Non-supported and Resin-supported Oligo(oxyethylenes) as Solid–Liquid Phase-transfer Catalysts. Effect of Chain Length and Head-group

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A series of oligo(oxyethylenes) containing 3—30 ethylene oxide residues and a number of polystyrene resin-supported analogues have been examined as phase-transfer catalysts in the reaction of solid potassium phenoxide with 1-bromobutane in toluene. With both groups of catalysts the activity increases with the length of the oligoether chain. This effect arises despite a fall in the ability of the oligoethers to solubilize the phenoxide, and must therefore be associated with an increase in the nucleophilicity of the phenoxide anion in the oligoether complexed ion pairs. A group of oligo(oxyethylenes) with three ethylene oxide residues and symmetrically substituted with different head-groups was also examined. One with 8-quinolyl end-groups proved to be as active as dibenzo-18-crown-6, whereas, somewhat surprisingly, a corresponding species with 2-methoxyphenyl substituents was a relatively poor catalyst. In this case the geometry of complexation might allow retention of intimate ion pair character. In the case of oligoethers with head-groups OH,OH; OH,OCH_3; and OCH_3,OCH_3 the presence of an hydroxy-group appears to enhance the ability to complex K^+, but simultaneously reduces catalytic activity, possibly because of interaction with the phenoxide counterion. As a result, the unsymmetrically substituted derivative is the most active catalyst providing an optimum balance of these factors. Two series of resin-supported analogues, one with three ethylene oxide residues in each oligoether chain and one with four, were also synthesised. In each case the derivative with an 8-quinolyl head-group and one related structure derived from 2-pyridylmethanol were the most active catalysts. Again the two species with a 2-methoxyphenyl head-group were less effective than anticipated. In the case of the oligoether chain with four ethylene oxide residues, the activity was somewhat better and there is some correlation with the reported complexing ability of analogous unbound species.

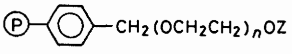
POLYMER-SUPPORTED phase-transfer catalysts represent just one group of supported species which have been developed over the last few years for use in organic synthesis.[1] They are active catalysts in both liquid–liquid and solid–liquid reactions and considerable progress has been made in understanding the mechanisms by which they operate.[2-4] Resin-supported oligo(oxyethylenes) are useful catalysts particularly in solid–liquid displacement reactions [5,6] and we have recently described our detailed mechanistic investigations of these.[7] We now report our findings on the effect of chain length and head-group of both resin-supported oligo(oxyethylenes) and some related non-supported oligoethers. As before, the model reaction chosen for study was the Williamson synthesis of n-butyl phenyl ether from solid potassium phenoxide and 1-bromobutane in toluene. The catalysts examined were the oligoethers (I)—(IX) and the polystyrene resin-supported species (X)—(XXIV).

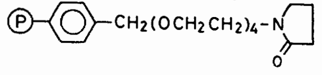
RESULTS

Syntheses of Resin-supported Catalysts.—Resins (X)—(XII) were prepared from chloromethylated polystyrene resins by reaction with the sodium salts of the corresponding oligo(ethylene glycol monoethers).[5] In the case of (X) and (XI) the resulting degree of substitution or loading (Table 2) corresponded very closely to the original level of chloromethylation as indicated by elemental microanalysis. However, with (XII) the loading of oligoether achieved was considerably lower. The remaining resin-bound species were prepared according to the Scheme. Catalysts (XIII)—(XV) were synthesised from a resin originally *ca.* 14% chloromethylated and by generating the monosodium salt of the glycol (VI) virtually 100% of oligoether chains were successfully attached to the resin support by one end only (XIII). Subsequent modification of the free hydroxy-groups was again reasonably efficient yielding the loading levels shown in Table 2. In contrast to this, catalysts (XVI)—(XXIV) were not so structurally well defined. Commencing with a resin *ca.* 40% chloromethylated, tetraethylene glycol could be attached by a single end to only *ca.*

$X(OCH_2CH_2)_nOY$

	X	Y	*n*
(I)	H	CH_3	3
(II)	H	Ph	3
(III)	H	CH_3	*ca.* 7
(IV)	H	CH_3	*ca.* 16
(V)	H	Ph	*ca.* 30
(VI)	H	H	3
(VII)	CH_3	CH_3	3
(VIII)	8-Quinolyl	8-Quinolyl	3
(IX)	2-Methoxyphenyl	2-Methoxyphenyl	3



