ethane (209 mg, 1.74 mmol) in $CHCl_3$ (5 mL). After 13 h the solvent was evaporated. Chromatography of the residue over alumina (3 × 50 cm) with hexane gave 213 mg (39%) of the major product **27** as a homogeneous (TLC, alumina, hexane) oil: NMR ($CDCl_3$) δ 2.1 (s, 9 H), 2.23 (s, 3 H); exact mass *m/e* 311.8451 (calcd for $C_5H_{12}{}^{80}Se_3$, *m/e* 311.8435). For analysis the material was distilled in a Kugelrohr apparatus; bp 110 °C (20 mm). Anal. Calcd for $C_5H_{12}Se_3$: C, 19.43; H, 3.91. Found: C, 19.61; H, 3.73.

Acknowledgment. Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work and to the National Research Council of Canada.

Registry No. 5, 29680-62-4; **6**, 29634-51-3; **10**, 71518-65-5; **11**, 71518-66-6; **12**, 71518-67-7; **13**, 66729-72-4; **14**, 66729-73-5; **15**, 71518-68-8; **16**, 71518-69-9; **17**, 67808-79-1; **18**, 71518-70-2; **19**, 71518-71-3; **20**, 53198-55-3; **21**, 63017-80-1; **22**, 71518-72-4; **23**, 69470-14-0; **24**, 67808-80-4; **25**, 71518-73-5; **26**, 71518-74-6; **27**, 66622-21-7; boron tribromide, 10294-33-4; benzeneselenol, 645-96-5; dimethyl diselenide, 7101-31-7; selenium, 7782-49-2; methyl iodide, 74-88-4; cyclopentanone, 120-92-3; estrone methyl ether, 1624-62-0; 5α-cholestan-3-one, 566-88-1; tricyclo[3.3.1.1^{3,7}]decan-2-one, 700-58-3; 4-*tert*-butylcyclohexanone, 98-53-3; nonan-5-one, 502-56-7; 3β-acetoxypregn-5-en-20-one, 1778-02-5; 3β-acetoxypregn-5-ene, 3090-79-7; undecanal, 112-44-7; 1-naphthaldehyde, 66-77-3; 2′-acetylnaphthalene, 93-08-3; acetophenone, 98-86-2; cholest-4-en-3-one, 601-57-0; 1,1,1-trimethoxyethane, 1445-45-0.

Homoallyl and Cyclopropylcarbinyl Carbonium Ion Formations under Strongly Basic Conditions[1]

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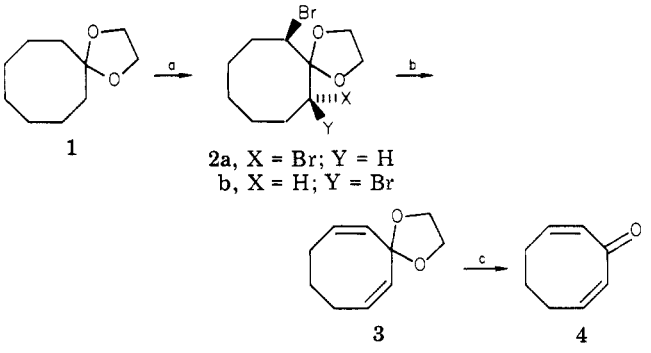
Treatment of *trans*-2,8-dibromocyclooctanone ethylene ketal with sodium hydroxide in refluxing methanol produced 2,7-cyclooctadienone ethylene ketal in yields of 71–79% and a mixture of 2-(2-cycloheptenyl)-2-methoxy-1,3-dioxolane (**15**) and 2-(*exo*-7-bicyclo[4.1.0]heptyl)-2-methoxy-1,3-dioxolane (**16**). The structures of the ortho ester side products were deduced from spectral and chemical methods. It was shown that the precursor of **15** was 2-bromocyclooct-7-enone ethylene ketal (**18**), and it was postulated that the intermediate which went on to **16** was 8-bromobicyclo[4.2.0]octan-7-one ethylene ketal (**25**). For the conversion of *trans*-2,7-dibromocycloheptanone ethylene ketal into the corresponding diene ketal, 2-(2-cyclohexenyl)-2-methoxy-1,3-dioxolane was found as a side product but not 2-(*exo*-6-bicyclo[3.1.0]hexyl)-2-methoxy-1,3-dioxolane. No rearrangement products were found with eliminations involving the ethylene ketals of *cis*-2,6-dibromo-4,4-dimethylcyclohexanone or *meso*-3,5-dibromo-4-heptanone. The involvement of intermediate carbonium ions is discussed.

In a previous report from this laboratory,[1b] it was shown that in the preparation of 2,7-cyclooctadienone (**4**) according to the reaction sequence developed by Garbisch (Scheme I),[2] the bis dehydrobromination step (**2** → **3**) was accompanied by interesting side reactions (apparently involving intermediate carbonium ions) which produced the ortho esters **15** and **16**. The structures of **15** and **16** were elucidated from spectral and analytical data, as well as from several chemical transformations (Schemes II and III).[3] Authentic samples of compounds **9** and **12** were prepared by independent routes,[4] while compounds **14a** and **14b** exhibited spectral properties identical with those reported for authentic materials.[5]

In a subsequent investigation, α,α'-dibromo ketals from the cycloheptyl and cyclohexyl frameworks as well as an acyclic system were subjected to the same elimination reaction conditions to find out what the effects of the smaller ring sizes would be on the side reactions. In this paper the results of that follow-up investigation are described; complete experimental details for the cyclooctyl system are also presented. Furthermore, additional information has been obtained which clarifies to some extent the origin of the ortho ester **16**.

Scheme I



a, Br_2/ether; b, NaOH/CH_3OH; c, 3% H_2SO_4.

Results

A. Cyclooctyl System. In the preliminary communication[1b] it was speculated that the homoallylic bromo ketal **18** (produced by the elimination of hydrogen bromide from dibromo ketal **2a**) ionized under the very polar reaction conditions to the homoallylic carbonium ion **19** and its cyclopropylcarbinyl counterpart **20**. Rearrangement of

(1) For a preliminary account of this work see: (a) Krabbenhoft, H. O. Abstracts, 8th Northeast Regional Meeting of the American Chemical Society, Boston, MA, June 25–28, 1978, No. ORGN 15. (b) Krabbenhoft, H. O. *J. Org. Chem.* **1978**, *43*, 4556.

(2) Garbisch, E. W., Jr. *J. Org. Chem.* **1965**, *30*, 2109.

(3) In actuality, mixtures of **5** and **6** were employed in the chemical degradations. Fortunately, in most cases the products resulting from reactions of **5** and **6** were separable and hence fully characterized; in those instances where separation was not achieved (i.e., with the carboxylic acids) the ^{13}C NMR spectra allowed definitive conclusions to be made.

(4) Karrer, P.; Keller, R.; Usteri, E. *Helv. Chim. Acta* **1944**, *27*, 237.

(5) (a) Musso, H. *Chem. Ber.* **1968**, *101*, 3710. (b) Ciganek, E. *J. Am. Chem. Soc.* **1971**, *93*, 2207. (c) Ishihara, T.; Ando, T.; Muranaka, T.; Saito, K. *J. Org. Chem.* **1977**, *42*, 666.

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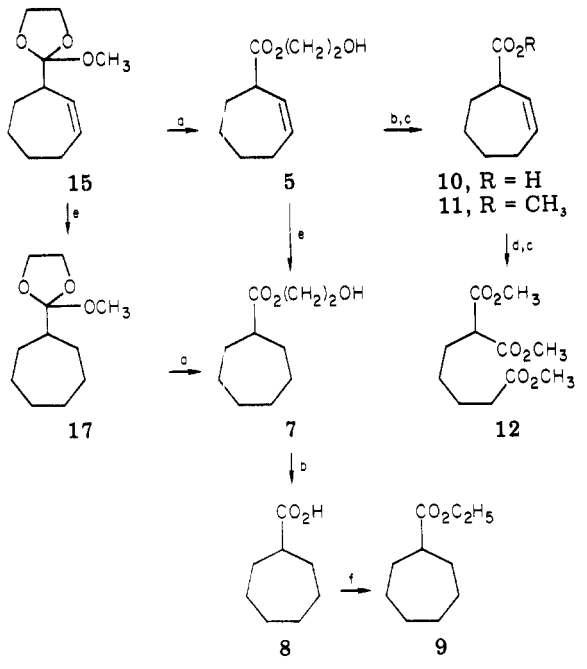
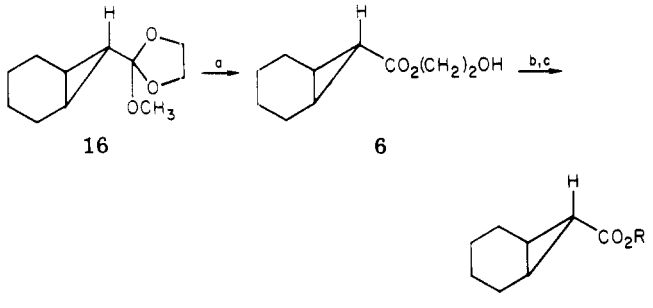
Scheme II



a, 3% H_2SO_4; b, KOH/aqueous C_2H_5OH; c, CH_3OH/H^+; d, $NaIO_4/KMnO_4/K_2CO_3$/aqueous acetone; e, H_2/Pd-C/C_2H_5OH; f, C_2H_5OH/H^+.

