increases dramatically with increased electron withdrawal (Figure 6; $\beta_{lg} = -0.95$[27]), while k_{-1} decreases slightly ($\beta = 0.2$[28]). The ethyl and chloroethyl hemiacetals have $k_{-1}/k_3 > 1$, and proton transfer therefore cannot be rate-limiting. A crossover is predicted when the leaving alcohol has a pK_{ROH} of ~ 13. The data for the acetaldehyde trifluoroethyl system illustrate the importance of the k_{-1} rate constant as well. With this hemiacetal k_3 has become large, but since the anion is a stronger base by ~ 1.5 pK_a units than the anion derived from the bromoketone, k_{-1} is also large, and k_{-1}/k_3 is still greater than unity.

(27) Because of the way pK_a is calculated, this β_{lg} is simply the value experimentally determined for OH^- catalysis minus 0.2.
(28) This arises because of the assumption of a 1/5 relationship between ΔpK_a and ΔpK_{ROH}.

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Kinetics of Amphiphilic Ketone Epimerizations in Cleavable Surfactant Hosts

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Abstract: The rate of epimerization and product equilibrium composition of eight amphiphilic ketone diastereomers were determined in aqueous base and in surfactants that were stable to strong base but were cleaved to nonsurfactant compounds upon mild acid workup. These cleavable surfactant hosts gave equilibria for the amphiphilic ketones similar to cetyltrimethylammonium bromide and dicetyldimethylammonium bromide, which were models for these structures. Furthermore, rates of ketone equilibration determined in these cleavable surfactant hosts indicate an appreciable catalytic effect for equilibration, as compared to equilibrations of the amphiphilic ketones in aqueous base alone. One of the ketone surfactant pairs was studied above and below its critical micelle concentration (cmc). Below the cmc, rates of equilibration were high and no diastereoselectivity was observed in the equilibration while above the cmc of the substrate, rates of equilibration were lower and the meso diastereomer was favored.

Molecular aggregates, such as micelles and lipid bilayer membranes, are important structures in biology and chemistry,[1-3] and they have functions such as emulsion polymerization catalysts,[4] structural components in complex biological systems,[5] and hosts for membrane-bound enzyme catalysts.[6] It has been established that these aggregates have important catalytic properties and their influence on rates of reactions has been reported on numerous occasions.[2,4,7-10] The effect of micelles and lipid bilayers on the stereochemical course of organic reactions has also been reported, and recent publications indicate a dramatic influence of aggregates on the rates of reactions of chiral reactants.[11-13]

We have recently reported that the hydrophobic effect can be used to perturb equilibria of two-chain ketone surfactants, such as **1-3**.[14,15] These epimerizable ketones exist as meso and (±) diastereomers, and the equilibrium ratio (base or acid catalyzed) of these diastereomers is 50:50 in isotropic fluids but is perturbed to as much as 90:10 in favor of the meso diastereomer if the base-catalyzed equilibrations are carried out in aqueous molecular aggregates. Equilibrations of **1-3** were also carried out in the presence of excess authentic micelle-forming cationic surfactant cetyltrimethylammonium bromide (CTAB) and with the bilayer-forming cationic surfactant dicetyldimethylammonium bromide (DDAB).[16-18] These surfactant hosts perturb the equilibrium ratios obtained from the twin-chain surfactants, as compared to equilibrations carried out without added cationic surfactants. While CTAB increases the meso/(±) product ratio for the 6,6′-linked ketone **2**, the equilibrium ratio for the 9,9′-linked ketone **3** decreases in CTAB relative to the value obtained in water alone. On the other hand, the bilayer-forming surfactant DDAB increases the equilibrium product ratio for both ketones **2** and **3**.

In the course of these studies with CTAB and DDAB, it became apparent that ketone equilibria were established faster in the presence of these cationic surfactants than was the case without these positively charged hosts.[15] Thus, equilibrium for **3** at 60 °C without CTAB or DDAB required over 200 h. On the other hand, the equilibrium for **3** could be established in a matter of a few hours at 60 °C with CTAB or DDAB present, and equilibrations could be achieved at 37 °C in a matter of days with these

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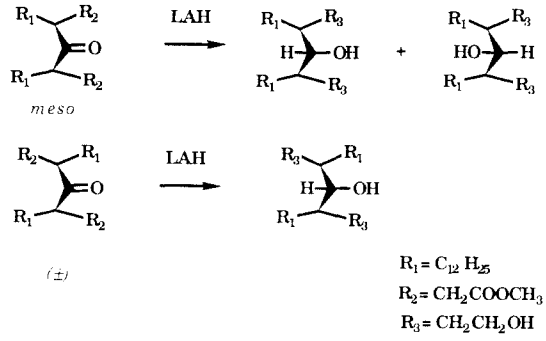
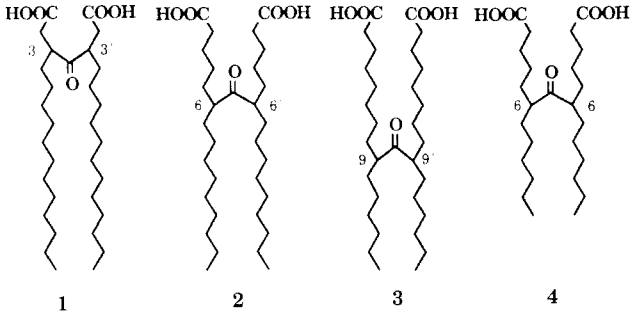
Scheme I



added cationic surfactants. Half-lives on the order of months were required at this temperature without added CTAB or DDAB. In order to explore this rate enhancement, preliminary kinetic studies were carried out. While reproducible analyses could be achieved for the equilibrium ratios obtained in these host surfactants, determination of the kinetics of approach to equilibrium was abandoned because of the difficulty of the extraction procedure involved in analysis of samples of **1–3**.

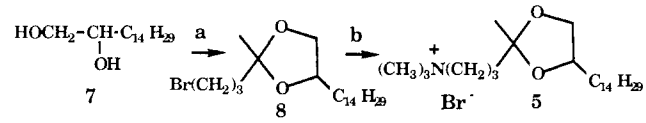


Cleavable (destructible) surfactants contain linkages separating their major lipophilic and hydrophilic portions that are stable under certain conditions but labile under other, mild conditions with respect to cleavage to nonsurfactant fragments. They facilitate the use of aqueous micellar/vesicular solutions as reaction media in applications requiring product isolation. After completion of a reaction, the surfactant is cleaved to allow straightforward extractive workup without the emulsion problems generally encountered with conventional surfactants. Several single-chain[19] and two double-chain[20] examples have been reported. The present study employed two new ketal-based surfactants, single-chain **5** and double-chain **6**. These surfactants are stable to the strong base conditions used to equilibrate ketones **1–3**, but they are cleaved upon a mild acid workup, allowing the ready extraction and analysis of the ketones by conventional HPLC techniques. We report here the results of a kinetic study of the epimerization of ketones **1–3** and the new ketone **4** in aqueous base and in the presence of the cleavable surfactants **5** and **6**.

