sulfoxides,[15] and sulfones[16] were synthesized according to literature procedures.

General Procedure for Desulfurization. The nickel reagent was prepared by mixing $\mathrm{NiBr_2{\cdot}DME}$ with 2 equiv of $\mathrm{Ph_3P}$ and 2 equiv of $\mathrm{LiAlH_4}$ in THF (ca. 30 mL) under nitrogen atmosphere. After the initial exothermic reaction subsided, the dark brown solution was stirred at room temperature for 30 min. Organosulfur compound was then syringed into 1–10 equiv (depending on the nature of the organosulfur substrate) of the nickel reagent described above. The mixture was stirred at room temperature for 1 day, quenched with saturated ammonium chloride solution (10 mL), and extracted with ether (3 × 25 mL). The combined organic solution was washed with brine solution, dried over anhydrous magnesium sulfate, and filtered. The filtrate was evaporated in vacuo to afford the residue, which was chromatographed on silica gel and eluted with hexane.

Desulfurization of 2-Naphthalenemethanethiol. According to the general procedure described above, the substrate (0.76 g, 4.4 mmol) was allowed to react with the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.97 g, 4.4 mmol), $\mathrm{Ph_3P}$ (2.4 g, 9.2 mmol), and $\mathrm{LiAlH_4}$ (0.21 g, 5.5 mmol) to yield 2-methylnaphthalene (0.50 g, 80%), which showed the same physical properties as those of the authentic sample.

Desulfurization of 2-Naphthalenemethanethiol with the Nickel Reagent Prepared from $\mathrm{LiAlD_4}$. According to the general procedure described above, the substrate (0.32 g, 1.8 mmol) was treated with the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.58 g, 1.9 mmol), $\mathrm{Ph_3P}$ (1.0 g, 3.8 mmol), and $\mathrm{LiAlD_4}$ (77 mg, 1.8 mmol) to give 2-methylnaphthalene-α-d_1 (0.12 g, 45%): ^{1}H NMR ($\mathrm{CDCl_3}$) δ 2.50 (s, 2.1 H), 7.2–8.0 (m, 7 H); ^{2}H NMR ($\mathrm{CHCl_3}$) δ 2.10 (t, J = 4.0 Hz); m/e 143.

Desulfurization of 2-Naphthalenethiol. According to the general procedure, the substrate (0.30 g, 1.9 mmol) was treated with the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.40 g, 1.8 mmol), $\mathrm{Ph_3P}$ (0.97 g, 3.7 mmol), and $\mathrm{LiAlH_4}$ (73 mg, 1.9 mmol) to give naphthalene (0.12 g, 50%), which exhibited properties identical with those of the authentic sample.

Desulfurization of 1-Decanethiol. Via the same method described above, the mercaptan (0.61 g, 3.5 mmol) was reduced by the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.76 g, 3.5 mmol), $\mathrm{Ph_3P}$ (1.9 g, 7.2 mmol), and $\mathrm{LiAlH_4}$ (0.14 g, 3.6 mmol) to afford *n*-decane (60%, GC yield[17]).

Desulfurization of 1-Adamantanethiol. By use of the general procedure, the sulfur compound (0.19 g, 1.1 mmol) was allowed to react with the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.39 g, 1.3 mmol), $\mathrm{Ph_3P}$ (0.61 g, 2.3 mmol), and $\mathrm{LiAlH_4}$ (47 mg 1.2 mmol) to afford adamantane (52% GC yield[17]).

Desulfurization of 9,9-Bis(phenylthio)fluorene (1a). Via the general procedure, **1a** (0.38 g, 1.0 mmol) was allowed to react with the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.62 g, 2.0 mmol), $\mathrm{Ph_3P}$ (1.1 g, 4.0 mmol), and $\mathrm{LiAlH_4}$ (76 mg, 2.0 mmol) to afford **1b** (0.14 g, 84%).

Desulfurization of 1,5-Diphenylpentane-1,5-dione Bis(dithioacetal) (2a). According to the general procedure depicted above, **2a** (0.40 g, 1.0 mmol) was treated with the nickel reagent prepared from $\mathrm{NiBr_2(Ph_3P)_2}$ (7.4 g, 10 mmol) and $\mathrm{LiAlH_4}$ (0.38 g, 10 mmol) to yield **2b** (0.13 g, 58%), which exhibited the same physical properties as those of the authentic sample.

