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Reactions in Microemulsion Media. Nucleophilic Substitution Reactions of Benzyl and *p*-Alkylbenzyl Chlorides[1]

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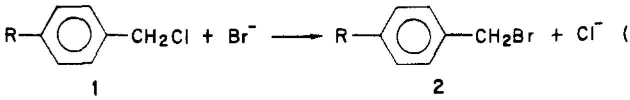
A kinetic and synthetic study of the nucleophilic displacement reaction of bromide ion with benzyl chloride (**1a**) and its *p*-ethyl-substituted (**1b**) and *p*-*n*-dodecyl-substituted (**1c**) analogues has been performed in microemulsions prepared from combinations of a 1.23:1 (w/w) mixture (S) of cetyltrimethylammonium bromide (CTABr) and 1-butanol, a 1:5 (w/w) KBr–H_2O solution (W), and hexane (O). The rates of reaction decreased differentially with increasing hexane content at a constant ratio of S:W to indicate that the interphase was the microemulsion reactive site. For microemulsion with respect to aqueous micellar and aqueous ethanol reaction media, solubilization of substrate was higher, initial reaction rates were comparable or slightly less, and overall conversions were greater.

Microemulsions are transparent, thermodynamically or kinetically stable solutions of water, oil, surfactant, and, in most cases, cosurfactant.[2] Structurally, they have been described as spherical droplets of a dispersed phase separated from a continuous phase by a surfactant interfacial layer.[3] Both water-dispersed-in-oil (w/o) and oil-in-water (o/w) microemulsions are possible. However, recent work has suggested that some systems may be bicontinuous.[4] Microemulsions can solubilize a wide variety of compounds simultaneously and offer the possibility of reagent compartmentalization and other effects. Thus, microemulsion catalysis represents an alternative to phase-transfer catalysis[5] and other techniques[6] for reaction of water-insoluble organic substrates with water-soluble reagents. Nevertheless, most of the chemical studies in microemulsions have had only kinetic objectives.[7] A few[1,8] have had synthetic, but none detailed kinetic *and* synthetic goals. Herein, we report the results of such a study of the nucleophilic substitution reaction of bromide ion with benzyl chloride (**1a**) and its *p*-ethyl (**1b**) and *p*-*n*-dodecyl (**1c**) analogues (eq 1).[9]



(1)

1 2

a, R = H; b, R = C_2H_5; c, R = *n*-$C_{12}H_{25}$

Results and Discussion

Microemulsions were formulated from combinations of hexane (O), a 1:5 (w/w) KBr–H_2O solution (W), and a 1.23:1 (w/w) mixture (S) of cetyltrimethylammonium bromide (CTABr) and 1-butanol. The pseudoternary phase diagram at 40 °C is given in Figure 1. The unhatched region corresponds to microemulsions and the hatched region to heterogeneous mixtures. Solutions 1–7 fall roughly along the dashed dilution line with respect to hexane and were used for the kinetic and synthetic runs. Their compositions are given in Table I. Note that along the dilution line the ratio of S:W remains constant.

In order to determine the w/o, o/w, or other character of the individual solutions, conductivity measurements and dispersion tests[10] were performed. Figure 2 contains a plot of the log of specific conductance (K) vs. weight percent hexane for solutions along the dilution line; K was about 10^4 $\mu\Omega^{-1}$ cm^{-1} for solutions with low hexane contents and decreased to 1.4 $\mu\Omega^{-1}$ cm^{-1} for solution 7. The values fell between those for 1:5 (w/w) KBr–H_2O and hexane, 1.8×10^5 and <0.2 $\mu\Omega^{-1}$ cm^{-1}, respectively. In the dispersion tests, solutions 2 and 3 dispersed into H_2O only, and 1 and 4–7 did not disperse into any of the solvents used, including hexane (see Experimental Section).

Taken as a whole, the conductivity and dispersion results do not allow an unambiguous description of the solutions. *Tentative* assignments are as follows: 1, aqueous mixed micelles of CTABr and 1-butanol; 2, o/w microemulsion; and 4–7, w/o microemulsions. Even though its dispersal into water and relatively high conductivity suggest that solution 3 has an aqueous external phase, it cannot be a classical o/w system on the basis of geometry. The spherical droplets of dispersed phase plus interphase cannot occupy a volume fraction greater than 0.74,[11] and for solution 3 the value is 0.80.[12] Thus, this solution may be bicontinuous[4] or consist of ill-defined aggregates.[13,14] In any event, the kinetic treatment below is according to a pseudophase model in which the solutions are assumed

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(1) For the previous paper in this series, see: Jaeger, D. A.; Ward, M. D.; Martin, C. A. *Tetrahedron*, in press.

(2) (a) Danielsson, I.; Lindman, B. *Colloids Surf.* **1981**, *3*, 391. (b) Friberg, S. E. *Ibid.* **1982**, *4*, 201.

(3) Prince, L. M., Ed. "Microemulsions: Theory and Practice"; Academic Press: New York, 1977.