Results

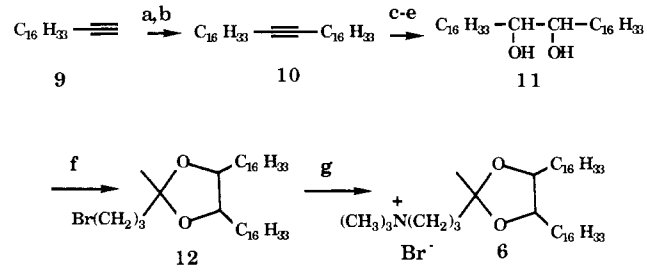
Synthesis of Ketones and Cleavable Surfactants. The ketones **1–4** were prepared as previously described.[14,15] The meso and (±) diastereomers were separated by reverse-phase liquid chromatography (C-18) with CH_3CN/H_2O mobile phase. The structures of the meso diastereomers of both **2** and **3** were solved by single-crystal X-ray analysis, while the identification of the diastereomers of **1** has not been rigorously established.[15] The meso diastereomers of **2** and **3** elute last on reverse-phase HPLC, and

Scheme II[a]



[a] (a) $Br(CH_2)_3COMe$, 4-$MeC_6H_4SO_3H$, C_6H_6; (b) Me_3N, MeOH.

Scheme III[a]



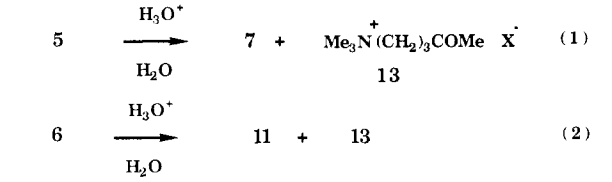
[a] (a) BuLi, hexane, THF; (b) $C_{16}H_{33}Br$, HMPA; (c) H_2, $Pd/BaSO_4$, hexane, EtOH; (d) H_2O_2/H_2O, HCO_2H, Bu_4NBr, C_6H_6; (e) KOH, MeOH, C_6H_6; (f) $Br(CH_2)_3COMe$, 4-$MeC_6H_4SO_3H$, C_6H_6; (g) Me_3N, MeOH.

this, coupled with the fact that the meso diastereomer is the favored diastereomer at equilibrium in micelles for both **2** and **3**, gives a tentative assignment of the **1** diastereomers. Crystals of **1** suitable for single crystal X-ray analysis could not be grown.

We considered other methods for proof of stereochemistry of the ketone diastereomers, and this led to the general solution illustrated in Scheme I for **1**. The meso diastereomers of the ketones **1–4** (as their dimethyl esters) reduce with lithium aluminum hydride to give two triol diastereomers, which can be separated by HPLC and identified by spectroscopic means, while the (±) diastereomers reduce to give only one product triol. This is the expected result based on the symmetry of the diastereomers, and it has been observed in every analogous example that we have investigated thus far (six pairs of epimeric amphiphilic ketone diastereomers including **1–4**). In every case studied, we have been able to separate the two triol diastereomers generated from the meso compound from the one triol coming from the (±) isomer by reverse-phase HPLC.

Surfactant **5** was prepared as illustrated in Scheme II. Ketal **8**, derived from diol **7** and 5-bromo-2-pentanone, gave **5** on reaction with trimethylamine in methanol. Surfactant **6** was synthesized as outlined in Scheme III. Alkyne **10**, obtained by alkylation of **9**, was converted to diol **11** through the corresponding alkene. With the same procedures used for **5**, **11** gave ketal **12**, which in turn yielded **6**.

Surfactants **5** and **6** undergo acid-catalyzed hydrolysis to yield nonsurfactant fragments **13**[19b] and diols **7** and **11**, respectively (eq 1 and 2).



The critical micelle concentration (cmc) of **5** in 0.01 M sodium bicarbonate at 25 °C is 6.9×10^{-5} M. In our kinetic studies utilizing **5**, vide infra, reactions were carried out at 60 °C. The temperature effect on the cmc of cationic surfactants is generally small,[4] and the cmc at 60 °C would be expected to be no more than 50% higher than the value determined at 25 °C, on the basis of analogy. The formation of vesicles from **6** was consistent with results obtained by gel filtration chromatography,[21] ^1H NMR line width narrowing,[22] and dynamic laser light scattering. Differential

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Table I. Kinetics and Equilibrium Constants for Epimerization of **1–3** in 1 M Aqueous Base at 60 °C

diacid	surfactant	10^6k_1, s^{-1}	10^6k_{-1}, s^{-1}	K_{eq}
1[a]	none	13 ± 1	2.0 ± 0.3	6.5 ± 1.0
1	**5**[b]	33 ± 2	5.0 ± 0.2	6.6 ± 1.0
2	none	17 ± 3	3.6 ± 0.2	4.7 ± 0.6
2	**5**[b]	180 ± 40	40 ± 2	4.5 ± 0.6
2	**6**[c]	120 ± 50	17 ± 3	7.1 ± 1.0
2	CTAB			5.2 ± 0.8[d]
2	DDAB			8.0 ± 1.0[d]
3	none	7.8 ± 0.2	3.0 ± 0.2	2.6 ± 0.3
3	**5**[b]	110 ± 20	49 ± 2	2.2 ± 0.2
3	**6**[c]	130 ± 40	39 ± 3	3.3 ± 0.8
3	CTAB[c]			1.8 ± 0.2[d]
3	DDAB			4.5 ± 0.6[d]

[a] Base used in this experiment was CsOH. KOH was used in all other experiments. Concentration of ketone was 1 mM in all experiments with no added surfactant. [b] 2 mM ketone, 17 equiv of surfactant. [c] 1 mM ketone, 18 equiv of surfactant. [d] Reference 15.

scanning calorimetry[23] of **6** gave a phase-transition temperature of 26 ± 2 °C.

By sonication, a vesicular solution of **6** was prepared in 0.050 M calcein[24] (pH 7.4) and then filtered through 0.4- and 0.2-μm polycarbonate filters. Gel filtration of the resultant solution on Sephadex G-25-80 with 0.0043 M phosphate buffer (pH 7.4; 0.10 M in NaCl and 0.0001 M in EDTA) as eluant gave a fraction containing vesicle-entrapped dye at the void volume. After the fraction was lysed with Triton X-100, its fluorescence increased ca. 10-fold, consistent with the initial presence of vesicles containing a high concentration of calcein whose fluorescence was self-quenched.[24]

A solution of **6** in D_2O was prepared by use of hand shaking, and its ^1H NMR spectrum was recorded. After the solution was sonicated for 1 h, the line width of the methylene signal decreased by a factor of 7 and the peak height increased by a factor of ca. 36, consistent with the formation of vesicles.[22]

A vesicular solution of **6** was prepared in the above pH 7.4 buffer and then filtered through 0.4- and 0.2-μm polycarbonate filters. Analysis of the filtrate by dynamic laser light scattering indicated a single size distribution with a hydrodynamic diameter 202 ± 58 nm. This size is consistent with both multilamellar and large unilamellar vesicles.[2]

Epimerization of Ketones 1–4. The rates of epimerization of the amphiphilic ketones **1–4** were determined in aqueous 1 M base and for **1–3** with 1 M base in the presence of the cleavable surfactants **5** and **6**. Analysis of the approach to equilibrium was monitored by reverse-phase HPLC, and kinetics were determined on at least duplicate runs from both diastereomers. The equilibrium distribution of diastereomers was measured after at least 5 half-lives, and in every case this equilibrium, K_{eq}, was the same within experimental error, when starting from either the meso or (±) diastereomer.

