POLYMER-SUPPORTED OLIGO(OXYETHYLENE)S, SULFOXIDES, AND CROWN ETHERS IN NUCLEOPHILIC SUBSTITUTION REACTIONS

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The efficiency of polymer analogues of oligo(oxyethylene)s and sulfoxides in the activation of nucleophilic substitution reactions were compared by testing to the reaction between sodium phenoxide and 1-bromooctane in 1,4-dioxane. With polymer analogues of crown ethers and polymer networks having the pseudo-crown ether structure the polymer effect can be achieved, i.e. a higher activation efficiency of the polymer analogue (in the L–S system) compared with the efficiency of the unimmobilized compound (in the homogeneous system). The results suggest that several molecules of the linear activator or of side active groupings (chains) on the polymer having the podand structure take part in the formation of the activation site (for the complex formation or solvation of the cation).

Organic reactions in a two-phase system water–organic solvent in the presence of ammonium or phosphonium salts, i.e. carried out by using the phase transfer catalysis (PTC)[1–3], were enriched by employing polymeric catalysts, or, more generally, polymeric activators of the type of polymeric quaternary salts, polymer analogues of dipolar aprotic solvents (polymeric cosolvents) and polymeric ionophores[4–11]. Basically, they act in nucleophilic substitution reactions in a uniform way, i.e. by releasing ions from the close ionic pair of the agent. Their application solves the problem of separation of the phase transfer medium from the product and that of the final purity of the product. If the medium can be dissolved in the organic phase, it can be precipitated, if it does not dissolve in the reaction medium, i.e. the system is a three-phase one (L–S–L), it can simply be filtered off. Another advantage, which can be added to those just mentioned, is easy manipulation, nontoxicity and repeated applicability. The disadvantage consists in the higher costs and the usually lower efficiency compared with low-molecular weight activation media.

During a few last years, we have focussed our studies in the field of polymeric activators of organic reactions on the research on the anhydrous system agent–substrate–polymeric activator in the homogeneous liquid phase or in the two-phase L–S system, in which the solution of the agent and substrate was the liquid phase

and the polymeric activator was the solid phase. In both cases easy separation of the polymeric activator after the reaction is preserved; in the case of the L–S system there is a possibility of conducting the process in a flow reactor, which seems attractive for industrial technologies. In earlier communications we have described the preparation procedures of polymer analogues of sulfur compounds, amides, ammonium salts, and oligoethers, along with their activation efficiency according to the types of activation compounds used[11–15]. This study is mainly focussed on the relation between the efficiency of polymeric activators and their low-molecular weight precursors.

In a two-phase L–S system each swollen particle of the activator is an internal reactor, which is entered by reaction components from the surrounding solution. In the swollen particle these components are in an immediate contact with the activation substance and the phase boundary loses its meaning. Of course, unlike the homogeneous system the activation substances cannot move unrestricted, because they are locally fixed. This view follows from the results obtained by an investigation of the activation efficiency of oligo(oxyethylene)s and sulfoxides in Williamson's synthesis of phenyl octyl ether by a reaction between sodium phenoxide and 1-bromooctane in anhydrous 1,4-dioxane at 75°C (Tables I and II). The activation efficiency of these compounds was characterized by using the specific rate constant, k_s, i.e. the observed rate constant (k) related to the unit concentration of the functional substance in the reaction mixture (c), or the specific rate constant k'_s, i.e. k related to the unit concentration of a certain functional group in the reaction mixture (c'). The relation between the activation efficiency of the polymeric activator and low-molecular weight activator (unimmobilized compound) was expressed as the immobilization effect, E, through the ratio k for the polymeric activator and the unimmobilized compound or its model. If $E > 1$, polymer effect is usually mentioned.

The testing reaction under investigation proceeds in the presence of tri(oxyethylene) (*I*) by one order of magnitude, and in the presence of tetra(oxyethylene) (*II*) and hepta(oxyethylene) (*III*) by two orders of magnitude more quickly than the uncatalyzed reaction[11] and can be conducted to a complete conversion of the the starting substrate to the expected product. The compounds ranging from tri- to hepta(oxyethylene)s bonded to the crosslinked poly(styrene-*co*-divinylbenzene) so that the podand structure predominates in the respective polymeric activator (*IV* to *VII*) have an activation efficiency lower by an order of magnitude, $E \leqq 0{\cdot}1$. Hence, it can be deduced that the complexation of the cation by unimmobilized compounds proceeds with participation of several molecules, which may be easy only if these molecules can freely move in the homogeneous solution. At the same time, the activation efficiency increases with increasing length of the oligomeric segment and each new oxyethylene constitutional unit has a more favourable effect than the given preceding unit (k'_s is not constant). The highest increase takes place after the fifth repeating constitutional unit has been incorporated (Fig. 1), which corresponds to

TABLE I

Activators. Specific amounts of functional groupings: c_o $(OCH_2CH_2)_n$ and/or $x(SO)$, $(c_o)_{OH}$ OH. Polymeric carriers: PS poly(styrene-*co*-divinylbenzene), PP catenapoly[bis(2,2,3,3-tetrafluoropropoxy)-λ^5-phosphazene], PVA poly(vinyl alcohol), PSBDOL poly(styrene-*co*-divinylbenzene)-*alt*-(2-butene-1,4-diol) (49 : 1 : 50 mole %), PSAA poly(styrene-*co*-divinylbenzene-*co*-allyl alcohol) (73·2 : 8·1 : 18·7 mole %). Specification of the carrier: number in brackets gives the mass fraction of the crosslinking monomeric unit (in %), exponent at PS denotes the degree of chloromethylation of the precursor, while at PP, PVA, PSBDOL, and PSAA it denotes the degree of substitution of the reactive monomeric unit of the precursor (mass fraction in %)

