H NMR: 7.43 (1H, $H_{4/5}$, br-d, J=7.3), 7.30 (2H, $H_{1,8}$, m), 7.24 (1H, $H_{5/4}$, m), 7.18 (1H, $H_{3/6}$, d,t, J=1.5, 7.3), 7.12 (3H, $H_{2,6/3,7}$, m), 4.47 (1H, H_{10}, d, J=1.8), 4.43 (1H, H_9, d, J=2.9), 3.59 (3H, -CO_2CH_3, s), 3.40 (1H, H_{12}, d,d, J=2.9, 9.9), 3.28 (1H, H_{11}, d,d, J=1.8, 10.3), 2.65 (1H, -SCH_2-, d,q, J=7.3, 12.1), 2.59 (1H, -SCH_2-, d,q, J=7.3, 12.1), 1.21 (3H, -CH_3, t, J=7.3). Anal. Calcd. for $C_{20}H_{20}O_2S$: C, 74.04; H, 6.21. Found: C, 73.94; H, 6.20.

1,4-Conjugate addition of 3a with ethanethiol.

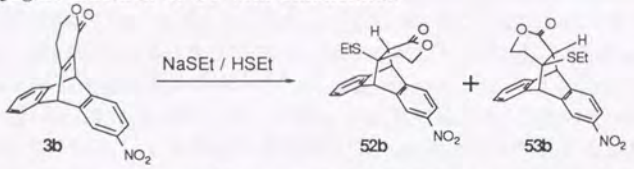


3a 52a

In the case of 6-membered ring lactones, the similar method as the 5-membered ring lactone **2** was used.

Adduct (52a): mp 239.0-239.5 ℃ (colorless prisms, recrystallized from ethyl acetate/*n*-hexane). ^{1}H NMR: 7.34 (3H, m), 7.23 (1H, d,d, J=3.3, 5.1), 7.19 (2H, m), 7.11 (2H, d,d, J=3.3, 5.5), 4.93 (1H, H_{10}, d, J=2.9), 4.72 (1H, H_{14}, d,t, J=1.8, 11.9), 4.30 (1H, H_9, s), 4.01 (1H, H_{14}, d,t, J=11.4, 3.7), 2.57 (1H, -SCH_2-, d,q, J=11.0, 7.3), 2.43 (1H, H_{11}, d, J=2.9), 2.30 (1H, -SCH_2-, d,q, J=11.0, 7.3), 1.88 (1H, H_{13}, br-d, J=14.7), 1.51 (1H, H_{13}, m), 1.13 (3H, -CH_3, t, J=7.3). Anal. Calcd. for $C_{21}H_{20}O_2S$: C, 74.97; H, 5.99. Found: C, 75.08; H, 5.97.

1,4-Conjugate addition of 3b with ethanethiol.

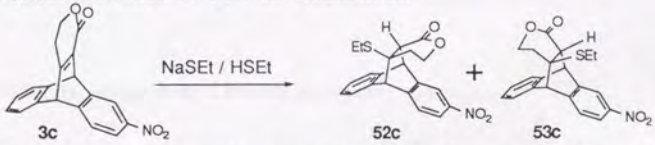


Two diastereomers were separated by preparative TLC (ethyl acetate: *n*-hexane 1:4).

***Anti*-adduct (52b)**: mp 200.0-201.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.13 (1H, H_1, d, J=2.2), 8.05 (1H, H_3, d,d, J=2.2, 8.1), 7.51 (1H, H_4, d, J=8.4), 7.39 (2H, $H_{5,8}$, m), 7.26 (2H, $H_{6,7}$, m), 5.08 (1H, H_{10}, d, J=2.9), 4.78 (1H, H_{14}, br-t, J=11.5), 4.47 (1H, H_9, s), 4.13 (1H, H_{14}, d,d,d, J=2.6, 3.7, 11.0), 2.61 (1H, -SCH_2-, d,q, J=11.0, 7.3), 2.48 (1H, H_{11}, d, J=2.9), 2.34 (1H, -SCH_2-, d,q, J=11.0, 7.3), 2.00 (1H, H_{13}, br-d, J=15.4), 1.47 (1H, H_{13}, d,d,d, J=3.3, 11.7, 15.0), 1.15 (3H, -CH_3, t, J=7.3). Anal. Calcd. for $C_{21}H_{19}NO_4S$: C, 66.12; H, 5.02; N, 3.67. Found: C, 65.84; H, 5.06; N, 3.37.

