presence of an internal standard. Half-lives were calculated by assuming a zero intercept. The results are presented in Table IV.

Solution-Phase Pyrolysis of (*E*)-14. Triene ester (370 mg) in cyclohexane (20 mL) is placed in a Carius tube, freeze–thaw degassed, and then pyrolyzed for 165 min at 200 °C. The NMR and GC analyses show only bridgehead olefin **26**. The pyrolysate is concentrated to yield 0.338 g of crude product. Kugelrohr distillation (100 °C, 0.3 mm) yields bridgehead olefin (0.309 g, 91%), which is 99% by VPC analysis.

Spectral Data of Bridgehead Olefins. 6-Oxobicyclo[3.3.1]-1(2)-nonene (19). NMR (C_6D_4) δ 1.6–2.7 (m, 11 H), 5.5 (m, 1 H); IR (CS_2, 0.052 mm) 3022 (m), 2952 (s), 2925 (s), 2886 (s), 2862 (s), 1712 (vs), 1630 (w), 1414 (w), 1343 (w), 1308 (w), 1279 (w), 1269 (w), 1240 (m), 1199 (m), 1161 (m), 1124 (w), 1070 (s), 1063 (s), 1040 (w), 980 (w), 949 (mw), 931 (w), 910 (w), 838 (m), 797 (s), 770 (w), 660 (w) cm^{-1}; UV (hexane) λ_{max} 193 nm; mass spectrum, *m/e* (EI, relative percent) 136 (29), 118 (3), 107 (6), 93 (40), 79 (100), 67 (14), 53 (18).

***exo*-4-Carbomethoxybicyclo[3.3.1]-1(2)-nonene (22).** NMR (C_6D_4) δ 1.0–2.2 (m, 9 H), 2.42 (complex t, J = 6.0 Hz, 2 H), 2.80 (m, 1 H), 3.34 (s, 3 H), 5.55 (t, J = 6.6 Hz, 1 H); IR (CS_2, 0.052 mm) 3010 (w), 2945 (s), 2925 (s), 2860 (m), 1733 (vs), 1622 (w), 1425 (m), 1340 (m), 1275 (m), 1245 (w), 1220 (nw), 1182 (s), 1170 (s), 1150 (ms), 1118 (w), 1085 (w), 1032 (w), 972 (w), 928 (w), 862 (w), 850 (w), 750 (w) cm^{-1}; UV (hexane) λ_{max} 207 nm; mass spectrum, *m/e* (EI, relative percent) 180 (24), 148 (30), 121 (45), 105 (46), 100 (29), 91 (77), 79 (100), 68 (47), 53 (39).

5-Oxobicyclo[4.3.1]-1(9)-decene (25). NMR (C_6D_6) δ 1.2–2.6 (m, 13 H), 5.36 (m, 1 H); IR (CS_2, 0.052 mm) 3030 (w), 2935 (s), 2880 (m), 2855 (m), 1705 (vs), 1335 (w), 1318 (w), 1259 (m), 1195 (w), 1180 (w), 1100 (m), 1020 (m), 930 (w), 893 (w), 808 (m), 615 (w) cm^{-1}; UV (hexane) λ_{max} 193, 233 sh, nm; mass spectrum, *m/e* (EI, relative percent) 150 (26), 135 (7), 122 (10), 107 (17), 93 (34), 79 (100), 67 (18), 55 (32).

***exo*-7-Carbethoxybicyclo[4.3.1]-1(9)-decene (26).** NMR ($CDCl_3$) δ 1.0–2.45 (m, 17 H), 4.14 (q, J = 7 Hz, 2 H), 5.57 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 177.14, 142.64, 123.80, 60.27, 47.41, 38.77, 35.35, 33.95, 31.21, 27.41, 25.82, 21.92, 14.28; IR (CS_2, 0.052 mm) 3038 (w), 2980 (m), 2932 (s), 2852 (m), 1731 (vs), 1651 (w), 1433 (m), 1370 (w), 1341 (w), 1300 (w), 1258 (m), 1239 (w), 1213 (w), 1173 (m), 1160 (m), 1142 (m), 109 (m), 1061 (w), 1038 (m), 855 (w), 812 (m), 791 (m) cm^{-1}; UV (hexane λ_{max} 199 nm; mass spectrum, *m/e* (EI, relative percent) 208 (7), 179 (2), 163 (4), 134 (100), 119 (25), 105 (28), 91 (91), 74 (74), 67 (60), 55 (43).

***endo*-7-Carbethoxybicyclo[4.3.1]-1(9)-decene (27).** NMR ($CDCl_3$) δ 0.9–2.8 (m, 16 H), 2.95 (t, J = 7 Hz, 1 H), 4.11 (q, J = 7 H, 2 H), 5.55 (m, 1 H); IR (CS_2, 0.052 mm) 3040 (w), 2980 (m), 2929 (s), 2858 (m), 1733 (vs), 1653 (s), 1435 (m), 1366 (m), 1333 (w), 1321 nw), 1252 (w), 1212 (w), 1100 (s), 1149 (s), 1097 (w), 1057 (w), 1021 (m), 966 (w), 910 (w), 851 (w), 818 (w), 792 (w) cm^{-1}; UV (hexane) λ_{max} 197 nm; mass spectrum, *m/e* (EI, relative percent) 208 (11), 179 (2), 163 (10), 134 (73), 120 (20), 105 (31), 93 (100), 79 (82), 67 (55), 55 (50).

6-Carbethoxybicyclo[4.3.1]-1(9)-decene (28). NMR ($CDCl_3$) δ 1.1–1.9 (m, 9 H), 1.9–2.4 (m, 6 H), 4.14 (q, J = 5 Hz, 2 H), 5.68 (t, J = 5 Hz, 1 H); IR (CS_2, 0.052 mm) 3035 (w), 2978 (m), 2930 Is), 2848 (m), 1728 (vs), 1652 (w), 1367 (w), 1299 (w), 1246 (s), 1237 (m), 1200 (m), 1175 (s), 1148 (w), 1104 (w), 1093 (w), 1070 (m), 1055 (m), 794 (m) cm^{-1}; UV (hexane) λ_{max} 198 nm; mass spectrum, *m/e* (CI, 2-methylpropane, relative percent) 209 (MH^+, 100), 163 (7), 161 (7), 135 (87), 134 (53), 133 (36).

