THEORY AND MODELING OF TRANSITION STRUCTURES OF ORGANIC REACTIONS

Apply modern techniques of ab initio quantum theory to characterize geometries and electronic structures of transition structures of organic reactions.

To understand rates and stereoselectivities.

To allow qualititative predictions.

To develop parameters for empirical calculations of (1) large molecular systems and (2) reactions in solution.

To design systems which bind selectively to the transition states of reactions, that is, to design catalysts.

Pericyclic Reaction Transition Structures

Characterization of hydrocarbon transition structures -
shapes
energies
charge distributions
substituent effects on energies, geometries

Hetero-Diels-Alder reactions

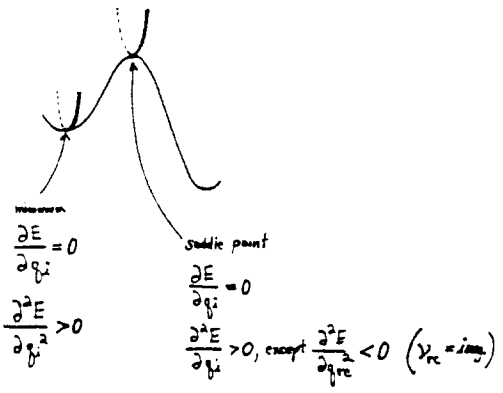
Intramolecular Diels-Alder reactions

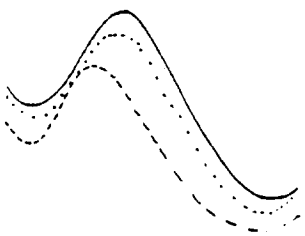
Radical and Photochemical Reactions

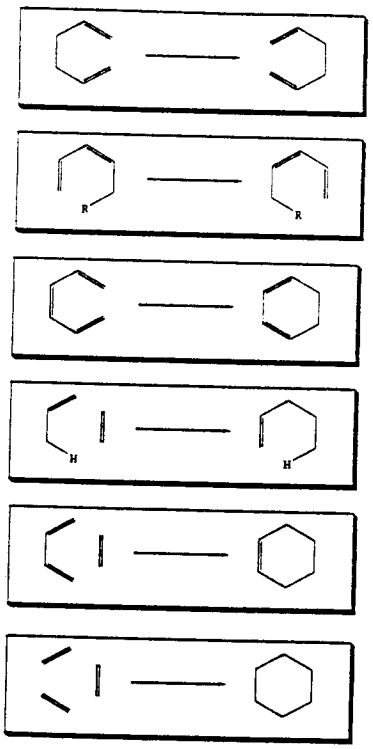
Alkyl radical cyclization reactions

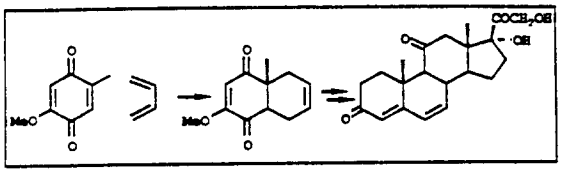
α-Acylalkyl radical cyclization reactions

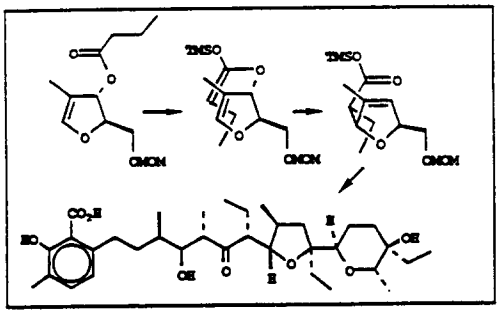
Enone photocycloadditions

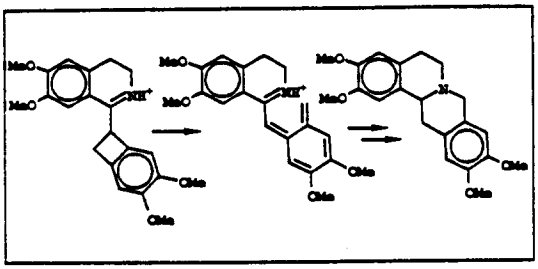


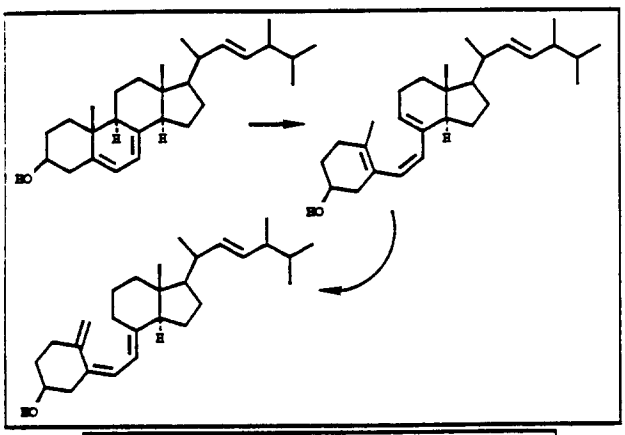


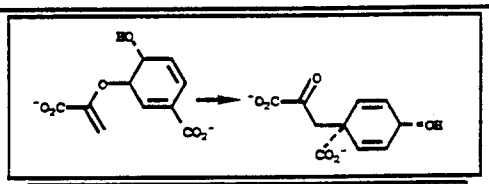


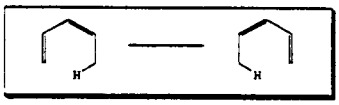


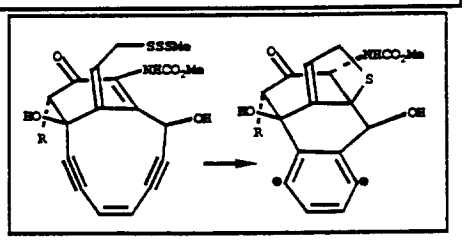


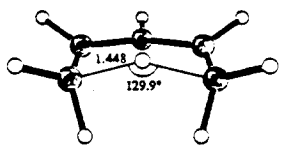








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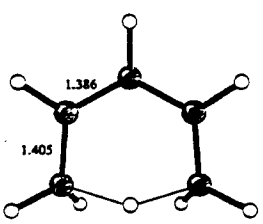
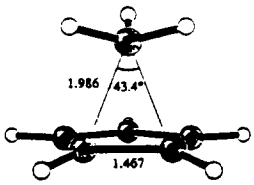
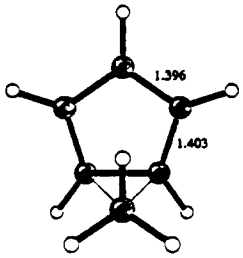
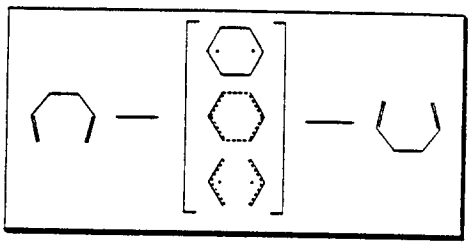
129.9°

