Pergamon

Tetrahedron 54 (1998) 12279–12288

TETRAHEDRON

On the Mechanism of the Diels-Alder Reaction of Enal Dienophiles. Competitive Reactivity and *Ab initio* Calculations Using a Transannular Probe

Yves L. DORY‡, Dennis G. HALL†¥, and Pierre DESLONGCHAMPS†*

† Laboratoire de synthèse organique,

‡ Laboratoire de modélisation moléculaire,

Département de chimie, Institut de Pharmacologie de Sherbrooke, Université de Sherbrooke, 3001, 12e avenue nord, Sherbrooke (Québec) Canada J1H 5N4

¥ Department of Chemistry, University of Alberta, Edmonton (Alberta) Canada T6G 2G2

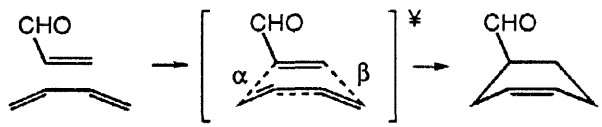
Received 12 June 1998; accepted 5 August 1998

Abstract: A sterically unbiased macrocyclic probe has been used to study the Diels-Alder reaction mechanism of enal dienophiles. All the results, theoretical as well as kinetical, converge to the conclusion that a virtually non-concerted zwitterionic mechanism is possible for certain cases of Lewis acid catalysis. This conclusion was reached because the zwitterionic limit intermediates obtained after the first step could arise either from favored [6.11] or disfavored [7.10] bicycle formation. These two opposite effects could assist or counteract asynchronicity. The analysis of these effects showed that asynchronicity highly stabilizes the Diels-Alder reaction transition state if the latter is geometrically favorable such as in the case of a [6.11] zwitterionic limit intermediate. Altogether, these results on the Diels-Alder cycloaddition involving enal dienophiles demonstrate the extreme sensitivity in transition state geometry in response to the most subtle structural changes in substrates.

Introduction

The acceleration of Diels-Alder reactions by Lewis acid catalysts has had a tremendous impact in organic synthesis since its discovery by Yates in 1961.[1] By coordinating with carbonyl-conjugated dienophiles, Lewis acids affect the reactivity and the diastereoselectivity outcome of the reaction. The detailed mechanistic nature[2] of such [4+2] cycloadditions involving non-polarized 1,3-dienes, however, remains elusive in spite of several reports outlining experimental results[3,4] and high level calculations[5,6].

It has now become generally accepted on the basis of calculations[6-9] and experimental arguments[10,11] that the uncatalyzed [4+2] cycloaddition of unsymmetrically activated dienophiles such as acrolein proceeds through a concerted asynchronous mechanism. Unequal development of the two incipient bonds presumably leads to an unsymmetrical transition state with more advanced bonding (shorter bond) at the β-site (Scheme 1) (Table 1, entry 3).[6]

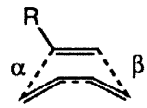


Scheme 1

Pierre Deslongchamps: *FAX:* (819) 820-6823. *E-MAIL:* pierre.deslongchamps@courrier.usherb.ca

0040-4020/98/$ - see front matter
PII: S0040-4020(98)00764-9

Table 1 *

Entry	R	
1	H	*2.21-2.21* [0.33-0.33]
2	Me	*2.22-2.21* [0.32-0.33]
3	C=O	*2.35-2.09* [0.26-0.38]
4	CO•••BH_3	*2.98-1.93* [0.08-0.48]

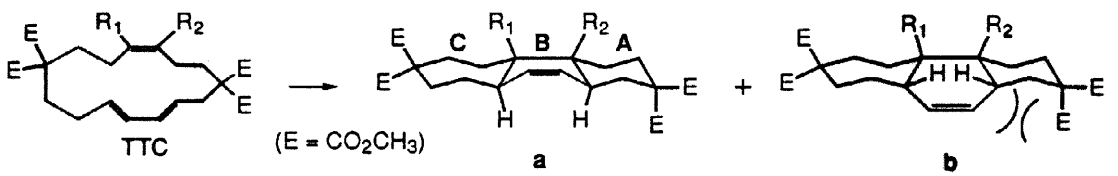
* Geometrical features of intermolecular transition structures (3-21G) related to transannular cases shown. For each transition structure, the forming bonds are given in Å in italics and the corresponding bond orders between brackets.

