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REACTIONS IN MICROEMULSION MEDIA. BOROHYDRIDE REDUCTION OF MONO- AND DICARBONYL COMPOUNDS'

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Abstract—Microemulsions were prepared at 26" from mixtures of hexanes (0), a 50 : 1 (w/w) solution (*W*) of 0.1 M KOH–$NaBH_4$, and a 1.23: 1 (w/w) mixture (S) of hexadecyltrimethylammonium bromide (HTABr) and 1-butanol. A pseudotemary phase map contained a significant microemulsion (μE) region, and μE's A and B (60: 35: 5 and 20: 10: 70 *S* : W: 0, respectively) were used for reduction of several monocarbonyl compounds [benzophenone (1a), benzaldehyde (2a), acetophenone (3a), and 1-phenyl-1-octadecanone (4a)], an α,β-unsaturated ketone [*trans*-4-phenyl-3-buten-2-one (6a)], and a diketone [4-(4'-benzoylphenyl)-2-butanone (7a)] at 26". For comparison purposes, reductions were also performed in aqueous 2-propanol (2–PrOH A and 2–PrOH B) prepared by the substitution of 2-propanol for the *S* and 0 components of μE's A and B. Generally, the reductions were slightly faster in the microemulsion media than in the corresponding aqueous 2-propanol media. The significantly slower reduction of 4a relative to that of 3a in μE B indicated that the interphase is the reactive site. With enone 6a, the influence of microemulsions on the competition between 1,2- and 1,4-reduction was determined. In μE's A and B there was 8% and 11% 1,4-reduction, respectively, whereas in 2–PrOH A and B there was only a trace. With diketone 7a, the reactivity of the aromatic carbonyl group relative to that of the aliphatic carbonyl group increased on going from 2-PrOH A and B to μE's A and B, respectively. For the sodium borohydride reduction of ketones, microemulsion catalysis is more effective than phase transfer catalysis or the use of a tetraalkylammonium borohydride in a hydrocarbon solvent.

Microemulsions are optically clear or translucent, thermodynamically-stable liquid dispersions of water in oil (w/o) and of oil in water (o/w)[2] that are stabilized by a surfactant and, in most cases, a cosurfacant such as a short-chain aliphatic alcohol. They can solubilize considerable amounts of a wide variety of materials ranging from nonpolar organic to ionic, inorganic compounds; moreover, they can simultaneously solubilize compounds from both ends of this spectrum. Thus, microemulsions hold potential as media for homogeneous reactions of organic substrates with ionic inorganic reagents. Indeed, there have been several reports of such reactions in microemulsions,[3] but very few of them have had synthetic objectives. Holt and Gonzalez have studied lactonization[4] and Diels–Alder[5] reactions and we a nucleophilic displacement reaction.'

The useful solvents for sodium borohydride reductions in terms of its solubihty and reactivity include water, methanol, ethanol, 2-propanol, and diglyme containing a protic solvent.[6] However, many relatively nonpolar organic compounds are insoluble in these solvents. It is for such compounds that microemulsions are attractive reaction media. Herein we report the formulation of microemulsions containing sodium borohydride, their use in the reduction of several carbonyl compounds, and a determination of the microemulsion reactive site.

RESULTS AND DISCUSSION

Microemulsions were prepared from mixtures of hexanes (0), a 50: 1 (w/w) solution (*W*) of 0.1 M KOH–$NaBH_4$, and a 1.23 : 1 (w/w) mixture (S) of hexadecyltrimethylammonium bromide (HTABr) and 1-butanol. The pseudotemary phase diagram was constructed by titration techniques at 26.0 ± 0.1" and is given in Fig. 1; compositions are on a weight basis. The unhatched region corresponds to microemulsions, and the hatched region to heterogeneous mixtures. The microemulsions were stable for periods of up to and beyond 48 h with respect to borohydride decomposition as determined by the lack of hydrogen evolution (visual inspection).'

Microemulsion (μE) compositions A and B (60 : 35 : 5 and 20 : 10 : 70 *S* : *W* : 0, respectively) were used for reductions at 26". Conductivity data[8] suggested that the former is an o/w and that the latter is most likely a w/o system. For comparison purposes, reductions were also performed analogously in aqueous 2-propanol solutions (2–PrOH A and 2–PrOH B) prepared by the substitution of 2-propanol for the *S* and 0 components of μE's A and B. Each reduction described below was followed with time by the ***direct analysis*** of the reaction mixture itself by reverse phase high performance liquid chromatography (HPLC) with calibrated ultraviolet detection.

An initial survey of borohydride reduction was performed with monocarbonyl compounds benzophenone (1a), benzaldehyde (2a), acetophenone (3a), and 1-phenyl-1-octadecanone (4a)(eqn 1). The initial molar ratio of $NaBH_4$ to substrate was 2: 1 in μE A and 2–PrOH A and 1: 2 in μE B and 2–PrOH B.

