(2 H, s, benzylic), 7.4 (4 H, s, ring). Anal. Calcd for $C_8H_9SO_2Cl$: C, 46.95; H, 4.43. Found: C, 47.05; H, 4.26.

(*p*-Chlorophenyl)methanesulfonyl chloride: ν_{max} (KBr) 3000, 2950, and 1091 (benzyl), 1313 (SO_2, asym, str), 1151 (SO_2, sym, str), 1357, and 1168 (SO_2Cl); δ_H (60 MHz; $CDCl_3$), 4.9 (2 H, s, benzylic), 7.5 (4 H, s, ring). Anal. Calcd for $C_7H_6SO_2Cl_2$: C, 37.35; H, 2.69. Found: C, 37.47; H, 2.57.

(*p*-Nitrophenyl)methanesulfonyl chloride: ν_{max} (KBr) 3000, 2870, and 1110 (benzyl), 1319 (SO_2, asym, str), 1135 (SO_2, sym, str), 1349, and 1167 cm^{-1} (SO_2Cl); δ_H (60 MHz; $CDCl_3$) 5.1 (2 H, s, benzylic), 7.4-8.5 (4 H, m, ring). Anal. Calcd for $C_7H_6NSO_4Cl$: C, 35.68; H, 2.57. Found: C, 35.80; H, 2.45.

(*p*-Methylphenyl)methanesulfonyl fluoride: ν_{max} (KBr) 3050, 2920, and 1113 (benzyl), 1280 (SO_2, asym, str), 1150 (SO_2, sym, str), 1400, and 1210 cm^{-1} (SO_2F); δ_H (60 MHz; $CDCl_3$) 2.4 (3 H, s, 4-Me), 4.8 (2 H, s, benzylic), 7.4 (4 H, s, ring). Anal. Calcd for $C_8H_9SO_2F$: C, 51.05; H, 4.82. Found: C, 50.97; H, 4.97.

(*p*-Chlorophenyl)methanesulfonyl fluoride: ν_{max} (KBr) 3000, 2870, and 1110 (benzyl), 1305 (SO_2, asym, str), 1150 (SO_2, sym, str), 1400, and 1207 cm^{-1} (SO_2F); δ_H (60 MHz; $CDCl_3$) 5.2 (2 H, d, J = 5 Hz, benzylic), 7.4 (4 H, s, ring). Anal. Calcd for $C_7H_6SO_2FCl$: C, 40.30; H, 2.90. Found: C, 40.43; H, 2.98.

(*p*-Nitrophenyl)methanesulfonyl fluoride: ν_{max} (KBr) 3000, 2870, and 1100 (benzyl), 1305 (SO_2, asym, str), 1149 (SO_2, sym, str), 1398, and 1213 cm^{-1} (SO_2F); δ_H (60 MHz; $CDCl_3$) 5.0 (2 H, d, J = 4 Hz, benzylic), 7.9-8.0 (4 H, d, J = 8 Hz, ring), 8.5-8.7 (4 H, d, J = 8 Hz, ring). Anal. Calcd for $C_7H_6NSO_4F$: C, 38.36; H, 2.76. Found: C, 38.50; H, 2.88.

Rate Constants. Rates were measured conductometrically[28] at three temperatures for each substrate ranging from 35.0 to 65.0 (±0.1) °C. Pseudo-first-order rate constants k_1(obsd) were determined by the Guggenheim method with a large excess of anilines, and second-order rate constants k_2 were obtained from the slope of a plot of k_1(obsd) vs (aniline) according to eq 3, where k_1 is the rate constant for methanolysis, which was found to be negligibly small compared with k_2 (vide supra). More than four aniline concentrations were used in the plot of eq 3 in all cases. Duplicate kinetic runs showed that the rates are reproducible to within ±3%. The average error limits in the values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are ±0.5 kcal·mol^{-1} and ±0.7 cal·mol^{-1}·k^{-1}, respectively.

Product Analysis. Products were identified by IR and TLC. The TLC results on the products from 1:1 phenylmethanesulfonyl halide-aniline reaction mixtures in *n*-hexane-ethyl acetate showed a distinct (single) spot (R_f 0.42) indicating no byproducts were involved. IR spectra[32] were taken on a Nicolet MX-1 FT-IR with KBr tablets; as the reaction proceeded, the pure characteristic peak of aniline at 1600-1650 cm^{-1} disappeared and the therminal -NH (sh) peak of aniline change to the intermediate -NH- (br) band at 3200-3500 cm^{-1}. Furthermore, the S-N bands (sh) were found to grow at 1350 cm^{-1}, confirming that the reaction proceeds as eq 4.

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Registry No. 4-$MeOC_6H_4CH_2SO_2Cl$, 110661-59-1; 4-$MeC_6H_4CH_2SO_2Cl$, 51419-59-1; $PhCH_2SO_2Cl$, 1939-99-7; 4-$ClC_6H_4CH_2SO_2Cl$, 6966-45-6; 4-$MeC_6H_4CH_2SO_2F$, 110661-60-4; $PhCH_2SO_2F$, 329-98-6; 4-$ClC_6H_4CH_2SO_2F$, 1513-29-7; 4-$O_2NC_6H_4CH_2SO_2F$, 110661-61-5; 4-$MeOC_6H_4NH_2$, 104-94-9; 4-$MeC_6H_4NH_2$, 106-49-0; $PhNH_2$, 62-53-3; 4-$ClC_6H_4NH_2$, 106-47-8; 4-$O_2NC_6H_4CH_2SO_2Cl$, 4025-75-6; 4-$MeOC_6H_4CH_2OH$, 105-13-5; 4-$MeC_6H_4CH_2OH$, 589-18-4; 4-$ClC_6H_4CH_2OH$, 873-76-7; 4-$O_2NC_6H_4CH_2OH$, 619-73-8; H_2NCSNH_2, 62-56-6.

Micellar Control of Organic Reactions: Propellane Substrates as Stereochemical Probes for Micellar Binding

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Abstract: Propellanediones and their reduction products have been used to demonstrate that micellar binding can control reaction diastereoselectivity. Borohydride reduction of the propellane carbonyl in an aqueous solution of a cationic surfactant provides clear evidence for this new kind of micellar perturbation of organic reactions. In addition to the expected rate enhancement that cationic micelles provide for the borohydride reduction, they direct the approach of the borohydride to one face of the reduction substrate. The source of this effect and its scope are explored. A correlation of micellar capabilities with substrate shape is presented. An explanation of these results is suggested. It is based on a particular model for the geometry of substrate-micelle binding and on micelle-directed attack of the prebound reagent.

The study of micellar effects on reaction stereochemistry has been an active area of investigation.[2] There have appeared in the literature a number of reports describing some limited success in attempts to use aqueous micelles and other aggregates to achieve optical induction.[2a] There is also ample precedent for the use of subtle changes in reaction stereochemistry as a diagnostic for particular capabilities of aqueous micelles to perturb a delicate balance among competing reaction pathways. Stereochemical probes of diazotate decomposition have provided insight into micellar influence on the partitioning of the carbocation-nitrogen-nucleofuge complex formed in that reaction[2b] and on the ability of the micelle to alter the balance among molecular rearrangement pathways.[2c] Changes in the stereochemistry of sulfonate solvolyses have revealed the enhanced nucleophilicity of surfactant sulfate head groups and their ability to compete with the nucleophilicity of water.[2d]

Our research program in the use of aqueous micelles to achieve synthetically useful perturbations of organic reactions has yielded successful control of olefin mercuration[3] and enone reduction.[4] We now report that in addition to such micelle-induced chemo-

(1) Research Career Development Awardee: NIH (1983-1988).

(2) (a) Sugimoto, T.; Matsumura, Y.; Imanishi, T.; Tanimota, S.; Okana, M. *Tetrahedron Lett.* **1978**, 3431. Goldberg, S. I.; Baba, N.; Green, R. L.; Pandian, R.; Stowers, J.; Dunlap, R. B. *J. Am. Chem. Soc.* **1978**, *100*, 6768. Baba, N.; Matsumura, Y.; Sugimoto, T. *Tetrahedron Lett.* **1978**, 4281. (b) Moss, R. A.; Talkowski, C. J.; Reger, D. W.; Powell, C. E. *J. Am. Chem. Soc.* **1973**, *95*, 5215. (c) Kirmse, W.; Rauleder, G.; Ratajczak, H. J. *J. Am. Chem. Soc.* **1975**, *97*, 4141. (d) Sukenik, C. N.; Bergman, R. G. *J. Am. Chem. Soc.* **1976**, *98*, 6613.