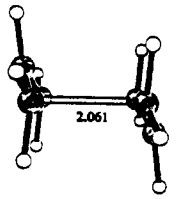

1.386
1.405

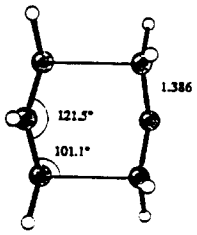

CH₃
CH₃


1.986
43.4°
1.467

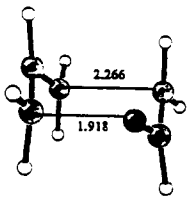

1.396
1.403

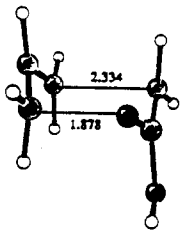


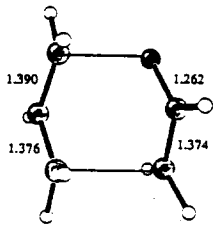

2.061

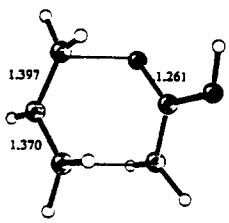

1.386
121.5°
101.1°

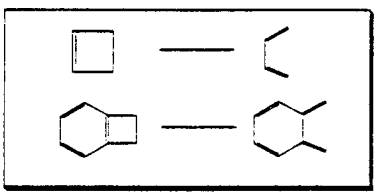

HO
HO

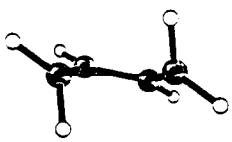

2.266
1.918

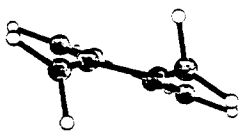

2.334
1.878

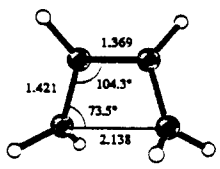

1.390
1.262
1.376
1.374

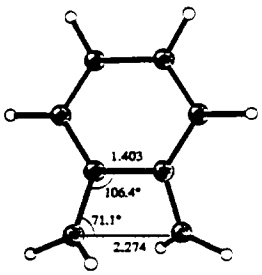

1.397
1.261
1.370

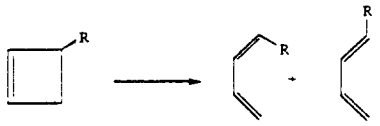






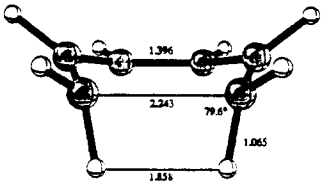

1.369
1.421
104.3°
73.5°
2.138


1.403
106.4°
71.1°
2.274



R	$E_{(in)}$-$E_{(out)}$
$-NH_2$	19.5 (17.5)
-OH	18.0 (17.2)
-F	17.3 (16.9)
$-CH_3$	6.6 (6.4)
$-NH_3^+$	7.8
-CCH	7.2
$-CO_2^-$	5.5
-H	0.0 (0.0)
-CN	4.6 (4.3)
$-CO_2H$	1.2 (2.3)
$-NO_2$	6.8 (7.4)
-CHO	-4.6 (-4.7)
$-CO_2H_2^+$	-6.3
-NO	-2.4 (-2.6)
$-BH_2$	-18.6 (-18.2)

3-21G (6-31G*//3-21G)
David C. Spellmeyer, E. Adam Kallel, and Andrzej Buda



C_{sp^3} C_{sp^3} C_{ts} H_{ax} = 57.9°
C_{sp^3} C_{sp^3} C_{ts} H_{eq} = -159.9°
C_{sp^3} C_{sp^3} C_{sp^3} C_{ts} = 33.2°
C_{sp^3} C_{sp^3} C_{sp^3} C_{sp^3} = 0.0°
H C_{sp^3} C_{sp^3} C_{sp^3} = -167.4°

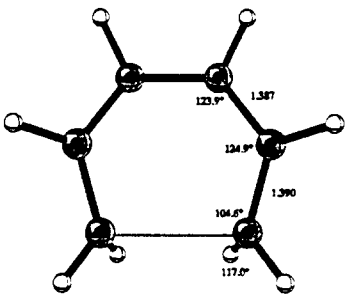
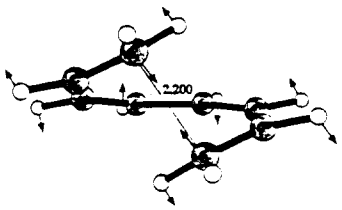
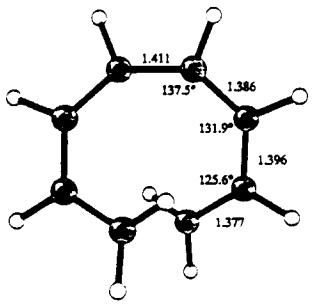


Figure 4: The 6-31G(d) disrotatory transition structure of cis-1,3,5-hexatriene to cyclohexadiene.



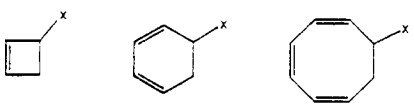
note no twist all in cyclic C skeleton



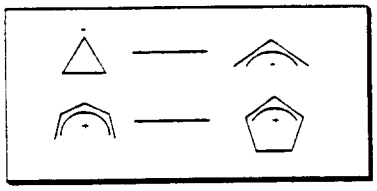
11.5 kcal/mol
$\Delta H^{\ddagger}$ = 15.1 kcal/mol Huisgen, *et al. Tetrahedron Lett.* 1969, *19*, 1461.

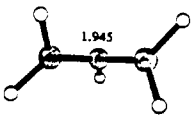
Figure 5: RHF/6-31G* conrotatory transition structure. (C_2)

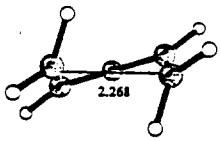
E_a(in) - E_a(out) MP2/6-31G*//6-31G*

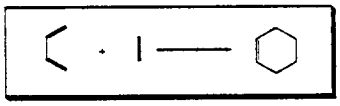


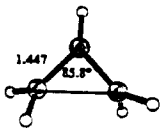
F	15.9	4.7	0.3
CH_3	5.1	3.9	-0.1
CHO	-6.1	0.0	0.0

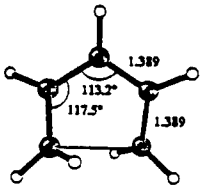


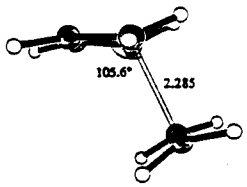

1.945

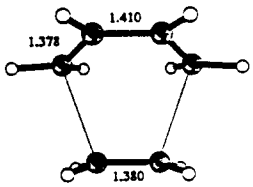

2.268

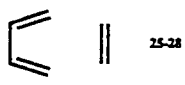


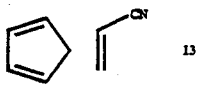

1.447
85.8°


1.389
113.2°
117.5°
1.389

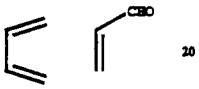

105.6°
2.285

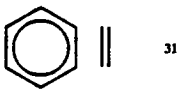

1.410
1.378
1.380


25-28


CN
13


24


CHO
20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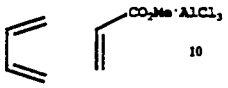
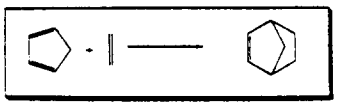
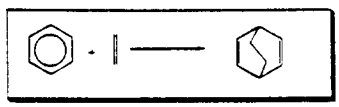
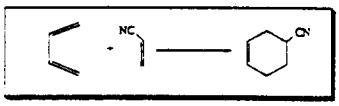
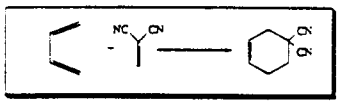
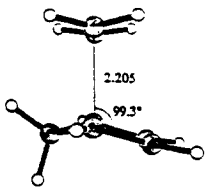

