Carbonium Ion Rearrangements in the Deltacyclane Ring System. III.[1] Solvolytic Reactions of C-5 Substituted *exo*- and *endo*-8-Deltacyclyl Brosylates

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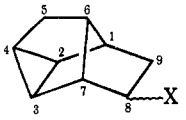
Abstract: The preparation of a series of C-5 substituted *exo*- and *endo*-8-deltacyclyl brosylates, *exo*- and *endo*-8-brosyloxydeltacyclan-5-one (**13b** and **17b**), *exo*- and *endo*-8-brosyloxydeltacyclan-5-one ethylene glycol ketal (**14** and **16b**), and *exo*- and *endo*-8-brosyloxydeltacyclan-5-one ethanedithiol ketal (*exo*-**19b** and *endo*-**19b**) is described. The rates of acetolysis of these substrates, relative to the rates of the parent brosylates, *exo*-8-deltacyclyl brosylate (*exo*-**1**-OBs) and *endo*-8-deltacyclyl brosylate (*endo*-**1**-OBs) (k_X/k_H), are used to determine the sensitivity to C-5 substitution ($\rho_{exo} = -2.68$, $\rho_{endo} = -1.63$). The acetolyses of *exo*- and *endo*-8-brosyloxydeltacyclan-5-one are nonstereospecific generating ratios of exo:endo unrearranged acetate of 87:13 and 89:11, respectively. The acetolyses of *exo*- and *endo*-ketal brosylate **14** and **16b** lead to unrearranged exo acetate, while acetolyses of *exo*- and *endo*-thioketal brosylate *exo*-**19b** and *endo*-**19b** generate ratios of unrearranged acetate:dihydro-*p*-dithiin **20** of 16:81 and 60:35, respectively. The mechanistic implications of these results are discussed.

Our interest in the chemistry of reactive intermediates in the deltacyclane ring system has been stimulated and maintained by the unique character of the carbonium ions and rearrangement pathways which are utilized as a consequence of solvolytic reactions of *exo*- and *endo*-8-substituted deltacyclane substrates. In our earlier studies,[1] we reported on several aspects of the chemistry of 8-substituted deltacyclane substrates which were of considerable help in characterizing carbonium ion rearrangements in this system. Acetolyses of *exo*-**1**-OBs, *endo*-**1**-OBs, and a mixture of *exo*-**1**-Cl and



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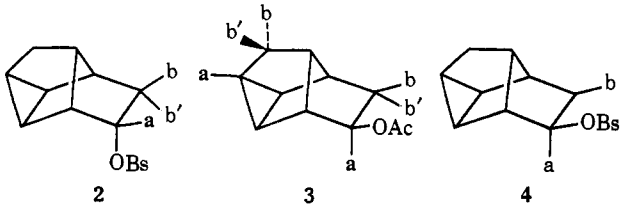
endo-**1**-Cl, deamination of a mixture of amines, *exo*-**1**-NH_2 and *endo*-**1**-NH_2, with nitrous acid in acetic acid, as well as oxidative decarboxylation of a mixture of *exo*-**1**-CO_2H and *endo*-**1**-CO_2H result in the generation of a single acetate, *exo*-**1**-OAc, with a stereoselectivity greater than 99.6%.

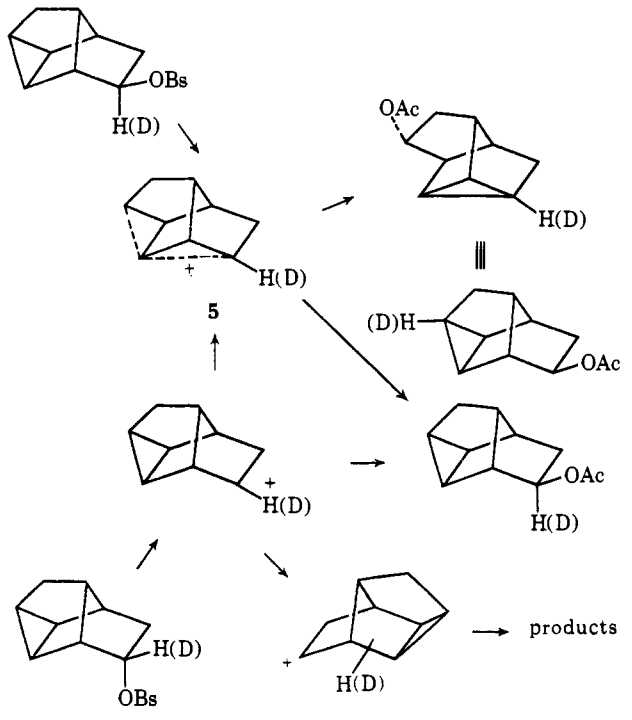
Deuterium tracer studies revealed that acetolysis of endo brosylate labeled at C-8 (position a in **2**) generates exo acetate **3** with deuterium distributed over positions a in **3**, while acetolysis of endo brosylate labeled at b and b′ in **2** produces **3** with deuterium distributed over positions b and b′. In each case the scrambling away from the original position in **2** was less than 50% (40 and 45%, respectively). Acetolysis of exo brosylate **4**



labeled at a gives exo acetate with deuterium distributed over positions a in **3**, while solvolysis of exo brosylate labeled at b in **4** generates exo acetate with deuterium distributed over positions b in **3**. The distribution of deuterium as measured by mass spectroscopy is 50:50 in the latter experiment.

The rates of acetolysis at 25.68° of *exo*-**1**-OBs, 2.61×10^{-4} sec^{-1} (anchimeric assistance $10^{5.3}$), and *endo*-**1**-OBs, 4.62×10^{-6} sec^{-1} (anchimeric assistance $10^{3.1}$), the nmr spectra of *exo*- and *endo*-**1**-OH in FSO_3H–SO_2 (only two protons downfield, τ 4.83), and the experimental facts that acetolysis of optically active *exo*-**1**-OBs results in 99% retention of optical activity, while acetolysis of *endo*-**1**-OBs produces product acetate with a 57% loss of optical activity, coupled with the data on the deuterium scrambling and the solvolytic course of the reaction, led us to suggest the reaction pathways outlined in Scheme I.[1a] Solvolysis of exo brosylate

Scheme I



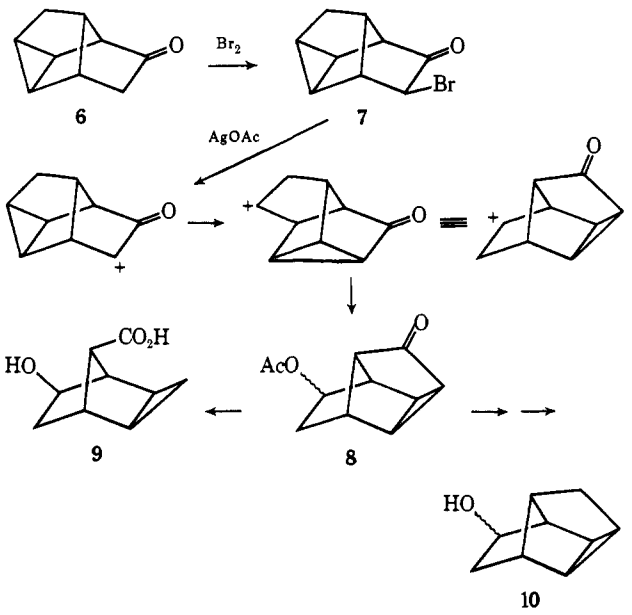
(1) For studies I and II, see (a) P. K. Freeman, D. M. Balls, and J. N. Blazevich, *J. Amer. Chem. Soc.*, 92, 2051 (1970); (b) P. K. Freeman and J. N. Blazevich, *Chem. Commun.*, 1357 (1969).