(3) (a) Link, C. M.; Jansen, D. K.; Sukenik, C. N. *J. Am. Chem. Soc.* **1980**, *102*, 7798. (b) Sutter, J. K.; Sukenik, C. N. *J. Org. Chem.* **1984**, *49*, 1295. (c) Sutter, J. K.; Sukenik, C. N. *J. Org. Chem.* **1982**, *47*, 4174. (d) Sukenik, C. N.; Link, C. M. In *Solution Behavior of Surfactants*; Mittal, K. L., Fendler, E. J., Eds.; Plenum: New York, **1982**; Vol. 2, pp 1007-1015.

(4) (a) Nikles, J. A.; Sukenik, C. N. *Tetrahedron Lett.* **1982**, *23*, 4211. (b) Nikles, J. A.; Mackey, S. M.; Sukenik, C. N., submitted for publication.

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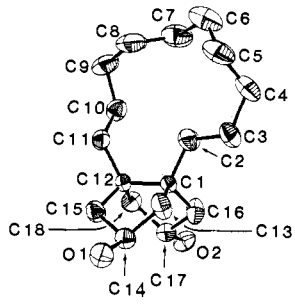
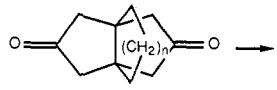


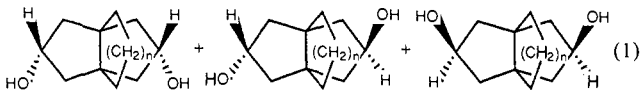
Figure 1. ORTEP of [10.3.3]propellane-*syn,syn*-14,17-diol.

selectivity and regioselectivity, cationic micelles can significantly alter the stereoselectivity of carbonyl reduction in substrates with particular structural features. This effect depends on substrate geometry and on specific interactions between the micelle and substrate. Our investigation of the basis of this effect has led us to new insight into both the geometry of micellar binding of organic substrates and the details of reagent binding to the micelle surface.

Aqueous micelles of cetyltrimethylammonium bromide (CTAB) were used as a medium for borohydride reduction of 4-*tert*-butylcyclohexanone (I), *trans*-1-decalone (II), and [10.3.3]propellane-14,17-dione (III, $n = 8$; eq 1). The two cyclohexanone-



III



anti,anti diol anti,syn diol syn,syn diol (1)

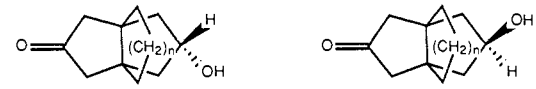
derived substrates can be treated as relatively flat molecules, while the propellane has well-differentiated faces with fused cyclopentanones in a Y-shaped framework. We compared reduction in aqueous CTAB (0.01 M, 10 × cmc) with that in water containing tetramethylammonium bromide (TMAB, 0.01 M), a nonaggregating analogue of CTAB. Reactions (room temperature, 24–72 h) containing 25:5:1 molar ratios of CTAB/TMAB to borohydride to substrate were homogeneous and went to completion.

Analysis of reaction products for the reductions of I and II was done by GC and for III by HPLC. I and II each yielded two isomeric alcohols, and III gave a mixture of three isomeric diols. Product identities for I and II were established as per literature reports.[5] The *anti-syn-* (*as-*) propellanediol with its two distinguishable CHOH groups was easily differentiated by NMR from the two symmetric diols. However, the assignment of which diol was syn,syn (ss) and which was anti,anti (aa) required the following crystallographic analysis.

Crystals of the *syn,syn*-propellanediol, as a monohydrate, were grown from wet ethyl acetate. X-ray analysis (Mo Kα radiation) by standard direct, Fourier, and difference Fourier methods and least-squares refinement on the 1157 unique reflections $3.0° \leq 2\theta \leq 47.5°$ and $I \geq 3\sigma(I)$ gave the agreement factors $R(F) = 0.054$ and $R_w(F) = 0.056$. Its structure (Figures 1 and 2) shows the five-membered rings puckered somewhat downward with the two hydroxyl groups facing outward. The angle between the two five-membered rings, as defined by the least-squares planes through atoms C(1), C(12), C(13), and C(15) (RMS dev = 0.056 Å) and C(1), C(12), C(16), and C(18) (RMS dev = 0.054 Å) is 116.4°. The mean angle between these planes and the planes defined by carbons C(13), C(14), C(15) and by carbons C(16), C(17), and C(18) is 143 (2)°. The quaternary carbons are in a nearly eclipsed conformation with the three torsion angles defined by C(2)–C(1)–C(12)–C(11), C(13)–C(1)–C(12)–C(15), and C(16)–C(1)–C(12)–C(18) at 15.4 (5), 10.8 (4), and 10.6 (4)°, respectively. The bond between the quaternary carbons C(1) and C(12) is lengthened to 1.597 (5) Å. All other bond lengths and all angles are as expected for 5-membered and 12-membered rings. The crystal lattice also contains a tetrahedrally disordered water molecular hydrogen bonded to the hydroxyls. The range of oxygen–oxygen contacts bridged by hydrogens is 2.728 (5)–2.864 (3) Å. These hydrogen bonds form an infinite sheet through the lattice lying in the *ab* plane at $z/c \simeq 0$ and 0.5.

Having unambiguously established the structures and stereochemistry of our reduction products, we turned to an analysis of product distributions. The ratio of isomeric alcohol products of both I and II is biased toward the thermodynamically favored (equatorial) alcohol. The reduction of I gives a 92:8 ratio of equatorial to axial alcohol, and the reduction of II shows a 90:10 preference. This ratio is the same for reduction in aqueous TMAB or aqueous CTAB. Borohydride reduction of I in CH_3OH gives 80% equatorial alcohol, and reduction of II yields 63% equatorial alcohol.[5] Thus, while aqueous borohydride provides a more selective reagent for cyclohexanone reduction, its stereoselectivity is not altered by a micellar environment.

The reduction of the propellanedione (eq 1) in aqueous TMAB gave a 22:48:30 mixture of aa/as/ss diols (overall 46:54 ratio of anti to syn hydroxyls). In micellar medium this ratio changed to 47:39:14 (67:33 overall anti to syn ratio). We thus began to explore not only the source of the micellar perturbation, but also whether the stereochemical partitioning is the same for the dione and for its stereoisomeric ketols,[6] and whether the change in stereochemistry would vary with the size of the polymethylene ring.



anti ketol syn ketol

To answer these questions, we obtained[7] III ($n = 2$, 20). We isolated and characterized[8] the ketol and diol isomers of these substrates and of III ($n = 8$) and examined the reaction of the diones and of each ketol. Assignment of both diol and ketol stereochemistry was made on the basis of the relative chemical shifts of the protons attached to the OH-bearing carbons [Table I, $\delta(H_A) < \delta(H_S)$].[9] This allowed us to extrapolate from the crystallography done for $n = 8$. These assignments were also confirmed by the successful synthesis of the cyclic oxalate of the $n = 20$ aa diol. The use of oxalate synthesis to prove diol stereochemistry had already been established by Ginsburg et al.[8] for the $n = 2$ system. Ketols were also correlated to diols by exclusive formation of the ss and as diols from the syn ketols and aa and as diols from the anti ketols.

(5) Monson, R. S.; Przybycien, D.; Barazr, A. *J. Org. Chem.* **1970**, *35*, 1700. Eliel, E. L.; Senda, Y. *Tetrahedron* **1970**, *26*, 2411.

(6) The overall product distribution would match the numbers obtained by multiplying the partition ratio for each step. Thus, assuming dione and ketols partition identically, the reduction of III ($n = 8$) in aqueous TMAB fits a 47% preference for anti ol formation in each reduction (calcd = 22:50:28; obsd = 22:48:30). For the CTAB reaction, the best fit assumes a 68% anti preference for each step (calcd 46:44:10; obsd = 47:39:14).

