1730, 1645, 1450, 1435, 1185 cm^{-1}. When a sample of this epimeric mixture was stirred with 0.3 equiv of lithium diisopropylamide in dry tetrahydrofuran or with 1 equiv of sodium methoxide in methanol, each at 20 °C for 2 days, the epimeric ratio was not changed. However, a sample kept at reflux for 7 days in a 1% sodium methoxide in methanol solution showed an epimeric ratio of 1.2:1.0 of the GC faster moving trans to the cis epimer.

Methyl 3,4-Epoxy-5-ethylcyclohexanecarboxylates (9). To 1.523 g (9.06 mmol) of the epimeric esters **8**, dissolved in 10 mL of dichloromethane, was added 2.00 g (14.4 mmol) of *m*-chloroperbenzoic acid at 0 °C.

After 20 h at 20 °C a saturated solution of Na_2SO_3 was added and the mixture was poured into chloroform. The separated organic phase was washed with saturated $NaHCO_3$, water, and brine, dried (Na_2SO_4), and concentrated under vacuum. Tube distillation (oven 50–60 °C) at 0.001 mm gave 1.337 g (80%) of a mixture of stereoisomeric epoxides; 100-MHz NMR ($CDCl_3$) δ 1.00 (t, 3 H), 3.20 (d, 2 H), 3.70 (s, 3 H); GC–mass spectrum with a 30-m SE 54 silica capillary column, showed three fractions in a ratio of 34:28:38, with relative retention times of 39, 43.5, and 45 min at 60 °C or 8.5, 10.3, and 11.0 min at 120 °C, which had identical fragmentation patterns except for a somewhat reduced fragment peak at 107 for the later fractions: *m/z* (relative intensity) 184 (M^+, 0.6), 169 (7), 155 (20), 125 (35), 124 (41), 115 (13), 109 (15), 107 (31 or 17) 100 (22), 97 (10), 96 (17), 95 (34), 91 (10), 87 (17), 83 (29), 81 (38), 79 (32), 77 (12), 71 (17), 70 (15), 69 (35), 68 (24), 67 (54), 65 (11), 59 (38), 57 (22), 56 (10), 55 (100), 54 (17), 53 (32). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.44; H, 8.67.

2-(2-Indol-3-yl-1-oxoethyl)-6-*endo*-hydroxy-7-ethyl-2-azabicyclo[2.2.2]octanes (10a,b). A solution of 390 mg (3.06 mmol) of tryptamine and 564 mg (3.06 mmol) of the stereoisomeric epoxides **9** in 3 mL of ethanol was heated at reflux for 12 h and then concentrated under vacuum. The residue was heated at 210–220 °C for 3.5 h, then cooled, and heated at reflux with 5 mL of methanol and 3 mL of 10% aqueous NaOH for 1 h. Concentration and partitioning of the residue between dichloromethane and successive portions of water, 5% HCl, and brine and concentration of the dried (Na_2SO_4) extract gave 444 mg (48%) of a white foam with TLC (silica, 1:1 $CHCl_3$:acetonitrile) R_f 0.41 for a major component and R_f 0.58 for a minor component. Crystallization from ethyl acetate and hexane gave a sample with mp ≈140 °C, recrystallized to 145–146 °C: mass spectrum, *m/z* (relative intensity) 312 (M^+, 23), 182 (13), 144 (47), 143 (100), 130 (48), 57 (21), 55 (22), 43 (48); IR (KBr) ν_{max} 3320, 2960, 2930, 2875, 1625, 1480, 1455, 1432, 1091, 1073, 745 cm^{-1}; 250-MHz NMR ($CDCl_3$ on sample mp 140 °C) δ 0.85 and 0.91 (two t, 1:1.3, 3 H), 1.21–1.45 (m, 3 H), 1.60–1.80 (m, 2 H), 1.93–2.36 (m, 3 H), 2.45–2.55 (m, 1 H), 3.03 (t, 2 H), 3.27–3.33 (m, 1.5 H), 3.62–3.88 (m, 1.5 H), 3.95–4.15 (m, 1 H), 7.06–7.25 (m, 3 H), 7.37 (d, 1 H), 7.64 (d, 1 H), 8.02 (s, 1 H). Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 73.19; H, 7.63; N, 8.80.