	Z	*n*
(X)	CH_3	3
(XI)	$C_9H_{19}-C_{11}H_{23}$	*ca.* 9
(XII)	Ph	*ca.* 30
(XIII)	H	3
(XIV)	8-Quinolyl	3
(XV)	2-Methoxyphenyl	3
(XVI)	H	4
(XVII)	Tosyl	4
(XVIII)	8-Quinolyl	4
(XIX)	2-Methoxyphenyl	4
(XX)	2-Pyridylmethyl	4
(XXI)	2-(1,4-Benzodioxanylmethyl)	4
(XXII)	2-Naphthyl	4
(XXIII)	Tetrahydrofuran-2-yl	4
(XXIV)		

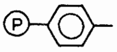
( = 2% crosslinked polystyrene resin beads)

TABLE 1

Rates of Williamson reactions catalysed by oligoethers in toluene at 105 °C [a]

Oligoether	10^5 Initial rate (l mol^{-1} s^{-1})	Loss of 1-bromobutane (%) (*t*/h)
(I)	9.10	98 (3)
(III)	10.5	98 (3)
(IV)	13.3	99 (2)
(V)	16.0	98 (2)
(IX)	2.61	71 (3)
(VI)	4.00	76 (3)
(VII)	5.00	63 (3)
(II)	10.5	97 (3)
(VIII)	21.1	*ca.* 100 (1.5)
Dibenzo-18-crown-6	19.5	*ca.* 100 (1.5)

[a] [1-Bromobutane]$_{\text{initial}}$ 0.24M; KOPh 2.0 mmol; catalyst 1.16 mmol of donor atom.

TABLE 2

Rates of Williamson reactions catalysed by resin-supported oligoethers in toluene at 105 °C [a]

Resin catalyst (loading, %) [b]	Quantity of catalyst (mmole of donor atom)	10^5 Initial rate (l mol^{-1} s^{-1})	Loss of 1-bromobutane (%) (*t*/h)
(X) (61)	1.16	10.0	93 (3)
(XI) (40)	1.16	11.8	98 (3)
(XII) (8)	1.16	16.0	96 (3)
(XV) (11)	0.58	1.10	35 (3)
(X) (10)	0.58	3.12	45 (3)
(XIII) (13)	0.58	4.10	70 (3)
(XIV) (7)	0.58	9.30	99 (3)
(XVII) (14)	1.16	4.11	83 (3)
(XVI) (27)	1.16	5.67	92 (3)
(XXIII) (14)	1.16	5.67	70 (3)
(XXIV) (14)	1.16	6.00	89 (2)
(XXI) (14)	1.16	6.78	90 (3)
(XIX) (14)	1.16	7.56	96 (2)
(XVIII) (14)	1.16	8.25	92 (3)
(XXII) (14)	1.16	9.77	93 (2)
(XXIV) (14)	0.58	2.44	80 (3)
(XXI) (14)	0.58	3.00	72 (3)
(XIX) (14)	0.58	3.22	69 (3)
(XXII) (14)	0.58	3.44	63 (3)
(XXIII) (14)	0.58	3.78	93 (3)
(XX) (14)	0.58	3.89	85 (3)
(XVIII) (14)	0.58	5.50	93 (3)

[a] [1-Bromobutane]$_{\text{initial}}$ 0.24M, $\overset{+}{\text{K}}\overset{-}{\text{O}}$Ph 2.0 mmol. [b] Percentage of resin aromatic groups substituted with the indicated oligoether.