Activator	Structure	c_o	$(c_o)_{OH}$
		mmol g^{-1}	
I	$H(OCH_2CH_2)_3OH$	6·66	6·66
II	$H(OCH_2CH_2)_4OH$	5·15	5·15
III	$H(OCH_2CH_2)_7OH$	3·06	3·06
IV	$PS(2)^{64}—CH_2—(OCH_2CH_2)_3OH(0·88)^a$	3·16	2·78
V	$PS(2)^{64}—CH_2—(OCH_2CH_2)_4OH(0·92)$	2·72	2·50
VI	$PS(2)^{64}—CH_2—(OCH_2CH_2)_5OH(0·95)$	2·44	2·12
VII	$PS(2)^{64}—CH_2—(OCH_2CH_2)_7OH(0·94)$	2·00	1·88
VIII	$PS(2)^{36}—CH_2—(OCH_2CH_2)_{6,4}O—CH_2—PS$	0·550	—
IX	$PS(2)^{69}—CH_2—(OCH_2CH_2)_{6,4}O—CH_2—PS$	1·11	—
X	$\left[\begin{matrix}(OCH_2CH_2)_{7,3}CH_2N^+(CH_3)_3\\ \vert\\ CH_2CH_2CH_2N^+(CH_3)_3\end{matrix}\right] 2\,Cl^-$	1·95	—
XI	$\left[\begin{matrix}(OCH_2CH_2)_{7,3}CH_2N^+(CH_3)_2—CH_2—PS\\ \vert\\ CH_2CH_2CH_2N^+(CH_3)_2—CH_2—PS(2)^{33}\end{matrix}\right] 2\,Cl^-$	0·836	—
XII	$\left[\begin{matrix}(OCH_2CH_2)_{55}CH_2N^+(CH_3)_2—CH_2—PS\\ \vert\\ CH_2CH_2CH_2N^+(CH_3)_2—CH_2—PS(2)^{33}\end{matrix}\right] 2\,Cl^-$	0·315	—
XIII	$C_6H_5CH_2N^+(CH_2CH_3)_3.Cl^-$	4·39[b]	—
XIV	$PS(2)^{36}—CH_2—N^+(CH_3)_2CH_2CH_2CH_3.Cl^-$	2·29[b]	—
XV	$PP^{59}—(OCH_2CH_2)_3OH(0·62)$	2·67	1·66
XVI	$PP^{64}—(OCH_2CH_2)_3OH(0·23)$	3·02	0·694
XVII	$PP^{30}—(OCH_2CH_2)_4OH(0·94)$	1·67	1·57
XVIII	$PP^{51}—(OCH_2CH_2)_4OH(0·34)$	2·07	0·704
XIX	$PP^{45}—(OCH_2CH_2)_5OH(0·64)$	1·66	1·06
XX	$PP^{64}—(OCH_2CH_2)_5OH(0·35)$	1·90	0·665

TABLE I
(*Continued*)

Activator	Structure	c_o	$(c_o)_{OH}$
		mmol g^{-1}	
XXI	PP[62]—$(OCH_2CH_2)_5OH$(0·07)	2·25	0·158
XXII	PP[30]—$(OCH_2CH_2)_7OH$(0·79)	1·54	1·22
XXIII	PP[69]—$(OCH_2CH_2)_7OH$(0·44)	2·20	0·968
XXIV	PVA[4]—O—$CH_2CH_2SOCH_2CH_3$	0·829	19·91
XXV	PVA[34]—O—$CH_2CH_2SOCH_2CH_3$	4·27	8·33
XXVI	PSBDOL(1)[7]—CH_2O—$CH_2CH_2SOCH_3$	0·720	8·99
XXVII	PSAA(8)[8]—CH_2O—$CH_2CH_2SOCH_2CH_3$	0·159	1·72
XXVIII	CH_3SOCH_3	12·80	—
XXIX	PS(1)[106]—CH_2—SO—CH_2—PS[c]	2·77	—
XXX	PS(1)[106]—CH_2—S—CH_2—PS[c]	3·10[d]	—
XXXI	PS(1)[106]—CH_2—SO_2—CH_2—PS[c]	2·64[e]	—
XXXII	PS(2)[100]—CH_2—$SOCH_3$	5·32	—
XXXIII	PS(2)[70]—CH_2—$SOCH_3$	4·45	—
XXXIV	PS(2)[36]—CH_2—$SOCH_3$	2·75	—
XXXV	PS(2)[100]—CH_2—$SOCH_2CH_2SOCH_2CH_3$	3·36	—
XXXVI	PS(2)[100]—CH_2—$SOCH_2CH_2SOCH_2CH_2SOCH_2CH_3$	2·50	—
XXXVII	$CH_3SOCH_2SOCH_3$	7·13	—
XXXVIII	PS(1)[15]—CH_2—$CH(SOCH_3)_2$	0·458	—
XXXIX	PS(1)[15]—CH_2—$NCH_2CH_2SCH_2CH_2$	0·885[d]	—
XL	PS(2)[69]—CH_2—$OCH_2CH_2NCH_2(CH_2OCH_2)_4CH_2$	2·19[f]	—
XLI	PS(2)[36]—CH_2—$OCH_2CH_2NCH_2(CH_2OCH_2)_4CH_2$	1·64[f]	—
XLII	PS(2)[9]—CH_2—$OCH_2CH_2NCH_2(CH_2OCH_2)_4CH_2$	0·430[f]	—
XLIII	$C_6H_5CH_2OCH_2CH_2NCH_2(CH_2OCH_2)_4CH_2$	2·83[f]	—
XLIV	PS(2)[69]—CH_2—$PO(C_6H_5)C_6H_3(OCH_2CH_2)_4O$	0·830	—
XLV	$HPO(C_6H_5)C_6H_3(OCH_2CH_2)_4O$	2·55	—

[a] Numerical value in brackets after OH denotes the mole fraction of pendent branches (here and onwards). [b] N^+. [c] Styrene monomeric unit substituted not only in the *p*-position. [d] S. [e] SO_2. [f] Only OCH_2CH_2 in the ring.