(4) (a) Scriven, L. E. In "Micellization, Solubilization, and Microemulsions"; Mittal, K. L., Ed.; Plenum Press: New York, 1977; Vol. II, p 877. (b) Clausse, M.; Peyrelasse, J.; Heil, J.; Boned, C.; Lagourette, B. *Nature (London)* **1981**, *293*, 636.

(5) Starks, C. M.; Liotta, C. "Phase Transfer Catalysis"; Academic Press: New York, 1978.

(6) For an example, see: (a) Regen, S. L. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 421. For a discussion, see: (b) Jaeger, D. A.; Frey, M. R. *J. Org. Chem.* **1982**, *47*, 311.

(7) For examples, see: (a) Mackay, R. A. *Adv. Colloid Interface Sci.* **1981**, *15*, 131. (b) Mackay, R. A. *J. Phys. Chem.* **1982**, *86*, 4756. (c) Mackay, R. A.; Hermansky, C. *Ibid.* **1981**, *85*, 739. (d) Bunton, C. A.; de Buzzaccarini, F. *Ibid.* **1982**, *86*, 5010. (e) Athanassakis, V.; Bunton, C. A.; de Buzzaccarini, F. *Ibid.* **1982**, *86*, 5002. (f) Bunton, C. A.; de Buzzaccarini, F.; Hamed, F. H. *J. Org. Chem.* **1983**, *48*, 2457, 2461, and references therein.

(8) (a) Gonzalez, A.; Holt, S. L. *J. Org. Chem.* **1982**, *47*, 3186. (b) Gonzalez, A.; Holt, S. L. *Ibid.* **1981**, *46*, 2594 (However, for a comment, see: Galli, C.; Mandolini, L. *J. Chem. Soc., Chem. Commun.* **1982**, 251). (c) Breslow, R.; Maitra, U.; Rideout, D. *Tetrahedron Lett.* **1983**, *24*, 1901. (d) Farques, R.; Maurette, M. T.; Oliveros, E.; Rivere, M.; Lattes, A. *Nouv. J. Chim.* **1979**, *3*, 487. (e) Sakellariou-Farques, R.; Maurette, M. T.; Oliveros, E.; Riviere, M.; Lattes, A. *J. Photochem.* **1982**, *18*, 101.

(9) Preliminary communication of results with **1a**: Martin, C. A.; McCrann, P. M.; Angelos, G. H.; Jaeger, D. A. *Tetrahedron Lett.* **1982**, *23*, 4651.

(10) Jones, S. C.; Dreher, K. D. *Soc. Pet. Eng. J.* **1976**, *16*, 161.

(11) Lissant, K. J. In "Emulsions and Emulsion Technology"; Lissant, K. J., Ed.; Marcel Dekker: New York, 1974; Part I, p 23.

(12) The calculation is based on droplets consisting of hexane plus all of the 1-butanol and CTABr with a density of 1 for the aqueous pseudophase and CTABr.

(13) Lindman, B.; Wennerstrom, H. In "Solution Behavior of Surfactants: Theoretical and Applied Aspects"; Mittal, K. L., Fendler, E. J., Eds.; Plenum Press: New York, 1982; Vol. I, p 3.

(14) In fact, neither structural character can be discounted for the other solutions.

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Table I. Reactions of 1a–c with Bromide Ion at 40 °C

	composition[a]					10^3k_ψ,[c] $\min^{-1}$		
soln	%S	%W	%O	[1], 10^3 M	δ_{obs}[b]	**1a**	**1b**	**1c**
1	70	30	0	20	61.850	4.0 (0.5)	6.6 (0.3)	
2	67	28	5	18	61.876	2.6 (0.2)	4.9 (0.2)	5.2 (0.4)
2a	67	28[d]	5	17		2.1 (0.4)		
3	57	24	19	16	62.007	1.8 (0.1)		
4	46	18	36	10	62.085	1.0 (0.1)	1.8 (0.2)	1.4 (0.1)
4a	46	19[d]	35	10		1.0 (0.1)		
5	36	15	49	8.1	62.190	1.0 (0.1)	1.5 (0.1)	
6	24	10	66	5.3	62.216	0.62 (0.06)		
7	15	6	79	3.1	62.320	0.32 (0.03)	0.45 (0.03)	0.27 (0.03)
7a	15	6[d]	79	3.6		0.40 (0.06)		

	composition		10^3k_ψ,[c] $\min^{-1}$		
soln	other media	[1], 10^3 M	**1a**	**1b**	**1c**
8	10% CTABr–H_2O	13	5.9 (0.4)	11 (2)	
9	10% CTABr–$CHCl_3$	19	2.6 (0.2)	4.2 (0.2)	
10	0.4 M KBr in 25% (v/v) H_2O–C_2H_5OH	20	1.2 (0.1)	2.4 (0.2)	2.2 (0.2)

[a] All compositions in weight percent unless noted otherwise. [b] Chemical shift of C-1 of 1-butanol (see Experimental Section). [c] Initial rate constant; each run was duplicated; estimated errors are in parentheses. [d] Aqueous pseudophase was H_2O.

