

The Effect of the Solvent on the Reactivity of Potassium Phenoxide in Nucleophilic Substitution Reactions.

Part IV. Cyclic Polyethers as Additives

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The rate of alkylation of potassium phenoxide with butyl bromide has been investigated in dioxane with small amounts of cyclic polyethers as additives. The cyclic ethers were either of the general formula dibenzo-3*n*-crown-*n* (*n* = 4, 5, 6, and 8) or belonged to the corresponding saturated series.

A comparison is made between the effect of tetraethylene glycol dimethyl ether and the various cyclic polyethers. The results indicate that the cyclic compounds are considerably better solvating agents than open-chain polyglycol ethers, measured by the induced reactivity on a phenoxide anion. Addition of 0.05 M of dicyclohexyl-18-crown-6 to a solution of 0.025 M K-phenoxide in dioxane increases the alkylation rate of the phenoxide by a factor of 1.5×10^4 .

The size of the cyclic ether cage is found to exert a pronounced effect, indicating that for the K^+ -ion there is an optimal cyclic ether ring diameter for which the maximum degree of solvation is achieved.

Hydrogenation or complete removal of one or both of the benzene rings are factors which make the oxygen atoms more basic and increase the solvating ability of the crown compounds.

In a previous paper (Part I)¹ it was shown that the rate of alkylation of potassium and sodium phenoxides in polyethylene glycol dimethyl ethers as solvents increases considerably with chain length from mono to hexaethylene glycol dimethyl ether. The same effect was obtained in isomerizations of olefinic hydrocarbons in a reaction system catalyzed by potassium-*t*-butylate, using the polyethers as solvents or additives.^{2,3} In these papers it is reported that the reaction rate depends chiefly upon the capacity of the solvent to solvate the alkali ion specifically, and furthermore that several oxygen atoms in the same polyether molecule contribute to solvation of the alkali ion.

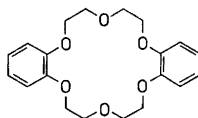
Pedersen⁴ synthesized cyclic ethers with a variety of ring sizes and substituents and showed that these compounds are able to form stable complexes with many salts of the alkali and alkaline earth metals. The complexes

were believed to be salt-polyether complexes formed by ion-dipole interaction between the cation and the oxygen atoms of the polyether ring with one molecule of polyether per discrete cation, regardless of its valence.

Haymore *et al.*⁷ found that dicyclohexyl-18-crown-6 forms complexes with a number of cations. Isolation of the complexes in crystalline form gave compounds with one or two ligands per cation.

In view of previous experience of the solvating effects of the polyethylene glycol dimethyl ethers it was obvious that some cyclic ethers could form complexes with alkali phenoxide and increase its anion reactivity. Kinetic investigations of the nucleophilic substitution reaction between K-phenoxide and butyl bromide were carried out with small additions of cyclic polyethers in order to compare the effect of this type of ether with that of the open-chain polyethylene glycol ethers. Dioxane was chosen as solvent because it is an ether with relatively poor cation solvating properties; it has a low dielectric constant, and the alkylation reaction in this solvent is extremely slow.

All the cyclic polyethers used in this investigation have the repeating unit C-C-O in the polyether ring. Their names are abbreviated according to Pedersen⁴ and the abbreviations describe, in order: (1) the number and kind of hydrocarbon ring; (2) the total number of atoms in the polyether ring; (3) the class name, crown; and (4) the number of oxygen atoms in the polyether ring. Dibenzo-18-crown-6, for example, has the following structural formula:



EXPERIMENTAL

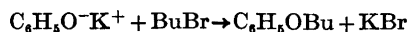
Reagents. Potassium phenoxide was prepared by the method of Kornblum and Lurie, as modified in Part I.¹ All cyclic polyethers were prepared by the methods of Pedersen.⁴ Dicyclohexyl-18-crown-6 was a gift from DuPont de Nemours Co. The melting points of the cyclic ethers were in good agreement with those reported, except for dibenzo-24-crown-8, which after repeated crystallization from heptane showed a constant melting point of 101.5°C. while Pedersen reports 113–114°C. However, in spite of this, our NMR-spectrum is identical with that obtained by Pedersen.