***Syn*-adduct (53b)**: mp 244.5-245.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.20 (1H, H_1, d, J=2.2), 8.12 (1H, H_3, d,d, J=2.2, 8.1), 7.51 (1H, H_4, d, J=8.4), 7.37 (1H, H_5, d,d, J=2.2, 4.8), 7.28 (1H, H_8, d,d, J=2.2, 4.8), 7.18 (2H, $H_{6,7}$, m), 5.06 (1H, H_{10}, d, J=2.9), 4.75 (1H, H_{14}, br-t, J=11.5), 4.47 (1H, H_9, s), 4.09 (1H, H_{14}, d,t, J=10.6, 3.3), 2.69 (1H, -SCH_2-, d,q, J=11.0, 7.7), 2.49 (1H, -SCH_2-, d,q, J=11.0, 7.7), 2.37 (1H, H_{11}, d, J=2.9), 1.95 (1H, H_{13}, br-d, J=15.4), 1.51 (1H, H_{13}, d,d,d, J=3.3, 11.7, 15.0), 1.18 (3H, -CH_3, t, J=7.7). Anal. Calcd. for $C_{21}H_{19}NO_4S$: C, 66.12; H, 5.02; N, 3.67. Found: C, 65.99; H, 4.87; N, 3.47.

1,4-Conjugate addition of 3c with ethanethiol.

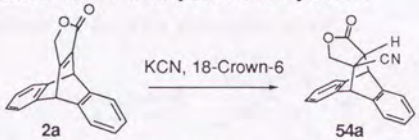


Two diastereomers were separated by preparative TLC (dichloromethane: *n*-hexane 2:3).

***Anti*-adduct (52c)**: ^{1}H NMR: 8.20 (1H, H_4, d, J=2.2), 8.06 (1H, H_2, d,d, J=2.2, 8.1), 7.39 (3H, $H_{1,5,8}$, m), 7.25 (2H, $H_{6,7}$, m), 5.09 (1H, H_{10}, d, J=2.9), 4.78 (1H, H_{14}, t, J=11.0), 4.45 (1H, H_9, s), 4.12 (1H, H_{14}, d,t, J=11.0, 3.3), 2.58 (1H, -SCH_2-, d,q, J=11.0, 7.3), 2.49 (1H, H_{11}, d, J=2.9), 2.31 (1H, -SCH_2-, d,q, J=11.0, 7.3), 1.97 (1H, H_{13}, br-d, J=15.0), 1.43 (1H, H_{13}, m), 1.14 (3H, -CH_3, t, J=7.3). HRMS Calcd. for $C_{21}H_{19}NO_4S$: 381.1035. Found: 381.1034.