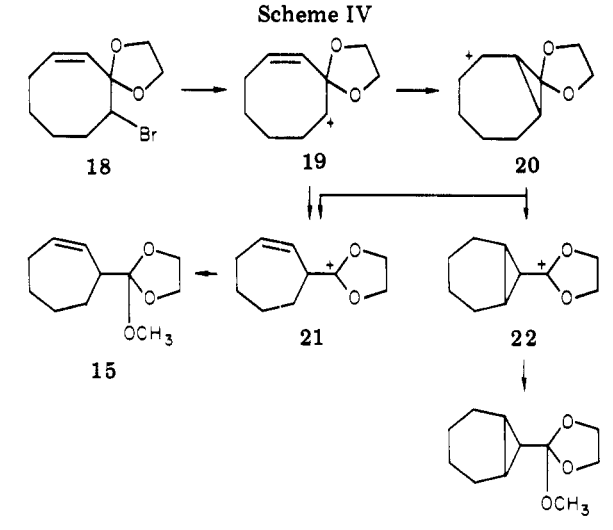
Scheme III



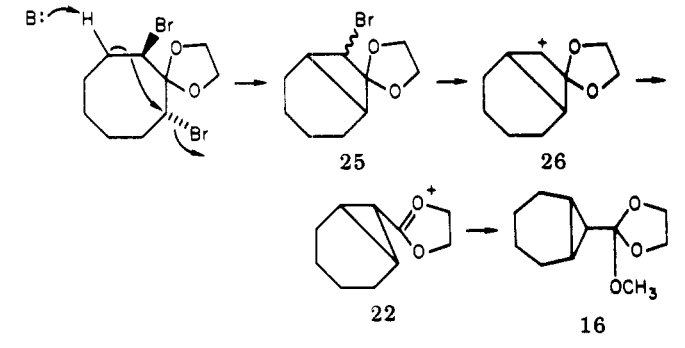
a, 3% H_2SO_4; b, KOH/aqueous C_2H_5OH; c, CH_3OH/H^+ or C_2H_5OH/H^+.

carbocations **19** and **20** utilizing the ethylene glyoxy unit gave ions **21** and **22** (stabilized by resonance with the adjacent oxygen atoms) which were trapped by methoxide/methanol to give the ortho esters **15** and **16** (Scheme IV).[6,7] Support for the proposal of Scheme IV was mixed. Thus, it was shown that methanolysis of distilled homoallylic ketal **18** (prepared by carrying out the elimination reaction to the extent that only a small amount of diene ketal **3** was formed) in the presence of anhydrous potassium carbonate gave ortho ester **15** *exclusively*. Likewise, treatment of homoallylic bromo ketal **18** in methanol with aqueous silver nitrate gave *quantitatively* ortho ester **15**, which under the reaction conditions was hydrolyzed to ester **5**.[9] These

Scheme IV



Scheme V



results are compatible with the intermediacy of homoallyl carbonium ions **19** and **21**. The fact that *no* cyclopropylcarbinyl products were formed was surprising in view of the results observed for the acetolysis of 3-cycloocten-1-yl brosylate, which gave bicyclo[5.1.0]octan-2-ols as the major products.[10]

It has now been determined that upon treatment of homoallylic bromo ketal **18** with methanolic sodium hydroxide at reflux (i.e., the conditions employed for the elimination reaction) *only* ortho ester **15** was formed (along with the major product diene ketal **3**; some starting material was also recovered). Thus, it was apparent that ortho ester **16** was *not* formed as indicated in Scheme IV. It should also be noted here than in the crude diene ketal (i.e., before distillation) *both* ortho esters **15** and **16** were present, thus discounting the possibility of a thermally induced isomerization of **15** to **16**; furthermore, resubjection of diene ketal **3** to the refluxing methanolic sodium hydroxide reaction conditions brought about no chemical changes.

Since the homoallylic bromo ketal **18** was not the precursor of the norcarane ortho ester **16**, there must have

(6) Interestingly, no ethers or alcohols derived by capture of cations **19** and **20** were found, suggesting that rearrangement to the much more stable carbonium ions **21** and **22** was very fast relative to the rate of interception by a nucleophile.

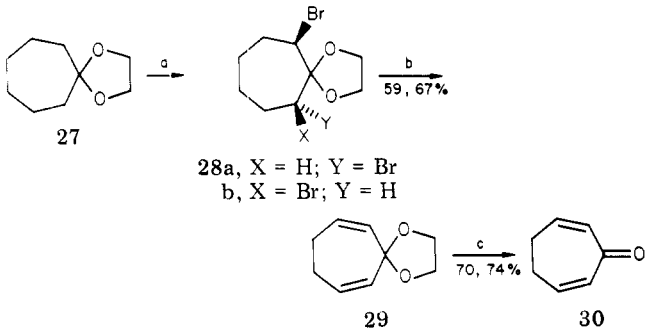
(7) Also somewhat surprising was the fact that **13** and 1-cycloheptenecarboxylic acid (**23**) (analyzed as their methyl esters **14a** and **24**,[8] respectively) which would be produced by the trapping of ions **21** and **22**, respectively, by hydroxide to give **5** and **6** followed by saponification (and in the case of **10**, isomerization to the α,β-unsaturated acid) were formed to the extent of only about 2%.

(8) The structure of ester **24** was confirmed by independent synthesis: (a) Ayerst, G. G.; Schofield, K. *J. Chem. Soc.* **1960**, 3445. (b) Mathur, K. C.; Saharia, G. S. *Indian J. Chem.* **1968**, *6*, 248. (c) Braidy, R. *Bull. Soc. Chim. Fr.* **1967**, 3489. See also: Froberg, J.; Magnusson, G.; Thoren, S. *Tetrahedron Lett.* **1975**, 1621.

(9) In contrast to this result, it was observed that both dibromo ketal **2a** and its monobromo counterpart were completely inert to the silver nitrate reaction conditions employed with the unsaturated bromo ketal **18**.

(10) Cope, A. C.; Peterson, P. E. *J. Am. Chem. Soc.* **1959**, *81*, 1643. See also: Friedrich, E. C.; Copper, J. D. *Tetrahedron Lett.* **1976**, 4397. Friedrich, L. E.; Wight, F. R. *J. Am. Chem. Soc.* **1970**, *92*, 1807. Cope, A. C.; Moon, S.; Park, C. H. *Ibid.* **1962**, *84*, 4850. Cope, A. C.; Moon, S.; Peterson, P. E. *Ibid.* **1962**, *84*, 1935.

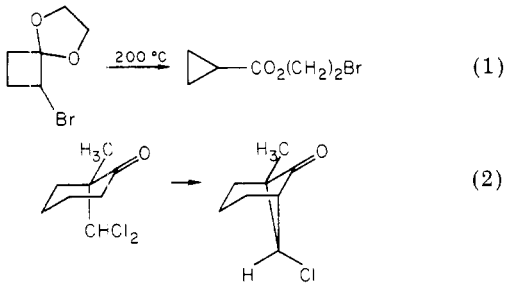
Scheme VI



27 28a, X = H; Y = Br; b, X = Br; Y = H 29 30

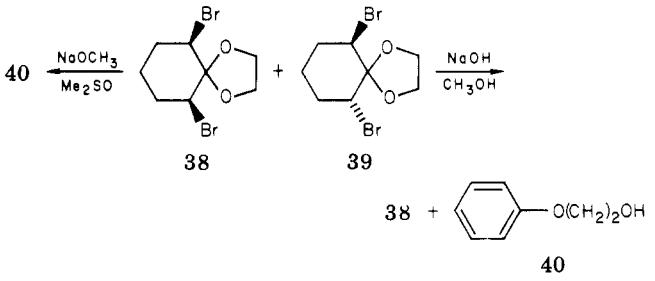
a, Br_2/ether; b, NaOH/CH_3OH; c, 3% H_2SO_4.

been another intermediate. An attractive possibility is the 8-bromobicyclo[4.2.0]octan-7-one ethylene ketal system **25** which could have arisen from a transannular 1,4-elimination reaction. Ionization of **25** to the cyclobutonium ion **26** followed (or accompanied) by rearrangement involving the ketal moiety would lead to carbonium ion **22**, which would be trapped by methoxide. These transformations are outlined in Scheme V. Among the evidence in support of the ring contraction of **25** are the results for the thermolysis of 2-bromocyclobutanone ethylene ketal (eq 1).[11a] Support for the feasibility of the suggested mode of formation of **25** derives from the well-established homo-Favorskii rearrangement (eq 2).[12,13]

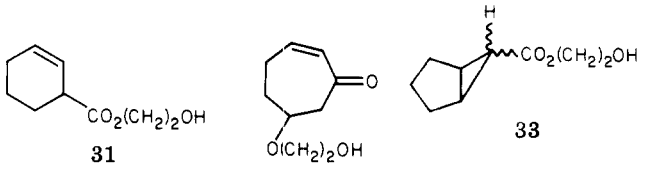


B. Cycloheptyl System. Scheme VI outlines the results obtained for the conversion of cycloheptanone ethylene ketal (**27**) to 2,6-cycloheptadienone (**30**); the yields indicated were similar to those reported previously.[2] Proton NMR analysis of the pot residues from the distillations of **30** revealed that they were virtually the same and, therefore, combined and distilled to provide three fractions. Fraction 1 was shown by carbon-13 NMR spectroscopy to be mostly cycloheptadienone **30**, fraction 2 was shown to be a mixture whose major constituents were 2-hydroxyethyl cyclohex-2-enecarboxylate (**31**) and 2,6-cycloheptadienone (**30**) in about a 1:1 ratio, and fraction 3 was shown to be a mixture whose major components were compounds **30–32** in the approximate ratio of 1:1:2, respectively. There was no indication that 2-hydroxyethyl bicyclo[3.1.0]hexane-6-carboxylate (**33**) was present to any significant extent. Compound **31** was purified by preparative gas chromatography and exhibited spectral characteristics similar to those of its next higher homologue **5**. The structural assignment of **32** is only tentative. The carbon-13 NMR spectral data (obtained on fraction 3) of **32** indicated the presence of $CH{=}CHCOCH_2$, $CHOCH_2CH_2OR$, and two different CH_2 groups. Purification of **32** by gas chromatography was not possible since the side-chain hydroxyethoxy group was thermally expelled to give mostly cycloheptadienone **30**. No further work was carried out with this material.

Scheme VII

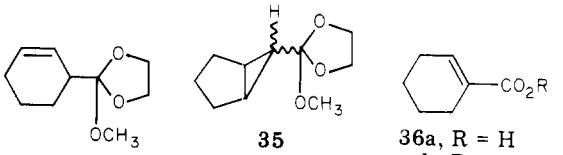


38 39 40



31 32 33

Examination of the carbon-13 NMR spectrum of the pot residue from the distillation of diene ketal **29** indicated the presence of diene ketal **29** and ortho ester **34** (in the ratio of about 1:2) along with a few minor components whose structures were not elucidated. There was, however, no evidence that suggested the presence of the cyclopropyl ortho ester **35**. Furthermore, *only* acid **36a** (analyzed as its methyl ester **36b**) was isolated after acidification of the **28** → **29** reaction mixture. The formation of 1-cyclohexenecarboxylic acid (**36a**) probably occurs as indicated in ref 7 for its next higher homologue **23**.



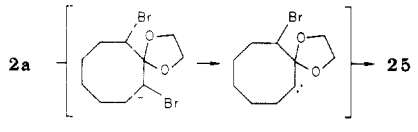
34 35 36a, R = H; b, R = CH_3

C. Cyclohexyl System. Bromination of cyclohexanone ethylene ketal (**37**) according to the general procedure[2] afforded in quantitative yield an approximately 1:1 mixture of the *cis*- and *trans*-2,6-dibromo ketals contaminated with a small amount of the corresponding ketones. The pure *cis*-dibromo ketal (**38**) was obtained by fractional crystallization from methanol; the trans isomer (**39**) was not isolated free of the cis isomer. Treatment of a 1:2 mixture of **38** and **39** with methanolic sodium hydroxide at reflux gave virtually all of the cis isomer (**38**) back and an 89% yield of 2-hydroxyethyl phenyl ether **40**. Similarly, subjection of pure *cis*-dibromo ketal to sodium methoxide in dimethyl sulfoxide at about 80 °C resulted in a 96% conversion to the aryl derivative **40**. These results, which are summarized in Scheme VII, were not unanticipated; a similar finding had been reported by Graff and Gilligan.[14]

(11) (a) Salaun, J.; Conia, J.-M. *Tetrahedron Lett.* **1968**, 4545; **1971**, 4023. Salaun, J.; Garnier, B.; Conia, J.-M. *Tetrahedron* **1973**, *29*, 2895. (b) Casadevall, E.; Pouet, Y. *Tetrahedron* **1975**, *31*, 757. (c) Baldwin, J. E.; Gand, J. E. *Tetrahedron Lett.* **1969**, 1101. (d) McElvain, S. M.; Weyna, P. L. *J. Am. Chem. Soc.* **1959**, *81*, 2579.