(7) Initial samples of III ($n = 2$) and its diols were obtained from Profs. D. Ginsburg and J. Cook. A close analogue of our $n = 20$ substrate is III ($n = 18$): Ashkenazi, P.; Kettenring, J.; Migdal, S.; Gutman, A. L.; Ginsburg, D. *Helv. Chim. Acta* **1985**, *68*, 2033. We note, but cannot reconcile, the conflict between our results and the reduction of III ($n = 18$) reported by: Ashkenazi, P.; Weinberg, O.; Zlota, A.; Ginsburg, D. *Recl. Trav. Chim. Pays.-Bas* **1986**, *105*, 254.

(8) III ($n = 2$) and its diols are reported in: Bhanumati, S.; Ashkenazi, P.; Migdal, S.; Ginsburg, D. *Helv. Chim. Acta* **1984**, *66*, 2703. Kapon, M.; Ashkenazi, P.; Ginsburg, D. *Tetrahedron* **1986**, *42*, 2555. The $n = 2$ ketols are reported in: Senegor, L.; Ashkenazi, P.; Ginsburg, D. *Tetrahedron* **1984**, *40*, 5271. III ($n = 8$) is reported in: Cook, J. M.; Yang, S. *J. Org. Chem.* **1976**, *41*, 1903. We made the assignments for the remaining ketols and diols.

(9) Tentative assignments for the $n = 2$ ketols and diols were made by: Askani, R.; Kirsten, R.; Dugall, B. *Tetrahedron* **1981**, *37*, 4437. Our values for the H's on the OH-bearing C's are based directly on our crystallography and that in ref 8. Our assignments of syn or anti (H_2/H_3, H_4/H_5) to the β hydrogens use our *J* values, the crystallographically determined geometries of the $n = 8$ *ss*-diol and all three $n = 2$ diols (graciously provided by M. Kapon, P. Ashkenazi, and D. Ginsburg), and a simple Karplus relationship.

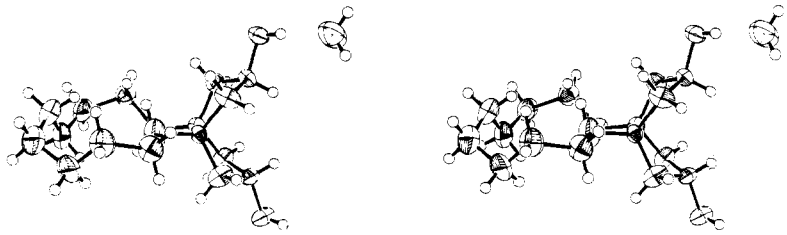
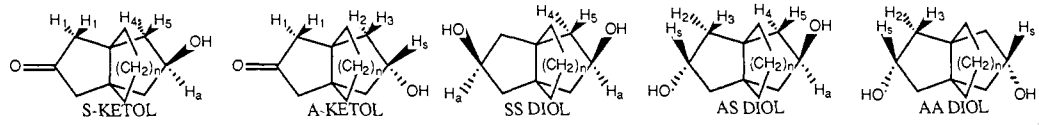


Figure 2. Stereoview of [10.3.3]propellane-*syn*,*syn*-14,17-diol hydrate.

Table I. ^{1}H NMR Data for Propellane Ketols and Diols (200 MHz, $CDCl_3$)[a]



n	compound	H_a	H_s	H_1 (J_{gem})	H_2 (J_{S2})	H_3 (J_{S3}) (J_{23})	H_4 (J_{A4})	H_5 (J_{A5}) (J_{45})	$(CH_2)_n$
2	*s*-ketol	4.56		2.07, 2.24 (18.7)			2.08 (7.9)	1.86 (3.9) (14.7)	1.43
2	*a*-ketol		4.60	2.25, 2.44 (19.0)	1.65 (4.1)	2.28 (8.1) (14.4)			1.39
8	*s*-ketol	4.41		2.10, 2.33 (19.3)			2.07 (7.7)	1.77 (5.3) (14.3)	1.42
8	*a*-ketol		4.51	2.32, 2.48 (18.8)	1.69 (4.1)	2.20 (7.8) (14.0)			1.39
20	*s*-ketol	4.39		2.11, 2.25 (18.5)			2.03 (7.4)	1.74 (5.6) (14.0)	1.31
20	*a*-ketol		4.45	2.25, 2.47 (19.0)	1.68 (3.8)	2.14 (7.5) (14.6)			1.25
2	*ss*-diol	4.38					1.90 (7.7)	1.64 (5.1) (14.0)	1.52
2	*as*-diol	4.41	4.55		1.67 (5.1)	2.16 (7.7) (14.0)	2.04 (8.0)	1.51 (5.8) (13.7)	1.49
2	*aa*-diol		4.46		1.84 (4.4)	2.11 (7.9) (14.2)			1.31
8	*ss*-diol	4.21					1.82 (6.9)	1.51 (9.2) (13.9)	1.37
8	*as*-diol	4.22	4.49		1.45	2.03	1.96	1.45	1.35
8	*aa*-diol		4.30		1.98 (4.3)	1.98 (8.5)			1.38
20	*ss*-diol	4.18					1.87 (6.6)	1.43 (9.3) (12.8)	1.26
20	*as*-diol	4.14	4.48		1.39	2.04	1.97	1.44	1.26
20	*aa*-diol		4.27		1.90 (6.1)	2.02 (14.5)			1.25

[a] δ units; *J*, Hertz.

Table II. Percentage Anti Alcohol Product Ratio from Propellane Substrates[a]

propellane, *n*	reactant	dione → *a*-ketol[b]	*a*-ketol → *aa*-diol,[c] obsd (calcd)	*s*-ketol → *as*-diol,[c] obsd (calcd)	dione → products[c] aa	as	ss
2	methanol	39	50 (51)	52 (48)	20	48	32
2	TMAB	44	51 (48)	50 (48)	21	50	29
2	CTAB	57	76 (80)	71 (72)	46	42	12
8	methanol	35	64 (63)	57 (54)	22	48	30
8	TMAB	36	60 (61)	56 (56)	22	48	30
8	CTAB	54	84 (87)	69 (70)	47	39	14
20	methanol	42	70 (67)	60 (60)	28	48	24
20	CTAB	62	86 (89)	67 (66)	55	32	13

[a] [TMAB] and [CTAB] = 10 mM; [substrate] (dione or ketol) = 0.4 mM. [b] [BH_4] = 0.1 mM, reaction time 1.5–3 h; remaining product is *syn*-ketol. [c] [BH_4] = 2 mM, reaction time 24–72 h; *syn*-ketols yield syn,syn and syn,anti diols; anti ketols yield syn,anti and anti,anti diols (no dione/ketol seen).

Since the $n = 20$ substrates were not soluble in aqueous TMAB, their CTAB reductions were referenced to reductions in methanol. All other reductions were done in aqueous TMAB, in methanol, and in CTAB (Table II). Isomer ratios of ketol products were assessed at <20% dione conversion. The results of the dione to ketol and ketol to diol reductions were compared with dione to diol reactions. The agreement between the independent measures of stereochemical partitioning is shown in the observed and calculated[6] values in Table II. It also guarantees that substrate binding and any realignment of ketol intermediates are faster than reduction. Finally, to be sure that all of our substrates were bound to CTAB micelles when reactions were done under micellar conditions, we used the method of Armstrong et al.[10] to measure the partition coefficients of our ketones, diones, and ketols between CTAB micelles and water (Table III). The partitioning could not be directly measured for the $n = 20$ dione and its ketols. However, since they do not dissolve to any measurable extent in water and they do dissolve in CTAB solution, they must be micelle bound to an even greater extent than the $n = 8$ system.

(10) (a) Armstrong, D. W.; Nome, F. *Anal. Chem.* **1981**, *53*, 1662. (b) Berthod, A.; Girard, I.; Gonnet, C. *Anal. Chem.* **1986**, *58*, 1356.

Table III. Micelle/Water Partition Coefficients of Reduction Substrates

ketone, dione, ketol	$10^{-5}K_{MW}$
tert-butylcyclohexanone	4.70
trans-1-decalone	6.30
[4.3.3]propellanedione	4.88
[4.3.3]propellane-*anti*-ketol	11.13
[4.3.3]propellane-*syn*-ketol	9.12
[10.3.3]propellanedione	11.13
[10.3.3]propellane-*anti*-ketol	23.90
[10.3.3]propellane-*syn*-ketol	23.90

For the six substrates ($n = 2$ and 8 diones, *anti*-ketols, and *syn*-ketols) where reductions in methanol and in TMAB could be compared, similar product distributions were obtained. Reductions in CTAB micelles were different. Thus, reduction in either methanol or TMAB is a satisfactory reference reaction for the aggregation-dependent alteration of propellane reduction stereochemistry seen in CTAB.