(1)

1a, R = C_6H_5 1b, R = C_6H_5
2a, R = H 2b, R = H
3a, R = CH_3 3b, R = CH_3
4a, R = n-$C_{17}H_{35}$ 4b, R = n-$C_{17}H_{35}$

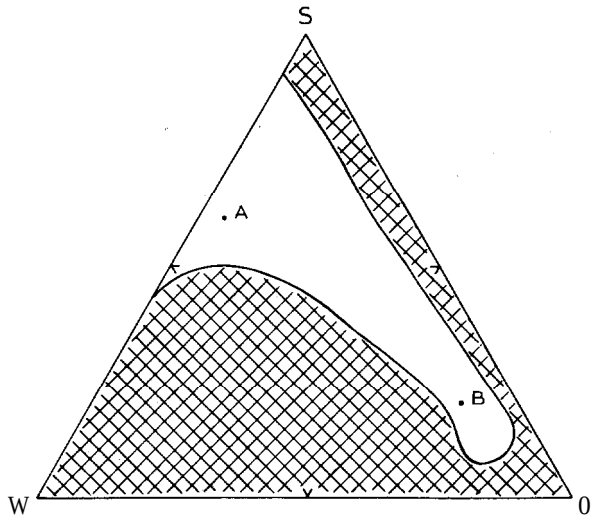


Fig. 1. Microemulsion pseudoternary phase diagram (O = hexanes; W = 50: 1 (w/w).0. 1 M KOH–$NaBH_4$; S = 1.23: 1 (w/w) HTABr–1–butanol.

The results for the reduction of **la** and **2a to** benzhydrol **(lb)** and benzyl alcohol **(2b),** respectively, are listed in Table 1. For **la, the** data indicate that the reaction was slightly faster in μE A than in 2–PrOH A, and that it proceeded at about the same rate in μE B and 2–PrOH B. Direct comparison of the results obtained in μE A and 2–PrOH A with those in μE B and 2–PrOH B cannot be made because the molar ratio of $NaBH_4$ to substrate was different in each set (see above). For **2a,** the reductions were very fast in all four media with no detectable rate differences. The results for the reduction of **3a** and **4a to 1-phenylethanol (3b)** and **1-phenyloctadecanol (4b),** respectively, are given in Table 2. For **3a, the** reductions were slightly faster in μE's A and B than in 2–PrOH A and 2–PrOH B, respectively. The results obtained with **4a are** noteworthy. It represents a high molecular weight, slightly polar substrate that would be expected to have limited solubility in conventional media used for $NaBH_4$ reductions.[6] Indeed, this was the case for **4a** in 2–PrOH A and 2–PrOH B and even in μE A. However, oil-rich μE B solubilized **4a** and allowed its reduction at the same concentration used for **la, 2a,** and **3a,** but at a rate about 18 times less than that for **3a.9** It is proposed that this difference results from the structural character of microemulsions and reflects the nature of the reactive site. Figure 2 depicts an **idealized microemulsion; curvature of the assumed spherical dispersed droplets has been ignored. In general, water, K^+, and Na^+ are confined to the aqueous pseudophase, hexanes to the oil pseudophase, and HTA^+ to the interphase. The counterions OH^-, BH_4^-, and Br^- are distributed between the aqueous pseudophase and the inter-**

Table 1. Reduction of la and 2a in microemulsions and aqueous 2-propanol

substrate[a]	time, min	% reduction[b,c] in μE A	2-PrOH A	μE B	2-PrOH B
1a	5	86			
	15		81		
	30	98	91	82	84
	60	100	99	90	88
	90			93	91
2a	1			100	100
	2		100		
	3	100			

[a]The concentration of 1a and 2a was 0.091 M in μE A and 2-PrOH A and 0.11 M in μE B and 2-PrOH B. [b]By direct calibrated HPLC analysis; values are from duplicate runs and are estimated to be ± 3%. [c]To 1b for 1a, and to 2b for 2a.

Table 2. Reduction of **3a** and **4a**[a] in microemulsions and aqueous 2-propanol

substrate[b]	time, min	% reduction[c,d] μE A	2-PrOH A	UEB	2 - m
3a (4a)	5	71	52		
	15	94	87		
	20	97			59
	25		95	85 (11)	76
	55			89 (20)	83
	115			96	91
	290			(55)	
	1385			(92)	

[a]The data for 4a are in parentheses. [b]The concentration of 3a was 0.092 m in μE A and 2-PrOH A and 0.11 m in μE B and 2-PrOH B. The concentration of 4a was 0.11 m in μE B. [c]By direct calibrated HPLC analysis; values are for duplicate runs and are estimated to he ± 3%. [d]To 3b for 3a, and to 4b for 4a.

