(±)-α-Lycorane (1). A mixture of **20** (349 mg) and $LiAlH_4$ (157 mg) in anhydrous ether–THF (1:1) (66 mL) (freshly distilled from $LiAlH_4$) was refluxed with stirring for 40 min. Excess of $LiAlH_4$ was decomposed at 0–5 °C with saturated aqueous Na_2SO_4 (4 mL) and a precipitate was filtered. The precipitate was washed well with ether and the combined organic layer was dried ($MgSO_4$). Evaporation of the solvent gave an oily residue. A mixture of the residue, 2% aqueous $PdCl_2$ (6.8 mL), concentrated HCl (1 mL), and active carbon (320 mg) in C_2H_5OH (20 mL) was shaken in a Parr hydrogenation apparatus (hydrogen pressure of 80 psi) at room temperature for 87 h. Usual workup of the mixture gave 219.1 mg of an oil, whose NMR spectrum showed no signals due to the benzyl group. A mixture of the crude residue, $KHCO_3$ (163 mg)–H_2O (2.3 mL), 37% formalin (3.5 ml), and concentrated HCl (1.6 mL) in CH_3OH (11.6 mL) was refluxed for 45 min. To the mixture was added concentrated HCl (1.6 mL) and refluxing was continued for 45 min. The same treatment as noted above gave 208.9 mg of an oil, which was chromatographed over Al_2O_3 (Grade II–III) (Merck Co., Ltd.) (12 g). Elution with benzene-*n*-hexane (24:1) gave 128 mg (50%) of (±)-α-lycorane (**1**), mp 85–92.5 °C, which was recrystallized from petroleum ether to yield 30 mg (11.7%) of colorless prisms, mp 95.5–97 °C. This was identical in all respects with an authentic sample[2b] (mp 96–97.5 °C), which was kindly provided by Drs. K. Kotera and Y. Hamada.

Acknowledgments. We wish to express our sincere thanks to Drs. K. Kotera and Y. Hamada, Central Research Laboratory of Shionogi Co., Ltd., and Professor R. K. Hill, University of Georgia, for their kind gifts of (±)-α- and (±)-γ-lycorane with their spectral data and of the lactam **3**. We are indebted to Dr. H. Yoshitake, Ube Kosan Co., Ltd., for his kind supply of a starting material. We are grateful to Dr. H. Hara for his useful discussion and to Misses Y. Arigaya and T. Umemura for their technical assistance. Thanks are also due to Misses T. Kawana and S. Komatsu of this Faculty for spectral measurements and to Sankyo Co., Ltd., for elemental analysis.

Registry No.—**1**, 63814-02-8; **3**, 63797-13-7; **5**, 63784-87-2; **8**, 63765-06-0; **9**, 63765-07-1; **10**, 63765-08-2; **11**, 63765-09-3; **12**, 63814-03-9; **13**, 63765-10-6; **14**, 63765-11-7; **14** pyrrolidine enamine, 63765-12-8; **15**, 63765-13-9; **17**, 63765-14-0; **20**, 63765-15-1; cyclohexanone, 108-94-1; 5-bromobenzo-1,2-dioxole, 2635-13-4; pyrrolidine, 123-75-1; benzylamine, 100-46-9.

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(10) The values of $J_{a,e}$ and $J_{a,a}$ corresponding to $\Phi \sim 45°$ and $\Phi \sim 170°$ as measured on a Dreiding model for **16** and **10** were 4.9 and 15.5 Hz, respectively.

(11) An exception where catalytic hydrogenation of 3a,4,5,6-tetrahydro-7-phenyloxindole gave *trans*-hexahydro-7-phenyloxindole is reported: A. N. Kost and I. P. Rudakova, *J. Gen. Chem. USSR* (*Engl. Transl.*), **35**, 140 (1965).

(12) Considering the $A^{1,3}$ strain[13] by interaction of the aryl and benzyl group in **18**, the unsaturated lactam (**19**) would have been formed predominantly at the initial stage.

(13) Cf. F. Johnson, *Chem. Rev.*, **68**, 375 (1968).

(14) Long-range coupling was likely responsible, though unchecked experimentally.