TABLE II

Specific rate constant, $k_s = k/c$, of the reaction between sodium phenoxide (0·25 mmol) and 1-bromooctane (1 mmol) in anhydrous 1,4-dioxane (1 ml of solution) with stirring (600 rpm) at 75°C. Symbols: c concentration of functional groupings, c_{OH} concentration of OH groups, k rate constant, k'_s specific rate constant related to unit concentration of OCH_2CH_2 and/or SO, E immobilization effect, ξ extent of reaction after 22 h

Activator	$c \cdot 10^2$ / mol l^{-1}	$c_{OH} \cdot 10^2$ / mol l^{-1}	System	$k \cdot 10^5$ / l mol^{-1} s^{-1}	$k_s \cdot 10^5$ / l^2 mol^{-2} s^{-1}	$k'_s \cdot 10^5$ / l^2 mol^{-2} s^{-1}	E	ξ
I	11·0	22·0	L	3·6	32·7	10·9	—	1·00
II	8·50	17·0	L	12	141	35·3	—	1·00
III	4·68	9·36	L	17	363	51·8	—	0·99
IV	6·00	5·28	L–S	0·19	3·2	1·1	0·10	0·20
V	5·44	5·00	L–S	0·38	7·0	1·8	0·05	0·40
VI	4·39	4·18	L–S	0·96	21·9	4·4	0·09[a]	0·51
VII	4·00	3·76	L–S	1·5	37·5	5·4	0·10	0·68
VIII	0·550	—	L–S	1·0	182	28·4	0·54[b]	1·00
IX	2·22	—	L–S	8·7	392	61·3	1·17[b]	1·00
X	1·91	—	L	9·3	487	68·4[c]	—	0·70
XI	1·67	—	L–S	22·8	1 365[d]	187[c]	2·80	1·00
XII	0·315	—	L–S	28·5	9 048	165[c]	2·41[e]	1·00
XIII	7·52	—	L	35·6	474	—	—	1·00
XIV	4·58	—	L–S	0·66	14·4	—	0·03[f]	0·08[g]
XV	6·68	4·14	L–S	0·24	3·6	1·2	0·11	0·18
XVI	7·75	1·74	L–S	0·29	3·8	1·3	0·12	0·26
XVII	4·18	3·92	L–S	0·60	14·4	3·6	0·10	0·40
XVIII	5·18	1·76	L–S	0·75	14·5	3·6	0·10	0·48
XIX	4·15	2·66	L–S	1·7	41·0	8·2	0·17[a]	0·76
XX	4·75	1·66	L–S	3·7	77·9	15·5	0·32[a]	0 93
XXI	2·25	0·158	L–S	4·7	209	42·7	0·86[d]	0·96
XXII	3·85	3·04	L–S	3·7	96·1	13·7	0·26	0·93
XXIII	5·50	2·42	L–S	8·0	145	20·8	0·40	0·97
XXIV	14·9	358	L–S	1·69	11·3	5·8	—	0·42[h]
XXV	19·2	37·5	L–S	2·61	13·6	6·8	—	0·84[h]
XXVI	1·44	17·98	L–S	1·11	77·1	38·5	—	0·70

the possibility of a single side chain to contribute to the complexation of the cation, because the chain itself is able to encompass the cation (to form a pseudo-crown ether loop). On the contrary, when hepta(oxyethylene) is bonded by both ends to the given polystyrene carrier, the efficiency of such polymeric activators (*VIII*, *IX*) is similar to that of unimmobilized compound. A suitable degree of functionalization

TABLE II
(*Continued*)

Activator	$c \cdot 10^2$ mol l^{-1}	$c_{OH} \cdot 10^2$ mol l^{-1}	System	$k \cdot 10^5$ l mol^{-1} s^{-1}	$k_s \cdot 10^5$ l^2 mol^{-2} s^{-1}	$k'_s \cdot 10^5$ l^2 mol^{-2} s^{-1}	E	ξ
XXVII	0·795	8·60	L–S	1·90	239	119	—	0·58
XXVIII	22·0	—	L	7·02	31·9	31·9	—	0·83
XXIX	6·94	—	L–S	2·09	30·0	30·0	0·94	0·95
XXX	7·75	—	L–S	0·80	10·3	10·3	0·32[i]	0·13
XXXI	6·60	—	L–S	1·41	21·4	21·4	0·67[i]	0·68
XXXII	25·0	—	L–S	0·51	2·0	2·0	0·06	0·37
XXXIII	22·0	—	L–S	0·51	2·3	2·3	0·07	0·37[h]
XXXIV	20·1	—	L–S	0·24	1·2	1·2	0·04	0·18
XXXV	8·40	—	L–S	0·50	6·0	3·0	—	0·38
XXXVI	6·22	—	L–S	0·54	8·7	2·9	—	0·33
XXXVII	4·06	—	L	6·94	171	85·4	—	1·00
XXXVIII	1·14	—	L–S	0·45	39·5	19·6	0·23	0·22
XXXIX	2·21	—	L–S	0·451	20·4	20·4	—	0·27
XL	5·48	—	L–S	164	2 993	599[j]	0·90	1·00[k]
XLI	4·10	—	L–S	159	3 878	776[j]	1·16	1·00[k]
XLII	1·08	—	L–S	24·7	2 287	459[j]	0·68	1·00[k]
XLIII	6·11	—	L	204	3 339	667[j]	—	1·00[k]
XLIV	2·08	—	L–S	11·7	562	112[j]	0·44	1·00[l]
XLV	2·09	—	L	26·8	1 282	256[j]	—	1·00[l]

[a,b] Related to k_s [a]234 and [b]334 determined for oligo(oxyethylene)s with the number of oxyethylene units, n, 5 and 6·4, respectively, by graphic interpolation in the k_s vs n dependence using data for *I*, *II*, *III*. [c] Oxyethylene group taken as the functional group. [d] 1 328 at c 836 mmol l^{-1} ($k = 11{\cdot}1 \cdot 10^5$ l mol^{-1} s^{-1}, $\xi = 0{\cdot}87$). [e] $(k'_s)_{XII}/(k'_s)_X$. [f] Related to $(k_s)_{XIII}$. [g] After 4 h. [h] After 23 h. [i] Related to $(k_s)_{XXVIII}$. [j] The ring supposed to contain five ligands. [k] After <1 h. [l] After 4–5 h.

is accompanied by the polymer effect ($E > 1$). In this case the obvious cause of the great difference in the activation efficiency is the network structure of the activators which has the character of the pseudo-crown ether structure, and the crown ethers are known to be more effective in the complexation of cations than the corresponding linear compounds, judging by the stability of the complexes. Itsuno and coworkers[16] also came to a similar conclusion regarding optimization of the length of the oligo(oxyethylene) chain and participation of oxyethylene units in the polymeric activator in order to produce the polymer effect when they investigated the initial rate of Williamson's alkylation of potassium phenoxide with 1-bromobutane in toluene in the presence of the network copolymer of styrene and α,ω-bis(*p*-vinylbenzyl)oligo(oxyethylene).