Table I. Acetolysis of C-5 Substituted Deltacyclyl Brosylates

Compd	Temp, °C	k_{exo}, sec^{-1} [a]	k_{rel}	Compd	Temp, °C	k_{endo} [a]	k_{rel}	k_{exo}/k_{endo}	σ^*
exo-1-OBs	25	2.61×10^{-4}	30,000	*endo*-1-OBs	25	4.62×10^{-6}	530	57	0.00
exo-**19b**	86.0	2.36×10^{-3}		*endo*-**19b**	85.5	2.40×10^{-4}			
	75.0	8.90×10^{-4}			75.0	8.18×10^{-5}			
	61.8	2.00×10^{-4}			61.8	1.86×10^{-5}			
	(25)	5.74×10^{-6}	660		(25)	2.12×10^{-7}	24	27	+0.84
14	85.7	1.61×10^{-3}		**16b**	85.7	1.84×10^{-4}			
	75.0	6.48×10^{-4}			75.0	6.41×10^{-5}			
	61.8	1.50×10^{-4}			61.8	1.48×10^{-5}			
	(25)	1.57×10^{-6}	180		(25)	1.82×10^{-7}	20	8.6	+1.04
13b	94.3	2.64×10^{-5}							
	84.5	9.96×10^{-6}		**17b**	85.9	1.09×10^{-5}			
	75.4	3.74×10^{-6}			75.0	3.59×10^{-6}			
	(25)	8.72×10^{-9}	1		(25)	8.72×10^{-9}	1	1	+1.65

[a] Each rate constant is the average of two runs.

Scheme II



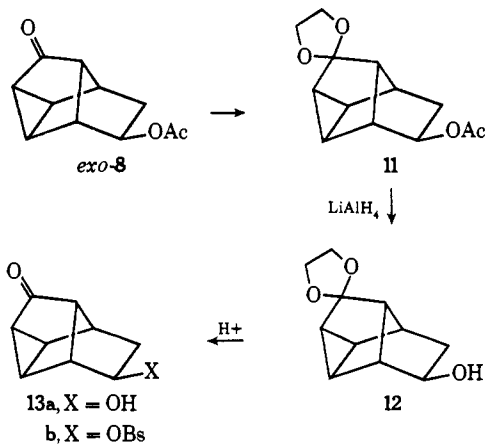
6 7 9 8 10

occurs with participation of the C-3–C-4 bond leading directly to symmetrical (C_2) delocalized carbonium ion **5**, while solvolysis of endo brosylate generates a classical 8-deltacyclyl ion initially, which may react with solvent, leak to delocalized ion **5** or rearrange by a sequence of alkyl shifts to an ion of enantiomeric configuration. Our investigation of secondary β-deuterium isotope effects on the solvolysis of labeled *exo*- and *endo*-1-OBs revealed a large isotope effect for the endo brosylate **2** (b = D), $k_H/k_D = 1.26 \pm 0.02$, and a reduced isotope effect for the exo brosylate **4** (b = D), $k_H/k_D = 1.14 \pm 0.02$,[1b] providing a similar pattern to that for secondary β-deuterium isotope effects in 2-norbornyl systems[2,3] and supporting the mechanistic picture presented in Scheme I.

It was felt that an interesting test of the charge distribution in the transition states for solvolysis of *exo*- and *endo*-8-deltacyclyl brosylates might be made by a study of the effect of substitution at C-5 on the rates of solvolysis of both endo and exo brosylates. In particular, electronegative substituents at C-5 should inhibit generation of positive charge at C-4. Accordingly, we prepared a series of C-5 substituted *exo*- (*exo*-1-OBs, *exo*-**19b**, **14**, and **13b**) and *endo*- (*endo*-1-OBs, *endo*-**19b**, **16b**, and **17b**) 8-deltacyclyl brosylates, using 8-acetoxydeltacylan-5-one (**8**) as the key synthetic intermediate. The synthesis of **8** from 8-deltacyclanone was accomplished by making use of the deltacyclyl cyclopropylethyl rearrangement as outlined in Scheme II. Treatment of bromo ketone **7** with silver acetate in acetic acid produces keto acetate **8** (92% exo and 8% endo) in 57% yield. Structure proof for **8** was accomplished by nmr spectral analysis and conversion of **8** to **10** by way of thioketal alcohol **19a** and reduction with hydrazine–KOH. Spin decoupling experiments carried out on *exo*-**8** (100 MHz, CCl_4 solvent) revealed a three proton system for $-CHOAcCH_2-$ at τ 5.07, 7.74, 8.40 ($J_{8,9n} = 6.0$, $J_{8,9x} = 2.1$, $J_{9x,9n} = 14$ Hz), while spin decoupling carried out on **8** (100 MHz, CCl_4, in the presence of shift reagent Eu(fod)$_3$) revealed a second three proton system consisting of three nonequivalent cyclopropane hydrogens, –CHCHCH– ($J_{2,3} = J_{3,4} = J_{4,2} = 6$ Hz).

Since saponification of the ester functional group at C-8 in **8** resulted in cleavage to hydroxy acid **9**, it was necessary to protect the keto group at C-5 in order to convert to *exo*-keto alcohol **13a** as outlined in Scheme III.

Scheme III



exo-**8** **11** **13a**, X = OH; b, X = OBs **12**

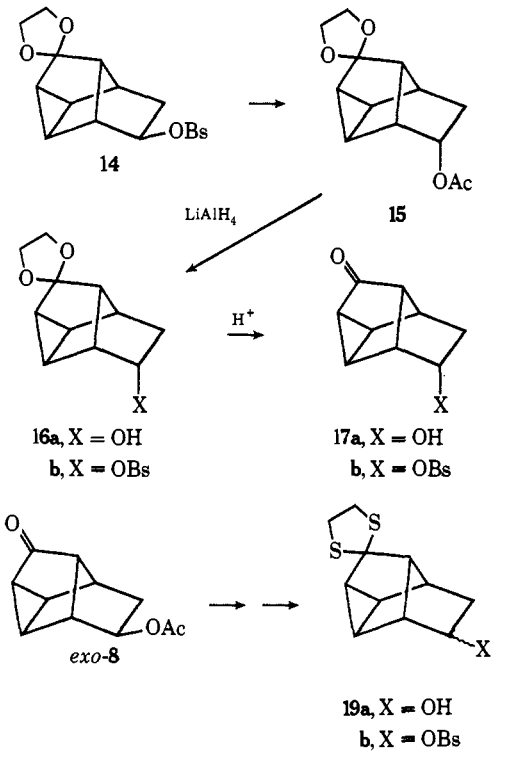
The SN2 displacement of brosylate by acetate, using the tetra-*n*-butylammonium acetate procedure of Murr

(2) J. P. Schaefer, M. J. Dagani, and D. S. Weinberg, *J. Amer. Chem. Soc.*, **89**, 6938 (1967); J. P. Schaefer and D. S. Weinberg, *Tetrahedron Lett.*, 2491 (1965); J. P. Schaefer, J. P. Foster, M. J. Dagani, and L. M. Honig, *J. Amer. Chem. Soc.*, **90**, 4497 (1968).