All experiments reported in Table I were at 60 °C and 1 or 2 mM in amphiphilic ketone with a 17- or 18-fold excess of the surfactant host. All solutions were clear and soapy, and there was no indication of precipitation of surfactant or ketone in any of the experiments. The epimerizations follow reversible first-order kinetics, as illustrated by eq 3 with $K_{eq} = k_1/k_{-1}$, and the rate

$$(\pm) \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{meso} \qquad (3)$$

constants could be extracted by standard data analysis.[25] Rate

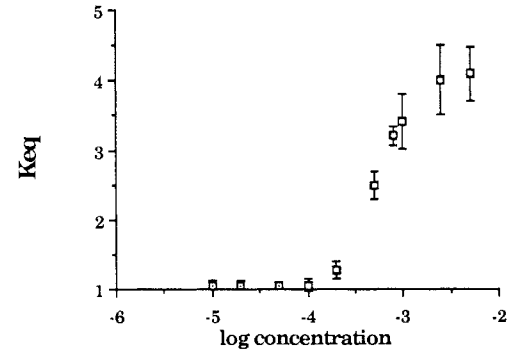

Figure 1. Equilibrium constant for **4** in 1 M KOH at 30 °C vs concentration.

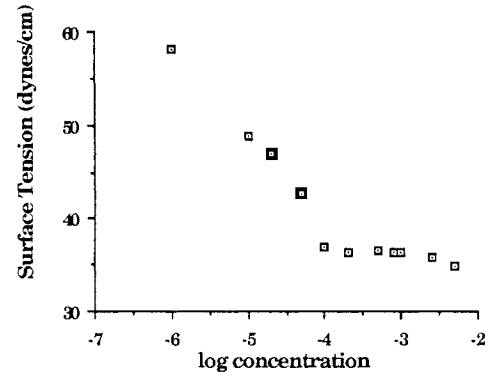

Figure 2. Surface tension for **4** at equilibrium in 1 M KOH at 30 °C vs concentration.

Table II. Rates of Equilibration of **4** in 1 M KOH at 30 °C[a]

concentration, M	10^6k_1, s^{-1}	10^6k_{-1}, s^{-1}
5×10^{-5}	41 ± 3	38 ± 3
1×10^{-3}	19 ± 1	5 ± 2
5×10^{-3}	7 ± 0.2	1.6 ± 0.4
15×10^{-3}	4 ± 0.3	0.8 ± 0.2

[a] For each concentration, at least 10 points were taken over 3 half-lives for both the meso and (±) diastereomers.

and equilibrium constants are presented in Table I. Equilibrium ratios for the ketones **2** and **3** obtained in CTAB and DDAB hosts are also shown.

The rates and equilibria for the diacid **4** were studied at several concentrations and at 30 and 60 °C. In Figure 1 are presented the equilibria established at 30 °C for this diacid at concentrations from 10^{-5} to 5×10^{-3} M. Equilibria obtained were determined from equilibration of both the meso and (±) diastereomers and at least triplicate analysis of duplicate experiments from each diastereomer was carried out. Results similar to the 30 °C experiments shown in Figure 1 were also obtained at 60 °C.

Surface tension experiments were also carried out with ketone **4**. The results of these experiments are presented in Figure 2. It should be noted that the surface tensions reported in Figure 2 represent the surface tension of a 1 M KOH solution of the equilibrium mixture of **4** at the particular concentration reported. At 0.001 M, for example, the surface tension determined is for the equilibrium mixture of **4** diasteromers obtained at this concentration (K_{eq} = 3.5 at 0.001 M, see Figure 1). At 10^{-4} M, the surface tension was determined after equilibrium was established, and this equilibrium was different than that determined at 0.001 M (K_{eq} = 1.05 at 10^{-4} M, see Figure 1). In this way the surface tensions report conditions identical with the conditions used to establish equilibrium at each concentration studied. Attempts were made to determine the cmc's of the pure diastereomers of the diacid **4** in 1 M KOH. Significant equilibration of the diacids occurred during the time required to make the surface tension measurement, however, and these experiments were thus abandoned. The rates of epimerization of the amphiphilic ketone **4** were determined in 1 M base in a manner similar to that reported

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for compounds **1–3**. These rates, determined now at four different concentrations of **4** from 0.05 to 15 mM are reported in Table II.

Discussion

The experiments reported here for the diacids **1–4** indicate that the state of aggregation of the diacid influences both the equilibrium constant for the diastereomers and the rate constants for equilibration. That the equilibrium is dependent on the state of aggregation is shown in Figure 1. At low concentrations of **4** ($<10^{-4}$ M), the equilibrium constant measured is within experimental error of 1.0. At these concentrations, **4** is present as the monomer, and these data indicate that there is no stereochemical preference for one diastereomer over the other as the monomer in water. Increasing the concentration of **4** results in a sharp increase in the equilibrium constant at $\sim 2 \times 10^{-4}$ M until at concentrations greater than 1 mM, K_{eq} exceeds 4.0. Surface tension experiments shown in Figure 2 support the notion that aggregation occurs for **4** at $\sim 2 \times 10^{-4}$ M. The meso diastereomer is favored in the aggregate relative to the (±) diastereomer, and the free energy preference for the former in molecular aggregates is in excess of 1.4 kcal/mol. The preference for the meso diastereomer of **1–3** in molecular aggregates has been discussed.[15] Stated simply, the preferred conformation at the carbonyl link of the two-chain surfactant makes the meso diastereomer a "good" amphiphile, while the (±) compound is not. Rates of equilibration are also dependent on the state of aggregation of the system, and the surfactants **5** and **6** were useful in facilitating the equilibrations.

Surfactants **5** and **6** were stable to the strongly basic conditions of the diacid epimerizations, but they were cleaved to the corresponding diols and water-soluble ketone **13** upon a mild acid workup, thereby allowing the ready extraction and analysis of the diacids by conventional HPLC techniques. Control experiments verified that accurate analyses of diacid ratios can be obtained by this workup procedure.

Micellar catalysis and inhibition are well-studied phenomena that result from the distribution of reactant(s) between the micellar pseudophase and bulk aqueous phase and different reaction rates in the two phases.[4] Specifically, ground- and transition-state stabilization/destabilization and electrostatic and hydrophobic effects can contribute to micellar catalysis/inhibition.