Compared with hepta(oxyethylene) which possesses end hydroxyl groups, hepta(oxyethylene) with its end tetraalkylammonium groups (*X*) is a somewhat more efficient activator. Bulky ionic groups either conformationally support the formation of a tridimensional cavity of the spiral type or lipophilize the activator; both effects are favourable for complexation of the cation in the system. Lipophilization support of the activation of the anion can also be interpreted by assuming that, with respect to the anion, the ionic double pair $Quat^+$**ip**$(Na^+)PhO^-X^-$ or the pair $Quat^+$**ip**PhO^- (after decomplexation following precipitation of the alkaline salt) is less close than **ip**$(Na^+)PhO^-$ (where **ip** denotes the type of the ionophoric shell). Quaternization of the corresponding dimethylamine precursor with chloromethylated poly(styrene-*co*-divinylbenzene) yields polymeric activator (*XI*) with an efficiency approximately three times higher than that of the unimmobilized ammonium salt, i.e. the polymer effect is considerable ($E = 2{\cdot}8$) and the increase in efficiency compared with the efficiency of a similar polymeric activator without the tetraalkylammonium grouping is quite distinct, too, $(k'_s)_{XI}/(k'_s)_{VIII} = 6{\cdot}6$. These data suggest that the conformational

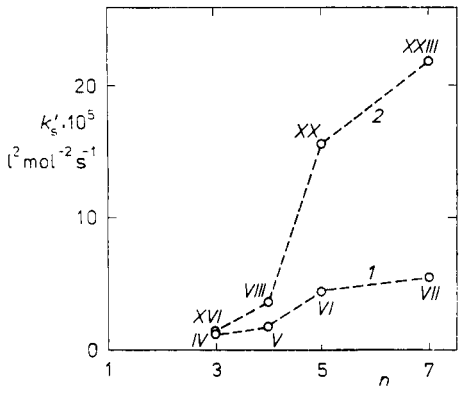
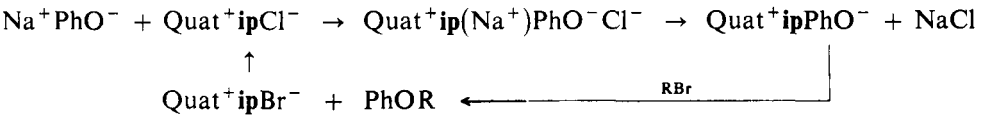


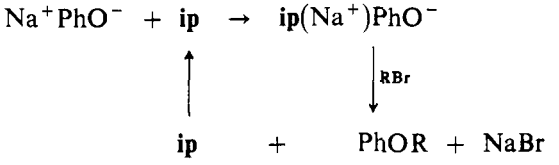
FIG. 1

Correlation between the specific rate constant k'_s of the testing reaction and the number of oxyethylene units in polymer analogues of oligo(oxyethylene)s as activators (denoted with numbers). Polymer carrier: *1* poly(styrene-*co*-divinylbenzene); *2* catenapoly[bis(2,2,3,3-tetrafluoropropoxy)-λ^5-phosphazene]

effect under consideration is not the true cause of the increased activation efficiency of the unimmobilized ammonium salt *X*. The several times higher number of oxyethylene units in the oligomeric segment of the polymeric activator of the given type (*XII*) results in a roughly proportional increase in efficiency at a high polymer effect, $E = 2{\cdot}41$. This proves that oxyethylene segments are a significant carrier of activation. The lower relative efficiency value, $(k_s')_{XII}/(k_s')_{VIII} = 5{\cdot}8$, may suggest a relative decrease in the cooperative effect of tetraalkylammonium groups. The fact that these groups play only a cooperative role in the structure of the polymeric activator is confirmed by the observed drastic drop in efficiency after binding of the activation efficient benzyltriethylammonium chloride (*XIII*) on the polymer carrier (cf. *XIV*, $E = 0{\cdot}03$). Thus, the cooperation effect most probably consists in that after complexation of the cation by a system of oxyethylene groups a precipitation decomplexation of the cation may already take place (its exclusion from an active role in the form of an insoluble halide) prior to the substitution reaction (reaction of the activated anion with the substrate),



while in the activation with the ionophoric polymeric activator without tetraalkylammonium groups in the activator's structure decomplexation of the cation sets in only by the substitution reaction,



Here, for steric reasons Quat$^+$**ip**PhO$^-$ (including the contribution of autocomplexation) is a less close ionic pair than **ip**(Na$^+$)PhO$^-$, and both these pairs are still less close than the pair Na$^+$PhO$^-$ (the essence of activation).

In the binding of oligo(oxyethylene) onto catenapoly(dichloro-λ^5-phosphazene) as the precursor of the carrier, catenapoly[bis(2,2,3,3-tetrafluoropropoxy)-λ^5--phosphazene] crosslinked polymers (*XV*–*XXIII*) are formed only when this modification reaction takes place. Their activation efficiency increases in the testing nucleophilic substitution reaction with the number of oxyethylene constitutional units, with the largest increase occurring with the fifth group (Fig. 1). In the case of tri- and tetra(oxyethylene) polymer analogue (*XV*–*XVIII*) the efficiency is independent of the type of the oligomeric side chains, i.e. of the chains being predominantly loose pendent branches (podand structure), or intra- or intermolecular

bridges. The immobilization effect is very unfavourable ($E = 0{\cdot}1$). The content of phosphacrown ether rings is obviously very low and the other oligomeric chains are too short to be complex-forming, and thus, activating. On the contrary, in the case of polymer analogues of penta- and hepta(oxyethylene) (*XIX*–*XXIII*) both the efficiency and immobilization effect are distinctly dependent on the structure of the activator and are higher if the content of oligo(oxyethylene) bridges or rings predominates over the content of loose pendent branches. Since the hydroxyl group is the end group just of these branches, the reaction rate in the given system and the efficiency of the activator increase with decreasing concentration of hydroxyl groups, i.e. with hydrophilicity of the activator (Fig. 2). Such relation is not global, however, as may be demonstrated on activators which bring active and hydroxyl groups into the system in amounts which do not correspond to each other. These activators are polyalcohols modified by the addition of alkyl vinyl sulfoxide. Poly(vinyl alcohol) by itself accelerates the substitution reaction only very weakly[14]. In applications of modified poly(vinyl alcohol) with a specific amount of hydroxyl groups, $(c_o)_{OH}$, 19·91 mmol g^{-1} (*XXIV*) and 8·33 mmol g^{-1} (*XXV*), when the concentrations of hydroxyl groups, c_{OH}, in the system differ by an order of magnitude, the efficiency of the corresponding polymeric activators in the system is approximately the same. On the contrary, in applications of the modified crosslinked *alt*-copolymer of styrene with 2-butene-1,4-diol (*XXVI*) and of the modified crosslinked copolymer styrene–allyl alcohol (*XXVII*), when c_{OH} in the system are roughly comparable, the efficiency of the corresponding polymeric activators differed by an order of magnitude.

