Hydroxy-5-methyl-4-undecanone (4f): IR (neat) 3400, 1700; NMR (CCl_4) 0.6–2.9 (m, 19 H), 2.0–2.5 (m, 3 H), 2.7–3.1 (b s, 1 H), 3.2–3.8 (m, 1 H).

1,5-Diphenyl-1-hydroxy-2-methyl-3-pentanone (4g): IR (neat) 3410, 1700; NMR (CCl_4) 0.70 (d, J = 6 Hz) and 1.05 (d, J = 10 Hz, 3 H), 2.2–3.9 (m, 4 H), 3.45 (m, 1 H), 3.2–4.0 (b s, 1 H), 4.53 (d, J = 6 Hz) and 4.76 (d, J = 10 Hz, 1 H), 7.05 (s, 5 H), 7.12 (s, 5 H). Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.77; H, 7.36. The erythro to threo ratio was determined by comparison of the ratio of benzylic protons appearing at 4.76 (erythro) and 4.53 (threo).

Registry No. **1a**, 66581-82-6; **1c**, 70280-36-3; **1e**, 70280-37-4; **1g**, 69583-57-9; **3a**, 62730-80-7; **3b**, 70280-44-3; **3c** (isomer 1), 71699-15-5; **3c** (isomer 2), 71699-16-6; **3d**, 70280-40-9; **3e**, 92694-77-4; **3f**, 92694-78-5; **3g**, 70280-45-4; **4a**, 62731-45-7; **4b**, 70280-38-5; **4e**, 70280-41-0; **4f**, 70280-42-1; **4g** (isomer 1), 77189-68-5; **4g** (isomer 2), 77189-62-9; **5**, 62510-08-1; LDA, 4111-54-0; BF_3OEt_2, 109-63-7; $TiCl_4$, 7550-45-0; $SnCl_4$, 7646-78-8; $C_6H_5CH{=}O$, 100-52-7; $C_8H_{17}CH{=}O$, 124-19-6; $C_5H_{11}CH{=}O$, 66-25-1; $ClCH_2CH(OCH_3)_2$, 97-97-2; $C_6H_5CH_2CH_2(CO)CH_2SiMe_3$, 92694-79-6; 5-chloro-4-methoxy-3-(phenylmethyl)pentan-3-one, 70280-48-7.

Hydrofluoric Acid Catalyzed Intramolecular Diels–Alder Reactions[1]

William R. Roush,*[2] Herbert R. Gillis, and Amy P. Essenfeld

Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received October 20, 1983

Studies of catalysis of intramolecular Diels–Alder reactions of trienes activated with substituted 2-hydroxyethyl esters are described. Triene esters **1**, **11**, **22**, and **26** cyclize in moderate to good yield (44–78%) when exposed to aqueous HF in acetonitrile at 23 °C. These results appear not to be the consequence of simple protic acid catalysis since trienes **5**, **13**, **14**, and **33** fail to cyclize under analogous conditions. Rather, a mechanism involving the cyclization of a reversibly generated dioxolenium ion (e.g., **16**) is proposed. Although very little relative asymmetric induction was realized, these hydrofluoric acid promoted cyclizations proved to be highly stereoselective otherwise. Products of endo cycloaddition were obtained exclusively in the cyclizations of **11**, **26**, and **30**, and the cyclization of **22** was more selective (96:4 mixture of endo and exo cycloadducts) than the Lewis acid assisted cyclization of methyl ester **35** (88:12). The method at present is limited to intramolecular cases since the cyclization of crotonate **41** with cyclopentadiene proceeded in very poor yield. Trienes possessing diene allylic alkoxyl groups (e.g., **38**) and (*Z*)-α,β-unsaturated dienophiles (e.g., **39**) are also unsuited substrates for this reaction.

For several years we have been interested in synthetic applications of intramolecular Diels–Alder reactions.[3,4] We have studied the stereochemistry of the cyclizations of activated deca-2,7,9-trienes and undeca-2,8,10-trienes and have shown that in many cases the best product ratios are obtained when the cycloadditions are performed in the presence of Lewis acids.[5] Unfortunately, a number of substrates decompose and fail to cyclize when exposed to Lewis acidic reagents. In addition, our preliminary studies of enantioselective intramolecular cycloadditions (which require Lewis acid catalysis for maximal stereochemical induction)[5b] afforded results far short of expectations based on bimolecular Diels–Alder analogies.[6]

In an attempt to extend Lewis acid catalysis to recalcitrant triene systems and to improve the facial selectivity in cyclizations of trienes possessing chiral dienophiles, we have studied the Lewis acid catalyzed cyclizations of trienes activated with 2-hydroxyethyl esters (cf. **1a**).[7] We imagined that treatment of such systems with an appropriate organometallic reagent (e.g., $EtAlCl_2$, $MeTiCl_3$,[8] or $MeNbCl_4$[9]) would effect cyclization via an internally coordinated alkoxymetal halide complex (e.g., **1a** → **2** → **3a**).[10] In principle, this would enable reactive or unstable functional groups to be isolated from the Lewis acid and, at the same time, restrict the number of degrees of freedom

(1) Portions of this work are described in the Ph.D. Thesis of H. R. Gillis, Massachusetts Institute of Technology, Cambridge, MA 1982.

(2) Holder of the Roger and Georges Firmenich Career Development Chair in Natural Products Chemistry, 1981–84; Fellow of the Alfred P. Sloan Foundation, 1982–84.

(3) Reviews: (a) Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 183. (b) Ciganek, B. *Org. React. (N.Y.)*, in press. (c) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (d) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10.

(4) See, for example: (a) Hall, S. E.; Roush, W. R. *J. Org. Chem.* **1982**, *47*, 4611. (b) Roush, W. R.; Peseckis, S. M. *Tetrahedron Lett.* **1982**, *23*, 4879. (c) Roush, W. R.; Myers, A. G. *J. Org. Chem.* **1981**, *46*, 1509. (d) Roush, W. R. *J. Am. Chem. Soc.* **1980**, *102*, 1390. (e) Roush, W. R.; Peseckis, S. M.; Walts, A. E. *J. Org. Chem.* **1984**, *49*, 3429.

(5) For leading references, see: (a) Roush, W. R.; Gillis, H. R. *J. Org. Chem.* **1982**, *47*, 4825. (b) Roush, W. R.; Gillis, H. R.; Ko, A. I. *J. Am. Chem. Soc.* **1982**, *104*, 2269. For other recent examples of catalyzed intramolecular Diels–Alder reactions, see: (c) Stork, G.; Clark, G.; Shiner, C. S. *J. Am. Chem. Soc.* **1981**, *103*, 4948. (d) Funk, R. L.; Zeller, W. E. *J. Org. Chem.* **1982**, *47*, 180. (e) Sternbach, D. D.; Rossana, D. M. *J. Am. Chem. Soc.* **1982**, *104*, 5853. (f) Bailey, M. S.; Brisdon, B. J.; Brown, D. W.; Stark, K. M. *Tetrahedron Lett.* **1983**, *24*, 3037. (g) Sakan, K.; Craven, B. M. *J. Am. Chem. Soc.* **1983**, *105*, 3732. (h) Shea, K. J.; Gilman, J. W. *Tetrahedron Lett.* **1983**, *24*, 657. (i) Attah-Poku, S. K.; Gallacher, G.; Ng, A. S.; Taylor, L. E. B.; Alward, S. J.; Fallis, A. G. *Ibid.* **1983**, *24*, 677. (j) See also the literature cited in ref 11.

(6) (a) Ensley, H. E.; Parnell, C. A.; Corey, E. J. *J. Org. Chem.* **1978**, *43*, 1610. (b) Boeckman, R. K., Jr.; Naegely, P. C.; Arther, S. D. *Ibid.* **1980**, *45*, 752. (c) Oppolzer, W.; Kurth, M.; Reichlin, D.; Moffatt, F. *Tetrahedron Lett.* **1981**, *22*, 2545. (d) Oppolzer, W.; Chapuis, C.; Dao, G. M.; Reichlin, D.; Godel, T. *Ibid* **1982**, *23*, 4781. (e) Oppolzer, W.; Kurth, M.; Reichlin, D.; Chapuis, C.; Mohnhaupt, M.; Moffatt, F. *Helv. Chim. Acta* **1981**, *64*, 2802. (f) Oppolzer, W.; Chapuis, C.; Kelly, M. *Ibid.* **1983**, *66*, 2358. (g) Helmchen, G.; Schmierer, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 208. (h) Choy, W.; Reed, L. A., III; Masamune, S. *J. Org. Chem.* **1983**, *48*, 1137. (i) Masamune, S.; Reed, L. A., III; Davis, J. T.; Choy, W. *J. Org. Chem.* **1983**, *48*, 4441. (j) Note added in proof. See also: Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1984**, *106*, 4261.

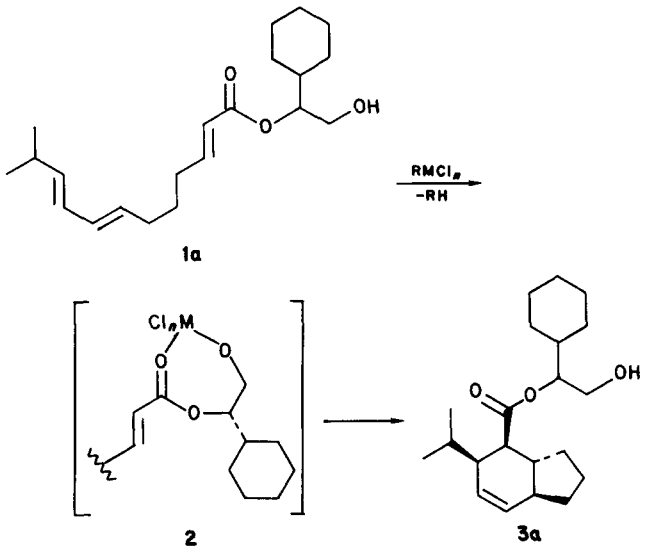
(7) These studies are decribed fully in ref 1.

(8) DeVries, H. *Recl. Chim.* **1961**, *80*, 866.

(9) Santini-Scampucci, C.; Riess, J. G. *J. Chem. Soc., Dalton Trans.* **1973**, 2436; **1974**, 1433.