2-(2-Indol-3-yl-1-oxoethyl)-6-*endo*-(tosyloxy)-7-*exo*-ethyl-2-azabicyclo[2.2.2]octane (11a). A solution of 222 mg (0.71 mmol) of the hydroxide **10** in 1 mL of pyridine was cooled to 0 °C and 135 mg (0.71 mmol) of *p*-toluenesulfonyl chloride added. After 2 h at 0 °C, 60 h at −25 °C, and 2 h at 20 °C, the reaction mixture was poured into 15 mL of iced water and extracted with dichloromethane. The extract was washed with brine, dried (Na_2SO_4), and concentrated to 291 mg (85%) of crude tosylate. Crystallization from methanol gave a sample with mp ≈148 °C which showed about 25% contamination by the 7-*endo*-ethyl epimer by NMR δ 0.86 (t, 0.25 × 3 H). A recrystallized sample had mp 156–157 °C: TLC (silica, 1.4:1 chloroform:acetonitrile) R_f 0.8; IR (KBr) ν_{max} 3260, 3060, 2960, 2920, 2873, 1655, 1579, 1455, 1350, 1196, 1185, 963, 866, 740 cm^{-1}; 250-MHz NMR ($CDCl_3$) δ 0.83 (t, 3 H), 1.0–1.50 (m, 4 H), 1.80–2.15 (m, 3 H), 2.39 (s, 3 H), 2.42–2.50 (m, 1 H), 3.00 (t, 2 H), 3.08–3.21 (m, 1 H), 3.43–3.50 (m, 1 H), 4.15–4.28 (m, 2 H), 7.09–7.29 (m, 5 H), 7.36–7.55 (m, 3 H), 7.63 (d, 1 H), 8.09 (s, 1 H). Anal. Calcd for $C_{26}H_{31}N_2O_4S$: C, 66.78; H, 6.68; N, 5.99; S, 6.86. Found: C, 66.71; H, 6.53; N, 5.84; S, 6.98.

5-Oxoibogamine (12). A suspension of 200 mg (0.43 mmol) of the tosylate **11** and 75 mg (0.64 mmol) of aluminum chloride in 20 mL of toluene was heated at 100 °C for 10 h. The cooled mixture was concentrated under vacuum and 25 mL of water was added to the residue. After 2 h the water was decanted and the residue triturated with ethanol to give 52 mg (42%) of the racemic lactam **12**. A sample recrystallized from methanol had mp 265–267 °C. HPLC: Micro Porasil 1 ft column, chloroform:acetonitrile 1.4:1, flow rate 1.5 mL/min, R_t 3.75 min; 250-MHz NMR ($CDCl_3$) δ 0.96 (t, 3 H), 1.35–1.56 (m, 3 H), 1.70–2.02 (m, 3 H), 2.19 (dt, 1 H), 2.65 (brd s, 1 H), 2.93–3.06 (m, 1 H), 3.10–3.38 (m, 3 H), 3.98 (s, 1 H at C21), 4.57 (p, 1 H), 7.04–7.19 (m, 2 H), 7.25 (d, 1 H), 7.45 (d, 1 H), 7.75 (s, 1 H). IR (KBr) ν_{max} 3240, 2960, 2935, 2875, 1644, 1618, 1462, 1369, 1330, 1248, 1161 cm^{-1}; IR (film) ν_{max} 3280 (NH), 1655 (CO) cm^{-1}. For comparison, a sample of natural ibogamine was oxidized to the corresponding lactam.[25] The racemic and nonracemic samples showed identical IR and 250-MHz NMR solution spectra and the same HPLC retention times.

***dl*-Ibogamine (1).** A solution of 22 mg (0.070 mmol) of the racemic lactam **12** was dissolved in 1 mL of dry tetrahydrofuran and added dropwise to 0.5 mL (0.5 mmol) of a 1 M solution of lithium aluminum hydride. The mixture was heated at reflux for 6 h and cooled, and 0.02 mL of water was added, followed by 0.02 mL of 15% NaOH and 0.06 mL of water. Filtration and concentration gave 15 mg (72%) of an oily product which corresponded by TLC (silica, 1% methanol in dichloromethane) R_f 0.35 to natural ibogamine. Preparative TLC and crystallization from aqueous ethanol provided a sample with mp 127–129 °C (lit.[10,12,14] mp 126–131 °C).