Epimerization and Deuterium Labeling of *endo*-7-Carbethoxybicyclo-[4.3.1]-1(9)-decene (27). Bridgehead olefin ester **27** (0.005 g, 0.24 mmol) is added to LDA (0.26 mmol) in THF (5 mL) at −78 °C. The reaction mixture is stirred at −78 °C for 1 h and then quenched with 1 mL of ethanol-*d*. After 15 min at −78 °C, the reaction is warmed, diluted with water, and extracted with ether (2 mL). The organic layer is washed with brine (2 × 11 mL) and dried (Na_2SO_4). The mixture is concentrated and analyzed by VPC. The product is predominantly exo ester **26** (97%) with a small amount (3%) of endo ester **27**. GC–MS analysis reveals that the exo diastomer has 11% deuterium incorporation while the endo had 83% deuterium incorporated. The endo ester, isolated by preparative VPC, has an ^1H NMR ($CDCl_3$) spectrum that is identical with nondeuterated *endo*-**27** except that the absorption at 2.9 ppm is absent.

Acknowledgment. Support of this work by the National Science Foundation is gratefully acknowledged. NMR and mass spectra were determined with spectrometers purchased with the assistance of NSF instrumentation grants.

Registry No. 1, 68695-14-7; **5**, 17844-21-2; **6**, 71304-43-3; **7**, 82865-49-4; **8**, 82865-50-7; **9**, 71304-44-4; **11**, 71304-41-1; (*E*)-**12**, 71304-45-5; (*Z*)-**1i**, 82865-51-8; **13**, 71304-42-2; (*E*)-**14**, 71304-46-6; (*Z*)-**14**, 71304-51-3; **15b**, 82865-52-9; **16a**, 82865-53-0; **16b**, 82865-54-1; **1m**, 68695-13-6; **18**, 17530-61-9; **19**, 71304-49-9; **20**, 71304-48-8; **22**, 82865-55-2; **23**, 82865-56-3; **2**, 61764-75-8; **25**, 71304-50-2; **26**, 71328-42-2; **27**, 71304-47-7; **28**, 82865-57-4; 3-hydroxy-6-methylene-1,7-octadiene, 82865-58-5; vinyl bromide, 593-60-2; *O*-(*tert*)-butyldimethylsilyl)-1,4-pentadien-3-ol, 82865-59-6; 2-(bromomethyl)-1,3-butadiene, 23691-13-6; ethyl 3-bromopropyl acetaldehyde acetal, 34399-67-2; 2-(bromomethyl)-1,3-butadiene, 23691-13-6; 5-methylene-6-hepten-1-ol, 74785-37-8; trimethylphosphonoacetate, 5927-18-4; 6-methylene-7-octen-1-ol, 82865-60-9; 4-bromo-1-butanol THP, 31608-22-7; ethyl (trimethylsilyl)acetate, 4071-88-9; triphenylphosphite methyliodide, 2065-66-9; methyl acetoacetate sodium salt, 34284-28-1; 8-methylene-3-carboethoxy-9-decen-2-one, 82865-61-0; formaldehyde, 50-00-0; 4-methylene-1-iodo-5-hexene, 17844-24-5; 7-methylene-3-carboethoxy-8-nonen-2-one, 82865-62-1; 1,5-dicarbomethoxybicyclo[3.2.0]heptane, 31947-23-6; 1-vinyl-5-carbomethoxybicyclo[3.2.0]heptane, 82865-63-2.

Synthesis and Chemistry of a Bridgehead Enol Lactone

Kenneth J. Shea* and Eiji Wada

Contribution from the Department of Chemistry, University of California, Irvine, California 92717. *Received December 9, 1981*

Abstract: Intramolecular Diels–Alder cycloaddition of ethyl 1-methylene-2-methyl-2-propenyl hex-2-enedioate (**6**) results in formation of bridgehead enol lactone **7** in high yield. The bridgehead enol lactone is a stable crystalline solid. Under mild acidic and basic conditions, the lactone bridge is cleaved to produce an enol or enolate ion in a high-energy boat conformation. Product stereochemistry of the cleavage reaction under basic or mildly acidic conditions reveals a rapid conformational relaxation to a low-energy chair conformer that undergoes highly stereoselective protonation. At higher Brønsted acidities, the apparent stereoselectivity of this protonation step diminishes. This is believed to be due to the onset of competing AS_E2 carbon–carbon double bond protonation, a process that results in formation of a product epimeric with that of the lactone cleavage reaction under milder acidic or basic conditions.

The intramolecular Diels–Alder reaction occupies a prominent position in contemporary organic synthesis.[1] Recently the scope of this reaction has been extended to include the synthesis of bicyclic bridgehead olefins.[2] This intramolecular cycloaddition reaction has proven to be sufficiently flexible to permit synthesis of a wide variety of functionalized bridgehead alkenes.[3] These compounds are of interest not only for providing an opportunity

(1) (a) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (b) Carlson, R. G. *Annu. Rep. Med. Chem.* **1974**, *9*, 270. (c) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63. (d) Kametami, T.; Nemoto, H. *Tetrahedron* **1981**, *37*, 3.

(2) Shea, K. J.; Wise, S. *J. Am. Chem. Soc.* **1978**, *100*, 6289.
(3) Shea, K. J.; Wise, S. *Tetrahedron* Lett. **1979**, 1011.

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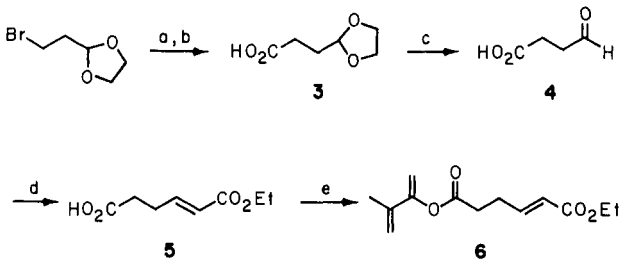
Scheme I



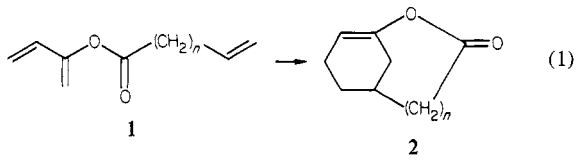
[a] Mg/Et_2O. [b] CO_2. [c] 0.5 N HCl. [d] Ph_3PCHCO_2Et. [e] $HCCC(CH_3)CH_2$, HgO, $Et_2O{\cdot}BF_3$, MeOH.

to establish the influence of a strained double bond on the chemical properties of organic functional groups[4,5] but also for their potential application in synthetic organic chemistry.[6]

This paper describes the first synthesis of a representative of a new class of molecules, bridgehead enol lactones (**2**). The compound, prepared by an extension of the intramolecular Diels–Alder reaction, permits evaluation of the influence of a torsionally distorted double bound on the chemistry of enol esters.