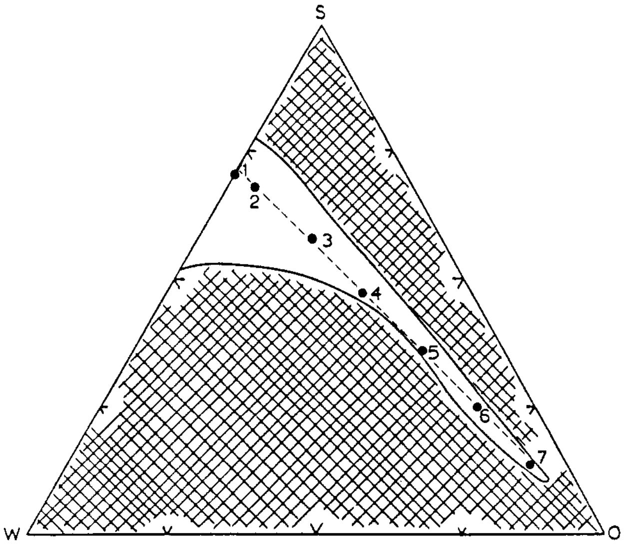


Figure 1. Microemulsion pseudoternary phase diagram at 40 °C.

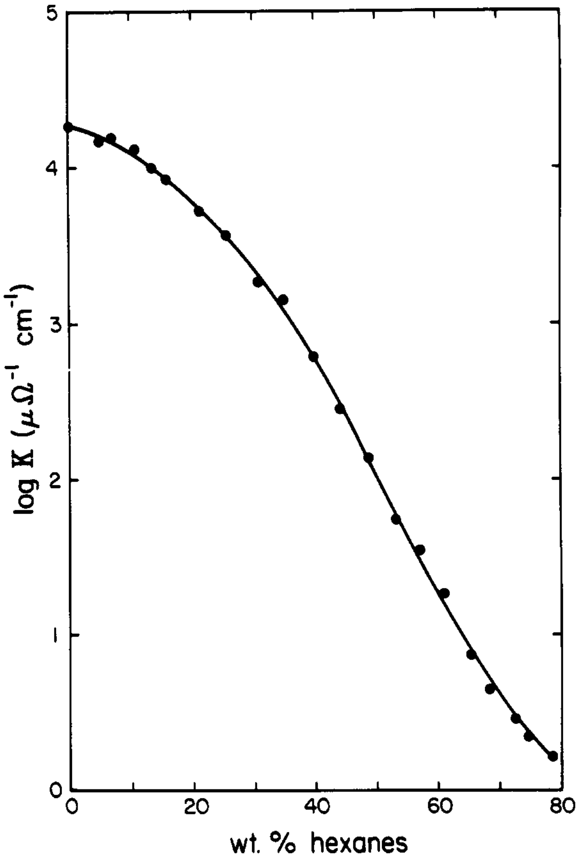
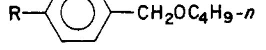


Figure 2. Log of specific conductance (K) vs. weight percent hexane for solutions along the dilution line of Figure 1.

to contain dispersed and continuous phases and is independent of o/w or w/o character.

The reaction of eq 1 was performed with **1a–c** at 40 °C under pseudo-first-order conditions in solutions 1–7 with [KBr]:[**1**] = 20 and total [Br^-]:[**1**] = 72 and in corresponding solutions 2a, 4a, and 7a without added KBr. It was also performed in aqueous micellar CTABr, inverse micellar CTABr in $CHCl_3$, and aqueous ethanol, solutions 8, 9, and 10, respectively, with [CTABr(KBr)]:[**1**] = 20. The observed pseudo-first-order rate constants, k_ψ, are given in Table I and correspond to the initial reaction period during which side products **3** and **4** were not formed (see below and Experimental Section).



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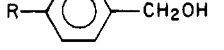

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a, R = H; b, R = C_2H_5; c, R = n-$C_{12}H_{25}$

A schematic representation of an idealized microemulsion is given below; curvature of the assumed spherical dispersed droplets has been ignored. Water and KBr are confined to the aqueous pseudophase, hexane to the oil pseudophase, and CTABr to the interphase, and 1-butanol and substrate **1** (not shown) are distributed between the interphase and the oil pseudophase. Second-order rate constants, k_2, are calculated below based on the assumption that reaction occurs only in the interphase and thus involves only Br^- bound to CTA^+. This assumption is supported by the identity of k_ψ values within experimental error obtained for **1a** in solutions with and without added KBr (2, 4, and 7 vs. 2a, 4a, and 7a, respectively). Thus, k_2 is defined by eq 2, where $[Br^-]_i$ is the concentration of Br^- in the interphase.