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Monochlorination of *n*-Alkyl Phenyl Ethers in Micellar Sodium Dodecyl Sulfate

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The effect of chain length on the regioselectivity and rate of monochlorination of C_6H_5OR (1: **a**, R = *n*-C_5H_{11}; **b**, R = *n*-C_9H_{19}; **c**, R = *n*-$C_{12}H_{25}$) with Cl_2 in micellar sodium dodecyl sulfate was determined. On going from **1a** to **1b** to **1c**, only modest changes were observed in the para/ortho product ratio and in relative rate. These results were interpreted to indicate that the hydrophilic character of C_6H_5O dominates the lipophilic character of R in the micellar reactivity of the ethers.

The ability of dynamic multimolecular surfactant aggregates to control the selectivity of organic reactions has been investigated with several systems.[2] Previously, we reported[3] that for monohalogenation of $C_6H_5OC_5H_{11}$-*n* with

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Table I. Monochlorination of *n*-Alkyl Phenyl Ethers[a]

entry	medium	ether nature	ether concn, M	Cl_2 concn, M	reactn time, min	% yld 2 + 3[b,c]	para/ortho ratio (2/3)[c]
1	0.20 M $NaDodSO_4$	1a	2.0×10^{-4}	1.0×10^{-3}	15	87 ± 2	3.77 ± 0.03
					30	98.0 ± 0.5	3.96 ± 0.03
2	0.20 M $NaDodSO_4$	1b	2.0×10^{-4}	1.0×10^{-3}	15	73 ± 5	4.05 ± 0.04
					30	92 ± 1	4.07 ± 0.06
3	0.20 M $NaDodSO_4$	1c	2.0×10^{-4}	1.0×10^{-3}	15	68 ± 2	4.9 ± 0.2
					30	88 ± 2	4.8 ± 0.1
4	H_2O	1a	8.7×10^{-5}	4.4×10^{-4}	15	89 ± 2	1.31 ± 0.04
					30	98 ± 1	1.35 ± 0.01
5	0.20 M $NaDodSO_4$	1a	8.7×10^{-5}	4.4×10^{-4}	15	33 ± 3	3.2 ± 0.1
					30	51 ± 3	3.4 ± 0.1
6	0.20 M $NaDodSO_4$	1a	0.032	0.018	1	46 ± 5	4.5 ± 0.3
					5	55 ± 3	4.4 ± 0.3
7	40:60 (v/v) H_2O–1,4-dioxane	1a	2.0×10^{-4}	2.0×10^{-4}	68[d]	44	3.2
					90[d]	74	3.2
8	40:60 (v/v) H_2O–1,4-dioxane	1b	2.0×10^{-4}	2.0×10^{-4}	68[d]	52	3.4
					90[d]	87	3.3
9	40:60 (v/v) H_2O–1,4-dioxane	1c	2.0×10^{-4}	2.0×10^{-4}	68[d]	49	3.6
					90[d]	85	3.2

[a] Entries 1–6 were performed at 25.0 ± 0.1 °C and 7–9 at 22 ± 3 °C. [b] For entries 1–6, by direct calibrated HPLC analysis of the reaction mixture with respect to the total amount of 1, 2, and 3; for entries 7–9, by calibrated GC analysis of the isolated product mixture containing an internal standard and based on the original amount of 1. The recovery of 1 + 2 + 3 with respect to the original amount of 1 was ca. 77% in entry 7 and essentially quantitative in entries 8 and 9. [c] Average deviations are given for the following numbers of individual runs: 4 for entry 1; 3 for 2–5; 2 for 6. [d] Time in hours.

several reagents, the para/ortho product ratios increase on going from H_2O to aqueous micellar media. Herein, we report the influence of chain length on the regioselectivity and rate of monochlorination of a series of C_6H_5OR (1: **a**, R = n-C_5H_{11}; **b**, R = n-C_9H_{19}; **c**, R = n-$C_{12}H_{25}$) in aqueous micellar sodium dodecyl sulfate ($NaDodSO_4$).

The ethers first were individually chlorinated with Cl_2 under several different homogeneous conditions (Table I). Unless noted otherwise, p-ClC_6H_4OR (**2**) and o-ClC_6H_4OR (**3**) were formed to the exclusion of 2,4-$Cl_2C_6H_3OR$ (**4**) and 2,6-$Cl_2C_6H_3OR$ (**5**) during the reaction period. In each case, the percent yield of **2** plus **3** and the para/ortho ratio (**2**/**3**) were determined. All three ethers were chlorinated in 0.20 M $NaDodSO_4$ by using a 2.0×10^{-4} M ether concentration and a 5:1 molar ratio of Cl_2 to 1 (entries 1–3). Ether **1a**, unlike **1b** and **1c**, has a detectable solubility in H_2O and an 8.7×10^{-5} M solution was chlorinated with a 5:1 molar ratio of Cl_2 to ether (entry 4). Analogous reactions were performed by using the same concentrations in 0.20 M $NaDodSO_4$ (entry 5). Chlorination of 0.032 M **1a**, a concentration approaching synthetic utility, was performed in 0.20 M $NaDodSO_4$; a small amount of **4a** and/or **5a**[4] was detected (entry 6). The three ethers were also chlorinated in 40:60 (v/v) H_2O–1,4-dioxane by using ether and Cl_2 concentrations of 2.0×10^{-4} M (entries 7–9).