Activation of the substitution reaction under investigation, i.e. activation of the anion of the agent by polymer analogues of linear oligo(oxyethylene)s consists in the complexation of the cation of the corresponding agent, similar to the complexation with ionophores. If the activator is a polymer network with sufficiently long

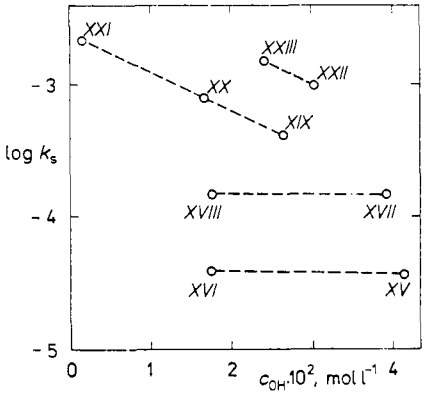


FIG. 2

Correlation between the specific rate constant (log k_s) of the testing reaction and the concentration of hydroxyl groups in the system in the presence of polyphosphazene analogues of tri(oxyethylene) *XV*, *XVI*, tetra(oxyethylene) *XVII*, *XVIII*, penta(oxyethylene) *XIX*–*XXI*, and hepta(oxyethylene) *XXII*, *XXIII*

oligo(oxyethylene) bridges between binding sites of the polymer carrier, the cation is complex-bonded in cavities of the network which imitate cavities of the crown ethers. Such activator shows the polymer effect ($E \gtrsim 1$). On the contrary, even though in the case of the podand structure of the activator loosely pendent oligomeric chains satisfy by their length the condition of loop formation which is necessary for the complexation of the cation similar to the transannular encapsulation in the true ionophore, the immobilization effect is unfavourable ($E < 1$). Hence, it can be seen that also in the homogeneous phase several molecules of soluble oligo(oxyethylene) participate in the complexation of the cation. No such cooperation is feasible in the application of a polymer analogue with locally fixed pendent branches. The same conclusions are reached by testing sulfoxides which activate the anion by forming a solvation shell around the cation of the nucleophilic agent. In the presence of dimethyl sulfoxide (*XXVIII*) at a concentration commensurate with that of the nucleophilic agent the reaction proceeds faster by almost two orders of magnitude than the uncatalyzed reaction. The polymer analogue of dimethyl sulfoxide having the strucure of a polymer network (*XXIX*) has the same efficiency as the unimmobilized compound ($E \approx 1$). The corresponding polymer analogues of dimethyl sulfoxide (*XXX*) and dimethyl sulfone (*XXXI*) are less active. The efficiency of polymeric activators with monotopically bound sulfoxides (*XXXII*–*XXXVI*) within a wide range of the degree of substitution of the polymer is lower by an order of magnitude; thus, the immobilization effect is very unfavourable ($E \leqq 0{\cdot}1$). Their efficiency increases slightly with the number of sulfinyl groups, but the contribution of each subsequent sulfinyl group in the linear sequence is always small ($\Delta k_s \sim 3\,l^2\,mol^{-1}\,.\,s^{-1}$). Although the activation efficiency of bis(methylsulfinyl)methane (*XXXVII*) is several times higher than that of dimethyl sulfoxide, binding to the polymer carrier through the central carbon atom which results in a forked position of sulfinyl groups in the respective polymer analogue (*XXXVIII*) again causes a strong decrease in efficiency and an unfavourable immobilization effect ($E = 0{\cdot}23$). A similar efficiency can be observed with the polymer analogue of 1,4-thiazinane (*XXXIX*).

With respect to the postulates mentioned above the activation efficiency of the polymer analogue of a suitably large crown ether should not be weaker in the given system than that of a free (dissolved) crown ether. On the contrary, the polymer effect could be anticipated ($E > 1$), because the complexation matrix at hand in the swollen particle of the polymeric activator is in the close vicinity of the agent. This indeed is so in the case of the polymer analogue of N-(2-hydroxyethyl)aza-15-crown-5 (*XL*–*XLII*) at the optimal degree of substitution (*XLI*), compared with the model N-(2-benzyloxyethyl)aza-15-crown-5 (*XLIII*). However, the polymer analogue of 4-(phenylphosphinoyl)benzo-15-crown-5 (*XLIV*) shows an efficiency which is distinctly weaker than the compound bound to the polymer carrier (*XLV*). In the case of compounds of this type, i.e. possessing a strong ability to undergo the transannular encapsulation of the cation, the activation efficiency of the respective polymer

analogue is also strongly affected by the rate of decomplexation of the cation, which in turn depends on the possibility of transport of the substrate to the complex, and later on, of the salt and the product from the immediate vicinity of the complexation ring. In such cases the immobilization effect will obviously depend on the permeability of the small channels in the swollen particle of the polymeric activator (accessibility of the active sites), and thus on the morphological structure of the polymer matrix, on steric requirements of the active substance, on the mode of binding of the compound onto the carrier (spacer), and on the degree of substitution of the polymer matrix.

EXPERIMENTAL

The IR spectra were recorded with a Perkin–Elmer 580B. The NMR spectra (δ in ppm, J in Hz) were recorded with Jeol 100 or Bruker WP-22 apparatuses (81·026 MHz ^{31}P, 200 MHz ^{1}H), GC analyses were carried out in a CHROM 5 apparatus (Laboratory Instruments, Prague; column 0·3 × 250 cm, SP 2100 (5%) in Inerton AW-DMCS, carrier gas N_2, FID).