Electrostatic effects are important and reasonably well understood for bimolecular reactions of micellar-bound substrates with ionic reagents in ionic micelles.[2,4] For example, electrostatic considerations would predict an increase or decrease in the observed rate for reaction of an anionic reagent with a substrate bound to a cationic or anionic micelle, respectively, relative to reaction in water. Inverse electrostatic effects on reactivity would result from the substitution of a cationic for an anionic reagent. In general, however, second-order rate constants for reactions within a micelle do not differ much from those in water. Thus, micellar catalysis of bimolecular reactions derives predominantly from the concentration of both reactants into the micellar pseudophase.[2,4]

We suggest that electrostatic effects are primarily responsible for the kinetic behavior of the epimerizations of diacids **1–4** with and without added surfactant. Table I shows that all of the epimerizations occurred more readily in cationic micelles than when no added surfactant was present.

Amphiphilic diacids **2** and **3** form molecular aggregates believed to be large micelles in 1 M KOH, as evidenced by dynamic laser light scattering and surface tension measurements.[14,15] Similar surface activity was observed for diacids **1** in 1 M CsOH. The kinetic experiments with diacids **1–3** without added surfactant were conducted significantly above the respective cmc's. Thus, the anionic character of the substrate micelles in 1 M base would be expected to inhibit the $^-$OH-catalyzed epimerizations, consistent with the above generalizations about electrostatic effects and with inhibition by anionic micelles in other systems.[26,27] This suggestion is supported by the results of our study of the diacid **4**. This diacid was chosen for examination since its cmc is higher than those of the more hydrophobic diacids **1–3**, and kinetics and equilibrations could thus be examined at concentrations where accurate analyses of the diacids were possible.

The kinetic data presented in Table II for equilibration of diacid **4** clearly demonstrate the inhibition of the reaction by the anionic aggregates formed from the diacid. At 5×10^{-5} M **4**, the forward and back rate constants for **4** are equal, within experimental error, and large (40×10^{-6} s^{-1}). At this concentration, we suggest that the diacid is present essentially in monomeric form and the rate obtained represents the rate of equilibration of the monomer. As the concentration is increased, the pseudo-first-order rate constants for the forward and back reaction decrease significantly. Thus at 15 mM the rate constant k_1 is 1 order of magnitude lower than that determined at 5×10^{-5} M and k_{-1} at 15 mM is nearly 50-fold lower than the corresponding rate constant determined at 5×10^{-5} M. It seems reasonable to suggest that the observed rate constants k_1 and k_{-1} should relate to a weighted average of the micellar rate constant and the monomeric rate constant as described in eq 4, where n is the mole fraction of diacid in micellar form.

$$k = [1 - n]k_{\text{monomer}} + [n]k_{\text{micelle}} \quad (4)$$

$$k_1 = [1 - n_{\pm}]k_{1,\text{monomer}} + [n_{\pm}]k_{1,\text{micelle}} \quad (5)$$

$$k_{-1} = [1 - n_{\text{meso}}]k_{-1,\text{monomer}} + [n_{\text{meso}}]k_{-1,\text{micelle}} \quad (6)$$

Equations 5 and 6 suggest that the rates are related to the fractions of diastereomers in the micellar and monomeric forms. One can also assume that $k_{1,\text{monomer}}$ is equal to the rate constant obtained at concentrations below the cmc (41×10^{-6} s^{-1}) and $k_{-1,\text{monomer}}$ is equal to 38×10^{-6} s^{-1}. Furthermore, the rate constants determined at 15 mM are determined at a concentration nearly 100 times that of the cmc, and these can be assumed to be close to k_{micelle}, 4×10^{-6} s^{-1} for k_1 and 0.8×10^{-6} s^{-1} for k_{-1}. With these assumptions and the rate data presented in Table II, we calculate that the mole fraction of micellized (±) diastereomer is 0.60 at 1 mM and 0.92 at 5 mM. For the meso diastereomer, we calculate the mole fraction of micellized meso **4** is 0.88 at 1 mM and 0.98 at 5 mM.

Equations 5 and 6 are simplifications and report average monomer and micellar mole fractions during the course of approach to equilibrium. In fact, as the equilibration occurs, the nature of the aggregate changes since the concentrations of the stereoisomers present in solution change over the course of the experiment. The cmc and the proportion of free and bound substrate will thus vary over the course of the kinetic experiment. Rates of approach to equilibrium appear linear over 3 half-lives, it should be noted.

Since the diacid substrates are amphiphilic, they should form mixed micelles with excess CTAB or **5** in aqueous base that are overall positively charged.[28] Under these conditions, micellar catalysis of diacid epimerization would be expected. There are many examples of bimolecular reactions of micellar-bound substrates with $^-$OH that are catalyzed by cationic micelles, including the hydrolyses of *p*-nitrophenyl acetate, hexanoate, and dodecanoate, where rate enhancements are on the order of 2–5.[27,29]

Micelle–ion interactions and the competition between counterions for a micellar surface have been treated quantitatively with the pseudophase ion exchange (PIE) model.[7,8,30–33] In the present

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(33) Bunton has presented an alternative to the PIE model based on a Poisson–Boltzmann distribution of ions with consideration of Coulombic and specific interactions (Bunton, C. A.; Moffatt, J. R. *J. Phys. Chem.* **1986**, *90*, 538; **1985**, *89*, 4166).

Table III. Relative Rate Constants with and without Surfactant for Epimerization of **1–3** in 1 M Aqueous Base at 60 °C

diacid	surfactant	k_1 rel	k_{-1} rel	K_{eq}[d]	5τ, h
1[a]	none	1	1	6.5 ± 1.0	64
1	**5**[b]	2.5	2.5	6.6 ± 1.0	24
2	none	1	1	4.7 ± 0.6	48
2	**5**[b]	10.5	11.1	4.5 ± 0.6	4.4
2	**6**[c]	7.1	4.7	7.1 ± 1.0	7.1
3	none	1	1	2.6 ± 0.3	89
3	**5**[b]	14.1	16.3	2.2 ± 0.2	6.2
3	**6**[c]	16.7	13.0	3.3 ± 0.8	5.7

[a] Base used in this experiment was CsOH; KOH was used in all other experiments. Concentration of ketone was 1 mM in all experiments with no added surfactant. [b] 2 mM ketone, 17 equiv of surfactant. [c] 1 mM ketone, 18 equiv of surfactant. [d] Error in K_{eq} was dependent on the accuracy of the HPLC analysis of percent meso values.

study, the competition is between Br^- and ^-OH for the surfaces of micellar CTAB and **5**. While a quantitative analysis of our system is inappropriate at such high concentrations of ^-OH and with mixed micelles, it seems sufficient to say that the positively charged micellar host concentrates the diacid substrates and ^-OH, and this results in catalysis of the epimerization.[34] Comparable effects are likely in vesicular hosts DDAB and **6**.[35] Some epimerization could also occur from monomeric diacid free from the surfactant host.

