THE EFFECT OF CROWN ETHER ON STERIC HINDRANCE TO BASE APPROACH IN BIMOLECULAR ELIMINATION: EVIDENCE AGAINST CLUMP AGGREGATE MODEL OF ION-PAIRED ALKOXIDE BASE*

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Received April 3rd, 1980

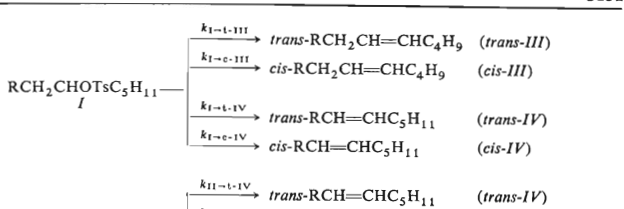
The effect of 18-crown-6-ether upon geometrical orientation and rates was investigated in tert-C_4H_9OK–tert-C_4H_9OH promoted *anti*-elimination from two homologous series of tosylates, $RCH_2CHOTsC_5H_{11}$ and $RCHOTsCH_2C_5H_{11}$ (R = H, CH_3, C_2H_5, n-C_3H_5, iso-C_3H_7, tert-C_4H_9). Steric requirements of the *cis*- and *trans*-stereoselective base species operating in the reaction in the absence and in the presence of the crown ether, respectively, have been assessed. An unambiguous distinction has been made between two pending models of the *cis*-stereoselective (ion-paired) base.

Crown ethers[1,2] (crowns) fill effectively coordination sites of alkali metal cations and convert contact ion pair monomers and oligomers ("associated"[3] species) into crown-complexed ions[2], ion pairs[4] or ion triplets[5,6] ("dissociated"[3] species). It makes from the crowns a very convenient tool for elucidation of base association effects in bimolecular elimination: as we already pointed out at earlier occasions[7–9], evidence on the operation of the associated and dissociated species of participating alkoxide base can be drawn simply from a comparison of the results obtained in the elimination performed in the absence and in the presence of an appropriate crown, respectively.

By this procedure, it has been demonstrated that both the associated and the dissociated species of tert-C_4H_9OK can participate in *anti*-elimination from open-chain tosylates[7,10] and halides[9,10,11] and exhibit divergent stereoselectivities, the former species preferring *cis*- whereas the latter *trans*-olefin formation.

In order to assess steric requirements of the two stereodivergent base species, we have now investigated the effect of 18-crown-6-ether upon orientation and rates in tert-C_4H_9OH–tert-C_4H_9OH promoted *anti*-elimination from two homologous series of tosylates, *I* and *II* (Scheme 1). The controversial[3,9–16] problem of *cis*-selectivity of the associated alkoxide base in *anti*-elimination has been thus resolved.

Part XLI in the series Elimination Reactions; Part XL: This Journal *45*, 2171 (1980).



R = H, CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, tert-C_4H_9

SCHEME 1

EXPERIMENTAL

Tert-butanol was dried by repeated distillation with potassium; the solvent contained less than 0·01% water (K. Fischer). The solution of potassium tert-butoxide was prepared by dissolving the clean potassium metal in tert-butanol and the concentration was determined titrimetrically. 18-Crown-6-ether[17] (31·7 g; 0·12 mol) was added to 500 ml of the 0·23M tert-C_4H_9OK–tert-C_4H_9OH solution and the resulting reagent was stored under nitrogen in a closed flask. The crown ether was dried *in vacuo* (13·3 Pa; 20°C) before use.

Kinetic procedure: About 1·5 mmol of the tosylate was weighted into 25 ml flask and treated with the stock solution of the crown-complexed base (20 ml). The flask equipped with a serum rubber cap was introduced into a thermostated bath kept at 25·4°C, aliquots (1·4 ml) were withdrawn at appropriate time intervals by a syringe and quenched by an immediate treatment with water (20 ml). Concentration of base in the samples was followed titrimetrically using 0·05M solution of hydrochloric acid.