***Syn*-adduct (53c)**: mp 241.0-242.0 ℃ (colorless prisms, recrystallized from ethyl acetate/*n*-hexane). ^{1}H NMR: 8.21 (1H, H_4, d, J=2.2), 8.11 (1H, H_2, d,d, J=2.2, 8.1), 7.47 (1H, H_1, d, J=8.1), 7.37 (1H, H_5, d,d, J=3.3, 5.5), 7.26 (1H, H_8, d,d, J=3.3, 5.5), 7.17 (2H, $H_{6,7}$, d,d, J=3.3, 5.5), 5.06 (1H, H_{10}, d, J=2.9), 4.72 (1H, H_{14}, d,t, J=1.5, 11.0), 4.46 (1H, H_9, s), 4.05 (1H, H_{14}, d,t, J=11.0, 3.3), 2.63 (1H, -SCH_2-, d,q, J=11.0, 7.7), 2.45 (1H, -SCH_2-, d,q, J=11.0, 7.3), 2.41 (1H, H_{11}, d, J=2.9), 1.93 (1H, H_{13exo}, br-d, J=15.4), 1.52 (1H, H_{13endo}, m), 1.17 (3H, -CH_3, t, J=7.3). Anal. Calcd. for $C_{21}H_{19}NO_4S$: C, 66.12; H, 5.02; N, 3.67. Found: C, 65.84; H, 4.96; N, 3.48.

1,4-Conjugate addition of 2a with potassium cyanide.

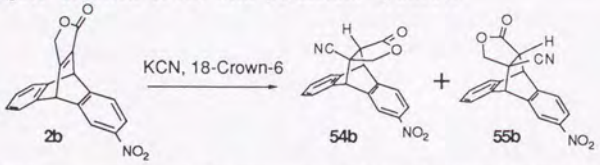


2a **54a**

A mixture of 41.1 mg (0.158 mmol) of **2a**, 27.5 mg (0.104 mmol, 0.66 equiv.) of 18-crown-6, 24.5 mg (0.376 mmol, 2.38 equiv.) of potassium cyanide and 2 mL of dichloromethane (methanol free) was stirred at 20 ℃ for 2.5 hrs. Then the mixture was poured into 50 mL of brine, and extracted with 60 mL of dichloromethane. The organic layer was washed with brine and dried over sodium sulfate, and evaporation of the solvent gave the mixture of 8.5 mg (0.0296 mmol, 19 %) of the adduct **54a** and 25.1 mg (0.0964 mmol, 61 %) of the substrate **2a**.

54a: mp 111 ℃ (colorless powder, recrystallized from *n*-hexane). ^{1}H NMR: 7.47 (1H, d,d, J=3.3, 5.5), 7.43-7.36 (3H, m), 7.28-7.24 (4H, m), 4.80 (1H, H_{10}, d, J=3.7), 4.57 (1H, H_{13exo}, d, J=10.3), 4.56 (1H, H_9, s), 4.00 (1H, H_{13endo}, d, J=9.9), 3.49 (1H, H_{11}, d, J=3.7). Anal. Calcd. for $C_{19}H_{13}NO_2 \cdot 1/8H_2O$: C, 78.81; H, 4.61; N, 4.84. Found: C, 78.71; H, 4.64; N, 4.80.

1,4-Conjugate addition of 2b with potassium cyanide.



2b **54b** **55b**

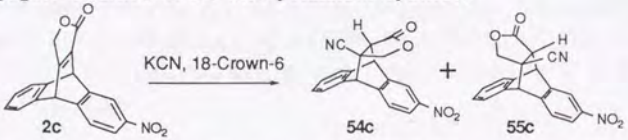
Two diastereomers were separated by preparative TLC (ethyl acetate: benzene 1:15).

***Anti*-adduct (54b)**: mp 201.0-202.5 ℃ (colorless needles, recrystallized from ethyl acetate/*n*-hexane). ^{1}H NMR: 8.29 (1H, H_1, d, J=2.2), 8.18 (1H, H_3, d,d, J=2.2, 8.4), 7.55 (1H, H_4, d, J=8.1), 7.52 (1H, H_8, m), 7.46 (1H, H_5, m), 7.33 (2H, $H_{6,7}$, m), 4.94 (1H, H_{10}, d, J=3.7),

4.71 (1H, H_9, s), 4.64 (1H, H_{13exo}, d, J=10.3), 4.06 (1H, H_{13endo}, d, J=10.3), 3.58 (1H, H_{11}, d, J=3.7). Anal. Calcd. for $C_{19}H_{12}N_2O_4$: C, 68.67; H, 3.64; N, 8.43. Found: C, 68.37; H, 3.56; N, 8.61.