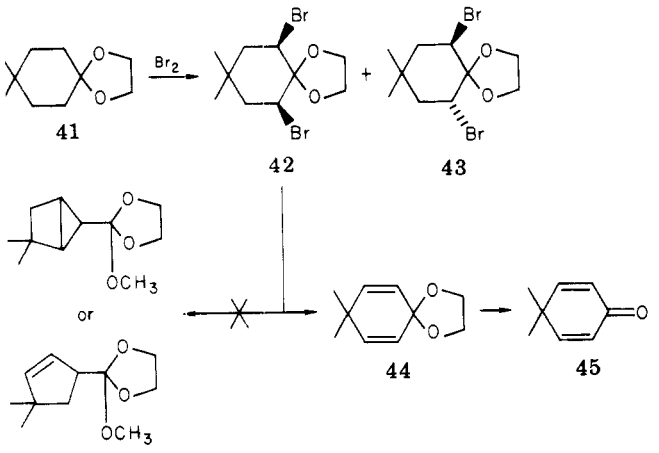
(12) Wenkert, E.; Bakuzis, P.; Baumgarten, R. J.; Leicht, C. L.; Schenk, H. P. *J. Am. Chem. Soc.* **1971**, *93*, 3208. Wenkert, E.; Bakuzis, P.; Baumgarten, R. J.; Doodrell, D.; Jeffs, P. W.; Leicht, C. L.; Mueller, R. A.; Yoshikoshi, A. *Ibid.* **1970**, *92*, 1617.

(13) It is also conceivable that bromo ketal **25** could have been generated via a carbene intermediate. However, such 1,4-insertions in the

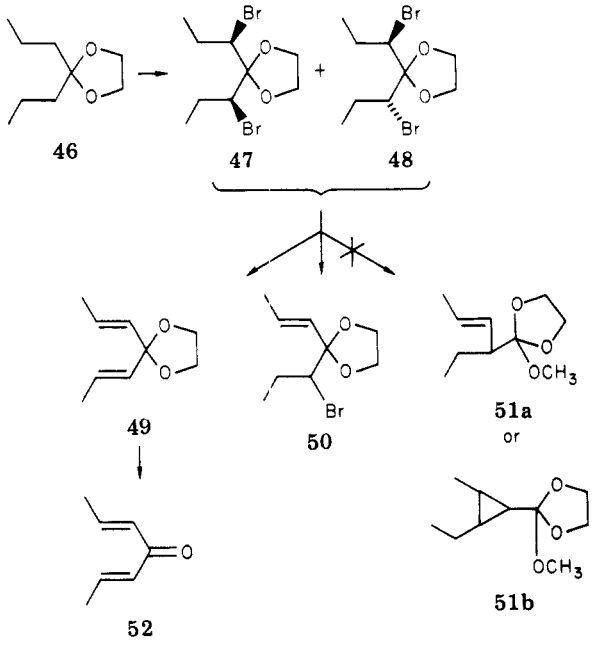


cyclooctane ring system are at present unknown; only 1,5-, 1,2-, and 1,3-insertions have been reported for carbenes in the cyclooctane system: Friedman, L.; Schecter, H. *J. Am. Chem. Soc.* **1955**, *77*, 4401.

Scheme VIII



Scheme IX

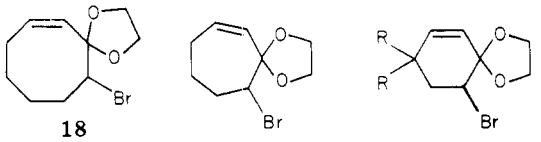


In order to avoid the formation of **40**, the 2,6-dibromo-4,4-dimethylcyclohexanone ethylene ketal system was prepared (crude yield 96%) in the usual fashion; an approximately 1:1 mixture of the cis (**42**) and trans (**43**) isomers was obtained from which the pure cis isomer **42** was isolated by fractional crystallization from methanol. Treatment of **42** with sodium hydroxide in methanol at reflux for 72 h resulted in no apparent reaction (94% recovery of **42**). (Garbisch had reported that under these conditions a reductive elimination occurred to produce a 76% yield of 2-cyclohexenone ethylene ketal.[2]) Treatment of **42** with sodium methoxide in dimethyl sulfoxide at about 80 °C for 72 h resulted in a 98% yield of diene ketal **44**; there was no indication of any ring-contracted derivatives. Hydrolysis of ketal **44** provided dienone **45** in 95% yield. Scheme VIII summarizes these results.

D. An Acyclic Substrate. In order to learn whether or not a cyclic structure was necessary for the side reaction(s) to occur, we treated a 9:1 mixture of *meso*-3,5-dibromoheptan-4-one ethylene ketal and its *d,l* isomer with methanolic sodium hydroxide at reflux; analytically pure diene ketal **49** was obtained in 84% yield after distillation. The distillation residue (which accounted for approximately 3% of the material balance) was shown to be mostly the unsaturated bromo ketal **50**; there was absolutely no evidence to suggest the formation of any side products such as **51a** or **51b**.[15] Hydrolysis of ketal **49** gave dienone **52** in 90% yield. Scheme IX details these results.

Discussion

On the basis of the above-mentioned results, the following conclusions can be drawn. (i) In the rearrangements of homoallylic bromo ketals (e.g., **18**) to olefinic ortho esters (e.g., **15**) ring sizes of at least seven are required. (ii) For the formation of cyclopropyl ortho esters (e.g., **16**) the ring size of the starting α,α'-dibromo ketal must be at least eight. (iii) Apparently neither type of rearrangement takes place with acyclic systems. In the absence of kinetic data it is not possible to rationalize these conclusions in a definitive manner. Qualitatively, however, it might have been expected that one would find relatively more olefinic ortho ester product from 2-bromocyclooct-7-enone ethylene ketal (**18**) and its cycloheptyl homologue **55** than from the cyclohexyl analogues **56** since it had been previously shown that the rates of bimolecular elimination of HBr (the process which competes with rearrangement) from cycloalkyl bromides with potassium ethoxide in ethanol decreases with increasing ring size [k_{rel} = 3.3 (cyclohexyl), 2.3 (cycloheptyl), and 1.0 (cyclooctyl)].[16] Since transannular reactions generally do not occur with ring systems of less than eight,[17] it was not surprising that cyclopropyl ortho esters were not formed from the α,α'-dibromo ketals of the cycloheptane and cyclohexane frameworks.

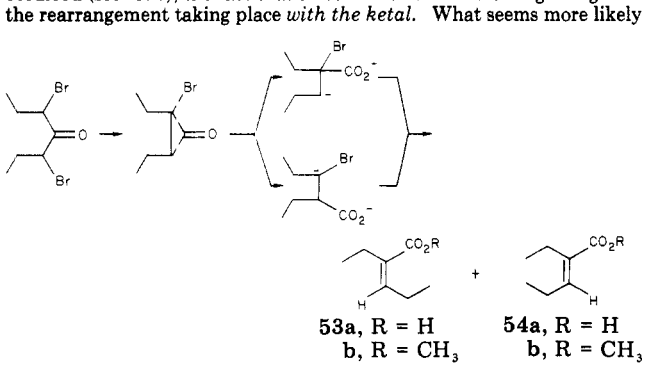


18 55 56a, R = H; b, R = CH_3

The most important finding from these studies[1] is that carbonium ions are probably involved in the side reactions even though the reaction conditions are strongly alkaline. Whether or not carbonium ions **19** or **26** were actually generated was not determined and remains, therefore, a

(14) Graff, M.; Gilligan, W. H. *J. Org. Chem.* **1967**, *32*, 3203. In their report, the authors did not specify the purity or the isomeric composition of dibromo ketals **38** and **39**; moreover, they obtained **40** in a maximum yield of only 39% (when potassium *tert*-butoxide was utilized as the base in dimethyl sulfoxide).

(15) However, upon acidification of the **47**/**48** → **49**/**50** reaction mixture (after having removed **49** and **50**) acids **53a** and **54a** (analyzed as their methyl esters **53b** and **54b**) were isolated in about 1% yield. While these data can be construed to suggest that a rearrangement has in fact occurred (see ref 7), the fact that **51** could not be detected argues against the rearrangement taking place *with the ketal*. What seems more likely



53a, R = H; b, R = CH_3 54a, R = H; b, R = CH_3

is merely a Favorski rearrangement with the dibromo ketone(s) (present as minor contaminants) followed by elimination of HBr.

(16) Zavada, J.; Krupicka, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1968**, *33*, 1393.

(17) Cope, A. C.; Martin, M. M.; McKervey, M. A. *Q. Rev., Chem. Soc.* **1966**, *20*, 119.

Table I. Carbon-13 NMR Chemical Shifts for Compounds 1-40[a,b]