The relative rates of epimerization of diacids **1–3** with and without surfactant **5** or **6** are presented in Table III. In all cases, the addition of **5** increased both k_1 and k_{-1} by approximately the same magnitude. For diacid **1** in cationic micellar **5**, k_1 increased from 1.3×10^{-5} to 3.3×10^{-5} s^{-1}, and k_{-1} from 2.0×10^{-6} to 5.0×10^{-6} s^{-1}. Since the forward and reverse rate constants increased equally (2.5-fold), the K_{eq} of 6.5 remained constant on the addition of surfactant **5**. Similar results were obtained for diacids **2** and **3**. The addition of the bilayer forming surfactant **6** increased the forward rate constant k_1 more than the reverse rate constant k_{-1} for both of the cases studied (see Table III).

The lack of an effect of micellar **5** on K_{eq} is consistent with the loosely organized structures of aqueous micelles.[2] The data suggest that the **5**-diacid mixed micelles differ from the diacid micelles primarily by the accumulation of ^-OH at their surfaces. Overall, this results in catalysis of epimerization but does not alter the equilibrium. The increase of K_{eq} on going from the diacid micelles to the **6**-diacid mixed vesicles may be due to either stabilization of the meso diastereomer or destabilization of the (±) diastereomer by the mixed vesicles relative to the diacid micelles. The data do not allow differentiation of these possibilities.

Diacids **2** and **3** are presumably more ordered in the bilayer structures formed from surfactant **6** than in the micellar structures formed from the surfactant **5**, in response to the greater order of vesicles compared to micelles.[2] In a bilayer, the carboxylate head groups of amphiphiles, such as **1–3**, should reside predominantly at the aggregate–water interface with the hydrocarbon tails oriented parallel to those of the surfactant host. It is perhaps this ordered bilayer environment, which offers considerably less flexibility for the alkyl chains of the substrate than a micellar environment, that reinforces the preference for the meso diastereomer relative to the (±) diastereomer. It should be noted that while effects on equilibria are noticeable and outside experimental error, a change in K_{eq} from 4.5 to 7.1 (diacid **2** in **5** and in **6**) amounts to only 0.3 kcal/mol at 60 °C.

The effects of **5** and **6** on equilibration times are also shown in Table III. The time required to reach equilibrium is taken as 5τ, where the half-life, τ, is equal to $\ln 2/(k_1 + k_{-1})$. Note that the rate enhancements experienced by the diacid substrates in the cationic surfactant hosts are in the order **3** > **2** > **1**. Thus, the greater the distance between the ketone linkage and the carboxylate groups, the greater the catalytic effect. This trend may reflect an electrostatic effect on local [^-OH] by the carboxylate groups that decreases with distance from them. Consequently, the effective [^-OH]'s experienced by the ketone linkages are in the order **3** > **2** > **1**.

(34) The PIE model may not be appropriate for counterions like ^-OH that bind inefficiently to micelles (Abuin, E. B.; Lissi, E.; Araujo, P. S.; Alexio, R. M. V.; Chaimovich, H.; Bianchi, N.; Miola, L.; Quina, F. H. *J. Colloid Interface Sci.* **1983**, *96*, 293). In any event, there will be electrostatic accumulation of ^-OH at the positively charged micelle surface.

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Summary

While there are many previous reports of kinetics on substrates associated with micelles and other aggregates, most of those earlier studies have relied on measurement of a colored reaction product, such as *p*-nitrophenoxide, to monitor reaction rate. Product isolation from surfactant aggregates is usually difficult, and the measurement of kinetics in such systems by product isolation is virtually impossible. The cleavable surfactants **5** and **6** make the isolation of amphiphilic products of micellar/vesicular reactions routine and allow measurement of the kinetics of epimerization of the diacids **1–3**.

These kinetic studies have shown that the epimerizations of amphiphilic diacids **1–3** in aqueous base are catalyzed by cationic micelle and bilayer-forming surfactants **5** and **6**, respectively. Such catalysis suggests the formation of mixed aggregates composed of diacid and surfactant.

Micelle-forming surfactant **5** increased the forward and reverse rates almost equally in each of the diacid epimerizations. Thus, the effect of **5**'s micelles on equilibrium was about the same as that of the diacid substrate's micelles. The lack of an effect of **5** on K_{eq} is consistent with the loosely organized nature of aqueous micelles.

With the bilayer-forming surfactant **6**, the reverse rates of epimerization of diacids **2** and **3** were increased to a lesser extent than the forward rates. Therefore, the values of K_{eq} increased relative to those obtained with micellar **2** and **3** alone. This differential in catalysis of the forward and reverse rates on going to surfactant **6** may be due to an increase in the energy of the (±) diastereomer or to a decrease in that of the meso diastereomer.

These interpretations for the diacids **1–3** are supported by experiments with the lower molecular weight diacid **4**. Equilibrations of this diacid above and below the cmc show that perturbation of the equilibrium from 1.0 to >4.0 is the result of aggregate formation, and furthermore, the rate of equilibration is dramatically reduced by formation of these negatively charged aggregates.

Experimental Section

General Procedures. ^1H (270 MHz, 300 MHz) and ^{13}C (67.8 MHz, 75.43 MHz) NMR spectra were recorded on JEOL FX-270 and Varian XL-300 spectrometers with Me_4Si as internal standard in $CDCl_3$. Electron impact (EI) high-resolution mass spectra (HRMS) were obtained on a VG-ZAB 1F spectrometer and at the Midwest Center for Mass Spectrometry (Lincoln, NE). Fluorescence measurements were made on a Perkin-Elmer LS-5 spectrometer. The cmc of **5** was measured as before.[36] The cmc of **4** was measured as reported earlier.[15] All melting points are uncorrected. Elemental analyses were performed by Atlantic Microlab (Atlanta, GA). Analytical HPLC was performed on two Altex Ultrasphere ODS analytical HPLC columns (5 μm, 4.6 mm × 25 cm) obtained from Beckman, Inc. An LDC Refractomonitor III was used for peak detection. THF was distilled from potassium and benzophenone immediately before use.

Synthesis of Surfactants and Data for Aggregates. (±)-6,8-Dihexyl-7-oxotridecanedioic Acid (4). The diacid was prepared as described for **1–3**:[15] ^1H NMR (300 MHz) δ 2.5 (br m, 2 H, α to ketone), 2.3 (t, 4 H, α to acid), 1.6 (br m, 8 H), 1.2 (br m, 26 H), 0.88 (t, 6 H, CH_3); ^{13}C NMR (75.4 MHz) δ 216.1, 179.9, 50.8, 33.9, 31.6, 30.8, 29.97, 29.4, 27.2, 26.9, 24.8, 22.6, 14.1. Anal. Calcd for $C_{25}H_{46}O_5$: C, 70.38; H, 10.87. Found: C, 70.63; H, 11.07.