***Syn*-adduct (55b)**: mp 244.0-245.5 ℃ (colorless prisms, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.35 (1H, H_1, d, J=1.8), 8.20 (1H, H_3, d,d, J=2.2, 8.1), 7.61 (1H, H_4, d, J=8.4), 7.45 (1H, $H_{8/5}$, m), 7.41 (1H, $H_{5/8}$, m), 7.32 (2H, $H_{6,7}$, m), 4.94 (1H, H_{10}, d, J=3.7), 4.71 (1H, H_9, s), 4.61 (1H, H_{13exo}, d, J=9.9), 4.04 (1H, H_{13endo}, d, J=10.3), 3.52 (1H, H_{11}, d, J=3.7). Anal. Calcd. for $C_{19}H_{12}N_2O_4$: C, 68.67; H, 3.64; N, 8.43. Found: C, 68.38; H, 3.57; N, 8.70.

1,4-Conjugate addition of 2c with potassium cyanide.

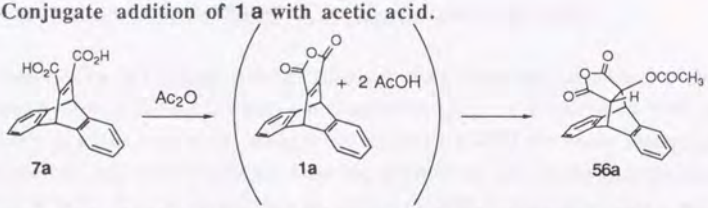


Two diastereomers were separated by preparative TLC (ethyl acetate: benzene 1:15).

***Anti*-adduct (54c)**: decomposes gradually (>150 ℃) (colorless powder, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.23 (1H, H_4, d, J=2.2), 8.18 (1H, H_2, d,d, J=2.2, 8.1), 7.59 (1H, H_1, d, J=8.1), 7.51 (1H, H_8, m), 7.47 (1H, H_5, m), 7.32 (2H, $H_{6,7}$, m), 4.95 (1H, H_{10}, d, J=3.7), 4.72 (1H, H_9, m), 4.63 (1H, H_{13exo}, d, J=10.3), 4.00 (1H, H_{13endo}, d, J=10.3), 3.58 (1H, H_{11}, d, J=3.7). HRMS Calcd. for $C_{19}H_{12}N_2O_4$: 332.0797. Found: 332.0799.

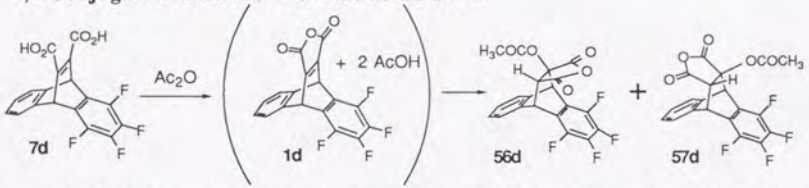
***Syn*-adduct (55c)**: dp 240.0 ℃ (colorless needles, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 8.31 (1H, H_4, d, J=2.2), 8.20 (1H, H_2, d,d, J=2.2, 8.1), 7.65 (1H, H_1, d, J=8.1), 7.43 (2H, $H_{5,8}$, m), 7.32 (2H, $H_{6,7}$, m), 4.95 (1H, H_{10}, d, J=3.7), 4.70 (1H, H_8, s), 4.60 (1H, H_{13exo}, d, J=9.9), 4.04 (1H, H_{13endo}, d, J=9.9), 3.54 (1H, H_{11}, d, J=3.7). Anal. Calcd. for $C_{19}H_{12}N_2O_4 \cdot 1/2H_2O$: C, 66.89; H, 3.84; N, 8.21. Found: C, 67.05; H, 3.94; N, 8.14.

