## REACTIONS IN MICROEMULSION MEDIA. NUCLEOPHILIC DISPLACEMENT

## REACTION OF BENZYL CHLORIDE WITH BROMIDE ION

Craig A. Martin, Patrick M. McCrann, George H. Angelos, and David A. Jaeger Department of Chemistry, University of Wyoming, Laramie, Wyoming 82071

<u>Abstract</u>: A kinetic and synthetic study of the reaction of benzyl chloride with bromide ion has been performed in microemulsions composed of cetyltrimethylammonium bromide, l-butanol, water, potassium bromide, and hexane; rates and yields of benzyl bromide formation decreased with increasing hexane content.

Microemulsions are transparent or translucent, thermodynamically-stable liquid dispersions of water and oil<sup>1</sup> that are stabilized by a surfactant and, in most cases, a cosurfactant such as a short-chain aliphatic alcohol. Both water-dispersed-in-oil (w/o) and oil-in-water (o/w) systems are possible. Microemulsions can simultaneously solubilize considerable amounts of dissimilar compounds and thus hold potential as media for homogeneous reactions of organic substrates with ionic, inorganic reagents. Since other methods used for such reactions (<u>i.e.</u>, rapid stirring, cosolvent, dipolar aprotic solvent, phase transfer catalysis) have their unique limitations, we have begun a delineation of this potential.<sup>2</sup>

For our initial study in microemulsion media, we have chosen the reaction of benzyl chloride  $(\underline{1})$  with bromide ion to give benzyl bromide  $(\underline{2})$  (eq 1), which has been and can be performed under other conditions. Therefore, the comparison of present with earlier results<sup>3</sup> will allow calibration of the efficacy of microemulsion catalysis.

$$c_{6}H_{5}CH_{2}C1 + Br \longrightarrow c_{6}H_{5}CH_{2}Br + C1 \qquad (1)$$

$$\frac{1}{2} \qquad \qquad 2$$

Microemulsions were prepared from combinations of hexane (0), a 1:5 (w/w)  $\text{KBr-H}_20$  solution (W), and a 1.23:1 (w/w) mixture (S) of cetyltrimethylammonium bromide (CTABr) and 1-butanol. A pseudoternary phase map was constructed at 40.0  $\pm$  0.1°C and is given in Figure 1; compositions are on a weight basis. The unhatched region corresponds to microemulsions, and the hatched region to heterogeneous mixtures.

<u>Kinetic Studies</u>. Runs 1-6 were performed at 40.0  $\pm$  0.1°C under pseudo first-order conditions in the corresponding microemulsion compositions<sup>4</sup> indicated along the dashed line of Figure 1 with [KBr]:[<u>1</u>] = 20:1 and total [Br]:[<u>1</u>] = 72:1. The observed initial pseudo first-order rate constants,  $k_{\psi}$ , are given in Table 1 for these and runs 7-9, which were performed in other media as indicated for comparison purposes with [CTABr(KBr)]:[<u>1</u>] = 20:1.

Figure 2 depicts an idealized microemulsion; curvature of the assumed spherical dispersed droplets has been ignored. Water and KBr are confined to the aqueous pseudophase, hexane to the oil pseudophase, CTABr to the interphase, and 1-butanol is distributed between the interphase and the oil pseudophase. Second-order rate constants,  $k_2$ , were calculated based on the assumption that reaction occurs only in the interphase and involves only Br bound to CTA<sup>+</sup>.<sup>5</sup> Thus, eq 2,



$H_20 + KBr$	aqueous pseudophase
CTABr + 1-BuOH	interphase
hexane + 1-BuOH	oil pseudophase

Figure 1. Microemulsion pseudoternary phase map.

Figure 2. Schematic representation of an idealized microemulsion.

adapted from Bunton and de Buzzaccarini,<sup>6</sup> can be applied, where  $V_i$  is the total interphase volume in a reaction mixture.<sup>7</sup> The fraction of 1-butanol in the interphase was estimated by <sup>13</sup>C NMR (67.8 MHz) according to eq 3.<sup>8</sup> The terms  $X_i$  and  $X_o$  are the mole fractions of 1-butanol in the interphase (polar) and oil pseudophase (nonpolar), respectively;  $\delta_i$ ,  $\delta_o$ , and  $\delta_{obs}$  are the chemical shifts (ppm <u>vs</u>. Me<sub>4</sub>Si) of carbon-1 of 1-butanol in a polar environment, in a nonpolar environment, and in a microemulsion, respectively.<sup>9</sup> Values of  $V_i$  were then calculated using the molar volumes of micellar CTABr (364 mL/mole)<sup>10</sup> and 1-butanol (92 mL/mole, from its density). If the minor amounts of dissociation of Br<sup>-</sup> from the interphase are neglected,<sup>11</sup> values of  $k_2$  are obtained as listed in Table 1 along with values of  $\delta_{obs}$ ,  $X_i$ , and  $V_i$ .