***meso*-6,8-Dihexyl-7-oxotridecanedioic Acid (4).** The diacid was prepared as described for **1–3**:[15] ^1H NMR (300 MHz) δ 2.5 (br m, 2 H, α to ketone), 2.3 (t, 4 H, α to acid), 1.6 (br m, 8 H), 1.2 (br m, 26 H), 0.88 (t, 6 H, CH_3); ^{13}C NMR (75.4 MHz) δ 216.2, 179.9, 50.9, 33.9, 31.7, 30.6, 30.2, 29.5, 27.3, 26.9, 24.8, 22.6, 14.1. Anal. Calcd for $C_{25}H_{46}O_5$: C, 70.38; H, 10.87. Found: C, 70.62; H, 11.05.

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2-Methyl-2-(3-bromopropyl)-4-tetradecyl-1,3-dioxolane (8). By a literature procedure,[19b] 8.00 g (31.0 mmol) of **7** (Aldrich, 90% recrystallized from MeOH, mp 69–70 °C) and 4.19 g (25.4 mmol) of 5-bromo-2-pentanone[37] gave 9.40 g (91%) of **8** as an oil: ^{1}H NMR δ 3.98–4.17 (m, 2 H, cis-OCHCHO), 3.38–3.56 (m, 3 H, CH_2Br, OCH), 1.98 (m, 2 H, CH_2CH_2Br), 1.79 (m, 2 H, $CH_2CH_2CH_2Br$), 1.15–1.68 (m containing a large singlet at 1.26 and singlet shoulders at 1.31 and 1.35, 29 H total, $(CH_2)_{13}$ and $OCCH_3$), 0.88 (t, 3 H, CH_3); IR (neat) 2920 (s), 2865 (s), 1455 (s), 1382 (m), 1305 (w), 1258 (m), 1115 (w), 1060 (s), 886 (m), 729 cm^{-1} (m); EI HRMS calcd for $C_{20}H_{38}{}^{79,81}BrO_2$ (M – CH_3) 389.2055 and 391.2037, found 389.2040 and 391.2067; calcd for $C_{18}H_{35}O_2$ (M – $CH_2CH_2CH_2Br$) 283.2636, found 283.2622; M was not observed.

[3-(4-Tetradecyl-2-methyl-1,3-dioxolan-2-yl)propyl]trimethylammonium Bromide (5). By a literature procedure,[19b] 8.40 g (20.7 mmol) of **8** was converted to **5**. Crude material was recrystallized two times from EtOAc to give 6.70 g (70%) of **5**: mp 113–180 °C; ^{1}H NMR δ 4.07 (m, 2 H, *cis*-OCHCHO), 3.38–3.69 (m + s at 3.49, 12 H total, $(CH_3)_3N$, CH_2N, and OCH), 1.65–1.98 (m, 4 H, $CH_2CH_2CH_2N$), 1.18–1.65 (m containing a large singlet at 1.26 and singlet shoulders at 1.31 and 1.35, 29 H total $(CH_2)_{13}$ and $OCCH_3$), 0.88 (t, 3 H, CH_3); IR (Nujol) 1252 (m), 1155 (w), 1100 (m), 1070 (w), 1041 (m), 940 (w), 900 (w), 820 cm^{-1} (w); cmc 6.9 × 10^{-5} M in 0.01 M $NaHCO_3$ (25 °C). By ^{13}C NMR spectroscopy (inverse gated spectrum; C-2 of dioxolane ring), this material consisted of an approximately 1:1 mixture of cis and trans diastereomers. Anal. Calcd for $C_{24}H_{50}BrNO_2 \cdot 0.25H_2O$: C, 61.45, H, 10.85. Found: C, 61.51, 61.44; H, 10.86, 10.92.

17-Tetratriacontyne (10). By a literature procedure,[38] 10.0 g (40.0 mmol) of **9** (Farchan) and 11.6 g (38.0 mmol) of 1-bromohexadecane (Aldrich) gave 15.3 g of crude product that was column chromatographed on basic alumina (Fisher, Brockman Activity I) packed in hexane with hexane elution to yield 13.4 g of **10**. Recrystallization of this material four times from hexane gave 11.4 g (63%) of **10**: mp 55–56.5 °C; ^{1}H NMR δ 2.14 (t, J = 7 Hz, 4 H, $CH_2C{\equiv}C$), 1.14–1.62 (m + s at 1.26, 56 H, $(CH_2)_{14}$), 0.88 (t, 6 H, CH_3); IR (KBr) 2916 (s), 2849 (s), 1472 (s), 1116 (m), 717 cm^{-1} (m). Anal. Calcd for $C_{34}H_{66}$: C, 85.99; H, 14.00. Found: C, 86.01; H, 13.95.

17,18-Tetratriacontanediol (11). A mixture of 4.04 g (8.52 mmol) of **10**, 142 mg of 5% Pd on $BaSO_4$ (Aldrich), 200 mL of EtOH, and 80 mL of hexane was held under 60 psi of H_2 at 25 °C for 5 h and then filtered and rotary evaporated. The resultant crude product was column chromatographed on silica gel packed in hexane with hexane elution to yield 3.73 g of alkene. Recrystallization of this material from 2:1:1 (v/v/v) hexane/MeOH/EtOAc gave 3.48 g (86%) of 17-tetratriacontene : mp 65–67 °C; ^{1}H NMR δ 5.35 (m, 2 H, CH=CH), 1.87–2.18 (m, 4 H, CH_2CH), 1.14–1.49 (m + s at 1.25, 56 H, $(CH_2)_{14}$), 0.88 (t, 6 H, CH_3); EI HRMS calcd for $C_{34}H_{68}$ 476.5322, found 476.5352.

A mixture of 6.17 g (13.0 mmol) of the above alkene, 107 mg (0.332 mmol) of Bu_4NBr (Aldrich), 52 mL (0.46 mol) of 30% H_2O_2/H_2O, 260 mL of 88% HCO_2H, and 320 mL of C_6H_6 was stirred at 45 °C for 24 h. The aqueous layer was extracted with three 25 mL portions of C_6H_6, and the combined organic layers were added to 260 mL of HCO_2H containing 107 mg of Bu_4NBr. The mixture was refluxed for 15 h, and the aqueous layer was extracted with three 25-mL portions of C_6H_6. The combined organic layers were added to a solution of 60 g of KOH in 350 mL of MeOH, and the resultant mixture was refluxed for 12 h, added to 150 mL of H_2O, and adjusted to pH 7 with concentrated hydrochloric acid. The aqueous layer was extracted with three 50-mL portions of C_6H_6. The combined organic layers were washed with saturated aqueous NaCl and rotary evaporated to give 6.51 g of **11**. Recrystallization of this material from 260 mL of EtOAc gave 6.24 g (94%) of **11** as a 1:1 mixture of erythro and threo diastereomers: mp 91–111 °C; ^{1}H NMR δ 3.51 and 3.60 (equal m's, 2 H total, $CHOH$, threo and erythro, respectively,[39] 1.94 and 1.78 (equal d's, J = 4 Hz for each, 2 H total, $CHOH$, threo and erythro, respectively[39]), 1.20–1.62 (m + s at 1.25, 60 H, $(CH_2)_{15}$), 0.88 (t, 6 H, CH_3); IR (Nujol) 3220 (s), 1115 (w), 1075 cm^{-1} (m); EI HRMS calcd for $C_{34}H_{70}O_2$ 510.5375, found 510.5328. Standard procedures[39,40] for alkene antihydroxylation with H_2O_2/HCO_2H failed with 17-tetratriacontene, presumably due to its extreme hydrophobic character.