1,4-Conjugate addition of 1a with acetic acid.



A mixture of the diacid **7a** (981 mg, 3.36 mmol) and 10 mL of acetic anhydride was refluxed for 1.2 hrs. Unreacted acetic anhydride was removed under reduced pressure, and the residue was flash-chromatographed (ethyl acetate: *n*-hexane 1:5) to give 470 mg (51 %) of the adduct **56a** as yellow powder, mp 175.0-177.5 ℃ (pale yellow flakes, recrystallized from ethyl acetate/ *n*-hexane). ^{1}H NMR: 7.48 (1H, d,d, J=5.5, 3.3), 7.42 (1H, d,d, J=5.5, 3.3), 7.34 (2H, $H_{(1,4)/(5,8)}$,m), 7.27-7.21 (4H, $H_{2,3,6,7}$, m), 4.82 (1H, H_9, d, J=4.0), 4.73 (1H, H_{10}, s), 3.33 (1H, H_{12}, d, J=3.7), 2.01 (3H, -OCOCH$_3$, s). Anal. Calcd. for $C_{20}H_{14}O_5$: C, 71.85; H, 4.22. Found: C, 71.59; H, 4.39.

1,4-Conjugate addition of 1a with acetic acid.



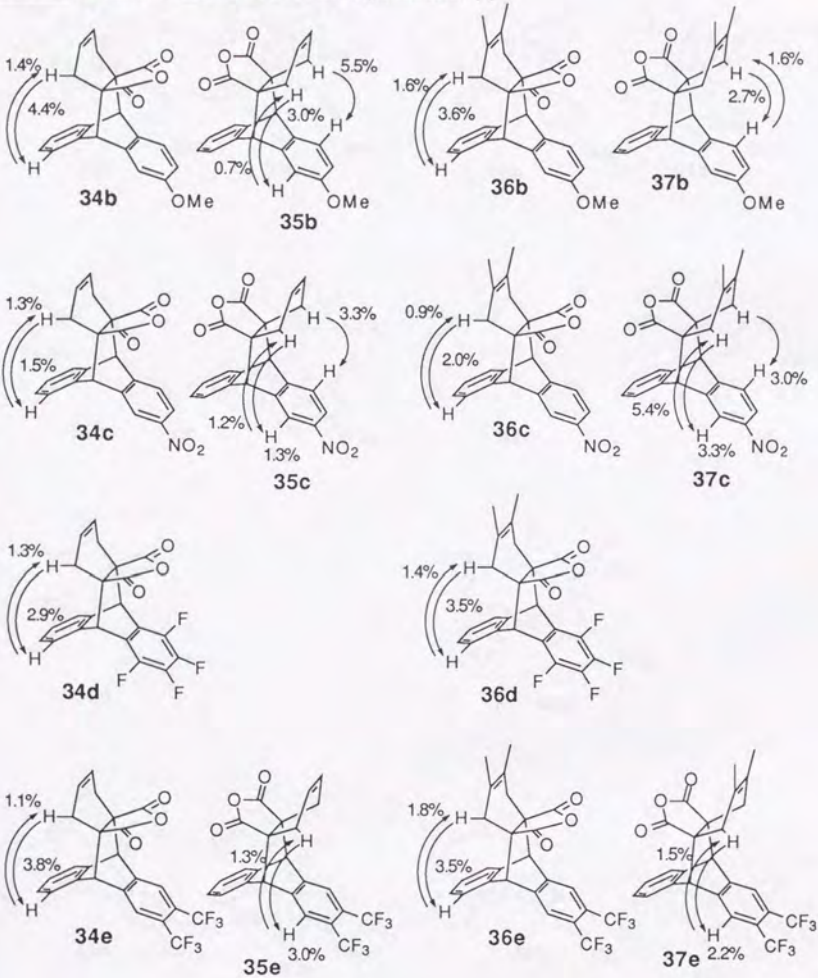
A mixture of the diacid **7d** (302 mg, 0.829 mmol) and 10 mL of acetic anhydride was heated at 75 ℃ for 11 hrs. Unreacted acetic anhydride was removed under reduced pressure, and the residue was dissolved in dichloromethane (methanol-free, 200 mL), washed with saturated aqueous sodium bicarbonate and brine, and was dried over sodium sulfate. The solvent was evaporated and the residue was washed with *n*-hexane to give 231 mg of a mixture of the adduct **56d**, **57d** and the anhydride **1d**. The integration values of ^{1}H-NMR indicate **1d** as 41.5 % and the adduct as 33.2 % yield, respectively. ^{1}H-NMR: 2.089 (3H, **57d**, -OCOCH$_3$, s), 2.024 (3H, **56d**, -OCOCH$_3$, s), and other peaks of the mixture.