CO2Me·AlCl3
10

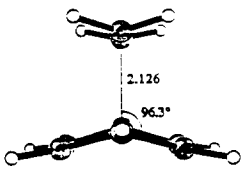


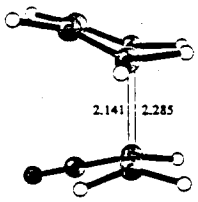


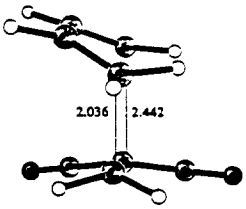

NC
CN

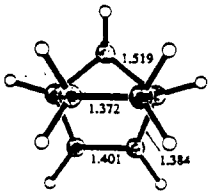

NC
CN
CN

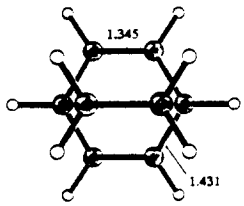

2.205
99.3°

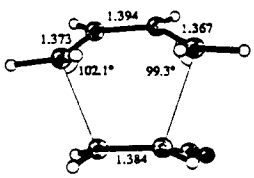

2.126
96.3°

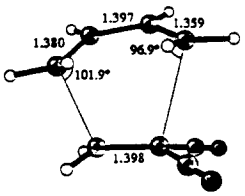

2.141
2.285

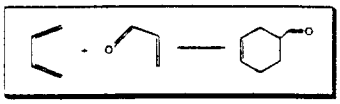

2.036
2.442

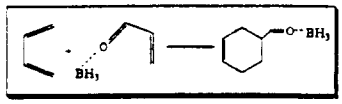

1.519
1.372
1.401
1.384

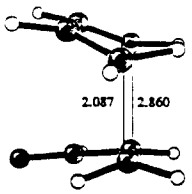

1.345
1.431

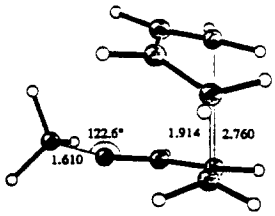

1.394
1.367
1.373
102.1°
99.3°
1.384

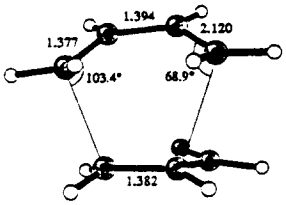

1.397
1.359
1.380
96.9°
101.9°
1.398

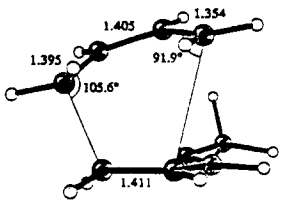


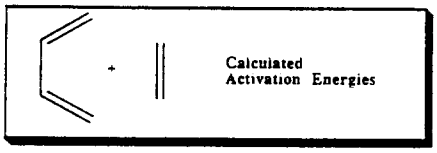








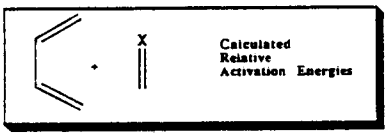




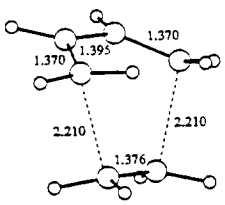
Theory Level	E_a
experimental	24-27
ST0-3G	36.0
3-21G	35.9
6-31G*//3-21G	45.1
6-31G*	45.0
MP2/6-31G*	17.6
CAS(4/4)SCF/4-31G	33.3

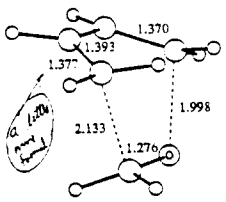
Beck
Bernardi
Robb
Schlegel

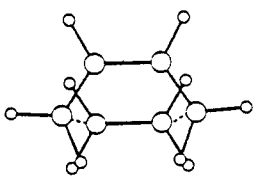
Houk
Wiest

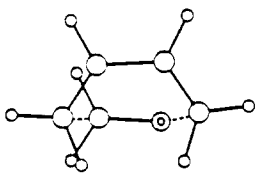


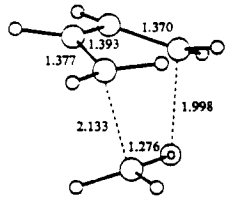
Dienophile		E_a(rel) 6-31G*//3-21G	E_a(rel) MP2
		0	0
		+4	+3
		-17	-14
	endo-H	+1	-2
	exo-H	+5	+3
	exo-B	-14	-9
	cyclic	-37	
	acyclic	-40	

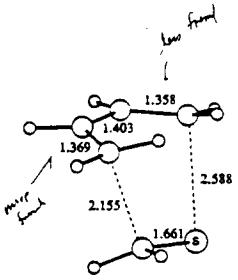


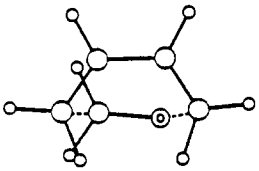


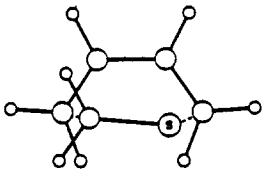


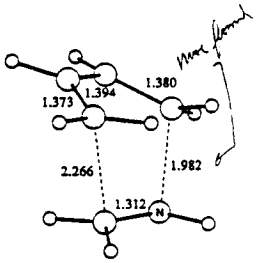


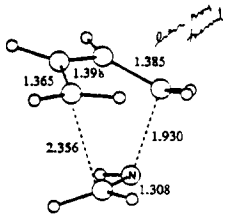

1.370
1.393
1.377
1.998
2.133
1.276
O

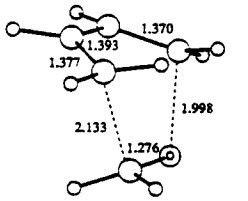

1.358
1.403
1.369
2.588
2.155
1.661
B

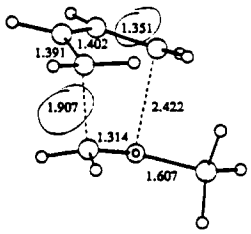

O

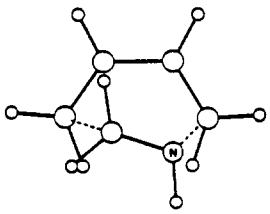

B

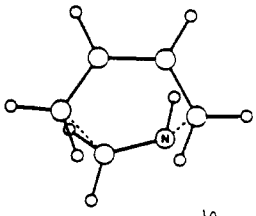

1.380
1.373
1.394
2.266
1.982
1.312
N


1.385
1.365
1.398
2.356
1.930
N
1.308


1.370
1.393
1.377
1.998
2.133
1.276
O


1.351
1.391
1.402
1.907
2.422
1.314
O
1.607


N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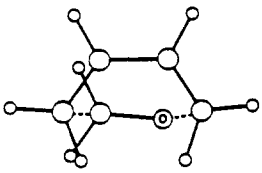
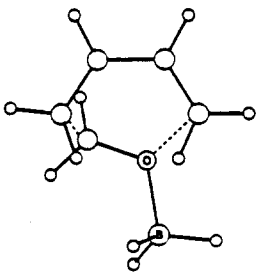
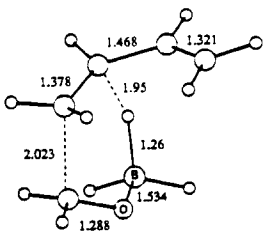
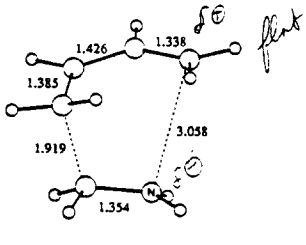
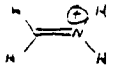
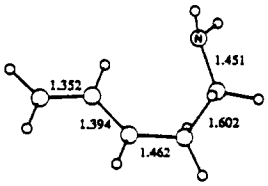