2-Methyl-2-(3-bromopropyl)-4,5-dihexadecyl-1,3-dioxolane (12). By a literature procedure,[19b] 2.00 g (3.92 mmol) of **11** and 0.815 g (4.94 mmol) of 5-bromo-2-pentanone[37] gave 2.25 g (87%) of **12** as a wax: ^{1}H NMR δ 3.35–4.12 (m, 4 H, CH_2Br, OCH), 1.96 (m, 2 H, CH_2CH_2Br), 1.75 (m, 2 H, $CH_2CH_2CH_2Br$), 1.17–1.56 (m + s at 1.25, 33 H, $(CH_2)_{15}$ and CH_3CO), 0.88 (t, 6 H, CH_3) IR (neat) 2839 (s), 1435 (m), 1365 (m), 1285 (w), 1236 (m), 1202 (w), 1083 (m), 884 (w), 711 cm^{-1} (w). EI HRMS calcd for $C_{38}H_{74}{}^{79,81}BrO_2$ (M – CH_3) 641.4873 and 643.4852, found 641.4890 and 643.4824; calcd for $C_{36}H_{71}O_2$ (M – $CH_2CH_2CH_2Br$) 535.5455, found 535.5486; M was not observed.

[3-(4,5-Dihexadecyl-2-methyl-1,3-dioxolan-2-yl)propyl]trimethylammonium Bromide (6). By a literature procedure,[19b] 5.00 g (7.60 mmol) of **12** was converted to 4.54 g of crude **6**. This material was column chromatographed on a 2 cm (i.d.) × 35 cm column of the aluminum used for **10** packed in $CHCl_3$ with elution by 200 mL of $CHCl_3$, followed by 250 mL of 1:1 (v/v) MeOH/$CHCl_3$. With the latter, 3.80 g of **6** was obtained, which was recrystallized from 20 mL of EtOAc to give 3.17 g (58%) of **6**: mp 120–170 °C; ^{1}H NMR δ 3.38–4.18 (m + s at 3.50, 13 H, $(CH_3)_3N$, CH_2N, OCH), 1.60–1.95 (m, 4 H, $CH_2CH_2CH_2N$), 1.15–1.60 (m + s at 1.25, 33 H, $(CH_2)_{15}$ and CH_3CO), 0.88 (t, 6 H, CH_3); IR (KBr) 2919 (s), 2851 (s), 1468 (m), 1381 (w), 1271 (w), 1215 (w), 1115 (m), 1064 (w), 958 (w), 911 (w), 721 cm^{-1} (m). By ^{13}C NMR (inverse gated spectrum; C-2 of dioxolane ring) this material was an approximately 2:1:1 mixture of three diastereomers: r-2, c-4, t-5; r-2, c-4, c-5; and r-2, t-4, t-5 (with respect to the dioxolane ring). Anal. Calcd for $C_{42}H_{86}BrO_2N \cdot 0.25H_2O$: C, 69.48; H, 12.08. Found: C, 69.56; H, 12.02.

Gel Filtration Chromatography.[21] Calcein (Eastman Kodak) purified[24,41] by column chromatography on Sephadex LH-20 was dissolved in H_2O by the addition of 1.0 M NaOH to give a 0.05 M solution (pH 7.4). In a 25-mL round-bottomed flask, a solution of 30.0 mg (0.0419 mmol) of **6** in 5.0 mL of $CHCl_3$ (spectral grade, J. T. Baker) was rotary evaporated to dryness and for an additional 20 min. Then, 5.0 mL of the above calcein solution was added, and the system was sonicated for 5 h (50 W, bath, 60 °C). The resultant vesicular solution was first filtered through two 25-mm 0.4-μm filters and then through two 25-mm 0.2-μm filters (polycarbonate, Nuclepore 110607 and 110606, respectively) with an ultrafiltration cell (Amicon Model 8010) at 40 psi of N_2. Then, 0.100 mL of the filtrate was eluted through a 1 cm (i.d.) × 31 cm column of Sephadex G-25-80 with 0.0043 M phosphate buffer (pH 7.4, 0.10 M in NaCl and 0.0001 M in EDTA).[42] The eluate was monitored at 254 nm (ISCO Model UA-5 absorbance monitor), and a 2.7-mL fraction containing vesicle-entrapped dye was collected at the void volume, as determined with the blue dextran 2000 (Pharmacia). With excitation at 490 nm, the fluorescence of the solution at 525 nm increased by ca. 10-fold at 25 °C after 0.20 mL of aqueous 10% (w/w) Triton X-100 was added and the solution was held at 60 °C for 1 h.

Dynamic Laser Light Scattering. To a thin film of 30.0 mg of **6**, as prepared above, was added 5.0 mL of the above phosphate buffer, and the system was sonicated for 5 h (50 W, bath, 60 °C). The resultant vesicular solution was filtered through the 0.4- and 0.2-μm filters, as above, and then analyzed at 25 °C with a Coulter Model N4 submicron particle analyzer (4 mW He Ne laser, 632.8 nm; 90° scattering angle). A single vesicle size distribution with a hydrodynamic diameter of 202 ± 58 nm was detected.

^{1}H NMR Line Width Measurements.[22] By use of hand shaking, 6.0 mg (0.0084 mmol) of **6** was dissolved in 1.0 mL of D_2O (99.96% D). The methylene signal at δ 0.3–2.6 in the ^{1}H NMR spectrum of the resultant solution had a line width of ca. 400 Hz at half-height. After the solution was sonicated for 1 h (50 W, bath, 60 °C), the line width of the methylene signal decreased to ca. 60 Hz, and the peak height increased by a factor of ca. 36.

Differential Scanning Calorimetry.[23] A vesicular solution, prepared as for the light scattering study, was added to a microconcentrator (30 000 MW cutoff, Amicon Centricon-30). The microconcentrator was centrifuged at 6000 rpm and 10 °C for 2 h. The resultant surfactant pellet was analyzed with a Perkin-Elmer Model DSC-1B differential scanning calorimeter. A phase-transition temperature of 26 ± 2 °C was detected.

Reduction of Ketones for Stereochemical Proof. Synthesis and Characterization of Triols. The two diastereomers for each diacid (3,3′-**1**, 6,6′-**2**, 9,9′-**3**, and **4**[15] were independently converted to the dimethyl esters with excess diazomethane. In a typical procedure, 10 mg (0.020 mmol) of diacid diastereomer was reacted with excess diazomethane in diethyl ether. After evaporation of residual CH_2N_2 by bubbling argon into the solution, the solvent was removed under reduced pressure. The residue

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was dissolved in dry THF, and 40 mg (1 mmol) of $LiAlH_4$ was added to the solution. Workup consisted of the dropwise addition of 40 μL of H_2O, 40 μL of 15% NaOH, and 120 μL of H_2O. The resulting white precipitate was filtered and discarded, and the solvent was removed under reduced pressure.

