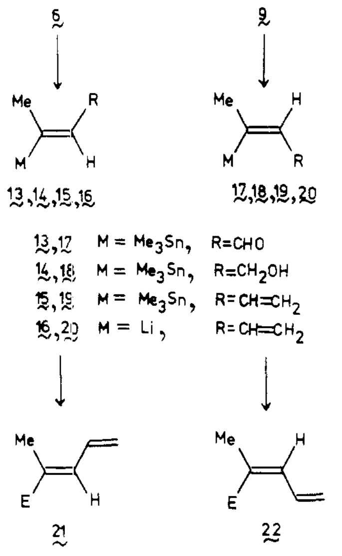
Scheme II



made for the reaction of lithium dialkylcuprates with α,β-acetylenic esters.[12,13] However, in the latter transformations, the "thermodynamically controlled" reactions did not lead to high stereoselectivity.

The possibility of employing the β-trimethylstannyl α,β-unsaturated esters **5**–**10** as precursors for stereochemically well-defined and isomerically pure vinyllithium[14] and related reagents appears to be very attractive. For example, reduction of the isomeric esters **6** and **9** with ~1 equiv of diisobutylaluminum hydride in pentane at −127 °C afforded the corresponding aldehydes **13** (86%) and **17** (82%), respectively.[15] Treatment of the latter substances with methylenetriphenylphosphorane in THF at room temperature gave the geometrically isomeric trimethylstannyl dienes **15** and **19** (74% and 72%, respectively). Interestingly, both of these substances underwent rapid and complete transmetalation when treated with 1.2 equiv of methyllithium in THF (−78 °C, 10 min). The resultant 4-lithio-1,3-pentadienes (**16** and **20**) reacted smoothly with a variety of electrophiles (E^+) to produce the corresponding substituted dienes (**21** and **22**, Scheme II). Some of the results we have obtained are summarized in Table I.

Table I. Reaction of the 4-Lithio-1,3-pentadienes 16 and 20 with Electrophiles

nucleophile	electrophile[a]	product (% yield)[b]
16	n-$C_8H_{17}Br$	21, E = n-C_8H_{17} (71)
16	RCH_2CH_2Br[c]	21, E = RCH_2CH_2[c] (69)
16	RCH_2CHO[c]	21, E = $RCH_2CH(OH)$[c] (82)
16	cyclopentanone	21, E = 1-hydroxycyclopentyl (74)
20	n-$C_8H_{17}Br$	22, E = n-C_8H_{17} (62)
20	RCH_2CHO[c]	22, E = $RCH_2CH(OH)$[c] (76)

[a] All reactions were carried out in THF solution. When the electrophile was an alkyl halide, the solution was stirred at −78 °C for 1 h, allowed to warm to room temperature over a period of 1 h, and then quenched with aqueous ammonium chloride. With carbonyl electrophiles, the solution was stirred at −78 °C for 1 h and treated at this temperature with aqueous ammonium chloride. [b] Yield of distilled, purified product. [c] R = 2-cyclopentenyl.

The potential inherent in the preliminary results described above would appear to be considerable. For example, reaction of **16** and **20** (or other lithio dienes derived from esters such as **5**–**10**) with electrophiles containing suitably placed dienophilic unsaturation would, presumably, produce intermediates which should undergo intramolecular Diels–Alder reactions. These possibilities, along with others, are being actively investigated.

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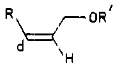
[12] Corey, E. J.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1969**, *91*, 1851.

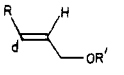
[13] Siddall, J. B.; Biskup, M.; Fried, J. H. *J. Am. Chem. Soc.* **1969**, *91*, 1853.

[14] The formation of vinyllithium reagents by transmetalation of trialkylvinylstannanes with an alkyllithium is well-known. For some recent reports, along with references cited therein, see: (a) ref 6; (b) Wollenberg, R. H. *Tetrahedron Lett.* **1978**, 717; (c) Chen, S. L.; Schaub, R. E.; Grudzinskas, C. V. *J. Org. Chem.* **1978**, *43*, 3450; (d) Collins, P. W.; Jung, C. J.; Gasiecki, A.; Pappo, R. *Tetrahedron Lett.* **1978**, 3187.