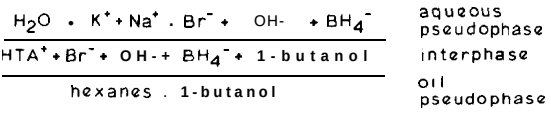
phase," and 1-butanol between the interphase and the oil pseudophase." Since 3a and 4a are essentially insoluble in water, there are two limiting possibilities for the reactive site in μE B, the oil pseudophase and the interphase. Reduction in the former would be expected to occur by a phase transfer process involving HTABH,. The reaction of 3a with HTABH, in benzene and 2-PrOH at 25" has been reported" to yield 0% and 59% of 3b after 4 h and 2 h, respectively, with the use of 50–100% excess HTABH,. From Table 2, it can be seen that after 25 min in μE B, 3a was 85% reduced. Thus it is very likely that not the oil pseudophase but the interphase is the reactive site, and the substantially greater reactivity of 3a over 4a supports this conclusion. On solubilization in a microemulsion, neutral organic compounds such as **3a** and **4a** should partition between the oil pseudophase and the more polar interphase. Due to the greater relative lipophilic character of **4a**, a lesser fraction of it should be solubilized at the interphase than of **3a**.[13] Thus, the much slower reduction of **4a**[14] is consistent with the model of Fig. 2 and strongly suggests that the interphase is the reactive site; on a time-averaged basis, there is simply less 4a than 3a at the interphase.[15] Others have observed[16] similar reactivity trends in w/o microemulsions for base-catalyzed hydrolyses of pnitrophenyl alkanoates.

A preparative reduction of 4a in μE B was performed under the conditions used for the kinetic runs of Table 2. Analysis of the reaction mixture by HPLC after four days indicated a 98% conversion of 4a to 4b. The isolation of **4b** in 93% yield involved the initial removal of HTA^+ by the addition of KPF, to precipitate HTAPF,.

The reduction of methyl benzoate (5) to benzyl alcohol (2b) (eqn 2) was attempted in μE A at 26" with a 2 : 1 molar ratio of $NaBH_4$ to 5. However, not unexpectedly the reduction was accompanied by saponification to potassium/sodium benzoate and transesterification to n-butyl benzoate as determined by HPLC analysis. Even when potassium hydroxide was deleted from μE A, analogous results were obtained, so the reduction of 5 was not studied further.

5 2b (2)

The α,β-unsaturated ketone 6a and diketone 7a were used in two studies of regioselectivity in borohydride reductions in μE's A and B. The molar ratio of $NaBH_4$ to 6a in μE A and 2-PrOH A was 2 :1, and in μE B and 2-PrOH B was 1 : 2. Both 1,2- and 1&reduction can occur to yield enol **6b** and ketone **6c**, respectively (eqn 3).[17] Under the conditions used, 1,4-reduction was monitored by the formation of alcohol **6d** because **6c** was undetectable due to its very rapid reduction to **6d** as demonstrated in a control (see Experimental). The results are summarized in Table 3. It is interesting to note that 1,4-reduction occurred in μE's A and B to greater extents than in 2-PrOH A and 2-PrOH B, respectively. Nikles and Sukenik have performed a similar study[18] with enone 6a in aqueous micellar HTABr and found 13% and 21% 1,4-reduction under non-micellar and micellar conditions, respectively.[19]

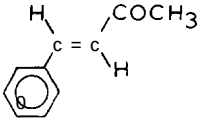


Pig. 2. Schematic representation of an idealized microemulsion.

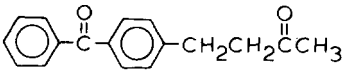
Table 3. Reduction of **6a**[a] in microemulsions and aqueous 2-propanol

	product mixture, %[b,c] in											
	μE A			2-PrOH A			μE B			2-PrOH B		
time, min	6a	6b	6d	6a	6b	6d	6a	6b	6d	6a	6b	6d
5	56	44	tr	71	29		76	24	tr	90	10	
45							24	71	5	52	48	tr
90		92	8		100	tr				33	67	tr
180							3	85	12	20	80	tr
1200		92	8					89	11		100	tr

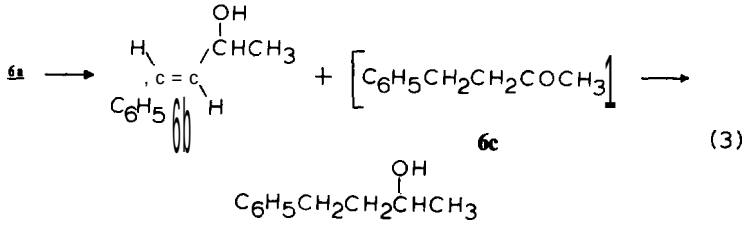
[a]The concentration of 6a was 0.090 M in μE A and 2-PrOH A and 0.11 M in μE B and 2-PrOH B. [b]By direct calibrated HPLC analysis; values are for duplicate runs and are estimated to be ± 5%. [c]For 6d, trace amounts (< ca. 4%) are indicated by tr.