(3) J. M. Jerkunica, S. Borčić, and D. E. Sunko, *Chem. Commun.*, 1488 (1968).

and Conkling,[4] was employed to convert *exo*-ketal brosylate **14** (from **12**) to *endo*-ketal acetate **15**, which was used to prepare *endo*-ketal alcohol **16a** and *endo*-keto alcohol **17a** as indicated in Scheme IV. *exo*-

Scheme IV



Keto acetate (*exo*-**8**) was converted to thioketal acetate **18** by treatment with ethanedithiol and boron trifluoride etherate. *exo*-Thioketal acetate **18** was then used to prepare *exo*- and *endo*-thioketal alcohols, *exo*-**19a** and *endo*-**19a**, by procedures entirely analogous to those described for the synthesis of **12** and **16a** starting with the related ketal acetate **11**.

The alcohols described were converted to brosylates by treatment with brosyl chloride in pyridine, and the rates of acetolysis in sodium acetate buffered acetic acid were measured and are presented in Table I. Least-squares fits of plots of the log of the relative rates for the exo brosylates, log k_x/k_H, *vs.* σ^* and of log k_x/k_H for the *endo*-brosylates *vs.* σ^* were constructed and yield a reaction constant $\rho = -2.68$ (correlation coefficient $= -0.983$) for the exo series and a $\rho = -1.63$ (correlation coefficient $= -0.991$) for the endo series.

An analysis of the acetolysis products of *exo*-keto brosylate **13b** and *endo*-keto brosylate **17b** by vpc, using a DEGS capillary column, reveals that solvent attack upon the carbonium ion (or ion pair) is much less stereoselective than attack upon the ion(s) formed in the acetolysis of unsubstituted *exo*- or *endo*-deltacyclyl brosylate (Table II).

Furthermore, product analysis of the acetolysis of *exo*- and *endo*-ketal brosylates (**14** and **16b**) reveals that only unrearranged *exo*-ketal acetate **11** is formed in either case. In contrast, acetolysis of *exo*-thioketal brosylate *exo*-**19b** yields unrearranged *exo*-thioketal acetate **18** and dihydro-*p*-dithiin **20** in a ratio of 16:81

(4) B. L. Murr and J. A. Conkling, *J. Amer. Chem. Soc.*, 92, 3465 (1970).

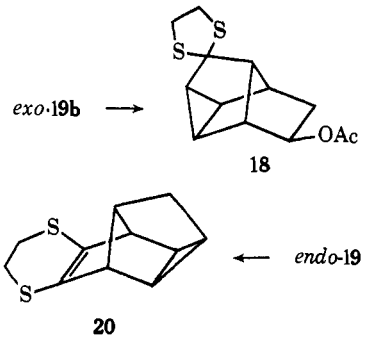


Table II. Acetolysis of *exo*- and *endo*-5-Keto-8-deltacyclyl Brosylates (**13b** and **17b**)

Brosylate	Acetolysis products, % *exo*-**8**	*endo*-**8**
13b	87	13
17b	89	11
1-OBs	>99.6	<0.4
	exo-**1**-OAc	*endo*-**1**-OAc

(97% overall yield). Acetolysis of *endo*-thioketal brosylate generates the same two components in a 60:35 ratio (overall yield, 95%). There was no detectable unrearranged endo acetate formed in the acetolysis of epimeric ketal and thioketal brosylates (<3% present by nmr).

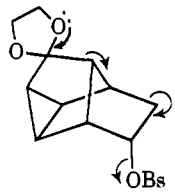
Discussion

The polar effect of substitution of C-5 on the acetolysis rates of the *exo*-8-deltacyclyl substrates is certainly more severe than on that of the endo substrates. In harmony with this we find a steady decrease in k_{exo}/k_{endo} as the value of σ^* is increased (Table I). The question arises as to whether these effects might be due to a major degree to a more severe dipole–dipole interaction ($C^{\delta+}$–$O^{\delta-}$ with $C^{\delta+}$–$O^{\delta-}$–Bs in **13b** and **17b**, for example) in the case of each endo epimer, making the assumption that the dipole-charge interactions in the transition states for the epimeric pairs will be nearly the same due to the charge dispersal expected for a developing brosylate anion in a hydrogen bonding solvent.[5] Thus, the introduction of a strong dipole at C-5 might raise the ground-state-energy level of the endo brosylate relative to the epimeric exo brosylate and, consequently mask the polar effect for the endo brosylate series. An inspection of models reveals, however, that the reverse is the case and that dipole–dipole interaction should raise the ground-state-energy level of the exo brosylate relative to epimeric endo brosylate. Since, in spite of this, we find greater deceleration for substitution of electronegative substituents at C-5 on the rates of acetolysis of exo brosylates than on those of the endo brosylates, our original suggestion that acetolysis of *exo*-8-deltacyclyl brosylate proceeds directly to delocalized intermediate **5** while *endo*-8-deltacyclyl brosylate generates a classical 8-deltacyclyl carbonium ion initially (Scheme I) is supported.

Although a large number of substituents have not been investigated, it is of interest to note that the regular behavior of the endo series contrasts with the erratic behavior found by Gassman for C-7 substituted *endo*-

(5) D. S. Noyce and B. E. Johnston, *J. Org. Chem.*, 34, 1252 (1969).

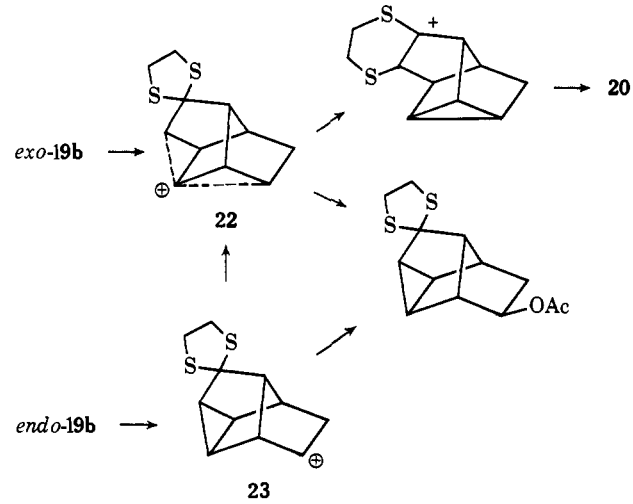
2-norbornyl tosylates.[6b] This is to be anticipated, since the positioning of the substituents on the deltacyclane ring system does not readily allow participation of the substituents by frangomeric or MeO-4 type mechanisms in the *endo*-deltacyclyl series.[6] Perhaps one could suggest the extended frangomeric process pictured in **21**; however, product analysis provides no evidence for such a process.



21

The stereoselectivities associated with the product-determining steps in these solvolytic reactions are in harmony with the rate data presented in Table I and with the mechanistic picture outlined in Scheme I. The suggestion may be made, in the light of the rate data of Table I, that the anchimeric assistance provided by the participation of the C-3–C-4 cyclopropane bond in the solvolytic reactions of the exo brosylates is completely inhibited in the case of *exo*-keto brosylate **13b**. We therefore anticipate that similar classical carbonium ions will be generated in the solvolyses of *exo*- and *endo*-keto brosylates **13b** and **17b** and find that this view is nicely reinforced by the formation of substantial quantities of *endo*-**8** as a consequence of the acetolyses of the epimeric keto brosylates (Table II). The lack of endo solvolysis product in the acetolysis of *endo*-1-OBs may be at least partially explained by suggesting that the actual trapping of the classical ion is a minor reaction pathway relative to the other alternative processes, which involve, presumably, delocalized product determining intermediates which protect against endo attack. In the acetolyses of thioketal *endo*-**19b** and *endo*-ketal **16b**, some endo product may have been formed and gone undetected by the nmr method used.