O

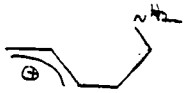

O
B

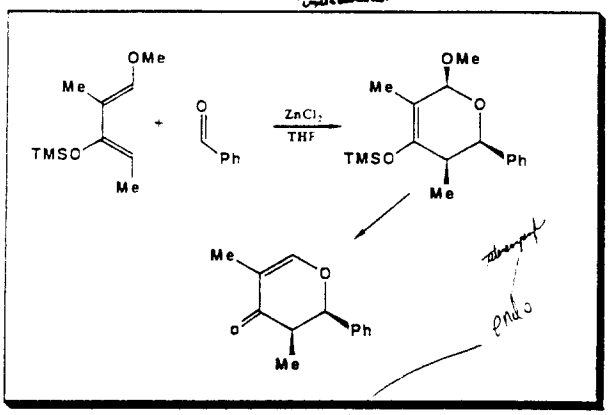

1.468
1.321
1.378
1.95
1.26
2.023
B
1.534
O
1.288

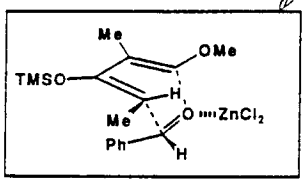

1.426
1.338
1.385
3.058
1.919
1.354
N

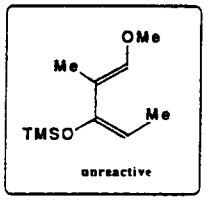

H
H
H
H


N
1.451
1.352
1.394
1.602
1.462

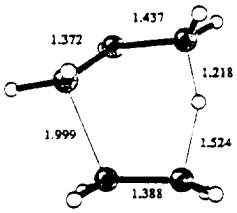

H2

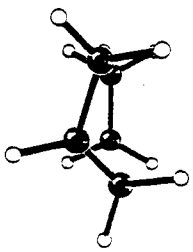


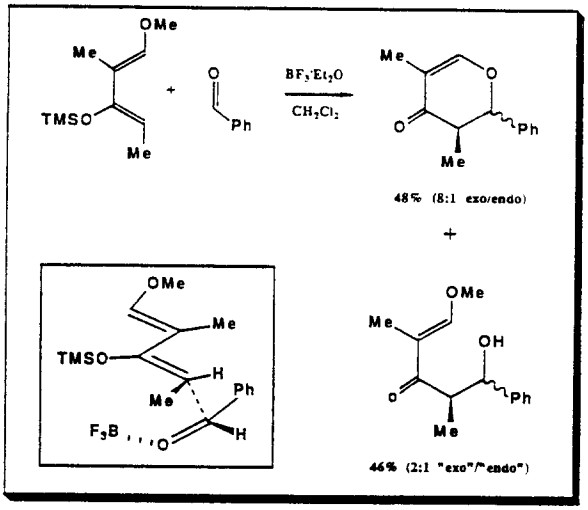




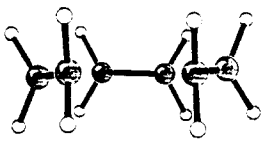
Danishefsky and Larson, 1982





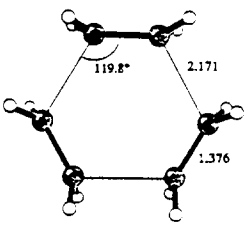


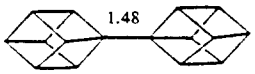
Danishefsky and Larson, 1982

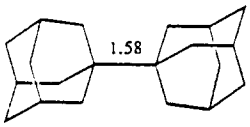


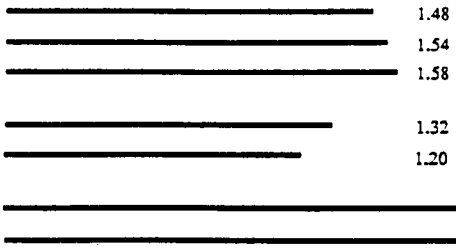
BOND LENGTHS IN TRANSITION STRUCTURES
OF PERICYCLIC REACTIONS

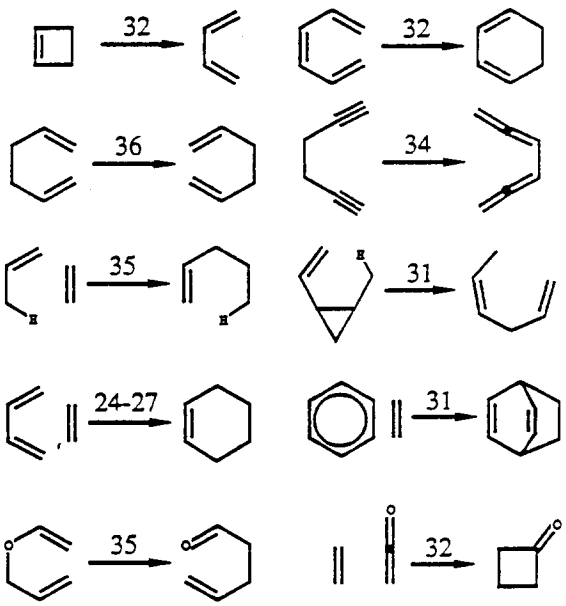
C--------C	2.19 - 2.26Å
C-------H	1.3-1.5Å
C=========C	1.36-1.42Å
C=========C	1.25-1.29Å
C H C	2.8-2.9Å

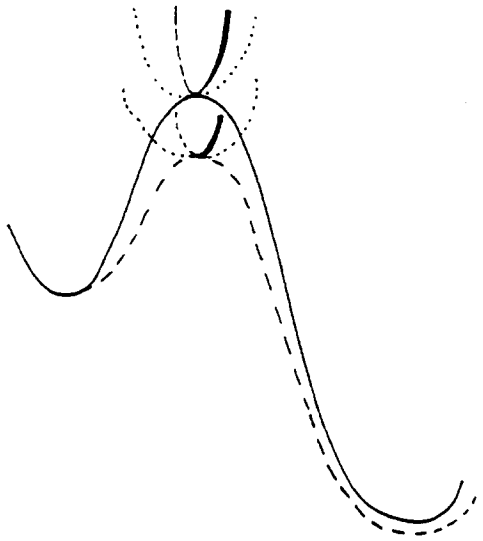












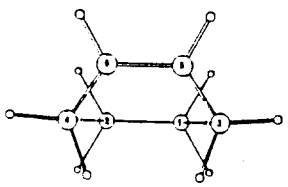
$$E_{total} = \sum_{bonds} \frac{1}{2} k_s (r - r_0)^2 (1 + CS (r - r_0)) + \sum_{angles} \frac{1}{2} k_b (\Theta - \Theta_0)^2 (1 + SF (\Theta - \Theta_0)^4$$

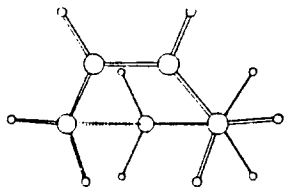
$$+ \sum_{stretch\ bend} \frac{1}{2} k_{sb} \left[(r_1 - r_0 (1)) + (r_2 - r_0 (2)) \right] (\Theta - \Theta_0)$$

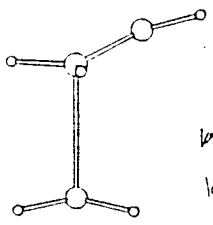
$$+ \sum_{dihedrals} \frac{V_1}{2} (1 + \cos \omega) + \frac{V_2}{2} (1 - \cos 2\omega) + \frac{V_3}{2} (1 + \cos 3\omega)$$

$$+ \sum_{\substack{VDW \\ r/r_v \le 3.311}} (\varepsilon_i \varepsilon_j)^{1/2} \left[2.90 \times 10^5 \, e^{-12.50 r / r_v} - 2.25 \left(\frac{r_v}{r} \right)^6 \right] + \sum_{\substack{VDW \\ r/r_v > 3.311}} (\varepsilon_i \varepsilon_j)^{1/2} 336.176 \left[\frac{r_v}{r} \right]$$

$$+ \sum_{dipole} \left[\frac{\mu_i \mu_j}{D r_{ij}^3} \right] (\cos \chi - 3 \cos \alpha_i \cos \alpha_j)$$







$C_1 \cdots C_3$ 2.21 Å; k = 1.0 md/Å

$C_2 \cdots C_4$ 2.21 Å; k = 1.0 md/Å

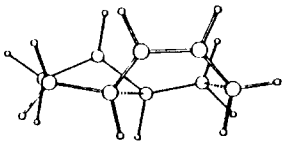
$C_4\text{-}C_8\ C_5\text{-}C_3$ $V_1 = V_3 = 0.0$; $V_2 = 15.0$ kcal/mol

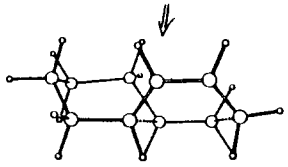
$H(C)\ C_8\ C_5\ H(C)$ $V_1 = V_3 = 0.0$; $V_2 = 15.0$ kcal/mol

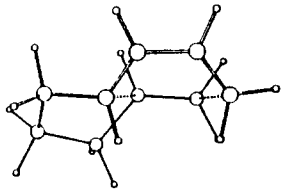
$H(C)\text{-}C_8\text{-}C_4 \cdots C_2$ $V_1 = V_3 = 0.0$; $V_2 = -7.5$ kcal/mol

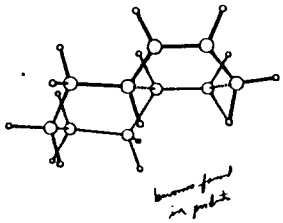
$H(C)\text{-}C_5\text{-}C_3 \cdots C_1$ $V_1 = V_3 = 0.0$; $V_2 = -7.5$ kcal/mol

$C_4 \cdots C_2\text{-}C_1\text{-}H(C)$ $V_1 = V_3 = 0.0$; $V_2 = -10.0$ kcal/mol