Secondly, in all instances, the effect of the micelles is to increase the relative amount of *anti*-ol formation, i.e., increase the extent to which hydride attack occurs from the side of the polymethylene

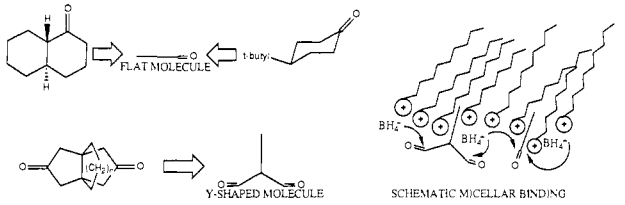


Figure 3. Schematic representation of micelle-bound substrates and ionic reagents.

bridge. Nonmicellar dione reduction always yields 39 ± 4% anti-ol vs 58 ± 4% for the micelle. *Anti*-ketol reduction shows parallel enhancements of *anti,anti*-diol production with increased polymethylene ring size in all media. The nonmicellar *anti*-ol production increases from 50 (n = 2) to 62 (n = 8) to 70% (n = 20), while there is a smaller variation with ring size for the micellar reaction (76 to 84 to 86%). Similarly, for *syn*-ketols, the extent of micellar enhancement of *anti*-ol production decreases from 21 to 13 to 7% as the polymethylene chain goes from 4 (n = 2) to 10 (n = 8) to 22 (n = 20). The stereochemistry of the nonmicellar reduction is more sensitive to changes in ring size than that of the micellar reduction.

The lack of a micellar effect on cyclohexanone and decalone reduction is reconciled with the micellar perturbation seen in the propellanes by the radial binding model shown in Figure 3. All of our substrates have large micellar binding constants (Table III). Both relatively flat molecules (I, II) and Y-shaped propellane molecules are radially bound to the micelle. This aligns the plane of a prochiral functional group in either a radial (for flat molecules) or tangential (for Y-shaped molecules) fashion. This mode of binding is useful in the selective monofunctionalization of flat systems[3] but allows equal access to both faces of the molecule; no change in reaction stereochemistry is seen. For molecules like III and its ketols, micellar complexation orients the faces of the reactive functionality where attack by the high local concentration of borohydride bound to the micelle surface[11] enhances *anti*-ol formation. This effect is seen for even small polymethylene rings. This explanation suggests, for the first time, that micellar enhancement of reaction rates by increased local reagent concentration carries with it a precomplexation of the reagent within the micelle Stern layer. Thus, an ionic reagent approaches the micelle-bound substrate from *within the micelle*.

We are exploring the scope of such directing effects and trying to reconcile them with spectroscopic evidence[12] for nonradial micellar binding. Alternative explanations of our micelle-induced diastereoselectivity are being tested both by experiment and computation. We are also comparing the extent of reaction control that can be achieved in the micelle with that which can be seen in other solution aggregates and in monolayer films.

Experimental Section

I. General Procedures. NMR spectra are reported in δ and were recorded on a Varian XL-200 spectrometer in $CDCl_3$ solvent. ^1H NMR spectra (200 MHz) are referenced to $CHCl_3$ at δ 7.24, and ^{13}C NMR spectra (50-MHz) are referenced to the center of the solvent triplet at δ 77.00. IR spectra were recorded on a Mattson Cygnus 25 FT-IR equipped with a water-cooled source and a TGS detector, operating at a resolution of 4 cm^{-1}. HPLC was performed on a Waters 590 pump equipped with a Rheodyne 7125 injector and a Waters 401 differential refractometer. GC analyses used a Perkin-Elmer 3920B gas chromatograph equipped with FID. TLC was done on aluminum-backed 0.2-mm 60F254 plates from EM Science and used phosphomolybdic acid as the visualization agent. Column chromatography (flash) was done with silica gel from Aldrich (230–400 mesh). Melting points were obtained on a Mel-Temp apparatus and are uncorrected. Elemental analyses were performed by Galbraith. Mass spectra (70 eV) were recorded at the Midwest Center for Mass Spectrometry, Lincoln, NE.

THF (Fisher) was distilled from purple solutions of Na benzophenone ketyl under N_2. EtOH (Aaper) was distilled under N_2 from Na metal. DMSO (Fisher) was fractionally distilled under vacuum. Benzene and toluene (Fisher) were fractionally distilled under N_2. Chlorotrimethylsilane (Aldrich) was treated with a small quantity of water and distilled from CaH_2 under N_2. 2-Propanol (Fisher) was dried over active 4-Å molecular sieves. Oxalic acid dihydrate (Aldrich) was pulverized and dried in a vacuum oven at 100 °C for 12 h. Water was doubly distilled, and all other solvents ($CHCl_3$, hexane, EtOAc, and CH_3OH) were Fisher HPLC grade (used as received). Cetyltrimethylammonium bromide from Sigma was crystallized twice from ethanol and dried in a vacuum oven. Diethyl malonate, 1,10-dibromodecane, 1,5-dibromopentane, $KClO_4$, dimethyl ketoglutarate, CaH_2, phosphomolybdic acid, cyclododecene, cyclohexane-1,2-dione, $NaBH_4$, and $(CH_3)_4NBr$ were used as received from Aldrich. $CuCl_2$ and LiCl (Fisher) were dried in a vacuum oven for 24 h. NH_4Cl, Mg, Na, NaCl, anhydrous $MgSO_4$, $NaHCO_3$, and acetic anhydride were used as received from Fisher.

II. Reduction Substrates. Synthesis and Characterization. A. *trans*-1-Decalone and *tert*-Butylcyclohexanone. These were used as received (Aldrich).

B. Propellanediones. Initial samples of [4.3.3]propellane-8,11-dione and [10.3.3]propellane-14,17-dione were gifts from Prof. David Ginsburg and Prof. James Cook. Synthesis of [4.3.3]propellane-8,11-dione was accomplished in two steps from cyclohexane-1,2-dione:[8] mp 198–200 °C (lit.[8] mp 173–174 °C); ^1H NMR 1.54 (s, 8 H), 2.24 and 2.44 (AB q, 8 H, J = 19 Hz); ^{13}C NMR 216.64 (2 C), 48.78 (4 C), 44.37 (2 C), 31.35 (2 C), 20.79 (2 C); IR ($CDCl_3$) 2948, 1738 cm^{-1}.

Synthesis of [10.3.3]propellane-14,17-dione was accomplished in three steps from cyclododecene:[8] mp 50–51.5 °C (lit.[8] mp 53–55 °C); ^1H NMR 1.39 (s, 20 H) 2.25 and 2.45 (AB q, 8 H, J = 19.5 Hz) [lit.[8] (60 or 100 MHz, $CDCl_3$) 1.40 (s, 20 H), 2.36 (s, 4 H), 2.45 (s, 4 H)]; ^{13}C NMR 217.35 (2 C), 50.43 (4 C), 49.92 (2 C), 34.29 (2 C), 27.34 (2 C), 26.07 (2 C), 23.61 (2 C), 23.23 (2 C); IR ($CDCl_3$) 2929, 1738 cm^{-1} [lit.[8] IR ($CHCl_3$) 2915, 2850, 1741 cm^{-1}].

Synthesis of [22.3.3]propellane-26,29-dione was achieved as follows.

1,20-Dibromoeicosane. A flame-dried, 1-L, three-neck flask equipped with a magnetic stirring bar, reflux condenser with a N_2 inlet, and a 500-mL pressure-equalized addition funnel was charged with 32 g (1.33 mol) of Mg turnings. A solution of 1,10-dibromodecane (80 g, 0.27 mol) in 400 mL of dry THF was dripped into the flask over a period of 1 h. (*Caution*: The addition must be performed slowly with occasional cooling in an ice bath to control the reaction.) Following completion of the addition, the stirring was stopped, and the solution of the di-Grignard reagent was cooled to 0 °C.