(10) Alkoxyaluminum dichlorides are excellent catalyst for Diels–Alder reactions: see ref 5a,b and Hashimoto, S.-I.; Komeshima, N.; Koga, K. *J. Chem. Soc., Chem. Commun.* **1979**, 437.

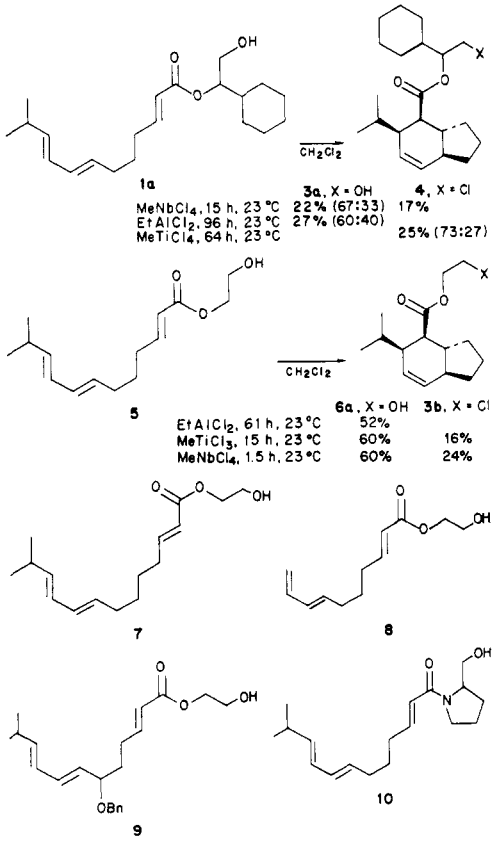
0022-3263/84/1949-4674$01.50/0



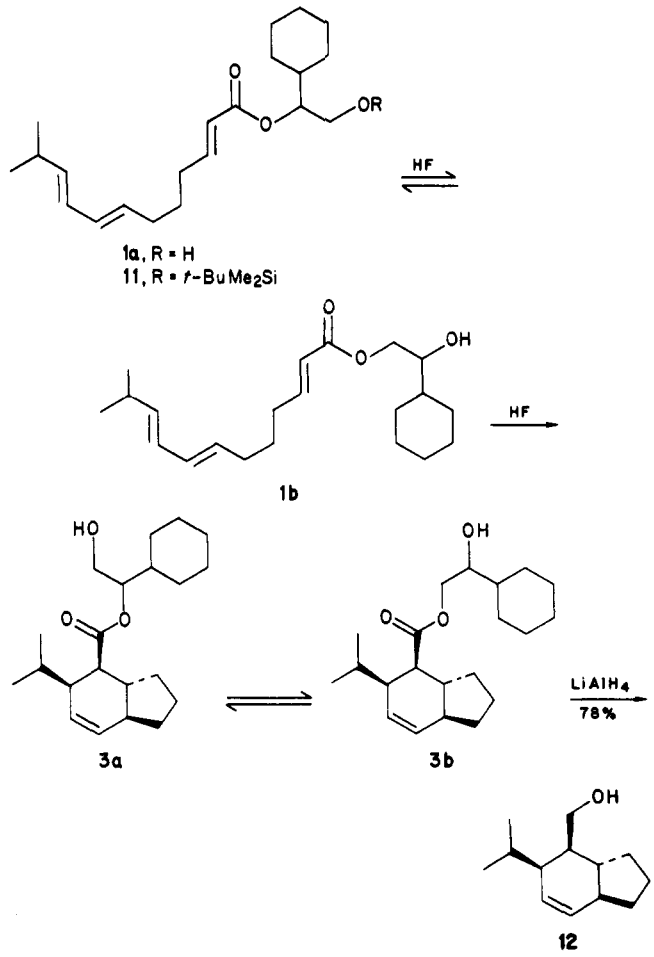
available to the chiral dienophile, thereby increasing dienophile facial selectivity.[11] In practice, however, our results with a variety of systems including 1 fell far short of our original objectives.[7,12]

(11) Several applications of this strategy to intramolecular Diels–Alder reactions of furans were reported by Mukaiyama during the initial stages of our work: (a) Takebayashi, T.; Iwasawa, N.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1107. (b) Mukaiyama, T.; Iwasawa, N. *Chem. Lett.* **1981**, 29. (c) Mukaiyama, T.; Takebayashi, T. *Ibid.* **1980**, 1013. (d) Mukaiyama, T.; Tsuji, T.; Iwasawa, N. *Ibid.* **1979**, 697.

(12) Initial results obtained with triene **5** were encouraging (see below; 0.9–0.95 equiv of stock solutions of the organometallic reagents were employed in each case). With **1**, however, the yield of cyclization products was much lower (25–39%) and the degree of stereochemical induction (diastereomer ratios are noted in parentheses next to product yields) was only moderate. Olefin polymerization was a serious problem with **7** and especially **8**, whereas triene **9** rapidly decomposed with evolution of benzyl alcohol when exposed to $EtAlCl_2$, $MeTiCl_3$, or $MeNbCl_4$. Finally, The $-AlCl_2$, $-TiCl_3$, and $-NbCl_4$ complexes of **10** were extremely inert (in the absence of excess organometallic reagent) and failed to cyclize within 16–20 h at 23 °C.



During these studies, however, we discovered a mechanistically interesting and potentially useful transformation. Prolonged exposure of (+)-**1a**, or its precursor *t*-$BuMe_2Si$ ether (**11**), to dilute aqueous HF in an acetonitrile–CH_2Cl_2



cosolvent mixture, conditions used originally for deprotection of **11**,[13] established an acyl transfer equilibrium between **1a** and **1b**. This reversible acyl transfer was accompanied by a slower, irreversible[14] Diels–Alder cyclization which afforded a (presumably equilibrium) mixture of adducts **3a** and **3b**. This Diels–Alder reaction required approximately 72 h to reach completion at 23 °C.[15] The major product from this reaction, **3b** (a mixture of diastereomers enantiomeric within the perhydroindene nucleus), was easily purified by SiO_2 chromatography (56% yield). Alternatively, the crude mixture of acyl transfer isomers was reduced with $LiAlH_4$ to afford alcohol **12**.[5b] In this manner, *t*-$BuMe_2Si$ ether **11** was converted directly into **12** in an overall yield of 78% without the necessity of isolating and purifying any intermediates. Since none of the cis-fused isomer of **12** was detected, the endo/exo selectivity of this cyclization was ≤98:2. Unfortunately, alcohol **12** so obtained was less than 1% optically pure as determined by comparison of its specific rotation to that

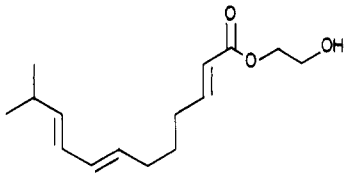
(13) Newton, R. F.; Reynolds, D. P. *Tetrahedron Lett.* **1979**, 3981.

(14) Control experiments established the stability of the products under the cyclization conditions.

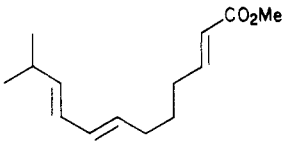
(15) Best results were realized when **1a** or **11** was treated with 2 equiv of 1.2% HF in a 19:20:1 mixture of CH_3CN, CH_2Cl_2 and H_2O. Acids other than hydrofluoric, however, were not successful catalysts for the cyclization of **1a** or **11**. In particular, triene **1a** was unaffected by acetic acid, trifluoroacetic acid catalyzed only acyl transfer, and dilute hydrochloric acid in CH_3CN–CH_2Cl_2 promoted rapid deconjugation of the dienophilic double bond as well as butadiene polymerization.

of optically pure material.[5b]

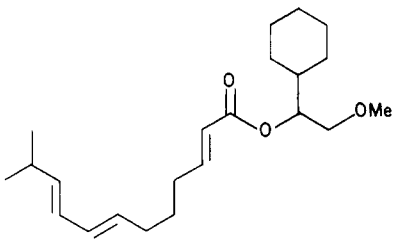
Proton-catalyzed *bimolecular* Diels–Alder reactions are well-known.[16] In addition, Stork has reported an example of an intramolecular Diels–Alder reaction catalyzed by trifluoroacetic acid.[5c] We suspect, however, that the results with **1a**/**11** are not the consequence of simple protic acid catalysis since attempts to effect the cyclizations of **5**, **13**, or **14**[17] with 4–8 equiv of HF under the usual conditions



5



13

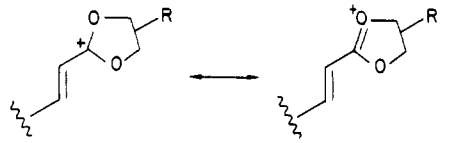


14

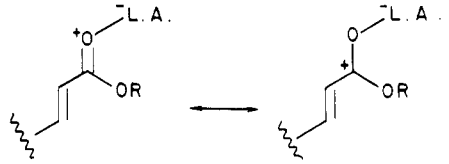
(48–72 h) were unsuccessful. In each instance, triene was recovered unchanged (91% recovery in the case of **14**) and cyclization products were not detected.

The experiments with **13** and **14** are particularly enlightening since they indicate that the *free* hydroxyl group in **1a**/**1b** is essential for cyclization to proceed. The mechanism which we propose to account for these observations is outlined in Scheme I. Central to this proposition is the reversible generation of dioxolenium ion **16**[18] which cyclizes irreversibly to **17**. This intermediate then hydrolyzes to a mixture of cycloadducts **3a** and **3b**. That triene **5** fails to cyclize under these conditions can be rationalized by noting that alkyl substituents are well-known to increase both the rate of formation and the thermodynamic stability of many types of ring systems.[19] In the case at hand, the presence of a bulky cyclohexyl group in **1** should facilitate closure to the dioxolane ring and increase the thermodynamic stability of the resulting hemiortho ester intermediate **15**. This would tend to increase both the rate of formation and the equilibrium concentration **15**, and hence the overall rate of cyclization, relative to the situation when unsubstituted triene **5** is employed as substrate.[18b] Additional data subsequently described is also consistent with this rationale.[20]

That **16** should cyclize readily to **17** seems reasonable from several points of view. First of all, dioxolenium **16**

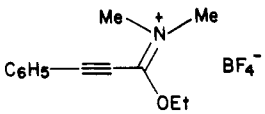


16

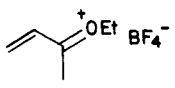


19 (L.A. = Lewis acid)

is electronically similar to the putative reaction intermediates (e.g., **19**) generated in Lewis acid catalyzed Diels–Alder reactions of α,β-unsaturated esters. NMR studies have shown that ions **19** are the dominant, if not sole, species present in solution when α,β-unsaturated carbonyl compounds are treated with various Lewis acids.[21] Second, Viehe has shown that acetylenic and vinylic amidium salts (e.g., **20**) are very reactive dienophiles in Diels–Alder



20



21

reactions with cyclopentadiene.[22] Finally, several examples of Diels–Alder reactions of α,β-unsaturated ketones catalyzed by Meerwein's salt ($Et_3O^+BF_4^-$) were recently reported.[23] These conversions probably proceed via onium salt intermediates such as **21** as the dienophile.