Results and Discussion

Our approach to the synthesis of bridgehead enol lactones is shown in eq 1. Intramolecular Diels–Alder cycloaddition of a

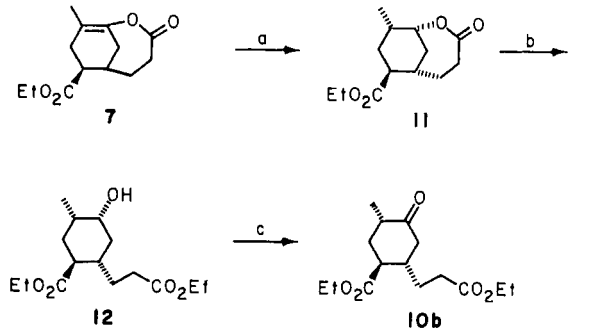


(1)

dienol ester of general structure **1** results in formation of the bridgehead olefin. The key structural feature of compound **1** is the dienol ester linkage. Simple 2-(acyloxy)-1,3-butadienes are mildly activated dienes in bimolecular Diels–Alder reactions.[7] Their synthesis has been achieved by several methods, including esterification of methyl vinyl ketones[8] and Lewis acid catalyzed condensation of carboxylic acids with conjugated enynes.[9] We have employed an adaption of this latter procedure to prepare dienol esters of general structure **1** from enynes. After several unsuccessful attempts at intramolecular cycloaddition of dienol esters,[10] we undertook a study of the synthesis and thermal chemistry of ethyl 1-methylene-2-methyl-2-propenyl hex-2-en-edioate (**6**). Its synthesis is outlined in Scheme I.

Although several syntheses of the acid aldehyde **4** have been reported,[11] we found carbonation of the organomagnesium reagent derived from 3-bromopropionaldehyde acetal[12] followed by acidification (pH 3), ether extraction, and deprotection (0.5 M HCl) to be the most convenient procedure for its preparation on a large scale (69% from bromo acetal). Acid aldehyde **4** is not isolated but is subjected to Wittig olefination conditions (Ph_3PCHCO_2Et) to yield the half-ester **5** (35%), as a crystalline solid.

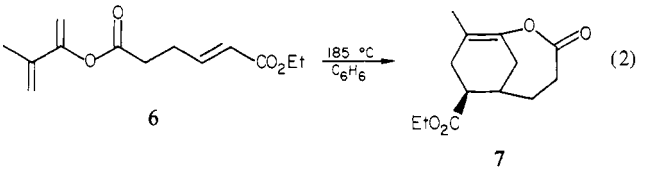
Scheme II



[a] $Pd/C-H_2$. [b] NaOEt, EtOH. [c] PDC/CH_2Cl_2.

Condensation of half-ester **5** and 2-methyl-1-buten-3-yne was accomplished in the presence of $HgO/BF_3{\cdot}OEt_2/MeOH$. The reaction presumably involves formation of a mercuric ester that undergoes electrophilic addition to the acetylenic group.[13] In situ protolytic cleavage of the vinyl–mercury bond produces dienol ester **6** and regeneration of an Hg^{II} species that can reenter the reaction sequence (HgO is present only in catalytic amounts). Dienol ester **6** was obtained in 60% yield together with 15% unreacted acid **5**.

Cycloaddition of dienol ester **6** was accomplished by heating



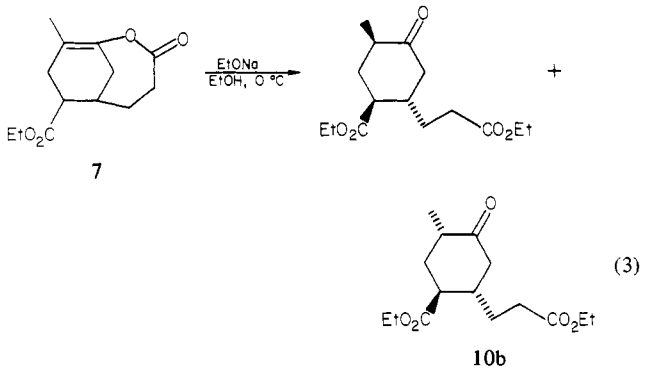
(2)

degassed 0.04 M solutions for 18 h at 185–188 °C. The crystalline bridgehead enol lactone **7** could be isolated by column chromatography (SiO_2) in 78% yield together with unreacted starting material (15%). The structure of the bridgehead enol lactone was established by a combination of ^1H and ^{13}C NMR spectra. The ^{13}C NMR spectrum revealed two olefinic carbon resonances at 145.33 and 122.59 ppm, consistent with an enol ester double bond,[14] in addition to carbonyl absorptions at 173.51 and 174.99 ppm. The infrared spectrum shows prominent absorptions at 1762 and 1733 cm^{-1} and a weaker absorption at 1685 cm^{-1}. Efforts to obtain a single crystal suitable for an X-ray crystal structure have not as yet been successful.

The cleavage reactions of bridgehead enol lactone **7** pose a variety of interesting mechanistic alternatives. Under basic conditions $B_{Ac}2$ lactone cleavage (carbonyl attack followed by acyl-oxygen cleavage) is expected to prevail.[15] This pathway will result in formation of a cyclohexanone enolate anion (**8**). Protonation (C or O) results in ketone or enol formation; this mixture is ultimately converted to ketones **10a** and **10b**. Information regarding the stereochemistry of these events can be extracted providing product stability under the reaction conditions can be established.