Determination of product composition: An aliquot of the reaction mixture (1·4 ml) withdrawn at the end of the reaction (10 half-times) was transferred into the 50 ml volumetric flask containing saturated aqueous sodium chloride (25 ml), pentane (1 ml) and a known amount of internal standard (ethylcyclohexane). The flask was made up to mark with water, shaken and a sample of the pentane layer injected into the vapour-phase chromatograph. The product composition data from the homologous series *I* and *II* are summarized in Tables I and II, respectively.

Evaluation of the kinetic data: The rate constant of the overall reaction (E2 plus S_N2), k_2^{tot}, were evaluated from the equation $k_2^{tot} = 2{\cdot}303/t(b - a) \cdot \log [a(b - x)/b(a - x)]$,where a and b are the initial concentrations (in mol l^{-1}) of the tosylate and of the base, respectively, and x is the fraction reacted at the time t (in s). The overall rate constant of elimination, k_{E2}^{tot}, was calculated from the equation $k_{E2}^{tot} = (\%\ E2)\ k_2^{tot}/100$, where % E2 is the percentage of olefinic products in the overall reaction determined by the vapour phase chromatography. The partial rate constants of the individual olefin-isomer formation, k_{E2}^{i}, were obtained from the equation $k_{E2}^{i} = (\%\ i)\ k_{E2}^{tot}/100$, where % i is the percentage of the given isomer in the resulting olefin mixture. The rate data from the series *I* and *II* are summarized in Tables III and IV, respectively.

Control experiments: Stability of products under the reaction conditions was checked by vapour-phase chromatography. No isomerisation has taken place in course of the elimination.

Vapour-phase chromatography: The alkene mixtures were analyzed on the Carlo Erba Fractovap GT apparatus equipped with digital integrator under the conditions reported in a previous paper[18].

TABLE I

Product Composition Data from the Reaction of the Tosylates *I*, $RCH_2CHOTsC_5H_{11}$, with 0·23M Solution of the Crown-Complexed Potassium Tert-Butoxide in Tert-Butanol at 25·4°C

R	% E2[a]	$RCH_2CH=CHC_4H_9$ (*III*)		$RCH=CHC_5H_{11}$ (*IV*)	
		% *trans*	% *cis*	% *trans*	% *cis*
H	95	15·7	7·0	77·3[b]	
CH_3	95	20·2	6·9	50·7	22·2
C_2H_5	80	32·8	14·7	39·3	13·2
n-C_3H_7	80	36·0[c]	14·0[c]	36·0[c]	14·0[c]
iso-C_3H_7	80	44·1	24·0	26·5	5·4
tert-C_4H_9	85	17·8	31·3	50·2	0·7

[a] The total contents of the olefinic products as determined by the internal standard method. [b] 1-Heptene. [c] Approximate value.

TABLE II

Product Composition Data from the Reaction of the Tosylates *II*, $RCHOTsCH_2C_5H_{11}$, with 0·23M Solution of the Crown-Complexed Potassium Tert-Butoxide in Tert-Butanol at 25·4°C

R	% E2[a]	$RCH=CHC_5H_{11}$ (*IV*)		$R^1R^2C=CHC_6H_{13}$ (*V*)	
		% *trans*	% *cis*	% *trans*	% *cis*
H	6	100[b]		—	—
CH_3	90	15·8	6·9	77·3[c]	
C_2H_5	90	20·0	6·4	52·0	21·6
n-C_3H_7	80	32·1[d]	15·4[d]	39·3[d]	13·2[d]
iso-C_3H_7	90	28·5	0·8	70·7[e]	
tert-C_4H_9	80	98·2	1·8	—	—

[a] The total contents of olefinic products as determined by the internal standard method. [b] 1-Heptene. [c] 1-Octene. [d] Approximate value. [e] Trisubstituted olefin ($R^1 = R^2 = CH_3$).