Desulfurization of Bis(2-naphthylmethyl) Sulfoxide. Via the general procedure, the sulfoxide (0.19 g, 0.58 mmol) was treated with the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (0.79 g, 2.6 mmol), $\mathrm{Ph_3P}$ (1.3 g, 5.1 mmol), and $\mathrm{LiAlH_4}$ (0.10 g, 2.7 mmol) to afford 2-methylnaphthalene (0.12 g, 70%).

Desulfurization of Ethyl 2-Naphthylmethyl Sulfone. According to the general procedure, a mixture of the sulfone (0.22 g, 0.94 mmol) and the nickel reagent prepared from $\mathrm{NiBr_2{\cdot}DME}$ (1.9 g, 6.0 mmol), $\mathrm{Ph_3P}$ (3.2 g, 12 mmol), and $\mathrm{LiAlH_4}$ (0.23 g, 6.0 mmol) to give 2-methylnaphthalene (0.12 g, 92%).

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Supplementary Material Available: Experimental procedures of the desulfurization of certain thiols, thioethers, and sulfoxides are available (2 pages). Ordering information is given on any current masthead page.

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(11) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*, 2nd ed.; Pergamon: Oxford, 1980.

(12) Urquhart, G. G.; Gates, J. W., Jr.; Connor, R. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 363.

(13) Wagner, R. B.; Zook, H. D. *Synthetic Organic Chemistry*; Wiley: New York, 1953; Chapter 32.

(14) Fieser, L. F. *J. Am. Chem. Soc.* **1954**, *76*, 1945. Wilson, S. R.; Georgiadis, G. M.; Khatri, H. N.; Bartmess, J. E. *J. Am. Chem. Soc.* **1980**, *102*, 3577.

(15) Oae, S. In *Organic Chemistry of Sulfur*; Oae, S., Ed.; Plenum: New York, 1977; Chapter 8.

(16) Truce, W. E.; Klingler, T. C.; Brand, W. W. In *Organic Chemistry of Sulfur*; Oae, S., Ed.; Plenum: New York, 1977; Chapter 10.

(17) GC yield was obtained by the integration of the peak on the chromatogram. Authentic sample was used for calibration.

Use of Polysorbate 80 (Tween 80) as a Phase-Transfer Catalyst[1a]

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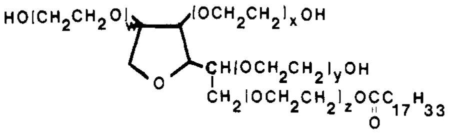
Polysorbate 80, also known as Tween 80 (1), has found extensive use as a surfactant and solubilizing agent, not only in chemical, biochemical, pharmacological, and medical research, but also in the food, cosmetics, and pharmaceutical industries. Recently,[2] its properties as an ionophore have been documented.



1

(w + x + y + z = 20)

Many ionophores, particularly the crown ethers which are so structurally similar to Polysorbate 80, have been found to be very effective phase-transfer catalysts.[3] The present work was initiated to determine whether Polysorbate 80 could also be used as an effective phase-transfer catalyst. Three reactions were studied: the cyanation of alkyl halides, the Williamson synthesis of ethers, and the base-catalyzed dehydrobromination of an alkyl halide.

Results and Discussion

Cyanation of Alkyl Halides (2). Cyanation of a series of alkyl halides and dihalides (2) was carried out by the method of Liotta et al.[4] as described in Starks and Liotta.[3a] This involves a solid–liquid system, in which solid KCN is acted upon by a solution of substrate and catalyst in acetonitrile at reflux for a set period of time: 1.5 h (Scheme Ia). The purpose was to compare our results using Polysorbate 80 to those reported by them using 18-crown-6 as a catalyst. Our results are summarized in Table I.

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(1) (a) Taken in part from the undergraduate theses of T.D.H. (1985), M.H. (1987), M.K. (1987), and D.F.S. (1985), University of Scranton. A preliminary report of this work was given at the 15th MARM of the ACS, Stockton State University, Pomona, NJ, May 1987. (b) Present address: Philadelphia College of Pharmacy and Science, Philadelphia, PA 19104.

