

Crown Ethers as Phase-transfer Catalysts in Two-phase Reactions

By DARIO LANDINI and FERNANDO MONTANARI*

(Centro C.N.R. e Istituto di Chimica Industriale dell'Università, Via C. Golgi 19, Milano 20133, Italy)

and FILIPPO M. PIRISI

(Istituto di Chimica Organica, Facoltà di Farmacia, Via Ospedale 72, Cagliari 09100, Italy)

Summary Crown ethers having aliphatic chains in the molecule, *e.g.* dicyclohexyl-18-crown-6, can be used as phase-transfer catalysts in anion promoted two-phase reactions.

Crown ethers form stable complexes with metal cations and, by increasing the dissociation of ion pairs, provide highly reactive, unsolvated anions.¹ They allow an alternative to dipolar aprotic solvents, yet their practical importance is limited because, at least in nucleophilic substitutions carried

out in homogeneous media, they must be employed in equimolecular amounts.

We have found that crown ethers, with a suitable structure, can be effectively used in catalytic amounts in two-phase organic aqueous systems. In these conditions they act as phase-transfer catalysts,² provided that aliphatic chains are bounded to the molecule so as to secure a partitioning of the crown ether-salt complex between the two phases.

As shown in Table 1, catalytic activity increases from

dibenzo-18-crown-6 (I) to benzo-15-crown-5 (II) and to dicyclohexyl-18-crown-6 (III), following the increase in aliphatic character of crown compounds and of related solubility¹ in organic media. On the basis of these data, (III) was chosen as catalyst in the reactions examined.

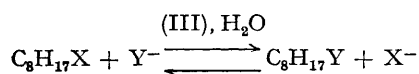
TABLE 1

Structural dependence of catalytic activity of crown ethers in the conversion of $n\text{-C}_8\text{H}_{17}\text{Br}$ into $n\text{-C}_8\text{H}_{17}\text{I}$ under phase-transfer conditions.

Reagent ^a	Crown ether ^b	Reaction time/h ^c	Yield/% ^d
KI	(I)	40	80
NaI	(II)	21	80
KI	(III)	3	100
KI	—	24	<4

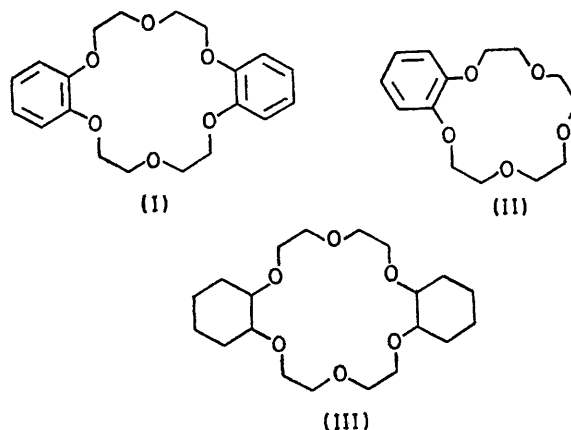
^a Saturated aqueous solution, 5 molar equivalents. ^b 0.05 Molar equivalents. ^c At 80°. ^d $n\text{-Octyl iodide}$.

Nucleophilic substitutions were carried out by stirring at 80–115° a mixture of an alkyl halide or a methanesulphonate and a saturated aqueous solution of an alkaline salt in the presence of catalytic amounts of (III). Under these conditions primary alkyl methanesulphonates afforded in high yields the corresponding halides and cyanides (Table 2).



As in phase-transfer catalysis by onium salts, the same substitutions are noticeably slower in alkyl halides, re-

as it does in the classical conditions of phase-transfer catalysis.² Preliminary data seem to indicate a poor selectivity of (III) between K^+ or Na^+ cations.



In addition we have found that in the presence of 0.05 molar equivalents of (III) alkylations of carbanions, oxidations and reductions can be as easily performed. Thus, benzyl methyl ketone was mono-alkylated with $n\text{-butyl bromide}$ in 50% aqueous NaOH to give 3-phenyl-2-heptanone (1.5 h, 80°, 93%). 1-Octene in benzene solution was oxidized to $n\text{-heptanoic acid}$ by stirring with a saturated aqueous solution of KMnO_4 at room temperature (45 min, exothermic reaction, 80%). 2-Octanone was reduced to

TABLE 2

Nucleophilic substitutions in octyl derivatives catalyzed by (III)^a under phase-transfer conditions.

Substrate	Reagent ^b	t°/C	Reaction		Product $n\text{-C}_8\text{H}_{17}\text{X}$, $\text{X} =$
			time/h	Yield/%	
$n\text{-C}_8\text{H}_{17}\text{OSO}_2\text{Me}$	KI	100	0.11	100	I
"	NaI	100	0.16	100	I
"	KBr	100	0.5	96	Br
"	NaBr	100	0.5	88	Br
"	KCl	100	3.0	89	Cl
"	NaCl	100	3.0	75	Cl
"	KF	115	42.0	65	F
"	KCN	100	0.3	90	CN
$n\text{-C}_8\text{H}_{17}\text{Br}$	KI	100	1.5	92	I
"	KI	80	3.0	100	I
$n\text{-C}_8\text{H}_{17}\text{I}$	KBr	80	3.0	40 ^d	Br
$n\text{-C}_8\text{H}_{17}\text{CH}(\text{OSO}_2\text{Me})\text{Me}$	KBr	100	2.5	67 ^e	$n\text{-C}_8\text{H}_{17}\text{CHBrMe}$

^a 0.05 Molar equivalents. ^b Saturated aqueous solution, 5 molar equivalents. ^c The products were characterized by g.l.c. retention times and by comparison (i.r. and/or n.m.r. spectra) with authentic samples. ^d 60% Of $n\text{-octyl iodide}$, same values after 26 h. ^e 16% 2-Octanol, 16% octenes, 1% 2-octyl mesylate.

actions being favoured by highly hydrophilic leaving groups.² In methanesulphonates, the apparent nucleophilicity scale is $\text{I}^- > \text{Br}^- > \text{Cl}^- > \text{F}^-$. Secondary substrates are less reactive than primary ones. In the Finkelstein reaction, whereas Br^- is quantitatively displaced by I^- , the inverse substitution goes to equilibrium after a partial conversion,

2-octanol in benzene solution with NaBH_4 and aqueous 2N NaOH (2.5 h, 80°, 92%).

These experimental results indicate that crown ethers may be at least as useful as onium salts in phase-transfer catalyzed reactions.

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¹ C. J. Federsen and H. K. Frensdorff, *Angew. Chem. Internat. Edn.*, 1972, 11, 16.

² C. M. Starks, *J. Amer. Chem. Soc.*, 1971, 93, 195; J. Dockx, *Synthesis*, 1973, 441; E. V. Dehmlow, *Angew. Chem. Internat. Edn.*, 1974, 13, 170.