Experimentally, sodium ethoxide–ethanol (0 °C, 30 min) gives an 85:15 ratio of epimeric keto diesters (**10a** and **10b**, eq 3). Stereochemical assignments were secured as follows. The multiplet from the methyne proton at carbon 2 for the *major* isomer was located in the 500-MHz ^1H NMR spectrum (2.44 ppm). Methyl decoupling resulted in collapse of this multiplet to a doublet of doublets (J = 13.13 Hz, J = 5.50 Hz) indicative of an axial hydrogen at carbon 2.[16] Since intramolecular Diels–Alder cy-

(4) See, for example: House, H. O.; Sieloff, R. F.; Van Derweer, D. *J. Org. Chem.* **1981**, *46*, 4639 and references cited therein.
(5) Shea, K. J. *Tetrahedron* **1980**, *36*, 1683.
(6) Shea, K. J.; Beauchamp, P. S.; Lind, R. S. *J. Am. Chem. Soc.* **1980**, *102*, 4544.
(7) Petrzilka, M.; Grayson, J. I. *Synthesis* **1981**, 753.
(8) (a) Thomas, A. F.; Ohloff, G. *Helv. Chem. Acta* **1970**, *53*, 1145. (b) Saucy, G.; Marbet, R. *Ibid.* **1967**, *50*, 2091.
(9) (a) Plaisance, C. B.; Casalo, P. F.; Levesque, G. *Makromol. Chem.* **1979**, *180*, 79. (b) Ansell, M. F.; Brooks, G. T. *J. Chem. Soc.* **1956**, 4518. (c) Hennion, G. F.; Nieuland, J. A. *J. Am. Chem. Soc.* **1934**, *56*, 1802.
(10) Shea, K. J.; Wada, E. *Tetrahedron Lett.* **1982**, 1523.
(11) (a) Bruce, R.; Sino, K.; Pitts, F. N. *Anal. Biochem.* **1971**, *41*, 271. (b) Schellenbergen, A.; Heinroth, I.; Huebner, G. *Hoppe-Seyler's Z. Physiol. Chem.* **1967**, *348*, 506. (c) Tsybina, N. M.; Protopopova, T. V.; Skoldinov, A. P. *Zh. Org. Khim.* **1970**, *6*, 269. (d) Watanabi, Y.; Yamashita, M.; Mitsudo, T.; Igami, M.; Takegami, Y. *Bull. Chem. Soc. Jpn.* **1975**, *48*, 2490.
(12) Buchi, G.; Wüest, H. *J. Org. Chem.* **1969**, *34*, 1122.
(13) Shoslakovskii, M. F.; Trofimov, B. A.; Atavin, A. S.; Lavrov, V. I. *Russ. Chem. Rev. (Engl. Transl.)* **1968**, *37*, 907.
(14) Levy, G. C.; Lichter, R. L.; Nelson, G. L. "Nuclear Magnetic *Resonance* Spectroscopy", 2nd ed., Wiley-Interscience: New York, 1980.
(15) For reviews of the mechanism of ester hydrolysis, see: (a) Bamford, C. H.; Tipper, C. F. H. *Compr. Chem. Kinet.* **1972**, 10, Chapter 2 and 3. (b) Ingold, C. K. "Structure and Mechanism in Organic Chemistry", 2nd ed.; Cornell University Press: New York, 1969; p 1131.

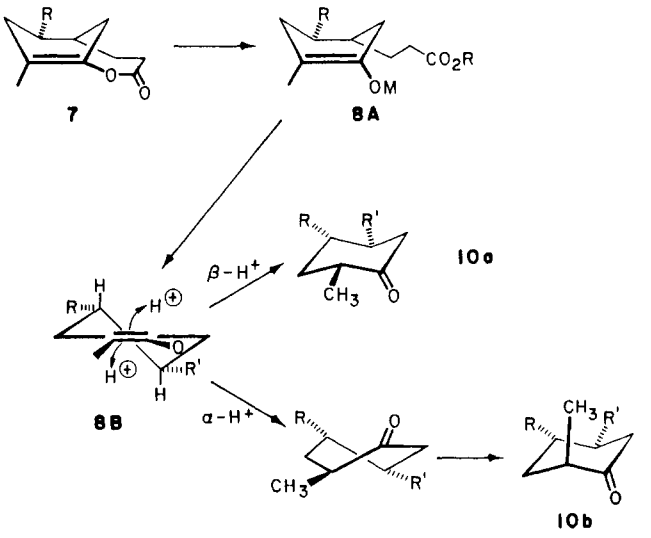


cloaddition is stereospecific at the dienophile,[4] the relative configuration of substituents at carbons 4 and 5 is fixed as trans; thus the major product is **10a**, the all-equatorial isomer. The *minor* component was shown to be an epimer of **10a** by equilibration studies (Et_3N, 100 °C) and by the stereochemical cycle shown in Scheme II. Catalytic reduction of bridgehead enol lactone at room temperature or below gives bicyclic lactone **11** (95%). Syn addition from the exo face of the bridgehead double bond[17] establishes the relative configuration of all substituents. Ethoxide cleavage of the lactone bridge produces a single cyclohexanol (**12**) in quantitative yield. Oxidation of this alcohol (PDC/CH_2Cl_2/room temperature) affords a product that is identical with the *minor* isomer resulting from base cleavage of bridgehead enol lactone (**10b**). Unambiguous stereochemical assignments of the ethoxide cleavage reaction of **7** is now possible—the product distribution is 85% **10a** and 15% **10b**. Equilibration studies of epimer **10b** under the EtONa/EtOH reaction conditions reveal this ratio of epimers represents an *equilibrium* mixture. It does not, therefore, provide information regarding the stereochemistry of the preceding events. Under milder basic conditions (Na_2CO_3/EtOH, room temperature, 44 h), conditions that do not result in significant product isomerization, the ratio of **10a**:**10b** is (90.5:9.5). The product ratio represents the end result of protonation of enol and/or enolate ions formed in the ring cleavage reaction. Since the initial enol (enolate) is produced in a high-energy boat conformation (Scheme III, **8A**), the product distribution is best understood by rapid conformational relaxation to one of two low-energy half-chair conformations (**8B**). The stereochemistry is established at the subsequent protonation step. This takes place with a strong preference for axial protonation from the β face at carbon 2 to produce the most stable chair conformation of cyclohexanone.