6a



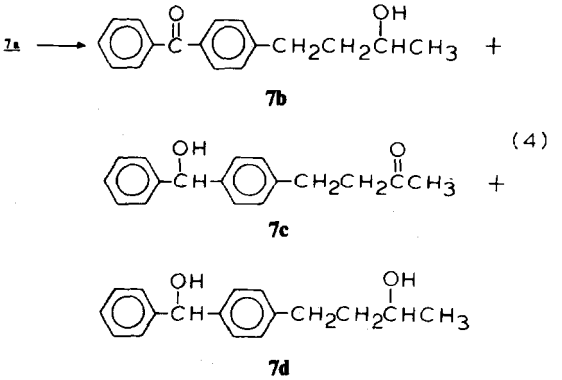
7a



6d

As noted above, the results with **3a** and **4a** strongly suggest that the interphase is the predominant site of borohydride reduction in μE B, and the same is assumed for μE A. Therefore, in principle it should be possible to reduce selectively one carbonyl group of a diketone if this group is preferentially solubilized in the interphase on a time-averaged basis. To study the possibility, **diketone 7a** was used. The aromatic carbonyl group of **7a** may prefer the interphase as a solubilization site more so than does the aliphatic carbonyl group; it has been demonstrated[13,20] with other systems that aromatic groups absorb at micelle-water interfaces.

Reduction of **diketone 7a** was performed in μE A and 2-PrOH A with a molar ratio of $NaBH_4$ to **7a** of 4:1, and in μE B and 2-PrOH B with a ratio of 1:1. Reduction products ketol **7b**, ketol **7c**, and diol **7d** were obtained (eqn 4), and the results are given in Tables 4 and 5. The regioselective reduction of the aromatic carbonyl group was not realized. However, a comparison of the reactivities of the two groups in μE A with those in 2-PrOH A indicates that the reactivity of the aromatic carbonyl group relative to that of the aliphatic carbonyl group was enhanced by a factor of about two in the microemulsion. The same conclusion can be drawn from the results in 2-PrOH B and μE B. For example, in Table 4 consider the product analysis at 2.5 min in μE A. Of the aromatic carbonyl groups originally present in **7a**, 32% of them [4% (**7c**) + 28% (**7d**)] were reduced at this time, and



7b

7c

7d

(4)

Table 4. Reduction of **7a**[a] in microemulsion A and aqueous 2-propanol solution A

	product mixture, %[b,c] in							
	μE A				2-PrOH A			
time, min	7a	7b	7c	7d	7a	7b	7c	7d
2					15	70	3	12
2.5	4	63	4	28				
S		53		47	2	15	tr	23
15		42		58		56		44
60		10		90		22		78
90		4		96		12		88.

[a]The concentration of 7a was 0.045 M in each solution. [b]By direct calibrated HPLC analysis; values are for duplicate runs and are estimated to be ± 3%. [c]Trace amount (< ca. 2%) is indicated bytr.

Table 5. Reduction of **7a**[a] in microemulsion B and aqueous 2-propanol solution B

	product mixture, %[b,c] in							
	μE B				2-PrOH B			
time, min	7a	7b	7c	7d	7a	7b	7c	7d
2					5 6 4 0		3	1
2.5	31	50	5	a				
15	1	55		44	.a	70	3	18
45		35		65	tr	64		36
75						55		45
120		15		85				
180		a		92				

[a]The concentration of 7a was 0.033 M in each solution. [b]By direct calibrated HPLC analysis; values are for duplicate runs and are estimated to be ± 3%. [c]Trace amount (< 1%) is indicated by tr.

the value for the aliphatic carbonyl groups was 91% [63% (7h) + 28% (7d)]. Thus, the relative reactivity ratio was 0.35 :1.[21] In 2-PrOH A at 2 min the conversions were 15% and 82% for the aromatic and aliphatic carbonyl groups, respectively, and the ratio was 0.18 : 1. At 5 min, the ratios were 0.47: 1 and 0.23: 1 in μE A and 2-PrOH A, respectively. In μE B the ratio was 0.22: 1 at 2.5 min and in 2-PrOH B was 0.10: 1 at 2min. At 15 min, the ratios were 0.44: 1 and 0.24: 1 in μE B and 2-PrOH B, respectively.

A comparison of the borohydride reductions above with those performed under phase transfer conditions with typical quatemary ammonium and phosphonium salts[22] indicates that the former are much faster. For example, **3a** underwent essentially complete reduction in μE's A and B in 20min and 115 min, respectively, whereas under phase transfer conditions with trioctylmethylammonium chloride in benzene/water at room temperature 2-octanone was only 80% reduced after 390 min.[23] This comparison is even more indicative of the greater reactivity of the microemulsion systems when one considers the fact that **3a** is expected to be intrinsically less reactive than 2-octanone in borohydride reduction due to the conjugating phenyl substituent.[14]

There have been other studies of carbonyl reduction with tetraalkylammonium borohydrides in aprotic media other than that mentioned above.[12] Raber *et al.*[24] have used tetraethyl- and tetrabutylammonium borohydride in dichloromethane; under these conditions diborane (produced by a reaction of borohydride with dichloromethane) participates in reduction. In benzene at room temperature, four

equivalents of tetrabutylammonium borohydride effected less than 3% reduction of 3a during 36 h.[24b] Apparently, the practical use of such borohydrides in hydrocarbon media requires the presence of a protic solvent or other electrophilic catalyst.[25]

In conclusion, for the sodium borohydride reduction of ketones, microemulsion catalysis is more effective than phase transfer catalysis or the use of a tetraalkylammonium borohydride in a hydrocarbon solvent. Furthermore, microemulsions are especially attractive media for the reduction of relatively nonpolar substrates.