H_2O ● KBr	aqueous pseudophase
CTABr + 1-BuOH	interphase
hexane + 1-BuOH	oil pseudophase

$$k_2 = k_\psi/[Br^-]_i \qquad (2)$$

The calculation of k_2 follows the kinetic treatment of Bunton and de Buzzaccarini.[7d] Initially, the volume ele-

Table II. Second-Order Rate Constants, k_m and k_2

				10^3k_m, min^{-1}			10^3k_2, M^{-1} min^{-1}		
soln	f_a^i	X_s^i	V_i, M^{-1}	1a	1b	1c	1a	1b	1c
1	1.0	0.20	0.15	26	43		3.9	6.5	
2	0.96	0.21	0.15	16	31	33	2.4	4.7	5.0
3	0.74	0.26	0.16	9.1			1.5		
4	0.60	0.29	0.17	4.5	8.2	6.4	0.76	1.4	1.1
5	0.43	0.37	0.19	3.6	5.3		0.68	1.0	
6	0.38	0.40	0.20	2.0			0.40		
7	0.21	0.51	0.23	0.83	1.2	0.70	0.19	0.28	0.16
8		1.0	0.36	7.9	15		2.8	5.4	
9		1.0	0.36	2.6	4.2		0.94	1.5	
10							3.0	6.0	5.5

ment of the reaction is neglected, and a second-order rate constant, k_m, is calculated from the following equations. In eq 3, β is the fraction of undissociated CTABr. In eq 3 and 4, for CTABr and 1-butanol, X_s^i and X_a^i are the mole

$$k_m = k_\psi/\beta X_s^i \tag{3}$$

$$X_s^i = 1 - X_a^i = n_s/(n_s + f_a^i n_a) \tag{4}$$

$$f_a^i + f_a^o = 1 \tag{5}$$

fractions constituting the interphase and n_s and n_a the molar amounts in the entire solution, respectively. In eq 5, f_a^i is the fraction of 1-butanol in the interphase, and f_a^o is that in the oil pseudophase. Values of f_a^i were estimated by ^{13}C NMR using eq 6,[15] wherein δ_{obs}, δ_i, and δ_o are the

$$\delta_{obs} = \delta_i f_a^i + \delta_o f_a^o \tag{6}$$

chemical shifts of carbon-1 of 1-butanol in a microemulsion, in a polar environment, and in a nonpolar environment, respectively. Values of δ_{obs} are given in Table I, and δ_i and δ_o are those for solution 1 and a 1-butanol–hexane solution, respectively (see Experimental Section). Resultant values of f_a^i and X_s^i are given in Table II. In a study[7d] of microemulsions composed of CTABr, 1-butanol, octane, and H_2O, β did not vary much with composition when the ratio of CTABr to 1-butanol was held constant. The average value, 0.76, was used in the calculation of k_m's listed in Table II.

From k_m, k_2 can be obtained with the use of eq 7 and 8, where V_i is the molar volume of the reactive site, which

$$k_2 = k_m V_i \tag{7}$$

$$V_i = X_s^i \bar{V}_s + X_a^i \bar{V}_a \tag{8}$$

is assumed to be the entire interphase, and $\bar{V}_s$ and $\bar{V}_a$ are the partial molar volumes of CTABr (0.36 M^{-1})[16] and 1-butanol (0.092 M^{-1}, from its density), respectively. Values of k_2 are given in Table II.[17,18]

Values of k_m and k_2 for solutions 8 and 9 were also calculated with the above kinetic treatment. For aqueous and inverse CTABr micelles, β = 0.75[19] and 1.0, respectively.

In the microemulsions, both k_ψ and k_2 for all three substrates decreased as the fraction of hexane increased, and this trend probably reflects a dilution effect. As the volume of the interphase decreased relative to that of the oil pseudophase, the fraction of **1** in the former, the reactive site, decreased too. For **1a** and **1b**, the values of k_2 decreased in the following order: solution 1 > 10 (aqueous ethanol) > 8 (aqueous micellar) > 9 (inverse micellar). The similar values in solutions 8 and 10 are consistent with the general observation that second-order rate constants for bimolecular reactions involving hydrophilic nucleophiles are about the same in aqueous cationic micelles and water.[20]

In solution 10, a homogeneous medium, **1b** and **1c** have essentially the same reactivity, which is greater than that of **1a**. These facts are in accord with the expected near identical σ values for p-C_2H_5 and p-n-$C_{12}H_{25}$ and with rate enhancement by p-alkyl substituents.[21] Note, though, that the relative reactivities of **1a**, **1b**, and **1c** change on going from solution 2 to 4 to 7. First, consider a comparison of **1b** and **1c**. The decrease in reactivity of **1c** follows from the partitioning of substrate between the oil pseudophase and the more polar interphase and from the latter as the reactive site as assumed above. Due to the greater overall lipophilic character of **1c** associated with the difference between ethyl and n-dodecyl, a lesser fraction of it than of **1b** is solubilized at the interphase as the oil content of a microemulsion increases.[22] However, the reactivities of **1b** and **1c** are the same in solution 2; apparently its oil pseudophase is not large enough to allow a manifestation of the partitioning effect. Second, consider a comparison of **1b** and **1c** with **1a**. The reactivities of the more lipophilic substrates *both* decrease relative to that of **1a** as the microemulsion oil content increases, consistent with the partitioning and active site arguments.