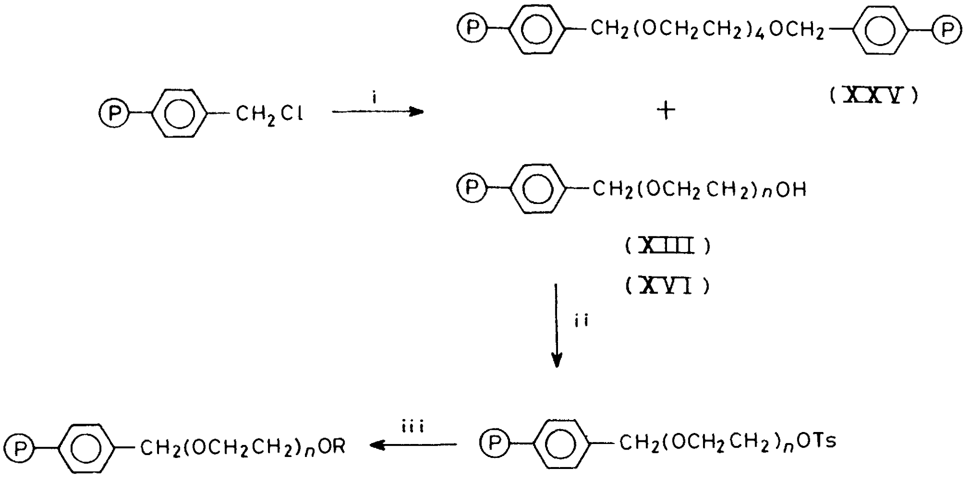
28% of resin aromatic groups, again calculated from elemental microanalyses. The remaining chloromethyl groups did undergo reaction as indicated by the loss of chlorine from the resin though these were presumably linked to each other by oligoether bridges as in (XXV) (Scheme). Subsequent modification of (XVI) to (XVII) yielded a loading of tosylated oligoether groups of *ca.* 14%. Conversion into the final species (XVIII)—(XXIII) was relatively efficient, producing comparable loadings of these head-groups (Table 2). Thus the resins (XVI)—(XXIII) contain not only oligoether chains with specific head-groups but also chains with residual hydroxy-groups and chains as bridging units. This situation is relevant in the interpretation of the catalytic activity of these materials.

Williamson Ether Synthesis.—These reactions were carried out on a small scale as previously described and were monitored employing normal quantitive g.l.c. methods. Initial rates were calculated from the gradients of 1-bromobutane decay curves. When the quantity of catalyst used contained 1.16 mmole of donor atom (O or O and N) gradients were drawn through curves at the 15 min interval, and this was extended to a 30 min interval when the catalyst quantity was halved. This procedure ensured a fair comparison when assessing rates of reaction.

Table 1 shows the results for the unbound oligoethers (I)—(IX), while the results for the various polymer-supported species are summarised in Table 2. The solubility of potassium phenoxide in toluene solutions of various oligoethers was measured by titration with hydrochloric acid using Methyl Red as the indicator and the results appear in Table 3.

DISCUSSION

Effect of Chain Length of Non-supported and Supported Oligo(oxyethylenes).—The results in Table 1 show clearly that for the oligo(ethylene glycol monoethers) (I) and (III)—(V) the catalytic activity increases significantly as the oligoether chain length increases, though (V) also has a phenyl rather than a methyl head-group. Furthermore, this trend is reflected in the resin-supported species (X)—(XII) (Table 2). With these catalysts there is also a large difference in loading, though it might be expected that if (XII) was loaded to the extent of (X), and retain its porosity, it would be an even more effective



SCHEME Reagents: i, HO(CH$_2$CH$_2$O)$_n$H; ii, *p*-CH$_3$C$_6$H$_4$SO$_2$Cl; iii, NaOR catalyst.[7] These conclusions confirm earlier reports in which oligo(ethylene glycol dimethyl ethers) were employed as exclusive solvents[8] and also effectively as phase-transfer catalysts with other solvents.[9,10] There is also agreement with experiments involving the use of much higher molecular weight poly(oxyethylenes).[11,12]

TABLE 3

Solubility of potassium phenoxide in toluene solutions of oligo(oxyethylenes)

Oligoether	Quantity of oligoether (mmol)[a,b]	Potassium phenoxide solubilised (mmol)[a]	Mole ratio phenoxide : oligoether
(I)	0.29	0.28	0.97
(II)	0.29	0.22	0.74
(IV)	0.067	0.20	2.4
(V)	0.039	0.05	1.4
(VI)	0.29	0.25	0.87
(VII)	0.29	0.037	0.13
None		$\ll 0.5$ p.p.m.[c]	

[a] 2 ml of solution. [b] 1.16 mmol of oxygen in each case. [c] Measured by atomic absorption flame photometry.

This trend could arise either because the longer chain species solubilise larger quantities of salt for a fixed quantity of donor oxygen atom, or the solubilised species become increasingly reactive as the chain length of oligoether is increased. The solubility measurements recorded in Table 3 show that for species (I), (IV), and (V) the weight of salt solubilised *falls* with increasing chain length of the oligoether, and the nominal number of oxygen donor atoms associated with each potassium ion rises accordingly. This is in broad agreement with related data in the literature.[12] Thus it appears that the enhanced catalytic activity is associated with an increased reactivity of the solubilised salt. The strength of complexation of arenediazonium[13] and sodium ions[14] is reported to increase with the chain length of oligoethers and so in our systems it seems likely that the trend in catalytic activity arises from an increase in the electrostatic shielding between the oligoether-complexed cation and the phenoxide counteranion, which effectively enhances the nucleophilicity of the latter.