The product ratios obtained upon the acetolysis of *exo*- and *endo*-thioketal brosylates, *exo*-**19b** and *endo*-**19b**, are also of considerable interest. The greater ratio of rearranged dihydro-*p*-dithiin **20**:unrearranged acetate **18** (81:16) from *exo*-thioketal brosylate relative to that (35:60) found for the *endo*-thioketal brosylate suggests a process favorable to rearrangement from exo substrate. Such a process might well be that in which *exo*-**19b** forms a bridged ion **22**, which may suffer attack at C-8 by solvent to form unrearranged acetate or intramolecular attack at C-4 by sulfur to follow a rearrangement pathway leading to **20**. Since there is no evidence for sulfur participation, the rate of acetolysis of *exo*-**19b** correlating well with a purely inductive effect for the thioketal group, it seems reasonable to represent the first formed intermediate without neighboring group interaction of sulfur. The solvolysis of *endo*-thioketal brosylate could then be pictured as generating classical ion **23** initially and this



either being trapped by solvent (57%) or leaking to **22** (43%), the overall process being completely analogous to that pictured in Scheme I.

Experimental Section

All melting points and boiling points are uncorrected. Infrared spectra were run on a Beckman Model IR-8 or a Perkin-Elmer 621 infrared spectrophotometer. Mass spectra were run on an Atlas CH7 or a Finnigan 1015 S/L mass spectrometer. Elemental analyses were performed by Alfred Bernhardt, Mikroanalytisches Laboratorium, 5251 Elbach Über Engelskirchen, Fritz-Pregl-Strasse 14–16, West Germany. Vpc analyses were performed on an F&M Model 700 chromatograph equipped with dual columns and thermal conductivity detectors, or on a Varian Aerograph Series 1200 chromatograph equipped with a flame ionization detector.

The following columns were used for vpc work: (1) 10 ft × 0.25 in. aluminum containing 10% Carbowax 20M on Anakrom 70–80 ABS, (2) 15 ft × 0.25 in. aluminum containing 15% QF-1 on Anakrom 70–80 ABS, (3) 3 ft × 0.25 in. aluminum containing 10% Carbowax 20M on Anakrom 70–80 ABS, (4) 10 ft × 0.25 in. aluminum containing 15% Carbowax 20M on Anakrom 70–80 ABS, and (5) 70 ft capillary column (stainless steel) coated with DEGS. Nmr spectra were obtained using a Varian Associates A-60 or HA-100 nmr spectrometer.

Product Analyses for Solvolytic Reactions of 5-Substituted 8-Deltacyclyl Brosylates. A. ***exo*-Ketal Brosylate 14.** To 270 mg (0.65 mmol) of *exo*-ketal brosylate **14** was added 20 ml of standard sodium acetate–acetic acid solution, and the resulting solution was heated to 67° for 6 hr. The solution was then neutralized by dropwise addition of saturated aqueous sodium bicarbonate, extracted with 3 × 100 ml of ether, washed once with aqueous sodium chloride, and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave an oil which was found to contain 0.147 g (0.62 mmol, 95% yield) of pure *exo*-ketal acetate **11** by vpc, using an internal standard and correcting for differences in molecular weight using Eastman's formula.[7] The product was shown to be *exo*-ketal acetate **11** by ir and nmr comparison with an authentic sample. No *endo*-ketal acetate could be detected by nmr analysis (<3% present). No other products were detected by vpc (column 1).

B. ***endo*-Ketal Brosylate 16b.** In a similar manner, 270 mg (0.65 mmol) of *endo*-ketal brosylate was heated to 67° for 36 hr. A yield of 0.150 g (0.63 mmol, 97% yield) of *exo*-ketal acetate **11** was obtained and identified as above. No *endo*-ketal acetate was detected by nmr analysis (<3% present). No other products were detected by vpc (column 1).

C. ***exo*-Thioketal brosylate *exo*-19b** (949 mg, 2.13 mmol) in 68 ml of standard sodium acetate–acetic acid solution was heated to 67° for 6 hr, and was worked up as above. A minor product, *exo*-thioketal acetate **18** (95 mg, 0.35 mmol, 16% yield), was obtained. No *endo*-thioketal acetate could be detected by nmr analysis (<3% present). The major product had a much shorter vpc retention time than *exo*-thioketal acetate **18** (column 3, 50 ml/min, 3 min *vs.* 16 min, 185°). The ratio of the two products was 16:81, thioketal acetate to major product. Physical properties of the major com-

(6) (a) P. G. Gassman and J. G. Macmillan, *J. Amer. Chem. Soc.*, **91**, 5527 (1969); (b) P. G. Gassman, J. L. Marshall, J. G. Macmillan, and J. M. Hornback *ibid.*, **91**, 4282 (1969); (c) P. G. Gassman and J. M. Hornback, *ibid.*, **91**, 4280 (1969); (d) P. G. Gassman and J. L. Marshall, *Tetrahedron Lett.*, 2429, 2433 (1968); (e) *J. Amer. Chem. Soc.*, **88**, 2822 (1966).

(7) R. H. Eastman, *J. Amer. Chem. Soc.*, **79**, 4243 (1957).

ponent are as follows: mp 53–57°; mass spectrum, parent peaks *m/e* 208 and 210; ir (neat) 3055 (cyclopropyl C–H stretching, C=C stretching); nmr (100 MHz, CCl_4) τ 8.3–8.6 (m, 5 H), 8.03 (broad singlet, 1 H), 7.47 (s, 2 H), 6.95 (s, 4 H, $-SCH_2CH_2S-$). The yield of the major product, characterized as dihydro-*p*-dithiin, **20**, was 358 mg (1.72 mmol, 81% yield). *Anal.* Calcd for $C_{11}H_{12}S_2$: C, 63.41; H, 5.81. Found: C, 63.21; H, 5.89.

To check the stability of *exo*-thioketal acetate **18** to the reaction conditions, 101 mg (0.377 mmol) was heated for 4 hr at 75° in 12 ml of standard HOAc–NaOAc solution. Work-up as above afforded 94 mg (0.35 mmol, 93% yield) of recovered thioketal acetate; no rearranged product could be detected by vpc.

D. *endo*-Thioketal brosylate *endo*-19b (280 mg, 0.63 mmol) in 20 ml of standard sodium acetate–acetic acid solution was heated to 67° for 36 hr, and worked up as above. Two product components were obtained: *exo*-thioketal acetate **18** (102 mg, 0.38 mmol, 60% yield) and dihydro-*p*-dithiin **20** (45 mg, 0.22 mmol, 35% yield). No *endo*-thioketal acetate was detected by nmr analysis (<3% present).

E. *exo*-Keto brosylate 13b (1.00 g. 0.00270 mol) was dissolved in 100 ml of sodium acetate–acetic acid solution and heated at 65° for 21 days and worked up as above. A yield of 0.39 g (0.00203 mol, 75% yield) of keto acetate **8** was obtained and identified by spectral comparison with an authentic sample. The product was found to consist of exo and endo acetate in a ratio of 87:13 by careful vpc analysis (column 5).

F. *endo*-Keto brosylate 17b (0.610 g, 0.00165 mol) was added to 50 ml of standard sodium acetate–acetic acid solution and heated to 61° for 21 days, working up as above. A yield of 0.24 g (0.00125 mol, 76% yield) of ketal acetate **8** was obtained which was found to consist of exo and endo acetates in a ratio of 89:11 by vpc analysis (column 5).