The kinetic data also allow one to discount the possibility that a significant fraction of the substitution reaction occurred in the oil pseudophase by a phase-transfer process involving CTABr. If this were the case, the more lipophilic a substrate, the greater its reactivity due to the partitioning effect.

Synthetic runs were performed with **1a**, and Table III contains the product distributions after 12 h at 40 °C. In solutions 1–7, [KBr]:[**1a**] = 10, and total [Br^-]:[**1a**] = 36. In solutions 2a, 4a, and 7a, [CTABr]:[**1a**] = 26, and in 7–9, [CTABr(KBr)]:[**1a**] = 10. The runs were not carried to completion and thus reflect the relative kinetic benefits of the various media under preparative conditions. In general, for solutions 1–7, the conversion of **1a** and the formation of side products **3a** and **4a** decreased with increasing hexane content. Note that even though the

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(15) Tricot, Y.; Kiwi, J.; Niederberger, W.; Grätzel, M. *J. Phys. Chem.* **1981**, *85*, 862.

(16) Güveli, D. E.; Kayes, J. B.; Davis, S. S. *J. Colloid Interface Sci.* **1981**, *82*, 307.

(17) Lower limit k_2's result because the calculation of V_i neglects contributions due to H_2O of hydration for CTABr and possible penetration of hexane.

(18) In ref 9, the k_2's for the microemulsion solutions are somewhat smaller due to the neglect of Br^- dissociation in their calculation.

(19) Fabre, H.; Kamenka, N.; Khan, A.; Lindblom, G.; Lindman, B.; Tiddy, G. J. T. *J. Phys. Chem.* **1980**, *84*, 3428.

(20) For examples, see: Bunton, C. A. *Catal. Rev.-Sci. Eng.* **1979**, *20*, 1 and references therein.

(21) The σ value for p-C_2H_5 is −0.15 (McDaniel, D. H.; Brown, H. C. *J. Org. Chem.* **1958**, *23*, 420). For relative rates of nucleophilic substitution reactions of benzyl and p-alkylbenzyl halides, see: Streitwieser, A., Jr. "Solvolytic Displacement Reactions"; McGraw Hill: New York, 1962; p 18.

(22) It is known that benzene is polar/surface active enough to prefer the interfacial region of an aqueous micelle (Mukerjee, P. In "Solution Chemistry of Surfactants"; Mittal, K. L., Ed.; Plenum Press: New York, 1979; Vol. I, p 153).

Table III. Solubility Limits of 1a and Product Distributions for Reactions of 1a after 12 h at 40 °C

				yield,[c] %			
soln	solubility limit, M	ρ (g/mL)[a]	initial [**1a**],[b] 10^3 M	**1a**	**2a**	**3a**	**4a**
1	0.87	0.95	40	14	76	8	2
2	0.84	0.94	37	8 (27)	83 (66)	7 (6)	2 (1)
2a		0.91	34	19	75	5	1
3	0.52	0.88	30	18 (33)	77 (63)	4 (3)	1 (1)
4	0.16	0.82	21	21 (41)	75 (57)	3 (2)	1 (0)
4a		0.80	20	48	52		
5	0.64	0.79	16	50	50		
6	1.9	0.72	11	64	36		
7	2.0	0.67	5.8	83 (79)	17 (21)		
7a		0.69	7.2	78	22		
8	0.10		28	23	66		11
9	>4.4		38	50	50		
10	0.47		40	55	44		1

[a] Density. [b] Initial concentrations in synthetic runs. [c] See text for values in parentheses.

presence of KBr in solutions 2, 4, and 7 had no effect on initial rates (Table I), it generally helped to drive the reaction further to completion. These facts suggest the operation of an ion-exchange process involving Br^- and Cl^-. It is known that the former binds more tightly to a CTA^+ interface.[19] Thus, over the course of a reaction, the ratio of $[Br^-]_i$ to $[Cl^-]_i$ will be greater in a solution with than in a corresponding solution without KBr, and as a consequence, a greater overall conversion results. Also note that k_ψ for aqueous micellar solution 8 was greater than those for solutions 1–7, but the overall conversions of **1a** were greater in solutions 1–4. Complete conversion of **1a** occurred in solutions 1–4 and 8 after 24 h with the formation of 10–25% side products **3a** and **4a**. After 4 days, complete conversion of **1a** to **2a** was obtained in solution 7 without side products. Table III also contains yields in parentheses for analogous runs made with total $[Br^-]:[1] = 7.2$; the conversions within the 12 h reaction period decreased as expected compared to those obtained with the fivefold higher ratio. Overall, in this study the yields of **2a** in the water-rich microemulsions equaled or exceeded those reported for phase-transfer[23a] and triphase[23b] catalyzed reactions.