EXPERIMENTAL

General procedures. All melting and boiling points are uncorrected. The ^{1}H NMR spectra were recorded with a JEOL FX-270 spectrometer (270 MHz), and $CDCl_3$ was used as solvent with TMS as internal standard. Infrared spectra were obtained on a Beckman Model IR-IO spectrophotometer with neat or Nujol mull samples between NaCl plates. Mass spectra were recorded on a Kratos MS-50 spectrometer at the Midwest Center for Mass Spectrometry at the University of Nebraska-Lincoln. The ionizing voltage was 70 eV, the filament current 500 μA, and the ion-source temperature 250"; direct insertion was used with ambient probe temperature. High performance liquid chromatography analyses were performed on two 25cm stainless steel columns packed with 10-μm LiChrosorb RP-18: column A, 4.6 mm (id) (Altex), and column B, 4.0 mm (id) (EM). Beckman Model 332 and 344 chromatographs were fitted with a column inlet filter (2μm) and a precolumn [3 cm x 4.6 mm (id): 10-μm LiChrosorb RP-18 (Brownlee)] between the sample injector and column. For detection and quantitation, Beckman Model 153 (254nm) and 165 (variable-wavelength) ultraviolet-visible detectors and a Hewlett-Packard Model 3390A reporting integrator were used. A backpressure regulator was attached to the outflow line of each detector. Preparative liquid chomatography separations were performed on a 25 cm x 21.2 mm (id) stainless steel column packed with 8-μm Zorbax ODS (du Pont). The Beckman Model 332 chromatograph, equipped with preparative pump heads, was used with a column inlet filter (2 μm) between the sample injector and column. The Beckman Model 153 detector, equipped with a preparative flow cell, was used for detection. For all analytical and preparative HPLC chromatography, mixtures of HPLC-grade H_2O and CH_3CN (J. T. Baker) were used at the compositions and flow rates indicated below.

Materials. Sodium borohydride (Alfa, 99%, powder) was used as received, and HTABr (Aldrich) was recrystallized twice from 4: 1 (v/v) CH_3COCH_3–CH_3OH (25"). The hexanes (J. T. Baker, HPLC grade), 1-butanol (Mallinckrodt, spectral grade), and 2-propanol (J. T. Baker, HPLC grade) were used as received. Benzophenone (1a) was recrystallized from hexane (25") to give material with m.p. 48–49°, and benzhydrol (1b) from 4: 1 (v/v) ether-hexane (25") to give material with m.p. 68-69". Benzaldehyde (2a), benzyl alcohol (2b), acetophenone (3a), 1-phenylethanol (3b), and methyl benzoate (5) were purified by distillation. The following materials (Aldrich) were used as received: *trans*-4-phenyl-3-buten-2-one (6a), m.p. 39–41°, 4-phenyl-2-butanone (6c), and 4-phenyl-2-butanol (6d). By the HPLC conditions used for analysis of reaction mixtures (see below), all materials were homogeneous except for 3b and 6c, which contained a trace of 3a and an unknown impurity, respectively, that were undetectable by ^{1}H NMR.

1-Phenyl-1-octadecanone (4a).[26] The preparation of 4a followed an established procedure.[26] Crude material was recrystallized once from 1: 1 (v/v) C_2H_5OH-ether (25°), twice from CH_3OH (25°), and three times from ether (−10°) to give 4a: m.p. 58-59" (lit m.p. 63.4–64.5°;[26] 59°[27]).

1-Phenyl-1-octadecanol (4b).[28] In standard fashion, reduction of 4a with $LiAlH_4$ in ether gave (70%) a white solid that was recrystallized from hexane (−10°) to yield 4b: m.p. 65–66° (lit[28] m.p. 65.8-66.5").

trans-4-Phenyl-3-buten-2-ol (6b).[29] The reduction of 6a with $LiAlH_4$ in ether at − 10" by a reverse addition procedure[30] yielded (83%) crude 6b as an oil, which by ^{1}H NMR and IR analysis contained starting material. This oil was subjected to preparative HPLC [eluant, 45 : 55 (v/v) CH_3CN–H_2O; flow rate, 21 ml/min; retention times: 6b, 8.5 min; 6a, 11.4 min]. The combined fractions containing 6b were rotary-evaporated to remove CH_3CN, and the aqueous residue was extracted twice with ether. The combined extracts were dried over Na_2SO_4 and rotary-evaporated to give 6b, m.p. 3638" (lit m.p. 35–36°;[29a] 33.5–34.5°[29b]), which was homogeneous by the HPLC analysis conditions used for reactions of 6a (se-e below).

4-(4′-Benzoylphenyl)-2-butanone (7a).[31] The procedure of Lansbury and: Peterson[31] was used to give (38%) 7a: m.p. 3637" (lit" m.p. 35–37°); ^{1}H NMR 6 7.70-7.82 (m, 4 H, ArH_{ortho} to CO), 7.53–7.64 (m, 1 H, ArH_{para}), 7.42–7.51 (m, 2 H, ArH_{meta}), 7.24-7.33 (m, 2 H, ArH_{meta}), 2.98 (t, J = 7.2 Hz, 2 H, CH_2), 2.81 (t, J = 7.2 Hz, 2 H, CH_2), 2.17 (s, 3 H, CH_3); IR (Nujol mull) 1710 (s) anh 1650 cm^{-1} (s).