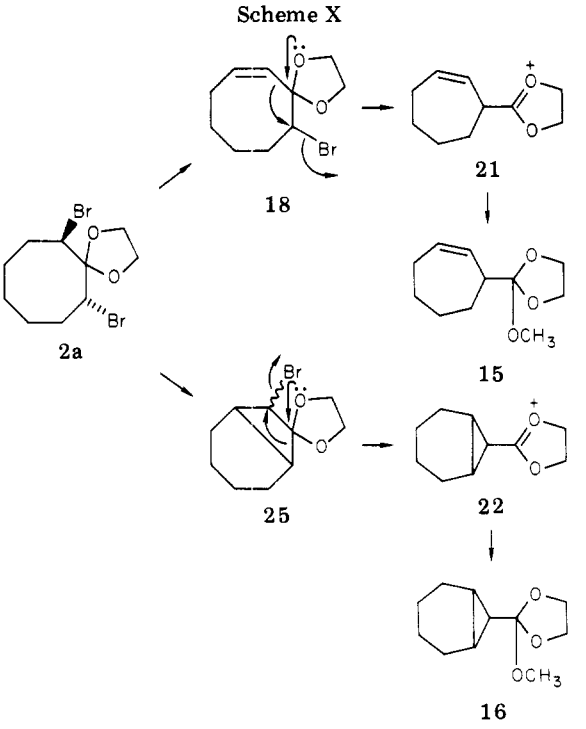
compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10	C-11
1	112.39	34.31	22.35*	28.15	24.68	(28.15)	(22.35)	(34.31)	64.25	(64.25)	
2a	111.46	58.12	25.72*	34.25*	24.65	(34.25)	(25.72)	(58.12)	67.69	(67.69)	
2b[c]	109.81	60.23	25.03*	34.79*	24.43	(34.79)	(25.03)	(60.23)	68.68+	66.52+	
3[d]	106.00	134.53	129.73	23.72	25.72	(23.72)	(129.73)	(134.53)	64.63	(64.63)	
4	193.23	135.93	141.59	25.04	27.14	(25.04)	(141.59)	(135.93)			
5[e]	46.10	133.36	130.28	30.61*	30.45*	28.53*	26.55*	175.72	66.16	60.84	
6	25.56	22.60	22.76	20.95	(20.95)	(22.76)	(22.60)	175.45	66.00	60.94	
7[f]	45.02	30.92*	28.42*	26.45*	(26.45)	(28.42)	(30.92)	177.44	65.79	60.56	
8[g]	45.06	30.81*	28.66*	26.48*	(26.48)	(28.66)	(30.81)	183.93			
9[h]	45.19	31.03*	28.56*	26.56*	(26.56)	(28.56)	(31.03)	176.79	60.05	14.34	
10a[i]	46.01	133.49	129.83	30.49*	30.49*	28.56*	26.59*	181.93			
11a[j]	46.09	133.09	130.71	30.68*	30.68*	28.64*	26.74*	175.34	51.68		
12	169.84	52.42	28.70*	24.76*	26.99*	33.70*	173.67	51.56	52.42	(169.84)	(51.56)
13[i]	25.69	22.76	23.40	20.94	(20.94)	(23.40)	(22.76)	181.71			
14a[j]	25.57	22.15	22.91	21.14	(21.14)	(22.91)	(22.15)	174.94	51.34		
14b[h]	25.79	22.13	22.83	21.05	(21.05)	(22.83)	(22.13)	175.00	60.09	14.30	
15[d,k]	47.09	133.94*	130.93*	31.30*	28.84*	28.54*	27.19*	124.91	65.72	(65.72)	48.79
16[d,l]	28.10	13.96	23.25	21.72	(21.72)	(23.25)	(13.96)	122.96	65.16	(65.16)	49.43
17[d]	46.05	29.05*	29.05*	27.36*	(27.36)	(29.05)	(29.05)	125.71	65.57	(65.57)	48.67
18[m]	108.67	60.89	32.09	27.73*	23.59*	22.08*	133.58+	131.76+	65.44	64.96	
23	136.43	146.36	32.23*	29.10*	27.24*	26.42*	25.92*	172.39			
24	136.83	144.33	32.39*	29.02*	27.68*	26.62*	26.13*	168.42	51.62		
27	113.00	38.60	22.61*	29.40*	(29.40)	(22.61)	(38.60)	64.07	(64.07)		
28a	110.14	57.72	31.24	23.44	(23.44)	(31.24)	(57.72)	66.66	(66.66)		
29	106.39	133.20	131.78	25.60	(25.60)	(131.78)	(133.20)	64.43	(64.43)		
30	192.50	133.50	144.33	27.30	(27.30)	(144.33)	(133.50)				
31	41.21	129.92	124.19	25.37*	24.70*	20.79*	174.99	66.24	61.25		
32[n]	200.78	49.07	74.14	32.97	25.94	148.27	132.89	70.19	61.73		
34[o]	42.80	128.79	127.08	25.43*	24.28*	21.93*	*p*	65.82	65.82	48.73	
37	108.98	35.35	24.10	25.35	(24.10)	(35.35)	64.22	(64.22)			
38	108.37	56.40	34.89	26.87	(26.87)	(34.89)	68.92	67.58			
39[q]	106.93	54.26	33.49	21.47	(21.47)	(33.49)	66.21	(66.21)			
40	158.79	114.59	129.49	120.89	(129.49)	(114.59)	69.27	60.74			

[a] Measured in $CDCl_3$ with internal Me_4Si unless specified otherwise. [b] Chemical shift assignments were made on the basis of general shielding parameters [Stothers, J. B. "Carbon-13 NMR Spectroscopy"; Academic Press: New York, 1970], relative signal intensities, and residual splitting patterns observed with off-resonance partially decoupled spectra; pairs or groups of signals which could not be rigorously assigned to specific carbons are indicated by the symbols * and +; values in parentheses are those of symmetry-related atoms. [c] Mixture of 2a and 2b. [d] In C_6D_6. [e] Mixture of 5 and 6. [f] Mixture of 6 and 7. [g] Mixture of 8 and 13. [h] Mixture of 9 and 14b. [i] Mixture of 10a and 13; see also ref 16b. [j] Mixture of 11a and 14a. [k] Mixture of 15 and 16. [l] Mixture of 16 and 17. [m] In $(CD_3)_2CO$. [n] Mixture of 30, 31, and 32. [o] Mixture with 29. [p] Not assignable. [q] Mixture of 38 and 39.

moot point, although it is noted that in previous studies dealing with the mechanisms of elimination reactions the occurrence of some E1 reaction under E2 conditions has been detected.[18] However, the maximum concentrations of base used were approximately 1 M, and the amounts of carbonium ion derived products (rearranged olefins) did not exceed 7% of the E2 reaction products. In the work described in this paper, the base concentrations were between 4.8 and 5.5 M; such high concentrations would normally be expected to completely suppress E1 reactions, such as the generation of **19** or **26**. However, it does seem reasonable that homoallylic cation **21** and cyclopropylcarbinyl cation **22** are real intermediates which are trapped by methoxide (Scheme X). There was apparently no interconversion between carbonium ions **21** and **22** as previously suggested.[1]

As pointed out in the preliminary communication,[1] the generation of cations in strongly basic media is a rarely encountered event.[19] That carbonium ions **21** and **22** can be formed under strongly basic conditions is probably attributable to the presence of the adjacent oxygens of the ethylene glyoxy moiety.

Scheme X



(18) Feit, I. N.; Saunders, W. H., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 1630. Colter, A. K.; McKelvey, D. R. *Can. J. Chem.* **1965**, *43*, 1282. Saunders, W. H., Jr.; Fahrenholtz, S. R.; Caress, E. A.; Lowe, J. P.; Schrieber, M. *J. Am. Chem. Soc.* **1965**, *87*, 3401. Brown, H. C.; Moritani, I. *Ibid.* **1954**, *76*, 455.

(19) Deoxidation (the reaction of alcohols with haloform in basic solution) probably involves carbonium ion intermediates; for a review see: Keating, J. T.; Skell, P. S. *Carbonium Ions* **1970**, 576, 617, 633.

Experimental Section

General Methods. Melting and boiling points are uncorrected. Infrared spectra were recorded as neat films for liquids or as

Table II. Carbon-13 NMR Chemical Shifts for Compounds 41-45[a]

compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7a	C-7e	C-8	C-9
41	109.12	36.76	31.28	29.50	(31.28)	(36.76)	27.99	27.99	64.10	64.10
42	108.60	53.79	47.57	35.19	(47.57)	(53.79)	24.42	31.34	68.80	67.43
43[b]	107.17	51.47	45.84	35.97	(45.84)	(51.47)	30.59	(30.59)	66.53	(66.53)
44	100.21	140.20	124.31	34.28	(124.31)	(140.20)	28.32	28.32	64.74	64.74
45	185.38	127.19	156.66	37.86	(156.66)	(127.19)	26.61	26.61		

[a] See Table I and footnotes *a* and *b*. [b] Mixture of 42 and 43.

Table III. Carbon-13 NMR Chemical Shifts for Compounds 46-52[a]

compd	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
46	14.53	17.36	39.78	111.80	(39.78)	(17.36)	(14.53)	65.03	(65.03)
47[b]	12.79	26.01	62.52	111.30	(65.52)	(26.01)	(12.79)	68.51	67.79
48[b]	12.26	25.20	61.96	*c*	(61.96)	(25.20)	(12.26)	67.95	(67.95)
49	17.38	126.76	131.80	107.04	(131.80)	(126.76)	(17.38)	64.57	(64.57)
50[d]	12.83	27.23	62.99	108.58	129.04	128.83	17.40	65.89	(65.89)
52	18.29	142.63	130.39	188.90	(130.39)	(142.63)	(18.29)		

[a] See Table I and footnotes *a* and *b*. [b] Mixture of 47 and 48. [c] Not assignable. [d] $In(CD_3)_2CO$.

chloroform solutions for solids with sodium chloride cells by using a Perkin-Elmer 457 spectrophotometer. Proton nuclear magnetic resonance spectra were measured with a Varian Associates T-60 instrument; the chemical shifts reported are referenced to internal tetramethylsilane. Carbon-13 NMR spectra were obtained with Varian CFT-20 or XL-100 spectrometers; the chemical shifts (Tables I-III) are referenced to internal tetramethylsilane. Electron-impact mass spectra were obtained with a Du Pont CEC 21104 mass spectrometer operated at 70 eV; field-ionization mass spectra were obtained with a Varian MAT 731 mass spectrometer. Gas chromatographic analyses and collections were carried out with a Varian Aerograph 1520 instrument equipped with a 5 ft × 1/4 in. aluminum column packed with 20% SE-30 on Chromosorb W. Elemental analyses were carried out by Galbraith Laboratories, Nashville, TN.

***trans*-2,8-Dibromocyclooctanone Ethylene Ketal (2a).** In a 3-L three-necked flask equipped with a dropping funnel charged with 110 mL (322 g, 2.016 mol) of bromine and fitted with a nitrogen inlet line, a mechanical stirrer, and a reflux condenser with a gas bubbler at its efflux were placed 170 g (1.00 mol) of cyclooctanone ethylene ketal and 1.5 L of anhydrous diethyl ether. The bromine was added dropwise under a continuously nitrogen-purged atmosphere over a period of about 90 min; the resulting dark orange solution was allowed to stir for several hours (overnight). To the solution was added in portions 454 g of anhydrous Na_2CO_3. The mixture was stirred for 90 min after which gas evolution had ceased. The mixture was then filtered and the filtrate concentrated to give 306.6 g of an off-white solid. The residue was taken up in 1 L of H_2O and then extracted with diethyl ether (1 × 400 mL, 2 × 300 mL), dried (Na_2CO_3), and concentrated to 37.0 g of a white solid. Crystallization of the combined solids from CH_3OH gave 269.2 g (82% yield) of **2a**: mp 73–74 °C (lit.[2] mp 74–75 °C); IR ($CHCl_3$) 1185, 1095, 1044, 975, 961 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.57–4.33 (m, 2 H, CHBr), 4.03 (s, 4 H, OCH_2CH_2O), 2.4–2.0 (m, 4 H), 1.8–1.4 (m, 6 H); MS (70 eV), *m/e* (rel intensity) 247, 249 (41.4, 41.9), 177, 179 (34.6, 35.0), 164, 166 (32.7, 32.8), 99 (100), 55 (100). Anal. Calcd for $C_{10}H_{16}Br_2O_2$: C, 36.61; H, 4.92; Br, 48.72. Found: C, 36.57; H, 4.87; Br, 48.56. Subsequent crystallizations from the mother liquor provided an additional 21.9 g of **2a** (mp 68–71 °C), bringing the total yield to 89%. A ^{13}C NMR spectrum of the final mother liquor (36.6 g) indicated that it was composed mostly of **2a** and some cis isomer **2b** as well as a little 2-bromo- and 2,8-dibromocyclooctanone.