The relative reactivities of the three ethers in micellar $NaDodSO_4$ were then determined. A 0.20 M $NaDodSO_4$ solution containing 6.7×10^{-5} M each of **1a**, **1b**, and **1c** with a 5:1 molar ratio of Cl_2 to total 1 was analyzed before the formation of any **4** and **5** (Table II).

The solubility limits of **1a** in H_2O and of **1a** and **1c** in 0.20 M $NaDodSO_4$ were determined and are given in the Experimental Section. It is evident that all chlorinations in this study were performed under conditions such that 1 was completely solubilized.[5]

Table II. Competitive Monochlorination of *n*-Alkyl Phenyl Ethers in 0.20 M $NaDodSO_4$ at 25.0 ± 0.1 °C[a]

ether	% reactn at 15 min[b,c]	para/ortho ratio (2/3)[c]
1a	82 ± 1	3.8 ± 0.1
1b	74 ± 1	4.0 ± 0.1
1c	67 ± 2	5.0 ± 0.1

[a] The concentration of each ether was 6.7×10^{-5} M and that of Cl_2 1.0×10^{-3} M. [b] For each ether, the percentage of 2 + 3 in the mixture of 1, 2, and 3 was determined by calibrated HPLC. [c] Average deviations are given for duplicate runs.

A comparison of entries 4 and 5 of Table I indicates that under otherwise identical conditions, the presence of 0.20 M $NaDodSO_4$ had a significant effect on the monochlorination of **1a**. Namely, the rate of reaction decreased, and the para/ortho ratio increased from 1.33 to 3.3 on the addition of $NaDodSO_4$. One-point, second-order rate constants were calculated from the data at 15 and 30 min to give average values of 4 (k_w) and 0.6 M^{-1} min^{-1} (k_m) for entries 4 and 5, respectively.[6] Thus, $k_m/k_w = 0.2$.

The greater para/ortho ratio in entry 5 is consistent with solubilization of **1a** by the $NaDodSO_4$ micelles and reaction therein. It is assumed that within a micelle a molecule of **1a** is oriented, on a time-averaged basis, with its somewhat hydrophilic C_6H_5O group in or near the Stern layer and its n-C_5H_{11} group extended into the micelle core.[7] For the purpose of discussion and in the absence of evidence to the contrary, it is also assumed that the solubilization and

(1) NSF Undergraduate Research Participant, summer 1981, and Kuehn Fellow (College of Arts and Sciences, University of Wyoming), summer 1984.

(2) For examples, see: (a) Sutter, J. K.; Sukenik, C. N. *J. Org. Chem.* **1984**, *49*, 1295. (b) Onyiriuka, S.; Suckling, C. J.; Wilson, A. A. *J. Chem. Soc., Perkin Trans. 2* **1983**, 1103. (c) Grieco, P. A.; Garner, P.; He, Z. *Tetrahedron Lett.* **1983**, *24*, 1897. (d) Turro, N. J. *Pure Appl. Chem.* **1981**, *53*, 259. (e) Breslow, R.; Kitabatake, S.; Rothbard, J. *J. Am. Chem. Soc.* **1978**, *100*, 8156. (f) de Mayo, P.; Syndes, L. K. *J. Chem. Soc., Chem. Commun.* **1980**, 994. (g) Jaeger, D. A.; Ward, M. D.; Martin, C. A. *Tetrahedron* **1984**, *40*, 2691 and references therein.

(3) Jaeger, D. A.; Robertson, R. E. *J. Org. Chem.* **1977**, *42*, 3298.

(4) These compounds were indistinguishable by the analysis employed (see Experimental Section).

(5) Initially, erroneously high para/ortho ratios were obtained for **1b** and **1c** in 0.02 M $NaDodSO_4$ under conditions which they were not completely solubilized (Robertson, R. E., Ph.D. Thesis, University of Wyoming, 1976).