[15] In each of these reductions, the aldehyde product was accompanied by a small amount (~5–7%) of the corresponding alcohol (**14** and **18**, respectively), which could be removed readily by column chromatography on silica gel. With regard to these latter substances, two items deserve explicit mention. First, both **14** and **18** could be oxidized smoothly and efficiently to the aldehydes (**13** and **17**, respectively) by treatment with barium manganate in dichloromethane.[16] Second, compounds **14** and **18**, along with the alcohols derived by reduction of **5**, **7**, **8**, **10**, and similar esters, should serve as convenient precursors of pure, geometrically isomeric vinyllithium reagents which correspond to the general d^3 synthons[17] i and ii.[18]



i



ii

[16] Firouzabadi, H.; Ghaderi, E. *Tetrahedron Lett.* **1978**, 839.

[17] For a stimulating review on methods of reactivity umpolung, see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 239.

[18] For some recent examples of reagents corresponding to similar d^3 synthons, see ref 14c and: Posner, G. H.; Ting, J.-S.; Lentz, C. M. *Tetrahedron* **1976**, *32*, 2281; Corey, E. J.; Wollenberg, R. H. *Tetrahedron Lett.* **1976**, 4705; Corey, E. J.; Bock, M. G.; Kozikowski, A. P.; Rama Rao, A. V.; Floyd, D.; Lipshutz, B. *Ibid.* **1978**, 1051.

Stereochemical Aspects of the Intramolecular Diels-Alder Reactions of Methyl Deca-2,7,9-trienoates. 1. Thermal Cyclizations

Summary: The intramolecular Diels–Alder reactions of **1**, **8**, **11**, and **12** preferentially afford *trans*-perhydroindene cycloadducts independent of dienophile stereochemistry.

Sir: The intramolecular Diels–Alder reaction has proven to be useful for the synthesis of many polycyclic compounds including natural products.[1] Despite the considerable research devoted to understanding the structural and stereochemical features of this reaction in recent years, the stereochemical aspects of the Diels–Alder reactions of trienes bearing terminal dienophile activating groups have been little studied. For these systems, it is tempting to assume that the stereochemistry of the major product can

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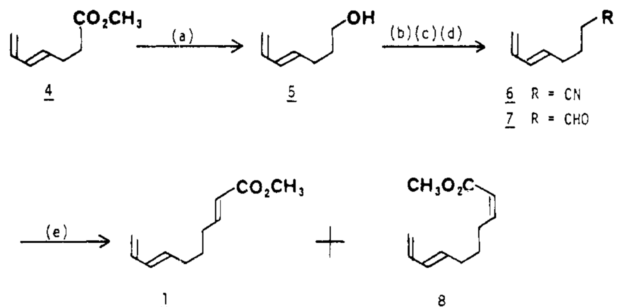
[1] (a) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (b) Oppolzer, W. *Synthesis* **1980**, 793. (c) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (d) Mehta, G. *J. Chem. Educ.* **1976**, *53*, 551. (e) Carlson, R. G. *Annu. Rep. Med. Chem.* **1974**, *9*, 270.

0022-3263/80/1945-4264$01.00/0

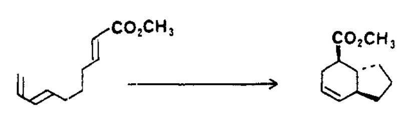
Scheme I[a]



4, 5, 6 R = CN, 7 R = CHO, 1, 8

[a] (a) $LiAlH_4$, Et_2O, 0 °C (79%); (b) CH_3SO_2Cl, Et_3N, CH_2Cl_2, 0 °C; (c) KCN, EtOH, reflux (77% from 5); (d) DIBAL, Et_2O, 0 °C; (e) $(C_6H_5)_3PCHCOOCH_3$ (47–60% of 1 and 4–5% of 8 from 6 in CH_2Cl_2).