Chemicals

Poly(oxyethylene), commercial product PEG 300 (Fluka). α-(3-Dimethylamino)propyl-ω-(dimethylaminomethyl)oligo(oxyethylene)[17], amount of basic groups 0·78 mol kg^{-1}. Chloromethylated poly(styrene-*co*-divinylbenzene) (98 : 1 mole %), 1·34 mmol Cl/g (r.s. 15%, Bio-Rad), chloromethylated poly(styrene-*co*-divinylbenzene) (98 : 2 mole %), 2·70 mmol Cl/g (r.s. 33%, Fluka) and chloromethylated poly(styrene-*co*-divinylbenzene) (98 : 2 mole %), 5·00 mmol Cl/g (r.s. 69%)[18] had grain size 200–400 μm. Benzyltriethylammonium chloride and maleic anhydride were purum grade, >98% (Fluka). Styrene (99·7%), divinylbenzene (56·7%) and allyl alcohol (purum, Fluka) were distilled prior to use. Polymerization initiators, 2,2′-azobis(isobutyronitrile), purum, >98% (Fluka), and dibenzoyl peroxide (Fluka) were recrystallized before use. Dimethyl sulfoxide was purum grade (Lachema, Brno), freshly distilled (over calcium hydride) before use. Alkyl vinyl sulfoxides wre prepared from alkyl 2-chloroethyl sulfoxides[14]. Methyl methylsulfinylmethyl sulfoxide, purum, 99% (Fluka), 1,4-thiazinane, purum, 98% (Fluka), and benzyl bromide (Lachema) were used as received. N-(2-hydroxyethyl)aza-15-crown-5 was an earlier preparation[15]. 1-Bromooctane (Fluka) was not specially purified and was distilled before use. Sodium phenoxide was prepared by reacting phenols with an equimolar amount of sodium ethoxide (or sodium methoxide) in ethanol and the raw product was recrystallized from ethanol (or a mixture hexane–benzene, 5 : 1 by vol.). Sodium hydride, a suspension in mineral oil (80%). The solvents were repurified before use by employing the usual procedures, toluene, tetrahydrofuran, and 1,4-dioxane were dried by distillation with sodium in a nitrogen atmosphere, N,N-dimethylformamide was dried over a molecular sieve 3A.

Preparation of Activators

Oligo(oxyethylene)s *I*–*III* were obtained by the fractionation of PEG 300 and dried in THF (1 mol l^{-1}) before use over a molecular sieve 3A. Preparations of a number of polymeric activators have been described in earlier communications: *IV*–*VII* (ref.[11]), *VIII*–*XI*, *XXI* (ref.[12]), *XIV* (ref.[13]), *XV*–*XX*, *XXII*, *XXIII* (ref.[19]), *XXIV*, *XXV* (ref.[14]), *XXIX*–*XXXI* (ref.[7]), *XXXII*,

XXXIV (ref.[18]), *XL—XLII* (ref.[15]). By employing procedures reported in an earlier communication[18], polymeric activators *XXXIII*, *XXXV*, and *XXXVI* were prepared in a similar way. Crown ether *XLV* (ref.[20]) was prepared in the Institute of Organic Chemistry of the Academy of Sciences of the Ukrainian S.S.R., Kiev.

Polymeric activator XII. To a suspension of 57·5 mg (0·155 mmol) of chloromethylated poly(styrene-*co*-divinylbenzene) (98 : 2 mole %) (2·70 mmol Cl/g) in 0·5 ml toluene, 0·93 ml water, and 410 mg α-(3-dimethylamino)propyl-ω-(dimethylaminomethyl)oligo(oxyethylene) (0·32 mmol basic groups) was added after the polymer had been swollen, and the mixture was heated at 60°C for 250 h under nitrogen. The insoluble polymer was separated, washed in methanol (3 × 150 ml), extracted (Soxhlet) with THF for 16 h, and dried (45°C, 23 Pa, 24 h). Yield 166 mg. Analysis: 63·28% C, 8·56% H, 2·82% Cl, 0·88% N. The contents of both chlorine and nitrogen correspond to the structure of a polymer with the fraction of constitutional units having bilaterally bound oligo(oxyethylene) 23·45 mole % (quaternization 71·06% theor.).

Polymeric activator XXVI. In 100 ml toluene, 3·27 g (33 mmol) of maleic anhydride, 6·8 mg 2,2′-azobis(isobutyronitrile) and a mixture of 3·41 g (32·7 mmol) styrene with 154 mg (0·66 mmol) divinylbenzene were gradually dissolved with stirring. The solution was heated to 55°C in a nitrogen atmosphere in order to start polymerization; the temperature of the reacting mixture was maintained at 80°C. One hour after turbidity had appeared the thin suspension was cooled, the product separated by filtration was extracted twice with 100 ml toluene (3 and 2 h), and dried in vacuo. Yield 6·76 g (100%) poly[(styrene-*co*-divinylbenzene)-*alt*-(maleic anhydride)] (49 : 1 : 50 mole %), specific amount of 2,5-dioxotetrahydrofuran-3,4-diyl constitutional units 4·93 mmol . $.g^{-1}$.

A mixture of 0·61 g of the copolymer (3 mmol constitutional anhydride units), 0·50 g (13·2 mmol) $LiAlH_4$, and 15 ml dry THF was heated with stirring at 60°C in a nitrogen atmosphere for 144 h, and unreacted $LiAlH_4$ was deactivated by adding (dropwise) 10 ml water and 5 ml 2M-H_2SO_4. The polymer was removed by filtration and washed gradually with 0·25M-H_2SO_4 (20 ml), water (100 ml), methanol (50 ml), ethyl acetate (50 ml), and chloroform (50 ml), and dried 48 h at room temperature and 133 Pa. Yield 0·54 g poly[(styrene-*co*-divinylbenzene)-*alt*-(2-butene-1,4-diol)] (49 : 1 : 50 mole %). IR spectrum (KBr disc): 3 600, 1 600, 1 100 cm^{-1} (insignificant absorption at 1 720 cm^{-1} corresponding to the insignificant amount of COOH). Analysis: 72·96% C, 7·85% H.

To a mixture of 0·2 g of the polymer carrier and 4 ml of dry DMSO, a solution of 64 mg (0·57 mmol) of sodium tert-butoxide in 1·5 ml of dry DMSO was added to the swollen polymer, and after 15 min 204·5 mg (2·27 mmol) methyl vinyl sulfoxide was also added. The reaction mixture was maintained with mild stirring at 75°C for 115 h. The polymer was extracted with 1,4-dioxane and ethanol (column with a glass filter) and dried at room temperature and a pressure of 133 Pa. In the IR spectrum (KBr disc) a new absorption band was recorded at 1 020 cm^{-1} (SO). According to an analytical determination of sulfur (2·30%), the addition resulted in a 3·70 mole % fraction of 1,2-bis[2-(methylsulfinyl)ethoxymethyl]ethylene constitutional units in the polymeric activator (7·40 theor.).