(15) Melting and boiling points are uncorrected. IR spectra were taken with a Hitachi Perkin-Elmer Model 225 grating spectrometer, unless otherwise noted. NMR spectra were recorded on a JEOL JNM-4H-100 spectrometer at 100 MHz in $CDCl_3$ solution (5–10%) using $(CH_3)_4Si$ as an internal standard. Mass spectra were measured with a Hitachi RMU-7M double-focusing mass spectrometer at 70 eV by direct insertion.

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(18) 5% CH_3OH–$CHCl_3$ solution was used as a developing solvent.

(19) A 215 Hitachi grating infrared spectrometer was used.

Behavior and Stability of Catalysts in Bi- and Triphase Transfer Catalysis

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Received July 15, 1977

Phase-transfer catalysis is becoming an increasingly important technique in organic synthesis.[2-7] However, very little is known about the behavior of the catalysts under biphase[2-6] and triphase conditions.[7]

Recently we observed that alkylation of thio reagents, by alkyl halides of low reactivity, gave poor yields (<20%) under biphasic conditions. Furthermore, with triphase systems, the repeatability of the reaction with the same catalyst (anion exchange resin) was not maintained after three runs.[8]

These facts prompted us to examine the chemical behavior, in classical PTC media, of various catalysts and anions (obtained from phenylacetonitrile, imidazole, phenol, thiophenol, and octylmercaptan) in the absence of alkylating reagent.

Under biphase catalysis conditions the catalysts used were: TEBA-Cl, TBAB, and CTAB.[9] The results, presented in Table I, show that the catalyst may be decomposed by alkylating the anion. This decomposition depends upon the nature of the anion and the structure of the ammonium catalyst. With TEBA-Cl and thiophenoxide this corresponds to 93% of the concentration of the catalyst. The results obtained are consistent with a nucleophilic substitution where the anion is the nucleophile and the tertiary amine is the leaving group (Scheme I). This is analogous to the dealkylation reactions of quaternary ammonium salts by nucleophilic sulfur reagents[11] or soft nucleophiles.[12,19]

Under triphase catalysis, the catalysts used were Dowex 1 × 8 and Dowex 11 anion exchange resins. Both resins are of the trimethylbenzylammonium type (Scheme II). During the reaction the gas evolved (a volatile amine if dequaternization occurred according to Scheme I) was trapped in a saturated solution of picric acid in ethanol. The results obtained show that without anion and for a reaction time of 6 h no picrate was formed, but with the anions of thiophenol and phenylacetonitrile a picrate did form.[10]

Although the decomposition of the quaternary ammonium catalyst (Scheme I) is in most cases only a secondary reaction, it can become more important for soft nucleophiles (RS⁻ >

Scheme I

$$Nu^- + RCH_2N^+R'_3\ \ X^- \xrightarrow{PTC} NuCH_2R + NR'_3 + X$$

Scheme II

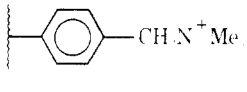

Table I. Alkylation (%) of Anions by Quaternary Ammonium Catalysts Under PTC Conditions

	Catalysts[9]		
Anions	TEBA-Cl[a]	TBAB	CTAB[b]
$C_6H_5CH^-CN$	85[c]	Traces[c]	
$C_3H_3N_2^-$ [i]	0.5[c]	0.6[e]	
$C_6H_5O^-$	0[c]	0[d]	0[c]
$C_6H_5S^-$	93[d]	90[d]	33[g]
	17[f]		
$C_8H_{17}S^-$	93[h]	90[e]	

[a] Only benzylation of the anion was detected. [b] Only methylation of the anion was detected. [c] 6 h at 60 °C. [d] 7 h at 70 °C. [e] 7 h at 60 °C. [f] 11 h at 30 °C, with 1.5 g of TEBA-Cl. [g] 7 h at 60 °C with 1.5 g of CTAB. [h] 7 h at 45 °C with 20% by weight sodium hydroxide. [i] Imidazole.

$R_3C^- > R_2N^- > RO^-$) and for substituents of the quaternary ammonium salt R_4N^+ which are easily displaced ($R = CH_2Ph > Me >$ alkyl). This, in turn, will have a dramatic effect on the yields of the phase transfer catalyzed reaction itself.