(2) Thoman, C. J. *J. Pharm. Sci.* **1986**, *75*, 983.

(3) (a) Starks, C. M.; Liotta, C. L. *Phase Transfer Catalysis: Principles and Techniques*; Academic Press: New York, 1978. (b) Weber, W. P.; Gokel, G. W. *Phase Transfer Catalysis in Organic Synthesis*; Springer-Verlag: New York, 1977.

(4) Liotta, C. L.; Cook, F. L.; Bowers, C. W. *J. Org. Chem.* **1974**, *39*, 3416.

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Scheme I

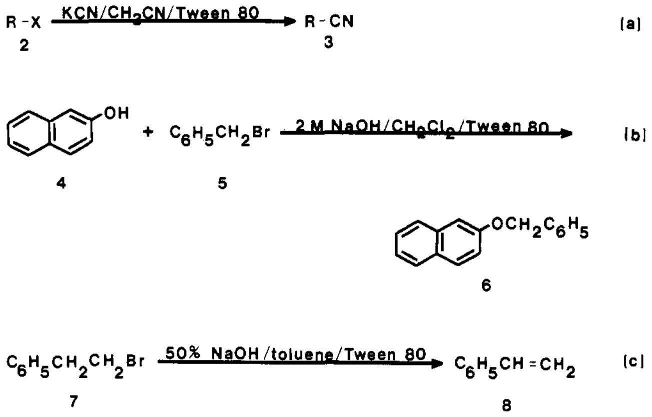

Table I. Cyanation of Alkyl Halides (2)[a]

substrate	product	% yield	
		Polysorbate 80	18-crown-6[b]
1,4-dibromobutane	adiponitrile	70	100
1,4-dichlorobutane	adiponitrile	33	95
1,3-dibromopropane	glutaronitrile	53	97
1,3-dichloropropane	glutaronitrile	26	97
cyclohexyl bromide	cyclohexyl nitrile	40	–
	cyclohexene	–	46
cyclohexyl chloride	cyclohexyl nitrile	37	–
	cyclohexene	–	32

[a] Using 0.045 mol of halide and 0.003 mol of Polysorbate 80 in 25 mL of acetonitrile and 0.18 or 0.09 mol dry KCN at reflux for 1.5 h. [b] From Starks and Liotta ref 3a, p 101, using the same molar proportions as above.

Polysorbate 80 is an effective catalyst in all cases, but not as effective as 18-crown-6. The higher yields with the crown ether over the same period of time are no doubt a reflection of the macrocyclic effect, which favors the cyclic ether. In our case, the higher yields with the bromides compared to the chlorides suggests that the process is reaction- rather than diffusion-controlled. Similar work[5] using tri-*n*-octylmethylammonium chloride (Aliquat 336) gave results comparable to ours. These workers[5] found that a small amount of water is needed for the cyanation to succeed. In our case, the water needed is provided by the Polysorbate 80, which contains 2–3% of it.

One glaring difference with the results of Liotto is the change of product (and process) with the cyclohexyl halides. Only elimination products are reported[4] using the crown ether, whereas our use of Polysorbate 80 produced only the substitution product. Apparently, the crown ether seems to enhance the basic qualities of cyanide ion more than the Polysorbate 80 does.

The Williamson Sythesis. The synthesis of benzyl β-naphthyl ether (6) from β-naphthol (4) and α-bromotoluene (5) was studied at a series of temperatures (Scheme Ib). The reaction was run for 2 h in a liquid–liquid system in the presence of a catalytic amount of Polysorbate 80. The results are shown in Table II.

Table II. Williamson Synthesis of Benzyl β-Naphthyl Ether (6)[a]

T, °C	yield,[b] mol	$10^7 k_1$, s^{-1}
20	0.00854 ± 0.0008	5.93
30	0.0172 ± 0.0016	11.94
37	0.0248 ± 0.0023	17.22
40	0.0320 ± 0.0009	22.22
42	0.0386 ± 0.0017	26.81
42[c]	0.0000	0.00

[a] Using 0.1 mol of β-naphthol (4) in 100 mL of 2 M NaOH and 0.2 mol of α-bromotoluene (5) and 9.1 mmol Polysorbate 80 (1) in 100 mL of CH$_2$Cl$_2$. [b] Based on three determinations each, except for the blank. [c] With no Polysorbate 80 (1) present.