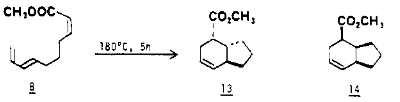
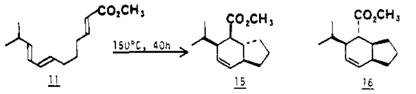
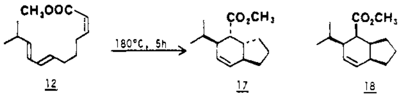
be predicted by the Alder endo rule. Such assumptions are encouraged by the general usefulness of this rule in intermolecular Diels–Alder reactions and by the report by House and Cronin that triene 1 cyclizes exclusively to trans-fused 2, the product of an endo cycloaddition reaction.[2] Indeed, this result is frequently cited[1] as evidence of the high selectivity of the intramolecular Diels–Alder reaction. However, we recently reported one example of a Diels–Alder reaction of an activated (*Z*,*E*,*E*)-deca-2,7,9-triene that violated the endo rule, and in other cases we have found that the cyclizations of (*E*,*E*,*E*)-trienes related to 1 are much less selective than expected in light of this precedent.[3] These results prompted us to reexamine the chemistry of 1[4] and to study a series of methyl (*E*,*E*,*E*)- and (*Z*,*E*,*E*)-deca-2,7,9-trienoates in order to define the stereochemical features of these Diels–Alder reactions. Toward this end we report herein on the thermal cyclizations of trienes 1, 8, 11, and 12. In the following communication we report on the Lewis acid catalyzed cyclizations of these trienes.[5]



1, 2

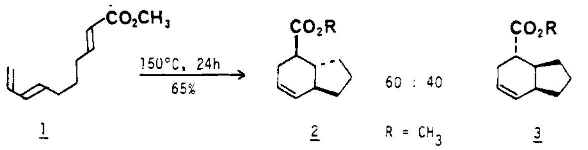
First, we consider a reexamination of the thermal chemistry of 1.[4] Triene 1 was prepared, starting from diene ester 4 (Scheme I), which is readily available from divinylcarbinol by an ortho ester Claisen rearrangement.[6] Reduction of 4 with $LiAlH_4$ in Et_2O (0 °C) afforded 79% of 5,[7a,b] which was converted into nitrile 6[7a,b] by mesylation (CH_3SO_2Cl, Et_3N, CH_2Cl_2, 0 °C) and substitution with KCN in refluxing EtOH (77% from 5). DIBAL reduction of 6 (1.1 equiv of DIBAL, Et_2O, 0 °C) afforded a volatile aldehyde, 7, which was not routinely purified. Condensation of crude 7 with a slight excess of [(carbomethoxy)methylidene]triphenylphosphorane in CH_2Cl_2 afforded 47–60% of 1[7a,8] and 4–5% of 8[7a,b] from 6.[9] The 250-MHz ^1H NMR spectrum of 1 so obtained revealed the presence of 7% of the *cis*-butadiene isomer, which undoubtedly derives from a minor product of the Claisen rearrangement.

Table I

reaction	yield,[a] %	trans/cis ratio[b]
 8, 13, 14	75	65:35[c]
 11, 15, 16	72	72:28[d]
 12, 17, 18	75	67:33[e]

[a] The combined yield of chromatographed products. [b] Ratio of trans-fused to cis-fused product. [c] GC analysis performed on a 10-ft, 4% SE-30/Chromosorb G column at 125 °C. [d] Inseparable by TLC or GC; product ratio assigned by NMR. [e] GC analysis performed at 150 °C on the column described in footnote *c*.

Cyclization of 1 at 150 °C (toluene, sealed tube, 24 h, 65%) afforded a 60:40 mixture (GC analysis) of cycloadducts 2 and 3. These compounds were separated by



1, 2, 9, 3, 10

the selective saponification procedure previously described[2] to afford the known acids 9 [mp 96.5–97.5 °C (lit.[2] mp 90–91 °C)] and 10 [mp 61.0–61.5 °C (lit.[2] mp 58.5–60 °C)]. Diazomethane esterification of 9 and 10 afforded 2 and 3, respectively, the spectroscopic properties of which were fully consistent with the published values. Clearly, the Diels–Alder reaction of 1 is much less selective than originally reported.[2] In fact, the cyclization of 1 is the least selective of all the decatrienoate Diels–Alder reactions studied to date (vide infra).

The results of the Diels–Alder reactions of the related trienes 8, 11,[7a,b,10] and 12[7a,b,10] are summarized in Table I.

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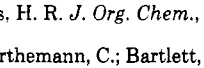
(2) House, H. O.; Cronin, T. C. *J. Org. Chem.* **1965**, *30*, 1061.

(3) Roush, W. R. *J. Org. Chem.* **1979**, *44*, 4008; *J. Am. Chem. Soc.* **1980**, *102*, 1390.