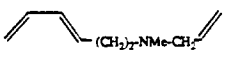




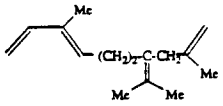
NONATRIENE
t / c = 26:74 (30:70)

DECATRIENE
t / c = 55:45 (48:52)

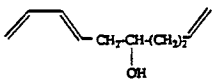
(613 K)



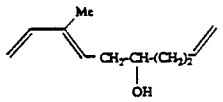
t / c = 55:45 (48:52)



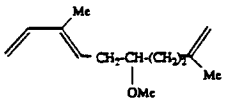
t / c = 92:8 (>95:5)



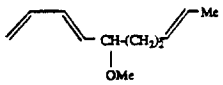
t / c = 60:40 (55:45)



t / c = 89:11 (>95:5)

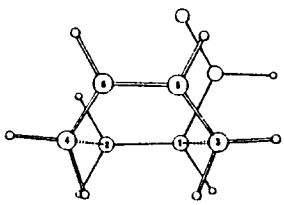


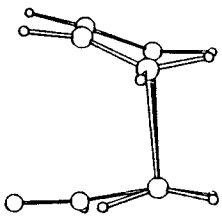
t / c = 90:10 (>95:5; OTHP, OTBDMS)

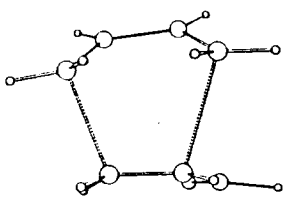


t / c = 26:74 (33:67; OTMS)

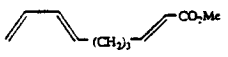
(413 - 518 K)



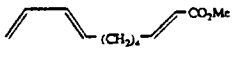




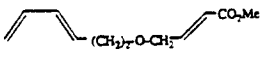
C_1—C_3	2.35 Å; k = 0.5 md/Å
C_2—C_4	2.07 Å; k = 1.5 md/Å
C.S. term	-1.0
$k_{stretching\text{-}bending}$	0.0 md/rad
C_4-C_6-C_5-C_3	$V_1 = V_3 = 0.0$; $V_2 = 15.0$ kcal/mol
H(C)-C_6-C_5-H(C)	$V_1 = V_3 = 0.0$; $V_2 = 15.0$ kcal/mol
H(C)-C_6=C_4—C_2	$V_1 = V_3 = 0.0$; $V_2 = -7.5$ kcal/mol
H(C)-C_5=C_3—C_1	$V_1 = V_3 = 0.0$; $V_2 = -7.5$ kcal/mol
C_4—C_2-C_1-H(C)	$V_1 = V_3 = 0.0$; $V_2 = -10.0$ kcal/mol
C_2=C_1-C=O	$V_1 = V_3 = 0.0$; $V_2 = 2.0$ kcal/mol
C_4—C_2-H(C)	0.0 md Å/rad^2
C_2—C_4-H(C)	0.0 md Å/rad^2



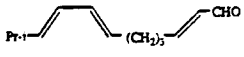
t / c = 64:36 (60:40)



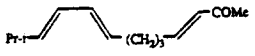
t / c = 60:40 (51:49)



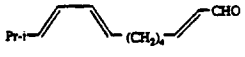
t / c = 62:38 (60:40)



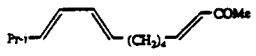
t / c = 82:18 (89:11)



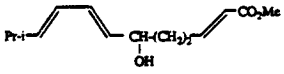
t / c = 77:23 (85:15)



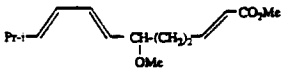
t / c = 77:23 (75:25)



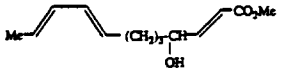
t / c = 73:27 (67:33)



t / c = 72:28 (70:30)

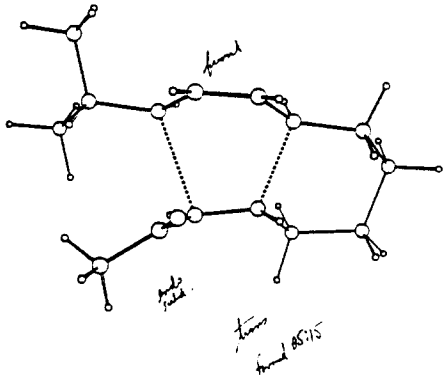


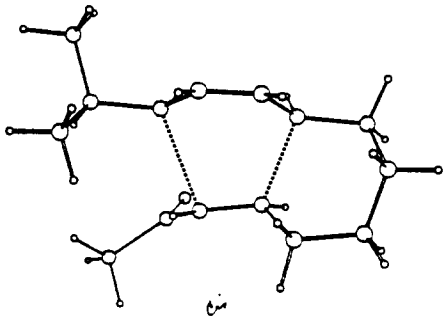
t / c = 75:25 (83:17; OBn)

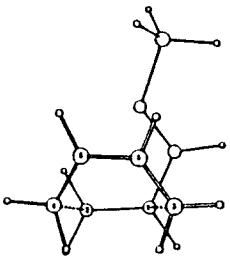


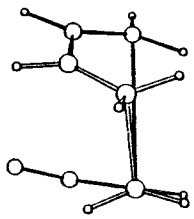
t / c = 60:40 (53:47)

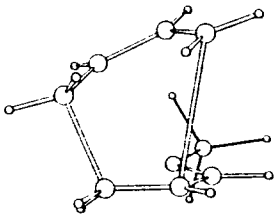
(413 - 443 K)





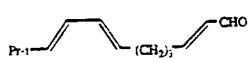




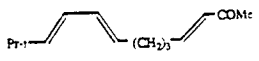


C_1—C_3	2.96 Å; k = 0.3 md/Å
C_2—C_4	1.93 Å; k = 1.7 md/Å
C.S. term	-1.0
$k_{stretching\text{-}bending}$	0.0 md/rad
C=O	μ = 4.0 D
C_4=C_6	μ = 1.5 D
C_4-C_6-C_5=C_3	$V_1 = V_3 = 0.0$; $V_2 = 15.0$ kcal/mol
H(C)-C_6-C_5-H(C)	$V_1 = V_3 = 0.0$; $V_2 = 15.0$ kcal/mol
H(C)-C_6-C_4—C_2	$V_1 = V_3 = 0.0$; $V_2 = -7.5$ kcal/mol
H(C)-C_5=C_3—C_1	$V_1 = V_2 = 0.0$; $V_3 = -7.5$ kcal/mol
C_4—C_2-C_1-H(C)	$V_1 = V_3 = 0.0$; $V_2 = -10.0$ kcal/mol
C_2=C_1-C=O	$V_1 = V_3 = 0.0$; $V_2 = 2.0$ kcal/mol
C_4—C_2-H(C)	0.0 md Å/rad²
C…C-H(C)	0.0 md Å/rad²

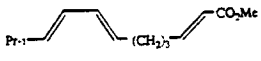
Catalyst



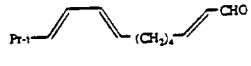
t / c = 99.6:0.4 (>99:1)



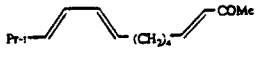
t / c = 99:1 (>99:1)



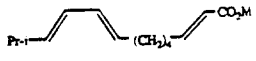
t / c = 93:7 (>99:1)



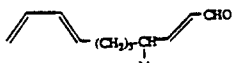
t / c = 99.6:0.4 (>99:1)



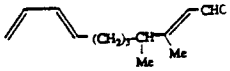
t / c = 99.6:0.4 (>99:1)



t / c = 92:8 (88:12)

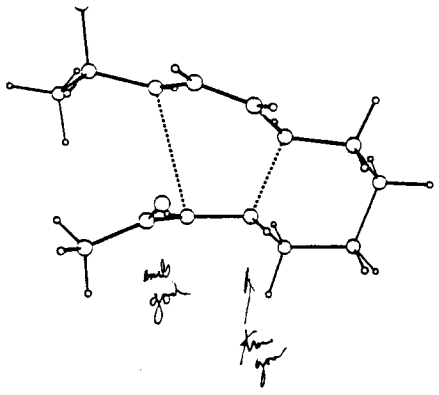


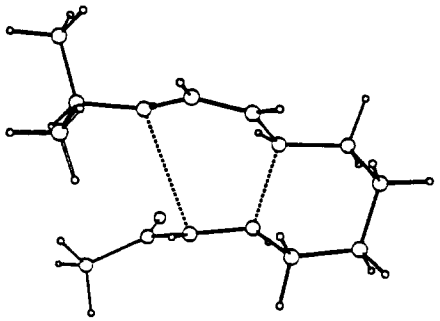
t / c = 98:2 (>95:5)