Preparation of *exo*-9-Bromodeltacyclan-8-one (7). To a rapidly stirred solution of 250 g (1.86 mol) of 8-deltacyclanone in 200 ml of ether was slowly added 350 g (2.18 mol) of bromine. A short induction period is required to build up a catalytic amount of hydrobromic acid. After this period the reaction is exothermic. Nitrogen was rapidly bubbled in to carry off hydrobromic acid. Additional ether was added during the reaction to maintain a constant volume. The reaction was then poured into a large beaker containing 200 ml of water. Sufficient sodium carbonate (10% solution) was added to neutralize any acid present. The ethereal layer was washed once with water and dried ($MgSO_4$). Evaporation of the solvent gave 345 g (1.62 mol, 87% yield) which was used without further purification. The bromo ketone product exhibits the following spectral characteristics: mass spectrum, parent peaks at *m/e* 212, 214; ir (neat) 3055 (cyclopropyl C–H stretching), 1751 (C=O), 1149, 826 cm^{-1}; nmr (60 MHz, CCl_4) τ 8.68 (m, 3 H, cyclopropyl protons), 8.30 (broad singlet, 2 H, $-CH_2-$ at C-5), 7.62 (s, 1 H, bridgehead proton), 7.50 (s, 2 H, bridgehead protons at C-1 and C-7), 5.94 (s, 1 H, CHBr).

Anal. Calcd for C_9H_9OBr: C, 50.75; H, 4.23. Found: C, 50.73; H, 4.27.

Preparation of *exo*-8-Acetoxydeltacyclan-5-one (*exo*-8). To a 3-l. three-necked flask equipped with a mechanical stirrer and reflux condenser was added 297 g (1.40 mol) of bromo ketone **7**, 1 l. of acetic acid, and 200 ml of acetic anhydride. The solution was stirred at reflux. Silver acetate (413 g, 2.46 mol) was then added over a period of 48 hr. The reaction was allowed to run for an additional 24 hr. Approximately 1 l. of acetic acid was then distilled and the remaining solution diluted with 200 ml of water. Ether (100 ml) was added and the contents were filtered. Sodium carbonate was added until the reaction was neutral to litmus paper. The aqueous layer was extracted with 3 × 200 ml of ether and washed three times with 100-ml portions of saturated salt solution and twice with 100-ml portions of water. The combined ether extracts were dried over anhydrous magnesium sulfate. Rotary evaporation of the ether gave 165 g of dark semisolid material. Distillation on a high vacuum line at 85–87° (1×10^{-5} mm) gave 153 g (0.80 mol, 57% yield) of product. Only one compound could be detected by vpc analysis (column 1, 180°, 70 ml/min, 29 min). Vpc analysis (column 5) showed a 92:8 ratio of *exo*:*endo*-keto acetate **8**. Distillation at higher temperature and pressure than that cited above was found to result in considerable decomposition and lower yields. The spectral characteristics of **8** are as follows: mass spectrum, *m/e* (rel intensity) 192 (6), 150 (20), 132 (36), 131 (56), 105 (28), 78 (62), 77 (36), 43 (100); ir (neat) 3055 (cyclopropyl C–H stretching), 1739 (C=O), 1245, 1163, 1042, 866, 838 cm^{-1}; nmr (100 MHz, CCl_4) τ 8.71 (t, 1 H, J = 6 Hz, cyclopropyl proton at C-4), 8.40 (doublet of triplets, 1 H, J = 14 Hz, 2 Hz, exo-C-9-proton), 8.22 (m, 3 H, cyclopropyl protons at C-3, C-2, bridgehead proton at C-6), 8.08 (s, 3 H, $-OCOCH_3$), 7.74 (doublet of doublets, 1 H, J = 14 Hz, 6 Hz, endo-C-9 proton), 7.32 (s, 1 H, bridgehead proton), 7.24 (s, 1 H, bridgehead proton), 5.07 (doublet of doublets, 1 H, J = 6.0 Hz, 2.1 Hz, –CHOAc).

Anal. Calcd for $C_{11}H_{12}O_3$: C, 68.73; H, 6.29. Found: C, 68.54; H, 6.22.

Preparation of *exo*-8-Acetoxydeltacyclan-5-one Ethylene Glycol Ketal (11). A solution of 10.0 g (0.052 mol) of *exo*-keto acetate *exo*-**8** and 6.1 ml of ethylene glycol in 91 ml of dry benzene containing 0.016 g of *p*-toluenesulfonic acid was heated at reflux for 9 hr, azoetropically separating the water formed using a Dean-Stark trap. The cooled benzene solution was decanted from the remaining ethylene glycol and then washed with 25 ml of 10% sodium carbonate and 25 ml of water. The organic layer was dried over anhydrous magnesium sulfate, and filtered, and the benzene removed by vacuum distillation, yielding 11.16 g (0.047 mol, 93% yield). The fairly pure crude *exo*-ketal acetate **11** obtained was used for subsequent steps with further purification due to its high boiling point. The product exhibits the following physical properties: ir (neat) 3055 (cyclopropyl C–H stretching), 1754 (C=O), 1117, 862 cm^{-1}; nmr (100 MHz, CCl_4) τ 8.86 (broad singlet, 3 H, cyclopropyl protons), 8.40 (doublet of triplets, 1 H, J = 14 Hz, 2 Hz, exo-methylene proton), 8.1 (broad singlet, 1 H, bridgehead proton at C-6), 7.88 (doublet of doublets, 1 H, J = 14 Hz, 7 Hz, endo-methylene proton), 7.64 (broad singlet, 2 H, bridgehead protons), 6.16 (d, 4 H, $-OCH_2CH_2O-$), 5.18 (doublet of doublets, 1 H, J = 6.8 Hz, 2.4 Hz, –CHOAc).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.01; H, 6.71.

Preparation of *exo*-8-Hydroxydeltacyclan-5-one Ethylene Glycol Ketal (12). To a rapidly stirred mixture of 3.5 g (0.092 mol) of lithium aluminum hydride and 160 ml of anhydrous ether in a three-necked flask equipped with a condenser was slowly added 22.5 g (0.095 mol) of *exo*-ketal acetate **11** in 100 ml of anhydrous ether. The resulting solution was stirred for 12 hr at room temperature. Saturated aqueous ammonium chloride was then slowly added and the solution was extracted with 3 × 200 ml of ether. The organic phase was washed with 3 × 25 ml of saturated salt solution and once with 25 ml of water. The combined ether extracts were dried over anhydrous magnesium sulfate. Evaporation of the ether solvent gave 16.0 g (0.083 mol, 87% yield) of white crystalline ketal alcohol **12**: ir (neat) 3413 (OH stretching), 3055 (cyclopropyl C–H stretching), 1116 cm^{-1}; nmr (100 MHz, CCl_4) τ 7.3–9.0 (m, 8 H), 6.42 (s, 1 H, –CHOH), 6.07 (broad singlet, 4 H, $-OCH_2CH_2O-$), 5.98 (doublet of doublets, 1 H, J = 7.0 Hz, 2.4 Hz, –CHOH).

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.79; H, 7.33.

Preparation of *exo*-8-Brosyloxydeltacyclan-5-one Ethylene Glycol Ketal (14). To a solution of 11.0 g (0.057 mol) of *exo*-ketal alcohol **12** in 180 ml of dry pyridine at 0° was added with stirring 19.0 g (0.074 mol) of *p*-bromobenzenesulfonyl chloride over a period of 30 min, keeping the temperature in the range 0–7°. The mixture was allowed to stir at room temperature for 2 hr and then stand in a refrigerator for 6 days. Crystalline pyridinium chloride was observed to form slowly. The solution was then poured into 200 g of ice and neutralized with a mixture of 6 *N* hydrochloric acid and ice to a pH of 2–4. The aqueous solution was extracted with 3 × 100 ml of ether. The ether layer was separated and washed successively with 25 ml of 5% hydrochloric acid, 25 ml of 10% sodium carbonate, 50 ml of saturated aqueous sodium chloride, and 25 ml of water. Drying over anhydrous magnesium sulfate and evaporation of the ether gave 18.0 g (0.044 mol, 77% yield) of brosylate. Recrystallization from an ether–pentane mixture (30:70) gave pure white crystalline brosylate: mp 95–97°; nmr (100 MHz, CCl_4) τ 8.88 (broad singlet, 3 H, cyclopropyl protons), 8.36 (doublet of triplets, 1 H, J = 14 Hz, 2 Hz, methylene proton), 8.28 (broad singlet, 1 H, bridgehead proton), 7.96 (doublet of doublets, 1 H, J = 14 Hz, 7 Hz, methylene proton), 7.60 (broad singlet, 1 H, bridgehead proton), 7.46 (broad singlet, 1 H, bridgehead proton), 6.18 (d, 4 H, $-OCH_2CH_2O-$), 5.33 (doublet of doublets, 1 H, J = 6.8 Hz, 2.3 Hz, –CHOBs).