(4) House and Cronin prepared 1 by a nonstereoselective route and were unable to obtain isomerically pure 1. They found that a *mixture* of 1 and i (ratio unknown) cyclizes to a mixture of 2 and 3, and they established that isomerically pure i cyclizes exclusively to 3. It was assumed that 2 is the sole cycloadduct of 1 even though the amount of degenerate cyclization of 1 to 3 could not be determined. Accordingly, this conclusion regarding 1 is uncertain, and we therefore decided to reexamine this question.



i

(5) Roush, W. R.; Gillis, H. R. *J. Org. Chem.*, following paper in this issue.

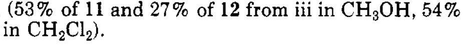
(6) Johnson, W. S.; Werthemann, C.; Bartlett, W. R.; Brockson, T. J.; Li, T.; Faulkner, D. J.; Peterson, M. R. *J. Am. Chem. Soc.* **1970**, *92*, 741. Divinylcarbinol was prepared by the method of: Ramsden, H. E.; Leebrick, J. R.; Rosenberg, S. D.; Miller, E. H.; Walburn, J. J.; Balint, A. E.; Cserr, R. *J. Org. Chem.* **1957**, *22*, 1602. The Claisen rearrangement affords 4 in 71% yield.

(7) (a) All new compounds were fully characterized by NMR, IR, and mass spectroscopy. (b) This compound or a crystalline derivative gave a satisfactory combustion analysis. (c) The elemental composition of this compound has been verified by high-resolution mass spectroscopy.

(8) Triene 1 was further characterized by condensation with maleic anhydride in refluxing benzene to give the known maleic anhydride Diels–Alder adduct: mp 96.5–97.5 °C (lit.[2] mp 96–97 °C); 84% yield. The maleic anhydride adduct[7a,b] of 8 had a melting point of 48.5–49 °C.

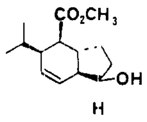
(9) The Wittig reaction of 7 in CH_3OH affords 35% of 1 and 18% of 8. See: House, H. O.; Jones, V. K.; Frank, G. A. *J. Org. Chem.* **1964**, *29*, 3327.

(10) Trienes 11 and 12 were synthesized as follows:

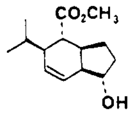


(i) Ac_2O, py (90%);[7a] (ii) Li_2CuCl_4, $BrMgCH_2CH_2CHOCH_2CH_2O$–, THF, −10 °C (65–70%)[7a,b] (iii) THF, H_2O, HOAc (80–85%); (iv) $(C_6H_5)_3PCHCOOCH_3$, (53% of 11 and 27% of 12 from iii in CH_3OH, 54% of 11 and 7% of 12 in CH_2Cl_2).

In each case, the major product contains a trans ring fusion. The structures of these compounds were assigned as follows.[11] Epimerization of 13[7a,c] with $NaOCH_3$ in CH_3OH (80 °C) followed by CH_2N_2 treatment afforded a 90:10 mixture of **2** and **13**. Similarly, **14**[7a,c] and **3** [**14** (47%) ⇄ **3** (53%)], **15**[7a,b] and **17**[7a,b] [**15** (15%) ⇄ **17** (85%)], and **18**[7a,c] and **16**[7a,c] (75% isolated yield of **16** from **18**) were correlated by ester epimerization. Isomers **15** and **16** prepared in this manner were identical in all respects with authentic samples prepared by deoxygenation of **19**[3] and **20**,[3] respectively [(i) NaH, CS_2, imidazole, THF, reflux, and then CH_3I; (ii) $(n\text{-}C_4H_9)_3SnH$, toluene reflux; 35% of **15** from **19** and 49% of **16** from **20**].[12]

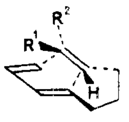


19

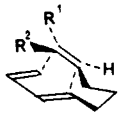


20

It is clear from inspection of this data that the selectivity for the trans-fused product is essentially independent of dienophile stereochemistry and that the endo rule fails to predict the outcome of the cyclizations of **8** and **12**.[13] This data also suggests that secondary orbital interactions are not significantly involved in determining the outcome of the cyclizations of trans trienes **1** and **11** since, to the extent that secondary orbital interactions stabilize an endo transition state, one expects to observe relatively more trans-fused product from the trans trienes and relatively more cis-fused product from the cis trienes. This tendency is not apparent in our data. In particular, **8** affords slightly more trans-fused product than does **1**. Rather, this selectivity is probably the consequence of strain and subtle nonbonded interactions within the chain bridging the diene and dienophile which destabilizes cis-fused transition state B relative to A, which leads to the major trans-fused products.[14]