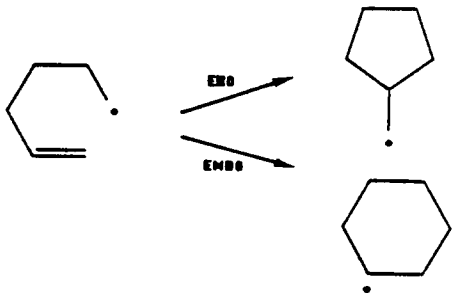


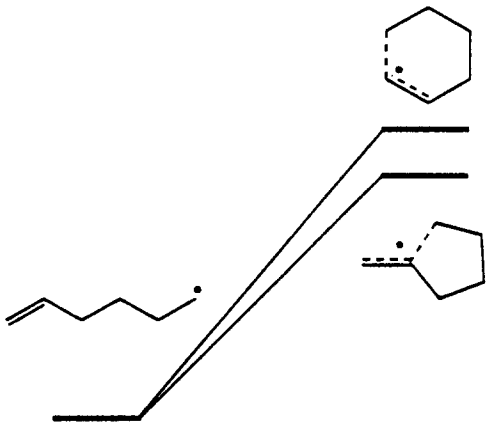
t / c = 99:1 (>95:5)

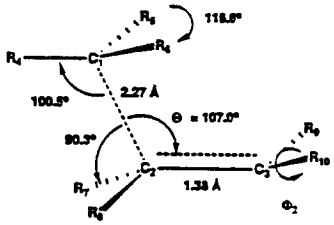
(195 - 296 K)





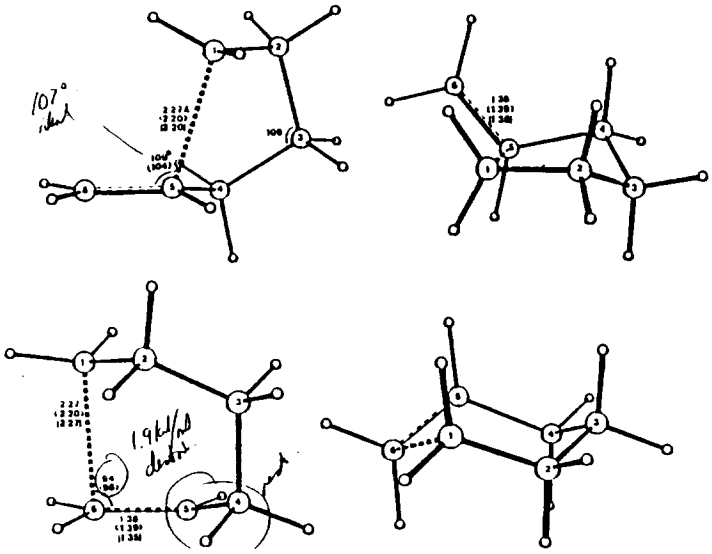




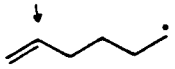
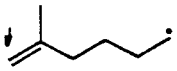
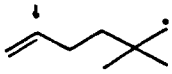
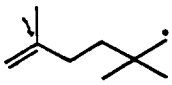
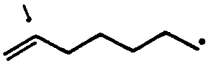
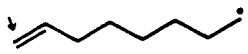
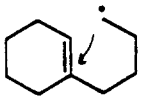


Spellmeyer - many calculations

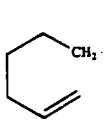
cf. Beckwith

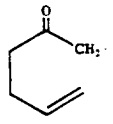


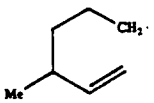
Exo/Endo Ratios

	Calculated	Experimental
	95/5	98/2
	41/59	40/60
	99/1	>99/1
	74/26	68/32
	97/3	89/11
	23/77	0/100
	82/18	55/45

Endo(6) : Exo(5)


2:98


93:7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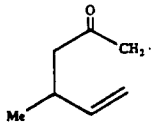
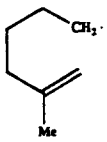
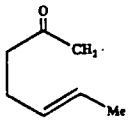
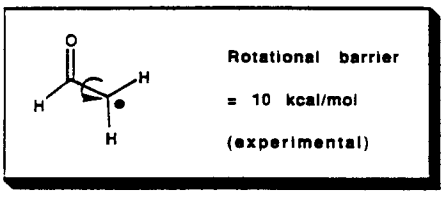
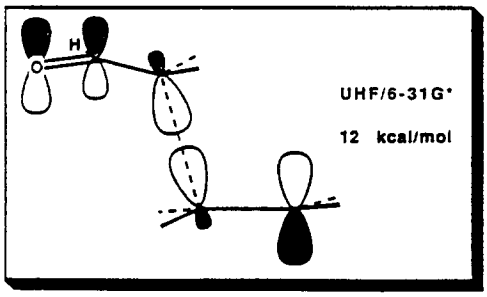

100:0


60:40

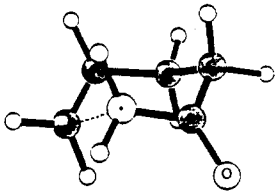

75:25

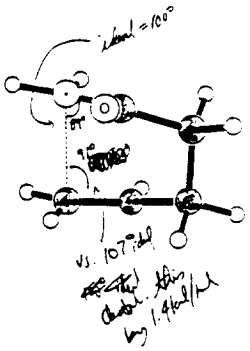


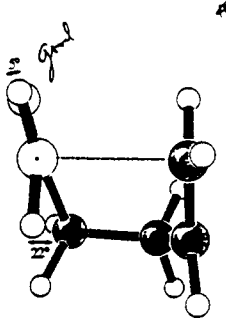
B-15



and endo-6 - more nearly planar

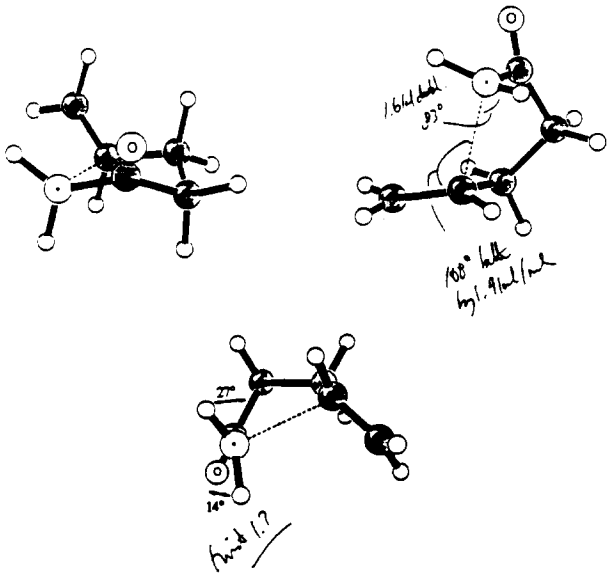




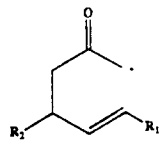


2.4 better

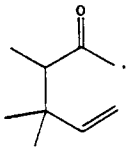
6-endo Exo



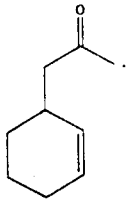
Calculated endo/exo ratio [ΔE]
Experimental endo/exo ratio [ΔΔG‡]



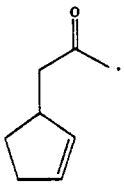
2: $R_1 = R_2 = H$
95:5 [2.0]
97:3 [2.3]
3: R_1 = Me, R_2 = H
68:32 [0.5]
75:25 [0.7]
4: R_1 = H, R_2 = Me
97:3 [2.4]
only endo [>2.5]



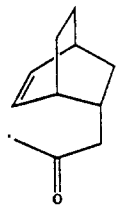
5
99:1 [3.0]
91:9 [1.6]



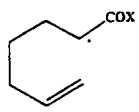
6
0:100 [-4.2]
only exo [<-2.5]