4-(4′-Benzoylphenyl)-2-butanol (7b).[31] The procedure of Lansbury and Peterson" was used. Reduction of diketone 7a gave (82%) an oil which by ^{1}H NMR analysis was pure 7b. However, by the HPLC analysis conditions used for reactions of 7a (see below), an unknown impurity was detected. The oil was subjected to preparative HPLC [eluant, 55 : 45 (v/v) CH_3CN–H_2O; flow rate, 16.8 ml/min; retention times: 7b, 9.0 min; impurity, 6.0 min] to give 7b as an oil: ^{1}H NMR δ 7.237.84 (m, 9 H, ArH), 3.86 (sextet, J = 7 Hz, 1 H, OCH), 2.68–3.00 (m, 2 H, $ArCH_2$), 1.65–1.88 (m, 3 H, CH_2CO and OH), 1.25 (d, J = 7 Hz, CH_3); IR (neat) 3450 (s), 3050 (w), 3010 (w), 2960 (m), 2920 (m), 1650 (s), 1600 (s), 1570 (w), 1440 (m), 1408 (m), 1370 (w), 1310 (s), 1270 (s), 1170 (m), 1140 (w), 1120 (m), 1060 (wj, 1010 (w), 928 (m), 913 (m), 830 (w), 780 (w), 725 (w), 690 cm^{-1} (s). High resolution mass spectrum M^+, 254.1311; Calc for $C_{17}H_{18}O_2$, 254.1307.

4-[4′-(Phenylhydroxymethyl)phenyl]-2-butanone (7c).[31] The procedure of Lansbury and Peterson" was used. Reduction of diketone 7a gave an oil which by 'HNMR contained ketol 7c in addition to diketone 7a, ketol 7b, and diol 7d. This material was subjected to preparative HPLC [eluant, 55: 45 (v/v) CH_3CN–H_2O; flow rate, 16.8 ml/min; retention times: 7c, 7.0 min; 7a, 12.5 *min;* 7b, 9.0 min; 7d, 5.5 min] to give ketol 7c as an oil: ^{1}H NMR δ 7.1 l-7.42 (m, 9 H, ArH), 5.81 (s, 1 H, OCH), 2.86 (t, J = 7 Hz, 2 H, CH_2), 2.73 (t, J = 7 Hz, 2 H, CH_2), 2.26 (s, 1 H, OH), 2.12 (s, 3 H, CH_3); IR (neat) 3420 (s), 3060 (w), 3030 (w), 2920 (w), 1710 (s), 1510 (w), 1490(w), 1450 (m), 1360 (m), 1280 (w), 1175 (m), 1020 (m), 790 (w), 720 (w), 690 cm-' (s). High resolution mass spectrum: M^+, 254.1303; Calc for $C_{17}H_{18}O_2$, 254.1307.

4-[4′-Phenylhydroxymethyl)phenyl]-2-butanol (7d).[31] In standard fashion, diketone 7a was reduced with $LiAlH_4$ in ether to give (98%) diol 7d, which contained a trace of ketol 7b by IR analysis. This material was purified by preparative HPLC [eluant, 55:45 (v/v) CH_3CN–H_2O; flow rate, 16.8 ml/min; retention times: 7d, 5.7 min; 7b, 9.0 min] to give diol 7d as an oil (mixture of racemates): ^{1}H NMR δ 7.08-7.48 (m, 9 H, ArH), 5.78 (s, 1 H, ArCH), 3.77 (sextet, J = 7 Hz, 1 H, OCH), 2.31-2.79 (br s overlapping with m, 3 H total, OH and $ArCH_2$), 1.42-1.80 (br s overlapping with m, 3 H total, OH and CH_2CO), 1.18 (d, J = 7 Hz, 3 H, CH_3); IR (neat) 3350 (s), 3050 (w), 3020 (w), 2960 (w), 2920 (m), 1600 (w), 1505 (w), 1485 (m), 1445 (m), 1370 (m), 1170 (m), 1115 (m), 1010 (s), 935 (w), 715 (m), 690 cm^{-1} (s).

Pseudoternary phase diagram. A pseudotemary phase diagram (Fig. 1) of surfactant, aqueous, and oil components was constructed at 26.0 ± 0.1" to give a region of clear, homogeneous solutions. The surfactant component (S) consisted of a 1.23 : 1 (w/w) mixture of HTABr and 1-BuOH, respectively, and the oil component (0) of hexanes. The

aqueous component (W) consisted of 50: 1 (w/w) 0.1 M KOH–$NaBH_4$. With a variation of S/W from 85 : 15 (w/w) to 10: 90 by increments of 5, samples of *S* and *W were* weighed (*ca.* 6 g total) into ground-glass stoppered bottles. Each sample mixture was then titrated with hexanes to give the points at which it turned from heterogeneous (cloudy) to homogeneous (clear) and then back to heterogeneous (visual observation). The resulting points were used to detemine the rough boundary of the microemulsion region, and thirty samples (cu. 1 g each) around this boundary were equilibrated at 26" for 48 to 72 h. They were then titrated with either 0 or *W* with equilibration at 26" for 48 to 72 h between additions. The resulting points gave Fig. 1.