Measurements of relative rates of the Diels-Alder reactions

A mixture of **1a** (4.1-5.9 mg, 0.015-0.022 mmol) and a substituted anhydride (**1x**, one of the anhydrides **x=b-e**, 0.014-0.022 mmol) was dissolved in 0.5 mL of CD_2Cl_2 in an NMR tube. To this solution is added 3.4-4.9 mg (0.041-0.060 mmol) of DMBD at ambient temperature. The sample tube was well shaken and loaded into the spectrometer, and all the measurements were conducted at 23 ℃. After 30 minutes from the addition of DMBD, signal accumulation was started (96 sec-duration for accumulation, and 1704 sec-interval of accumulation).

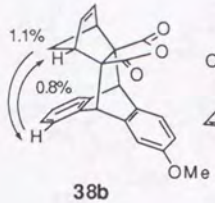
Signal integration values of the starting materials (**1a** and **1x**) and the products (**36a**, **36x** and **37x**) were obtained in each measurement ^{1}H NMR, and thus the relative values of $[S_H]$, $[S_X]$, $[P_H]$ and $[P_X]$ are given for **eq. 1**. Therefore, $\ln(([S_X]+[P_X])/[S_X])$ can be plotted against $\ln(([S_H]+[P_H])/[S_H])$ to give straight lines with regression more than 0.9995, and then the relative value of the second-order rate constants (k_X/k_H) were obtained from the slope of the lines. Then the k_X/k_H is distributed into the values of *anti*- and *syn*-side of the dienophile in proportion to the *anti/syn* product ratio.

NOE measurements in ^{1}H-NMR spectroscopy.

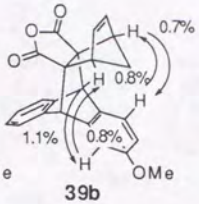


^{1}H NOE measurements:

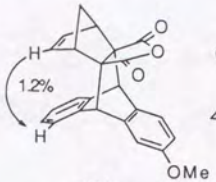
Products of Diels-Alder reactions with BD and DMBD



38b



39b



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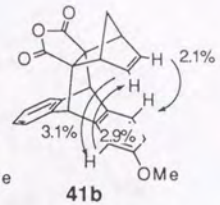

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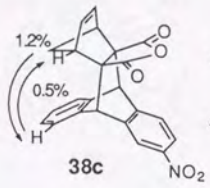
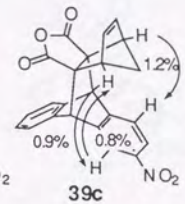


38c



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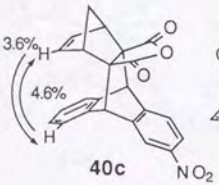

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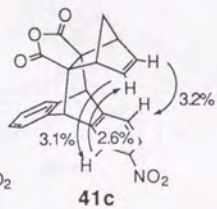
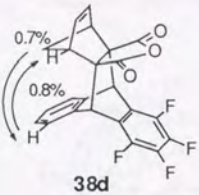