We were interested in the scope of this cycloaddition process and consequently studied a number of additional examples (see Table I). The cyclization of **22** (via **23**) proceeded smoothly to give a 96:4 mixture of endo (**24**) and exo (**25**) alcohols in 76% yield following reduction of the mixture of crude cycloadducts. It is interesting to note that the cyclization of **23** is much more stereoselective than the Lewis acid assisted cyclization of methyl ester **35**.[5a] The results with **26**, **30**, and **33** reemphasize the dependence of the efficiency of cyclization on the substitution pattern of the glycol ester. In fact, these results parallel the trend expected for a pathway involving dioxolenium ion intermediates based on the equilibrium constants for acetonide formation from the various diols.[24] We believe that it

(16) (a) Rubin, W.; Steiner, H.; Wassermann, A. *J. Chem. Soc.* **1949**, 3046. (b) Rodgman, A.; Wright, G. F. *J. Org. Chem.* **1953**, *18*, 465. (c) Wassermann, A. "Diels–Alder Reactions"; Elsevier: Amsterdam, 1965; pp 65–71.

(17) Triene **14** was prepared by treating **1a** with NaH and CH_3I in DME at 23 °C (48% yield). An inseparable mixture (55:45) of acyl transfer isomers was obtained and was used as such in the experiments described in text. One isomer only is shown for convenience.

(18) (a) The generation and reactivity of hemiortho ester intermediates has been reviewed recently: Deslongchamps, P. "Stereoelectronic Effects in Organic Chemistry"; Pergamon Press: Oxford, 1983, Chapter 3. (b) For kinetic and mechanistic studies on the generation of hemiortho esters and dioxolenium ions from glycol monoesters, see: McClelland, R. A.; Ahmad, M.; Bohonek, J.; Gedge, S. *Can. J. Chem.* **1979**, *57*, 1531. Guthrie, J. P. *Ibid* **1977**, *55*, 3562.

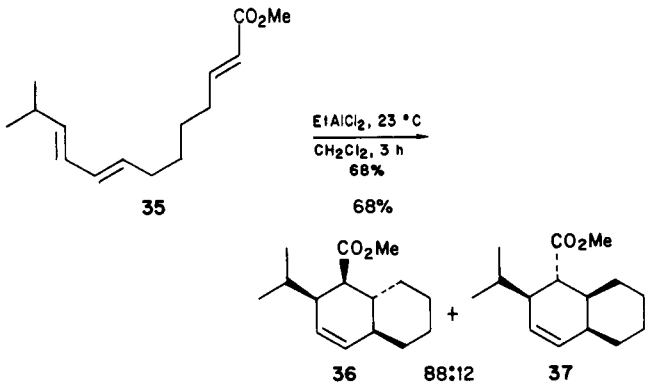
(19) For a review, see: Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962; Chapter 7.

(20) A referee, however, has suggested that the difference in reactivity of **1a**, **5**, **13**, and **34** may be due to differences in the basicity of their esters and thus their susceptibility to protonation and HF catalysis. Increasing alkyl substitution in the ester alkoxy moiety is known to increase the polarization of the carbonyl group (Dybal, J.; Stokr, J.; Schneider, B. *Collect. Czech. Chem. Commun.* **1982**, *47*, 2027) and increases the equilibrium constant of association with proton donors (Kamlet, M. J.; Solomonovici, A.; Taft, R. W. *J. Am. Chem. Soc.* **1979**, *101*, 3734. Gramstad, T. *Spectrochim. Acta* **1963**, *19*, 497). We believe that the failure of methyl ether **14** to cyclize under conditions which effect smooth conversion of **11** (or **1a**) to a mixture of **3a** and **3b** is inconsistent with this proposal and therefore favor the dioxolenium ion pathway discussed in text.

(21) Childs, R. F.; Mulholland, D. L.; Nixon, A. *Can. J. Chem.* **1982**, *60*, 801, 809.

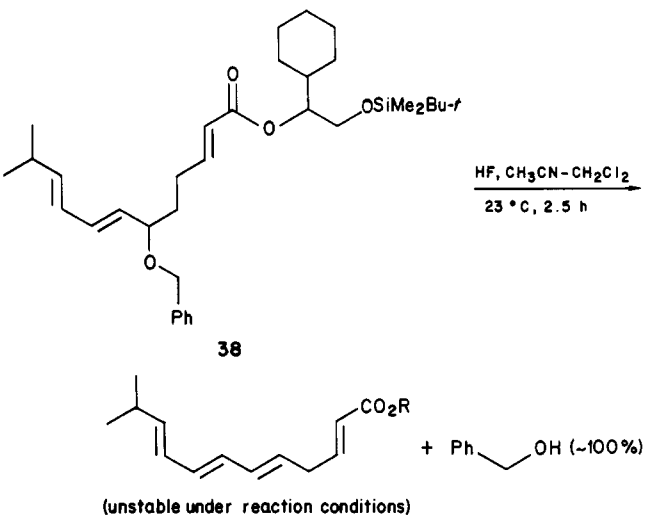
(22) (a) Baum, J. S.; Viehe, H. G. *J. Org. Chem.* **1976**, *41*, 183. (b) Viehe, H. G.; Baum, J. S., unpublished results. We thank Prof. Viehe for providing a copy of Dr. Baum's research report.

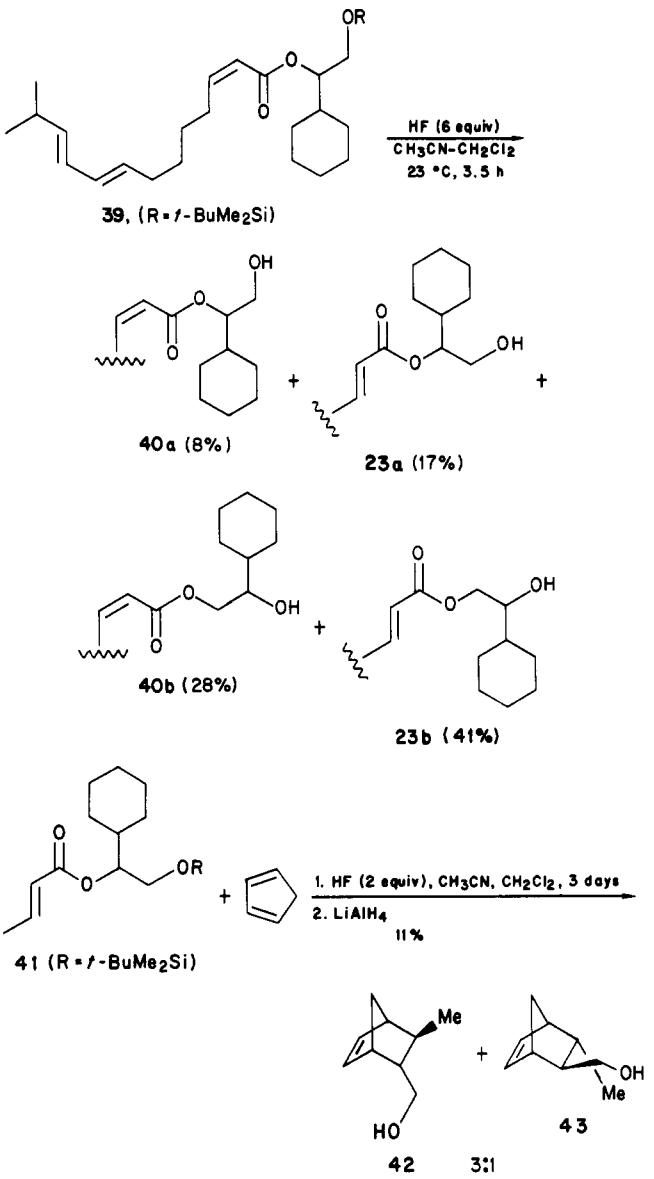
(23) Sasaki, T.; Ishibashi, Y.; Ohno, M. *Tetrahedron Lett.* **1982**, *23*, 1693.



should be possible to use this paradigm to design more efficient dienophilic ligands.

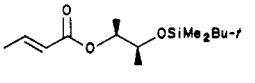
Although this cyclization protocol constitutes the mildest set of reaction conditions which we have used to catalyze intramolecular Diels–Alder reactions, these conditions are still far too acidic for diene allylic ethers to survive. For example, treatment of **38** in the prescribed manner afforded near quantitative yields of benzyl alcohol after a 2.5-h reaction period. (*Z*)-α,β-Unsaturated esters are also unsuited as the dienophilic component, for rapid double-bond isomerization precedes intramolecular cyclization. Exposure of ester **39** to 6 equiv of the HF–acetonitrile reagent for 3.5 h at 23 °C, for example, afforded 8% of deprotected (*Z,E,E*)-triene **40a**, 28% of acyl transfer isomer **40b**, 17% of (*E,E,E*)-triene **23a**, and 41% of its acyl transfer isomer **23b**. Prolonged exposure of **40a** or **40b** to the HF system afforded only products of cyclization of **23**. Finally, all attempts thus far to apply this procedure to bimolecular Diels–Alder reactions has met with very limited success (cf. the reaction of **41** with cyclopentadiene).[25]





(24) Anteunis, M.; Rommelaere, Y. *Bull. Chim. Soc. Belg.* **1970**, *79*, 523.