Conductivity measurements. The following conductivities (μmho/cm) were measured with a Yellow Springs Instrument (YSI) Model 31 conductivity bridge equipped with a YSI Model 3403 conductance cell with a cell constant of 1 cm^{-1}: μE A, 11,800; μE B, 57; hexanes (HPLC grade), < *0.2;* 50 : 1 (w/w) 0.1 M KOH–$NaBH_4$, 50,000; H_2O (distilled from $KMnO_4$, then boiled). < 0.2.

Reductions. The following general procedure was used. To a 50ml glass-stoppered round-bottomed flask was added 2.5 g, 5.0 g, or 10.0 g of the reaction medium (μE's A and B a&l 2–PrOH A and 2–PrOH B), which was-then equilibrated at 26° (at least 90 min for μE B and at least 45 min for the others). Then the appropriate amount of substrate was added to give: a 2 : 1 molar ratio of $NaBH_4$ to substrate for la, **2a**, **3a**, and **6a** in μE A and 2–PrOH A; a 1 : 2 molar ratio for the same substrates and **4a** in μE B and 2–PrOH B; a 4: 1 molar ratio for **7a** in μE A and 2–PrOH A; and a 1: 1 molar ratio for **7a** in μE B and 2–PrOH B. Samples (5 to 20 μl) of the reaction mixture were then removed by syringe at appropriate times and analyzed by HPLC; those aliquots that could not be analyzed immediately were added to melting point capillaries, frozen at once in liquid N,, and then stored at -10" until analyses could be made. For comparison purposes, "complete" reaction corresponded to the disappearance of > 95% of substrate. All reaction mixtures remained homogeneous throughout the time needed for complete reaction except that for diketone **7a** in 2–PrOH B; this system was slightly turbid immediately after the addition of 7a and ***became Very*** turbid (without phase separation) after 30 min.

The HPLC analysis conditions were as follows: (substrate: HPLC column, detection wavelength, eluant composition, flow rate, retention times of substrate and products): la: column A, 254 nm, 65 : 35 (v/v) CH_3CN–H_2O, 1 ml/min, la, 8.0 min, lb 6.0 min; **2a**: column A, 254 nm, 45: 55 (v/v) CH_3CN–H_2O, 1 ml/min, **2a**, 8.5 min, **2b**, 6.0 min; **3a**: column A, 254 nm, 45 : 55 (v/v) CH_3CN–H_2O, 1 ml/min, **3a**, 8.5 min, **3b**, 6.5 min; **4a**: column B, 254 nm, CH_3CN, 2 ml/min, **4a**, 25.5 min, **4b**, 24.0 mio; **6a**: column B, 220 nm, 20 : 80 (v/v) CH_3CN–H_2O, 2 ml/min, **6a**, 33.0 min, **6b** 26.0 min, **6c**, 35.5 mio, **6d**, 29.0 min; **7a**: column B, 254 nm, 55 : 45 (v/v) CH_3CN–H_2O, 1 ml/min, 7a. 11.6 min. **7b**, 9.0 min, **7c**, 7.1 min, **7d**, 5.8 min. The data for the various reductions are listed in Tables l-5.

The reduction of methyl benzoate (5) was attempted using the above procedure. To 10 g of μE A was added 0.124 g of 5 to give a 0.091 m solution. Uncalibrated analysis by HPLC [column A, 254 nm 65: 35 (v/v) CH_3CN–H_2O, 1 ml/min] at various times indicated the presence of substantial amounts of sodium (potassium) benzoate (retention time, 3.8 mio) and n-butyl benzoate (11.4 min) in addition to that of **2b** (4.5 min) and 5 (6.2 min). An analogous run was performed in a microemulsion prepared without KOH. Lesser amounts of sodium benzoate and n-butyl benzoate were detected.

Calibration factors for HPLC analyses. For the HPLC conditions employed for the analyses of reaction mixtures (see above), detector response factors relating each substrate to its reduction product(s) were determined with the use of known mixtures of these materials: la-lb, 51: 1, respectively; **2a**–**2b**, 123 : 1, respectively; **3a**–**3b**, 64 : 1, respectively; **4a**–**4b**, 24: 1, respectively; **6a**–**6b**–**6c**–**6d**, 1.2 : 2 : 1 : 1, respectively; and **7a**–**7b**–**7c**–**7d**, 34 : 31 : 1 : 1, respectively.

Control on HPLC analyses. To a 5.0 g aliquot of μE A equilibrated at 26" was added 57.7 mg (0.229 mmol) of diketone **7a** to give a 0.046 m solution. After 2.5 min, a sample was withdrawn and analyzed by HPLC with the same conditions used for the other reductions of **7a** above (Table 4), except that the flow rate was 0.5 ml/min. Other identical reaction mixtures were prepared and analyzed similarly at 2.5 min but with flow rates of 1 and 2 ml/min. The results of the aoalyses at the three different flow rates were within 3% of one another. Thus, it is apparent that minimal reduction occurred within a sample of a reaction mixture subsequent to its injection into the HPLC chromatograph.