Table III also contains solubility limits for **1a** in the various media. Although aqueous micellar solution 8 gave the largest k_ψ, it solubilized the smallest amount of **1a** and is therefore the least suited for practical synthesis. Indeed, in Table I, a run for **1c** could not be made in solution 8 due to its limited solubility. Of solutions 1–7, hexane-rich 5–7 can solubilize more **1a** (molar basis) than the total amount of Br^-, and all, except 4, more **1a** than KBr.

Attempts were made to isolate products from synthetic runs with **1a**. Aqueous $NaClO_4$ was added to a reaction mixture to precipitate $CTAClO_4$, followed by extraction of the filtrate with hexane. Only 61% of the product mixture was recovered. In part, this low yield resulted from losses due to codistillation of **1a** and **2a** with hexane and 1-butanol during rotary evaporation of extracts. It is clear that the synthetic application of microemulsions will require simplified and more efficient product isolation procedures, which "destructible" (cleavable) surfactants[6b,24] should facilitate.

Experimental Section

General Procedures. All melting and boiling points are uncorrected. The ^1H NMR spectra were recorded at 60 and 270 MHz on Varian EM-360 and JEOL FX-270 spectrometers, respectively, with $CDCl_3$ as solvent and Me_4Si as internal standard. The ^{13}C NMR spectra were obtained at 67.8 MHz on the latter instrument. High-resolution mass spectra were recorded on a VG-ZAB 1F spectrometer (70 eV; direct insertion; probe and ion source temperatures, ambient and 210 °C, respectively). Conductivity measurements were performed on a Yellow Springs Instruments (YSI) Model 31 conductivity bridge with a YSI Model 3403 conductivity cell (cell constant = 1 cm^{-1}). High-performance liquid chromatography (HPLC) analyses were performed on a Beckman Model 332 chromatograph equipped with a column inlet filter (2 μm) and a precolumn [3 cm × 4.6 mm i.d.; 10-μm LiChrosorb RP-18] between the sample injector and column [25 cm × 4.0 (EM) or 4.6 mm i.d. (Altex); 10-μm LiChrosorb RP-18]. Solvents were HPLC-grade H_2O and CH_3CN (J. T. Baker). For detection and quantitation, a Beckman Model 153 (254 nm) ultraviolet detector and a Hewlett-Packard Model 3390A reporting integrator were used. Gas chromatography (GC) analyses and preparative separations were performed on a Varian Model 2700 chromatograph equipped with a 6 ft × $^1/_4$ in. column packed with 4% SE-30 on 60–80-mesh AW Chromosorb W. Densities were measured at 40.0 ± 0.1 °C in a 10-mL pycnometer. Benzyl chloride (**1a**), bromide (**2a**), and alcohol (**4a**) were reagent grade. Elemental analyses were performed by Atlantic Microlab, Atlanta, GA.

Kinetic Measurements. The following general procedure was used. To 10.0 g of the reaction medium, equilibrated at 40.0 ± 0.1 °C for 30–90 min, was added **1** to give the following molar ratios: $[KBr]:[1] = 20$ (total $[Br^-]:[1] = 72$) in solutions 1–7; $[CTABr]:[\mathbf{1a}] = 52$ in solutions 2a, 4a, 7a; and $[CTABr(KBr)]:[1] = 20$ in solutions 8, 9, and 10. The reaction mixture was held at 40.0 ± 0.1 °C, and over the first 1–2 half-lives, 9–12 aliquots were withdrawn and analyzed by calibrated HPLC with gradient CH_3CN-H_2O elution. The value of k_ψ was calculated as the slope of the initially linear portion of a plot of log $([1]_0/[1]_t)$ vs. t, were $[1]_0$ and $[1]_t$ are the initial and time t concentrations of **1**, respectively. Each plot was linear (correlation coefficient > 0.97) until side products **3** and **4** were detected (not during the first half-life for all runs, nor during the second for some). Aliquots that could not be analyzed immediately were frozen in melting point capillaries in liquid N_2 and stored at −15 °C. Each solution remained homogeneous during the course of the reaction. Results are summarized in Table I.

Synthetic Runs. The following general procedure was used. To 10.0 g of the reaction medium, equilibrated at 40.0 ± 0.1 °C, was added an amount of **1** twice that used in the corresponding kinetic run. After 12 h at 40 °C, the reaction mixture was analyzed as in the kinetic runs. The use of anisole as an internal standard in some analyses demonstrated that the relative yields corresponded to absolute yields. Results are summarized in Table III.

