Reduction of [m.3.3]Propellane Ketones in Solution Aggregates[1]

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The reduction of [m.3.3]propellane diones and ketols has been studied in water containing cationic, anionic, and zwitterionic surfactants. From the rate and stereochemistry of the reductions done in these media, the binding of neutral substrates and ionic reagents to surfactant aggregates has been probed. Surface interactions of these variously charged aggregates have been studied, and the behavior of aggregates with like charge but different structure (cationic aqueous micelles, vesicles, and reverse micelles) has been compared. A picture of charge distribution at the surface of amine oxide zwitterionic micelles has emerged. The oriented propellane binding (polymethylene ring aligned with surfactant tails and fused five-membered rings tangential to the aggregate surface) first proposed for propellanes bound to cationic micelles has been confirmed and extended to cationic vesicles and to amine oxide micelles.

We have recently reported the ability of cationic aqueous micelles to perturb the stereochemistry of the reduction of [m.3.3]propellane diones and ketols.[3] We suggested that micellar enhancement of hydride attack from the same face as the polymethylene ring was attributable to an oriented binding of the propellane substrate that directed reagent attack from within the micelle to one face of the molecule. Specifically, this involved a radial orientation of the polymethylene chain and placement of the two oxygen-bearing five-membered rings tangential to the micelle surface. The present paper considers how this attack of micelle-bound reducing agent on an oriented substrate can be altered by modifying the structure of the surfactant aggregate. Would changing the micellar surface from cationic to anionic or zwitterionic alter the observed diastereofacial selectivity of reagent approach? Would changing the morphology of the cationic aggregate from an aqueous micelle to a vesicle or a reverse micelle significantly alter substrate binding and reduction chemistry? The effect of these changes on both the rate and stereochemistry of propellane carbonyl reduction has afforded us insight into aggregate structure and into details of micellar binding of both neutral substrates and ionic reagents.

Results

Both the [m.3.3]propellane substrates and products have been described previously.[3,4] The reduction of dione to ketols to diols (Scheme I, $m = n + 2$, $n = 2$, 8, 10, 20) summarizes the reactions involved. In addition to extending our studies[3] of aqueous micelles of cetyltrimethylammonium bromide (CTABr), we have used this same surfactant with either a tosylate (CTATos) or borohydride ($CTABH_4$) counterion. Double-tailed cationic surfactants based on didodecyldimethylammonium cations with either bromide (DDABr) or hydroxide (DDAOH) counterions were used for vesicle and reverse micelle formation. Sodium dodecyl sulfate (SDS) was used to form anionic micelles, and dodecyldimethylamine oxide (DDAO) solutions provided zwitterionic micelles.

The product distributions obtained from the borohydride-mediated double reduction of diones to diols and from the reductions of diones to ketols or ketols to diols are shown in Tables I and II. Reductions in CTABr, CTATos, DDAO, and SDS micelles, in water with added tetramethylammonium bromide (TMABr) or trimethylamine oxide (TMAO), and in methanol are included. The $m = 4$ and $m = 10$ systems could be investigated in water with no surfactant, while the $m = 12$ and $m = 22$ systems lacked sufficient water solubility and could only be referenced to a methanol control reaction. Calculated ketol to diol percentages in Table II are obtained by combining the dione to ketol and dione to diol results and knowing that the two ketol isomers have comparable binding constants.[3]

There was little or no effect on product stereochemistry by changing the concentration of the reactive borohydride counterion of a cationic micelle. Adding a large excess of $NaBH_4$ or using $CTABH_4$ as both surfactant and reducing agent had no effect on the reduction stereochemistry of the $m = 22$ dione and very slightly enhanced the "anti" selectivity for the $m = 10$ dione relative to what was seen in CTABr with $NaBH_4$.