Anal. Calcd for $C_{17}H_{17}O_5SBr$: C, 49.40; H, 4.14. Found: C, 49.57; H, 4.12.

Preparation of *exo*-8-Hydroxydeltacyclan-5-one (13a). To 4.0 g (0.021 mol) of *exo*-ketal alcohol **12** was added 25 ml of ethanol and 4.6 ml of 5% aqueous sulfuric acid. The mixture was rapidly stirred for 7 hr at room temperature. Ethyl alcohol was then re-

moved from the mixture by rotary evaporation (heating was avoided, as it will cause some decomposition of the keto alcohol). The solution was extracted with 3 × 50 ml of ether, and the ether extracts were washed with 10 ml of 10% sodium carbonate, three times with 15 ml of saturated salt water, and once with 10 ml of water. The ether layer was dried over anhydrous magnesium sulfate and filtered, and solvent evaporated to give 2.5 g (0.017 mol, 81% yield) of *exo*-keto alcohol **13a**. No further attempt was made to purify the product due to its instability: ir (neat) 3448 (OH stretching), 3055 (cyclopropyl C–H stretching), 1751 (C=O), 1075, 1042, 840 cm^{-1}; nmr (100 MHz, $CHCl_3$) τ 8.68 (t, 1 H, J = 6 Hz, cyclopropyl proton), 8.3 (m, 1 H, methylene proton), 8.2 (m, 3 H, cyclopropyl proton at C-3, C-2, bridgehead proton at C-6), 7.68 (doublet of doublets, 1 H, J = 14 Hz, 7 Hz, methylene proton), 7.32 (broad singlet, 2 H, bridgehead proton), 6.38 (s, 1 H, –CHOH), 5.82 (doublet of doublets, 1 H, J = 7.0 Hz, 2.4 Hz, –CHOH).

Anal. Calcd for $C_9H_{10}O_2$: C, 71.78; H, 6.71. Found: C, 71.87; H, 7.16.

Reduction of *exo*-8-Hydroxydeltacyclan-5-one Ethanedithiol Ketal (*exo*-19a). Thioketal alcohol *exo*-**19a** (0.80 g, 0.0035 mol), 15 ml of triethylene glycol, 5 ml of 95% hydrazine hydrate, and 2.4 g (0.045 mol) of KOH were added to a 25-ml flask attached to a micro distillation still. The mixture was stirred and heated to 90°. A slow evolution of gas began, which was collected in an inverted cylinder. Final heating of the flask was accomplished at 135–140° for 2 hr. The reaction vessel was cooled and the contents were transferred to a separatory funnel, diluted with 50 ml of water, and extracted three times with ether. The ether extracts were washed with saturated salt solution and dried over anhydrous magnesium sulfate. Rotary evaporation of solvent gave 0.36 g (0.0026 mol, 74% yield) of product. A vpc collected sample (column 4, 100 ml/min, 14 min) was identical by spectral comparison with an authentic sample of *exo*-8-deltacyclyl alcohol.

Preparation of *exo*-8-Brosyloxydeltacyclan-5-one (13b). To a stirred solution of 4.10 g (0.027 mol) of *exo*-keto alcohol **13a** in 75 ml of pyridine at 0° was added 8.0 g (0.031 mol) of *p*-bromobenzenesulfonyl chloride over a period of 1 hr, maintaining the temperature between 0 and 7°. The solution was stirred an additional hour at room temperature, allowed to stand in a refrigerator for 10 days, and then worked up as described above for brosylate **14**. Recrystallization from a 90:10 pentane–ether mixture gave white crystalline brosylate: mp 94–95°; nmr (100 MHz, CCl_4) τ 8.6–8.0 (m, 1 H, cyclopropyl proton), 8.0–8.4 (m, 4 H), 7.79 (doublet of doublets, 1 H, J = 14 Hz, 6.5 Hz, endo-methylene proton), 7.33 (broad singlet, 1 H, bridgehead proton), 7.16 (broad singlet, 1 H, bridgehead proton), 5.15 (doublet of doublets, 1 H, J = 6.5 Hz, 2.4 Hz, –CHOBs).

Anal. Calcd for $C_{15}H_{13}O_4SBr$: C, 48.79; H, 3.55. Found: C, 48.51; H, 3.49.

Preparation of *endo*-8-Acetoxydeltacyclan-5-one Ethylene Glycol Ketal (15). To 200 ml of dry benzene, 13.0 g (0.045 mol) of tetra-*n*-butylammonium acetate (**4**) and 11.0 g (0.027 mol) of *exo*-ketal brosylate **14** were added and the resulting reaction mixture was heated at 58° for 15 hr in a tightly stoppered flask. The resulting dark solution was then distilled under reduced pressure to remove the benzene. Ether (200 ml) was added and the solution was washed several times with 100-ml portions of saturated salt water, 10% sodium carbonate, and water. The organic layer was dried with anhydrous magnesium sulfate, and the solvent evaporated to give 6.0 g (0.025 mol, 93% yield) of *endo*-ketal acetate **15**: ir (neat) 3055 (cyclopropyl C–H stretching), 1730 (C=O), 1362, 1250, 1125 cm^{-1}; nmr (100 MHz, CCl_4) τ 8.4–9.0 (m, 6 H, cyclopropyl, bridgehead, and methylene protons), 8.04 (s, 3 H, $OCOCH_3$), 7.64 (m, 1 H, bridgehead proton), 7.38 (m, 1 H, bridgehead proton), 6.22 (d, 4 H, $-OCH_2CH_2O-$), 5.02 (doublet of triplets, 1 H, J = 9.8 Hz, 3.4 Hz, –CHOAc).

Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 66.01; H, 6.71.

Preparation of *endo*-8-Hydroxydeltacyclan-5-one Ethylene Glycol Ketal (16a). To a rapidly stirred solution of 2.80 g (0.074 mol) of lithium aluminum hydride in 400 ml of anhydrous ether was slowly added 8.0 g of *endo*-ketal acetate **15** in 50 ml of ether. The reaction was allowed to stir for 14 hr at room temperature, and then worked up as described above for **12**, giving 6.0 g (0.031 mol, 91% yield) of white solid *endo*-ketal alcohol; mass spectrum parent peak at *m/e* 194; ir (neat) 3390 (OH stretching), 3055 (cyclopropyl C–H stretching), 1361, 1124, 1008 cm^{-1}; nmr (100 MHz, CCl_4) τ 7.9–9.0 (m, 7 H, cyclopropyl, methylene, bridgehead protons, and CHOH), 7.72 (broad singlet, 1 H, bridgehead proton), 7.62 (broad singlet, 1 H, bridgehead proton), 6.20 (d, 4 H, $-OCH_2CH_2O-$), 5.73 (doublet of triplets, 1 H, J = 9.6 Hz, 3.8 Hz, –CHOH).