(6) The reaction of p-ClC_6H_4OMe with Cl_2 in 99:1 (v/v) $MeCO_2H$–H_2O is first order each in ether and Cl_2 (Bradfield, A. E.; Jones, B. *J. Chem. Soc.* **1928**, 1006). The calculations of k_w and k_m (using concentrations for the solution as a whole) were based on the assumption that the same is true for the present system.

(7) For discussions of micelle structure and solubilization, see: (a) Fendler, J. H. "Membrane Mimetic Chemistry"; Wiley-Interscience: New York, 1982; pp 9–23. (b) Mukerjee, P. In "Solution Chemistry of Surfactants"; Mittal, K. L., Ed.; Plenum Press: New York, 1979; Vol. I, p 153.

reactive sites for **1a** (and **1b** and **1c** as discussed below) are similar, if not one and the same. The former assumption is strongly supported by a ^1H NMR study[8] of the microenvironment of $C_6H_5OC_6H_{13}$-*n* in $NaDodSO_4$ micelles; the ortho protons were found to reside in a less polar environment than does the para proton. These results indicate that the former are located farther from the micelle surface, consistent with the orientation described above. Earlier, we demonstrated by UV spectroscopy that Cl_2 resides mainly in the aqueous pseudophase of an aqueous micellar solution.[3] Thus, in its attack on **1a** within a micelle, the para position is more accessible, and as a result of this differential shielding, the para/ortho ratio is greater than in H_2O alone.

Of course, there are other related factors which potentially can influence the micellar para/ortho ratio, including the polarity of the reactive site. It is known that the Stern layer of a $NaDodSO_4$ micelle has an effective dielectric constant less than that of H_2O and about that of EtOH/MeOH.[9] The results obtained in H_2O–1,4-dioxane (entry 7, Table I) suggest that the para/ortho ratio increases as the polarity of the reaction medium decreases.[10]

In entry 1, a higher concentration of **1a** was used than in entry 5. The resultant larger para/ortho ratio most likely reflects a greater partitioning of **1a** into the micellar pseudophase. The para/ortho ratios of 4.06 and 4.8 obtained in entries 2 and 3 with **1b** and **1c**, respectively, reflect reaction only in the micellar pseudophase since they are essentially insoluble in H_2O. The two values perhaps resulted from different reactive sites. Indeed, for the series **1a**, **1b**, and **1c**, the time-averaged position of the C_6H_5O group within a $NaDodSO_4$ micelle might move sequentially inward from the micelle–H_2O interface as the relative lipophilic character increases. If the reactive sites mirror these shifts, increases in para/ortho selectivity could result from enhanced differential shielding of the ortho positions. Thus, the increase on going from **1b** to **1c** is consistent with such movement. However, if analogous changes occur on going from **1a** to **1b**, they are not clearly manifested in the para/ortho selectivity since the respective values in 0.20 M $NaDodSO_4$ are almost the same. In any event, the similar ratios obtained for entries 1, 2, and 5 indicate that most of **1a** reacted in the micellar pseudophase in entries 1 and 5. No microenvironmental differences for **1a**, **1b**, and **1c** in 0.20 M $NaDodSO_4$ were detected by UV spectroscopy. But this method is relatively insensitive to such changes for these ethers (see Experimental Section). The results of entries 7–9 for chlorinations of **1a–c** in H_2O–1,4-dioxane indicate that the length of the alkyl chain has no intrinsic effect on the para/ortho ratio.

In entry 6, the regiochemical effects persisted under conditions which are close to being synthetically useful. The somewhat higher para/ortho ratio as compared to those of entries 1 and 5 resulted in part from the minor amount of dichlorination yielding **4a** and/or **5a**, in which **3a** is expected to be more reactive than **2a** due to micellar shielding as outlined above.[11,12]

Table III. Physical Properties of Ethers[a]

ether	bp, °C (mmHg)	ether	bp, °C (mmHg)
1b	123–125 (0.15)	**3c**	163–165 (0.10)
1c[b]	160–162 (0.15)	**4b**	153–155 (0.10)
2b	148–150 (0.20)	**4c**	183–185 (0.10)
2c	30.5–33[c]	**5a**	65–67 (0.005)
3d	138–140 (0.10)		

[a] Satisfactory analytical data (±0.4% for C and H) were obtained for all new compounds. [b] Van Duzee, E. M.; Adkins, H. *J. Am. Chem. Soc.* **1935**, *57*, 147. [c] Melting point.