(25) (a) Excess cyclopentadiene (2 equiv) was used in the Diels–Alder reaction with crotonate **41**. Control experiments establish that no reaction occurred in the absence of HF. (b) The identity and stereochemistry of adducts **42** and **43** was confirmed by comparison with authentic samples; see, Abraham, R. J.; Coppell, S. M.; Ramage, R. *Org. Magn. Reson.* **1974**, *6*, 658. (c) No Diels–Alder reaction was observed when **41** was treated with isoprene or cyclohexadiene in the HF system. (d) The Diels–Alder reaction of cyclopentadiene and dienophile ii also proceeded in low yield (10–12% of **42–43** after $LiAlH_4$ reduction).



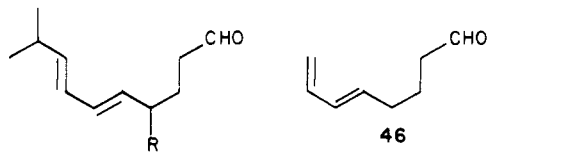
ii

Synthesis of Cyclization Substrates. All triene esters were prepared by Wadsworth–Emmons–Horner condensations[26] of readily available aldehydes **44–47**[4d,5a,b] with phosphonate reagents **48–51**. The latter were prepared by selective monosilylation of the parent glycol followed by acylation with bromoacetyl bromide and pyridine and then treatment with triethyl phosphite in hot toluene. Crotonate **41** was prepared by DCC-mediated esterification of crotonic acid and 1-cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethanol.

Experimental Section

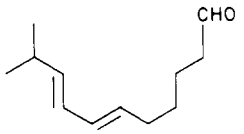
^1H NMR spectra were measured at 250 and 270 MHz on Bruker 250- and 270-MHz instruments and at 60 MHz on Perkin-Elmer R-24B and Varian T-60 instruments. Chemical shifts are reported in δ units relative to internal Me_4Si. Infrared spectra were measured on a Perkin-Elmer Model 283B infrared spectrophotometer and were calibrated with the 1601-cm^{-1} absorption of polystyrene. Low-resolution mass spectra were measured at 70 eV on a Varian MAT 44 instrument. High-resolution mass spectra were provided by the Facility supported by NIH Grant RR00317 (principal investigator, Professor K. Biemann) from the Biotechnology Resources Branch, Division of Research Resources, and were obtained on a CEC 21-110B high-resolution mass spectrometer equipped with a PDP-1145 based computer system

(26) Wadsworth, W. S., Jr. *Org. React. (N.Y.)* **1977**, *25*, 73.

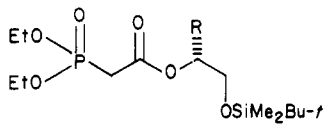


44, R = H
45, R = $OCH_2C_6H_5$

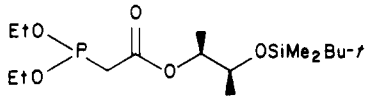
46



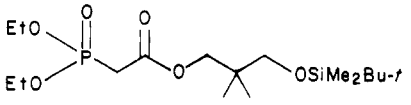
47



48, R = H
49, R = C_6H_{11}



50



51

to process data recorded on photographic plates. Melting points were recorded on a Fisher-Johns hot stage melting point apparatus and are uncorrected. Optical rotations were measured on a Perkin-Elmer 144 polarimeter using a 1-cm^3 capacity quartz cell (10-cm path length). Concentrations are reported in units of g/100 mL. Elemental analyses were performed by Robertson Laboratory, Inc., Florham Park, NJ.

All reactions were conducted in oven-dried (120 °C) or flame-dried glassware under atmospheres of dry argon or nitrogen. All solvents were purified before use: ether, THF, and DME were distilled from sodium benzophenone ketyl; CH_2Cl_2 and Me_2SO were distilled from CaH_2; toluene was distilled from sodium metal. Preparative thin-layer chromatography (TLC) was performed on 20 × 20 cm plates coated with 0.5- and 1.5-mm thickness of silica gel containing PF 254 indicator (Analtech). Unless indicated otherwise, compounds were eluted from the adsorbents with ether or ethyl acetate. Column chromatography was performed by using activity I Woelm silica gel. All chromatography solvents were distilled prior to use.

(*R*)-1-Cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (Diethoxyphosphinyl)acetate (49). A solution of 1.50 g (10.4 mmol) of >97% ee[27] (*R*)-(−)-1-cyclohexyl-1,2-ethylene glycol (prepared from (*R*)-(−)-mandelic acid[28]) in 12 mL of dry CH_2Cl_2 was treated with 51 mg (0.42 mmol) of (dimethylamino)pyridine and 1.26 g (12.5 mmol) of triethylamine. *tert*-Butyldimethylsilyl chloride (1.66 g, 10.9 mmol) was then added and the reaction stirred for 15 h at 23 °C. The mixture was then diluted with 15 mL of 1 N aqueous HCl and extracted with ether (3 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and filtered. The solvents were evaporated in vacuo to afford 2.83 g of crude monosilyl ether (theoretical yield, 2.68 g): NMR (60 MHz, CCl_4) δ 3.34 (m, 3 H), 2.13 (br s, 1 H), 1.30 (m, 11 H), 0.77 (s, 9 H), 0.00 (s, 6 H). The crude alcohol was dissolved in 25 mL of dry CH_2Cl_2 containing 0.99 g (12.5 mmol) of dry pyridine. This solution was cooled to 0 °C and 2.42 g (12 mmol) of bromoacetyl bromide was then added. The reaction was allowed to warm gradually to 23 °C over 1.5 h while being stirred vigorously. It was then diluted with 25 mL of 1 N aqueous HCl and processed according to the procedure described for preparation of **50**. The crude bromo ester was purified by chromatography on 75 g of SiO_2 using 5% ether–hexane as eluant (25 mL fractions). Fractions 8–15 yielded 3.22 g (82% from glycol) of bromo acetate as a clear colorless liquid: TLC, R_f 0.7 (5% ether–hexane); NMR (60 MHz, CCl_4) δ 4.77 (q, J = 5.2 Hz, 1 H), 3.82 (s, 2 H), 3.76 (d, J = 7.2 Hz, 2 H), 1.42 (m, 11 H), 0.95 (s, 9 H), 0.08 (s, 6 H); IR (neat) cm^{-1} 2925, 1734, 1454, 1402, 1274, 1115, 992; the low-resolution mass spectrum showed no parent ion; high-resolution mass spectrum, calcd for $C_{16}H_{31}{}^{79}BrO_3Si$ 378.19836, found 378.19973.

The above bromide (3.22 g, 8.50 mmol) was dissolved in 6 mL of dry toluene and treated with 1.56 g (9.40 mmol) of triethyl phosphite at reflux for 5 h. The toluene was then evaporated in vacuo to afford the crude product which was purified by chromatography on 90 g of SiO_2 using ether as eluant (25-mL fractions). Fractions 12–25 yielded 3.51 g (95%) of phosphonate **49** as a clear colorless liquid: TLC, R_f 0.75 (ether); $[\alpha]^{25}{}_D$ +5.2° (*c* 10, EtOH); NMR (60 MHz, CCl_4) δ 4.35 (q, J = 4.2 Hz, 1 H), 3.77 (q, J = 7.6 Hz, 4 H), 3.30 (d, J = 4.2 Hz, 2 H), 2.50 (d, J = 22 Hz, 2 H), 1.12 (m, 11 H), 0.99 (t, J = 7.6 Hz, 6 H), 0.58 (s, 9 H), −0.32 (s, 6 H); IR (CH_2Cl_2) cm^{-1} 2925, 1730, 1458, 1388, 1272, 1112, 1030; the high-resolution mass spectrum showed no parent ion, calcd for $C_{16}H_{32}O_6PSi$ (P − *t*-Bu) 379.17056, found 379.17999. Anal. Calcd for $C_{20}H_{41}O_6PSi$: C, 55.02; H, 9.47. Found: C, 55.24; H, 9.64.

***threo*-1,2-Dimethyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (Diethoxyphosphinyl)acetate (50).** *d,l*-2,3-Butanediol, 3.00 g (33.3 mmol), was dissolved in 70 mL of dry THF and the solution was cooled to −78 °C under argon. *n*-Butyllithium in hexane (13.1 mL, 2.4 M, 31.5 mmol) was added dropwise, and then the reaction was allowed to warm to 23 °C over a 1-h period. *tert*-Butyldimethylsilyl chloride (4.60 g, 30.0 mmol) was then introduced as a 20-mL solution in dry THF. The mixture was stirred for 0.5 h and a catalytic amount of imidazole (0.1 g) was then added. The mixture was stirred (12 h), then diluted with 70 mL of saturated aqueous $NaHCO_3$, and extracted (3 × 70 mL) with ether. The combined ether extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo to afford a clear pale yellow liquid (6.15 g, 99%) consisting of crude monosilyl ether: NMR (60 MHz, CCl_4) δ 3.67 (m, 3 H), 1.08 (d, J = 7.0 Hz, 6 H), 0.92 (s, 9 H), 0.05 (s, 6 H).

The above crude alcohol was dissolved in 85 mL of dry CH_2Cl_2 and cooled to 0 °C under argon. Pyridine (2.90 g, 36.7 mmol) was introduced followed by bromoacetyl bromide (7.27 g, 36.0 mmol), and the reaction was then allowed to warm to 23 °C and stirred for 1 h. The mixture was diluted with 90 mL of 1 N aqueous HCl and then extracted (3 × 130 mL) with ether. The combined ether extracts were washed with 30 mL of saturated aqueous $NaHCO_3$, dried over Na_2SO_4, and filtered. Evaporation of the solvents in vacuo afforded a cloudy yellow liquid which was purified by chromatography on 200 g of SiO_2 using 5% ether–hexane as eluant (25-mL fractions were collected). Fractions 15–33 afforded 4.82 g (50% based on butanediol) of bromo ester (TLC, R_f 0.6, one development in 5:1 hexane–ether): NMR (^1H, 60 MHz, CCl_4) δ 4.80 (m, 1 H), 3.90 (m, 1 H), 3.78 (s, 2 H), 1.25 (d, J = 6.5 Hz, 3 H), 1.13 (d, J = 6.0 Hz, 3 H), 0.90 (s, 9 H), 0.05 (s, 6 H); IR (neat) cm^{-1} 2942, 1733, 1460, 1372, 1277, 1105, 1038. A parent ion was not observed in the low-resolution mass spectrum.