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.86; H, 7.22.

Preparation of *endo*-8-Brosyloxydeltacyclan-5-one Ethylene Glycol Ketal (16b). To a solution of 5.0 g (0.026 mol) of *endo*-ketal alcohol **16a** was added 80 ml of dry pyridine, and the solution was cooled to 0–5°. *p*-Bromobenzenesulfonyl chloride (8.0 g, 0.0313 mol) was added over 30 min, maintaining the temperature at 0–7°. The solution was stirred an additional 15 min at 0°, and finally 15 min at room temperature. After standing in a refrigerator for 10 days, the reaction mixture was worked up as described above for brosylate **14**. Recrystallization of crude brosylate from a 70:30 pentane–ether mixture yielded 9.0 g (0.022 mol, 85% yield) of crystalline brosylate: mp 79–81°; nmr (100 MHz, CCl_4) τ 8.86 (t, 1 H, J = 6 Hz, cyclopropyl proton at C-4), 8.0–8.4 (m, 5 H, cyclopropyl, bridgehead, and methylene protons), 7.62 (broad singlet, 1 H, bridgehead proton), 7.38 (broad singlet, 1 H, bridgehead proton), 6.16 (m, 4 H, $-OCH_2CH_2O-$), 5.09 (doublet of triplets, 1 H, J = 9.6 Hz, 3.8 Hz, –CHOBs).

Anal. Calcd for $C_{17}H_{17}O_5SBr$: C, 49.40; H, 4.14. Found: C, 49.26; H, 4.15.

Preparation of *endo*-8-Hydroxydeltacyclan-5-one (17a). To 3.3 g (0.017 mol) of *endo*-ketal alcohol **16a** was added 21 ml of methanol and 3.9 g of 5% sulfuric acid. The mixture was rapidly stirred for 5 hr at room temperature and then worked up as in the analogous preparation of keto alcohol **13a** above. *endo*-Keto alcohol, 1.1 g (0.007 mol, 36% yield), was obtained: ir (neat) 3401 (OH stretching), 3055 (cyclopropyl C–H stretching), 1742 (C=O), 1074, 1042, 840, 794 cm^{-1}; nmr (100 MHz, CCl_4) τ 8.74 (m, 2 H, cyclopropyl protons), 7.75–8.74 (m, 4 H), 7.33 (m, 2 H, bridgehead protons), 6.68 (s, 1 H, –CHOH), 5.58 (doublet of triplets, 1 H, J = 9.5 Hz, 3.5 Hz, –CHOH).

Preparation of *endo*-8-Brosyloxydeltacyclan-5-one (17b). To a stirred solution of 2.12 g (0.014 mol) of *endo*-keto alcohol **17a** in 40 ml of pyridine cooled to 0° in an ice bath was added 4.0 g (0.016 mol) of *p*-bromobenzenesulfonyl chloride over a period of 30 min, maintaining the temperature at 0–7°. The solution was stirred an additional 15 min at 0°, and finally 15 min at room temperature. The pyridine mixture was allowed to stand in a refrigerator for 10 days and then worked up as in preparation of brosylate **14** above, giving 3.9 g (0.0095 mol, 67% yield) of *endo*-keto brosylate **17b**. Recrystallization of a portion of the brosylate from 90:10 pentane–ether solution gave white crystalline brosylate: mp 94–95°; nmr (100 MHz, $CHCl_3$) τ 8.6–8.9 (m, 3 H, cyclopropyl protons), 8.1–8.4 (m, 2 H), 7.8–8.1 (m, 1 H), 7.38 (broad singlet, 1 H, bridgehead proton), 7.14 (broad singlet, 1 H, bridgehead proton), 5.08 (doublet of triplets, 1 H, J = 9.5 Hz, 3.4 Hz, –CHOBs).

Anal. Calcd for $C_{15}H_{13}O_4SBr$: C, 48.79; H, 3.55. Found: C, 49.08, H, 3.80.

Preparation of *exo*-8-Acetoxydeltacyclan-5-one Ethanedithiol Ketal (18). Boron trifluoride etherate (2 ml) was slowly added to a stirred solution of 25.0 g (0.13 mol) of keto acetate **8** in 20 ml of ethanedithiol which was cooled in an ice–salt bath. An immediate exothermic reaction occurred, at which time the solution turned milky white and very viscous. The reaction was allowed to stir an additional 5 min, and then 10 ml of ether was added. The organic layer was washed several times with 10% aqueous sodium hydroxide solution, followed by saturated salt solution, to remove excess ethanedithiol. Drying the ethereal layer over anhydrous magnesium sulfate, filtration, and rotary evaporation of the solvent gave 31.1 g (0.11 mol, 89% yield) of waxy solid thioketal acetate. Spectral data on a vpc collected sample are as follows: ir (neat) 3055 (cyclopropyl C–H stretching), 1727 (C=O), 1236, 1036, 1015 cm^{-1}; nmr (100 MHz, $CHCl_3$) τ 8.75 (m, 2 H, cyclopropyl protons), 8.38 (m, 2 H, cyclopropyl, methylene protons), 8.02 (s, 3 H, $-OCOCH_3$), 7.92 (broad singlet, 1 H, bridgehead proton), 7.82 (d, 1 H, J = 14 Hz, 7 Hz, endo-methylene proton), 7.62 (broad singlet, 2 H, bridgehead protons), 6.78 (s, 4 H, $-SCH_2CH_2S-$), 5.12 (doublet of doublets, 1 H, J = 7.0 Hz, 2.4 Hz, –CHOAc).

Anal. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.17; H, 6.02. Found: C, 58.16; H, 5.89.

Preparation of *exo*-8-Hydroxydeltacyclan-5-one Ethanedithiol Ketal (*exo*-19a). Thioketal acetate **18** (20.0 g, 0.075 mol) in 50 ml of ether was added to a rapidly stirred mixture of 2.6 g (0.068 mol) of lithium aluminum hydride in 100 ml of anhydrous ether at room temperature. The reaction was allowed to stir for 12 hr and then worked up as described above for alcohol **12**, giving 16.5 g (0.074 mol, 99% yield) of thioketal alcohol *exo*-**19a**: ir (neat) 3390 (OH

stretching), 3055 (cyclopropyl C–H stretching), 1073, 1040, 1005, 833 cm^{-1}; nmr (100 MHz, $CHCl_3$) τ 8.84 (m, 2 H, cyclopropyl protons), 8.52 (doublet of triplets, 1 H, J = 14 Hz, 2 Hz, methylene proton), 8.44 (m, 1 H), 7.90 (doublet of doublets, 1 H, J = 14 Hz, 7 Hz, methylene proton), 7.84 (broad singlet, 1 H, bridgehead proton), 7.68 (broad singlet, 2 H, bridgehead protons), 6.74 (s, 4 H, $-SCH_2CH_2S-$), 5.88 (doublet of doublets, 1 H, J = 7.0 Hz, 3.5 Hz, CHOH).

Anal. Calcd for $C_{11}H_{14}OS_2$: C, 58.37; H, 6.23. Found: C, 58.74; H, 6.07.