2,7-Cyclooctadienone Ethylene Ketal (3). In a 2-L flask equipped with a condenser with a gas bubbler were placed 164.0 g (0.500 mol) of dibromo ketal **2a**, 164 g (4.1 mol) of NaOH, and 850 mL of absolute CH_3OH. The mixture was heated at reflux under a static nitrogen atmosphere for 72 h. After the mixture was allowed to cool to room temperature, the reaction was processed by diluting with H_2O (2 L) and extracting with diethyl ether (7 × 200 mL); the combined extracts were dried ($MgSO_4$) and concentrated with a rotary evaporator to provide 82.9 of crude **3** as light yellow liquid. ^1H and ^{13}C NMR spectral and gas chromatographic analyses indicated that the material consisted of a mixture of about 80% **3** and 20% of a mixture of **15** and **16** (in a ratio of about 3:4). Distillation utilizing a heated 30 cm × 4 cm column packed with glass helices afforded 61.5 g (74%) of **3** [bp 133–135 °C (31 mmHg)] of greater than 95% purity according to ^1H and ^{13}C NMR spectral data and gas chromatographic analysis: IR 3020, 1660, 1095, 950 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.7–5.1 (m, 4 H, HC=CH), 3.92 (s, 4 H, OCH_2CH_2O), 2.6–2.1 (m, 4 H), 1.9–1.4 (m, 2 H); MS (70 eV), *m/e* (rel intensity) 166 (8.3, M^+), 138 (21.7), 125 (21.0), 99 (27.2), 91 (41.5), 81 (49.2), 79 (80.7), 39 (100). In other similar preparations of **3**, yields of 72, 71, 76, and 79% were obtained. The residues remaining after the distillations of **3** are referred to as PR-I.

2,7-Cyclooctadienone (4). CAUTION! 4 Is a Severe Vesicant. In a separatory funnel were placed 49.0 g (0.295 mol) of diene ketal **3**, 100 mL of diethyl ether, and 80 mL of 3% aqueous H_2SO_4 solution. The mixture was shaken for 5 min and then processed by separating the layers and extracting the aqueous phase with diethyl ether (1 × 75 mL, 2 × 40 mL). The combined ether layers were washed with H_2O (1 × 50 mL) and saturated aqueous $NaHCO_3$ solution (1 × 50 mL), dried (Na_2SO_4), and concentrated to 37.1 g of a light yellow liquid. Distillation employing a 200 mm × 18 mm Vigreux column provided 34.2 g (95%) of pure **4**: bp 107–110 °C (26 mmHg); IR 3023, 2960, 2887, 2879, 1642, 1610, 1463, 1404, 1290, 1270, 1227, 1153, 848, 667 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.4–5.8 (m, 4 H, HC=CH), 2.5–2.0 (m, 4 H), 1.9–1.5 (m, 2 H); MS (70 eV), *m/e* (rel intensity) 122 (13.3), 94 (46.5), 81 (100), 80 (31.2), 79 (59.2), 68 (65.8), 66 (54.2), 53 (76.2). In several other preparations of **4** the yields ranged from 92 to 99%. The residues remaining after the distillations of **4** are referred to as PR-II.

2-Hydroxyethyl 2-Cycloheptenecarboxylate (5). Gas chromatographic analysis of PR-II revealed that the material was composed of two rather polar liquids (**5** and **6**), which were the major components (in approximately equal amounts), a little dienone **4**, and a few other very minor constituents which were not considered further. Pure samples of **5** for spectral and analytical data were obtained by preparative vapor-phase chromatography: IR 3450, 3030, 1735, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.73–5.57 (m, 2 H, HC=CH), 4.17–3.50 (A_2B_2 m, 4 H, $CO_2CH_2CH_2OH$), 3.4–3.1 (m, 1 H, $CHCO_2$), 3.03 (s, 1 H, OH; the signal was concentration dependent and disappeared upon treatment with D_2O), 2.3–1.3 (m, 8 H); MS (70 eV), *m/e* (rel intensity) 185 (3.2, M + 1), 184 (1.3, M^+), 95 (100), 94 (70.3). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.27; H, 8.93.

2-Hydroxyethyl *exo*-Bicyclo[4.1.0]heptane-7-carboxylate (6). The procedure was the same as for **5**. IR 3440, 1725, 1190, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.10–3.50 (A_2B_2 m, 4 H, $CO_2CH_2CH_2OH$), 2.83 (s, 1 H, OH; the signal was concentration dependent and disappeared upon treatment with D_2O), 2.1–1.0 (m, 11 H); MS (70 eV), *m/e* (rel intensity) 185 (4.6, M + 1), 184 (2.4, M^+), 123 (72.0), 122 (100), 95 (46.1), 94 (50.8). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.14; H, 8.78.

2-Hydroxyethyl Cycloheptanecarboxylate (7). A solution of 2.50 g of PR-II (consisting of mostly **5** and **6** in a 1:1 ratio) in

200 mL of 95% C_2H_5OH was hydrogenated over 0.210 g of 5% Pd on carbon with an internal pressure of approximately 5 psig with a Parr shaker for 1.5 h at room temperature. Filtration and concentration on a rotary evaporator gave 2.31 g of a yellow liquid whose gas chromatographic analysis indicated two major components in about a 1:1 ratio. Samples of the major components were obtained by preparative gas chromatography. The more polar major component was shown to be **5**. The less polar major constituent was identified as being **7**: IR 3450, 2930, 2860, 1730, 1189, 1140 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.1–3.5 (A_2B_2 m, 4 H, $CO_2CH_2CH_2OH$), 3.00 (s, 1 H, OH), 2.6–2.2 (m, 1 H, $CHCO_2$), 2.1–1.2 (m, 12 H); MS (70 eV), *m/e* (rel intensity) 187 (1.1, M + 1), 125 (21.6), 124 (18.9), 97 (42.8), 96 (14.0), 55 (100). Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.25; H, 9.52.

Ethyl Cycloheptanecarboxylate (9). In a 50-mL round-bottomed flask equipped with a condenser were placed 1.5 g of the 1:1 mixture of **7** and **5** described above, 20 mL of 50% C_2H_5OH, and 0.6 g of KOH. The mixture was then heated on a steam bath for 6 h. After being cooled to room temperature, the mixture was diluted with H_2O (100 mL) and washed with diethyl ether (2 × 25 mL). The aqueous solution was then acidified with concentrated HCl solution and extracted with diethyl ether (1 × 25 mL) and CH_2Cl_2 (4 × 25 mL). The combined extracts were dried ($MgSO_4$) and concentrated to give 1.1 g of light yellow liquid whose IR and ^1H NMR spectra showed the material to be a carboxylic acid (presumably **8** and **13**). The crude material was dissolved in 50 mL of absolute C_2H_5OH, 2 drops of concentrated sulfuric acid were added, and the solution was heated at reflux for 16 h. After the mixture cooled to room temperature, the reaction was worked up by adding 100 mL of H_2O and extracting with diethyl ether (5 × 25 mL). The combined extracts were washed with H_2O (1 × 25 mL), saturated aqueous $NaHCO_3$ solution (1 × 25 mL), and H_2O (1 × 25 mL), dried ($MgSO_4$), and concentrated to 0.75 g of golden yellow liquid which was shown by gas chromatography and ^{13}C NMR spectroscopy to be composed primarily of ethyl esters **9** and **14b**. Samples of **9** for spectra were obtained by preparative gas chromatography: IR 2927, 2860, 1730, 1186, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.94 (q, J = 7 Hz, 2 H, OCH_2CH_3), 2.6–2.1 (m, 1 H, $CHCO_2$), 2.1–1.0 (m, 12 H), 1.17 (t, J = 7 Hz, OCH_2CH_3). For comparison of these spectral data with those of authentic material, **9** was also prepared independently from the commercially available acid **8** by the above procedure in 91% yield.

Methyl 2-Cycloheptenecarboxylate (11a). A solution of 2.6 g of PR-II (consisting mostly of **5** and **6** in about a 1:1 ratio), 2.0 g of KOH, and 40 mL of 50% C_2H_5OH was heated at reflux for 6 h. After being allowed to cool to room temperature, the reaction mixture was diluted with H_2O (100 mL), washed with diethyl ether (3 × 30 mL), acidified with concentrated HCl solution, and extracted with CH_2Cl_2 (4 × 50 mL). The combined extracts were dried ($MgSO_4$) and concentrated to 1.62 g of brown liquid (crude mixture of **10a** and **13**). An additional 1.58 g of crude **10a** and **13** was prepared from 2.8 g of PR-II. The two batches of **10a** and **13** were combined, treated with 100 mL of CH_3OH and 2 drops of concentrated H_2SO_4 solution, and then heated at reflux for several hours (overnight). After being allowed to cool to room temperature, the reaction mixture was diluted with H_2O (300 mL) and extracted with diethyl ether (1 × 100 mL, 6 × 50 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ solution (2 × 50 mL), 5% aqueous NaOH solution (2 × 60 mL), H_2O (1 × 50 mL), and saturated aqueous NaCl solution, dried ($MgSO_4$), and concentrated to give 3.2 g of a golden yellow liquid whose gas chromatographic analysis indicated that the material was composed of two major components in about a 1:1 ratio. Samples of **11a** (the less polar constituent) for spectral data were obtained by preparative gas chromatography: IR 3035, 2930, 1735, 1205, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.7–5.3 (m, 2 H, HC=CH), 3.53 (s, 3 H, CH_3), 3.3–3.0 (m, 1 H, $CHCO_2$), 2.3–1.0 (m, 8 H); MS (70 eV), *m/e* (rel intensity) 154 (10.1, M^+), 122 (27.4), 95 (100), 94 (40.7). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.22; H, 9.09. The more polar component of the mixture was shown to be **14a** (see below for spectral data).

Dimethyl α-(Carbomethoxy)pimelate (12). Method A. In a 1-L round-bottomed flask were placed 1.78 g of the above mixture of **11a** and **14a**, 200 mL of acetone, 1.0 g of sodium carbonate dissolved in 50 mL of water, 7.5 g of sodium periodate in 100 mL of water, 0.5 g of potassium permanganate in 70 mL of water, and an additional 50 mL of acetone. The mixture was stirred for several hours (overnight). The reaction was processed by removing most of the acetone on a rotary evaporator, adding 5% aqueous sodium hydroxide solution until basic, washing with diethyl ether (4 × 100 mL), acidifying with concentrated hydrochloric acid, and extracting with diethyl ether (4 × 100 mL); the combined extracts were dried ($MgSO_4$) and concentrated to 1.40 g of a brown liquid which was taken up in 80 mL of absolute methanol, treated with 2 drops of concentrated sulfuric acid, and heated at reflux for several hours (overnight). The reaction was worked up by adding 400 mL of water, extracting with diethyl ether (1 × 100 mL, 5 × 50 mL), washing the combined extracts with saturated aqueous sodium bicarbonate solution (1 × 50 mL), 5% aqueous sodium hydroxide solution (1 × 50 mL), and water (1 × 50 mL), drying (K_2CO_3), and concentrating to 0.71 g of golden liquid. Gas chromatographic analysis revealed one major component and several other (minor) components. The major component was isolated by preparative gas chromatography and shown to be the triester **12**: IR 1752, 1745, 1200, 1165 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.57 [s, 6 H, $CH(CO_2CH_3)_2$], 3.50 [s, 3 H, $CH_2CO_2CH_3$], 3.27 [t, J = 7 Hz, 1 H, $CH(CO_2CH_3)_2$], 2.23 [t, J = 7 Hz, $CH_2CO_2CH_3$], 2.0–1.0 [m, 6 H, $(CH_2)_3$].