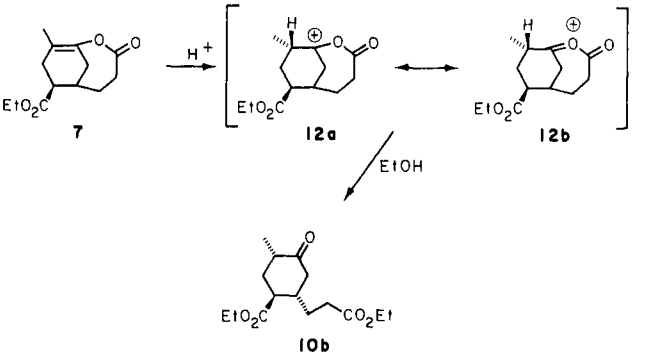
The stereoselectivity of this reaction (Scheme III) is consistent with previous stereochemical studies of kinetic protonations of cyclohexanone enolate anions, although in the present example the stereoselectivity is significantly higher than that previously observed.[18,19] The relative time scales of conformational relaxation vs. proton transfer[20] and the observed product stereochemistry (a preference for epimer **10b** would be expected if protonation were to occur prior to conformational relaxation) argue for the sequence of events shown in Scheme III.

The gross stereochemical results do not permit a distinction between the stereochemistries of protonation of enol of enolate

Scheme III



Scheme IV



anion, although current evidence[21] favors rapid oxygen protonation to produce initially enol rather than carbon protonation to yield cyclohexanone.

The acid-catalyzed cleavage of bridgehead enol lactone **7** can proceed by either $B_{Ac}2$ ester cleavage (oxygen protonation–acyl-oxygen bond cleavage) or by initial carbon protonation (AS_E2). In the acid-catalyzed hydrolysis of simple vinyl acetates, i.e., isopropenyl acetate, both mechanisms contribute to the overall reaction.[22,23]

The importance of the AS_E2 contribution to the acid-catalyzed hydrolysis of **7** can be readily established since protonation at carbon 2 from the exo face fixes the relative configuration of the methyl group resulting in exclusive formation of **10b**.

When **7** was treated with several drops of HCl in ethanol at 20 °C, keto didesters **10a** and **10b** were obtained in a ratio of 84:16. This product distribution is similar to that from the base-catalyzed ethanolysis experiments. Since the products are only slightly epimerized under these conditions,[24] the similarity

(16) Jackman, L. M.; Sternhill, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: London, 1969; p 288.

(17) Stereochemical studies of the addition of reagents to bridgehead double bonds proceed almost without exception in an exo-syn manner.[5]

(18) For a general discussion of the stereochemistry of enolate protonation, see: (a) Lamaty, G. "Isotopes in Organic Chemistry. Volume 2. Isotopes in Hydrogen Transfer Processes"; Bunal, E.; Lee, C. C., Ed.; Elsevier: Amsterdam, 1976; Chapter 2. (b) House, H. O. "Modern Synthetic Reactions"; W. A. Benjamin: New York, 1972; pp 501.

(19) For the most pertinent references regarding the stereochemistry of cyclohexanone enolate protonation, see: (a) House, H. O.; Trost, B. M. *J. Org. Chem.* **1965**, *30*, 1341, 2502. (b) House, H. O.; Tefertiller, B. A.; Olmstead, H. O. *Ibid.* **1968**, *33*, 935. (c) Reference 18a.

(20) (a) Rates of conformational relaxation are on the time scale of bond rotations ($k_{max} = 10^{12}\ M^{-1}\ s^{-1}$). (b) Rates of proton transfer ($k_{max} = 10^{10}\ M^{-1}\ s^{-1}$). Eigen, M. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 1.

(21) See, for example, ref 20b and (a) Stuehr, J. *J. Am. Chem. Soc.* **1967**, *89*, 2826. (b) Ringold, J.; Malhotra, S. K. *Ibid.* **1962**, *84*, 3402. (c) Ringold, J.; Malhotra, S. K. *Ibid.* **1964**, *86*, 1997. (d) Ringold, J.; Malhotra, S. K. *Ibid.* **1965**, *87*, 3228.

(22) Mechanistic studies of acid-catalyzed hydrolysis of vinyl acetates: (a) Kring, E. V.; Jenkins, G. I.; Bacchetta, V. L. *J. Phys. Chem.* **1960**, *64*, 947. (b) Noyce, D. S.; Pollack, R. M. *J. Am. Chem. Soc.* **1969**, *91*, 119, 7158. (c) Attia, S. Y.; Berry, J. P.; Koshy, K. M.; Leung, Y. K.; Lyzniki, E. P.; Nowlan, V. J.; Oyama, K.; Tidwell, T. T. *Ibid.* **1977**, *99*, 3401. (d) Euranto, E. K.; Hautoniemi, L. *Acta Chem. Scand.* **1969**, *23*, 1288. (e) Novak, M.; Loudan, G. *J. Org. Chem.* **1977**, *42*, 2499.

(23) Mechanistic studies of base-catalyzed hydrolysis of vinyl acetates: (a) Euranto, E. K.; Alhoniemi, A. *Acta Chem. Scand.* **1972**, *26*, 855. (b) Evans, C. G.; Thomas, J. D. R. *J. Chem. Soc. B* **1971**, 1502. (c) Sharma, R. C.; Sharma, M. M. *Bull. Chem. Soc. Jpn.* **1970**, 642.

(24) A pure sample of **10b** under the reaction conditions was converted to a 36.9:63.1 mixture of **10a**:**10b**. A summary of ethanolysis conditions and epimerization results is given in the Experimental Section.

of product composition for both acid- and base-catalyzed ethanolysis implies similar reaction intermediates. Thus, the initially formed high-energy boat conformation of the enol (**8A**, Scheme III, M = H) relaxes to the chair conformation (**8B**) prior to protonation. The slightly lower ratio of **10a**:**10b** under acidic conditions may be due to differences in the stereochemistry of carbon proton addition to enols vs. enolates, to medium effects, or more likely, to a small component of competing AS_E2 ethanolysis.

The fraction of AS_E2 hydrolysis of vinyl acetates under acidic conditions is known to be a function of acid strength:[22c] rate-limiting proton addition to carbon becomes the principal reaction pathway at higher Brønsted acidities. Evidence for a competing AS_E2 reaction pathway may be obtained from a study of the ratio of **10a**:**10b** as a function of acidity. We have examined this ratio and have found that it decreases from 85:15 in dilute hydrochloric aicd to 73:27 in a medium of higher Brønsted acidity. Since product isomerization does not occur under the reaction conditions (see Experimental Section), this change in product ratio is mechanistically significant. These results suggest that under more strongly acidic conditions we are observing the onset of C-2 protonation with formation of the bridgehead carbonium ion, although this reaction pathway probably does not contribute to more than 10% of the overall reaction.[25] Since hydrolysis of simple enol esters at high acid concentration proceeds almost completely by the AS_E2 mechanism, the reluctance of bridgehead enol ester **7** to react by this pathway may be due to the instability of bridgehead carbonium ion **12**[26] (Scheme IV). This instability could more than offset the increase in reactivity (proton affinity) expected of a torsionally distorted carbon–carbon double bond.[27]

These results underscore the interesting mechanistic differences that emerge between simple enol esters and bridgehead enol esters.