Quality and purification of the other reagents and solvents have been described in Parts I and II.^{1,5}

Procedure. Dried potassium phenoxide was dissolved in dioxane to give a concentration somewhat higher than desired for the kinetic experiments. The solution was transferred to a 100 ml round bottom flask containing the weighed amount of polyether and left to equilibrate for about 3 days. After analysis of its phenoxide concentration 50 ml of the dioxane solution were transferred to the reaction flask. This flask was equipped with a side arm, into which butyl bromide was pipetted. The required amount of dioxane was added to the butyl bromide to give the desired concentration of the reactants. The reaction flask was then stoppered and placed in a constant temperature bath (25°C). The reaction was started by rapidly mixing the reagents. Aliquots were withdrawn from the reaction mixture at regular intervals for analysis of unreacted phenoxide, applying the method described in Part I.¹

The reaction flask had a stopcock connected to the upper part of its neck, and nitrogen was slowly introduced through this stopcock every time the glass stopper of the flask was removed for sampling. The whole procedure, including the preparation of the phenoxide solution, transportation of the solutions and the kinetic run itself, was carried out in an atmosphere of nitrogen.

Table 1. Effect of polyether additives in the reaction between potassium phenoxide and butyl bromide in dioxane.



Temperature: 25°C $[\text{BuBr}]_0 = 0.05$ or 0.10 mol l⁻¹

$[\text{C}_6\text{H}_5\text{OK}]_0 = 0.020$ mol l⁻¹

r_1 = initial consumption of phenoxide in mol l⁻¹ sec⁻¹.

Run No.	Additive	$\frac{[\text{Additive}]}{[\text{Phenoxide}]_0}$ in %	$r_1/[\text{BuBr}]_0$ 10 ⁵ sec ⁻¹
1	None	—	0.01 ^s
2	Tetra-EGDME ^a	5.4	0.015
3		20	0.030
4		62	0.071
5		100	0.11
6		Dibenzo-12-crown-4	5.4
7	Dibenzo-15-crown-5	1	0.011
8		5.4	0.023
9		20	0.062
10		50	0.15
11		76	0.22
12		Dibenzo-18-crown-6	1
13		5.4	0.37
14		20	1.9
15		30	3.1
16		Dibenzo-24-crown-8	1
17		5.4	0.075
18		15	0.20
19		Benzo-15-crown-5	5.4
20	Benzo-18-crown-6	5.4	1.00
21	Dicyclohexyl-18-crown-6	5.4	2.80
22		30	15.0
23		49	33.0
24		100	87.0
25		128	104
26		153	112
27		206	117
28		Bis(<i>t</i> -butylbenzo)-18-crown-6	5.4
29		100	13.0
30		153	15.0
31		201	15.0
32		Dimethyl sulphoxide	100

^a Abbreviation for tetraethylene glycol dimethyl ether.

RESULTS AND DISCUSSION

Table 1 gives the results of the phenoxide alkylation with butyl bromide in dioxane with varying amounts of additives. In addition to the cyclic polyethers are included results with the linear ether tetraethylene glycol dimethyl ether and with dimethyl sulphoxide. The amount of additive is given in mol % of the initial phenoxide concentration and the reaction rate as a first order experimental rate constant. For three of the cyclic polyethers, dibenzo-15-crown-5, dibenzo-18-crown-6, and dibenzo-24-crown-8, the maximum additions are limited by the solubility of the potassium phenoxide-polyether complex in dioxane.

An addition of tetraethylene glycol dimethyl ether equivalent to the phenoxide concentration gives a rate increase of 11 compared to pure dioxane (run 5), while the corresponding rate increase with dimethyl sulphoxide is only 1.4 (run 32). This is in accordance with the results reported by Ugelstad *et al.*² in conjugation isomerizations of fatty acids with K-*t*-butylate as catalyst, where a 1 % (vol.) addition of tetra-EGDME to diethyl ether is 8 times as powerful as the same amount of dimethyl formamide. The opposite effect, however, is found when tetra-EGDME and DMSO are used as pure solvents. In the reaction between K-phenoxide (0.025 M) and butyl chloride⁵ the reaction rate is shown to be 16 times higher in DMSO than in tetra-EGDME.

The higher solvating power of tetra-EGDME when applied as additive in small amounts has been ascribed to the cooperation of several oxygen atoms in the same molecule in the solvation of the alkali cation. When the solvating oxygen atoms belong to a single molecule the solvation of the cation involves a smaller loss in configurational entropy than would be the case with several molecules. When tetra-EGDME and DMSO are used as pure solvents the difference in configurational entropy disappears, and in this case DMSO gives a higher reactivity than tetra-EGDME.

It appears from Table 1 that all the cyclic polyethers studied in this investigation are considerably more effective in increasing the reactivity of potassium phenoxide than the linear tetra-EGDME when applied as additives in small amounts. Some of the cyclic ethers increase the reaction rate by several orders of magnitude. An addition of bis(*t*-butylbenzo)-18-crown-6 equivalent to the phenoxide concentration leads to an alkylation rate 1300 times faster than in pure dioxane (run 29), the same amount of dicyclohexyl-18-crown-6 causes a 8700 fold rate increase (run 24), while a corresponding addition of tetra-EGDME, as mentioned above, only gives a rate increase of 11.