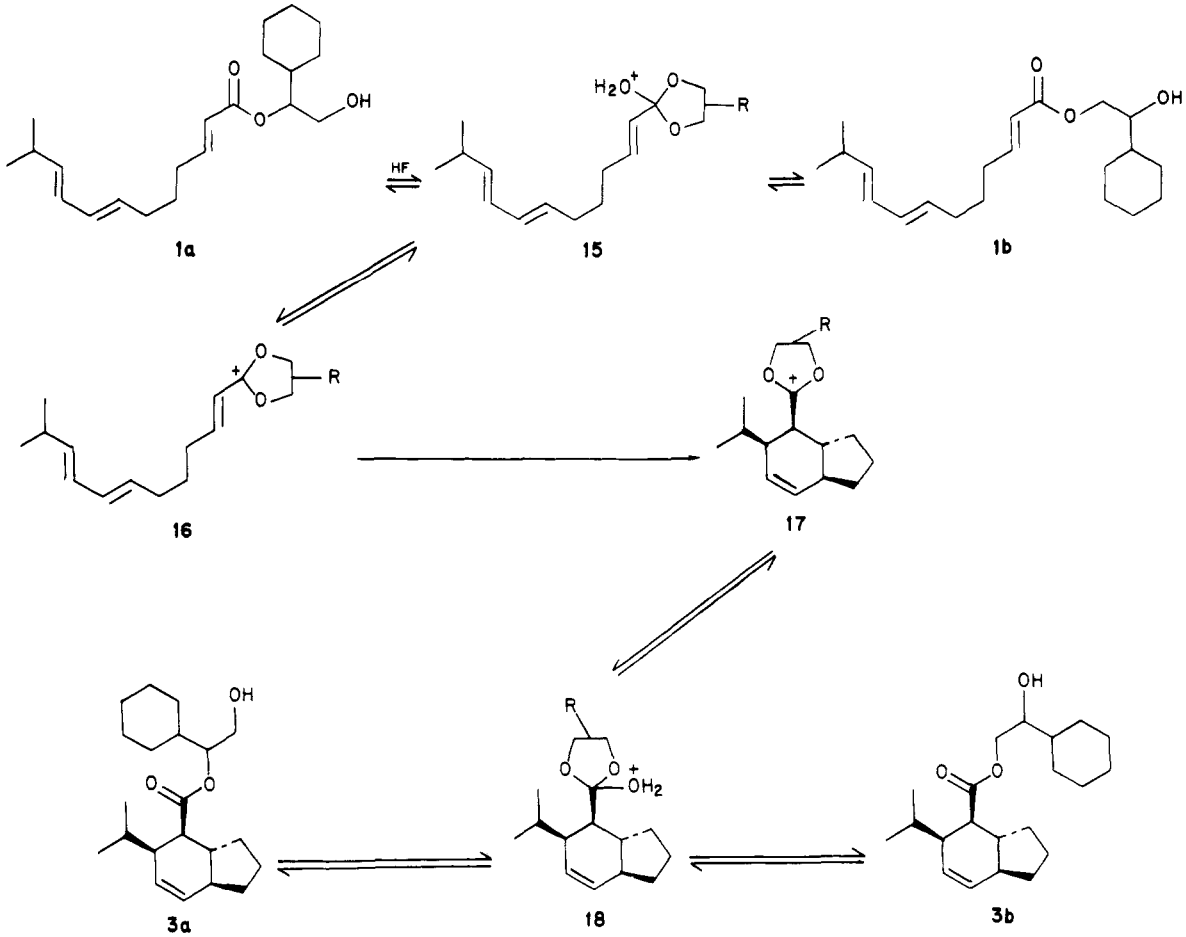
The bromo ester (4.78 g, 14.7 mmol) was dissolved in 6 mL of dry toluene and treated with 2.57 g (15.5 mmol) of triethyl phosphite. This mixture was refluxed for 3 h under argon. All volatile components were removed in vacuo and the crude phosphonate was purified by chromatography on 150 g of SiO_2 using ether as eluant (25-mL fractions were collected). Fractions 20–39 yielded 5.10 g (91%) of **50** as a clear colorless liquid: TLC, R_f 0.7 (Et_2O); NMR (60 MHz, CCl_4) δ 4.69 (m, 1 H), 4.10 (q, J = 7.5 Hz, 4 H), 3.85 (m, 1 H), 2.77 (d, J = 21 Hz, 2 H), 1.26 (m, 12 H), 0.87 (s, 9 H), 0.04 (s, 6 H); IR (neat) cm^{-1} 2938, 1738, 1461, 1387, 1269, 1111, 1030; the low- and high-resolution mass spectra showed no parent ions, calcd for $C_{12}H_{26}O_6PSi$ (P − *t*-Bu) 325.12362, found 325.12146. Anal. Calcd for $C_{16}H_{35}O_6PSi$: C, 50.24; H, 9.22. Found: C, 50.53; H, 9.16.

(*R*)-1-Cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (*E,E,E*)-11-Methyldodeca-2,7,9-trienoate (11). A solution of 890 mg (2.04 mmol) of phosphonate **49** in 13 mL of dry DME was cooled to 0 °C. Sodium hydride (108 mg, 2.24 mmol, 50% oil dispersion) was then introduced and the mixture stirred vigorously at 0 °C until gas evolution ceased. The reaction was allowed to warm gradually to 23 °C (over 10 min), and aldehyde **44** (407 mg, 2.45 mmol) was then introduced as the neat liquid. This mixture

(27) Optical purity determinations were performed by using the Mosher ester technique: Dale, J. A.; Mosher, H. S. *J. Org. Chem.* **1970**, *35*, 4002. Dale, J. A.; Dull, D. L.; Mosher, H. S. *Ibid* **1969**, *34*, 2543.

(28) Hirano, T.; Inoue, S.; Tsuruta, T. *Makromol. Chem.* **1976**, *177*, 3237.

Scheme I. Proposed Mechanism for Acid-Catalyzed Cyclization of 1



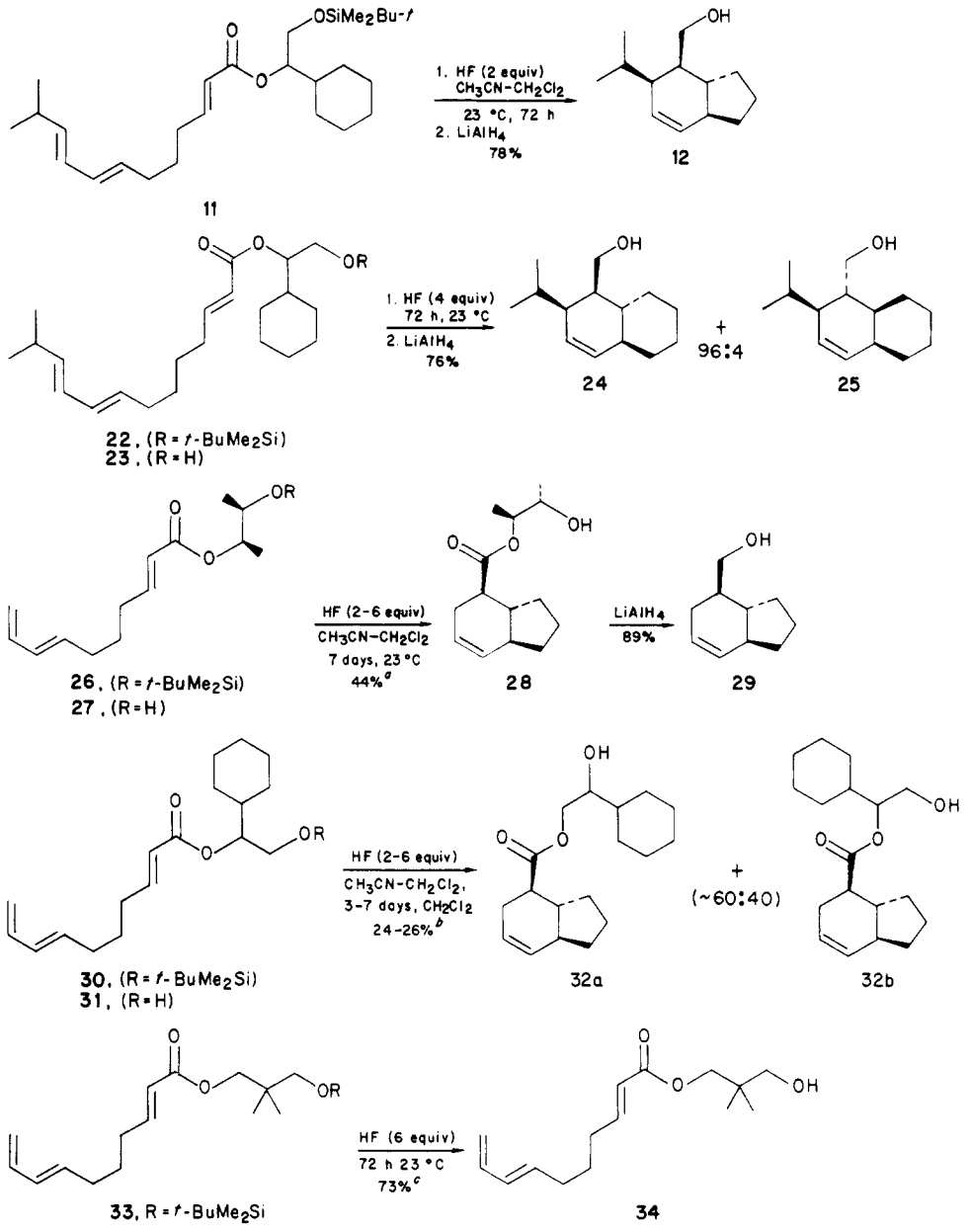
was stirred vigorously for 3 min and then promptly diluted with 15 mL of saturated aqueous $NaHCO_3$. The mixture was extracted with ether (3 × 20 mL). The combined ether extracts were dried over Na_2SO_4, filtered, and concentrated in vacuo to afford a clear pale yellow liquid. The crude product was purified by chromatography on 70 g of SiO_2 using 4% ether–hexane as eluant (25-mL fractions were collected). Fractions 15–22 yielded 737 mg (81%) of triene **11** as a clear colorless liquid: TLC, R_f 0.5 (two developments in 10% ether–hexane); NMR (60 MHz, CCl_4) δ 6.84 (dt, J = 15.5, 7.0 Hz, 1 H), 6.58 (m, 5 H), 4.63 (m, 1 H), 3.61 (d, J = 4.6 Hz, 2 H), 2.12 (m, 3 H), 1.63 (m, 15 H), 0.94 (d, J = 7.0 Hz, 6 H), 0.86 (s, 9 H), −0.06 (s, 6 H); IR (neat) cm^{-1} 2924, 1714, 1648, 1451, 1380, 1356, 1250, 1122; mass spectrum, m/e 448 (parent ion); high-resolution mass spectrum, calcd for $C_{27}H_{48}O_3Si$ 448.33412, found 448.33723.