41c



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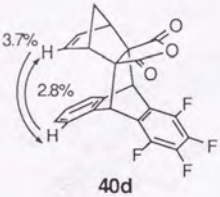

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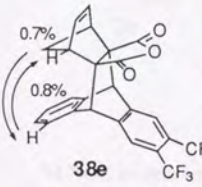

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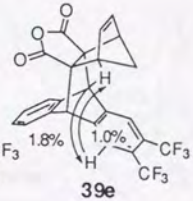

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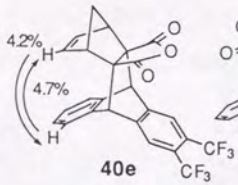

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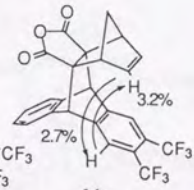
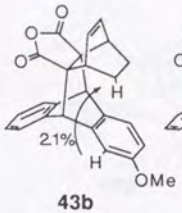


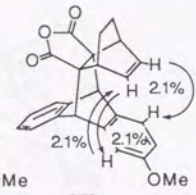
41e

^{1}H NOE measurements:

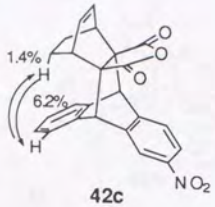
Products of Diels-Alder reactions with CPD



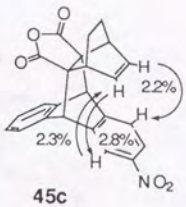
43b



45b



42c



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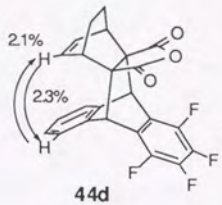
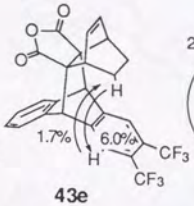
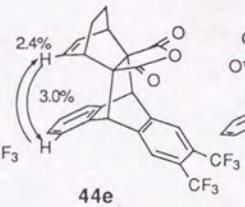


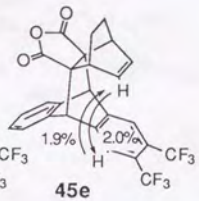
44d



43e

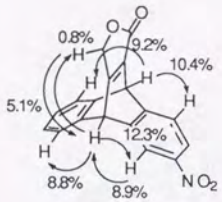


44e

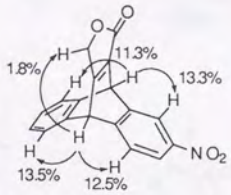


45e

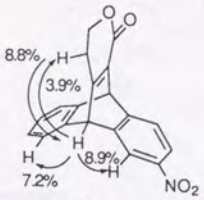
^{1}H NOE measurements:
Products of Diels-Alder reactions with CHD