The increase in reaction rate when tetra-EGDME is replaced by a cyclic polyether is believed to be caused by the greater ability of the latter to solvate the K⁺-ion and thus make the phenoxide anion of the ion-pair a stronger nucleophilic reagent. Several effects may possibly account for this difference. The dominant advantage of the cyclic compounds is the fact that the oxygen atoms in the polyether ring are arranged beforehand in a position suitable for a concerted solvating action. In the case of the linear ether the solvation process involves a considerable loss in freedom for rotation. In addition, the formation of a curled polyglycol ether molecule with a "free hole" available for the potassium ion necessitates the breaking off of interactions between

dioxane molecules and segments of the linear ether. There is also possibly a steric effect favouring the cyclic ether. The repelling forces between the $-\text{CH}_3$ groups on each end of a polyglycol dimethyl ether chain, which normally are too far away from each other for a mutual interaction, may be a considerable factor in a solvating situation when the ether molecule is curled up around an alkali cation. This steric hindrance is absent in the case of cyclic ethers.

Comparing the dibenzo- $3n$ -crown- n compounds, where n is the number of oxygen atoms in the polyether ring, the results in Table 1 indicate that there is a direct relationship between the size of the ring and the rate of the phenoxide alkylation reaction. Calculations from molecular models show that $n = 4$ gives a diameter of the cyclic ether cage of about 1.8 Å, $n = 5$ gives 2.7 Å, $n = 6$ about 4.0 Å, and $n = 8$ a diameter greater than 4 Å.⁴ The runs 6, 8, 13, and 17 with 0.0011 M (5.4 % of the phenoxide concentration) of the cyclic polyethers dibenzo-12-crown-4, dibenzo-15-crown-5, dibenzo-18-crown-6, and dibenzo-24-crown-8 show an increase in alkylation rate with increasing number of oxygen atoms in the ring up to the maximum at $n = 6$. A marked drop in rate is, however, observed when n is increased further to 8.

Dibenzo-12-crown-4 with a diameter of 1.8 Å is obviously too small for the K^+ -ion of 2.66 Å to fit into it, even though the solvation power of this cyclic ether is considerably better than that of tetra-EGDME (*cf.* runs 2 and 6). Dibenzo-15-crown-5 has a cage just large enough for the K^+ -ion, but run 8 shows that this cyclic ether is no better than the dibenzo-12-crown-4 as far as promoting the alkylation reaction is concerned.

A very marked increase in alkylation rate is obtained with 6 oxygen atoms in the cyclic ether ring (runs 12–15). With a cyclic ether hole of 4.0 Å, as in dibenzo-18-crown-6, the cage obviously is large enough for complete enclosure of the K^+ -ion. Runs 20–27 with monobenzo-18-crown-6 and dicyclohexyl-18-crown-6 show that an even better solvation effect of the crown-6 ring is achieved when one benzene ring is removed or both benzene rings are completely hydrogenated. The increase in basicity of the oxygen atoms in the cyclic ether ring increases their interaction with the cation and results in more powerful solvation.

For $n = 8$ (runs 16–18) the cyclic ether cage apparently has become too large. In this case the mutual interactions between the K^+ -ion and the oxygen atoms of the cyclic ether ring are too weak to keep the cation inside the cage. Moreover, molecular models show that when the cyclic ethers have seven or more oxygen atoms in the polyether ring, the oxygen atoms cannot be arranged in a coplanar configuration.

This change in reactivity with the size of the cyclic polyether ring is in accordance with the results of Pedersen, who estimated the degree of complex formation with K^+ -ions by ultraviolet spectroscopy and solubility measurements of potassium salts.⁴

Fig. 1, drawn from the results of runs 21–27, shows that increasing additions of dicyclohexyl-18-crown-6 cause an increase in reaction rate up to about 0.04 M, corresponding to 200 % of the initial K -phenoxide concentration. At this point the complex formation is complete and the rate is that of potassium phenoxide existing completely in the form of solvent-separated ion-pairs.

The runs of Table 2 are carried out with varying concentrations of K-phenoxide and with dicyclohexyl-18-crown-6 as additive. The cyclic ether is in each run added in excess so as to give complete complex formation. In Fig. 2

Table 2. Rates of alkylation of potassium phenoxide with butyl bromide at different concentrations of phenoxide, using 200 % of dicyclohexyl-18-crown-6.

Temperature 25°C. $[\text{BuBr}]_0 = 0.050 \text{ mol l}^{-1}$.

r_i = initial consumption of phenoxide in $\text{mol l}^{-1} \text{ sec}^{-1}$.