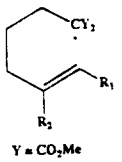
7
1:99 [-3.0]
only exo [<-2.5]



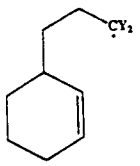
8
0:100 [-3.6]
only exo [<-2.5]



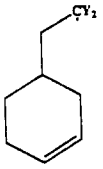
9: X = OMe
12:88 [-1.4]
7:93 [-1.8]
10: X = OtBu
9:91 [-1.6]
8:92 [-1.7]
11: X = tBu
15:85 [-1.2]
25:75 [-0.8]



12: $R_1 = R_2 = H$
8:92 [-1.6]
10:90 [-1.5]
13: R_1 = H, R_2 = Me
92:8 [17]
only endo [>2.5]
14: R_1 = Me, R_2 = H
0:100 [-5.2]
only exo [<-2.5]



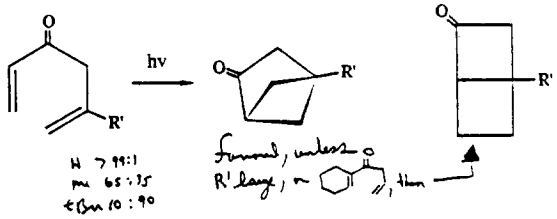
15
0:100 [-6.5]
only exo [<-2.5]

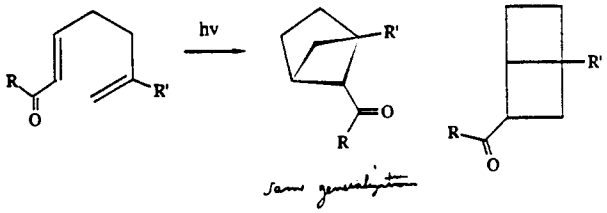


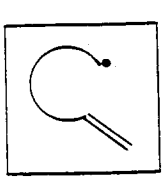
16
3:97 [-2.3]
only exo [<-2.5]

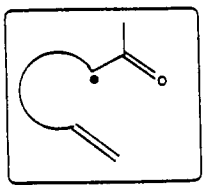
Crossed Closure

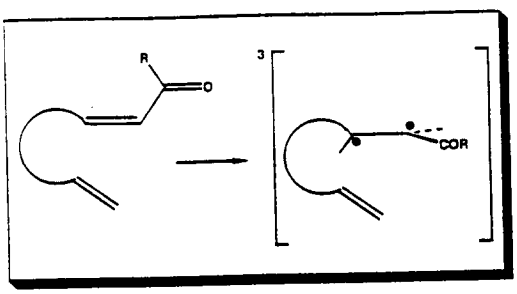
Straight Closure

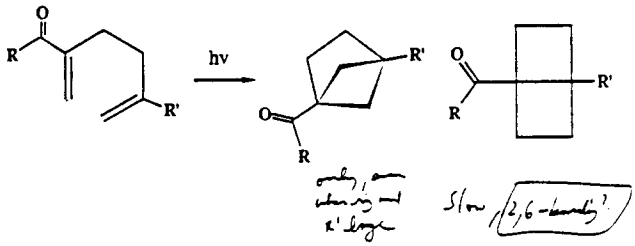




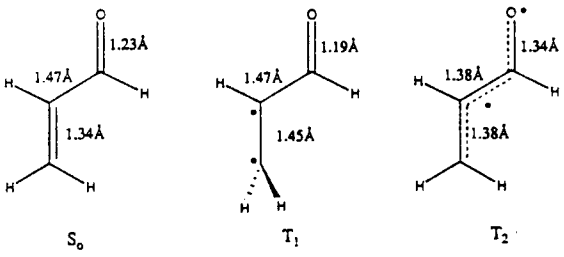








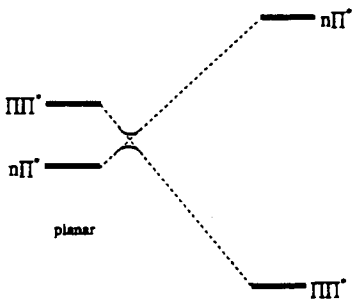
UMP4/6-31G*//UMP2/6-31G*

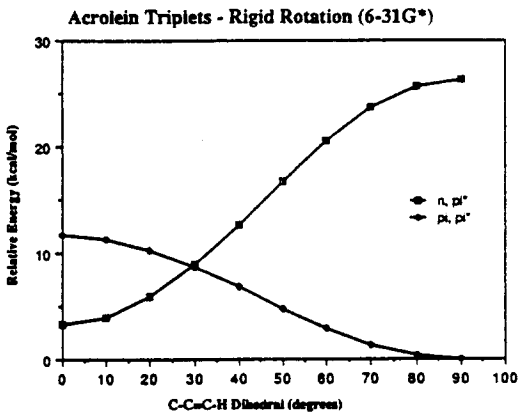


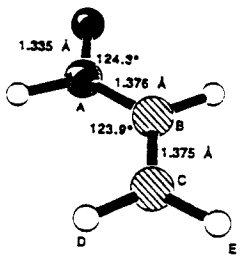
S_o T_1 T_2

$\pi\pi^*$ $n\pi^*$

0 +10 kcal/mol



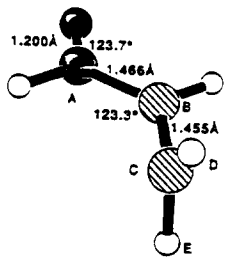




$\emptyset_{abcd}$ = 0°

$\emptyset_{abce}$ = 180°

S_o

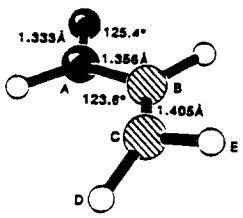


$\emptyset_{abcd}$ = -93°

$\emptyset_{abce}$ = 93°

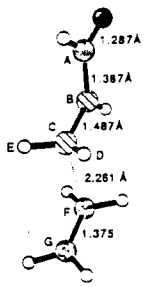
$T_1 = \pi\pi^*$

UMP4//
UMP2/6-31G*



$\emptyset_{abcd}$ = 45°

$\emptyset_{abce}$ = -165°

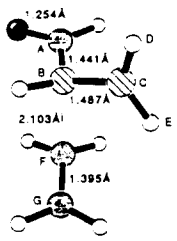


Φ_{abcd} = -71°

Φ_{abce} = 71°

θ_{cfg} = 107.9°

17A



Φ_{abcd} = 117°

Φ_{abce} = -73°

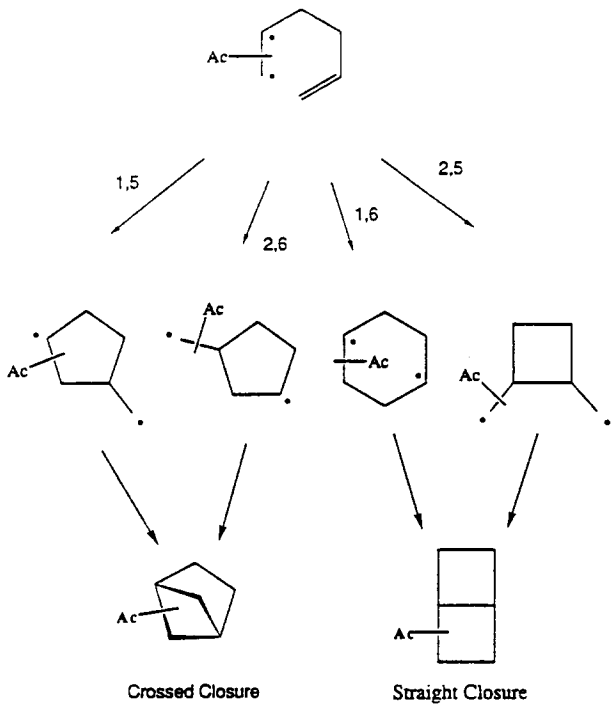
θ_{cfg} = 107.6°

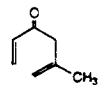
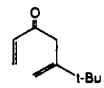
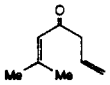
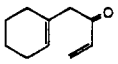
18A