 $k_2 = k_{\psi} V_i / (\text{moles Br} \text{ bound to interphase})$  (2)  $\delta_{\text{obs}} = X_i \delta_i + X_o \delta_o$  (3)

In runs 1-6, the decreases in both  $k_{\psi}$  and  $k_2$  as the fraction of hexane increases probably reflect a dilution effect. As the volume of the interphase decreases relative to that of the oil pseudophase, the fraction of <u>1</u> in the former, the reactive site, decreases also. Relative to  $k_2$  for the reaction in aqueous CTABr micelles (run 7), those for the microemulsions are uniformly lower, again most likely due to a dilution effect. It is interesting to note the similarity of the  $k_2$  values for runs 7 and 9; within the micellar pseudophase the reaction is neither catalyzed nor inhibited relative to that in aqueous ethanol.

<u>Synthetic Studies</u>. The approximate upper solubility limits for <u>1</u> in the various media are given in Table 2. Although micellar solution 7 gave the largest value of  $k_{\psi}$ , it solubilized the smallest amount of <u>1</u> and is therefore the least suited for practical synthesis. Hexane-rich microemulsions 4-6 can solubilize more <u>1</u> (molar basis) than the total amount of Br<sup>-</sup> present, and all microemulsions, except 3, more <u>1</u> than KBr.<sup>12</sup>

The reaction media of Table 1 were used in synthetic studies; Table 2 records the product distributions after 12 h at 40.0°C. In solutions 1-6,  $[KBr]:[\underline{1}] = 10:1$  and total  $[Br]:[\underline{1}] = 36:1$ ; in solutions 7-9,  $[CTABr(KBr)]:[\underline{1}] = 10:1$ . Water-rich microemulsions 1-3 gave the highest

run	run reaction medium microemulsions		$[1], 10^3 M 10^3 k_{\psi}^{a}, \min^{-1}$		<sup>δ</sup> obs	X <sub>i</sub>	V <sub>i</sub> , <sup>b</sup> mL	10 <sup>3</sup> k <sub>2</sub> , <sup>c</sup> M <sup>-1</sup> min <sup>-1</sup>		
	% S	% W	<u>% 0</u>							
1	67	28	5	18	2.6	(0.2)	61.876	0.96	7.3	1.9
2	57	24	19	16	1.8	(0.1)	62.007	0.74	5.5	1.2
3	46	18	36	10	1.0	(0.1)	62.085	0.60	4.1	0.62
4	36	15	49	8.1	1.0	(0,1)	62,190	0.43	2.9	0.51
5	24	10	66	5.3	0.62	(0.06)	62,216	0.38	1.8	0.31
6	15	7	78	3.1	0.32	(0.03)	62.320	0.21	1.0	0.14
	otl	her me	dia							
7	10% (w/w	w) CTA	Br-H <sub>2</sub> O	13	5.9	(0.4)			1.0 <sup>d</sup>	2.9 <sup>e</sup>
8	10% (w/v	w) CTA	Br-CHC13	19	2.6	(0.2)			1.0 <sup>d</sup>	0.96 <sup>f</sup>
9	9 0.40 M KBr in 25%			20	1.2	(0.1)				3.0
	(v/v)	H <sub>2</sub> 0-C	2 <sup>н</sup> 5 <sup>он</sup>							

Table 1. Reaction of Benzyl Chloride with Bromide Ion in Microemulsion and Other Media at 40.0°C.

<sup>a</sup>Initial rate constant; each run was duplicated; estimated errors are in parentheses. For a typical run, 7-9 points were taken within the first half-life, during which side products 3 and 4 were not detected. Direct analyses of reaction mixture aliquots were made by calibrated HPLC [4.6 mm (i.d.) x 25 cm 10  $\mu$  LiChrosorb RP-18; aqueous CH<sub>3</sub>CN gradient elution; 254 nm UV detection]. <sup>b</sup>Calculated interphase volume in 10 g of reaction mixture. <sup>c</sup>For all but run 9, calculated with eq 2. <sup>d</sup>Volume of CTABr. <sup>e</sup>Calculated with  $\alpha = 0.25$  (ref. 11). <sup>f</sup>Calculated with  $\alpha = 0$ .

Table 2. Solubility Limits of <u>1</u> in Microemulsion and Other Media and Product Distributions after 12 h at  $40.0^{\circ}$ C.

solubility limit		initial [ <u>1</u> ], 10 <sup>3</sup> M <sup>a</sup>	yields, % <sup>b</sup>				
of <u>1</u> , M	soln		<u>1</u>	2	<u>3</u>	<u>4</u>	
0.84	1	37	8 (27)	83 (66)	7 (6)	2 (1)	
0.52	2	30	18 (33)	77 (63)	4 (3)	1 (1)	
0.16	3	21	21 (41)	75 (57)	3 (2)	1 (0)	
0.64	4	16	50	50	0	0	
1.9	5	11	64	36	0	0.	
2.0	6	5.8	83 (79)	17 (21)	0 (0)	0 (0)	
0.10	7	28	23	66		11	
>4.4	8	38	50	50			
0.47	9	40	55	44		1	

<sup>a</sup>Initial concentration in the synthetic runs. <sup>D</sup>Relative yields by HPLC; controls with an internal standard (anisole) indicated that they adequately represent absolute yields.