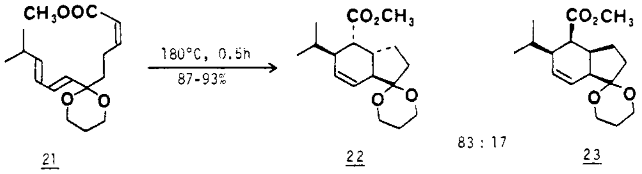
A



B

endo-1,11 R_1 = $COOCH_3$, R_2 = H exo-1,11
exo-8,12 R_1 = H, R_2 = $COOCH_3$ endo-8,12

In retrospect, the lack of secondary orbital control and the failure of the endo rule in these cases is not surprising since studies of the Diels–Alder reactions of open-chain dienes and dienophiles have shown that this rule is well obeyed only at low temperatures.[15] The energy difference separating the endo and exo transition states of such systems is usually small, and many violations of the endo rule are known.[15,16] The preferential formation of the trans-fused product and the lack of secondary orbital control illustrated by these examples are consistent with the cases previously reported from our laboratory[3] and appear to be general for trienes of this type.[17,18] Although the selectivity for the trans-fused product is slight in the cases reported herein, more highly functionalized 2,7,9-decatrienes are more selective for the trans-fused product, ratios of 83:17 not being uncommon; for example, the exo cyclization of **21** to **22** is the key step in an improved synthesis of the perhydroindenone precursor of dendrobine.[19] In certain cases, the selectivity of these Diels–Alder reactions is significantly improved by using Lewis acids. An account of the latter results appears in the accompanying communication.[5]