Rate acceleration through complexation of the dienophile carbonyl with a Lewis acid results in enhanced polarization of the dienophile with the consequence of further increasing the asynchronous character of the cycloaddition.[3,5,6,9] Yet, only in a few extreme cases of highly polarized or charged components is there a claim for a stepwise ionic mechanism[12-15]. No such evidence exists for the Lewis acid catalyzed reaction of enal dienophiles with non-polarized 1,3-dienes. In such cases the Alder *cis* rule has always been observed. This stands as a strong argument in favor of concertedness in bond formation but may not disprove the possibility for a stepwise stereospecific mechanism. If a concerted mechanism is operative, assessing the degree of incipient bonding asynchronicity is a very challenging experimental problem. In addition, transition state geometry is likely substrate sensitive, as suggested by a recent study on steric substituent effects.[4] In the absence of relevant quantitative experimental models, transition states were calculated for the acrolein (complexed or not) butadiene prototype reaction in gas phase.[6,8b] The *ab initio* transition structure obtained by Houk for the uncatalyzed reaction is significantly unsymmetrical at the RHF/3-21G level with respective β and α-bond lengths of 2.09 Å and 2.35 Å compared to 2.21 Å for the synchronous ethylene-butadiene case (entry 1). Under BH_3 coordination, the resulting species may point toward a change of mechanism from a concerted to a pseudo-zwitterionic one. Indeed, a highly asynchronous transition structure having essentially no α-bonding (β = 1.91 Å, α = 2.76 Å) was suggested for the endo approach, despite inadequate curvature for that structure. However, as no intermediates could be detected, Houk concluded that the process is still concerted, albeit possibly stepwise in solution, owing to charge separation.[6] The possibility for extreme asynchronicity has even led Yamabe to suggest another mechanism, a hetero [2+4] / Claisen rearrangement pathway.[15] This surprising mechanism was actually the result of a thorough IRC[16] *ab initio* study starting from an endo BF_3 catalyzed acrolein-ethylene transition structure.

In this report, we bring the most insightful data obtained on transition state geometry for non-catalyzed and Lewis-acid activated Diels-Alder reactions involving enal dienophiles. To this end, a novel model system using two macrocyclic probe compounds was studied by competitive kinetics and data are supported by RHF/3-21G *ab-initio* calculations.

Transannular Probe System

As previously described, model 15-membered macrocyclic trienes **1/2** (Scheme 2) undergo a transannular Diels-Alder (TADA) reaction to afford *trans-syn-trans* and *cis-syn-cis* A.B.C.[6.6.7] tricyclic products in various diastereomeric ratios.[17] The selectivity of the process is actually best explained with the "asynchronous transition state" theory. For the purpose of this work, macrocycles **1** and **2** can be mutually considered as sterically unbiased. Indeed, a permutation of the formyl substituent between the two vinylic positions on the dienophile (R_1 and R_2) should not affect significantly the balance of steric interactions encountered in transition states derived from both macrocycles.[18] In both cases, the malonate moieties are oriented away from the formyl substituent in the A.B.C. chair-boat-twist-chair transition structure.



1 R_1 = CHO, R_2 = H
2 R_1 = H, R_2 = CHO

Scheme 2

Therefore, any difference in reaction rates between nearly-identical substrates **1** and **2** should stem from electronic effects at the transition state level. In principle, with increasing asynchronicity in bond formation, macrocycle **1** should show a higher reactivity compared to **2**. Indeed, faster β-bonding in **1** effects closure of the 6-membered ring A, whereas the much less favored 7-membered ring C forms predominantly in **2**. For example, as an indication of this effect in such transannular systems, fundamental studies in our laboratory indicate that the TADA reaction temperature of analogous 14-membered macrocyclic trienes, leading to A.B.C [6.6.6] tricyclic products, is approximately 100°C inferior compared to **1/2**.[19] If one extrapolates this analysis, as shown in Figure 1, complete β-bond closure in **1** leads to a [6.11] bicyclic zwitterionic intermediate. On the other hand, **2** would generate a [7.10] bicyclic intermediate. Clearly, the latter situation is disfavored compared to the case of macrocycle **1** because six- and eleven-membered ring closures are generally strongly preferred to seven- and ten-membered ring closures[20]. Thus, the relative reactivity difference of **1/2** can be associated with the degree of asynchronicity between the β and α incipient bonds.