Preparation of *exo*-8-Brosyloxydeltacyclan-5-one Ethanedithiol Ketal (*exo*-19b). *p*-Bromobenzenesulfonyl chloride (15.0 g, 0.056 mol) was added in small portions over 1 hr to a stirred solution of 11.0 g (0.049 mol) of *exo*-thioketal alcohol *exo*-**19a** in 200 ml of dry pyridine. A temperature of 0–7° was maintained during the addition. The mixture was stirred for 1 hr at room temperature, allowed to stand in a refrigerator for 8 days, and worked up as described for brosylate **14**. Upon recrystallization from a 70:30 pentane–ether mixture, 18.0 g (0.040 mol, 82% yield) of crystalline brosylate was obtained: mp 119–121°; nmr (100 MHz, $CHCl_3$) τ 8.82 (t, 2 H, J = 6 Hz, cyclopropyl protons at C-2, C-3), 8.38 (t, 1 H, cyclopropyl proton), 8.28 (doublet of triplets, 1 H, J = 14 Hz, 2 Hz, methylene proton), 7.89 (doublet of doublets, 1 H, J = 14 Hz, 7 Hz, methylene proton), 7.84 (broad singlet, 1 H, bridgehead proton), 7.64 (broad singlet, 1 H, bridgehead proton), 7.48 (broad singlet, 1 H, bridgehead proton), 6.76 (broad singlet, 4 H, $-SCH_2-CH_2S-$), 5.20 (doublet of doublets, 1 H, J = 6.8 Hz, 2.3 Hz, –CHOBs).

Anal. Calcd for $C_{17}H_{17}O_3S_3Br$: C, 45.83; H, 3.84. Found: C, 45.97; H, 3.95.

Preparation of *endo*-8-Acetoxydeltacyclan-5-one Ethanedithiol Ketal. To 19.0 g (0.043 mol) of *exo*-thioketal brosylate *exo*-**19b** was added 21.0 g (0.074 mol) of tetra-*n*-butylammonium acetate in 50 ml of dry benzene. The flask was tightly sealed, and the contents were heated to 60° for 16 hr and worked up as described for endo acetate **15**, giving 10.5 g (0.039 mol, 89% yield) of *endo*-thioketal acetate as a waxy solid: mp 65–66° (vpc collected); ir (neat) 3055 (cyclopropyl C–H stretching), 1724 (C=O), 1361, 1245, 1125, 1031 cm^{-1}; nmr (60 MHz, CCl_4) τ 8.3–8.8 (m, 4 H), 8.17 (d, 1 H, J = 14 Hz, methylene proton), 8.05 (s, 3 H, $-OCOCH_3$), 7.85 (m, 1 H, bridgehead proton), 7.68 (broad singlet, 1 H, bridgehead proton), 7.44 (broad singlet, 1 H, bridgehead proton), 6.80 (s, 4 H, $-SCH_2-CH_2S-$), 4.93 (doublet of triplets, 1 H, J = 9.8 Hz, 3.4 Hz, –CHOAc).

Anal. Calcd for $C_{13}H_{16}O_2S_2$: C, 58.17; H, 6.02. Found: C, 58.13; H, 5.78.

Preparation of *endo*-8-Hydroxydeltacyclan-5-one Ethanedithiol Ketal (*endo*-19a). *endo*-Thioketal acetate (13.0 g, 0.048 mol) in 50 ml of ether was added to a rapidly stirred solution of 2.5 g (0.066 mol) of lithium aluminum hydride in 150 ml of ether. The mixture was stirred at room temperature for 12 hr and worked up as described for alcohol **12**, giving 9.5 g (0.042 mol, 88% yield) of waxy solid *endo*-thioketal alcohol: mp 90–93°; nmr (100 MHz, $CHCl_3$) τ 8.8–8.35 (m, 4 H), 7.8–8.2 (m, 2 H), 7.72 (broad singlet, 1 H, bridgehead proton), 7.52 (m, 1 H, bridgehead proton), 7.04 (s, 1 H, –CHOH), 6.76 (s, 4 H, $-SCH_2CH_2S-$), 5.60 (doublet of triplets, 1 H, J = 9.5 Hz, 3.5 Hz, –CHOH).

Anal. Calcd for $C_{11}H_{14}OS_2$: C, 58.37; H, 6.23. Found: C, 58.11; H, 6.12.

Preparation of *endo*-8-Brosyloxydeltacyclan-5-one Ethanedithiol Ketal (*endo*-19b). To a stirred solution of 8.0 g (0.034 mol) of *endo*-thioketal alcohol *endo*-**19a** in 120 ml of pyridine was added 11.0 g (0.043 mol) of *p*-bromobenzenesulfonyl chloride over 1 hour while the temperature was maintained at 0–7°. The solution was stirred an additional 0.5 hr at room temperature and then allowed to stand in a refrigerator for 10 days. The reaction was worked up as described for brosylate **14**. Recrystallization of the brosylate from a 70:30 pentane–ether mixture gave 14.0 g (0.031 mol, 91% yield) of product: mp 127.5–129°; nmr (100 MHz, $CHCl_3$) τ 8.58 (m, 2 H), 8.42 (m, 2 H), 7.8–8.4 (m, 2 H), 7.66 (broad singlet, 1 H, bridgehead proton), 7.52 (m, 1 H, bridgehead proton), 6.80 (d, 4 H, $-SCH_2CH_2S-$), 5.03 (doublet of triplets, 1 H, J = 9.4 Hz, 3.6 Hz, –CHOBs).

Anal. Calcd for $C_{17}H_{17}S_3O_3Br$: C, 45.83; H, 3.84. Found: C, 45.84; H, 3.92.

Kinetic Measurements. The acetolysis conditions and analytical methods were similar to those employed in our initial study.[1b]

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Polyfunctional Catalysis. IV. Oxy Acid Catalysis of the Mutarotation of Tetramethyl-D-glucose in Benzene

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Abstract: An experimental study of the mutarotation of 2,3,4,6-tetramethyl-D-glucose (TMG) in benzene has been performed. The rate law for all of the catalysts studied is rate = $(k_1 + k_1')$[catalyst]{[TMG] − $[TMG]_e$}, where $[TMG]_e$ is the concentration of α-tetramethylglucose at equilibrium. The activation parameters, relative to the catalyst–substrate complex, are: (1) diphenyl phosphate, $\Delta H^{\pm}$ = 14.1 kcal/mol and $\Delta S^{\pm}$ = −10.8 gibbs/mol at a standard state of 1 mol/l. at 25°; (2) benzenephosphinic acid, $\Delta H^{\pm}$ = 14.9 kcal/mol and $\Delta S^{\pm}$ = −8.8 gibbs/mol; (3) trichloroacetic acid, $\Delta H^{\pm}$ = 14.1 kcal/mol and $\Delta S^{\pm}$ = −15.4 gibbs/mol; (4) benzoic acid, $\Delta H^{\pm}$ = 13.2 kcal/mol and $\Delta S^{\pm}$ = −21.4 gibbs/mol; (5) 2-pyridone, $\Delta H^{\pm}$ = 13.2 kcal/mol and $\Delta S^{\pm}$ = −22.7 gibbs/mol; (6) pyrazole, $\Delta H^{\pm}$ = 13.2 kcal/mol and $\Delta S^{\pm}$ = −30.2 gibbs/mol; (7) 2-aminopyridine, $\Delta H^{\pm}$ = 13.2 kcal/mol and $\Delta S^{\pm}$ = −24.6 gibbs/mol; and (8) picric acid, $\Delta H^{\pm}$ = 12.7 kcal/mol and $\Delta S^{\pm}$ = −28.4 gibbs/mol. Brønsted plots of catalytic activity *vs.* pK_{H_2O} suggest that strong oxy acids act as tautomeric catalysts for the mutarotation of tetramethylglucose in nonpolar solvents.

In a previous paper, we proposed that the catalysis of chemical reactions by tautomeric molecules was a general phenomenon.[2] We called this type of catalysis *tautomeric catalysis*, defined a tautomeric catalyst as "a molecule that repeatedly cycles between two or more

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