Cationic vesicles made by sonicating an aqueous suspension of DDABr or from a solution of DDAOH in water gave the same product distribution for BH_4^- reduction of the $m = 22$ dione to diols as is seen in CTABr or $CTABH_4$ micelles. This was in contrast with results obtained in cationic reverse micelles of DDABr in benzene/water mixtures (Table III). While these experiments showed no dependence on the water/surfactant ratio (water pool size), they gave product distributions for both dione and ketol substrates that greatly differed from all other cationic aggregates.

Finally, we have observed large differences in the rates of reduction of the propellane substrates in the various media. Rate enhancements of approximately a factor of 8 (varying with substrate structure) for BH_4^- reduction in CTABr micelles have been reported.[5] Kinetics measurements on propellane ketols show an enhancement of a factor of 7 for the [10.3.3] syn ketol in CTABr relative to its reduction rate in water. This is supplemented by a qualitative appraisal of relative rates that emerged from our stereochemical studies, which required either very low degrees of conversion to observe dione to ketol ratios or complete conversion in the dione to diol experiments. This yielded the following relative rate order: $CTABH_4$ micelles > CTABr micelles $\simeq$ DDABr/DDAOH cationic vesicles > CTATos micelles $\simeq$ DDAO micelles > H_2O (with or without nonaggregating additives) $\gg$ DDABr reverse micelles $\simeq$ SDS micelles. With the concentrations of surfactant and BH_4^- used in our experiments, the reduction rate in methanol was similar to that in CTABr micelles.

(1) Taken in part from the Ph.D. Thesis of A.N., Case Western Reserve University, 1988.
(2) NIH Research Career Development Awardee (1983–1988).
(3) Natrajan, A.; Ferrara, J. D.; Youngs, W. J.; Sukenik, C. N. *J. Am. Chem. Soc.* **1987**, *109*, 7477.
(4) Natrajan, A.; Ferrara, J. D.; Hays, J. D.; Colonell, J.; Youngs, W. J.; Sukenik, C. N., submitted for publication.
(5) Menger, F. M.; Bonicamp, J. M. *J. Am. Chem. Soc.* **1981**, *103*, 2140.

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Scheme I. Reduction of [*m*.3.3]Propellane Diones and Ketols (*m* = *n* + 2)

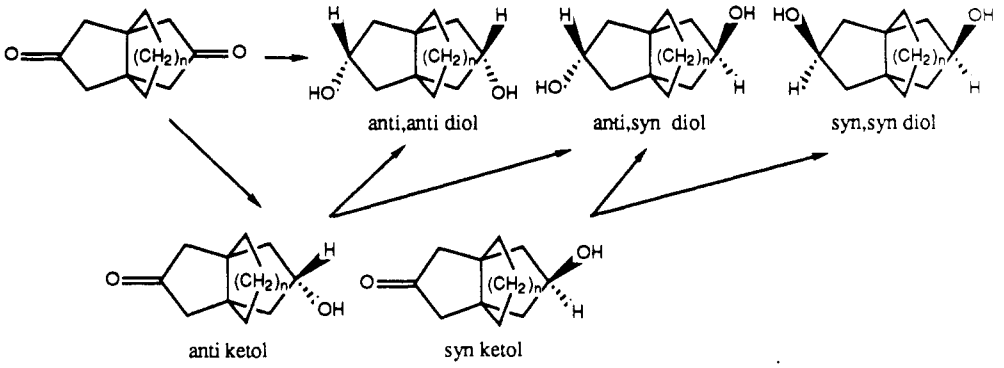

Table I. Distribution of Diols from Reducing [*m*.3.3]Propellane Diones[a]

	[4.3.3]			[10.3.3]			[12.3.3]			[22.3.3]		
medium	aa	sa	ss	aa	sa	ss	aa	sa	ss	aa	sa	ss
MeOH	20	48	32	22	48	30	20	42	38	28	48	24
TMABr[b]	21	50	29	22	48	30						
TMAO[c]	19	53	28	26	46	28						
CTABr[b]	46	42	12	47	39	14	48	33	19	55	32	13
CTATos[b]	29	48	23				52	30	18			
CTATos[d]				52	34	14	52	30	18	56	32	12
DDAO[c]	25	47	28	51	35	14	53	30	17	57	30	13

[a] [dione] = 0.4 mM; [BH_4] = 2 mM; 1–3 days; pH 12, adjusted with 1 M NaOH. [b] [TMABr], [CTABr], [CTATos] = 10 mM. [c] [DDAO], [TMAO] = 20 mM; [dione] = 0.8 mM; [BH_4] = 8 mM; 3–4 days. [d] [CTATos] = 2.7 mM; [dione] = 0.11 mM; [BH_4] = 0.54 mM.