(*R*)-1-Cyclohexyl-2-hydroxyethyl (*E*,*E*,*E*)-11-Methyldodeca-2,7,9-trienoate ((+)-1a). To a solution of 1.40 g (3.13 mmol) of *t*-$BuMe_2Si$ ether **11** in 2 mL of CH_2Cl_2 was added 3.5 mL of a 19:1 mixture of CH_3CN and 48% aqueous HF. This mixture was stirred at 23 °C for 3 min, then *promptly* diluted with 10 mL of saturated aqueous $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 15 mL). The combined extracts were filtered through a cotton plug and concentrated in vacuo to afford a clear pale yellow liquid. The crude product was purified by chromatography on 25 g of SiO_2 using 3:1 hexane–ether as eluant (25-mL fractions). Fractions 9–19 yielded 871 mg (83%) of pure (+)-**1a**: TLC, R_f 0.4 (2:1 hexane–ether); $[\alpha]^{25}_D$ +4.5° (c 13, EtOH); NMR (250 MHz, $CDCl_3$) δ 6.98 (dt, J = 15.4, 7.0 Hz, H_3), 5.97 (m, 2 H), 5.85 (dt, J = 15.4, 1.5 Hz, H_2), 5.55 (m, 2 H), 4.74 (m, $H_{1'}$), 3.74 (m, 2 H, H_2; when this signal is saturated by double irradiation, the signal at 4.74 collapses to a doublet (J = 7.8 Hz)), 2.29 (m, 1 H), 2.20 (dq, J = 1.5, 7.7 Hz, 2 H, H_4), 2.08 (br q, J = 7.0 Hz, 2 H, H_6), 1.96 (m, 1 H), 1.70 (m, 6 H), 1.56 (q, J = 7.4 Hz, 2 H, H_5), 1.17 (m, 5 H), 0.98 (d, J = 6.6 Hz, 6 H); IR (neat) cm^{-1} 3440, 2924, 1712, 1649, 1447, 1360, 1263, 1188; the low-resolution mass spectrum showed no parent ion. Anal. Calcd for $C_{21}H_{34}O_3$: C, 75.41; H, 10.25. Found: C, 75.16; H, 10.08.

(*R*)-2-Cyclohexyl-2-hydroxyethyl (*E*,*E*,*E*)-11-Methyldodeca-2,7,9-trienoate (1b). To a solution of 400 mg (0.89 mmol) of triene **11** in 0.2 mL of CH_2Cl_2 was added 1 mL of a 19:1 mixture of CH_3CN and 48% aqueous HF. The reaction was stirred for 25 min at 23 °C and then worked up as in the previous procedure to afford a clear yellow liquid. The crude mixture of products was applied to 60 g of SiO_2 and eluted with 3:1 hexane–ether (25-mL fractions). Fractions 29–45 yielded 198 mg (66%) of **1a**, whereas fractions 19–25 afforded 33 mg (11%) of **1b** as a clear colorless liquid: TLC, R_f 0.55 (2:1 hexane–ether); NMR (250 MHz, $CDCl_3$) δ 7.01 (dt, J = 15.8, 7.0 Hz, H_3), 5.99 (m, 2 H), 5.88 (dt, J = 15.8, 1.5 Hz, H_2), 5.58 (m, 2 H), 4.30 (dd, J = 11.7, 3.3 Hz, $H_{1'cis}$), 4.11 (dd, J = 11.7, 12.0 Hz, $H_{1'trans}$), 3.63 (m, $H_{2'}$; when this signal is saturated by double irradiation, the signals at 4.11 and 4.30 both collapse to doublets (J = 11.7 Hz)), 2.34 (m, 1 H), 2.23 (dq, J = 1.5, 7.3 Hz, 2 H, H_4), 2.09 (br q, J = 7.0 Hz, 2 H, H_6), 2.06 (br s, 1 H), 1.89 (m, 1 H), 1.77 (m, 5 H), 1.58 (q, J = 7.3 Hz, 2 H, H_5), 1.21 (m, 5 H), 1.01 (d, J = 6.6 Hz, 6 H); IR (CH_2Cl_2) cm^{-1} 3588, 3480, 2922, 1711, 1648, 1443, 1376, 1245, 1179; mass spectrum, m/e 334 (parent ion); high resolution mass spectrum, calcd for $C_{21}H_{34}O_3$ 334.25080, found 334.25006.

(*R*)-1-Cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (*E*,*E*,*E*)-12-Methyltrideca-2,8,10-trienoate (22). Triene **22** was prepared in 65% yield from aldehyde **47**[5a] and phosphonate **49** by using the procedure described for the synthesis of **11**: TLC, R_f 0.6 (5% ether–hexane); NMR (250 MHz, $CDCl_3$) δ 6.93 (dt, J = 15.6, 7.0 Hz, H_3), 5.96 (m, 2 H), 5.80 (dt, J = 15.6, 1.1 Hz, H_2), 5.54 (m, 2 H), 4.77 (q, J = 4.8 Hz, $H_{1'}$), 3.68 (m, 2 H; this signal collapses to a sharp singlet when the resonance at 4.77 is saturated by double irradiation), 2.29 (m, 1 H), 2.18 (br q, J = 5.9 Hz, 2 H, H_4), 2.04 (q, J = 6.6 Hz, 2 H, H_7), 1.68 (m, 7 H), 1.42 (m, 4 H), 1.16 (m, 4 H), 0.97 (d, J = 7.0, 6 H), 0.84 (s, 9 H), 0.01 (s, 3 H), 0.00 (s, 3 H); IR (neat) cm^{-1} 2930, 1718, 1652, 1460, 1359,

Table I. HF-Catalyzed Intramolecular Diels–Alder Reactions



[a] Triene **27** was recovered (14%). [b] Triene **31** was recovered (28–34%) as a mixture of acyl transfer isomers. [c] No products of cyclization were detected.

1253, 1126, 1100; the low-resolution mass spectrum showed no parent ion. Anal. Calcd for $C_{28}H_{50}O_3Si$: C, 72.67; H, 10.89. Found: C, 72.55; H, 11.20.

***threo*-1,2-Dimethyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (*E,E*)-Deca-2,7,9-trienoate (26).** Triene **26** was prepared in 59% yield from aldehyde **46**[5b] and phosphonate **50** by using the procedure described for the synthesis of **11**: TLC, R_f 0.65 (10% ether–hexane); NMR (60 MHz, CCl_4) δ 6.93 (dt, J = 15.4, 7.0 Hz, 1 H), 5.90 (m, 4 H), 4.98 (m, 3 H), 3.93 (m, 1 H), 2.20 (m, 4 H), 1.63 (m, 2 H), 1.23 (d, J = 4.2 Hz, 3 H), 1.10 (d, J = 4.2 Hz, 3 H), 0.92 (s, 9 H), 0.05 (s, 6 H); IR (neat) cm^{-1} 2930, 1718, 1702, 1603, 1460, 1371, 1254, 1172, 1111, 1038; mass spectrum, m/e 353 (parent ion). Anal. Calcd for $C_{20}H_{36}O_3Si$: C, 68.13; H, 10.29. Found: C, 68.27; H, 10.07.

(*R*)-1-Cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (*E,E*)-Deca-2,7,9-trienoate (30). Triene **30** was prepared in 61% yield from aldehyde **46** and phosphonate **49** by using the procedure described for the synthesis of **11**: TLC, R_f 0.65 (10% ether–hexane); NMR (250 MHz, $CDCl_3$) δ 6.96 (dt, J = 15.4, 7.0 Hz, H_3), 6.32 (dt, J = 16.9, 10.3 Hz, H_9), 5.84 (dt, J = 15.4, 1.5 Hz, H_2), 5.68 (dt, J = 15.1, 7.0 Hz, H_7), 5.11 (br d, J = 16.9 Hz, H_{10syn}), 4.98 (br d, J = 10.3 Hz, H_{10anti}), 4.81 (br q, J = 4.8 Hz, $H_{1'}$), 3.71 (m, 2 H; this multiplet collapses to a sharp singlet when the resonance at 4.81 is saturated by double irradiation), 2.22 (dq, J = 1.1, 7.2 Hz, 2 H, H_4), 2.13 (br q, J = 7.3 Hz, 2 H, H_6), 1.72 (m, 6 H), 1.59 (br quint, J = 7.3 Hz, 2 H, H_5), 1.58 (s, 1 H), 1.12 (m, 5 H), 0.88 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H); IR (neat) cm^{-1} 2921, 1716, 1650, 1447, 1252, 1171, 1123, 1000; high-resolution mass spectrum, calcd for $C_{24}H_{42}O_3Si$ 406.29032, found 406.29280.

2,2-Dimethyl-3-[(*tert*-butyldimethylsilyl)oxy]propyl (*E,E*)-Deca-2,7,9-trienoate (33). Triene **33** was prepared in 60% yield from aldehyde **46**[5b] and phosphonate **51** by using the procedure described for the synthesis of **11**: TLC, R_f 0.8 (10% ether–hexane); NMR (250 MHz, $CDCl_3$) δ 6.95 (dt, J = 15.8, 7.0 Hz, H_3), 6.32 (dt, J = 16.9, 10.3 Hz, H_9), 6.10 (dd, J = 15.1, 10.2 Hz, H_8), 5.85 (dt, J = 15.8, 1.5 Hz, H_2), 5.68 (dt, J = 15.1, 7.4 Hz, H_7), 5.11 (dd, J = 16.9, 1.4 Hz, H_{10syn}), 4.99 (dd, J = 10.2, 1.4 Hz, H_{10anti}), 3.93 (s, 2 H), 3.36 (s, 2 H), 2.24 (dq, J = 1.4, 8.1 Hz, 2 H, H_4), 2.14 (br q, J = 7.4, 2 H, H_6), 1.58 (quint, J = 7.4 Hz, 2 H, H_5), 0.90 (s, 6 H), 0.88 (s, 9 H), 0.02 (s, 6 H); IR (neat) cm^{-1}

2945, 1723, 1653, 1602, 1471, 1400, 1364, 1257, 1096; the low-resolution mass spectrum showed no parent ion.