Since normal PTC reaction conditions necessitate a 5% molar concentration of the catalyst, the side products obtained by dealkylation of the catalyst will never exceed 5% yield; e.g., the alkylation of thiophenol by 1-bromooctane has been studied, using several ammonium catalysts, without evidence of decomposition of the catalyst.[13] On the other hand, when reagents of low reactivity are used the effect is more pronounced; e.g., when thiophenol is reacted with 2-bromothiophene or 2-bromothiazole the yield of the reaction with the bromide is 0–4% while the alkylation by the ammonium salt corresponds to 55–85% of the concentration of the catalyst (see Experimental Section).

Furthermore, one must note that for continuous processes, where the catalyst is recycled, even a slow quaternary ammonium salt decomposition will lead to the disappearance of the catalyst and to an eventual termination of the phase transfer catalysis process.

One way to circumvent this inconvenience is the use of more stable catalysts such as crown ethers,[13-14] but their use for large scale synthetic purposes is still difficult.[15] One other possibility is the use of polyglymes, which can be considered as noncyclic crown ethers. They are stable, easily available, and could be used both under bi-[17] and triphase conditions.[18] We are presently studying these possibilities further.

In summary, the results reported in this study can be used to explain the origin of side products, low yields, and nonconstancy of the performances of supported catalysts in phase-transfer catalysis.

Experimental Section

The phase-transfer catalysts and nucleophiles are commercial products. They have been used without further purification. The quantitative determinations of alkylated compounds have been made by GLC with a IGC 120FB Intersmat instrument or with a coupled GLC-mass spectrometer Varian Mat111.

Procedure for Biphase Conditions (Table I). The general experimental procedure was as follows: 3 g of the anion precursor, 1 g of catalyst, and 40 mL of sodium hydroxide (50% by weight) were stirred for 6–11 h at 30–70 °C. The organic layer was directly analyzed by GLC.

Procedure for Triphase Conditions. The general experimental procedure was as follows: 1.5 g of resin, 4 mL of sodium hydroxide (50% by weight), and 0.5 g of anion precursor were stirred at 80 °C for 3 h. The gas evolved was trapped in a solution of picric acid in ethanol. The picrate was filtered. The melting point was measured with a Koffler apparatus.

Procedure for 2-Bromothiazole: 5.5 g of thiophenol (0.05 mol), 8.2 g of 2-bromothiazole (0.05 mol), 1.09 g of CTAB, 100 mL of NaOH (50% by weight), and 150 mL of benzene were reacted with stirring for 24 h at 70 °C. The analysis of the organic layer by GLC showed 4% of 2-thiazolyl phenyl thioether and 55% of methyl phenyl thioether (from the catalyst CTAB). The above reaction with the same compounds, except NaOH (25% by weight), TBAB as catalyst, and a reaction time of 10 h at 80 °C gave 0% of 2-thiazolyl phenyl thioether and 84% of butyl phenyl thioether.

Procedure with 2-Bromothiophene: 5.5 g of thiophenol (0.05 mol), 8.2 g of 2-bromothiophene (0.05 mol), 0.7 g of TBAB, and 100 mL of NaOH (50% by weight) were reacted for 10 h at 80 °C. Less than 1% of 2-thiophenyl phenyl thioether and 85% of butyl phenyl thioether was detected from the catalyst.

Registry No.—Phenylacetonitrile, 140-29-4; imidazol, 288-32-4; phenol, 108-95-2; thiophenol, 108-98-5; octanethiol, 111-88-6; TEBA-Cl, 56-37-1; TBAB, 1643-19-2; CTAB, 57-09-0; Dowex 1 × 8, 12627-85-9; Dowex 11, 9049-12-1; 2-bromothiazole, 3034-53-5; 2-thiazolyl phenyl thioether, 33342-67-5; methyl phenyl thioether, 100-68-5; butyl phenyl thioether, 1126-80-3; 2-bromothiophene, 1003-09-4; 2-thiophenyl phenyl thioether, 16718-12-0.

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