From symmetry arguments, it is evident that after subjection to the above procedure the (±) diastereomer yields *one* triol and the meso diastereomer yields *two* triols. These triols were separated by normal-phase flash chromatography (50/50 EtOAc/hexane) or by RP-HPLC (99/1/0.1 or 955/45/1 CH_3OH/H_2O/AcOH). The later eluting ketone diacid diastereomer yields two triols in all cases (**1**–**4**). The stereochemistry of the later eluting isomer for the 6,6′ and 9,9′ diacids was confirmed as the meso diastereomer by X-ray crystal structure determinations.[15] The stereochemical assignment for the 3,3′ diacid diastereomers was made by chemical methods, as described above. The characterization data for the 3,3′ triols follow.

3,3′ triol diastereomer A from the (±) diacid diastereomer 1: RP-HPLC t_R 30 min (0.7 mL/min, 99/1/0.1 CH_3OH/H_2O/AcOH); ^{13}C NMR (75.4 MHz) δ 76.4, 61.3, 39.6, 37.9, 32.8, 31.9, 31.7, 30.3, 30.0, 29.7, 29.4, 27.35, 26.7, 26.4, 26.0, 22.7, 14.1; ^1H NMR (300 MHz) δ 3.7 (br m, 4 H), 3.4 (br m, 1 H), 1.7 (br m, 4 H), 1.4 (br, 48 H), 0.85 (t, 6 H); HRMS M + Li calcd 491.5016, observed 491.5015.

3,3′ triol diasteromer B from the meso diacid diastereomer 1: RP-HPLC t_R 22 min (0.7 mL/min, 99/1/0.1 CH_3OH/H_2O/AcOH); ^{13}C NMR (75.4 MHz) δ 75.9, 60.3, 38.0, 33.2, 31.9, 30.1, 29.7, 29.35, 28.1, 27.2, 22.7, 14.1; ^1H NMR (300 MHz) δ 3.7 (br m, 4 H), 3.4 (br m, 1 H), 1.7 (br, 4 H), 1.3 (br, 48 H), 0.85 (t, 6 H); HRMS M + Li calcd 491.5016, observed 491.4998.

3,3′ triol diastereomer B′ from the meso diacid diastereomer 1: RP-HPLC t_R 36 min (0.7 mL/min, 99/1/0.1 CH_3OH/H_2O/AcOH); ^{13}C NMR (75.4 MHz) δ 60.0, 38.9, 31.9, 30.7, 30.0, 29.7, 29.35, 26.7, 22.7, 14.1; ^1H NMR (300 MHz) δ 3.75 (br m, 2 H), 3.65 (br m, 2 H), 3.4 (br t, 1 H), 1.8 (2 H), 1.65 (2 H), 1.3 (br, 48 H), 0.85 (t, 6 H); HRMS M + Li calcd 491.5016, observed 491.5023.

Kinetic Methods. Equilibrations for kinetic runs were carried out in custom-designed long-neck flasks equipped with a Teflon stopcock, which could be opened for the removal of aliquots. The reaction vessel was submerged approximately 6–8 in. deep into the oil bath, and aliquots were removed at the appropriate time via syringe. The oil bath was equipped with a thermistor and an ultrasensitive relay (Princo T-688) connected to heating coils. The bath was stirred and maintained at 60.0 ± 0.1 °C during the equilibrations. The epimerization kinetics for the approach to equilibrium were studied by using both (±) and meso as the starting diacid diastereomer.

In a typical experiment, (±) or meso diastereomer was placed in the flask, and titrated KOH (1.0 ± 0.01 N) or KOH/surfactant stock solution was added. The solution was vortexed and immediately placed into the constant temperature bath. Each aliquot was quenched immediately after removal with 10% HCl(aq). In cases where hydrolyzable surfactant was present, 10 min was allowed to assure the complete cleavage of the surfactant. This solution was extracted with CH_2Cl_2 (three times, 50 mL), and the organic layer was dried (Na_2SO_4) and filtered. The solvent was then removed under reduced pressure. Any solid present was filtered before injection onto the HPLC.

The ratio of meso/(±) for each time point was measured in at least triplicate by RP-HPLC. In general, the diacids were analyzed, but occasionally contamination hindered analysis. In such cases, it was necessary to convert the diacid to the dimethyl esters with diazomethane before analysis. Control experiments verified that valid analyses within reasonable error limits were obtained by using the above procedures.

The forward and reverse rate constants were calculated from the percent meso values determined at various time points during diacid equilibrations with either the (±) or meso diastereomer as starting material. In either case, percent meso values were converted to molar concentrations for the kinetic analysis. The simple equilibrium which was studied is represented in eq 3 (see text).

Equations 7a and 7b show the relationship of the forward and reverse rate constants to the raw kinetic data with either (see reference 25 for derivation) the (±) or meso diastereomer as starting material. The extraction of the individual rate constants is possible since K_{eq} values are known.

$$\ln [([\pm]_t - [\pm]_{eq})/([\pm]_{intial} - [\pm]_{eq})] = -(k_1 + k_{-1})_t \quad (7a)$$

$$\ln [([meso]_t - [meso]_{eq})/([meso]_{initial} - [meso]_{eq})] = -(k_1 + k_{-1})t \quad (7b)$$

The τ values, or half-lives, are defined as ln 2 times the reciprocal of the sum of the forward and reverse rate constants in this particular equilibrium.[25] The time required for these epimerizations to reach equilibrium starting with either diastereomer is taken as 5 times the half-life τ.

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Registry No. (±)-**1**, 112925-82-3; *meso*-**1**, 112925-84-5; (±)-**2**, 103346-29-8; *meso*-**2**, 103346-30-1; (±)-**3**, 103346-27-6; *meso*-**3**, 103346-28-7; (±)-**4**, 114838-50-5; *meso*-**4**, 114838-51-6; *cis*-**5**, 114838-52-7; *trans*-**5**, 114838-62-9; **6** (isomer 1), 103346-30-1; **6** (isomer 2), 114838-59-4; **6** (isomer 3), 114838-60-7; **7**, 6920-24-7; **8**, 114838-54-9; **9**, 629-89-0; **10**, 114838-55-0; *erythro*-**11**, 114838-56-1; *threo*-**11**, 114838-57-2; **12**, 114838-58-3; 5-bromo-2-pentanone, 3884-71-7; 1-bromohexadecane, 112-82-3; tetratriacontene, 57-09-0; (±)-13,15-bis(2-hydroxyethyl)-14-heptacosanol, 114838-61-8; *meso*-13,15-bis(2-hydroxyethyl)-14-heptacosanol (isomer 1), 114924-35-5; *meso*-13,15-bis(2-hydroxyethyl)-14-heptacosanol (isomer 2), 114924-36-6.