The yield of solid product isolated was temperature-dependent. These single results at each temperature can lead to the (admittedly tentative) pseudo-first-order rate constants[6] found in Table II. An Arrhenius curve (r = 0.9969) based on them produces an energy of activation of 12.18 kcal/mol, which compares favorably with the literature value of 13.9 kcal/mol,[7] determined using tetra-*n*-butylammonium bisulfate as the catalyst.

Table III. Dehydrohalogenation of β-Phenethyl Bromide[a]

T, °C	$10^5 k_1$, s^{-1}	T, °C	$10^5 k_1$, s^{-1}
25[b]	0.00	48	22.07
38	10.12	53	25.78
43	16.07	35[c]	130

[a] Using 36.6 mmol of (β-bromoethyl)benzene (7) and 0.83 mmol of Polysorbate 80 (1) in 10 mL of toluene and 20 mL of 50% NaOH. [b] Run without the presence of Polysorbate 80 (1). [c] From ref 10, using 0.2 M (β-bromoethyl)benzene (7) and 0.2 M PEG-600 and 60% aqueous KOH.

Dehydrobromination. The base-catalyzed dehydrobromination of β-phenethyl bromide (7) in a liquid–liquid system was studied at various temperatures (Scheme Ic). The course of the reaction was followed via gas chromatography, using the decrease of the β-phenethyl bromide peak area to determine the rates, and toluene as an internal standard. The results are shown in Table III.

From this data, an energy of activation of 12.63 kcal/mol is determined for the reaction. Halpern and his co-workers[8] have reported an energy of activation of only 7.43 kcal/mol for this same reaction catalyzed by tetra-*n*-octylammonium bromide. They cite Levenspiel[9] to the effect that "E_a = 0–10 kcal/mol for diffusion-controlled processes and usually over 15 kcal/mol for chemical reaction control". They conclude that, under their conditions (using toluene–50% NaOH at 74.5 °C and a stirring rate of 750 rpm), the conversion is diffusion controlled. Our intermediate E_a does not allow us to decide on how the process is controlled.

Kimura and Regen[10] studied this reaction using polyethylene glycols and glymes as catalysts. They discovered that the glymes, in which the terminal hydroxy groups of the PEG's have been alkylated, gave no reaction and concluded that terminal hydroxy groups were necessary for transport of the hydroxide ion into the organic layer. The three free terminal hydroxy groups in Polysorbate 80 allow such a transfer.

Polysorbate 80 as a Phase-Transfer Catalyst. Polysorbate 80 is certainly an effective phase-transfer catalyst for these reactions. It has definite advantages over the more commonly used catalysts. It is significantly cheaper than the common alternative substances.[11] It is much less toxic than either the tetraalkylammonium salts or the crown ethers, and it is stable under most conditions;

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(5) Bram, G.; Loupy, A.; Pedoussout, M. *Bull. Soc. Chim. Fr.* **1986**, 124.

(6) Montanari, F.; Quici, S.; Tundo, P. *J. Org. Chem.* **1983**, *48*, 199.

(7) Freedman, H. H.; Dubois, R. H. *Tetrahedron Lett.* **1975**, 3251.

(8) Halpern, M.; Sasson, Y.; Rabinovitz, M. *J. Org. Chem.* **1984**, *49*, 2011.

(9) Levenspiel, O. *Chemical Reaction Engineering*; Wiley: New York, 1972; Chapter 14.

(10) Kimura, Y.; Regen, S. L. *J. Org. Chem.* **1983**, *48*, 195.

(11) The costs of 10 mmol of typical catalysts: 18-crown-6, $3.62 (25-g bottle); tetra-*n*-butylammonium bromide, $1.40 (25-g bottle); Polysorbate 80, $0.19 (500-mL bottle). All from Aldrich.

(12) Reference 3a, Table I, p 60.

the ammonium salts, in contrast, are somewhat unstable under basic conditions.[10] Finally, Polysorbate 80 is more versatile than individual crown ethers in carrying cations of varying sizes, since it is not constrained by a preformed cavity of a specific size.