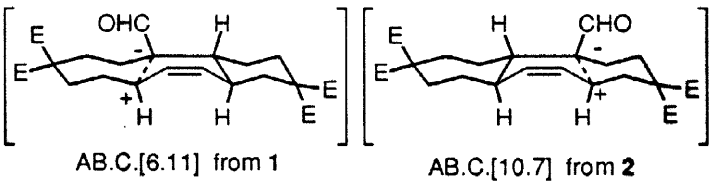


Fig. 1. Limit *endo* asynchronous transition structures for macrocycles **1** and **2**.

Competitive Reaction Kinetics of 1 and 2

One-point comparative kinetic assays were carried out by allowing the reactions to proceed similarly for both **1** and **2** at definite temperatures and times. The non-catalyzed assays were carried out at 120°C in degassed toluene solution sealed in pyrex tubes. The Lewis acid catalyzed runs were performed under a nitrogen atmosphere. They were initiated by addition of the Lewis acid solution and were stopped by adding a neutralizing aqueous solution. The conversion percentages of macrocycles **1** and **2** into tricyclic products were measured by ^1H NMR integration of representative singlet signals on the crude reaction mixtures. This method was reproducible and allowed the calculation of first order constants showing reactivity trends which are clearly valuable for the present study (Table 2).

Table 2. Kinetic data for the TADA reactions of **1** and **2**

Conditions	Solvant	Toluene		Dichloromethane	
	Temperature	120°C	25°C		
	Time	180 min	30 min		30 s
	Lewis acid	no	$SnCl_4$	BF_3•OEt_2	
Macrocycle **1**	Conversion %	94	96	100	74
	$K_1 \times 10^{-3}$ min^{-1}	16	105	/	16300
Macrocycle **2**	Conversion %	28	< 2	48	0
	$K_2 \times 10^{-3}$ min^{-1}	1.8	0.65	22	/
	K_1 / K_2	9	> 160	740 (16300/22)	

Model macrocycle **1** was moderately more reactive than regioisomer **2** by almost one order of magnitude (K1/K2=9) under thermal activation only (120°C). On the other hand, activation with Lewis acids at room temperature showed a dramatic rate difference between **1** and **2**. Either with excess $SnCl_4$ in toluene or with a stronger acid like BF_3•OEt_2,[21] in dichloromethane, hundred fold relative constants were obtained. The K1/K2 value of 160 found under $SnCl_4$ catalysis is a minimal figure since no product conversion was observed with macrocycle **2** and it was attributed a value delimited by the sensitivity of NMR detection. The use of BF_3•OEt_2 in CH_2Cl_2 showed faster macrocycle consumption and allowed measurement of the disappearance of both macrocycles under different time scales. It gave an impressive K1/K2 value of 740, which translates into more than 3.9 kcal/mol difference in activation energy between the two reactions. A competitive assay performed with an equimolar mixture (BF_3•OEt_2, CH_2Cl_2, RT, 30 sec) of **1** and **2** even resulted in a mixture containing

totally unreacted **2** along with TST tricycle **1a** originating from complete consumption of **1**. The spectacular rise in rate differentiation upon Lewis acid catalysis points toward a possible change of mechanism from asynchronous concerted to a virtually non concerted one.