Product Isolation. The following represents an exhaustive isolation. To 51.4 g of solution 2 was added 1.42 g (11.2 mmol) of **1a** ($[KBr]:[\mathbf{1a}] = 1.8$ and total $[Br^-]:[\mathbf{1a}] = 6.4$). The reaction mixture was held at 40 °C for 12 h. Then 200 mL of hexane and 50 mL of H_2O were added *without phase separation*, followed by a solution of 15 g of $NaClO_4 \cdot H_2O$ in 50 mL of H_2O. The precipitated $CTAClO_4$ was removed by filtration and washed with three 100-mL portions of hexane. The combined hexane layers

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were washed twice with 50-mL portions of H_2O and dried (Na_2SO_4). Rotary evaporation left 1.63 g of an oil. The aqueous washes and the original aqueous filtrates were combined and continuously extracted for 25 h with hexane, which was dried (Na_2SO_4) and rotary evaporated to give 34.8 mg of an oil. The $CTAClO_4$ from above was slurried with 300 mL of hexane, filtered, and then washed further with two 100-mL portions of hexane. These combined hexane solutions were dried (Na_2SO_4) and rotary evaporated to leave 0.123 g of an oil. The $CTAClO_4$ was then continuously extracted with hexane in a Soxhlet extractor for 24 h. Rotary evaporation of the hexane after drying (Na_2SO_4) left no additional oil. The oil recovered from the above operations, 1.79 g total, *contained* 1.8 *mmol* of **1a**, 3.8 *mmol* of **2a**, 1.0 *mmol* of **3a**, and 0.28 mmol of **4a** by ^1H NMR analysis with anisole as internal standard. The combined amounts represent a recovery of 61% with respect to starting material. A control demonstrated that **1a** codistills with 1-butanol and hexane on rotary evaporation, and the same is assumed for **2a**.

Phase Diagram. The CTABr (Aldrich) was recrystallized twice from 4:1 (v/v) MeCOMe–MeOH at 25 °C, the KBr was reagent grade, and the solvents were HPLC (H_2O and hexane) and spectral grade (1-butanol, Mallinkrodt). The hexane contained 85% *n*-hexane plus isomers. The S component consisted of a 1.23:1 (w/w) mixture of CTABr and 1-butanol, the W coponent of a 1:5 (w/w) KBr–H_2O solution, and the O component of hexane. The tentative phase boundaries of the pseudoternary phase diagram at 40.0 ± 0.1 °C were determined by preparing solutions along the S/O and S/W axes and titrating with W and O, respectively. Mixtures were prepared along both sides of these boundaries and equilibrated for 2–3 days, and their phase behavior was noted by visual inspection. Then they were titrated with small amounts of either O or W, equilibrating 2–3 days between titrations.

Dispersion Tests. One drop of a solution was added to 1 mL of a given solvent [H_2O, 1:5 (w/w) KBr–H_2O, 1-butanol, hexane], and it was noted whether or not the drop immediately dispersed to give a homogeneous system. The results are summarized in the text.

^{13}C NMR Spectra. The δ_{obs} values were obtained with solutions 1–7 containing <1% Me_4Si and D_2O substituted for H_2O, and the δ_o value (62.443) with a hexane solution containing 5% 1-butanol and <1% Me_4Si (coaxial D_2O lock). The δ_i value (61.850) was taken as δ_{obs} of solution 1.

4-Ethylbenzyl Chloride (1b). According to a standard procedure,[25] 4-ethylbenzyl alcohol (**4b**) (Aldrich) was converted with PCl_3 and pyridine in Et_2O into **1b**: bp 64–66 °C (8 mmHg); lit.[26] bp 81–82 °C (11 mmHg).

4-*n*-Dodecylbenzyl Chloride (1c). According to the literature,[27] 1-phenyldodecane (Aldrich) was chloromethylated with paraformaldehyde and PCl_3 in MeOH to give **1c**: mp 34.5–35.5 °C; lit.[27] mp 35.5–36 °C.

4-Ethylbenzyl Bromide (2b). By an established procedure,[25] **4b** was converted to **2b**: bp 71–72 °C (7 mmHg); lit. 84 °C (0.8 mmHg),[28] 70 °C (0.1 mmHg).[29]

4-*n*-Dodecylbenzyl Bromide (2c). A literature procedure[30] was used to convert **4c**[27] into **2c**. Recrystallization of crude material from MeOH at 5 °C gave **2c**: mp 45–46 °C; ^1H NMR (270 MHz) δ 7.10–7.34 (AA′BB′, 4 H, Ar H), 4.49 (s, 2 H, CH_2Br), 2.58 (t, J = 7.5 Hz, 2 H, $ArCH_2$), 1.51–1.65 (m, 2 H, $ArCH_2CH_2$), 1.25 (s, 18 H, $(CH_2)_9CH_3$), 0.88 (t, 3 H, CH_3). Anal. Calcd for $C_{19}H_{31}Br$: C, 67.24; H, 9.21. Found: C, 67.37, H, 9.23.