Effect of Head-group of Non-supported Oligo(*oxyethylenes*).—In the case of the unbound symmetrically disubstituted oligoethers (VI)—(IX) the trend in catalytic activity is (VIII) $>$ (VII) $>$ (VI) $>$ (IX), with the bisquinolyl derivative (VIII) being as effective as dibenzo-18-crown-6. The replacement of both hydroxy-groups of oligo(ethyleneglycols) by *certain* lipophilic species is known to increase their ability to solubilise sodium salts in benzene.[12] Furthermore, molecules such as (VIII) and (IX) with rigid donor end-groups are known to form stable crystalline complexes with a variety of Group I and II metal salts,[15] and with this combination of factors it is not surprising how effective the catalyst (VIII) actually is. The poor performance of (IX), however, is very difficult to understand. An earlier indication that species such as these might not be good complexing entities has more recently been proved incorrect,[16] as they do indeed readily form crystalline complexes. One possibility that remains is that the conformation of the oligoether-complexed potassium ion may still in this case allow close approach of the phenoxide counteranion, hence reducing the nucleophilicity of the latter. Why this might be so is not clear, but certainly the relatively poor catalytic activity is also reflected somewhat in the supported species (XV) and (XIX).

A comparison of the catalysts (I), (VI), and (VII) is also interesting. Whereas the order of reactivity in catalysis is (I) $>$ (VII) $\geqslant$ (VI), the order of ability to solubilise potassium phenoxide is (I) $\geqslant$ (VI) $\gg$ (VII). Hence, although (I) solubilises *ca.* 7 times more salt than (VII) the difference in reaction rates is only *ca.* 2. On the other hand, (VI) is *ca.* 6 times more effective than (VII) in solubilising the salt and yet has comparable catalytic activity. These variations can be explained by balancing the strength of cation complexation with the extent of electrostatic interaction with the phenoxide counteranion in each ion pair species. It seems likely that the presence of an hydroxy-end-group increases the ability of the oligoether to complex with the cation,[12] but at the same time provides the possibility of stronger interaction, *via* hydrogen-bonding, with the anion. The oligoether (I), therefore, represents a compromise structure capable of achieving strong complexation with potassium ion, while simultaneously not deactivating the phenoxide counteranion too much. Oligoether (VII) complexes less effectively, while (VI) interacts too strongly with the anion.

Effect of Head-group of Resin-supported Oligo(*oxyethylenes*).—While the activity of the various oligoethers is attenuated somewhat when supported on a resin they are still very effective catalysts. Furthermore, the influence of the different head-groups is largely retained. This appears most clearly with species (X) and (XIII)—(XV) containing three ethylene oxide residues. The structures of this group of catalysts are fairly well defined, and the rates of catalysed reactions varied by a factor of *ca.* 9, with the 8-quinolyl derivative (XIV) again being the most effective. Furthermore, the corresponding 2-methoxyphenyl derivative (XV) is surprisingly poor. Non-supported oligoethers carrying a *single* rigid donor end group are known to form stoicheiometric crystalline compounds with sodium and potassium salts,[17] with a species analogous to (XIV) being particularly effective. In contrast, the unbound oligoether corresponding to (XV) produced complexed salts with no simple stoicheiometry, and this factor may be related to its performance in catalysis. The oligoether containing an additional ethylene oxide residue did give a complex with a definitive 1 : 1 stoicheiometry, and indeed the resin bound species (XIX), again with an extra ether residue, also showed a relative improvement in catalysis.

The second group of resin bound catalysts (XVI)—(XXIV) with four ethylene oxide residues in each oligoether chain showed smaller variations in catalytic activity. While this may be due to the longer chains, since rates of reaction were only of the same order of magnitude as before, it is more likely that it arises because significant proportions of the bound species do not have specific head-groups. Within this group, however, the 8-quinolyl derivative (XVIII) and the structurally closely related 2-pyridylmethyl derivative (XX), are most active. Perhaps somewhat surprisingly the 2-naphthyl species (XXII) with no additional donor atom in its head-group, is also relatively high in activity. However, since the comparison was made on the basis of molar equivalents of donor atoms, not of oligoether chains, it can be argued that the figures for (XXII) are somewhat flattering. Similarly, the catalyst (XXI) with the 2-(1,4-benzodioxanyl)methyl head-group possesses one extra heteroatom, located such that it is unlikely to be involved in complexation. This comparison on the basis of molar equivalents of potential donor atoms is therefore likely to bias the result for this catalyst towards the low side.