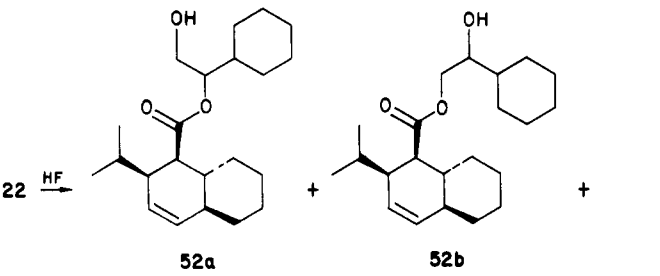
2,2-Dimethyl-3-hydroxypropyl (*E*,*E*)-Deca-2,7,9-trienoate (34). Attempts to cyclize **33** by using the HF–CH_3CN–CH_2Cl_2 protocol subsequently described (see also Table I) were completely unsuccessful. Triene **34** was recovered in 73% yield by silica gel chromatography: TLC, R_f 0.6 (1:1 hexane–ether); NMR (250 MHz, $CDCl_3$) δ 6.97 (dt, J = 15.6, 7.0 Hz, H_3), 6.29 (dt, J = 16.9, 10.3 Hz, H_9), 6.04 (dd, J = 15.1, 10.3 Hz, H_8), 5.82 (dt, J = 15.6, 1.5 Hz, H_2), 5.65 (dt, J = 15.1, 7.0 Hz, H_7), 5.08 (br d, J = 16.9 Hz, H_{10syn}), 4.98 (dd, J = 10.6, 0.7 Hz, H_{10anti}), 3.98 (s, 2 H, $H_{1'}$), 3.27 (br d, J = 5.9 Hz, 2 H, $H_{3'}$), 2.30 (br t, J = 6.3 Hz, 1 H), 2.21 (dq, J = 1.1, 7.2 Hz, 2 H, H_4), 2.10 (br q, J = 7.0 Hz, H_6), 1.56 (dq, J = 8.6, 7.0 Hz, 2 H, H_5), 0.91 (s, 6 H); IR (CH_2Cl_2) cm^{-1} 3615, 3500, 2933, 1706, 1649, 1600, 1473, 1369, 1308, 1175, 1042; mass spectrum, m/e 252 (parent ion); high-resolution mass spectrum, calcd for $C_{15}H_{24}O_3$ 252.17255, found 252.17422.

1-Cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl Crotonate (41). To a solution of 500 mg of crotonic acid (5.8 mmol) and 600 mg (2.32 mmol) of 1-cyclohexyl-2-(*tert*-butyldimethylsilyl)ethanol (see procedure for preparation of **49**) in 10 mL of dry CH_2Cl_2 was treated with a solution of 28 mg (0.23 mmol) of 4-(dimethylamino)pyridine and 1.20 g (5.81 mmol) of DCC in 10 mL of CH_2Cl_2. The mixture was stirred for 36 h at room temperature and then was filtered to remove dicyclohexylurea which had precipitated. The urea was washed with 25 mL of dry CH_2Cl_2 and the combined filtrates were concentrated in vacuo. Ester **41** was purified by flash column chromatography (40-mm column, 3:1 hexane–ether) to afford 680 mg (89%) of **41** and 50 mg (8%) of recovered alcohol. Data for **41**: TLC, R_f 0.70 (3:1 hexane–ether); $[\alpha]^{23}_D$ −8.8° (c 1.13, $CHCl_3$); NMR (250 MHz, $CDCl_3$) δ 6.94 (dq, J = 15.5, 6.9 Hz, 1 H), 5.82 (dd, J = 15.5, 1.6 Hz, 1 H), 4.76 (br q, J = 5.1 Hz, 1 H), 3.67 (m, 2 H), 1.85 (dd, J = 6.9, 1.6 Hz, 3 H), 1.70–0.92 (m, 11 H), 0.84 (s, 9 H), 0.00 (s, 6 H); IR (neat) cm^{-1} 2930, 2850, 1720, 1655, 1445, 1255, 1180, 1000, 965, 830. Anal. Calcd for $C_{18}H_{34}SiO_3$: C, 66.21; H, 10.49. Found: C, 66.31; H, 10.34.

(*R*)-1-Cyclohexyl-2-[(*tert*-butyldimethylsilyl)oxy]ethyl (*Z*,*E*,*E*)-12-Methyltrideca-2,8,10-trienoate (39). A solution of 2.77 g (6.79 mmol) of phosphonate **49** in 40 mL of dry THF was added dropwise to a −40 °C solution of 10.4 mmol of LDA in 40 mL of THF (prepared in situ from 1.32 g (13.1 mmol) of diisopropylamine and 4.55 mL of 2.3 M *n*-BuLi in hexane). The mixture was stirred for 15 min at −40 °C and then 940 mg (5.22 mmol) of aldehyde **47**[5a] in 40 mL of dry THF was added dropwise. The reaction was stirred for 10 min at −40 °C and then warmed to room temperature and stirred for 6 h. The reaction was diluted with 100 mL of saturated NaCl solution and extracted with CH_2Cl_2 (3 × 100 mL). The organic extracts were passed through a cotton plug and concentrated in vacuo to afford 3.7 g of the crude product. TLC analysis (9:1 hexane–ether) indicated that this material consisted of a mixture of **22** (R_f 0.7; major product) and **39** (R_f 0.83). These isomers were separated by flash column chromatography (50-mm column, 19:1 hexane–ether as eluant) to afford 1.14 g (45%) of **22** and 0.51 g (20%) of **39**: NMR (250 MHz, $CDCl_3$) δ 6.17 (dt, J = 11.5, 7.4 Hz, 1 H), 5.95 (m, 2 H), 5.75 (d, J = 11.6 Hz, 1 H), 5.54 (m, 2 H), 4.78 (br q, J = 4.6 Hz, 1 H), 3.68 (m, 2 H), 2.63 (m, 2 H), 2.28 (m, 1 H), 2.05 (m, 2 H), 1.72–1.00 (m, 15 H), 0.97 (d, J = 6.8 Hz, 6 H), 0.84 (s, 9 H), 0.00 (s, 6 H); IR (CH_2Cl_2) 2930, 2855, 1710, 1640, 1455, 1245, 1180, 835 cm^{-1}. Anal. Calcd for $C_{28}H_{50}O_3Si$: C, 72.67; H, 10.89. Found: C, 72.91; H, 10.70.

General Procedure for HF-Catalyzed Cyclizations (See Table I). The appropriate triene was dissolved in a mixture prepared from 19 parts CH_3CN, 20 parts CH_2Cl_2, and 1 part 48% aqueous HF; the concentration of HF in this system is roughly 0.7 M. The quantity of HF solution added (i.e., the number of molar equivalents of HF relative to triene) is indicated in Table I. The reaction mixtures so prepared were stirred vigorously at 23 °C and monitored by TLC. Additional CH_2Cl_2 was added if two phases separated during the course of the reaction.[29] Each reaction was quenched with excess saturated $NaHCO_3$ and extracted (3×) with CH_2Cl_2. The combined extracts were filtered through a cotton plug and the solvents removed in vacuo. The crude products were then chromatographed over silica gel or reduced with $LiAlH_4$. All yields reported in Table I are for products isolated by chromatography.

Samples of the major products **3b**, **52b**, and **32a** from the cyclizations of trienes **11** (or **1**), **22**, and **30**, respectively, were



obtained by direct chromatography of the cyclization mixtures. It was not possible, however, to obtain pure samples of the corresponding acyl transfer isomers **3a**, **52a**, and **32b** from these experiments. These minor products, in general, cochromatographed with unreacted triene isomers[30] and with other unidentified reaction side products. As a consequence, it was generally most convenient to reduce the product mixtures with $LiAlH_4$ before product isolation.

Adduct **3b** appeared to be a nearly equal mixture of two diastereomers (enantiomeric within the perhydroindene nucleus) by high-field NMR analysis. Adduct **52b** was approximately a 1:1.5 mixture of diastereomers.[31] Cycloadducts **28** and **32a** were mixtures of two diasteromers,[31] with one slightly predominating over the other. We were not able to separate any of these diastereomeric mixtures by SiO_2 chromatography.

The following specific procedure is representative. A solution of 108 mg (0.234 mmol) of triene **22** in 1 mL of CH_2Cl_2 was treated with 0.95 mL of CH_3CN and 0.05 mL of 48% aqueous HF (1.2 mmol, 5 equiv). The resulting mixture was stirred for 72 h at 23 °C and then was worked up as described above in the general procedure. The crude product, consisting primarily of **52a**, **52b**, and a small amount of uncyclized **23** and exo cycloadducts, was dissolved in 5 mL of dry ether and treated with 38 mg (1 mmol) of $LiAlH_4$. This mixture was stirred for 30 min at 23 °C, then was cooled to 0 °C, quenched with excess methanol, and worked up in the usual manner. The crude product was chromatographed (0.5-mm silica gel preparative plate, 2:1 hexane–ether) to give 37 mg (76%) of a 96:4 mixture of alcohols **24** and **25**. Authentic samples of these alcohols were prepared by $LiAlH_4$ reduction of **36** and **37**.[5a]

(2*R*)-2-Cyclohexyl-2-hydroxyethyl 5β-(2-Propyl)-2,3,3aβ,4,5,7aα-hexahydroindene-4β-carboxylate (3b). This diastereomeric mixture[31] was isolated in 56% yield from the cyclization of triene **11**: TLC for the mixture of diastereomers, R_f 0.7 (2:1 hexane–ether); mp 76–77 °C; $[\alpha]^{25}_D$ +7.8° (c 6.4, EtOH); NMR (250 MHz, $CDCl_3$) δ 5.99 (br d, J = 9.9 Hz, 1 H), 5.59 (dt, J = 9.9, 2.6 Hz, 1 H), 4.27 (dd, J = 11.7, 2.9 Hz, first diastereomer), 4.11 (dd, J = 11.7, 11.4 Hz, first diastereomer), 4.21 (dd, J = 10.9, 4.2 Hz, second diastereomer), 4.07 (dd, J = 10.9, 12.1 Hz, second diastereomer), 3.60 (m, 1 H; the four previous signals collapse to doublets, J = 11.7 Hz, J = 11.7 Hz, J = 10.9 Hz, and J = 10.9 Hz, respectively, when this signal is saturated by double irradiation), 2.78 (dd, J = 11.4 Hz, 7.7 Hz, H_4), 2.65 (m, 1 H), 0.99 (d, J = 7.0 Hz, 3 H), 0.87 (d, J = 7.0 Hz, 3 H); IR (CH_2Cl_2) cm^{-1} 3598, 3470, 2930, 1726, 1638, 1447, 1371, 1328, 1184, 1142; mass spec-

(29) We have recently observed that the reactions remain homogeneous when performed in CH_3CN without CH_2Cl_2 as a cosolvent.