The major problem with the use of Polysorbate 80 as a phase-transfer catalyst lies in its separation from product after reaction. It is very difficult to recover the catalyst, but this is not really a problem since it is so inexpensive. Separation can be accomplished by sending the concentrated reaction mixture through a column of activated alumina before final distillation.

Experimental Section

Melting points were determined on a Fisher-Johns block and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 1310 spectrophotometer; NMR spectra on a Varian T-60 spectrometer; and the gas chromatograms on a Perkin-Elmer Model 3920B instrument. The Polysorbate 80 (Aldrich) was used as sold.

General Preparation of Alkyl Nitriles (3).[4] Dry KCN (11.7 g, 0.18 mol for disubstitution; 5.85 g, 0.09 mol for monosubstitution) was placed in a 50-mL round-bottom flask with a solution of 0.045 mol of alkyl halide or dihalide (2) and 5.00 g (0.0038 mol) of Polysorbate 80 (1) in 25 mL of dry acetonitrile. The fluid mixture was refluxed for 1.5 h with vigorous magnetic stirring, after which it was cooled and evaporated to one-third its volume. After addition of 50 mL of distilled water, the mixture was extracted three times with 10-mL portions of CH_2Cl_2. The combined extracts were dried over anhydrous $MgSO_4$, concentrated to 5 mL, and chromatographed on a column of activated alumina. Removal of the solvent was followed by distillation of the product, which was identified by boiling point and IR and NMR spectra. The yields are shown in Table I.

Adiponitrile: bp 198 °C (30 mmHg) [lit. bp 180 °C (20 mmHg)].

Glutaronitrile: bp 160 °C (30 mmHg) [lit. bp 160.4 °C (22 mmHg)].

Cyclohexyl cyanide: bp 180 °C (lit. bp 184 °C).

Williamson Synthesis of Benzyl β-Naphthyl Ether (6). A solution of β-naphthol (4) (14.42 g, 0.01 mol) in 100 mL of 2 M NaOH was added to a solution of α-bromotoluene (5) (34.21 g, 0.2 mol) and Polysorbate 80 (1) (11.92 g, 9.1 mmol) in 100 mL of CH_2Cl_2 in a 500-mL, three-neck, round-bottom flask. The immiscible mixture was stirred vigorously with a magnetic stirrer for 2 h at constant temperature (±0.2 °C). The mixture was then separated, and the aqueous layer was extracted twice with 100-mL portions of CH_2Cl_2, with the washings being added to the original CH_2Cl_2 layer. Evaporation of the CH_2Cl_2 left a thick, yellow-orange paste, which was triturated with 50-mL portions of glacial acetic acid until all color was removed. Recrystallization from hot 95% EtOH produced benzyl β-naphthyl ether as small white flakes, mp 95–98 °C (lit. mp 99–100 °C). The product's identity was confirmed by IR and NMR spectroscopy. The yields varied with temperature, as shown in Table II.

Dehydrobromination of β-Phenethyl Bromide (7). To 20 mL of 50% NaOH in a 100-mL three-neck flask immersed in a constant-temperature bath was added a solution of β-phenethyl bromide (7) (6.78 g, 36.6 mmol) and Polysorbate 80 (1) (1.09 g, 0.83 mmol) in 10 mL of toluene. Stirring was begun, and the system was allowed to equilibrate for 2–3 min. Then, 0.5-mL samples were withdrawn by syringe every 15 min. Each was centrifuged at 4500 rpm for 3 min, and then 1 μL of the organic layer was removed and injected into the gas chromatograph; the remaining sample was then replaced in the reaction mixture. The column used was a 10% SAE 30 (methyl silicone gum), and a temperature program was used to facilitate separation: the oven was held at 110 °C for 1 min after injection and then increased by 32 °C/min to a final temperature of 230 °C. Retention times were toluene, 85 s; styrene (8), 130 s; β-phenethyl bromide (7), 240 s. The initial integration of the β-phenethyl bromide peak was taken as 100% of that material (36.6 mmol), and subsequent integrations compared to that. The toluene was used as an internal standard.