A 2-L, two-neck, flame-dried flask with a magnetic stirring bar and a N_2 inlet was charged with 122 g (0.53 mol) of 1,5-dibromopentane in 200 mL of dry THF and 32 mL of a 0.1 M solution of Li_2CuCl_4 in THF.[13] This was cooled thoroughly to 0 °C in an ice-salt bath, and the previously prepared di-Grignard reagent was added via syringe over 10–15 min. Following completion of the addition, the black reaction mixture was stirred for 3 h at 0 °C under N_2 and then quenched with 300 mL of saturated NH_4Cl solution. The whole mixture was transferred to a 2-L separatory funnel, and the THF layer was separated. The aqueous layer was extracted with 300 mL of $CHCl_3$. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product mixture was subjected to Kugelrohr distillation to remove unreacted 1,5-dibromopentane. The residue was filtered through silica gel (hexane eluent). Vacuum removal of the hexane afforded 60 g of material, which was subjected to a second Kugelrohr distillation. An initial fraction [bp 130–140 °C (0.07 mm)] was mainly monobromides, while the second fraction [bp 170–180 °C (0.05 mm)] was the desired dibromide: yield 18 g, (15%); mp 62–64 °C; ^1H NMR 1.24 (s, 32 H), 1.83 (m, 4 H), 3.39 (t, 4 H, J = 6.9 Hz); ^{13}C NMR 33.99 (2 C), 33.82 (2 C), 29.66 (6 C), 29.60 (2 C), 29.53 (2 C), 29.43 (2 C), 28.75 (2 C), 28.17 (2 C).

2,23-Dicarbethoxytetracosanedioic Acid Diethyl Ester. A 1-L, three-neck, flame-dried flask equipped with a magnetic stirring bar, a reflux condenser with a N_2 inlet, and a 500-mL pressure-equalized addition funnel was charged with Na (3.8 g, 170 mmol) and 400 mL of dry ethanol. After all the sodium had been consumed, the solution was heated to reflux, and diethyl malonate (25 mL, 170 mmol) was added via a syringe. The reaction was stirred at reflux for 45 min. To the refluxing solution was added 18.2 g (41.4 mmol) of 1,20-dibromoeicosane in 200 mL of dry THF over a period of 20 min. The reaction was refluxed for 3–5 h, cooled to room temperature, and then quenched with 100 mL of saturated NH_4Cl solution. The mixture was concentrated under vacuum, and the aqueous solution left behind was extracted with EtOAc (3 × 150 mL). The combined EtOAc extracts were washed with H_2O, dried over $MgSO_4$, and filtered, and the solvent was removed under reduced pressure. The crude product mixture was subjected to Kugelrohr

(11) Bunton, C. A.; Carrasco, N.; Huang, S. K.; Paik, C. H.; Romsted, L. S. *J. Am. Chem. Soc.* **1978**, *100*, 5420.
(12) Menger, F. M.; Carnahan, D. W. *J. Am. Chem. Soc.* **1986**, *108*, 1297.
(13) Tamura, M.; Kochi, J. *Synthesis* **1971**, 303.

distillation to remove unreacted diethyl malonate. The residue (24.7 g) was purified by flash chromatography (15:85, EtOAc/hexane) to yield 17.25 g (70%) of the desired tetraester as a waxy solid: ^{1}H NMR 1.22 (m, 52 H), 1.85 (m, 4 H), 3.28 (t, 2 H, J = 7.6 H), 4.16 (q, 8 H, J = 7.1 Hz); ^{13}C NMR 169.52 (4 C), 61.19 (4 C), 52.07 (2 C), 29.75 (10 C), 29.58 (2 C), 29.38 (2 C), 28.78 (2 C), 27.36 (2 C), 14.12 (4 C); IR ($CDCl_3$) 2920, 1742, 1727, 1271, 1153, 1095 cm^{-1}.

1,24-Tetracosanedioic Acid Diethyl Ester. A 250-mL single-neck flask equipped with a magnetic stirring bar and a reflux condenser was charged with 100 mL of DMSO, 17.25 g (29 mmol) of the tetraester, 6.78 g (116 mmol) of NaCl, and 2.7 mL (145 mmol) of H_2O. The mixture was heated (140 °C, 24 h). It was cooled and partitioned between $CHCl_3$ and H_2O. The $CHCl_3$ layer was separated, and the aqueous layer was extracted with $CHCl_3$ (2 × 100 mL). The combined organic extracts were washed exhaustively with H_2O, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude diester (12.25 g) was purified by flash chromatography (5:95, EtOAc/hexane) to yield 7.0 g (60%) of the desired diester as a white solid: mp 59–61 °C; ^{1}H NMR 1.22 (m, 38 H), 1.58 (m, 4 H), 2.25 (t, 4 H, J = 7.5 Hz), 4.01 (q, 4 H, J = 7.1 Hz); ^{13}C NMR 173.86, 60.10, 34.39, 29.68, 29.59, 29.45, 29.25, 29.14, 24.98, 14.24; IR ($CDCl_3$) 2931, 1741, 1187, 1034 cm^{-1}.

2-Oxocyclotetracosanol. In a 1-L, three-neck, flame-dried flask equipped with a mechanical stirrer, a reflux condenser with a N_2 inlet, and a pressure-equalized addition funnel was placed 350 mL of dry toluene. The addition funnel was charged with a solution of 6.5 g (14.3 mmol) of the diester and 45 mL of TMSCl (358 mmol) in 150 mL of dry toluene. Sodium (1.316 g, 57.2 mmol) was introduced into the flask, and the toluene was brought to a reflux. The molten sodium was dispersed by stirring at high speed for a few minutes. The stirring rate was then reduced, and the solution in the addition funnel was added over a period of 12 h. After the addition was complete, the reaction was refluxed for an additional 1 h, cooled to 0 °C, and filtered quickly under a stream of Ar. (*Caution*: The finely dispersed Na metal in the filter funnel is pyrophoric and should be quenched carefully with dry 2-propanol.) The filtrate was concentrated under vacuum, and to the residue was added 150 mL of THF and 15 mL of 1 N HCl. The solution was stirred at room temperature. After 1.5 h, solid $NaHCO_3$ (~2 g) was added, and the THF was removed under vacuum. The aqueous suspension left behind was diluted with H_2O (100 mL) and extracted with $CHCl_3$ (3 × 75 mL). The combined $CHCl_3$ extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude acyloin was purified by flash chromatography (15:85, EtOAc/hexane) and isolated as a white waxy solid: yield 4.4 g (85%); ^{1}H NMR 1.31 (s, 42 H), 2.61–2.27 (m, 2 H), 3.50 (d, 1 H, J = 4.6 Hz), 4.18 (m, 1 H); IR ($CDCl_3$) 3571–3295, 2924, 1709, 1239, 1044 cm^{-1}.

Cyclotetracosane-1,2-dione. In a 500-mL, two-neck flask with a magnetic stirring bar and a N_2 inlet were placed 4.2 g (11.5 mmol) of the acyloin, 200 mL of dry DMSO, and 100 mL of acetic anhydride. The solution was stirred at room temperature under N_2 for 16 h and then poured into a 1-L Erlenmeyer flask containing 400 mL of a 1:1 mixture of EtOAc and saturated $NaHCO_3$ solution. More solid $NaHCO_3$ was added until the evolution of CO_2 ceased. The whole mixture was then transferred into a 2-L separatory funnel, and the EtOAc layer was separated. It was washed three times with saturated $NaHCO_3$ solution and five times with H_2O, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude diketone was purified by flash chromatography (5:95, EtOAc/hexane) to yield 3.0 g (72%) of a yellow wax, which was used directly for the next reaction.

[22.3.3]Propellane-26,29-dione. To a solution of cyclotetracosane-1,2-dione (3 g, 8 mmol) in 17 mL of dry benzene in a 100-mL two-neck flask with a magnetic stirring bar and N_2 inlet were added 3.1 g (18 mmol) dimethyl ketoglutarate and a solution of 1 g (18 mmol) of KOH in 30 mL of dry CH_3OH. The reaction was stirred at room temperature under N_2 for 2 weeks. The solvent was removed under vacuum, and the residue was extracted with hexane (4 × 50 mL). To the residue was added 60 mL of 6 N HCl, and the suspension was heated at reflux for 7 h. The mixture was then cooled to room temperature and extracted with $CHCl_3$ (3 × 75 mL). The combined $CHCl_3$ extracts were washed with saturated $NaHCO_3$ solution and water, dried over $MgSO_4$, filtered, and concentrated under vacuum. The propellanedione was purified by flash chromatography (1:4, EtOAc/hexane) and obtained as a waxy solid: yield 2.8 g (78%); recrystallization from hexane/EtOAc/*i*-PrOH gave colorless crystals, mp 43–45 °C; ^{1}H NMR 1.24 (s, 40 H), 1.48 (m, 4 H), 2.24 and 2.42 (AB q, 8 *H*, J = 19 Hz); ^{13}C NMR 216.55, 49.31, 48.80, 34.28, 29.77, 29.00, 28.56, 28.46, 29.19, 25.12; IR ($CDCl_3$) 2929, 2856, 1737 cm^{-1}. Anal. Calcd: C, 81.02; H, 11.78. Found: C, 81.22; H, 11.46.