(30) All trienes used in the studies described herein contained 7–10% of *cis*-1,3-diene isomers which do not undergo intramolecular Diels–Alder reactions.

(31) Enantiomeric within the trans-fused bicyclic ring system.

trum, m/e 334 (parent ion); high-resolution mass spectrum, calcd for $C_{21}H_{34}O_3$ 334.25080, found 334.25041.

(1*R*)-1-Cyclohexyl-2-hydroxyethyl 5β-(2-Propyl)-2,3,3aβ,4,5,7aα-hexahydroindene-4β-carboxylate (3a). Data obtained on a 2:1 mixture of diastereomers[31] obtained from the $MeNbCl_4$-promoted cyclization of triene **1a**[12] (TLC for the mixture, R_f 0.7, two developments in 2:1 hexane–ether): NMR (250 MHz, $CDCl_3$) δ 5.97 (br d, J = 10.3 Hz, 1 H), 5.56 (dt, J = 10.3, 3.3 Hz, 1 H), 4.78 (m, this signal integrates for only 0.33 protons), 4.70 (m, this signal integrates for 0.67 protons), 3.72 (m, 2 H; the signals at 4.78 and 4.70 each collapse to broad doublets (J = 6.2 Hz) when this multiplet is saturated by double irradiation); 2.76 (dd, J = 11.2, 7.7 Hz, H_4-major diastereomer), 2.75 (dd, J = 11.5, 7.7 Hz, H_4-minor diastereomer), 2.63 (m, 1 H), the isopropyl signals of the major diastereomer (0.96 (d, J = 7.0 Hz, 0.85 (d, J = 7.0 Hz)), and of the minor diastereomer (0.97 (d, J = 7.0 Hz), 0.85 (d, J = 7.0 Hz)); IR (CH_2Cl_2) cm^{-1} 3600, 3475, 2924, 1717, 1643, 1432, 1372, 1325, 1244, 1182, 1141; the low-resolution mass spectrum shows a parent ion at m/e 334; high-resolution mass spectrum, calcd for $C_{21}H_{34}O_3$ 334.25080, found 334.25394.

(2*R*)-2-Cyclohexyl-2-hydroxyethyl 6β-(2-Propyl)-1,2,3,4,4aβ,5,6,8aα-octahydronaphthalene-5β-carboxylate (52b). This mixture of diastereomers[31] was isolated in 53% yield from the cyclization of triene **22**: TLC, R_f 0.7 (1:1 hexane–ether); NMR (250 MHz, $CDCl_3$) δ 5.56 (s, 2 H), 4.13 (m, 2 H), 3.57 (m, 1 H), 2.63 (dd, J = 11.8, 7.4 Hz, H_5), 2.44 (m, 1 H), 0.94 (d, J = 7.0 Hz, 3 H), 0.85 (d, J = 7.0 Hz, 3 H); IR (neat) cm^{-1} 3475, 2922, 1716, 1651, 1447, 1369, 1252, 1160, 1131; mass spectrum, m/e 348 (parent ion); high-resolution mass spectrum, calcd for $C_{22}H_{36}O_3$ 348.26645, found 348.27063.

5β-(Hydroxymethyl)-6β-(2-propyl)-1,2,3,4,4aβ,5,6,8aα-octahydronaphthalene (24). Obtained in 76% overall yield as a 96:4 mixture with the isomeric alcohol **25** by reduction of the crude product mixture from the hydrofluoric acid catalyzed cyclization of triene **22**: TLC of the mixture, R_f 0.5 (1:1 hexane–ether); NMR (250 MHz, $CDCl_3$) δ 5.64 (ddd, J = 10.2, 1.6, 2.6 Hz, 1 H), 5.54 (br d, J = 10.2 Hz, 1 H), 3.85 (d br d, J = 10.3, 5.2 Hz, 1 H), 3.65 (br t, J = 10.1 Hz, 1 H), 2.26 (m, 1 H), 1.98 (m, 1 H), 1.77 (m, 5 H), 0.98 (d, J = 7.0 Hz, 3 H), 0.84 (d, J = 7.0 Hz, 3 H); IR (neat) cm^{-1} 3335, 2925, 1649, 1464, 1447, 1376, 1081, 1042, 1008; mass spectrum, m/e 208 (parent ion). Anal. Calcd for $C_{14}H_{24}O$: C, 80.70; H, 11.62. Found: C, 80.92; H, 12.01.

One of the isopropyl doublets (J = 7.0 Hz) from the minor isomer **25** in the NMR spectrum of this mixture appeared at δ 0.77. The ratios **24** and **25** in such mixtures were determined by integration of the isopropyl signals.

***threo*-1,2-Dimethyl-2-hydroxyethyl 2,3,3aβ,4,5,7aα-hexahydroindene-4β-carboxylate (28):** TLC, R_f 0.7 (2:1 hexane–ether; two developments); NMR (250 MHz, $CDCl_3$) δ 5.81 (br d, J = 10.2 Hz, 1 H), 5.56 (dq, J = 9.9, 3.3 Hz, 1 H), 4.88 (m, 1 H), 3.86 (m, 1 H), 2.50 (dt, J = 7.0, 10.3 Hz, H_4), 2.36 (m, 2 H), the methyl signals of the major diastereomer[31] (1.19 (d, J = 6.2 Hz), 1.15 (d, J = 6.2 Hz)) and the minor diastereomer (1.18 (d, J = 6.2 Hz), 1.15 (d, J = 6.2 Hz)), this region of the spectrum integrates for a total of 6 H; IR (CH_2Cl_2) cm^{-1} 3590, 2940, 1718, 1638, 1417, 1372, 1243, 1170, 1082; mass spectrum, m/e 238 (parent ion); high-resolution mass spectrum, calcd for $C_{14}H_{22}O_3$ 238.15690, found 238.15216.

$LiAlH_4$ reduction of **28** afforded alcohol **29**[5b] in 89% yield.

Acknowledgment. This research was supported by grants from the National Science Foundation (Grant No. 8106987-CHE) and the National Institutes of Health (GM-26782).

Registry No. (+)-**1a**, 92126-38-0; **1b**, 92126-39-1; **11**, 92126-40-4; **22**, 92126-41-5; **23**, 92126-42-6; (±)-**26**, 92126-43-7; (±)-**27**, 92126-44-8; **30**, 92126-45-9; **31**, 92126-46-0; **33**, 92126-47-1; **34**, 92126-48-2; **39**, 92126-49-3; **41**, 92126-50-6; **49**, 92126-51-7; *dl*-**50**, 92126-52-8; HF, 7664-39-3.

Solvent Effects on the Rates and the Activation Parameters for the Methoxymercuration of *p*-Substituted Styrenes

Adolphus Lewis

Department of Chemistry, Howard University, Washington, D.C. 20059

Received May 14, 1984

The second-order rate constants and the activation parameters for the methoxymercuration of a series of para-substituted styrenes have been determined in four methanol/*p*-dioxane mixtures—X_{MeOH} varied from 1.00 to 0.791. For each styrene log k is a linear function of X_{MeOH}. The average value of the slopes of the correlation lines is 8.25 ± 0.32 which suggests the involvement of eight–nine MeOH molecules in the rate-determining transition state. For each solvent identical linear plots of log k vs. σ and σ^+ are obtained. At 25 °C, the values of ρ (av −3.26 ± 0.05) and ρ^+ (av −2.86 ± 0.05) are independent of the solvent's composition. For each styrene ΔG^* increases as the methanol concentration deceases; however, $\delta\Delta G^*$ is constant. While $\delta\Delta G^*$ varies linearly with σ and σ^+, in no case is $\delta\Delta H^*$ linearly related to $\delta\Delta S^*$. In anhydrous methanol this reaction series is isoenthalpic; however, this is not the case for either of the methanol/*p*-dioxane mixtures. On the basis of the ΔS^* values, the reaction series approaches an isoentropic state as the methanol concentration decreases.

Introduction

In our last report[1] on the methoxymercuration of para-substituted styrenes, because of the trend in the large negative values of ΔS^* found in anhydrous methanol and the rate reductions obtained upon adding *p*-dioxane to the kinetic mixture, in the case of *p*-bromostyrene, we proposed that solvents affect the rates of this reaction by altering either the concentration of the "reactive" mercury species and/or the stability of the rate-determining transition state. To better understand the role of the solvent, we studied the solvent effects on both the second-order rate constants and the activation parameters for this reaction.

The most widely accepted mechanism for this reaction is the Ad_E2 mechanism.[2-10] According to it, the rate-de-

(1) Lewis, A.; Azoro, J. *J. Org. Chem.* **1981**, *46*, 1764.

(2) Lucus, H. J.; Hepner, F. R.; Winstein, S. *J. Am. Chem. Soc.* **1939**, *61*, 3102.
(3) Chatt, J. *Chem. Rev.* **1951**, *48*, 7.
(4) Zerirov, N. S. *Russ. Chem. Rev.* **1965**, *34*, 527.
(5) Matteson, D. S. "Organometallic Reaction Mechanisms of the Nontransition Elements"; Academic Press: New York, 1974; Chapter 5.

0022-3263/84/1949-4682$01.50/0