yields of  $\underline{2}$  but also the greatest amounts of side products, benzyl butyl ether ( $\underline{3}$ ) and benzyl alcohol ( $\underline{4}$ ). In general, the conversion of  $\underline{1}$  and the formation of  $\underline{3}$  and  $\underline{4}$  decreased with increasing hexane content. These decreases are a consequence of decreasing rates since the molar ratio of total Br<sup>-</sup> to  $\underline{1}$  is constant in solutions 1-6. Table 2 also contains yields in parentheses for analogous runs made with total [Br<sup>-</sup>]:[ $\underline{1}$ ] = 7.2:1; they decreased somewhat or remained essentially unchanged relative to those obtained with the five-fold higher ratio. Almost complete reaction of  $\underline{1}$  results when water-rich solutions 1-3 and 7 stand overnight; side products  $\underline{3}$  and  $\underline{4}$  then constitute 10-25% of the product mixtures.

Overall, the conversions of 1 to 2 in the water-rich microemulsions equal or exceed those

reported for phase transfer<sup>3a</sup> and triphase<sup>3b</sup> catalyzed reactions. Organic products can be isolated by the addition of aqueous  $NaClO_4$ ·H<sub>2</sub>O to precipitate  $CTAClO_4$ , followed by hexane extraction of the filtrate.<sup>13</sup>

<u>Acknowledgment</u> is made to the U.S. Army Research Office and to the Marathon Oil Company for support of this research, and to the National Science Foundation for a departmental grant (CHE-8026553) for the purchase of a JEOL FX-270 NMR spectrometer.

## References and Notes

- (a) Prince, L. M., Ed. "Microemulsions: Theory and Practice"; Academic Press: New York, 1977. (b) Danielsson, I.; Lindman, B. <u>Colloids Surf.</u> <u>1981</u>, <u>3</u>, 391.
- Microemulsions have been used previously as reaction media; for examples, see Mackay, R. A. <u>Adv. Colloid Interface Sci. 1981</u>, <u>15</u>, 131, and references therein. However, to our knowledge, only one study has had synthetic objectives (Gonzales, A.; Holt, S. L. <u>J. Org. Chem.</u> <u>1981</u>, <u>46</u>, 2594); it used detergentless microemulsions.
- (a) Jonczyk, A.; Ludwikow, M.; Makosza, M. <u>Angew. Chem., Int. Ed. Engl.</u> <u>1978</u>, <u>17</u>, 62. (b) Regen, S. L. <u>J. Org. Chem.</u> <u>1977</u>, <u>42</u>, 875.
- Dispersion tests and conductivity and other data indicate that 1 and 2 are o/w and 6 is w/o the results for 3-5 are inconclusive.
- 5. This assumption is supported by the fact that for runs <u>without KBr</u> corresponding otherwise to 1, 3, and 6, the same k<sub>i</sub> values were obtained within experimental error.
- 6. Bunton, C. A.; de Buzzaccarini, F. J. Phys. Chem. 1981, 85, 3142.
- 7. Lower-limit k<sub>2</sub>'s result because the calculation of V<sub>i</sub> neglects contributions due to water of hydration for CTABr and possible penetration of hexane.
- 8. Tricot, Y.; Kiwi, J.; Niederberger, W.; Grätzel, M. J. Phys. Chem. 1981, 85, 862.
- 9. The  $\delta_{obs}$  and  $\delta_i$  (61.850) values were obtained with microemulsions and a 70:30 (w/w) S-W solution, respectively, containing <1% Me<sub>4</sub>Si and D<sub>2</sub>O substituted for H<sub>2</sub>O, and the  $\delta_o$  value (62.443) with a hexane solution containing 5% 1-butanol and <1% Me<sub>4</sub>Si (coaxial D<sub>2</sub>O lock.)
- 10. Güveli, D.E.; Kayes, J. B.; Davis, S. S. J. Colloid Interface Sci. 1981, 82, 307.
- 11. With the assumption that the dissociation equilibrium in these media is the same as that for aqueous micellar CTABr (Fabre, H.; Kamenka, N.; Khan, A.; Lindblom, G.; Lindman, B.; Tiddy, G. J. T. J. Phys. Chem. 1980, 84, 3428), a dissociation constant was calculated (K = 8.3 x 10<sup>-2</sup> M) and used to determine α, the fraction of Br<sup>-</sup> dissociated from the interphase (CTABr) in the presence of KBr. In runs 1-6, α decreases from 0.05 to 0.01, respectively.
- 12. Of course, high conversions in the present reaction can be obtained only with total [Br<sup>-</sup>]: [1] >1.
- The low recoveries obtained (ca. 50%) resulted from losses due to co-distillation (demonstrated for <u>1</u> and assumed for <u>2</u>) with hexane and l-butanol during rotary-evaporation of extracts and thus do not fairly represent the ability to isolate organic products from microemulsions. In any event, the use of destructible surfactants (Jaeger, D. A.; Frey, M. R. J. Org. Chem. <u>1982</u>, <u>47</u>, 311; Jaeger, D. A.; Ward, M. D. <u>ibid</u>. <u>1982</u>, <u>47</u>, 2221) will simplify product isolation from microemulsions.