Benzyl *n*-Butyl Ether (3a). Under N_2, 0.575 g (25.0 mmol) of Na and 2.67 g (36.0 mmol) of 1-butanol were added to 10 mL of hexamethylphosphoramide (distilled from CaO). Then 3.17 g (25.0 mmol) of **1a** was added, and the resultant solution was held at 70 °C for 4 h and added to a mixture of hexane and H_2O. The hexane layer was washed 3 times with water and once with aqueous saturated NaCl and dried (Na_2SO_4). Rotary evaporation left 2.1 g of crude material which was distilled to give 1.33 g (32%) of **3a**.[31]

4-Ethylbenzyl *n*-Butyl Ether (3b). The procedure for **3a** was used to give (50%) **3b**: bp 68–70 °C (0.2 mmHg); ^1H NMR (60 MHz) δ 7.17 (s, 4 H, Ar H), 4.42 (s, 2 H, $ArCH_2O$), 3.40 (t, J = 6.0 Hz, 2 H, CH_2O), 2.63 (q, J = 7.4 Hz, 2 H, $ArCH_2$), 1.40–1.80 (m, 4 H, $CH_3CH_2CH_2CH_2$), 1.23 (t, J = 7.5 Hz, 3 H, $ArCH_2CH_3$), 0.93 (t, J = 7.5 Hz, 3 H, CH_3). Preparative GC (145 °C) gave an analytical sample. High-resolution mass spectrum (HRMS): M^+, 192.1520; calcd for $C_{13}H_{20}O$, 192.1514.

4-*n*-Dodecylbenzyl *n*-Butyl Ether (3c). To 50 mL of 1-butanol (distilled from BaO under N_2) was added 0.35 g (15 mmol) of Na, followed by 0.24 g (0.71 mmol) of **2c** after the Na dissolved. The resultant solution was stirred at 25 °C overnight and then at 70 °C overnight and added to a mixture of H_2O and hexane. The aqueous layer was extracted twice with hexane, and the combined hexane layers were washed once with aqueous 5% $NaHCO_3$ and twice with aqueous saturated NaCl and then dried (Na_2SO_4). Rotary evaporation left 0.28 g of an oil. Preparative GC (200 °C) gave **3c**: ^1H NMR (270 MHz) δ 7.10–7.30 (AA′BB′, 4 H, Ar H), 4.46 (s, 2 H, $ArCH_2O$), 3.46 (t, J = 6.5 Hz, 2 H, OCH_2CH_2), 2.58 (t, J = 7.5 Hz, 2 H, $ArCH_2$), 1.50–1.70 (m, 4 H, $ArCH_2CH_2$ and OCH_2CH_2), 1.18–1.50 (m, with s at 1.25, 20 H, $(CH_2)_9CH_3$ and $OCH_2CH_2CH_2CH_3$), 0.91 (t, 6 H, CH_3). HRMS: M^+, 332.3073; calcd for $C_{23}H_{40}O$, 332.3079.

4-*n*-Dodecylbenzyl Alcohol (4c). A literature procedure[32] was used to prepare 4-*n*-dodecylbenzoyl chloride from 1-phenyldodecane with oxalyl chloride and $AlCl_3$ in CH_2Cl_2. The acid chloride was hydrolyzed in aqueous sodium hydroxide, and 4-*n*-dodecylbenzoic acid was precipitated by acidification with hydrochloric acid. Extraction with ether yielded crude material that was recrystallized from H_2O–C_2H_5OH to give (63%) 4-*n*-dodecylbenzoic acid: mp 92–95 °C; lit.[33] mp 93–95 °C. With MeOH and H_2SO_4 this material was converted to methyl 4-*n*-dodecylbenzoate: bp 168–170 °C (0.05 mmHg); ^1H NMR (270 MHz) δ 7.94 (d, J = 8.1 Hz, 2 H, Ar $H_{2,6}$), 7.23 (d, J = 8.1 Hz, 2 H, Ar $H_{3,5}$) 3.89 (s, 3 H, CH_3O), 2.64 (t, J = 8.1 Hz, 2 H, $ArCH_2$), 1.53–1.70 (m, 2 H, $ArCH_2CH_2$), 1.25 (s, 18 H, $(CH_2)_9CH_3$), 0.88 (t, 3 H, CH_3). HRMS: M^+, 304.2391; calcd for $C_{20}H_{32}O_2$, 304.2401. In standard fashion, reduction of the ester with $LiAlH_4$ in Et_2O gave (87%) of crude material that was recrystallized from hexane to yield **4c**: mp 50–51 °C; lit.[27] mp 50.5–51 °C.

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Registry No. **1a**, 100-44-7; **1b**, 1467-05-6; **1c**, 104-37-0; **2b**, 57825-30-6; **2c**, 92186-08-8; **3a**, 588-67-0; **3b**, 777-90-2; **3c**, 92186-09-9; **4b**, 768-59-2; Br^-, 24959-67-9; KBr, 7758-02-3; H_2O, 7732-18-5; Cl_3P, 7719-12-2; CTABr, 57-09-0; 4-*n*-dodecylbenzoyl chloride, 53097-40-8; methyl 4-*n*-dodecylbenzoate, 92186-10-2; 1-butanol, 71-36-3; hexane, 110-54-3; 1-phenyldodecane, 123-01-3; paraformaldehyde, 30525-89-4; 4-*n*-dodecylbenzoic acid, 21021-55-6.

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