Run	[phenoxide] mol l^{-1}	$r_i/[\text{BuBr}]_0$ 10^5 sec^{-1}
33	0.0137	89
27	0.0193	117
34	0.0265	166

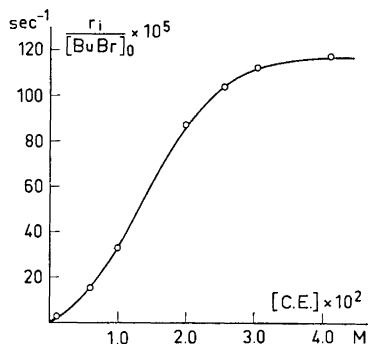


Fig. 1. Effect of cyclohexyl-18-crown-6 on the alkylation rate of potassium phenoxide with butyl bromide. Temp. 25°C. $[\text{phenoxide}]_0 = 0.020 \text{ M}$.

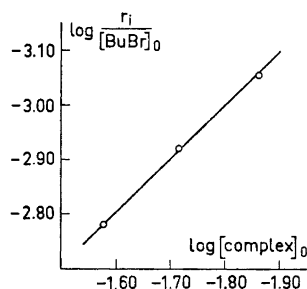


Fig. 2. Plot of $\log r_i/[\text{BuBr}]_0$ versus $\log [\text{complex}]$ for the alkylation of potassium phenoxide in dioxane with dicyclohexyl-18-crown-6 as additive. Temp. 25°C. $[\text{BuBr}]_0 = 0.05 \text{ M}$.

these runs are plotted as $\log(r_i/[\text{BuBr}]_0)$ versus $\log[\text{complex}]$ with the latter taken to be equal to the initial phenoxide concentration. The slope of the straight line is found to be very close to one, and accordingly the order of the alkylation reaction with respect to the phenoxide-cyclic ether complex must be equal to one. This indicates that the reacting entity is the phenoxide⁻, K⁺-cyclic ether complex existing as single ion-pairs.

In a previous paper (Part III)⁶ it was shown that replacing the K⁺-ion by a Bu₄N⁺-ion results in a very great increase in the reactivity of the phenoxide in dioxane solution. Contrary to the sodium and potassium phenoxide alkylation reactions in aprotic solvents^{1,5} the alkylation of tetra-butylammonium phenoxide is of first order with respect to the phenoxide even in a low polarity solvent like dioxane, and it was concluded that also in this case the

reacting entity is a single ion-pair. The enhanced reactivity of the quaternary ammonium phenoxide was explained by a strongly reduced cation-anion interaction energy, and this is also the most probable explanation for the high reactivity caused by the complex formation with the cyclic polyethers.

In Table 3 the maximum rate obtainable by addition of dicyclohexyl-18-crown-6 at a K-phenoxide concentration of 0.025 M is compared to the rate in pure tetra-EGDME and to the effect of replacement of the \bar{K}^+ -ion with Bu_4N^+ .

Table 3. Effect of solvents and additives in the alkylation of K-phenoxide with butyl bromide.

$[\text{phenoxide}]_0 = 0.025 \text{ mol l}^{-1}$. Temp. 25°C .

r_1 = initial consumption of phenoxide in $\text{mol l}^{-1} \text{ sec}^{-1}$.

Solvent	Additive	$r_1/[\text{BuBr}]_0 \times 10^5 \text{ sec}^{-1}$
Dioxane	—	0.01 ^b
Tetra-EGDME	—	150 ^b
Dioxane	Dicyclohexyl-18-crown-6	150
Dioxane	Bu_4NBr^a	$\sim 400^b$

^a Addition of a slight excess of Bu_4NBr to a solution of K-phenoxide in dioxane leads to formation of Bu_4N -phenoxide and precipitation of KBr.

It appears that an addition of 0.05 M of dicyclohexyl-18-crown-6 to dioxane gives the same reactivity of the phenoxide anion as in pure tetra-EGDME. The quaternary ammonium phenoxide is somewhat more reactive, indicating that the charge of the nitrogen atom is more effectively shielded in a quaternary ammonium cation with relatively long alkyl chains than the charge of a solvated potassium ion.

In dimethyl sulphoxide and dimethyl formamide the alkylation rate of K-phenoxide is even higher than that of the tetrabutylammonium phenoxide in dioxane, about $2 \times 10^{-2} \text{ sec}^{-1}$.⁵ K-phenoxide is 40–50 % dissociated at a concentration of 0.025 M in these highly polar solvents,⁶ and the kinetic results may be taken to indicate that in aprotic solvents the free phenoxide is about 10 times as reactive as the most reactive ion-pair.

Acknowledgement. We gratefully acknowledge the support of *Norges Teknisk-Naturvitenskapelige Forskningsråd* for this investigations.

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Received January 11, 1971.

Acta Chem. Scand. 25 (1971) No. 8