Preparative reduction of 1-phenyl-1-octadecanone (**4a**). To 2.5 g of μE B at 26° was added 93.5 mg (0.270 mmol) of **4a** to give a concentration of 0.11 m with a $NaBH_4$ to **4a** molar ratio of 1: 2. The reaction mixture was held at 26" for 4 davs and was then analyzed by HPLC with the same conditions used for the reduction of **4a** above (Table 2). The reduction of **4a** to **4b** was 98% complete. To the reaction mixture, which contained 0.279 g (0.766 mmol) of HTABr, was added a solution of 0.218 g (1.18 mmol) of KPF, in 5 ml of H_2O. A white precipitate of $HTAPF_6$ formed immediately, and the mixture was shaken well and allowed to stand for 30min. It was then filtered twice through a fritted-glass funnel, and the solid in the funnel was washed with two 10 ml portions of hexane. The aqueous layer was extracted with three 25 ml portions of hexane. All hexane layers were combined and dried over Na_2SO_4, and rotary-evaporation left 87.6 mg (93%) of **4b**, m.p. 61–64°, which was homogeneous by ^1H NMR analysis.

Solubilities of 1-phenyl-1-octaakcanone (**4a**) **in *various media. The*** approximate solubilities at 26" of **4a** in 2.5 g aliquots each of μE A, 2-PrOH A, and 2–PrOH B, all prepared without $NaBH_4$, were determined by visual inspection. Each medium was equilibrated at 26" for at least 1 h before the addition of **4a**, and then the mixture was shaken and allowed to stand at 26" with intermittent shaking. For μE A, an amount of **4a** equivalent to 25% of the molar amount of **3a** used in this medium (Table 2) was added, most of it remained undissolved after 24 h. When a 10% equivalent of **4a** was added to μE A, most of it dissolved after 5 h, but it was still incompletely dissolved after 24 h. For 2–PrOH A, an amount of **4a** equivalent to 4% of the molar amount of **3a** used in this medium was added; most of it remained undissolved after 24 h. For 2–PrOH B, an amount of **4a** equivalent to 10% of the molar amount of **3a** used in this medium was added; most of it remained undissolved after 24 h. Wheo a 4% molar equivalent of **4a** was added to 2–PrOH B, some of it dissolved after 5 h, but it was still incompletely dissolved after 24 h.

Control on the reduction of enol **6b**. A 0.10 m solution of **6b** in μE B at 26" was prepared (molar ratio of $NaBH_4$ to **6b** = 0.5 : 1). At 5 mio and 1410 min, analysis by HPLC with the conditions used for the reduction of enone **6a** (see above) indicated the presence of only **6b**. Thus, **6b** does not undergo reduction to give alcohol **6d**.

Control on the reduction of 4-phenyl-2-butanone (**6c**). ***The*** reduction of 7.9 mg (0.053 mmol) of **6c** in 4.85 g of μE B was performed at 26° using the general reduction procedure above. The initial concentration of **6c**, 0.011 m, corresponds approximately to that of alcohol **6d** present after complete reaction of enone **6a** in μE B (Table 3). Therefore, the initial molar ratio of $NaBH_4$ to **6c** was 5: 1. After 10 min, 89% of **6c** was reduced to **6d**, and a second run under identical conditions gave the same result. Thus, **6c** is much more reactive than **6a**, and it is reasonable that it does not accumulate to allow its detection by HPLC.

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"It is realized that there is a difference between the intrinsic reactivities of **3a** and **4a** with respect to reduction by BH_4^-. For example, Brown and Ichikawa [H. C. Brown and K. Ichikawa, *J. Am.* Chem. *Soc.* 84, 373 (1962)] found that phenyl ethyl ketone is 1.8 times less reactive than **3a** with respect to $NaBH_4$ in 2-PrOH at 25". This difference is due to steric effects since. all alkyl groups have about the same polar effect [M. Char-ton, *J. Am.* Chem. *Soc.* 97, 3691 (1975)]. As the alkyl chain length increases to 17 in **4a** an additional modest decrease in intrinsic reactivity is expected. In a study of the hydroxide ion-catalyzed hydrolysis of a series of p-nitrophenyl esters in *water* at 25°, Guthrie [J. P. Guthrie, *J. Chem. Soc. Chem. Commun.* 897 (1972)] found that the decanoate ester was only 4.3 times less reactive than the acetate ester. The rate decrease was ascribed to coiling of the alkyl group back on itself with a resultant shielding of the ester carbonyl group. For **4a** in the oil pseudophase, the coiling effect is less important because an alkyl group is reasonably expected to be more extended in this medium than in water. For **4a** at the interphase, the coiling effect likewise is less important because. of its probable orientation with the benzoyl group in the interphase and the alkyl group extended into the oil pseudophase.

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