The competition runs of Table II indicate that the micellar reactivity order is **1a** > **1b** > **1c**, and they accord with the percent yields and para/ortho ratios of entries 1, 2, and 3 of Table I. The order is consistent with sequential inward movement of the C_6H_5O group within a micelle to less polar microenvironments. However, the reactivity of **1a** undoubtedly reflects a minor amount of chlorination in the aqueous pseudophase, which in fact may be responsible for the difference between **1a** and **1b**. Bradfield and Jones[13] reported that for the series *p*-$ClC_6H_4OC_nH_{2n+1}$-*n* with *n* = 2 through 16, the rate of ortho chlorination with Cl_2 in $MeCO_2H$–H_2O at 20 °C is almost invariant. In the present system it is probable that the length of the alkyl chain likewise has no intrinsic effect on the rate of monochlorination.

In related work, Suckling and co-workers[2b] have observed regiochemical effects in the chlorination of C_6H_5OH with Me_3COCl in micellar $NaDodSO_4$ that are consistent with those obtained with **1**. The para/ortho ratio *decreased* on the addition of $NaDodSO_4$ to 9:1 (v/v) H_2O–MeCN. The time-averaged orientation of C_6H_5OH's oxygen with respect to the micelle surface is *opposite* to that of **1**'s oxygen as determined by ^1H NMR.[8] As a result, for C_6H_5OH the ortho positions are more exposed than the para position to attack from the aqueous pseudophase. Breslow has obtained dramatic regiochemical control in the cyclodextrin-catalyzed monochlorination of C_6H_5OMe.[14]

Overall, it is evident that variation of the alkyl group has minimal effect on the rate and regioselectivity of micellar monochlorination of **1**. Indeed, the hydrophilic character of the C_6H_5O group dominates the lipophilic character of R.

Experimental Section

General Procedures. ^1H NMR spectra were recorded at 270 MHz with $Me_3SiCD_2CD_2CO_2Na$ as internal standard in D_2O. Critical micelle concentrations (cmc) were determined as described previously.[3] Glassware exposed to micellar solution was cleaned with hydrofluoric acid, rinsed with H_2O, dilute aqueous NH_3, H_2O, dilute nitric acid, H_2O, and HPLC-grade H_2O, and dried at 110 °C. The following procedures were used unless noted otherwise. UV spectra were obtained with matched 1-cm quartz cuvettes. Solutions of **1** in H_2O and $NaDodSO_4$–H_2O were prepared by sonication (Branson B-12 and B-32H sonicators; 12 h; bath H_2O reached ca. 50 °C), equilibration overnight at 25 °C, and filtration (0.45 μm Nylon).

Materials and Solvents. Ethers **1a**, **2a**, **3a**, and **4a** have been described previously.[3] Each of the remaining ethers was prepared by a Williamson procedure[15] with the appropriate combination of *n*-alkyl bromide/chloride and phenol.[16] Except for **1c**, frac-

(8) Suckling, C. J.; Wilson, A. A. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1616.

(9) (a) Mukerjee, P.; Cardinal, J. R.; Desai, N. R. In "Micellization, Solubilization, and Microemulsions"; Mittal, K. L., Ed.; Plenum Press: New York, 1977; Vol. I, p 241. (b) Sudhölter, E. J. R.; van de Langkruis, G. B.; Engberts, J. B. F. N. *Recl. Trav. Chim. Pays-Bas* **1980**, *99*, 73.

(10) For the uncatalyzed chlorination of C_6H_5OMe with Cl_2 in aprotic media of high and low dielectric constants (ε) the para/ortho ratio increases and decreases, respectively, with a decrease in ε (Seguchi, K.; Asano, T.; Sera, A.; Goto, R. *Bull. Chem. Soc. Jpn.* **1970**, *43*, 3318).

(11) The relative rates of reaction for C_6H_5OMe, *o*-ClC_6H_4OMe, and *p*-ClC_6H_4OMe with Cl_2 in 99:1 (v/v) $MeCO_2H$–H_2O at 20 °C are 650:3.6:1, respectively (Jones, B.; Richardson, E. N. *J. Chem. Soc.* **1956**, 3939).

(12) Furthermore, the aggregate character most likely changes on going from the lower to higher [**1a**], e.g., from micelle to microemulsion.

(13) Bradfield, A. E.; Jones, B. *Trans. Faraday Soc.* **1941**, *37*, 726.

(14) Breslow, R.; Kohn, H.; Siegel, B. *Tetrahedron Lett.* **1976**, *17*, 1645 and references therein.