We are continuing with our studies of the synthesis and chemistry of bridgehead enol esters with particular attention to their potential application in synthetic organic chemistry.

Experimental Section[28]

3-(2-Dioxolanyl)propionic Acid (3).[11] A solution of 3-bromopropionaldehyde acetal[12] (21 g, 0.116 mol) in THF (60 mL) was added dropwise to a stirred suspension of magnesium turnings (10 g, 0.411 mol) in THF (200 mL) at 15–20 °C under an atmosphere of nitrogen. After completion of addition the mixture is stirred for 1 h (20–23 °C) and then cooled to −40 °C. A large excess of powdered dry ice was added with stirring followed by saturated NH_4Cl and water. The reaction mixture was filtered through glass wool, concentrated, and then extracted with ether (100 mL). The aqueous solution was acidified to pH 3 (methyl orange indicator), extracted with ether (6 × 150 mL), dried ($MgSO_4$), and concentrated to yield 13 g (77%) of 3-(2-dioxolanyl)propionic acid (**3**): ^1H NMR (80 Hz, $CDCl_3$) δ 9.44 (br s, 1 H, OH), 4.97 (t, 1 H, J = 4 Hz, O_2CH), 3.91 (m, 4 H, CH_2O), 2.48 (apparent t, 2 H, J = 6.6 Hz, CH_2CO_2), 1.99 (m, 2 H).

Ethyl Hex-2-enedioate (5). A solution of acid acetal **3** (1.44 g, 10 mmol) in 0.5 N HCl was stirred for 12 h at room temperature. The resulting solution was saturated with NaCl, extracted with ether (5 × 40 mL), dried ($MgSO_4$), and concentrated to give crude acid aldehyde **4** (0.90 g, 90%).[11]

The crude acid aldehyde **4** and Ph_3PCHCO_2Et (7.0 g, 20 mmol)[29] in THF (50 mL) was refluxed for 24 h under an atmosphere of N_2. The reaction mixture was concentrated and the resultant oil stirred with 10% aqueous Na_2CO_3 (60 mL) for 1 h. The solution was extracted with CH_2Cl_2 (2 × 30 mL), acidified (concentrated HCl, pH 3), extracted with ether (5 × 40 mL), and dried ($MgSO_4$). Concentration of the extracts gave crude **5** (800 mg, 46%). Purification (SiO_2, CH_2Cl_2:Et_2O 85:15) gave (605 mg, 35%) pure crystalline product: mp 33–36 °C; IR (film) 3500–3000 br, 1750–1690 br, 1658, 1320, 1250, 1230, 1150 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 8.0 (br s, 1 H, OH), 6.96 (m, 1 H, $RO_2CC(H)$=), 5.86 (d, 1 h, J = 15.6 Hz, =C(H)CH_2), 4.20 (q, 2 H, J = 7.1 Hz, CH_2CH_3), 2.53 (d, 4 H, J = 2.7 Hz, CH_2CH_2), 1.37 (t, 3 H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 177.7, 166.6, 146.6, 122.4, 60.5, 32.3, 27.0, 14.2. Anal. Calcd for $C_8H_{11}O_4$: C, 55.79; H, 7.02. Found: C, 55.78; C, 7.05.

Ethyl 1-Methylene-2-methyl-2-propenyl Hex-2-enedioate (6). A mixture of red HgO (0.36 g, 1.67 mmol) $BF_3{\cdot}OEt_2$ (0.12 mL) and MeOH (0.12 mL) was warmed for 5 min at 50–55 °C and then cooled to room temperature. To this suspension is added **5** (2.1 g, 12.2 mmol) in Et_2O (5 mL) followed by 2-methylbuten-3-yne (5 mL, 60 mmol). The resulting reaction mixture is stirred for 17 h at room temperature and then extracted with Et_2O. The ether extracts are washed with H_2O and saturated $NaHCO_3$ and dried ($MgSO_4$). Concentration gave an oil (4.5 g) that was chromatographed twice on SiO_2 (100 g, Et_2O:hexane 12.5:87.5) to give 1.80 g (60%) of pure diester **6**: IR (film) 1760, 1725, 1716, 1668, 1603, 1265, 1135, 1038, 890 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.15–6.75 (m, 1 H, $CH_2C(H)$=), 5.88 (d, 1 H, J = 1 Hz, $RCO_2C(H)$=), 5.10 (apparent d, 2 H, =CH_2), 5.01 (br s, 1 H, =CH), 4.87 (br s, 1 H, =CH), 4.19 (q, 2 H, J = 7.1 Hz, CH_2CH_3), 2.70–2.50 (m, 4 H, CH_2CH_2), 1.93 (br s, 3 H, CH_3C=), 1.28 (t, 3 H, J = 7.1 Hz, CH_3CH_2); ^{13}C ($CDCl_3$) δ 170.3, 166.2, 153.5, 146.0, 136.8, 122.8, 113.8, 103.3, 60.3, 32.5, 27.2, 19.4, 14.3. Acidification of the mother liquor (concentrated HCl, pH 3) and ether extractions gave, after drying and concentration, 0.30 g (15%) of unreacted starting material (**5**). Dienol diester **6** was not stable as a neat liquid. Following purification it was immediately carried through the next step.

***exo*-7-Carbethoxy-9-methyl-2-oxabicyclo[4.3.1]dec-1(9)-en-3-one (7).** A dry, degassed benzene solution (13 mL) of diester **6** (128 mg, 0.538 mmol) containing a catalytic amount of hydroquinone was heated in a Carius tube for 18 h at 185–188 °C. Concentration and purification of the residue by chromatography on silica gel (4:1 hexane–ether) gave starting diester **6** (20 mg, 15%) (TLC, R_f 0.55, 4:1 hexane–ether) and bridgehead enol lactone **7** (100 mg, 78%, 92% net) (TLC, R_f 0.33, 4:1 hexane–ether). Recrystallization from pentane afforded an analytical sample of the cycloadduct **7**: mp 54–55 °C; IR (CCl_4) 1762, 1733, 1685, 1180, 1160, 1115, 1050 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.17 (q, 2 H, J = 7.1 Hz, OCH_2), 2.73 (m, 1 H, RO_2CCH), 2.6–1.6 (complex m, 9 H, ring H's), 1.78 (br s, 3 H, C=CCH_3), 1.27 (t, 3 H, J = 7.1 Hz, CH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 175.0, 173.5, 145.3, 122.6, 60.8, 44.6, 37.1, 34.1, 33.7, 33.0, 31.3, 15.1, 14.2; mass spectrum, m/e (EI, relative percent) 238 (10), 210 (33), 193 (14), 109 (100); M, $C_{13}H_{18}O_4$ requires 238.1205, found 238.1201.