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(11) Spectroscoic data for **2**: NMR ($CDCl_3$, 250 MHz) δ 5.76 (br d, *J* = 10.0 Hz, 1 H), 5.52 (dq, *J* = 10.0, 3.0 Hz, 1 H), 3.61 (s, 3 H), 2.53 (dt, *J* = 7.0, 10.2 Hz, H_4), 2.35 (m, 1 H); IR (neat) 1735, 1640 cm^{-1}; mass spectrum, *m/e* 180 (parent ion). For **3**: NMR ($CDCl_3$, 250 MHz) δ 5.99 (dm, *J* = 10 Hz, 1 H), 5.74 (dm, *J* = 10 Hz, 1 H), 3.69 (s, 3 H), 2.43 (m, 1 H), 2.33 (m, 1 H), 2.20 (m, 1 H); IR (CCl_4) 1735, 1650 cm^{-1}; mass spectrum, *m/e* 180 (parent ion). For **9**: NMR ($CDCl_3$, 250 MHz) δ 5.83 (br d, *J* = 10 Hz, 1 H), 5.60 (dq, *J* = 10, 3 Hz, 1 H), 2.55 (dt, *J* = 10.7, 6.2 Hz, H_4), 2.36 (m, 1 H); IR (CCl_4) 3300–2500 (br), 1750, 1705, 1635 cm^{-1}; mass spectrum, *m/e* 166 (parent ion). For **10**: NMR ($CDCl_3$, 250 MHz) δ 5.75 (dm, *J* = 10 Hz, 1 H), 5.71 (dm, *J* = 10 Hz, 1 H), 2.45 (m, 1 H), 2.36 (m, 1 H), 2.25 (m, 1 H); IR (CCl_4) 3300–2500 (br), 1750 (weak), 1705, 1650 cm^{-1}; mass spectrum, *m/e* 166 (parent ion). For **13**: NMR ($CDCl_3$, 250 MHz) δ 5.86 (br d, *J* = 10 Hz, 1H), 5.60 (dm, *J* = 10 Hz, 1 H), 3.67 (s, 3 H), 3.00 (dd, *J* = 3.6, 6.6 Hz, H_4), 2.47 (dm, *J* = 17.5 Hz, 1 H), 2.29 (dm, *J* = 17.5 Hz, 1 H); IR (neat) 1730, 1640 cm^{-1}; mass spectrum, *m/e* 180 (parent ion). For **14**: NMR ($CDCl_3$, 250 MHz) δ 5.61 (m, 1 H), 5.42 (br d, *J* = 10 Hz, 1 H), 3.69 (s, 3 H), 2.82 (ddd, *J* = 3.8, 5.6, 11.6 Hz, H_4), 2.70 (m, 1 H), 2.50 (m, 1 H); IR (CCl_4) 1735, 1650 cm^{-1}; mass spectrum, *m/e* 180 (parent ion). For **15**: NMR ($CDCl_3$, 250 MHz) δ 5.95 (d, *J* = 10.0 Hz, 1 H), 5.55 (ddd, *J* = 10.0, 4.4, 2.6 Hz, 1 H), 3.65 (s, 3 H), 2.70 (dd, *J* = 11.4, 7.7 Hz, H_4), 2.60 (m, 1 H), 1.98 (m, 1 H), 0.96 (d, *J* = 7 Hz, 3 H), 0.84 (d, *J* = 7 Hz, 3 H); IR (neat) 1740, 1640 cm^{-1}; mass spectrum, *m/e* 222 (parent ion). For **16**: NMR ($CDCl_3$, 250 MHz) δ 5.89 (dt, *J* = 10, 4 Hz, 1 H), 5.58 (br d, *J* = 10 Hz, 1 H), 3.71 (s, 3 H), 2.37 (m, 3 H), 2.11 (dd, *J* = 10.8, 11.3 Hz, H_4), 0.99 (d, *J* = 7 Hz, 3 H), 0.80 (d, *J* = 7 Hz, 3 H); IR (CH_2Cl_2) 1735, 1650 cm^{-1}; mass spectrum, *m/e* 222 (parent ion). For **17**: NMR ($CDCl_3$, 250 MHz) δ 5.95 (dt, *J* = 10, 1.5 Hz, 1 H), 5.56 (dt, *J* = 10, 3 Hz, 1 H), 3.66 (s, 3 H), 2.81 (d, *J* = 4.9 Hz), 2.33 (m, 1 H), 0.95 (d, *J* = 7 Hz, 3 H), 0.92 (d, *J* = 7 Hz, 3 H); IR (neat) 1735, 1640 cm^{-1}; mass spectrum, *m/e* 222 (parent ion). For **18**: NMR ($CDCl_3$, 250 MHz) δ 5.81 (dt, *J* = 10, 2.5 Hz, 1 H), 5.70 (br d, *J* = 10 Hz, 1 H), 3.60 (s, 3 H), 2.93 (t, *J* = 4.9 Hz, H_4), 2.44 (m, 2 H), 0.99 (d, *J* = 7 Hz, 3 H), 0.92 (d, *J* = 7 Hz, 3 H); IR (neat) 1740, 1650 cm^{-1}; mass spectrum *m/e* 222 (parent ion).

(12) Barton, D. H. R.; McCombie, S. W. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1574.

(13) Control experiments were performed to establish that each of the cyclizations described herein is a kinetically controlled process.

(14) The greater relative stability of transition state A is apparent on examination of Dreiding models. First, bonding distances seem to be more easily attained in transition state A than in B if one considers the transition state geometry calculated by: Kikuchi, O. *Tetrahedron* **1971**, *27*, 2791. (It is important to keep in mind that the Diels–Alder reaction transition state cannot simply be described by assuming that the dienophile approaches the diene from a direction *directly above* the diene, since this arrangement of reacting components does not lead to the correct geometry of the initial boat cyclohexene Diels–Alder adduct. Rather, one must move the reacting components with respect to one another until the boat cyclohexene geometry is achieved.) Second, an eclipsing interaction between the C(4) methylene and C(8) H occurs in transition state B but not in A. On the basis of the product distribution data, transition state A is ~0.5–0.8 kcal mol^{-1} more stable than B for **1**, **8**, **11**, and **12**.

(15) Reviews: (a) Sauer, J. *Angew. Chem., Int. Ed. Engl.* **1967**, *6*, 16; (b) Onishenko, A. S. "Diene Synthesis" (English translation); Israel Program for Scientific Translations: Jerusalem, 1964. (c) Martin, J. G.; Hill, R. K. *Chem. Rev.* **1961**, *61*, 537.

(16) For example, see: Berson, J. A.; Hamlet, Z.; Mueller, W. A. *J. Am. Chem. Soc.* **1962**, *84*, 297.