Table II. Percent Anti Alcohol from Diones and Ketols

			anti ketol → aa diol[b]		syn ketol → sa diol[b]	
propellane	medium	dione → anti ketol[a]	obsd	calcd	obsd	calcd
[4.3.3]	MeOH	39	50	51	52	48
[4.3.3]	TMABr	44	51	48	50	48
[4.3.3]	TMAO[c]	40		48		53
[4.3.3]	CTABr	57	76	80	71	72
[4.3.3]	DDAO[c]	47		60		53
[4.3.3]	SDS[d]	41				
[10.3.3]	MeOH	35	64	63	57	54
[10.3.3]	TMABr	36	60	61	56	56
[10.3.3]	TMAO[c]	40		65		53
[10.3.3]	CTABr	54	84	87	69	70
[10.3.3]	DDAO[c]	65		79		60
[10.3.3]	SDS[d]	40				
[12.3.3]	MeOH	37	58	54	39	40
[12.3.3]	CTABr	57	82	84	53	56
[12.3.3]	DDAO[c]	67		79		48
[12.3.3]	SDS[d]	39				
[22.3.3]	MeOH	42	70	67	60	60
[22.3.3]	CTABr	62	86	89	67	66
[22.3.3]	DDAO[c]	64		89		64
[22.3.3]	SDS[d]	43				

[a] [TMABr], [CTABr] = 10 mM; [dione] = 0.4 mM; [BH_4] = 0.1 mM; 1.5–3 h; pH 12, adjusted with 1 M NaOH; <20% dione consumed. [b] [TMABr], [CTABr] = 10 mM; [ketol] = 0.4 mM; [BH_4] = 2 mM; 24 h; pH 12. [c] [DDAO], [TMAO] = 20 mM; [dione] = 0.8 mM; [BH_4] = 0.8 mM; 3 h. [d] [SDS] = 25 mM; [dione] = 0.5 mM; [BH_4] = 2.5 mM; *m* = 4: 12 h, *m* = 10: 48 h, *m* = 12, 22: 120 h.

Discussion

Reactions in methanol, SDS micelles, TMABr, and TMAO all yield comparable product ratios for any given substrate. The observation that TMABr and TMAO yield the same, methanol-like, product distributions requires that changes in product distribution seen with cationic and zwitterionic micelles are genuinely aggregate dependent. This is in contrast to the situation with SDS micelles where micellar binding of substrate molecules allows solubilization of the otherwise water-insoluble *m* = 22 substrates, yet these anionic aggregates show no induced changes in reduction product distribution. Substrates that are reduced in SDS-containing media are not being reduced on

Table III. Percent Anti Alcohol by Reduction in DDABr/Benzene Reverse Micelles[a]

propellane	[H_2O]/[DDABr]	dione → anti ketol	anti ketol → anti,anti diol	syn ketol → syn,anti diol
[4.3.3]	4	42	36	37
[10.3.3]	4	39	43	45
[22.3.3]	1		47	
[22.3.3]	2		43	
[22.3.3]	3		44	
[22.3.3]	4	48	47	46

[a] [DDABr] = 15 mM; [BH_4] = 3 mM; [substrate] = 0.6 mM; 55 °C; 2.5–3 h (dione → ketols) (<20% dione consumed); 24–72 h (ketols → diols).