Method B. In a 100-mL round-bottomed flask equipped with a magnetic stirbar and a Friedrich condenser were placed 50 mL of absolute methanol, 10 mL of benzene, and 0.65 g (0.028 g-atom) of sodium. After the sodium had been consumed, 3.72 g (0.0280 mol) of dimethyl malonate was added, followed by the addition of 5.00 g (0.0256 mol) of methyl 5-bromopentanoate. The resulting solution was heated at reflux under nitrogen for several hours (overnight). The reaction was processed as follows: after being cooled to room temperature, the mixture was filtered (to remove the precipitated sodium bromide byproduct), concentrated (to remove the solvents), and dissolved in diethyl ether (100 mL). The ethereal solution was washed with water (1 × 50 mL), dried ($MgSO_4$), and concentrated to give 5.48 g of a clear, colorless liquid whose gas chromatogram showed one major peak and a few very minor peaks. Distillation [bp 113–115 °C (160 μmHg)] provided 4.67 g (74%) of **12**.

Methyl *exo*-7-Bicyclo[4.1.0]heptanecarboxylate (14a). The procedure was the same as for **11a**. IR 1727, 1450, 1440, 1310, 1196, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.50 (s, 3 H, CO_2CH_3), 2.0–1.0 (m, 11 H); MS (70 eV), *m/e* (rel intensity) 154 (100, M^+), 123 (43.3), 122 (58.5), 111 (61.7), 100 (35.6), 95 (73.9), 94 (57.7), 93 (24.8), 81 (51.4), 80 (75.6), 79 (51.9), 67 (72.4), 55 (60.1), 41 (82.2). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.31; H, 9.30.

Ethyl *exo*-7-Bicyclo[4.1.0]heptanecarboxylate (14b). The procedure was the same as for **9**. IR 1725, 1450, 1430, 1310, 1190, 1171 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.91 (q, J = 6.5 Hz, 2 H, $CO_2CH_2CH_3$), 2.0–1.0 (m, 9 H), 1.20 (t, J = 6.5 Hz, 3 H, $CO_2CH_2CH_3$); MS (70 eV), *m/e* (rel intensity) 168 (70.6, M^+), 140 (58.8), 139 (26.4), 123 (79.6), 122 (57.4), 97 (54.5), 95 (79.5), 94 (53.0), 81 (61.1), 80 (100), 67 (77.9), 55 (92.1), 41 (86.3).

2-(2-Cycloheptenyl)-2-methoxy-1,3-dioxolane (15) and 2-(*exo*-7-Bicyclo[4.1.0]heptyl)-2-methoxy-1,3-dioxolane (16). From the pot residue (PR-I) from the distillation of diene ketal **3**, the mixture of ortho esters **15** and **16** was isolated by preparative gas chromatography: IR 3035, 2930, 1450, 1245, 1186, 1095, 1078, 1032 cm^{-1}; ^1H NMR (C_6D_6) δ 6.0–5.4 (m, HC=CH), 3.7–3.3 (m, OCH_2CH_2O), 3.10 (s, OCH_3), 3.03 (s, OCH_3), 2.9–2.5 (m, $CH(OR)_3$ of **15**), 2.3–0.9 (m); MS (70 eV), *m/e* (rel intensity) 198 (5.0, M^+), 167 (18.0), 166 (45.3), 103 (74.2), 95 (30.2), 58 (100). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.17; H, 8.94.

2-Cycloheptyl-2-methoxy-1,3-dioxolane (17). A solution of 2.0 g of PR-I, 5.0 mL of triethylamine, and 200 mL of 95% ethanol was hydrogenated over 0.210 g of 5% palladium on carbon at an internal pressure of about 5 psig with a Parr shaker for 1.5 h at room temperature. Filtration and concentration gave 2.05 g of colorless liquid (PR-IH) whose gas chromatogram indicated one very major component and a few very minor components. Preparative gas chromatography provided samples of the major component, which was shown to be a mixture of the ortho esters **16** and **17**: IR 2930, 1452, 1306, 1246, 1183, 1075, 1030 cm^{-1}; ^1H NMR (C_6D_6) δ 3.6–3.3 (m, OCH_2CH_2O), 3.05 (s, OCH_3), 2.98 (s, OCH_3), 2.2–1.0 (m).

2-Bromocyclooct-7-enone Ethylene Ketal (18). In a 300-mL round-bottomed flask equipped with a magnetic stirbar and a condenser were placed 20.0 g (0.061 mol) of dibromo ketal **2a**, 10 g (0.25 mol) of sodium hydroxide, and 175 mL of methanol. The mixture was heated at reflux for 30 h, allowed to cool to room temperature, and worked up by diluting with water (350 mL) and extracting with pentane (6 × 70 mL). The combined extracts were dried ($MgSO_4$) and concentrated to give 11.6 g of a white semisolid, which was triturated with pentane, filtered, and concentrated to give 5.8 g of a light yellow liquid whose ^1H NMR spectrum showed it to be about a 2:1 mixture of **18** and **2a**, respectively. The residue (5.7 g) was shown to be almost all **2a**. The residue was taken up in 150 mL of methanol, treated with 5.8 g (0.145 mol) of sodium hydroxide, heated at reflux 30 h, and then processed as described above to give 0.75 g of an approximately 3:1 mixture of **18** and **2a**, respectively. The two batches of mixtures of **18** and **2a** were combined and distilled to provide 3.74 g of **18** [bp 66–69 °C (0.25 mmHg)] as a clear, colorless liquid whose spectral data indicated that the material was at least 95% pure **18**: IR 3030, 2960, 1655, 1170, 1095, 1025, 961, 952, 918, 708, 654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.5–5.3 (m, 2 H, HC=CH), 4.1–4.0 (m, 1 H, CHBr), 3.67 (s, 4 H, OCH_2CH_2O), 2.6–1.2 (m, 8 H); MS (70 eV), *m/e* (rel intensity) 248, 246 (3.6, 3.5 M^+), 205, 203 (1.8, 1.7), 168 (37.3), 125 (100), 81 (26.5), 55 (22.8).

Methanolysis of 2-Bromocyclooct-7-enone Ethylene Ketal (18). In a 100-mL round-bottomed flask were placed 498 mg (2.02 mmol) of homoallylic bromo ketal **18**, 50 mL of anhydrous methanol, and 552 mg (3.99 mmol) of anhydrous potassium carbonate. The mixture was heated at reflux for 1 week, after which it was processed by adding water (100 mL), extracting with pentane (5 × 25 mL), washing the combined extracts with water (1 × 25 mL) and saturated aqueous sodium chloride solution (1 × 25 mL), drying (K_2CO_3), and concentrating to 401 mg of a light yellow liquid whose ^{13}C NMR spectra revealed that the material was a mixture composed of ortho ester **15** and ketal **18** in a ratio of about 1:1.

Treatment of 2-Bromocyclooct-7-enone Ethylene Ketal (18) with Silver Nitrate in Aqueous Methanol. In a 30-mL beaker were placed 498 mg (2.02 mmol) of homoallylic bromo ketal **18** and 10 mL of anhydrous methanol. To this stirred solution was added a solution of 378 mg (2.23 mmol) of silver nitrate in 2 mL of water; silver bromide precipitated almost instantaneously. After stirring for 1 h, the reaction was worked up by pouring the mixture into 150 mL of diethyl ether, filtering, washing the filtrate with saturated aqueous sodium chloride solution, drying ($MgSO_4$), and concentrating to 398 mg (98% yield) of ester **5**.

Treatment of 2-Bromocyclooct-7-enone Ethylene Ketal (18) with Methanolic Sodium Hydroxide. In a 50-mL round-bottomed flask equipped with a magnetic stirbar and a condenser were placed 1.24 g (0.00502 mol) of homoallylic bromo ketal **18**, 2.0 g (0.05 mol) of sodium hydroxide, and 12 mL of absolute methanol. The solution was heated at reflux for 24 h, after which the reaction mixture was worked up by diluting with water (60 mL), extracting with diethyl ether (6 × 50 mL), washing the combined extracts with water (1 × 25 mL) and saturated aqueous sodium chloride solution (1 × 25 mL), drying (K_2CO_3), and concentrating to 0.66 g of light yellow liquid whose ^{13}C NMR spectrum revealed that the material was composed of only compounds **3**, **15**, and **18** in an approximate ratio of 7.7:1:2.4, respectively.

Methyl 1-Cycloheptenecarboxylate (24). In the preparation of diene ketal **3** from 109.33 g (0.33 mol) of dibromo ketal **2a** according to the procedure given above, the aqueous (basic) solution remaining after the extractions with diethyl ether was acidified with concentrated sulfuric acid and extracted with methylene chloride (1 × 200 mL, 3 × 100 mL); the combined extracts were dried ($MgSO_4$) and concentrated to give 2.10 g of brown liquid, which was taken up in 175 mL of methanol, treated with 2 drops of sulfuric acid, and heated at reflux for several hours (overnight). The reaction was processed by adding 200 mL of 10% aqueous sodium hydroxide solution, extracting with methylene chloride (4 × 50 mL), drying the combined extracts over $MgSO_4$, and concentrating to give 1.08 g of a light brown liquid whose ^{13}C NMR spectrum showed that the material was composed of **24** and **14a** in a ratio of about 3.5:1, respectively. Ester **24** was also prepared independently by dehydration of cycloheptanone cyanohydrin followed by saponification and esterification.[8] IR 3020, 2920, 1710, 1645, 1440, 1287, 1256, 1207, 1150, 1068, 747 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.13 (t, J = 6.5 Hz, HC=C), 3.50 (s, 3 H, CO_2CH_3), 2.7–2.4 (m, 2 H), 2.3–1.9 (m, 2 H), 1.8–1.1 (m, 6 H); MS (70 eV), *m/e* (rel intensity) 154 (71.6, M^+), 123 (31.5), 95 (100), 94 (65.6), 87 (54.4), 79 (57.3), 67 (56.1), 41 (58.4).