● = OXYGEN

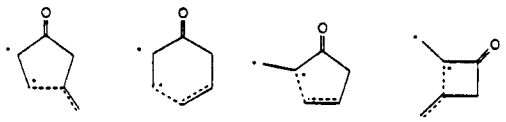
◔ = CARBON

⊘ = RADICAL

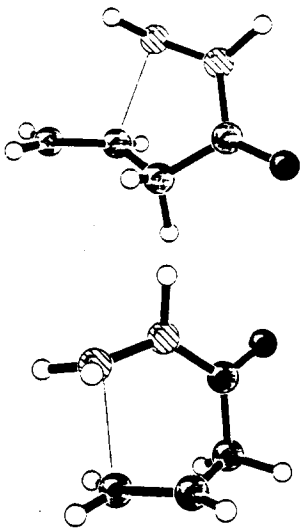


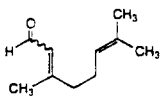
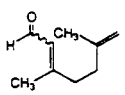
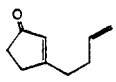
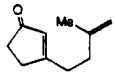
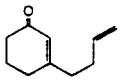
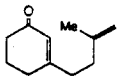
Compound	Calc. Ratio for Crossed/Straight Closure	Exp. Ratio for Crossed/Straight Closure
	100:0	100:0
	76:24	61:39
	1:99	10:90
	100:0	100:0
	99:1	77:23
	95:5	93:7
	32:68	43:57
	2:98	0:100

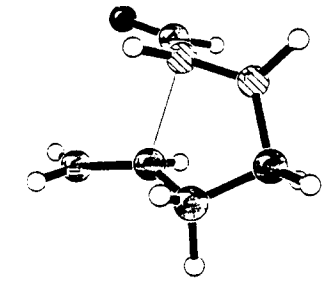
Relative Energy of Transitions States for 1,5-Hexadien-3-one (kcal/mol)

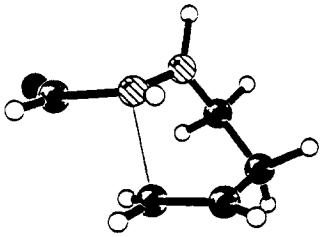


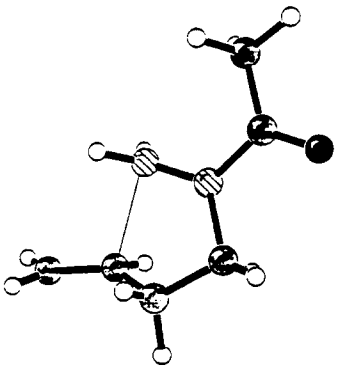
Twisted	0.0	3.6	24.3	31.1
Planar	26.0	27.3	40.3	44.0

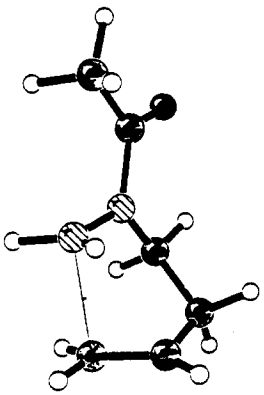


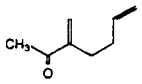
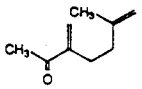
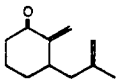
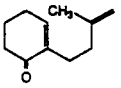
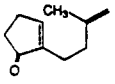
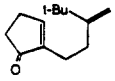
Compound	Calc. Ratio for Crossed/Straight Closure	Exp. Ratio for Crossed/Straight Closure
	100:0	100:0
	12:88	22:78
	0:100	10:90
	0:100	0:100
	98:2	74:26
	10:90	13:87



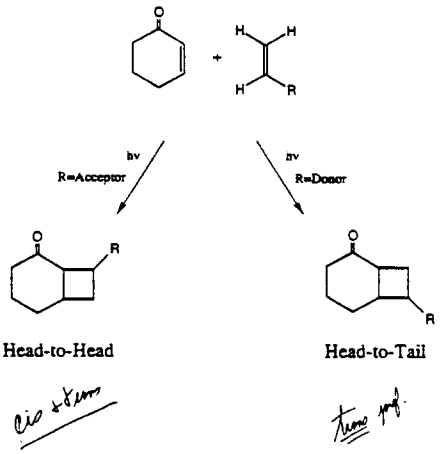


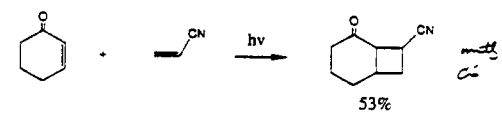




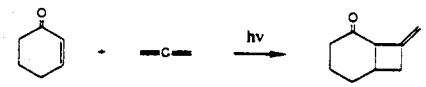
Compound	Calc. Ratio for Crossed/Straight Closure	Exp. Ratio for Crossed/Straight Closure
	100:0	100:0
	100:0	100:0
	100:0	100:0
	100:0	100:0
	94:6	100:0
	44:56	100:0

Regioselectivity of 2+2 Photocycloaddition





53%



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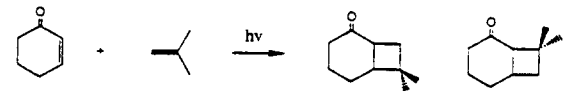
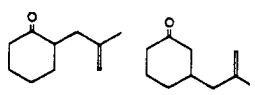
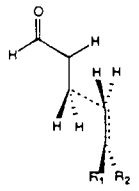


33% 6%

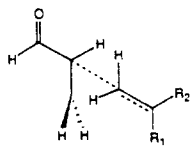


14% 8%

67%



β

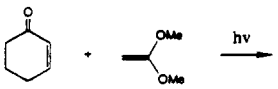
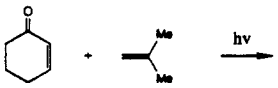
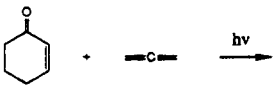
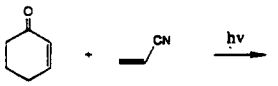


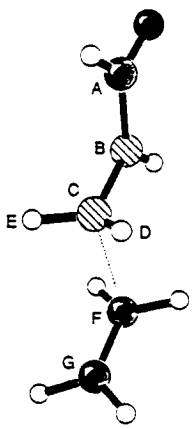
α

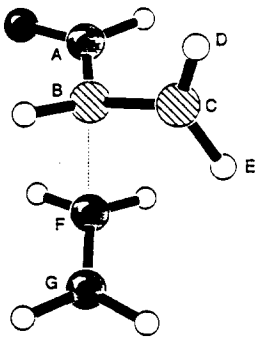
(R1, R2)	ΔE(β-α) PMP2/6-31G*	PMP3/6-31G*	Exp.
(H, CN)	1.8	-0.9	-0.7
(=CH2)	2.0	-0.6	<-2.0
(H, H)	2.2	-0.3	--
(H, Me)	3.7	0.3	0.1
(Me, Me)	4.0	0.5	0.5
(H, OMe)	5.8	1.7	>2.0

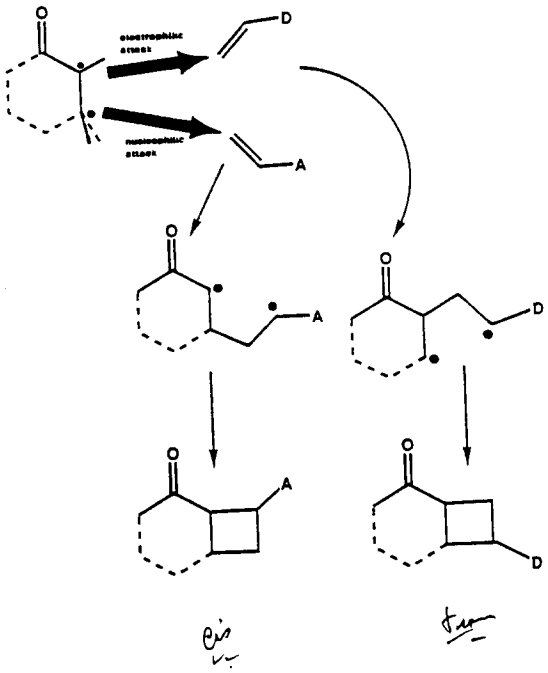
Trend O.K.

not calibrated well by B-L Method

	Trans-Fused	Cis-Fused
	49%	21%
	47%	19%
	27%	7%
	0%	55%
	0%	53%







epi

trans