Transition State Calculations

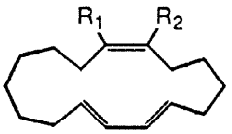
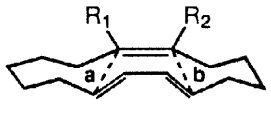
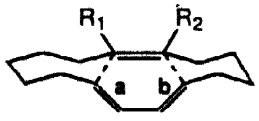
Since experimental results agree well with the concept of favored [6.11] and disfavored [7.10] bicyclic zwitterionic intermediates, we wanted to validate these ideas by means of theoretical calculations. Obviously, the size of the systems at stake is detrimental to high accuracy treatment and we had recourse to the *ab initio* RHF/3-21G level of theory.[22] Nevertheless, even this basis set is still too large to allow easy modelling of the TADA reactions arising from cyclopentadecatrienes **1** and **2**. Indeed, these macrocycles contain 29 heavy atoms and 32 hydrogens and the four methyl esters lead to numerous rotamers. This situation renders the localization of transition states awkward. Since Diels-Alder reactions are kinetically driven, the transition structures are truly the significant species and must be characterized. Thus, the problem was simplified by swapping the ester groups for hydrogen atoms.[23] In fact, as discussed above, such a drastic transformation of the molecules should not disturb the reaction profiles to a large extent because these esters are distant from the reaction site. Their effect is only steric as it enhances the TST selectivity by destabilizing the CSC transition state in which one axial ester in ring A bumps into the diene in the latter transition structure (Scheme 2).

Consequently, the molecules which were finally calculated[24] are shown in Table 3. The macrocycles input files were derived from a parent macrocycle (**1**: with R = $SnBu_3$) whose structure was known from its X-ray crystal analysis.[27] Only chair-boat-twist-chair transition structures were considered, because such conformations would minimize steric interactions if the esters were to be present. This approach was used to closely mimick the actual cases in terms of backbone shapes because it has already been successfully used by us to study related transannular reactions.[23] Finally, an attempt to evaluate the possible steric bias of the formyl group was carried out by replacing it with a methyl group and a hydrogen atom (entries 5-7). In the latter case, which is the reference, one sees the effect of the macrocycle itself on the TST/CSC selectivity. Not surprisingly, there is none, as shown by the fact that the TST and CSC transition states (entry 5) have identical activation energies (45.9 Kcal/mol, the zero point energy correction was not calculated). This simply indicates that the macrocycle shape does not influence on its own the endo/exo ratio of adducts. In fact, as already mentioned, the TST adducts are always the major products presumably due to the steric discrimination disfavoring the competing CSC transition states (Scheme 2). Since the calculations do not explicitly take into account the ester groups largely responsible for the TST/CSC selectivity, it turns out that the calculated CSC transition structures are somewhat irrelevant as far as their energies are concerned. On the other hand, their geometrical features are meaningful and follow the same trend as the corresponding TST transition structures. For clarity, the following discussion will only take the favored TST transition structures into consideration.

From the reference TST transition state ($R_1 = R_2 = H$, entry 5) one important geometrical characteristic can be drawn out: the transition structure shows dissymmetry. The forming bonds have different lengths, 2.18 Å on the incipient six-membered ring side and 2.27 Å for the seven-membered ring counterpart. However, this dissymmetry is only apparent because as many electrons are fed into the two forming bonds as shown by their

bond orders[28] which are equal (0.31). Therefore, the length of a bond does not always accurately reflect its electron density. In this case, it may reflect the lesser ease at which the 7-membered ring forms on a mechanical standpoint alone.

Table 3 *

Entry	R_1	R_2	 macrocycle	 TST t.s.	 CSC t.s.
5	H	H	-578.72052	-578.64734 (45.92) *2.27-2.18* [0.31-0.31]	-578.64738 (45.90) *2.31-2.13* [0.32-0.35]
6	Me	H	-617.54058	-617.46003 (50.54) *2.30-2.17* [0.29-0.32]	-617.45832 (51.62) *2.35-2.13* [0.29-0.34]
7	H	Me	-617.54009	-617.46110 (49.57) *2.23-2.23* [0.31-0.30]	-617.46187 (49.08) *2.25-2.22* [0.33-0.32]
8	C=O	H	-690.81276	-690.74783 (40.74) *2.56-1.96* [0.21-0.45]	-690.74563 (42.12) *2.53-1.97* [0.24-0.43]
9	H	CO	-690.81180	-690.74192 (43.85) *2.12-2.34* [0.36-0.24]	-690.74374 (42.70) *2.12-2.33* [0.37-0.26]
10	CO•••BH_3	H	-717.08477	-717.03884 (28.82) *2.96-1.99* [0.06-0.42]	-717.03355 (32.14) *2.83-1.92* [0.11-0.47]
11	H	CO•••BH_3	-717.08391	-717.02863 (34.69) *2.06-2.50* [0.42-0.15]	-717.02564 (35.56) *2.04-2.53* [0.41-0.16]

* Energies are indicated in a.u. and enthalpies of activation in kcal/mol between brackets. For each transition structure, the forming bonds **a** and **b** are given in Å in italics and the corresponding bond orders between brackets.