(15) Smith, R. A. *J. Am. Chem. Soc.* **1933**, *55*, 3718.

(16) Of the ethers **5**, only **5a** was prepared and characterized.

tional distillation or recrystallization from EtOH gave material pure by GC and/or HPLC analysis (see below); **1c** was sublimed at 120 °C (0.02 mmHg). Table III summarizes the physical data. The $NaDodSO_4$ (BDH, specially pure) was recrystallized[17] at 0 °C three times from H_2O and two times from absolute EtOH, with an Et_2O wash before each recrystallization, to give material with a cmc at 25 °C of 7.5×10^{-3} M without hysteresis (lit.[18] 8.1×10^{-3} M). For reaction mixtures, HPLC-grade or doubly-distilled H_2O was used and for HPLC analyses, the former and HPLC-grade MeCN. 1,4-Dioxane was purified[19] and distilled from $LiAlH_4$ immediately before use.

Chlorination of 2.0×10^{-4} M 1 in 0.20 M $NaDodSO_4$. Cl_2 was collected in H_2O at 0 °C, diluted to ca. 0.025 M, and standardized with $Na_2S_2O_3$–KI.[20] It was stored at 10 °C and was periodically restandardized. A typical procedure follows. To 50 mL of 0.20 M $NaDodSO_4$ was added 0.01 mmol of **1**. Aqueous Cl_2 (ca. 0.8 mL) was added to 20 mL of the resultant solution to give 1.0×10^{-3} M Cl_2, and samples were analyzed by HPLC at 15 min intervals until **4**/**5** were detected beyond 45 min. In an analogous fashion, chlorination was performed with 0.87×10^{-4} M **1a** and 4.4×10^{-4} M Cl_2 in 0.20 M $NaDodSO_4$. Results are summarized in Table I.

Chlorination of 0.032 M 1a in 0.20 M $NaDodSO_4$. To 30 mL of 0.20 M $NaDodSO_4$ was added 190 mg (1.16 mmol) of **1a**. Then 2.5 mL of 0.11 M aqueous Cl_2 was added to 13.1 mL of the resultant solution to give 0.032 M **1a** and 0.018 M Cl_2. Samples were analyzed by HPLC at 1 and 5 min; results are summarized in Table I.

Chlorination of 1a in Water. To 100 mL of H_2O was added 1.42 mg of **1a** (8.7×10^{-5} M). Aqueous Cl_2 (ca. 0.35 mL) was added to 20 mL of the resultant solution to give 4.4×10^{-4} M Cl_2. Samples were analyzed by HPLC at 15-min intervals; results are summarized in Table I.

Chlorination of 1 in Aqueous 1,4-Dioxane. A typical procedure follows for chlorination of **1** in 40:60 (v/v) H_2O–1,4-dioxane with [1] and $[Cl_2] = 2.0 \times 10^{-4}$ M. To 0.10 mmol of **1** was added 300 mL of 1,4-dioxane and 191.1 mL of H_2O followed by 8.9 mL of 0.0112 M aqueous Cl_2. After the reaction, 5 mg of Na_2SO_3 was added, followed by saturation with NaCl. The resulting 1,4-dioxane layer was separated and the aqueous layer extracted with four 100-mL portions of hexane. Upon combination of the hexane extracts and 1,4-dioxane layer, an aqueous layer separated. The organic layer was dried (Na_2SO_4) and rotary-evaporated to leave the product mixture, which was analyzed by GC after the addition of an internal standard. Controls demonstrated that **2** and **3** do not fractionate during isolation. Results are summarized in Table I.

Competition Runs in 0.20 M $NaDodSO_4$. To 100 mL of 0.20 M $NaDodSO_4$ were added 1.1 mg of **1a**, 1.5 mg of **1b**, and 1.8 mg of **1c** (0.0067 mmol each). Aqueous Cl_2 (ca. 0.8 mL) was added to 20 mL of the resultant solution to give 1.0×10^{-3} M Cl_2. Samples were analyzed by HPLC at 15 min; results are summarized in Table II.

Analysis of Reaction Mixtures. The product yields and para/ortho ratios for entries 1–6 of Table I and for Table II resulted from *direct analyses* of the reaction mixtures by calibrated HPLC on a 25 cm × 4.0 mm (i.d.) column of 10-μm Li-Chrosorb RP-18 (EM) with MeCN–H_2O elution using the chromatograph, UV detector (254 nm), and reporting integrator described previously.[21] $NaDodSO_4$ and excess Cl_2 eluted first, followed by the organic products. Controls in a more reactive system[2g] demonstrated that little, if any, reaction of substrate occurs in a sample subsequent to its injection into the chromatograph.