Table IV. Reverse Micelle Effect on Syn Alcohol Production

propellane	medium	anti ketol → sa diol	syn ketol → ss diol	dione → overall syn ol ss + 0.5 sa diol[b]
[4.3.3]	DDABr reverse micelles	64	63	61
[4.3.3]	TMABr/TMAO/MeOH controls[a]	50	49	55
[4.3.3]	CTABr aqueous micelles	24	29	33
[10.3.3]	DDABr reverse micelles	57	55	59
[10.3.3]	TMABr/TMAO/MeOH controls[a]	38	44	53
[10.3.3]	CTABr aqueous micelles	16	31	34
[22.3.3]	DDABr reverse micelles	55	54	53
[22.3.3]	MeOH control reaction	30	40	48
[22.3.3]	CTABr aqueous micelles	14	33	29

[a] Average of nonsurfactant-containing control reactions. [b] Calculated overall propensity for formation of syn alcohol from both dione and ketol reduction.

the micelle due to repulsion of the borohydride anion from the anionic micelle surface. The reaction on the micelle is so slow that even reaction in water, which is strongly disfavored by the low substrate solubility, can compete. The net result is an extremely slow reaction whose rate is inversely proportional to substrate hydrophobicity and whose product distribution reflects a reaction that is occurring in the bulk aqueous phase.

Cationic vesicles with OH^- and/or Br^- and/or BH_4^- counterions are indistinguishable from each other and from comparable simple micelles in their influence on reaction stereochemistry. The enhanced rigidity of the vesicle structure and surface ion competition effects all have little impact on propellane solubilization, orientation, and reduction stereochemistry. Both the spontaneously formed hydroxide vesicles[6] and the sonicated bromide vesicles solubilize and orient the propellane substrates in a way that is comparable to that seen in simple cationic micelles. This can be contrasted to a number of other aggregate-bound reactions with demonstrable sensitivity to aggregate rigidity.[7] The binding of our propellane substrates near the micelle surface is anisotropic, but still fluid enough not to be measurably affected by these variations in aggregate structure.

The only exception to this uniform behavior of cationic aggregates in water is seen when a very hydrophobic counterion, tosylate, is added. It has been shown[8] that the strongly bound tosylate can displace borohydride from a cationic micelle surface. This suggested that CTATos should both slow the rate of propellane reduction and allow water-like stereochemistry to be manifest even in the presence of a cationic aggregate. We observed that tosylate counterions slowed the overall reduction rate, consistent with a displacement of BH_4^- ions from the micelle surface. For the [4.3.3] system, the most hydrophilic of our substrates, this also resulted in a reaction stereochemistry that was nearly water-like. For more tightly bound propellane substrates,[9] even the lowered levels of micelle-bound BH_4^- are sufficient for all reduction to still occur within the aggregate. Tosylate displacement of BH_4^- and/or substrate is most easily detected for the least tightly bound substrates.

A novel perturbation of reaction stereochemistry in a cationic aggregate is seen in the DDABr reverse micelles in benzene. These reactions were extremely slow, presumably due to the propellane substrate spending most of its time in the bulk benzene phase, away from the borohydride-containing water pool. When reaction did occur, it showed two new features. First, all other aggregates showed comparable perturbation of reaction stereochemistry for both dione and ketol substrates. Dione reduction in reverse micelles proceeds with the same stereochemistry seen in bulk aqueous medium, while product distributions for the ketols in reverse micelles resemble neither the bulk water reductions nor those in the cationic aqueous aggregates. Second, all previously observed alterations in product stereochemistry relative to the aqueous and methanol controls showed enhanced formation of anti alcohol (hydride attack from the same side as the polymethylene ring). These aggregates show a small but consistent enhancement of syn alcohol formation regardless of polymethylene chain length or stereochemistry of the starting ketol (Table IV). We could not compare the reverse micelle results to reductions in benzene (with or without water) with no surfactant, since such mixtures were all heterogeneous and gave no evidence of propellane reduction.