Interestingly, adding a methyl group at position R_1 (entry 6) or R_2 (entry 7) does not affect much neither the bond lengths **b** (6-membered ring side) and **a** (7-membered ring side) nor the corresponding bond order indexes which remain relatively constant (0.29 to 0.32). The same marginal steric effect was also observed in intermolecular cases (entries 1 and 2, Table 1) since the absence (entry 1) or presence (entry 2) of a methyl substituent on the dienophile led to almost identical transition state geometries, where the bond lengths and bond orders are remarkably close to the transannular examples disclosed in entries 5-7.

This constancy validates the assumption that the macrocyclic probe compounds (**1**/**2**) under consideration are sterically unbiased and reinforces the value of the previous kinetic data to address the current problem. The accuracy of the calculations was confirmed by the activation energies obtained, 50.54 kcal/mol when R_1 = Me and 49.57 when R_2 = Me ($\Delta\Delta E^{\ddagger}$ = 0.97 kcal/mol), showing that the latter case is favored. This theoretical result is in agreement with experiments carried out with R_1 or R_2 = CH_2OMOM.[18]

Armed with this reliable tool, the aldehyde groups were introduced and it was therefore assumed that their steric effect could be safely neglected. Under thermal conditions (entries 8 and 9), the calculated $\Delta\Delta E^{\ddagger}$ was 3.11 kcal/mol (43.85 - 40.74) in favor of R_1 = CHO. Experimentally (Table 2), macrocycle **1** (R_1 = CHO) was consumed 9 times faster than macrocycle **2** (R_2 = CHO) at 120°C. Both structures show asynchronicity; in particular the lowest energy one (R_1 = CHO) which presumably tends to form a [6.11] bicyclic intermediate in

which the ring junction bond has a length of 1.96 Å (bond order: 0.45). The lagging bond a is much longer with a length of 2.56 Å and a bond order index of 0.21. The bond order figures indicate that the bond b contains twice as many electrons as bond a at the transition state. This ratio in bond formation is less dramatic when the aldehyde is positioned at the other end of the dienophile (entry 9). In fact the geometry in the latter case closely matches the intermolecular transition structure involving butadiene and acrolein (entry 3) both in terms of bond lengths and bond orders. It comes out of these observations that the asynchronicity of the process is enhanced when the forward bond generates a favored 6-membered ring and remains identical to that of the intermolecular reference (entry 3) when the forward bond leads to the formation of a 7-membered ring case. Catalysis of these reactions by means of BH_3 increases the phenomenon of asynchronicity in a drastic way since the lagging bonds are almost non existent at the transition state level. This is particularly true when the lagging bond leads to a 7-membered ring (entry 10) and less so when the same bond yields a 6-membered ring (entry 11). The lengths of these bonds are 2.96 Å and 2.50 Å respectively which correspond to bond order indexes of 0.06 and 0.15. The advanced bonds behave in a similar way in both cases since the bond orders are the same (0.42). It is interesting to notice that only the transannular catalyzed transition state whose advanced forming bond belongs to a 6-membered tether ring (entry 10) closely matches the intermolecular situation (entry 4) in terms of bond lengths and bond orders.

The most asynchronous transition structure (bond order ratio: 0.42/0.06 = 7, entry 10) is favored energetically over the less asynchronous one (bond order ratio: 0.42/0.15 = 2.8, entry 11) by 5.87 kcal/mol. Such a large reactivity difference agrees satisfactorily with the experimental result of **1** and **2**.

It therefore appears general that the larger the asynchronicity the better the reaction rate (related to $\Delta E^{\ddagger}$), since this trend was also observed for the non-catalyzed reactions (entry 8, bond order ratio: 0.45/0.21, $\Delta E^{\ddagger}$ = 40.74 kcal, entry 9, bond order ratio: 0.36/0.24 = 1.5, $\Delta E^{\ddagger}$ = 43.85 kcal/mol).