C. Propellane Ketols. Preparative separations of ketol isomers used a Whatman Partisil Magnum-9 (10 μm) 9.4 mm × 50 cm column. Separation conditions are listed in Table IV. The ketol mixtures were obtained by the partial reduction procedure illustrated for [22.3.3]-propellane-26,29-dione.

Table IV. HPLC Separations of Dione/Ketol Mixtures

propellane	solvent: hexane	solvent: EtOAc	solvent: *i*-PrOH	flow, mL/min	retention time, min: dione	*a*-ol	*s*-ol
[4.3.3]	57	38	5	8.3	5.8	8.0	10.0
[10.3.3]	75	20	5	6.6	5.9	10.4	12.0
[22.3.3]	85	10	5	8.3	4.5	8.0	9.2

Table V. Preparative HPLC Separations of Diol Isomers

substrate	solvent system: MeOH	solvent system: H_2O	flow, mL/min	retention time, min: ss	sa	aa
[4.3.3]propellane	50	50	5	5.6	8.5	15.7
[10.3.3]propellane	80	20	5	6.9	8.4	14.9
[22.3.3]propellane	95	5	7	10.8	13.5	22.5

To a solution of 200 mg (0.45 mmol) of [22.3.3]propellane-26,29-dione in 25 mL of methanol was added 4 mg (0.11 mmol) of sodium borohydride. The reaction was stirred at room temperature for 1.5 h and then quenched with acetic acid. The methanol was removed under vacuum, and the residue was partitioned between ethyl acetate and H_2O (1:1, 100 mL). The ethyl acetate layer was separated and washed with H_2O and brine. This solution was dried over $MgSO_4$, and solvent was removed under vacuum. The crude ketol mixture (~0.2 g) was subjected to HPLC to isolate the individual ketol isomers. Material recovered: dione 140 mg; *anti*-ketol 16 mg, 27% of reacted dione; *syn*-ketol 22 mg, 37% of reacted dione.

Characterization of the individual ketol isomers from each propellane substrate is based on the following data. ^{1}H NMR data are listed in Table I. 8-Keto[4.3.3]propellan-11-*anti*-ol: mp 122–123.5 °C; IR (CCl_4) 3590–3250, 2922, 1738, 1173, 1072, 1024, 1000 cm^{-1} (lit.[8] IR, 3620, 2950, 1745 cm^{-1}). 8-Keto[4.3.3]propellan-11-*syn*-ol: mp 137–139 °C; IR (CCl_4) 3553–3320, 2925, 1741, 1168, 1086, 1023, 1005 cm^{-1} (lit.[8] IR, 3620, 2950, 1745 cm^{-1}). 14-Keto[10.3.3]propellan-17-*anti*-ol: waxy solid; IR (CCl_4) 3590–3303, 2927, 1736, 1181 cm^{-1}. 14-Keto[10.3.3]-propellan-17-*syn*-ol: waxy solid; IR (CCl_4) 3590–3303, 2930, 1736, 1179 cm^{-1}. 26-Keto[22.3.3]propellan-29-*anti*-ol: waxy solid; IR (CCl_4) 3553–3250, 2938, 1741, 1178, 1053, 1025 cm^{-1}. 26-Keto[22.3.3]propellan-29-*syn*-ol: waxy solid; IR (CCl_4) 3571–3250, 2938, 1740, 1175, 1047 cm^{-1}.

III. Reduction Products: Isolation and Characterization. A. *cis* and *trans-tert*-butylcyclohexanols and the two isomers of *trans*-1-decalols are known compounds[5] and were identified by their chromatographic behavior.

B. Ketol isomers from each propellane substrate were isolated and charaterized as discussed above. Diol isomers from each propellane substrate were isolated by HPLC with an IBM ODS (5 μ) 10.0 mm × 25 cm column. Separation conditions are listed in Table V. The diol mixtures were obtained by reduction of each propellanedione with excess $NaBH_4$. The following procedure for [10.3.3]propellane-14,17-dione is typical.

To a solution of 160 mg (0.6 mmol) of [10.3.3]propellane-14,17-dione in 25 mL of CH_3OH was added 109 mg (3 mmol) of $NaBH_4$. The reaction was stirred (room temperature, 12 h) and then quenched with HOAc. The CH_3OH was removed under vacuum and the residue partitioned between EtOAc and water (100 mL, 1:1). The organic layer was separated, and the aqueous layer was extracted with EtOAc (2 × 25 mL). The combined organic extracts were washed with brine and dried over $MgSO_4$, and solvent was removed under vacuum. Diol isomers were purified by HPLC: syn,syn (24 mg, 17%), syn,anti (41 mg, 29%), anti,anti (19 mg, 14%).

Characterization of the individual diol isomers is based on the ^{1}H NMR data listed in Table I and on the following data. [4.3.3]Propellane-8,11-*anti,anti*-diol: mp 115–117 °C (lit.[8] mp 122–123 °C); IR ($CDCl_3$) 3500–3152, 2923, 1262, 1231, 1132, 1036 cm^{-1}. [4.3.3]Propellane-8,11-*syn,anti*-diol: mp 137.5–139 °C (lit.[8] mp 140 °C; IR ($CDCl_3$) 3500–3179, 2921, 1230, 1138, 1105, 1049, 1006 cm^{-1}. [4.3.3]-Propellane-8,11-*syn,syn*-diol: mp 163–165 °C, (lit.[8] mp 164 °C); IR ($CDCl_3$) 3446–3090, 2921, 1244, 1108, 1046, 1019 cm^{-1}. [10.3.3]-Propellane-14.17-*anti,anti*-diol: mp 98–99 °C; IR (Nujol) 3405–3071, 1103, 1075, 1062, 1042 cm^{-1}. [10.3.3]Propellane-14,17-*syn,anti*-diol: mp 137–138 °C; IR (Nujol) 3464–3071, 1234, 1143, 1068, 1051, 1005 cm^{-1}. [10.3.3]-Propellane-14,17-*syn,syn*-diol: mp 170–172 °C; IR (Nujol) 3384–3125, 1261, 1104, 1067, 1046, 1022 cm^{-1}. [22.3.3]Propellane-26,29-*anti,anti*-diol: mp 112–113 °C; IR (CCl_4) 3429–3071, 2929, 1240,

1138, 1047 cm^{-1}. [22.3.3]Propellane-26,29-*syn,anti*-diol: mp 127.5–128.5 °C; IR (CCl_4) 3500–3107, 2943, 1167, 1261, 1048 cm^{-1}. [22.3.3]Propellane-26,29-*syn,syn*-diol: mp 109–110 °C; IR (CCl_4) 3500–3080, 2943, 1261, 1167, 1048 cm^{-1}.

IV. Stereochemistry of Diols and Ketols. For the [4.3.3] series, crystal structures for each diol isomer have been published,[8] and our assignments were made by comparison with authentic samples provided by Prof. David Ginsburg.

For the [10.3.3] series, the crystal structure of the syn,syn isomer provided an unambiguous basis to assign all three diols. The procedures used to obtain this crystal structure are described below.