EXPERIMENTAL

Materials.—Catalysts (I) (Fluka), (II) (Lankro Chemicals), (III) (Pfaltz and Bauer), (IV) (Pfaltz and Bauer), (V) (Lankro Chemicals), (VI) (Aldrich), and (VII) (Koch-Light Laboratories) were dried over molecular sieves before use. In some cases, when carrying out reactions to attach these to resins, drying was achieved *in situ* by using a slight excess of sodium hydride. Catalysts (VIII) and (IX) were prepared from 1,8-dibromo-3,6-dioxaoctane by reaction with the sodium salts of 8-hydroxyquinoline and 2-methoxyphenol respectively, essentially as described in the literature.[15,16] Catalyst (VIII) remained as an oil[15] even after purification by column chromatography while (IX) was obtained as a solid with m.p. 75—77 °C.

Resin-supported Catalysts.—All of these were prepared from 2% crosslinked polystyrene resin (Bio Beads SX2). These beads were chloromethylated as previously reported[18] and oligoether chains were attached as before.[5] The species with specific head-groups, (XIV), (XV), (XVIII)—(XXIV), were synthesised according to the Scheme. In the case of (XIV) and (XV) the precursor was made by attaching (VI) to the resin by one end only, whereas the precursor (XVI) for the remaining catalysts was made using tetraethylene glycol. As an example, the preparation of (XV) will be described.

Preparation of (XIII).—Typically, into a 500 ml baffled round-bottomed flask were placed (VI) (98.4 g, 0.656 mol), toluene (70 ml), and tetraethylene glycol dimethyl ether (30 ml). Sodium hydride (3.15 g, 0.066 mol) was added slowly with stirring. The resultant mixture was agitated by rotation[19] and heated to 100 °C for 30 min until the evolution of hydrogen ceased. Chloromethylated polymer resin (22.1 g, 0.026 mol Cl) was added and the resultant mixture rotated at 100 °C under nitrogen for 80 h. The polymer was collected by filtration and washed successively with aqueous tetrahydrofuran (3 : 1), aqueous tetrahydrofuran containing 10% HCl, aqueous tetrahydrofuran, and finally tetrahydrofuran itself. After extracting the product for 6 h in a Soxhlet using tetrahydrofuran it was vacuum dried at 30 °C to yield resin (23.4 g), $\nu_{max.}$ (KBr) 1 100 cm^{-1} [Found: C, 85.15; H, 7.95; Cl, 0.3; O (by difference) 6.55%].

All manipulations of the resin were carried out with care to avoid weight losses, as the change in weight was used to estimate the change in the ' average molecular weight ' of a resin segment. The residual level of chloromethylation and degree of substitution by the oligoether chain were then calculated from the chlorine and oxygen microanalyses respectively using the method previously reported.[18] In the case of attaching tetraethylene glycol it was also possible to make an estimate of the fraction of oligoether chains attached by a single end and those present effectively as crosslinks.

Tosylation of (XIII).—Into a 100 ml baffled flask were placed methylene chloride (20 ml) and (XIII) (4.00 g, *ca.* 4 mmol OH). Tosyl chloride (7.63 g, 0.04 mol) in methylene chloride (10 ml) and pyridine (1 ml) were added and the resultant solution rotated for 24 h at room temperature. The polymer was collected by filtration and washed successively with methylene chloride and acetone before being extracted for 6 h with acetone in a Soxhlet extractor. After drying at 40 °C in a vacuum oven for 24 h, product (4.47 g) was obtained, $\nu_{max.}$ (KBr) 1 360, 1 185, and 1 100 cm^{-1} (Found: C, 82.75; H, 7.45; S, 2.55%).

Preparation of (XV).—2-Methoxyphenol (0.953 g, 7.7 mmol) and potassium hydroxide (0.39 g, 6 mmol) were dissolved in refluxing ethanol (30 ml). Tosylated (XIII) (2.02 g, 1.5 mmol S) was added and the mixture refluxed for 16 h. The resin was collected by filtration and washed successively with a dilute solution of sodium hydroxide in aqueous ethanol (50%), a dilute solution of sodium hydroxide in aqueous acetone (50%), water, aqueous acetone (50%), and finally acetone. After extracting with acetone for 6 h the resin was dried overnight under vacuum at 40 °C to yield the product (XV) (1.95 g), $\nu_{max.}$ (KBr) 1 250 and 1 100 cm^{-1} (Found: C, 85.85; H, 7.9; S, 0.0%).

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