General Conclusion

Both calculation and experimental results fully support the limit transition structure model shown in Figure 1. Because the [7.10] limit case is much less favored than the [6.11] one, calculations outlined on entries 9 and 11 show a resistance effect to asynchronicity when compared to their regioisomeric cases (entries 8, 10). Experimentally, macrocycle **2** is less reactive than **1** as it must find thermodynamic balance by fighting extreme asynchronicity to avoid a disfavored geometrical situation at transition state level. With macrocycle **1**, electronic (bonding asynchronicity) and mechanical (favored [6.11] limit structure) variables work in the same direction with the benefit of a higher reactivity. Although no quantitative assessment of bond asynchronicity can be drawn from it, this study clearly demonstrates the extreme sensitivity of transition state geometry in response to the most subtle structural changes in substrates. However, in the most favorable cases of Lewis acid catalysis such as with macrocycle **1**, a virtually non-concerted zwitterionic mechanism can be envisioned.

Experimental Section

Experimental details: macrocyclic substrates **1** and **2** were prepared as described in reference 29. One-point competitive kinetics: 1) Thermal reactions: clean isovolumic pyrex tubes (20 cm long, ext. diam.: 0.9 cm, int. diam.: 0.5 cm) were washed and prepared according to: Ciganek, E. In Organic Reactions. Vol. 32, Edited by: Dauben, W.G., Wiley: New York, 1984, p. 96. A 1.0 mg sample of macrocycle in 1.0 mL of degassed toluene was then transferred and sealed under vacuum. The tubes were heated in the temperature-controlled (+0.1°C) oven of a GC instrument for temperatures and times indicated in Table 2. The use of additives like a tertiary amine as an acid scavenger or a radical inhibitor did not affect the reactions. 2) Catalyzed reactions: Lewis acids were purchased from Aldrich Chemical Co. Reactions were performed at c.a. 0.1 M concentrations and employed excess Lewis acids (≥3 eq.) owing to the chelating abilities of the diester groups. 3) Conversion percentages were determined by measuring peak height and surface of representative signals on a Bruker AC 300 instrument (relaxation delay: 5.0 sec.).

Acknowledgements

This research was supported by the Natural Sciences and Engineering Research Council of Canada (NSERCC, Ottawa) and by the "Ministère de l'Éducation" (FCAR, Québec).

References and notes

(1) Yates, P.; Eaton, P. J. *Am. Chem. Soc.* **1960**, *82*, 4436.

(2) For a review on mechanistic aspects of the Diels-Alder reaction, see: Sauer, J.; Sustmann, R. *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 779.

(3) Tolbert, L.M.; Ali, M.B. *J. Am. Chem. Soc.* **1984**, *106*, 3806.

(4) Dai, W.-M.; Lau, C.W.; Chung, S.H.; Wu, Y.D. *J. Org. Chem.* **1995**, *60*, 8128.

(5) Branchadell, V.; Oliva, A.; Bertran, J. *J. Mol. Struct. (Theochem)* **1986**, *138*, 117.

(6) Birney, D.M.; Houk, K.N. *J. Am. Chem. Soc.* **1990**, *112*, 4127.

(7) Storer, J.W.; Raimondi, L.; Houk, K.N. *J. Am. Chem. Soc.* **1994**, *116*, 9675, and references therein.

(8) For review articles, see: (a) Houk, K.N.; Li, Y.; Evanseck, J.D. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 682. (b) Houk, K.N.; González, J.; Li, Y. *Acc. Chem. Res.* **1995**, *28*, 81. (c) Dewar, M.J.S.; Jie, C. *Acc. Chem. Res.* **1992**, *25*, 537.

(9) (a) Houk, K.N. *J. Am. Chem. Soc.* **1973**, *95*, 4092. (b) Houk, K.N.; Strozier, R.W. *Ibid.* **1973**, *95*, 4094. (b) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley and Sons: New York, 1976, p. 163.

(10) Gajewski, J.J.; Peterson, K.B.; Kagel, J.R.; Huang, Y.C.J. *J. Am. Chem. Soc.* **1989**, *111*, 9078.