Polymeric activator XXVII. A homogeneous mixture of 3·75 g (36 mmol) styrene, 0·92 (4 mmol) divinylbenzene, 11·61 g (200 mmol) allyl alcohol, and 179 mg dibenzoyl peroxide was divided into ampoules so that each ampoule (10 cm^3) contained 4·5 ml. The mixture was bubbled through with nitrogen, the ampoules were sealed and heated in a bath to 150°C for 30 h. On cooling, the joined reaction mixtures were poured into ethanol (100 ml), the precipitated polymer was washed with ethanol and left to stand in it overnight. The filtered product was dried in vacuo at 50°C. Yield 2·44 g (15%). According to the analysis (found 89·04% C, 7·90% H), the product

was attributed the structure of poly(styrene-*co*-divinylbenzene-*co*-allyl alcohol) (73·2 : 8·1 : : 18·7 mole %).

After the polymer had swollen, 1 ml of a solution of 10 mg (0·089 mmol) potassium tert-butoxide in dry DMF was added to a mixture of 50 mg polymer carrier, and after 10 min 300 mg (2·88 mmol) ethyl vinyl sulfoxide was added. The reaction mixture was maintained 144 h at 75°C with mild stirring. The polymer was extracted with DMF and methanol and dried in vacuo at room temperature. The IR spectrum (KBr disc) contained a band of the SO group at 1 020 cm^{-1}. According to the analytical determination of sulfur (0·51%), addition resulted in the fraction 1·58 mole % of 1-[2-(ethylsulfinyl)ethoxymethyl]ethylene constitutional units in the polymeric activator.

Bis(methylsulfinyl)methane (XXXVII). To a mixture of 8·11 g (65·4 mmol) methyl methylthiomethyl sulfoxide and 80 ml glacial acetic acid cooled in a bath with ice, 7·4 ml of 30% hydrogen peroxide was added, and the reaction mixture was stirred at room temperature 8 h, then diluted with 700 ml dichloromethane, neutralized with solid potassium carbonate, and filtered. The solution was dried (Na_2SO_4), the solvent was evaporated, and the raw product was purified in a silica gel column (mixture ethyl acetate–methanol 9 : 1 to 1 : 1 as eluent). Yield 4·45 g (48·6%). IR spectrum (dichloromethane): 2 960, 2 600, 1 750, 1 710, 1 390, 1 280, 1 230, 1 050, 940 cm^{-1}. For $C_3H_8O_2S_2$ (140·2) calculated: 25·70% C, 5·75% H, 45·75% S; found: 25·52% C, 5·69% H, 45·61% S.

Polymeric activator XXXVIII. To a mixture of 2 g (2·68 mmol) chloromethylated poly(styrene-*co*-divinylbenzene) (99 : 1 mole %) (1·34 mmol Cl/g) and 10 ml dry THF, a solution of 589 mg (4·2 mmol) bis(methylsulfinyl)methane in 50 ml dry THF and 160 mg sodium hydride (oil suspension) was added, the mixture was stirred at room temperature 24 h and then heated under reflux ($CaCl_2$ closure). After that, the mixture was cooled, 20 ml of a THF–H_2O (1 : 1 by vol.) mixture was added, the polymer was removed by filtration, washed gradually (50 ml) with methanol, dichloromethane, diethyl ether, and dried (50°C/27 Pa, 24 h). According to the analytical determination of sulfur (2·94%), a 5·37 mole % fraction of 1-{4-[2,2-bis(methylsulfinyl)-ethyl]phenyl}ethylene constitutional units in the polymeric activator was reached (35·87% theor.).

Polymeric activator XXXIX. To a mixture of 0·5 g (0·67 mmol) chloromethylated poly(styrene-*co*-divinylbenzene) (99 : 1 mole %) (1·34 mmol Cl/g) and 15 ml dry THF, 170 mg (1·61 mmol) 1,4-thiazinane and 80 mg sodium hydride (oil suspension) was added, and the mixture was maintained under reflux ($CaCl_2$ closure) 42 h. After that it was cooled, 10 ml water was added, the polymer was removed by filtration, washed gradually (25 ml) with water, methanol, dichloromethane, diethyl ether, methanol, dichloromethane, and diethyl ether, and dried at room temperature and pressure 27 Pa (24 h). According to the analytical determination of nitrogen (1·24%), a fraction of 10·51 mole % of 1-{4-[(1,4-thiazine-4-yl)methyl]phenyl}ethylene constitutional units in the polymeric activator was reached (70·07% theor.).

N-[2-(*Benzyloxy*)*ethyl*]*aza*-15-*crown*-5 (XLIII). To a mixture of 90 mg sodium hydride (oil suspension) and 10 ml dry THF, a solution of N-(2-hydroxyethyl)aza-15-crown-5 was added, the mixture was diluted with dry THF to 30 ml, and 393 mg (2·3 mmol) benzyl bromide was added dropwise with stirring. The reaction mixture was stirred at room temperature 3 h, heated under reflux ($CaCl_2$ closure) for 2 h, cooled, and diluted with 30 ml water. The product was extracted with chloroform (3 × 20 ml), the chloroform solution was dried ($MgSO_4$) and filtered, and the solvent was distilled off at reduced pressure. Yield 0·73 g (91%). ^1H NMR spectrum (Jeol, deuteriochloroform, TMS): 7·31 m, 5 H (C_6H_5); 4·51 s, 2 H ($C_6H_5CH_2$); 2·85 m, 3·64 m.