(17) (a) To date we have examined the cyclizations of 12 different methyl deca-2,7,9-trienoates, seven of which contain cis dienophiles. In all cases, the trans-fused product predominates. (b) The failure of the endo rule also extends to methyl undeca-2,8,10-trienoates. These results will be reported separately: Roush, W. R.; Hall, S. E., unpublished results.

(18) Exception: placement of the activating group on the bridge separating the diene and the dienophile shifts the selectivity to the cis-fused product: Bajorek, J. J. S.; Sutherland, J. K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 1559. With 1,2-diactivated dienophiles, the trans-fused product is formed almost exclusively: Gschwend, H. W.; Lee, A. O.; Meier, H.-P. *J. Org. Chem.* **1973**, *38*, 2169; Gschwend, H. W.; Meier, H.-P. *Angew. Chem.* **1972**, *84*, 281; Gschwend, H. W. *Helv. Chim. Acta* **1973**, *56*, 1763; Auerbach, J.; Weinreb, S. M. *J. Org. Chem.* **1975**, *40*, 3311; White, J. D.; Sheldon, B. G.; Solheim, B. A.; Clardy, J. *Tetrahedron Lett.* **1978**, 5189; Cox, T. T. *J. Chem. Soc., Chem. Commun.* **1975**, 903. A terminal activating group is essential for maximum selectivity: Oppolzer, W.; Fehr, C.; Warneke, J. *Helv. Chim. Acta* **1977**, *60*, 48; Roush, W. R.; Peseckis, S. M., unpublished results.

(19) Roush, W. R.; Gillis, H. R. *J. Org. Chem.*, in press.

Stereochemical studies of other systems are in progress.

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Stereochemical Aspects of the Intramolecular Diels–Alder Reactions of Methyl Deca-2,7,9-trienoates. 2. Lewis Acid Catalysis

Summary: The Lewis acid catalyzed intramolecular Diels–Alder reactions of all-trans trienes **1** and **2** afford exclusively the trans-fused cycloadducts; in contrast, mixtures of cis- and trans-fused cycloadducts are obtained from the catalyzed cyclizations of trienes **3** and **4**, the cis dienophile isomers of **1** and **2**.

Sir: We have studied the intramolecular Diels–Alder reactions of a series of methyl deca-2,7(*E*),9-trienoates and have found that the thermal cyclizations of these trienes preferentially afford trans-perhydroindene cycloadducts independent of dienophile stereochemistry.[1] The selectivity for the trans-fused product ranges from 60:40 in the least favorable case to a maximum of 83:17. Hopeful that the selectivity of these cyclizations could be altered or improved by Lewis acid catalysis,[2] we have initiated studies on this problem. We are pleased to report herein that the Diels–Alder reactons of trienes **1**–**4**[1] are subject to catalysis and that *in the presence of Lewis acids all-trans trienes 1 and 2 afford exclusively the corresponding trans-fused cycloadducts.*

Previous attempts to catalyze intramolecular Diels–Alder reactions have met with limited success. Prior to this study, only three examples of catalyzed intramolecular Diels–Alder reactions had been reported.[3,4] The rate accelerations observed in these cases have been only modest, and changes in product selectivity of the type frequently encountered in catalyzed bimolecular Diels–Alder reactions[2] were unknown. The results reported in Table I for **1** and **2** represent the first significant examples of both phenomena in an intramolecular Diels–Alder reaction. Whereas the thermal cyclizations require temperatures of at least 150 °C for a practical rate of cyclization, the catalyzed reactions are conveniently performed at temperatures below 50 °C—*in most cases at room temperature*—depending on the Lewis acid employed. These two reactions are also highly stereoselective, as noted above.

Typically, these cyclizations were performed by adding a Lewis acid to a solution of triene in CCl_4 or CH_2Cl_2 under an inert atmosphere, except for the reactions catalyzed by menthoxyaluminum dichloride[5] which were performed in a toluene–CH_2Cl_2 cosolvent mixture.[6] In most cases, stoichiometric quantities of Lewis acid were required for complete cyclization. The progress of the reactions was monitored by TLC or ^1H NMR spectroscopy. When complete as judged by these analytical methods, the reactions were worked up by aqueous extraction, and the cyclization products were then isolated by standard techniques.