***trans*-2,7-Dibromocycloheptanone Ethylene Ketal (28a).** In a 2-L, three-necked, round-bottomed flask equipped with a dropping funnel charged with 55 mL (161 g, 1.01 mol) of bromine, a mechanical stirrer, and a reflux condenser were placed 78.1 g (0.5 mol) of ketal **27** and 750 mL of anhydrous diethyl ether. A flow-through nitrogen purge was hooked up to the system with a bubbler at the efflux end of the condenser. The bromine was discharged dropwise. After the addition of the bromine was complete, the orange solution was stirred for about 1 h and then treated with 235 g (2.2 mol) of anhydrous sodium carbonate, and the resulting mixture was stirred for several hours (overnight). The mixture was then filtered and concentrated to give 154.67 g (99% crude yield) of dibromo ketal **28a** whose ^{13}C NMR spectrum indicated that the material was virtually the pure trans isomer: IR 2945, 2900, 1457, 1145, 1108, 1035, 955 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.6–4.4 (m, 2 H, CHBr), 3.80 (s, 4 H, OCH_2CH_2O), 2.4–1.5 (m, 8 H); MS (70 eV), *m/e* (rel intensity) 233, 235 (100, 99.8), 177, 179 (50.8, 49.6), 153 (21.2), 152 (19.8), 99 (94), 55 (66.9). In another preparation of **28a**, the yield was also 99%.

2,6-Cycloheptadienone Ethylene Ketal (29). In a round-bottomed flask equipped with a magnetic stirbar and a condenser were placed 78.5 g (0.25 mol) of dibromo ketal **28a**, 500 mL of methanol, and 82 g (2.05 mol) of sodium hydroxide. The mixture was heated at reflux for 72 h. After the reaction mixture was allowed to cool to room temperature, 1 L of water was added and the mixture extracted with ether (7 × 200 mL); the combined extracts were dried (K_2CO_3) and concentrated to 35.58 g of golden yellow liquid which was then distilled to provide 25.32 g (67%) of virtually pure diene ketal **29**: bp 124–126 °C (29 mmHg); IR 3030, 2950, 2880, 1408, 1100, 970, 948, 829, 800 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.1–5.6 (m, 4 H, HC=CH), 3.95 (s, 4 H, OCH_2CH_2O), 2.3–2.2 (m, 4 H); MS (70 eV), *m/e* (rel intensity) 152 (41.2, M^+), 151 (20.6), 108 (35.3), 107 (44.1), 91 (58.8), 80 (82.4), 79 (100), 77 (35.3), 68 (26.5), 65 (29.4). In another preparation of **29**, the distilled yield was 59%.

2,6-Cycloheptadienone (30). In a separatory funnel were placed 22.57 g (0.148 mol) of diene ketal **29**, 50 mL of diethyl ether, and 30 mL of 3% aqueous sulfuric acid. The mixture was shaken for 5 min. The layers were then separated, and the aqueous phase was extracted with diethyl ether (3 × 25 mL). The combined organic layers were washed with water (1 × 25 mL), dried ($MgSO_4$), and concentrated to give 14.27 g (88% crude yield) of **30** as a light yellow liquid, which was distilled [bp 98–103 °C (30 mmHg)] to provide 12.00 g (74%) of **30**: IR 3035, 2940, 1645, 1610, 1464, 1410, 1296, 1263, 1195, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.9–6.5 (m, 2 H, HC=CHC=O), 6.08 (d, J = 2 Hz, 2 H, HC=CHC=O), 2.6–2.3 (m, 4 H, CH_2CH_2); MS (70 eV), *m/e* (rel intensity) 108 (31.2, M^+), 80 (71.7), 79 (100), 77 (25.6). In another preparation (0.5-mol scale) of dienone **30**, the yields of crude and distilled material were 84 and 70%, respectively.

2-Hydroxyethyl 2-Cyclohexenecarboxylate (31). The pot residues from the distillations of two preparations of dienone **30** were combined (total amount of material = 14.8 g) and distilled to provide three fractions: (1) 4.4 g, bp 65–95 °C (120 μmHg), mostly dienone **30**; (2) 8.3 g, bp 95–110 °C (120 μmHg), an approximately 1:1 mixture of dienone **30** and ester **31**; (3) 1.7 g, bp 110–120 °C (120 μmHg), mostly enone **32** along with some dienone **30** and ester **31**. Ester **31** was isolated by preparative gas chromatography and exhibited the following spectral characteristics: IR 3460, 3040, 2950, 1735, 1650, 1453, 1180, 890 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.80 (s, 2 H, HC=CH), 4.3–3.6 (A_2B_2 m, 4 H, $CHOCH_2CH_2OH$), 3.52 (s, 1 H, OH), 3.3–2.8 (m, 1 H, $CHOCH_2CH_2OH$), 2.2–1.2 (m, 6 H); MS (70 eV), *m/e* (rel intensity) 171 (<1, M + 1), 108 (22.2), 81 (100), 80 (77.8). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.38; H, 8.27.

Methyl 1-Cyclohexenecarboxylate (36b). In the preparation of diene ketal **29** from 314 g (1.0 mol) of dibromo ketal **28** according to the procedure given above, the aqueous (basic) solution remaining after the extractions with diethyl ether was processed as described for ester **24** to give 5.13 g of dark brown liquid after esterification whose gas chromatogram revealed the presence of

one very major component and several minor components. Preparative gas chromatography provided samples of the major component which was shown to be ester **36b** by comparison of its spectral properties with those reported[20] in the literature for authentic **36b**: IR 3010, 2945, 1712, 1652, 1439, 1280, 1250, 1090, 750, 706 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1–6.9 (m, 1 H, HC=C), 3.72 (s, 3 H, OCH_3), 2.5–2.1 (m, 4 H), 1.8–1.5 (m, 4 H); MS (70 eV), *m/e* (rel intensity) 140 (37.5, M^+), 109 (25), 108 (25), 81 (100), 80 (55.0), 79 (37.5).

Preparation of *cis*- and *trans*-2,6-Dibromocyclohexanone Ethylene Ketals (38 and 39). The procedure was the same as that for the preparation of **28a** except that cyclohexanone ethylene ketal **37** was substituted for cycloheptanone ethylene ketal **27**. Concentration provided 150.6 g (100% crude yield) of a white paste which upon trituration with methanol and filtration provided 40.1 g of a white solid (mp 89–92 °C) which was shown by ^{13}C NMR spectroscopy to be mostly (>95%) *cis*-dibromo ketal **38**. Concentration of the methanolic filtrate provided 110.5 g of light yellow liquid which was shown by ^{13}C NMR spectroscopy to be a 1:2 mixture of the *cis*- and *trans*-dibromo ketals **38** and **39**, respectively. Recrystallization of **38** from methanol gave 36.5 g of pure **38**: mp 97.5–99 °C (lit.[21] mp 100 °C); IR ($CHCl_3$) 2955, 2910, 1450, 1320, 1199, 1093, 1024, 960, 916, 655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.58 (s, 4 H, OCH_2CH_2O), 4.4–4.1 (m, 2 H, CHBr), 2.5–1.4 (m, 6 H); MS (70 eV), *m/e* (rel intensity) 302, 300, 298 (16.2, 32.2, 21.1), 221, 219 (37.7, 33.2), 179, 177 (88.4, 100).

2-Hydroxyethyl Phenyl Ether (40). Method A. As in the preparation of diene ketal **29**, 75.0 g (0.25 mol) of the 1:2 mixture of dibromo ketals **38** and **39**, 82 g (2.05 mol) of sodium hydroxide, and 500 mL of methanol were heated at reflux for 40 h. The reaction was processed by diluting with water (1 L) and extracting with pentane (4 × 200 mL). The combined extracts were dried (K_2CO_3) and concentrated to 25.0 g of a slightly yellow solid whose ^1H NMR spectrum was virtually identical with that obtained previously for pure **38**. The aqueous phase was then further extracted with diethyl ether (5 × 25 mL); the combined extracts were dried ($MgSO_4$) and concentrated to 20.4 g (89% crude yield) of hydroxy ether **40** as a golden brown liquid: IR 3400, 3080, 3045, 2940, 1605, 1500, 1250, 1085, 1050, 757, 693 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.7–7.0 (m, 5 H, C_6H_5), 4.07 (br s, 4 H, OCH_2CH_2O), 3.6–3.3 (1 H, OH).

Method B. In a 500-mL round-bottomed flask were placed 30.0 g (0.10 mol) of *cis*-dibromo ketal **38**, 54.0 g (1.0 mol) of sodium methoxide, and 200 mL of dimethyl sulfoxide (which had been dried over activated 3A molecular sieves). The resulting mixture was heated under a nitrogen atmosphere at approximately 78 °C for 48 h. After being cooled to room temperature, the reaction mixture was poured into 1 L of water and the flask rinsed with 200 mL of water. The resulting solution was extracted with diethyl ether (4 × 150 mL), and the combined extracts were washed with water (1 × 100 mL), dried ($MgSO_4$), and concentrated to give 11.5 g of **40** as a golden yellow liquid. The remaining aqueous solution was acidified by the dropwise addition of 32 mL of concentrated sulfuric acid and extracted with diethyl ether (4 × 150 mL), and the combined extracts were treated as above to give an additional 1.7 g of **40**, bringing the total crude yield to 96%.

Preparation of *cis*- and *trans*-2,6-Dibromo-4,4-dimethylcyclohexanone Ethylene Ketals (42 and 43). In a 2-L three-necked flask equipped with a dropping funnel charged with 40 mL (117.2 g, 0.733 mol) of bromine, a mechanical stirrer, and a condenser with a gas bubbler at its efflux end were placed 59.0 g (0.347 mol) of 4,4-dimethylcyclohexanone ethylene ketal (**41**)[22] and 500 mL of diethyl ether. With a flow-through nitrogen atmosphere, the bromine was discharged dropwise and then treated in a fashion similar to that described above for **2a**. Concentration provided 125.2 g of a brown solid/liquid mixture. Methanol was then added and the slurry filtered to give 36.4 g the cis isomer **42** [mp 120–122 °C (lit.[2] mp 123–124 °C)]. Recrystallization from methanol provided 29.0 g of **42**: mp 120–124 °C; IR ($CHCl_3$) 2965, 2910, 1180, 1086, 1045, 960 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.5–4.1 (m, 2 H, CHBr), 4.33 (s, 4 H, OCH_2CH_2O), 2.2–1.8 (m, 4 H), 1.0 (s, 6 H, 2 CH_3); MS (70 eV), *m/e* (rel intensity) 177, 179 (100, 94.3). The filtrate was concentrated to give 82.7 g of a clear brown liquid whose ^{13}C NMR spectrum revealed that the material was mostly about a 1:2 mixture of the cis and trans isomers **42** and **43**.

4,4-Dimethylcyclohexadienone Ethylene Ketal (44). The procedure was the same as that in method B for compound **40**. Processing provided 14.3 g (98%) of **44**: IR 3035, 2960, 2880, 1222, 1179, 1110, 1022, 960, 763 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.90 (d, J = 10 Hz, 2 H, **H**C=CH), 5.62 (d, J = 10 Hz, 2 H, HC=C**H**), 3.98 (s, 4 H, OCH_2CH_2), 1.12 (s, 6 H, 2 CH_3); MS (70 eV), *m/e* (rel intensity) 166 (100, M^+), 151 (52.0), 136 (58.6), 121 (45.8), 91 (89.2), 79 (83).