Polymeric activator XLIV. To a solution of 1·00 g (2·55 mmol) 4-(phenylphosphinoyl)-1,2-

-benzo-15-crown-5 (*XLV*) in 4 ml dry 1,4-dioxane, 109 mg (2·5 mmol) sodium hydride (oil suspension, 55%) was added, the mixture was stirred at room temperature 2 h, 270 mg (1·35 mmol) chloromethylated poly(styrene-*co*-divinylbenzene) (98 : 2 mole %) (5·00 mmol Cl/g) was added, the reaction mixture was heated and kept in a closed vessel with mild stirring (magnetic) at 95—100°C for 192 h. Then it was cooled, the polymer was removed by filtration, washed gradually (30 ml) with THF, ethanol, water, acetone, chloroform, hexane, and dried at 90°C/133 Pa for 48 h. Yield 0·41 g. IR spectrum (KBr disc): 3 400, 3 050, 3 020, 2 920, 2 860, 1 590, 1 510, 1 450, 1 440, 1 260, 1 230, 1 130, 810 cm^{1-}. According to the analysis, a 16·35 mole % fraction of 1-{4-[(2,3,5,6,8,9,11,12-octahydro-1,4,7,10,13-benzopentaoxacyclopentadecin-15-yl-phenylphosphoryl)methyl]phenyl}ethylene constitutional units in the polymeric activator was reached (23·70% theor.).

4-(*Phenylphosphinoyl*)*benzo*-15-*crown*-5 (XLV). To a mixture of 5·21 g (15 mmol) 4-bromobenzo-15-crown-5 and 0·30 g (1·3 mmol) anhydrous $NiBr_2$, 4·15 g (18 mmol) diisopropyl phenylphosphonite was added dropwise with stirring at 185—190°C in dry argon within 15 min. The reaction mixture was maintained at this temperature for 15—20 min, cooled, dissolved in 100 ml benzene, and washed with a 2% aqueous ammonia solution (25 ml three times). Benzene was removed by evaporation, the residue was recrystallized from a heptane–benzene mixture (6 : 1 by vol.), and 5·1 g (75%) 4-[phenyl(isopropoxy)phosphinoyl]benzo-15-crown-5 was obtained, m.p. 108—110°C. ^{1}H NMR spectrum (Bruker, deuteriochloroform, HMDS): 1·25 d, 3 H (^3J(H, H) = 6); 1·28 d, 3 H (^3J(H, H) = 6); 3·60—4·13 m, 16 H; 4·49—4·66 m, 1 H; 6·67 to 7·78 m, 8 H. ^{31}P NMR spectrum (Bruker, hexadeuterioacetone, 85% H_3PO_4): 28·78. For $C_{23}H_{31}O_7P$ (450·5) calculated: 61·32% C, 6·94% H, 6·88 P; found: 60·85% C, 6·93% H, 7·08% P.

To a suspension of 1·52 g (40 mmol) $LiAlH_4$ in 40 ml dry THF, 4·32 g (40 mmol) chloro(trimethyl)silane was added at −80°C with stirring in dry argon; on reaching room temperature, the stirring continued for 24 h. After that, the mixture was again cooled to −80°C, and 13·5 g (30 mmol) 4-[phenyl(isopropoxy)phosphinoyl]benzo-15-crown-5 in 70 ml THF was added with stirring, the temperature of the reaction mixture was raised to room temperature within three hours, and the mixture was maintained at this temperature for another 12 h. Then 1·52 ml water, 1·52 ml 15% NaOH, and 3 ml water were gradually added to the mixture, the precipitate was removed by filtration, the filtrate was evaporated, and the residue was dissolved in 100 ml diethyl ether. The precipitate formed after 12 h was removed by filtration and recrystallized from isopropyl alcohol. Yield 6·8 g (58%) of *XLV*, m.p. 98—101°C. ^{1}H NMR spectrum (Bruker, hexadeuterioacetone, HMDS): 3·50—4·00 m, 16 H; 6·86—8·00 m, 8 H; 7·91 d, 1 H (^1J(H, P) = = 479). ^{31}P NMR spectrum (Bruker, deuteriochloroform, 85% H_3PO_4): 17·5 d (^1J(P, H) = = 476). For $C_{20}H_{25}O_6P$ (392·4) calculated: 61·22% C, 6·42% H, 7·89% P; found: 59·69% C, 39% H, 8·20% P.

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REFERENCES

1. Makosza M., Serafinova B.: Rocz. Chem. *39*, 1223 (1965).
2. Brandström A., Gustavii K.: Acta Chem. Scand. *23*, 1215 (1969).
3. Starks C. M.: J. Am. Chem. Soc. *93*, 195 (1971).
4. Tomoi M., Ford W. T.: J. Am. Chem. Soc. *103*, 3821 (1981).

5. Regen S. L., Mehrotta A., Singh A.: J. Org. Chem. *46*, 2182 (1982).
6. Nee G., Seyden-Penne J.: Tetrahedron *38*, 3485 (1982).
7. Janout V., Čefelín P.: Collect. Czech. Chem. Commun. *47*, 1818 (1982).
8. Kondo S., Ohta K., Tsuda K.: Makromol. Chem., Rapid Commun. *4*, 145 (1983).
9. Kimura Y., Regen S. L.: J. Org. Chem. *48*, 195 (1983).
10. Cinquini M., Colonna S., Molinari H., Montanari F., Tundo P.: J. Chem. Soc., Chem. Commun. *1976*, 394.
11. Janout V., Čefelín P., Tur D. R., Vinogradova S. V.: Polym. Bull. (Berlin) *15*, 303 (1986).
12. Valter B., Masař B., Janout V., Hrudková H., Čefelín P., Tur D. R., Vinogradova S. V.: Makromol. Chem. *192*, 1549 (1991).
13. Janout V., Masař B., Hrudková H., Čefelín P.: J. Chem. Soc., Chem. Commun. *1989*, 213.
14. Hrudková H., Čefelín P., Janout V.: Collect. Czech. Chem. Commun. *52*, 2204 (1987).
15. Valter B., Janout V., Hrudková H., Čefelín P., Lukyanenko N. G., Bassok S. S., Kulygina E. Yu.: Polym. Bull. (Berlin) *22*, 261 (1989).
16. Itsuno S., Moue I., Ito K.: Polym. Bull. (Berlin) *21*, 365 (1989).
17. Masař B., Janout V., Čefelín P.: Makromol. Chem. *189*, 2330 (1988).
18. Janout V., Hrudková H., Čefelín P.: Collect. Czech. Chem. Commun. *49*, 1563 (1984).
19. Janout V., Čefelín P., Provotorova N. P., Tur D. R., Vinogradova S. V.: J. Polym. Sci., Polym. Chem. Ed. *25*, 3489 (1987).
20. Markovskii L. N., Kalchenko V. I., Parkhomenko N. A., Atamas L. I., Aleksyuk O. A.: *Abstracts of the 15th Int. Symp. on Macrocyclic Chemistry, Odessa 1990*, p. 53.

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