In aqueous micelles, reagent attack occurs predominantly from the inside of the aggregate and thus shows preference for attack on the same face as the polymethylene ring. In the reverse micelles, we suggest that reagent attacks from the direction of the water pool while the propellane is at least somewhat oriented with its polymethylene chain away from the water pool. This orientation is independent of chain length, as in aqueous micelles, but it may be sensitive to the difference between dione and ketol substrates. Also, just as ketols are better bound than diones to aqueous micelles,[3] there may also be a difference in the strength of their interactions with the head groups of the reverse micelles.

Finally, we address the results obtained in zwitterionic micelles. Amine oxide micelles show a small enhancement over the rate of reaction in water. However, their reactions are distinctly slower than in cationic micelles. Second, for all except the [4.3.3] substrates, the stereochemistry seen for these systems is comparable to that seen in cationic micelles. We see these results as support for the following concept recently suggested by Bunton.[10]

Dodecyldimethylamine oxide is formally neutral. However, as a zwitterionic surfactant, it has negatively

(6) (a) Brady, J. E.; Evans, D. F.; Kachar, B.; Ninham, B. W. *J. Am. Chem. Soc.* **1984**, *106*, 4279. (b) We have been alerted by Prof. C. A. Bunton to the possibility that the spontaneous formation of vesicles (rather than micelles) with hydroxide counterions may be concentration dependent. Since our results are the same for the hydroxide (spontaneous) and the bromide (sonication) systems, this does not alter our work or its interpretation.

(7) Kunitake, T.; Okhata, Y.; Ando, R.; Shinkai, S.; Hirakawa, S. I. *J. Am. Chem. Soc.* **1980**, *102*, 7877. Also see: Fendler, J. H.; Hinze, W. L. *J. Am. Chem. Soc.* **1981**, *103*, 5439.

(8) Bunton, C. A.; Carrasco, N.; Huang, S. K.; Paik, C. H.; Romsted, L. S. *J. Am. Chem. Soc.* **1978**, *100*, 5420.

(9) Binding constants for the $m = 4$ and $m = 10$ diones and ketols to CTABr micelles are reported in ref 3. Due to the viscosity of the CTATos solutions, a direct measure of propellane binding to such micelles could not be obtained.

(10) Bunton, C. A.; Mhala, M. M.; Moffat, J. R. *J. Org. Chem.* **1987**, *52*, 3832.

charged oxygens extending out from positively charged nitrogens. Upon micellization, the overall neutrality of the micelle is maintained, but this is not necessarily true for specific layers of the micelle surface. If micelles can be even crudely approximated as spheres, the negative charge density on the micelle surface will be smaller than the positive charge density. This is because, on average, the anionic domain extends slightly further away from the micelle core and is thus spread over a larger surface area. In addition to this effect, it is also true that the pH-dependent hydration of the (formal) oxide anion reduces the negative charge density of the surface more effectively than it attenuates the positive charge of the ammonium moiety. Admittedly, this effect will be small at pH 12. Nevertheless, either oxide protonation (as seen at low pH) or anion hydration and hydrogen bonding make the amine oxide begin to resemble an ammonium hydroxide. The result is that the micelle surface, within a limited radius, has a net positive charge and attracts anions, though less strongly than cationic micelles. Moreover, like cationic micelles, ion competition effects are to be expected. Thus, with OH^- and BH_4^- as the only anions in a DDAO micellar solution, there is an accumulation of the less hydrated BH_4^- at the micelle surface. The reductions of propellanes in DDAO micelles are thus comparable to the results seen in CTATos micelles. For hydrophobic substrates, reaction occurs exclusively at the micelle surface and micellar enhancement of anti alcohol formation is seen, just like in the aqueous cationic aggregates. Less hydrophobic substrates exhibit stereochemistry suggesting a combination of reactions in water and in the micelle.