4,4-Dimethylcyclohexadienone (45). In a separatory funnel were placed 11.40 g (0.0687 mol) of diene ketal **44**, 75 mL of diethyl ether, and 25 mL of 3% aqueous sulfuric acid. The mixture was shaken for 5 min, the layers were then separted, and the organic layer was washed with water (1 × 25 mL), dried ($MgSO_4$), and concentrated to give 7.67 g (92% yield) of **45** as a light yellow liquid. Distillation [bp 108–109 °C (40 mmHg)] provided 7.15 g of material: IR 3040, 2975, 1664, 1633, 1471, 1405, 1258, 1107, 860 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.94 (d, J = 11 Hz, 2 H, C**H**=CHCO), 6.18 (d, J = 11 Hz, 2 H, CH=C**H**CO), 1.33 (s, 6 H, $(CH_3)_2$); MS (70 eV), *m/e* (rel intensity) 122 (36.1, M^+), 107 (17.7), 94 (40.6), 79 (100), 77 (69.6).

***meso*- and *d,l*-3,5-Dibromo-4-heptanone Ethylene Ketals (47 and 48).** The procedure was the same as that for the preparation of dibromo ketal **28a** except that 79.0 g of 4-heptanone ethylene ketal **46** (prepared in the usual fashion) was used. Filtration and concentration provided 154.0 g (97% crude yield) of an approximately 9:1 mixture of **47** and **48**, respectively, as a light yellow liquid: IR 2985, 1458, 1294, 1200, 1112, 1070, 960, 815 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.6–4.0 (m, CHBr), 4.32 (s, OCH_2CH_2O), 2.3–1.5 (m, CH_2CH_3), 1.12 (t, J = 7.5 Hz, CH_2CH_3); MS (70 eV), *m/e* (rel intensity) 193, 195 (100, 98.1).

(*E,E*)-Hepta-2,5-dien-4-one Ethylene Ketal (49). A mixture of 150.0 g (0.47 mol) of the above **47**/**48** dibromo ketal mixture, 164 g (4.1 mol) of sodium hydroxide, and 1 L of methanol was heated at reflux for 48 h. After being cooled to room temperature, the reaction mixture was diluted with water (2 L) and then extracted with pentane (5 × 200 mL). The combined extracts were washed with water (1 × 100 mL), dried ($MgSO_4$), and concentrated to 64.6 g of crude **49** as a light yellow liquid, which was distilled through a 6-in. glass helices packed column [bp 85–90 °C (23 mmHg)] to provide 60.6 g (84% yield) of pure diene ketal **49**: IR 3042, 2975–2890, 1673, 1620, 1450, 1293, 1222, 1155, 1081, 1040, 1030, 965 cm^{-1}; ^1H NMR (C_6D_6) δ 6.2–5.3 (m, 4 H, CH=CH), 3.67 (s, 4 H, OCH_2CH_2O), 1.60 (d, J = 6 Hz, 6 H, CH_3); MS (70 eV), *m/e* (rel intensity) 154 (6.0, M^+), 139 (47.1), 69 (100). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.87; H, 8.76. The distillation pot residue (3.3 g) was shown to be mostly bromo enone ketal **50**: IR 3040, 2970, 2885, 1673, 1455, 1385, 1288, 1205, 1150–1020, 975, 813 cm^{-1}; ^1H NMR (C_6D_6) δ 6.3–5.3 (m, 2 H, HC=CH), 4.2–3.5 (m, 5 H, CHBr and OCH_2CH_2O), 2.2–1.5 (m, 2 H, CH_3CH_2), 1.58 (d, J = 5.5 Hz, 3 H, C=CHC**H**$_3$), 1.00 (6, J = 8.0 Hz, 3 H, CH_2CH_3); MS (70 eV), *m/e* (rel intensity) 224, 226 (<1, M^+), 113 (100), 69 (60). Acidification of the aqueous (basic) solution followed by extraction with diethyl ether (5 × 200 mL), washing the combined extracts with water (1 × 100 mL), drying ($MgSO_4$), and concentrating provided 1.9 g of golden brown liquid which was dissolved in 150 mL of methanol and treated with a few drops of concentrated sulfuric acid. The resulting solution was heated at reflux for several hours (overnight). The reaction was processed by adding 300 mL of 10% aqueous sodium hydroxide solution, extracting with pentane (1 × 100 mL, 3 × 75 mL), drying the combined extracts ($MgSO_4$), and concentrating to provide 1.2 g of a light yellow liquid which according to gas chromatographic analysis consisted of two major components (**53b** and **54b**) in a ratio of about 5:1; preparative gas chromatography provided samples of the two components for spectral data.[23] **53b**: IR 3030, 2970, 1720, 1645, 1230, 1138 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.87 (t, J = 6.5 Hz, 1 H, HC=C), 3.77 (s, 3 H, CO_2CH_3), 2.7–2.1 (m, 4 H, 2 CH_3CH_2), 1.10 (6, J = 7.0 Hz, 6 H, 2 CH_3CH_2); MS (70 eV), *m/e* (rel intensity) 142 (75.0, M^+), 127 (50.0), 111 (41.7), 95 (41.7), 83 (36.7), 67 (55.0), 55 (100). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.53; H, 10.17. **54b**: IR 3030, 2975,

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2880, 1718, 1648, 1309, 1242, 1152, 1107 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.73 (6, J = 7.5 Hz, 1 H, HC=C), 3.77 (s, 3 H, CO_2CH_3), 2.6–2.0 (m, 4 H, 2 CH_3CH_2), 1.07 (t, J = 7.0 Hz, 3 H, CH_3CH_2), 1.02 (t, J = 7.0 Hz, 3 H, CH_3CH_2); MS (70 eV), m/e (rel intensity) 142 (46.1, M^+), 127 (28.9), 113 (35.5), 111 (30.3), 95 (23.7), 83 (42.1), 67 (47.4), 59 (28.9), 55 (100).

(*E*,*E*)-Hepta-2,5-dien-4-one (52).[24] In a separatory funnel were placed 53.8 g (0.349 mol) of distilled diene ketal **49**, 100 mL of diethyl ether, and 50 mL of cold 3% aqueous sulfuric acid. The mixture was shaken for several minutes and then worked up in the usual manner to provide 29.2 g (90%) of **52** as a pale yellow liquid: IR 3040, 1670, 1618, 1449, 1308, 1300, 1210, 975 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.93 (d of q, J = 16 and 6 Hz, 2 H, CH_3CH=CH), 6.33 (d, J = 16 Hz, 2 H, CH_3CH=CH), 1.95 (d of d, J = 6 and 1 Hz, CH_3CH=CH); MS (70 eV), m/e (rel intensity) 110 (21.4, M^+), 95 (20.7), 69 (100).

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Registry No. 1, 183-03-9; **2a**, 68434-69-5; **2b**, 71718-31-5; **3**, 1728-35-4; **4**, 1073-76-3; **5**, 68434-73-1; **6**, 68434-74-2; **7**, 71718-32-6; **8**, 1460-16-8; **9**, 32777-26-7; **10a**, 68434-75-3; **11a**, 64187-85-5; **12**, 65844-65-7; **13**, 21448-77-1; **14a**, 36744-59-9; **14b**, 4729-30-0; **15**, 68434-70-8; **16**, 71718-33-7; **17**, 68434-72-0; **18**, 68434-76-4; **23**, 4321-25-9; **24**, 56745-53-0; **27**, 184-26-9; **28a**, 71718-34-8; **29**, 71718-35-9; **30**, 1192-93-4; **31**, 71718-36-0; **32**, 71718-37-1; **36b**, 18448-47-0; **37**, 177-10-6; **38**, 71718-38-2; **39**, 71718-39-3; **40**, 122-99-6; **41**, 49783-32-6; **42**, 1728-28-5; **43**, 71718-40-6; **44**, 71718-41-7; **45**, 1073-14-9; **46**, 41329-93-5; **47**, 71718-42-8; **48**, 71718-43-9; **49**, 71718-44-0; **50**, 71718-45-1; **52**, 71718-46-2; **53a**, 71718-47-3; **53b**, 71718-48-4.

Acyclic Stereoselection. 4. Assignment of Stereostructure to β-Hydroxycarbonyl Compounds by Carbon-13 Nuclear Magnetic Resonance

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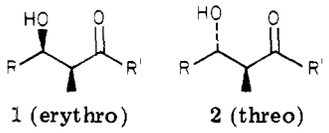
^{13}C NMR spectra for over 40 sets of β-hydroxycarbonyl compounds possessing diastereoisomerism were recorded. Empirical observations were made which allow the assignment of stereostructure to these compounds. A model for the preferred conformations of these molecules was developed which accounts for the observed chemical shift trends.

We have recently been interested in the use of the aldol condensation as a means for establishing chiral centers in acyclic systems in a controlled fashion.[1,2] Consequently, we desired a method to reliably ascertain the stereochemical outcome of any particular aldol condensation. We have found that ^{13}C NMR is an excellent tool for this determination. Diastereomeric β-hydroxycarbonyl compounds exhibit consistent ^{13}C NMR chemical shifts on the basis of which stereostructure may be assigned.

Results

α-Methyl-β-hydroxycarbonyl Compounds. When aldol condensations between ethyl carbonyl compounds and aldehydes are carried out as previously described,[1,2] erythro and threo diastereomeric products **1** and **2** may be produced. For these model studies, the R groups (incorporated from the aldehyde portion) include Ph, *p*-NO_2Ph, *p*-MeOPh, Et, *i*-Pr, *t*-Bu, $(Ph)_2CH$, and $PhCH(CH_3)$. The R′ groups (incorporated from the ethyl carbonyl compound) include H, OH, O-alkyl, *i*-Pr, *t*-Bu, Et, Ph, $C(CH_3)_2OMe_3Si$, and mesityl. The resonances that are of the greatest interest to us are those present in all compounds **1** and **2**, namely, the methyl, carbinol, and methine carbons. Table I lists the resonances observed for these three carbons in a number of diastereomeric pairs, along with resonances for some compounds for which we have only a single isomer.



1 (erythro) 2 (threo)

We take as a typical case from this table the adduct produced from reaction of methyl propionate with benzaldehyde (R′ = OMe, R = Ph). The erythro carbinol absorption is found at 73.6 ppm, while that in the threo isomer occurs at 76.3 ppm. Similar upfield shifts are observed for the other two resonances in the erythro isomer. In fact, in all the compounds listed in Table I, we note an upfield shift of the carbons in the erythro isomer compared with those in the threo isomer. This shift is smaller for methine carbons than for the other two.

In Table II the chemical shift ranges for each carbon in each isomer are given. In the carbinol and methyl signals, we note a slight overlap between the ranges for a given isomer in all compounds studied. However, Table I shows a minimum separation of 1.1 ppm in carbinol and methyl resonances of diastereomeric pairs. The maximum separation observed is 5 ppm. The methine carbons, being more directly affected by R′, show a much wider chemical

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