Crystals of [10.3.3]propellane-*syn,syn*-14,17-diol were obtained from wet ethyl acetate by slow evaporation at room temperature over a period of a few months. The crystals were of orthorhombic habit elongated along one axis (1 mm × 1 mm × 20 mm). A crystal suitable for X-ray diffraction was cleaved from one of these crystals and was mounted on a Syntex $P2_1$ diffractometer. The Laue symmetry ($2/m$) and the systematic absences (hkl, $h + k = 2n + 1$, $h0l$, $l = 2n + 1$) define the space group $C2/c$. The unit cell was determined by least-squares refinement of 15 reflections with 2θ values between 20.0 and 30.0° giving a = 39.440 (16) Å, b = 7.096 (2) Å, c = 13.327 (2) Å, β = 106.85 (2)°, V = 3569.7 (16) $Å^3$, and Z = 8. The data were collected at room temperature from $3.0° \leq 2\theta \leq 47.5°$. The intensities of three check reflections were monitored for decay with no apparent change during data collection. The density of the crystal determined by flotation in aqueous NaCl is 1.10 g cm^{-3}, while the calculated density is 1.11 g cm^{-3}.

The structure was solved by direct methods.[14] Least-squares refinement of the non-hydrogen atoms and subsequent difference Fourier syntheses gave the positions of the hydrogens on O(1), O(2), O(3), C(14), and C(17). All the methylene hydrogens were calculated at ideal positions (d = 0.950 Å) and thermal parameters (+1 $Å^2$ of the bonded carbon).[15] Anisotropic refinement of all non-hydrogen atoms with all the hydrogens "riding" in this model gave final agreement factors R = 0.054 and R_w = 0.056 for data $I \geq 3\sigma(I)$ and R = 0.12 and R_w = 0.072 for data $I \geq 0$.

For the [22.3.3] series, assignment based on the trend in NMR data (Table I) was augmented by the synthesis of the cyclic oxalate of the anti,anti isomer. The procedure for oxalate formation was based on that reported by Ginsburg for [4.3.3]propellane-8,11-*anti,anti*-diol.[8] A 50-mL single-neck flask equipped with a magnetic stirring bar, Dean–Stark trap, and a reflux condenser was charged with 20 mL of dry benzene, a crystal of *p*-toluenesulfonic acid, 10 mg (23 μmol) of diol, and 2 mg (23 μmol) of anhydrous oxalic acid. The solution was heated at reflux for 24 h and cooled to room temperature, the benzene was removed under vacuum, and the residue was partitioned between CH_3Cl and water (50 mL, 1:1). The $CHCl_3$ layer was separated, washed with H_2O, and dried over $MgSO_4$. Evaporation of the solvent yielded a waxy solid, which was chromatographed (15:85, EtOAc/hexane) to yield 4 mg (36%) of the oxalate: ^1H NMR (s, 44 H), 2.02 (d, 8 H, J = 5.86 Hz), 5.31 (t, 2 H, J = 5.86 Hz); IR ($CDCl_3$) 1760, 1734, 1262, 1200 cm^{-1}; MS (70 eV), m/z no M^+ detected, 458.4544 (6%, M – CO_2), 431.4212 (23%, M – C_2O_3), 413.4076 (9%), 412.4054 (33%, M – $C_2O_3 \cdot H_2O$), 385.3918 (12%).

V. Reduction of [*n*.3.3]Propellanediones to [*n*.3.3]Propellane Ketols. Reaction in Methanol. The following procedure for the reduction of [22.3.3]propellane-26,29-dione to the corresponding ketols is typical. To a solution of 9 mg (20 μmol) of [22.3.3]propellane-26,29-dione in 50 mL of MeOH was added a solution of 0.19 mg (5 μmol) of $NaBH_4$ in 0.5 mL of 1 M NaOH. The reaction was stirred at room temperature for 2–3 h and then quenched with acetic acid. The methanol was removed under vacuum, and the residue was partitioned between EtOAc and H_2O (50 mL, 1:1). The EtOAc layer was separated, washed with H_2O, dried over $MgSO_4$, filtered, and concentrated under vacuum. TLC (EtOAc) indicated no diol. The crude ketol mixture was analyzed by HPLC. The relative amounts of the two ketol isomers remained unchanged when base was omitted from the above procedure or when the reaction was done at a higher concentration.

Reaction in TMAB. The procedure for the reduction of [10.3.3]-propellane-14,17-dione is typical. A suspension of 5.5 mg (20 μmol) of [10.3.3]propellane-14,17-dione in a solution of 77 mg (0.5 mmol) of TMAB in 50 mL of H_2O was warmed (50 °C) and stirred (1 h) until a clear solution was obtained. The solution was cooled, $NaBH_4$ added, and the reaction quenched with HOAc (as in the MeOH reaction). This was extracted with EtOAc (25 mL). The EtOAc extract was washed with H_2O, dried over $MgSO_4$, and concentrated under vacuum. TLC (EtOAc) indicated no diol. The ketol mixture was analyzed by HPLC.

Reaction in CTAB. The procedure used for [10.3.3]propellane-14,17-dione is typical. It parallels the TMAB procedure but instead used a solution of 182 mg (0.5 mmol) of CTAB in 50 mL of H_2O. The reaction was stirred at room temperature for 1.5 h and then quenched with acetic acid. The solution was transferred to two 50-mL centrifuge tubes with 1 g of NaCl and 2 g of $KClO_4$ each. Ethyl acetate (5 mL) was added to each tube. These mixtures were shaken vigorously and then centrifuged for 5 min. The EtOAc layer in each tube was removed, and the extraction procedure was repeated twice. The combined EtOAc extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was filtered through a plug of silica gel (EtOAc eluent, 8–10 mL) to remove surfactant. TLC (EtOAc) indicated no diol. Evaporation of the EtOAc afforded the crude ketol mixture which was analyzed by HPLC.

VI. Reduction of Propellane Ketols to Propellanediols. Reaction in MeOH. The following procedure for 14-keto[10.3.3]propellan-17-*anti*-ol is typical. To a solution of 4 mg (14.5 μmol) of the ketol in 36 mL of MeOH was added a solution of 2.7 mg (72.5 μmol) of $NaBH_4$ in 0.36 mL of 1 M NaOH. The reaction was stirred at room temperature for 24–48 h and then quenched with acetic acid. The methanol was removed under vacuum, and the residue was partitioned between EtOAc and H_2O (50 mL, 1:1). The EtOAc layer was separated, and the aqueous layer was extracted with EtOAc. The combined EtOAc extracts were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. TLC (EtOAc) indicated no ketol. The crude diol mixture was analyzed by HPLC. The relative amounts of the two diols remained unchanged when base was omitted and solid sodium borohydride was added.

Reaction in TMAB. The following procedure for 14-keto[10.3.3]-propellan-17-*anti*-ol is typical. A suspension of 4 mg (14.5 μmol) of the ketol in a solution of 56 mg (0.36 mmol) of TMAB in 36 mL of H_2O was warmed (~50 °C) and stirred (1 h) until a clear solution was obtained. This was cooled to room temperature. $NaBH_4$/NaOH was added as with the MeOH procedure. The reaction was stirred at room temperature for 72 h and then quenched with acetic acid. This was extracted with EtOAc (2 × 25 mL). The combined EtOAc extracts were washed with brine, dried over $MgSO_4$, and concentrated under vacuum. TLC (EtOAc) indicated no ketol. The crude diol mixture was analyzed by HPLC.

Reaction in CTAB. The procedure used for 14-keto[10.3.3]propellan-17-*anti*-ol is typical. It parallels the TMAB reaction but instead uses a solution of 132 mg (0.36 mmol) of CTAB in 36 mL of H_2O. This was cooled to room temperature, and $NaBH_4$/NaOH was added as in the CH_3OH reaction. After 24 h at room temperature, the reaction was quenched with acetic acid and worked up as described for the dione to ketol reaction in CTAB. TLC (EtOAc) of the crude diol product indicated no ketol. This mixture was analyzed by HPLC.

VII. Reduction of [*n*.3.3]Propellanediones to the Corresponding Diols. Reaction in MeOH. The procedure for the reduction of [10.3.3]propellane-14,17-dione is typical. To a solution of 5.5 mg (0.02 mmol) of the dione in 50 mL of MeOH was added a solution of 3.8 mg (0.1 mmol) of $NaBH_4$ in 0.5 mL of 1 M NaOH. The reaction was stirred at room temperature for 24–48 h, quenched with acetic acid, and worked up as described for other MeOH reactions. TLC (EtOAc) indicated no dione or ketol. The crude diol mixture was analyzed by HPLC.