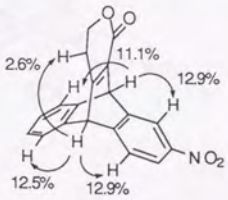
2b



2c

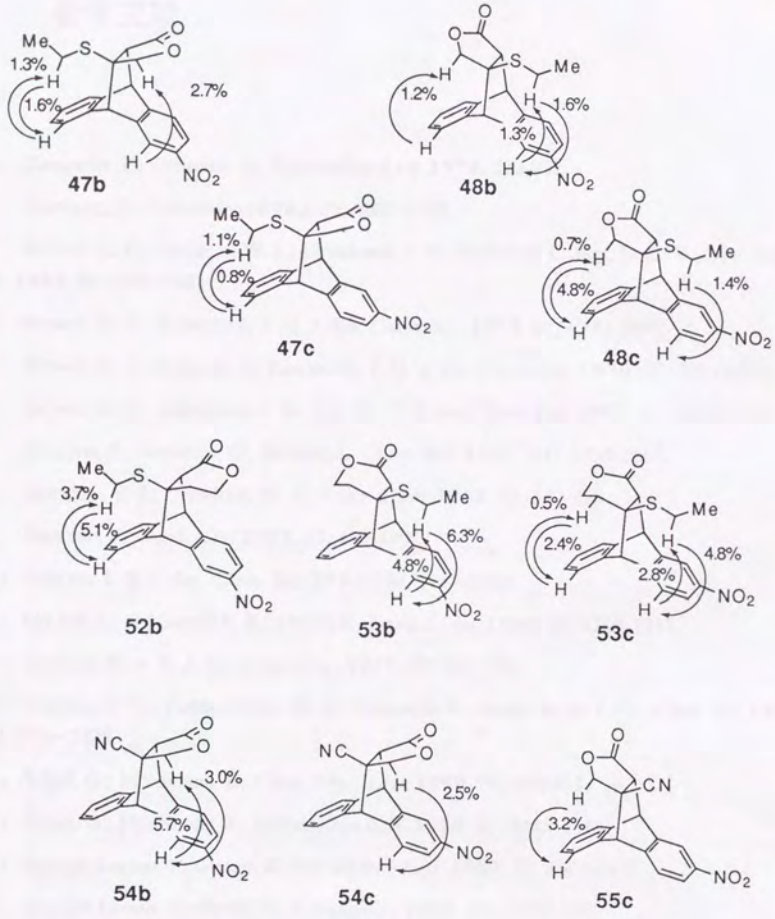


3b



3c

^{1}H NOE measurements:
Nitro substituted lactones



^{1}H NOE measurements:

Products of 1,4-conjugate additions

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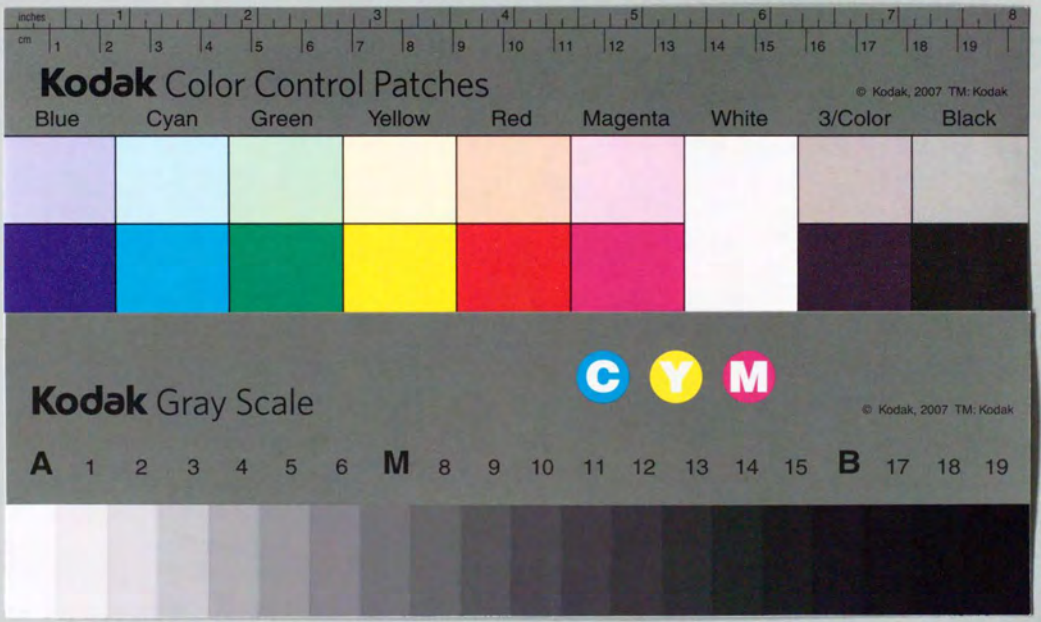
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