Ethanolysis of Bridgehead Enol Lactone 7. To a NaOEt solution prepared from Na (100 mg, 4.35 mmol) and dry EtOH (28 mL) was added bridgehead enol lactone **7** (100 mg) in EtOH (3 mL) at −7 °C (ice–salt bath). The solution was stirred for 30 min at −7 °C and then treated with saturated NH_4Cl. The resulting suspension was extracted with ether (3 × 30 mL), and the combined extracts were washed (H_2O) and then dried ($MgSO_4$). Concentration of the extracts gave an oil (110 mg) which was chromatographed on silica gel (4:1 hexane–ether) and gave chromatographically pure keto diester **10b**, 3.5 mg (TLC, R_f 0.5; 4:1 hexane–ether), intermeidate fractions containing mixtures of **10a** and **10b**, 81.5 mg, and chromatographically pure keto diester **10a**, 20 mg (TLC, R_f 0.48; 4:1 hexane–ether), for a combined yield of 87.5%.

Major isomer, *r*-2-methyl-*c*-4-carbethoxy-*t*-5-[2-(ethoxycarbonyl)-ethyl]cyclohexanone (**10a**): IR (film) 1726, 1716 1255, 1180, 1025 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 4.14 (two overlapping q, 4 H, J = 7.1 Hz, OCH_2) 2.75–1.88 (m, 8 H), 1.88–1.49 (m, 3 H), 1.26 (two overlapping t, 6 H, J = 7.1 Hz, CH_2CH_3), 1.1 (d, 3 H, J = 6.2 Hz, $HCCH_3$); ^{13}C NMR (C_6D_6) δ 208.0, 173.6, 172.5, 60.4, 60.2, 48.7, 45.0, 43.3, 40.6, 37.9, 30.9, 29.9, 14.2 (3-CH_3); ^1H NMR (500 MHz, $CDCl_3$) δ 2.44, C_2–CH_3 decoupling (d,d, 1 H, J_{AX-AX} = 13.13 Hz, J_{AX-EQ} = 5.50, C_2H).

Anal. Calcd for $C_{15}H_{24}O_5$: C, 63.36; H, 8.49. Found: C, 63.36; H, 8.51.

Minor isomer, *r*-2-methyl-*t*-4-carbethoxy-*c*-5-[2-(ethoxycarbonyl)-ethyl]cyclohexanone (**10b**): ^1H NMR (80 MHz, $CDCl_3$) δ 4.17 (apparent p, 4 H, J = 7.1 Hz, OCH_2CH_3), 2.75–2.00 (m, 8 H), 2.0–1.5 (m, 3 H), 1.27 (two overlapping t, 6 H, J = 7.1 Hz, CH_2CH_3), 1.06 (d, 3 H, J = 6.5 Hz, $HCCH_3$); ^{13}C NMR (C_6D_6) δ 209.5, 173.9, 172.2, 60.5, 60.2, 43.4, 42.6, 41.8, 38.5, 33.1, 31.7, 28.9, 15.0, 14.3, (2-CH_3).

Stereochemical Correlation. *exo*-7-Carbethoxy-*endo*-9-methyl-2-oxabicyclo[4.3.1]decan-3-one (11). To a suspension of 10% Pd–C (2.5 mg) in dry ethyl acetate was added bridgehead enol acetate **7** in ethyl acetate

(25) This value assumes that under acidic conditions the product ratio difference is due to formation of **10b** via the AS_E2 pathway.

(26) Fort, R. C.; Schleyer, P. von R. *Adv. Alicyclic Chem.* **1966**, *1*, 284.

(27) Torsionally distorted carbon–carbon double bonds have significantly enhanced proton affinities. For example, bicyclo[3.3.1]non-1-ene is protonated in acetic acid: Becker, K. B. *Helv. Chem. Acta* **1977**, *60*, 94 and ref 5.

(28) **General Information.** Infrared spectra were recorded on a Perkin-Elmer 238 spectrophotometer. ^1H NMR spectra were determined with Varian EM 360 (60 MHz), Varian FT 80A (80 MHz), or Bruker WM 250 (250 MHz) spectrometers. ^{13}C NMR spectra were determined at 22.62 MHz with a Bruker WH-90 spectrometer. ^1H and ^{13}C NMR shifts are reported as δ values relative to internal Me_4Si. ^1H NMR coupling constants are reported in Hz and refer to apparent multiplicities. High-resolution mass spectra were determined at the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, NE. Low-resolution mass spectra were determined on a Finnigan 4000 GC/MS/DS. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

(29) Maercker, A. *Org. React.* (*N.Y.*) **1965**, *14*, 270.

(1 mL) at 0 °C under H_2. Approximately 2.5 mL of hydrogen was absorbed over 110 min. The reaction mixture was passed through a short plug of silica gel. The crude product was shown by VPC to consist of a mixture of lactone **11** (95.4%) and starting material (4.6%). Chromatography on silica gel (1:1 hexane–ether) gave pure lactone **11**, 18 mg (75%): IR (neat film) 1726, 1716, 1175, 1025 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.38 (br s, 1 H, HCO bridgehead), 4.17 (q, 3 H, J = 7.1 Hz, OCH_2CH_3), 2.81 (apparent t, 2 H), 2.56 (m, 2 H), 2.35–1.52 (m, 7 H), 1.26 (t, 3 H, J = 7.1 Hz, CH_2CH_3), 1.05 (d, 3 H, J = 6.1 Hz, CH_3CH); ^{13}C NMR ($CDCl_3$) δ 174.0, 173.5, 78.5, 66.3, 44.9, 34.7, 33.5, 29.2, 28.3, 26.5, 25.9, 18.3, 14.3.