Calibrated GC analyses (Table I, entries 7–9) based on internal standards were performed on a Varian Model 2700 chromatograph with He elution and thermal conductivity detection using column C and the integration method of our earlier report.[3]

The yields determined by HPLC are based only on the relative amounts of **1**, **2**, and **3**. However, the GC-based results of Table I and of our earlier study,[3] coupled with the fact no other products were detected, suggest that the HPLC results fairly represent absolute yields. Furthermore, the HPLC and GC analyses gave comparable para/ortho ratios. For chlorination of **1a** in H_2O the former yielded 1.33 and the latter 1.65.[3,22]

UV Spectroscopy. UV spectra were determined as follows. 0.20 M $NaDodSO_4$: **1a**, 272 nm (ε 1954), 278 (1494); **1b**, 272 (1947), 278 (1529); **1c**, 272 (2053), 278 (1764). H_2O: **1a**, 268 nm (ε 1269), 275 (1107). 40:60 (v/v) H_2O–1,4-dioxane: **1a–c**, 272 nm (ε 1806 ± 45), 278 (1492 ± 38). *n*-Heptane: **1a–c**, 272 nm (ε 2073 ± 38), 278 (1924 ± 37). MeCN: **1a–c**, 270 nm (ε 1679 ± 31), 277 (1340 ± 24). In 0.20 M $NaDodSO_4$, [1] = 1.0×10^{-4} M, and in H_2O, [**1a**] = 5.2×10^{-5} M. For the latter, 10-cm quartz cells were used.

Ether Solubility Limits in 0.20 M $NaDodSO_4$ and H_2O. Saturated solutions in 0.20 M $NaDodSO_4$ were prepared from excess **1a** and **1c**. The UV absorptions at 272 nm and the appropriate ε's above gave the solubility limits: 0.040 M and 0.0035 M for **1a** and **1c**, respectively.

Determination of the solubilities of **1** in H_2O by the same procedure was complicated by the formation of emulsions as detected by UV absorbance above 300 nm, which was absent in the spectra of 5.2×10^{-5} M **1a** in H_2O and of all ethers in other media. In fact, for **1b** and **1c** the resultant aqueous systems were visually turbid. A second filtration of the latter through 0.22-μm cellulose removed some but not all of the turbidity. When the amount of excess **1a** was reduced, emulsions were not detected, and a solubility limit of 1.1×10^{-4} M was obtained. In our earlier study,[3] a value of 6.7×10^{-5} M resulted from the following procedure. A mixture of excess **1a** and H_2O at 25 °C was stirred for 2 h and allowed to stand for 40 h. A sample was taken with the exclusion of undissolved ether at the surface and its UV spectrum recorded. Use of this method for **1b** and **1c** gave no detectable absorption. Even though no λ_{max} were observed for the turbid **1b** and **1c** solutions above, the absorbances at 268 nm were used to calculate an upper solubility limit of 3×10^{-5} M for the two ethers.

Control on the Stability of $NaDodSO_4$ during the Sonication Procedure. A 0.20 M solution of $NaDodSO_4$ in D_2O was sonicated for 12 h. By ^1H NMR, no hydrolysis occurred as determined by the absence of *n*-$C_{12}H_{25}OH$; <5% would have been detected.

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Registry No. **1a**, 2050-04-6; **1b**, 36588-31-5; **1c**, 35021-68-2; **2b**, 95248-98-9; **2c**, 95248-99-0; **3b**, 95249-00-6; **3c**, 95249-01-7; **4b**, 95249-02-8; **4c**, 95249-03-9; **5a**, 95249-04-0.

Supplementary Material Available: Detailed HPLC analysis conditions including retention times and calibration factors and GC conditions including internal standards and calibration factors (2 pages). Ordering information is given on any current masthead page.

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(22) However, this comparison involves runs with different concentrations of **1a** and Cl_2. The earlier para/ortho ratios[3] for chlorination of **1a** in aqueous $NaDodSO_4$ are not expected to be the same as those of Table I because different [$NaDodSO_4$]'s (0.02 and 0.20 M, respectively) were used. A para/ortho ratio depends on the fraction of the reaction occurring in the micellar pseudophase, which is a function of [$NaDodSO_4$].