Conclusions

[*m*.3.3]Propellane diones and ketols are solubilized in micelles and vesicles with a specific orientation that places their cyclopentanone rings tangential to the aggregate surface. In this way, BH_4^- that is bound to such aggregates is biased to attack from within the micelle surface (i.e., from the direction of the polymethylene ring). Interestingly, amine oxide surfactants yield micelles that, effectively, resemble cationic aggregates, even at high pH. Thus, the surfaces of both ammonium and amine oxide micelles evidence significant BH_4^- binding. Charge repulsion from the surface of anionic micelles prevents any detectable reduction from occurring on those micelles. A complementary binding configuration exists in reverse micelles. BH_4^- is held in the water pool and the orientation of the binding now introduces a small bias for attack from the direction of the water pool (i.e., from the direction opposite the polymethylene ring).

Experimental Section

General. HPLC was performed on a Waters 590 pump equipped with a Rheodyne 7125 injector and a Waters 401 differential refractometer. TLC was done on aluminum-backed 0.2-mm 60F254 plates from EM Science and used phosphomolybdic acid as visualization agent. Column chromatography (flash) was done with silica gel from Aldrich (230–400 mesh). Cetyltrimethylammonium bromide (Sigma) was recrystallized twice from ethanol and dried in a vacuum oven. Cetyltrimethylammonium *p*-toluenesulfonate (Sigma) was recrystallized twice from 2-propanol and dried in a vacuum oven. Cetyltrimethylammonium borohydride (Sigma) was used as received. Sodium dodecyl sulfate (Bio-Rad) was recrystallized twice from 95% ethanol. A plot of its surface tension vs concentration showed no hysteresis. Didodecyldimethylammonium bromide (Sigma) was recrystallized twice from ethyl acetate. Rexyn 201 was obtained from Fisher. Water was doubly distilled, and all other solvents ($CHCl_3$, hexane, EtOAc, and CH_3OH) were Fisher HPLC grade (used as received). $NaBH_4$, dodecyldimethylamine, and trimethylamine oxide were used as received from Aldrich.

The source, characterization, and chromatography of all propellane diones, ketols, and diols have been described,[3,4] except for the analytical HPLC of the [12.3.3] system. Ketol analyses were performed on a Whatman Partisil 10, 4.6 mm × 25 cm column using hexane/EtOAc/*i*-PrOH in a ratio of 75:25:5 at a flow of 0.8 mL/min. Retention times (in minutes) were 7.5 (dione), 11.5 (anti ketol), and 13.3 (syn ketol). Diols were analyzed on an IBM ODS-RP C_{18} (5 μm) 4.5 mm × 25 cm column using an 85:15 MeOH/water mixture and a flow of 1 mL/min. Diol retention times were 7.2 (ss), 8.5 (as), and 13.6 (aa) min. 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 for the [12.3.3] system: dione, 0.76; ketols, 0.55; diols, 0.28.

Dodecyldimethylamine Oxide. In a 500-mL single-neck flask equipped with a magnetic stirring bar was placed dodecyldimethylamine (45 g, 0.222 mol). The amine was cooled to 0 °C and H_2O_2 (25 g, 30% solution) was added over a period of 30 min. The reaction was stirred for 2 h. Benzene was added to the slurry, and the benzene–water azeotrope was repeatedly distilled off till the distillate was clear. Remaining benzene was removed and crude amine oxide was twice recrystallized from acetone. Its cmc (surface tension, 2.0×10^{-3} M) matched literature values.[11]

Reductions of [4.3.3]-, [10.3.3]-, and [22.3.3]propellane diones and ketols in CTABr, TMABr, and MeOH have been described.[3] Procedures for other media follow.

Reduction of [*m*.3.3]Propellane Diones to Ketols. (1) Reduction in DDAO. The reduction of [10.3.3]propellane-14,17-dione is typical. A suspension of dione (4 mg, 14 μmol) in a solution of DDAO (80 mg, 0.35 mmol) in 17.5 mL of H_2O was warmed and stirred till a clear solution was obtained. The solution was cooled to room temperature, and $NaBH_4$ (0.5 mg, 14 μmol) in 175 μL of 1 M NaOH was added. The reaction was stirred at room temperature for 3 h and quenched with HOAc. NaCl was added, and the solution was extracted with EtOAc (2 × 25 mL). The combined EtOAc extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was filtered (silica gel, EtOAc, 8–10 mL) to remove surfactant. TLC (EtOAc) indicated no diol. Evaporation of the EtOAc afforded the crude reaction product mixture, which was analyzed by HPLC.