The yield of cyclization product depends on the choice and amount of Lewis acid used, as triene polymerization competes with cyclization in nearly all of the examples reported in Table I. This problem is most serious with triene **4** and when $BF_3{\cdot}Et_2O$, $TiCl_4$, or $SnCl_4$ is used as catalyst. Polymerization is also a problem with $AlCl_3$ and $EtAlCl_2$,[7] two of the more efficient Lewis acids used in this study, but is minimized by limiting the amount of these reagents employed (entries 3, 4, 6, 7, 14, 15). Best results were obtained with **1** with $AlCl_3$, $EtAlCl_2$, Et_2AlCl, or menthoxyaluminum dichloride, and these reagents were therefore the only Lewis acids studied with **2**–**4**. Although acceptable yields of cycloadducts from **2** and **3** were obtained using $AlCl_3$, we favor use of $EtAlCl_2$, Et_2AlCl, or menthoxyaluminum dichloride because of their mildness and ease of handling.[8]

In contrast to the excellent selectivity and good yields of product realized with **1** and **2**,[9] the catalyzed cyclizations of cis trienes **3** and **4** are not improved relative to the thermal reactions either in terms of product yield or in terms of a significant change in product selectivity. The moderate change in selectivity realized with **4** and the lack of a change with **3** imply that increased secondary orbital control resulting from an interaction between the ester carbonyl and the Lewis acid,[10] which presumably accounts for the increased selectivity with **1** and **2**,[2] is insufficient to overcome the transition-state preference for the trans-fused product noted in the thermal cyclizations.[1,11]

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(1) Roush, W. R.; Ko, A. I.; Gillis, H. R. *J. Org. Chem.*, preceding paper in this issue, and references cited therein.

(2) Lewis acid catalysis is very effective in improving the selectivity of bimolecular Diels–Alder reactions; see: Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976; pp 161–165; Houk, K. N.; Strozier, R. W. *J. Am. Chem. Soc.* **1973**, *95*, 4046; Houk, K. N. *Acc. Chem. Res.* **1975**, *11*, 361 and references therein.

(3) (a) Wenkert, E.; Naemura, K. *Synth. Commun.* **1973**, *3*, 447. (b) DeClercq, P. J.; Van Royen, L. A. *Ibid.* **1979**, *9*, 771. (c) Mukaiyama, T.; Tsuji, T.; Iwasawa, N. *Chem. Lett.* **1979**, 697. See also: Mukaiyama, T.; Iwasawa, N.; Tsuji, T.; Narasaka, K. *Ibid.* **1979**, 1175.

(4) Unsuccessful attempts have also been reported: (a) Parker, K. A.; Adamchuk, M. R. *Tetrahedron Lett.* **1978**, 1689; (b) Evans, A. J. Ph.D. Thesis, University of Minnesota, 1975.

(5) Hayakawa, Y.; Fueno, T.; Furukawa, J. *J. Polym. Sci.* **1967**, *5*, 2099. Racemic menthoxyaluminum dichloride was used throughout this study. The chiral catalyst has been previously applied to bimolecular Diels–Alder reactions: Hashimoto, S.-I.; Korneshima, N.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 437.

(6) The $AlCl_3$-catalyzed cyclizations of **1** and **3** performed in toluene give poor results, owing to Friedel–Crafts reaction with the solvent.

(7) $EtAlCl_2$ has previously been used as a catalyst for ene reactions: Snider, B. B.; Rodini, D. J.; Conn, R. S. E.; Sealfon, S. *J. Am. Chem. Soc.* **1979**, *101*, 5283.

(8) $EtAlCl_2$ and Et_2AlCl are commercially available as 25% solutions in either hexane (Alfa) or toluene (Aldrich). Menthoxyaluminum dichloride is conveniently prepared in situ from menthol and $EtAlCl_2$ (toluene).

(9) The lower yields of **7** from **2** are in part a consequence of the volatility of this compound.

(10) Evidence that such complexation occurs is provided by the observation that the ^1H NMR signals for the methoxyl groups and C(3) H of **1**–**4** are shifted in the presence of 1.0 equiv of $EtAlCl_2$. Invariably, the methoxyl signal is shifted upfield, whereas the resonance for C(3) H is shifted downfield.

(11) Control experiments established that mixtures of **5** and **6**, **7** and **8**, **9** and **10**, and **11** and **12** are stable toward $EtAlCl_2$ under the conditions reported in Table I. Thus, it is unlikely that the product ratios reported for other Lewis acids reflect selective decomposition of the cis-fused cycloadducts.

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