Alkyl Substituted Aza-macrobicyclic Polyethers: Highly Efficient Catalysts in Two-phase Reactions

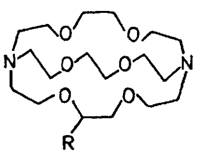
By Mauro Cinquini and Fernando Montanari*
(*Centro C.N.R. e Istituto di Chimica Industriale dell'Università, Via C. Golgi* 19, *Milano* 20133, *Italy*)
and Pietro Tundo
(*Istituto di Chimica Organica dell'Università, Via Bidone* 36, *Torino* 10125, *Italy*)

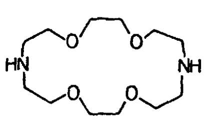
Summary Alkyl substituted aza-macrobicyclic polyethers are highly efficient catalysts in anion promoted two-phase reactions, such as nucleophilic substitutions, *C*-alkylations, cyclopropanations, and borohydride reductions.

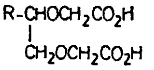
Large organic cations derived from elements of groups V or VI are normally used as catalysts in phase-transfer reactions.[1] A similar catalytic activity has been found for crown ethers,[2,3] especially for those having a high organophilic character.[2] Other factors being equal, the reactivity of the anion must increase with the distance from the cation within the ion pair.

Aza-macrobicyclic polyethers, which are able completely to surround the cation, are powerful anionic activators.[4] We have found that these systems are highly efficient catalysts in aqueous, organic two-phase reactions, provided that alkyl chains confer a sufficient organophilicity to the molecule.

Compounds (Ia) and (Ib) were prepared by condensation of diaza-18-crown-6 (II) with the chlorides of acids (IIIa) and (IIIb), respectively, followed by reduction with diborane of the resulting cyclic diamide.†


(Ia) $R = n\text{-}C_{14}H_{29}$
(Ib) $R = n\text{-}C_{11}H_{23}$
(Ic) $R = H$


(II)

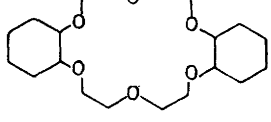


$$\begin{array}{l}R\text{-}CHOCH_2CO_2H\\ \quad|\\ \quad CH_2OCH_2CO_2H\end{array}$$

(IIIa) $R = n\text{-}C_{14}H_{29}$
(IIIb) $R = n\text{-}C_{11}H_{23}$

$n\text{-}C_{16}H_{33}\overset{+}{P}Bu^n_3\ Br^-$

(IV)


(V)

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† Compounds (Ia) and (Ib) were isolated as $NaBF_4$ complexes, m.p. 91·5—92·5 °C and 94·5—95·5 °C, respectively, and used as such. Elemental analyses, m.s., i.r. and ^1H n.m.r. data for (Ia,b) and (IIIa,b) are in agreement with the assigned structures.

TABLE

Substrate[a]	Reagent	Catalyst[g]	T/°C	Time/h	Yield/%[j]	Product[k]
n-$C_8H_{17}Br$	KI[b]	(Ia)	60	0·2	100	n-$C_8H_{17}I$
"	"	(Ib)	60	0·5	92	"
"	"	(Ic)	60	14	90	"
"	"	(IV)	60	1	93	"
"	"	(V)[h]	80	3	100	"
n-$C_8H_{17}Cl$	"	(Ia)	80	5	77	"
"	"	(Ib)	80	4	85	"
"	"	(IV)	80	24	80	"
"	KCN[b]	(Ia)	80	5	93	n-$C_8H_{17}CN$
"	"	(IV)	80	5	94	"
n-$C_8H_{17}OSO_2Me$	KF[b]	(Ib)[i]	120	4	85	n-$C_8H_{17}F$
"	"	(IV)[i]	120	2	94	"
n-$C_8H_{17}Br$	PhSNa[c]	(Ia)	20	0·1	100	n-$C_8H_{17}SPh$
"	"	(IV)	20	0·1	100	"
n-$C_6H_{13}CH(Br)Me$	KI[b]	(Ia)	80	3	86	n-$C_6H_{13}CH(I)Me$
"	"	(IV)	80	6	89	"
$PhCH_2COMe$	Bu^{n}Br[d]	(Ia)	20	0·75	94	PhCH(Bu^n)COMe
"	"	(IV)	20	2·5	90	"
"	"	(V)[h]	80	1·5	93	"
n-$C_6H_{13}COMe$	$NaBH_4$[e]	(Ia)	20	4	97	n-$C_6H_{13}CH(OH)Me$
"	"	(IV)	20	6	78	"
"	"	(V)[h]	80	2·5	92	"
$PhCH{=}CH_2$	NaOH[f], $CHCl_3$	(Ia)	20	24	60	$PhCHCCl_2CH_2$

[a] Benzene was used as solvent in the borohydride reduction, otherwise no solvent was used for the substrate; the reactions were carried out with a saturated aqueous solution of the reagent. [b] 5 Mol. equiv. [c] 1 Mol. equiv. [d] 1·2 Mol. equiv. in 50% aq. NaOH. [e] 1·5 Mol. equiv. [f] 2·5 Mol. equiv. [g] 0·05 Mol. equiv. [h] From ref. 2. [i] 0·1 Mol. equiv. [j] By g.l.c. analysis. [k] The products were characterized by g.l.c. retention time and by comparison (i.r. and ^{1}H n.m.r. spectra) with authentic samples.

The catalytic activity of (Ia) and (Ib) has been tested for some classical nucleophilic substitutions, as well as for alkylation at carbon, cyclopropanation, and borohydride reduction, and compared with that of hexadecyltributylphosphonium bromide (IV)[1] and of perhydrodibenzo-18-crown-6 (V)[2] (see Table). The catalytic activities of (Ia) and (Ib) are of the same order of magnitude, and in most of the cases examined are higher than that of the phosphonium salt (IV) and much higher than that of the crown ether (V).

Catalytic activity depends, however, on the nature of the reaction; being particularly high in Br–I and Cl–I substitutions, in the reduction with BH_4^-, and in alkylation, and comparable to that of the phosphonium salt (IV) in Cl–CN and OSO_2Me–F substitutions. Cyclopropanation is much slower than the other reactions examined and seems to be less sensitive to the nature of the catalyst.‡

The simple aza-macrobicyclic polyether (Ic) still shows some catalytic activity, which is much lower than that of (Ia) and (Ib), apparently because of its great solubility in water coupled with a low solubility in organic solvents.

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‡ In the case of crown ethers it was found[5] that cyclopropanation is probably favoured by the presence of aromatic rings in the catalyst.

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