(2) Reduction in TMAO. The reduction of [10.3.3]propellane-14,17-dione is typical. It parallels the DDAO reaction but uses a solution of TMAO (56 mg, 0.5 mmol) in 50 mL of H_2O with dione (5.5 mg, 0.02 mmol) and $NaBH_4$ (0.8 mg, 0.02 mmol). The reaction was worked up as described above, but with no silica gel filtration. Crude product, showing no diol (TLC, EtOAc), was analyzed by HPLC.

(3) Reduction in DDABr Reverse Micelles. The reduction of [22.3.3]propellane-26,29-dione is typical. To a solution of DDABr (0.173 g, 0.374 mmol) in 25 mL of dry benzene was added $NaBH_4$ (2.8 mg, 0.0748 mmol) in aqueous NaOH (27 μL), pH 12. The suspension was sonicated and shaken (10 min) till a clear solution was obtained. Dione (7 mg, 0.015 mmol) was added, and the reaction flask was fitted with an air condenser and warmed to 55 °C for 3 h. It was then cooled to room temperature and quenched with acetic acid. The benzene was removed under vacuum, and the residue was filtered (silica gel, EtOAc, 10 mL). The EtOAc eluent was washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The crude product mixture showed no diol (TLC, EtOAc) and was analyzed by HPLC.

(4) Reduction in SDS. The reduction of [10.3.3]propellane-14,17-dione is typical. A suspension of dione (6.5 mg, 0.024 mmol) in a solution of SDS (360 mg, 1.2 mmol) in 50 mL of H_2O was warmed and stirred till a clear solution was obtained. After the solution cooled to room temperature, $NaBH_4$ (4.7 mg, 125 μmol) was added as a solution in 0.5 mL of 1 M NaOH. After 48 h the reaction was quenched with acetic acid. The solution was transferred to two 50-mL centrifuge tubes with 1 g of NaCl and 2 g of $BaCl_2$ each. EtOAc (5 mL) was added to each tube;

(11) (a) Benjamin, L. *J. Phys. Chem.* **1964**, *68*, 3575. (b) Herrmann, K. W. *J. Phys. Chem.* **1962**, *66*, 295.

the mixtures were shaken vigorously and 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 (silica gel, EtOAc, 8–10 mL). TLC (EtOAc) indicated no diol. Evaporation of the EtOAc afforded the crude reaction product mixture, which was analyzed by HPLC.

Reduction of Propellane Ketols to Diols in DDABr Reverse Micelles. The reduction of [22.3.3]propellane-26-keto-29-*anti*-ol is typical. To DDABr (90 mg, 0.2 mmol) in 13 mL of dry benzene was added $NaBH_4$ (1.5 mg, 40 μmol) in 14 μL of pH 12 aqueous NaOH. The suspension was shaken and sonicated (10 min) till a clear solution was obtained. Ketol (3.5 mg, 7.85 μmol) was added, and the flask was fitted with an air condenser and warmed to 55 °C for 3 days. The reaction was cooled and quenched with HOAc, the benzene was removed under reduced pressure, and the residue was filtered (silica gel, EtOAc, 10 mL). The EtOAc eluent was washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was chromatographed (silica, EtOAc) to remove unreacted ketol (R_f ketol 0.64, R_f diols 0.31). The diol fractions were combined, concentrated under vacuum, and analyzed by HPLC.