The hydrogenation was found to be a sensitive reaction, often giving two as yet unidentified side products at times as the major product. The temperature of the reduction was found to be important in minimizing these side reactions; optimum yields were obtained at or below room temperature.

Cyclohexanol 12. A solution of bicyclic lactone **11** (11 mg, 0.046 mmol) in ethanol (2 mL) was added to a solution of NaOEt (50 mg Na) in ethanol (10 mL) at 0 °C under an atmosphere of N_2. The reaction mixture was stirred at 0 °C for 30 min, treated with saturated NH_4Cl, and concentrated. The residue was extracted with ether, washed (H_2O), and dried ($MgSO_4$). Concentration gave an oil, 14 mg (100%): IR (film) 3450 (OH), 1726 (C=O), 1265, 1170, 1150, 1090, 1030 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 4.12 (two partially superimposed q, 4 H, J = 7.1 Hz, OCH_2), 3.97 (d, t, 1 H, J = 11.3, 4.4 Hz, HOC*H*), 2.5–1.35 (m, 12 H), 1.24 (two partially superimposed t, 6 H, J = 7.1 Hz, CH_2CH_3), 0.95 (d, 3 H, J = 7.1 Hz, CH_3CH).

Oxidation of Cyclohexanol 12. Cyclohexanol **12** (12.5 mg, 0.04 mmol) in CH_2Cl_2 (2 mL) was added to a stirred suspension of pyridinium chlorochromate (56 mg, 0.26 mmol) in CH_2Cl_2 (2 mL). After stirring for 20 min, the reaction mixture was filtered through silica gel and concentrated to give 14 mg of crude product. VPC analysis indicated a mixture of starting material (64%) and ketone product (34%). Further oxidation with pyridinium chlorochromate (200 mg, 6 mmol) for 1 h in CH_2Cl_2 at room temperature followed by washing gave 9.5 mg of an oil (76%) that was shown by VPC to be a mixture of starting material (13%) and ketone (87%). The ketone product had an identical VPC retention time (two columns) and spectral properties (^1H and ^{13}C NMR), with the *minor* product (**10b**) resulting from acid or base cleavage of bridgehead enol lactone **7**.

Stereochemical Studies of the Hydrolysis of Bridgehead Enol Lactone 7. Pure samples of bridgehead enol lactone **7** were subjected to the indicated reaction conditions. After the specified amount of time, the reaction mixtures were quenched with water, neutralized and extracted with ether, filtered through a short plug of silica gel, and concentrated. The product mixture was analyzed by VPC with a 50-m SE-30 capillary column; retention times: **7**, 14.91 min, **10b**, 16.01 min, **10a**, 16.15 min. The results are summarized below. The stability of keto diesters **10a** and **10b** under a variety of reaction conditions is also given below.

The following ethanolysis experiments of enol lactone **7** are averages of at least two runs. The reagents, temperature, time, and final product distribution [**7**:(**10a** + **10b**) (ratio)] are specified as follows:

Base Cleavage. NaOEt/EtOH (0.15 M), −6 °C, 30 min, 0:100 (85:15); NaOEt/EtOH (0.02 M), −2 °C, 30 min, 0:100 (84.9:15.1); Na_2CO_3/EtOH (0.1 M), 20 °C, 44 h, 1.8:95.6 (90.5:9.5).

Acid Cleavage. HCl/EtOH (0.05 M), 20 °C, 9 H, 0:96.8 (81:19); HCl/EtOH (0.1 M), 20 °C, 10 h, 3.1:94.7 (83.5:16.5); HCl/EtOH (0.1 M), −40 °C, 8 h, 65.4:32.6 (82.8:17.2); H_2SO_4/EtOH (0.1 M), 20 °C, 5 min, 81.5:17.0 (73:27).

Epimerization of Keto Diesters 10a and 10b. The epimerization experiments are average of at least two runs. The *initial* isomer ratio (**10a**:**10b**), reagents, temperature, time, and *final* isomer ratio (**10a**:**10b**) are specified as follows:

Base Epimerization. 5:95, NaOEt/EtOH (0.08 M), −2 °C 30 min, 86:14; 0:100, $NaCO_3$/EtOH (0.1 M), 20 °C, 44 h, 53:47; 90:10, Et_3N (neat), 100 °C, 24 h, 87.4:12.6.

Acid Epimerization. 0:100, HCl/EtOH (0.1 M), 20 °C, 36.9:63.1; 5:95, H_2SO_4/EtOH (0.1 M), 20 °C, 5 min, 5:95.

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Registry No. 3, 4388-56-1; **4**, 692-29-5; **5**, 82979-04-2; **6**, 82979-05-3; *exo*-**7**, 82979-06-4; **10a**, 82979-08-6; **10b**, 82979-07-5; **11**, 82979-09-7; **12**, 82979-10-0; 3-bromopropionaldehyde ethylene acetal, 18742-02-4; 2-methyl-1-buten-3-yne, 78-80-8.

Chiral and Stereochemical Control via Intramolecular Diels–Alder Reaction of *Z* Dienes[1]

Stephen G. Pyne,[2a] Mark J. Hensel,[2b] and P. L. Fuchs*

Contribution from the Department of Chemistry, Purdue University, West Lafayette, Indiana 47907. *Received November 24, 1981*

Abstract: Chiral *Z* dienes undergo intramolecular Diels–Alder reaction with enones to afford cis-fused products with complete stereo- and enantiospecificity.

The intramolecular Diels–Alder reaction of *E* dienes is a valuable and often-used strategy in organic synthesis.[3] A limitation associated with this expedient is that an *E* diene (**1**) has two relatively easily accessible transition states (endo, exo) which, in many instances, afford mixtures of cis- and trans-fused products (**2**, **3**). This problem is further exacerbated by the introduction of an additional asymmetric center at the pentadienylic position of the diene (**1**, X ≠ H). In this latter instance, it is possible for a mixture of four products (**2**α, **2**β, **3**α, **3**β) to result from the intramolecular Diels–Alder reaction (Scheme I). There have been a number of recent notable examples utilizing just such strategy; however, in many of these cases, a mixture of products was observed.[4-7]

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(2) (a) Postdoctoral Research Associate; (b) Graduate Research Associate.

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(5) Often the product (**2**) derived from the "endo" transition state is highly favored; however, there are numerous cases[6,7] where mixtures of products or products (**3**) derived only from the "exo" transition state are formed.

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