Reaction in TMAB. The procedure for the reduction of [10.3.3]-propellane-14,17-dione is typical. A suspension of 5.5 mg (0.02 mmol) of the dione in a solution of 77 mg (0.5 mmol) of TMAB in 50 mL of H_2O was warmed (50 °C) and stirred (1 h) until a clear solution was obtained. This was cooled to room temperature, and $NaBH_4$/NaOH solution was added as in the CH_3OH reaction. The reaction was stirred at room temperature for 72 h, quenched with acetic acid, and worked up as described for the TMAB reactions above. TLC (EtOAc) showed no dione or ketol. The crude diol mixture was analyzed by HPLC.

Reaction in CTAB. The procedure for [10.3.3]propellane-14,17-dione is typical. It parallels the TMAB procedure but uses a solution of 0.182 g (0.5 mmol) of CTAB in 50 mL of H_2O. It was stirred at room temperature for 24 h, quenched with acetic acid, and worked up as described for the CTAB reactions above. TLC (EtOAc) showed no dione or ketol. Concentration of the EtOAc eluent afforded the crude diol mixture, which was analyzed by HPLC.

Reactions of Ketone Substrates. Procedures for the reduction of *tert*-butylcyclohexanone and *trans*-1-decalone in CTAB and TMAB are identical with those described for the reduction of propellanedione to diols. Analytical GC was performed with a 6 ft × $^1/_8$ in. column with 15% Carbowax-20M as the stationary phase and He as the carrier gas. At 135 °C and a flow of 55 mL/min, the retention times for *cis*- and

(14) (a) Main, P.; Fiske, S. J.; Hulls, S. E.; Lessinger, L.; Germain, G.; Declerq, J. P.; Woolfson, M. M. *Multan 80. A System of Computer Programmes for the Automatic Solution of Crystal Structures from X-ray Diffraction Data*; Universities of York and Louvain: York, England, and Louvain, Belgium, 1980. (b) The UCLA Crystallographic Computing Package, Nov 1985.

(15) (a) Hamilton, W. C.; Ibers, J. A. In *Hydrogen Bonding in Solids*; W. A. Benjamin: New York, 1968. (b) Churchill, M. R. *Inorg. Chem.* **1973**, *12*, 1213.

Table VI. Analytical HPLC Separations for Propellane Reduction Mixtures

substrate	solvent system hexane	EtOAc	*i*-PrOH	flow, mL/min	retention time, min dione	*a* ol	*s* ol
[4.3.3]	57	38	5	1.0	7.6	10.0	13.0
[10.3.3]	75	20	5	0.8	7.1	11.5	13.3
[22.3.3]	85	10	5	1.0	5.1	9.3	10.8

substrate	solvent system MeOH	H_2O	flow, mL/min	retention time, min aa	sa	ss
[4.3.3]	50	50	1.0	15.1	9.2	7.2
[10.3.3]	80	20	1.0	13.6	8.6	7.2
[22.3.3]	95	5	1.0	18.0	11.9	10.1

trans-tert-butylcyclohexanol were 5.4 and 7.0 min, respectively. At 135 °C and a flow of 80 mL/min, the retention times for the axial and equatorial *trans*-1-decalols were 9.5 and 11.1 min, respectively.

VIII. HPLC and TLC Analyses of Propellane Reduction Products. HPLC propellaneketol analyses were performed on a Whatman Partisil 10, 4.6 mm × 25 cm column. Diols were analyzed on an IBM ODS-RP C_{18} (5 μm) 4.5 mm × 25 cm column. Retention times and separation conditions are recorded in Table VI.

TLC (EtOAc eluent) of the propellane reductions was used to verify the presence or absence of diones, ketols, and diols. The following R_f values were found. [4.3.3]: dione, 0.54; ketols, 0.36; aa diol, 0.16; as diol, 0.19; ss diol, 0.26. [10.3.3]: dione, 0.76; ketols 0.55; diols, 0.28. [22.3.3]: dione, 0.82; ketols, 0.64; diols 0.31.

IX. Partition Coefficients of the Reduction Substrates. The partition coefficients (Table III) of the reduction substrates between CTAB micelles and water were measured by HPLC as described by Armstrong.[10] An IBM RP-C_8 (5 μm) 4.5 mm × 25 cm column was used. The void volume of the column (determined with NaI) was 2.16 mL. From the total volume of the column (3.98 mL), the volume of the stationary phase was found to be 1.82 mL. Using [CTAB] = 5, 7.5, and 10 mM, substrate retention volumes were measured and the K_{MW} values calculated assuming an aggregation number of CTAB of 100.

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Supplementary Material Available: Tables listing the crystallographic data collection details, data reduction and refinement procedures, bond lengths, bond angles, positional parameters, and thermal parameters of the syn,syn propellanediol (n = 8) (6 pages); tables of calculated and observed structure factors (11 pages). Ordering information is given on any current masthead page.

Conversion of Cyclobutane to Bicyclobutane by Base-Catalyzed 1,3-Dehydrohalogenation Reaction: A Mechanistic Study[1]

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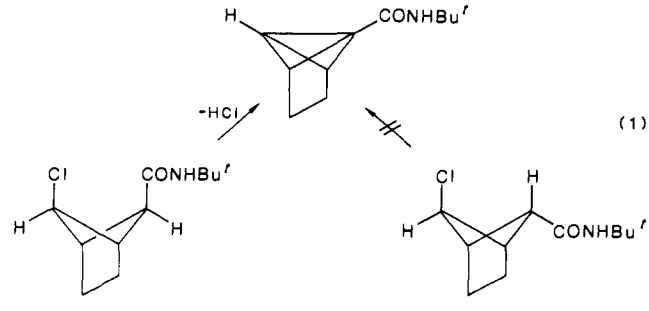
Abstract: The kinetics of the *t*-BuOK–*t*-BuOH-induced 1,3-dehydrohalogenation of the geometrical isomers of cyclobutanes **2–5** to give the corresponding bicyclobutanes was investigated. Substitution of H by Cl or Me on the carbon bearing the leaving group (substrates **1–3**) caused rate reduction by a factor of 2 only. The cyano-activated substrates with Cl as a leaving group (substrates **1** and **3**) underwent syn–anti isomerization under the reaction conditions. Substrate **2**, which due to local symmetry lacks the geometrical syn and anti isomerism, was found to undergo ^3H incorporation during the course of the reaction. In the presence of crown ether, elimination rate constants were significantly enhanced compared to those for isomerization. Negligible isomerization was detected in the reactions of the bromo derivatives **4s** and **4a** as well as in those of the two carbonyl-activated substrates **5a** and **5s**. The effect of added crown ether on the elimination rate constants for the last two substrates was relatively small. The leaving group element effect (k^{Br}/k^{Cl}) was found to be 71 for the pair **4s**/**3s** and 30 for the pair **4a**/**3a**. On the basis of the analysis of the element effect and supporting data it was concluded that the elimination from the cyano-activated substrates occurs from the hydrogen-bonded carbanion whereas an $(E1cB)_1$ mechanism was assigned to the reactions of the carbonyl-activated substrates. The results obtained in this study combined with literature data suggest a low probability for a concerted 1,3-elimination reaction in the cyclobutane–bicyclobutane system.

The 1,3-elimination reaction was the key step in the first successful synthesis of bicyclobutane performed by Wiberg et al. about 30 years ago.[2] In spite of its continually being one of the most useful and popular methods for the preparation of bicyclobutanes,[3] this reaction is at best only poorly understood. The stereochemical issue, for example, has been addressed in only three papers, and each of these gave rise to a different conclusion. Thus, Meinwald and co-workers[4] found that the leaving group (chlorine) can depart from an *axial* position when the proton assumes an equatorial position (eq 1) whereas the isomer with both the H and the Cl in the axial positions was found to be unreactive.



(1)

Several years later, Hall and co-workers[5] demonstrated in a very

(1) This is part 14 in the series "Cyclobutane–Bicyclobutane System". For part 13, see: Hoz, S.; Basch, H.; Cohen, D. *J. Am. Chem. Soc.*, in press.
(2) Wiberg, K. B.; Ciula, R. P. *J. Am. Chem. Soc.* **1959**, *81*, 5261.
(3) For a comprehensive review on the chemistry of bicyclobutane, see: Hoz, S. In *The Chemistry of the Cyclopropyl Group*; Rappoport, Z., Ed.; Wiley: New York, in press.
(4) Meinwald, J.; Swithenbank, C.; Lewis, A. *J. Am. Chem. Soc.* **1963**, *85*, 1880.

0002-7863/87/1509-7483$01.50/0