Reduction of [m.3.3]Propellane Diones to Diols. (1) Reduction in DDAO. The reduction of [10.3.3]propellane-14,17-dione is typical. A suspension of [10.3.3]propellane-14,17-dione (5.5 mg, 20 μmol) in a solution of DDAO (115 mg, 0.5 mmol) in 25 mL of H_2O was warmed and stirred till a clear solution was obtained. It was cooled to room temperature and $NaBH_4$ (3.8 mg, 0.1 mmol) was added as a solution in 0.25 mL of 1 M NaOH. The reaction was stirred at room temperature for 4 days and then worked up as described for the dione to ketol conversion. The crude diol mixture showed no dione or ketol (TLC, EtOAc) and was analyzed by HPLC.

(2) Reduction in TMAO. The procedure parallels the one described for the dione to ketol conversion but instead uses a solution of TMAO (56 mg, 0.5 mmol), [10.3.3]propellane-14,17-dione (5.5 mg, 20 μmol), and $NaBH_4$ (3.8 mg, 0.1 mmol) in 50 mL of H_2O reacting at room temperature for 4 days. The crude diol mixture showed no dione or ketol (TLC, EtOAc) and was analyzed by HPLC.

(3) Reduction in CTATos. The reduction of [10.3.3]propellane-14,17-dione is typical. A suspension of dione (3 mg, 10.9 μmol) in a solution of CTATos (122 mg, 0.27 mmol) in 100 mL of H_2O was warmed and stirred. A clear, viscous solution was obtained. The solution was cooled and $NaBH_4$ (2 mg, 0.053 mmol) in 1 mL of 1 M NaOH was added. The reaction was stirred at room temperature for 2 days and quenched with acetic acid. The solution was transferred to four 50-mL centrifuge tubes with 1 g of NaCl and 2 g of $KClO_4$ in each. EtOAc (5 mL) was added to each tube; the mixtures were shaken vigorously and centrifuged for 5 min. The EtOAc layer in each tube was removed, and the extraction was repeated twice. The combined EtOAc extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The residue was filtered (silica gel, EtOAc) to remove surfactant. TLC of the eluent showed no ketol. Evaporation of the EtOAc afforded the crude diol mixture, which was analyzed by HPLC.

(4) Reduction in Cationic Vesicles. To a solution of DDAOH[6a] (50 mL, 0.005 M) was added [22.3.3]propellane-26,29-dione (11 mg, 25 μmol). The suspension was warmed and stirred till a clear solution was obtained. After cooling to room temperature, the pH of the solution was adjusted to 12 using 1 M NaOH. $NaBH_4$ (3 mg, 79 μmol) was added. The reaction was stirred at room temperature for 24 h and then quenched with HOAc. Workup was identical with that described for the CTATos reaction. The crude product mixture showed no dione or ketol (TLC, EtOAc) and was analyzed by HPLC. The procedure in DDABr vesicles was the same, but instead used a solution of DDABr (4 mM) prepared by sonicating a suspension of 46 mg of DDABr in 25 mL of water.

Kinetic Measurements. A Cary 2300 UV–visible–near-infrared spectrophotometer with 3-mL quartz cuvettes and a water-jacketed cell compartment was used. The decrease in ketol absorbance at 290 nm was monitored with time. Plots of ln ($A - A_\infty$) vs time were linear and their slopes yielded the unimolecular rate constants. Bimolecular rate constants were calculated from these, knowing the concentration of borohydride used. The instrument base line was set for either CTABr or DDAO in pH 12 aqueous NaOH. The procedure for the reduction of [10.3.3]-propellane-14-keto-17-*anti*-ol is typical. To a 3-mL quartz cuvette was transferred 2.97 mL of a solution of the ketol in 0.01 M CTABr. The cuvette was placed in the spectrophotometer to thermally equilibrate at 25 °C. $NaBH_4$ solution (30 μL) in pH 14 aqueous NaOH was added via a syringe (total concentration of $NaBH_4$ = 10 mM, total concentration of ketol = 1 mM). Spectra (248–324 nm) were collected at 7-min intervals, till no further change in absorbance could be detected.

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