(11) The stereoselectivities of some intramolecular Diels-Alder (IMDA) reactions have been interpreted in terms of the "asynchronized concerted mechanism" theory, thereby constituting additional arguments in favor of this theory. For a review on the IMDA reaction and a discussion on this aspect, see: Roush, W.R. In Comprehensive Organic Synthesis, Vol. 4, Edited by Trost, B.M.; Pergamon Press: Oxford, 1991, p. 513.

(12) Woodward, R.B.; Katz, T.J. *Tetrahedron* **1959**, *5*, 70.

(13) (a) Thompson, H.W.; Melillo, D.G. *J. Am. Chem. Soc.* **1970**, *92*, 3218. (b) Gupta, R.B.; Franck, R.W. *J. Am. Chem. Soc.* **1987**, *109*, 5393. (c) Jensen, F.; Foote, C.S. *J. Am. Chem. Soc.* **1987**, *109*, 6376. (d) Baran, J.; Mayr, H.; Ruster, V.; Klärner, F.-G. *J. Org. Chem.* **1989**, *54*, 5016. (e) Gassman, P.G.; Gorman, D.B. *J. Am. Chem. Soc.* **1990**, *112*, 8624.

(14) Sustmann, R.; Sicking, W. *J. Am. Chem. Soc.* **1996**, *118*, 12562.

(15) (a) Yamabe, S. Dai, T.; Minato, T. *J. Am. Chem. Soc.* **1995**, *117*, 10994.

(b) Garcia, J.I.; Mayoral, J.A.; Salvatella, L. *J. Am. Chem. Soc.* **1996**, *118*, 11680.

(16) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363.

(17) Hall, D.G.; Müller, R.; Deslongchamps, P. *Can. J. Chem.* **1995**, *73*, 1695.

(18) In support with this assumption, analogous cyclopentadecatrienes (R_1 or R_2 = CH_2OMOM in lieu of CHO) were found to give similar ratios,[17] and a very close reactivity factor (Krel ≥ 2 in favor of R_2 = CH_2OMOM).

(19) Deslongchamps, P. *Pure and Appl. Chem.* **1992**, *64*, 1831.

(20) Approximate relative rate constants for ring closure on a model cyclization reaction are as follows: $K_{6/7}$ = 2 x 10^2, $K_{11/10}$ = 3 (Eliel, E.; Wilen, S.H. Stereochemistry of Organic Compounds, Wiley: New York, 1994, p. 678). The $K_{11/10}$ factor for **1/2** could be further substantiated due to the presence of unsaturations.

(21) Laszlo, P.; Teston, M. *J. Am. Chem. Soc.* **1990**, *112*, 8750.

(22) Binkley, J.S.; Pople, J.A.; Hehre, W.J. *J. Am. Chem. Soc.* **1980**, *102*, 939.

(23) Dory, Y.L.; Soucy, P.; Drouin, M.; Deslongchamps, P. *J. Am. Chem.Soc.* **1995**, *117*, 518.

(24) *Ab initio* computational procedure: All the calculations were done at the RHF 3-21G level. The first input files for GAMESS[25] were the corresponding fully characterized AM1[26] transition structures. The saddle point searches were carried out in cartesian coordinates. The computed AM1 hessian matrices were fed into GAMESS. Finally, when the saddle points were located, the hessian matrices were not recomputed at the 3-21G level of theory due to system limitations. Thus zero point energies corrections could not be applied.

(25) Schmidt, M.W.; Baldridge, K.K.; Boatz, J.A.; Elbert, S.T.; Gordon, M.S.; Jensen, J.H.; Koseki, S.; Matsunaga, N.; Nguyen, K.A.; Su, S.J.; Windus T.L.; Dupuis, M.; Montgomerey, J.A. *J.Comput. Chem.* **1993**, *14*, 1347.

(26) Dewar, M.J.S.; Zoebisch,E.G.; Healy, E.F.; Stewart, J.J.P. *J. Am. Chem. Soc.* **1985**, *107*, 3902.

(27) Falardeau, G.; Deslongchamps, P.; Drouin, M. Unpublished results.

(28) Mayer, I. *Chem. Phys. Lett.* **1983**, *97*, 270.

(29) Hall, D.G.; Müller, R.; Deslongchamps, P. *Can. J. Chem.* **1995**, *73*, 1675.