TABLE III

Rate Constants of Elimination in the Reaction of the Tosylates *I*, $RCH_2CHOTsC_5H_{11}$, with 0·23M Solution of the Crown-Complexed Potassium Tert-Butoxide in Tert-Butanol at 25·4°C

R	$10^4 k_{E2}$	$RCH_2CH{=}CHC_4H_9$ (*III*)		$RCH{=}CHC_5H_{11}$ (*IV*)	
		$10^4 k_{trans}$	$10^4 k_{cis}$	$10^4 k_{trans}$	$10^4 k_{cis}$
H	122	19·1	8·5	94·4[a]	
CH_3	67	13·5	4·6	34·0	14·9
C_2H_5	33	10·8	4·8	13·0	4·4
n-C_3H_7	22	7·9	3·1	7·9	3·1
iso-C_3H_7	14	6·1	3·4	3·7	0·8
tert-C_4H_9	9	1·6	2·8	4·5	0·06

[a] The rate constant of 1-heptene formation.

TABLE IV

Rate Constants of Elimination in the Reaction of the Tosylates *II*, $RCHOTsCH_2C_5H_{11}$, with 0·23M Solution of the Crown-Complexed Potassium Tert-Butoxide in Tert-Butanol at 25·4°C

R	$10^4 k_{E2}$	$RCH{=}CHC_5H_{11}$ (*IV*)		$R^1R^2C{=}CHC_6H_{11}$ (*V*)	
		$10^4 k_{trans}$	$10^4 k_{cis}$	$10^4 k_{trans}$	$10^4 k_{cis}$
H	11	11[a]		—	—
CH_3	108	17·0	7·5	83·5[b]	
C_2H_5	58	11·6	3·7	30·2	12·5
n-C_3H_7	28	9·0	4·3	11·0	3·7
iso-C_3H_7	25	7·1	0·2	17·7[c]	
tert-C_4H_9	1·3	1·28	0·02	—	—

[a] The rate constant of 1-heptene formation. [b] The rate constant of 1-octene formation. [c] The rate constant of the trisubstituted ($R^1 = R^2 = CH_3$) olefin formation.

RESULTS AND DISCUSSION

Mechanistic assumptions: As we pointed out previously[15,16,19], interpretation of geometrical orientation and rates in tert-C_4H_9OK–tert-C_4H_9OH promoted elimination from the tosylates *I* and *II* is complicated by a competition of *anti*- and *syn*-pathways. In the reaction performed in the absence of crowns, an approximate dissection of the overall *trans*/*cis* ratios[15] as well as of the overall elimination

rates[16,19] into the corresponding *anti* and *syn* components has been already made. In the presence of equimolar amounts of 18-crown-6-ether, it is assumed that the reaction is a clean *anti*-elimination. A practically complete suppression of *syn*-elimination by the crown from the *anti-syn* competition has been demonstrated[7,8] in tert-C_4H_9OK–tert-C_4H_9OH promoted reaction of conformationally mobile tosylates, including those which are extraordinarily prone[7] to eliminate in the *syn*-fashion.

Effect of 18-*Crown-6-ether and Alkyl Substitution upon* trans/cis *Ratios in* anti-*-Elimination*

Table V compares the ratios in which *trans-* and *cis-IV* alkenes arose from the homologous tosylates *II* in the tert-C_4H_9OK–tert-C_4H_9OH promoted *anti*-elimination in the absence and in the presence of the crown. In the absence of the crown, the values of *trans-IV*/*cis-IV* ratios are always lower than unity and almost insensitive to steric variation of the substituent R. In the presence of the crown, on the other hand, the values are always higher than unity and increase sharply with branching the substituent R. Almost identical values were obtained previously[15] in the elimination performed with tert-C_4H_9OK in the dipolar solvent dimethylformamide, also renown for its cation-coordinating ability (Table V; figures in parentheses).

A qualitatively similar effect of the crown upon geometrical orientation is found in the tosylate series *I* (Table VI). The anomalously low values of *trans-III*/*cis-III* ratios obtained for the branched tosylates *I* (R = iso-C_3H_7 and R = tert-C_4H_9) in the presence of the crown and also in dimethylformamide (figures in parentheses) arise assumedly from steric interference between the substituent *R* and tosyloxy group (*cf.* "neohexyl anomaly" in ref.[15]).

TABLE V

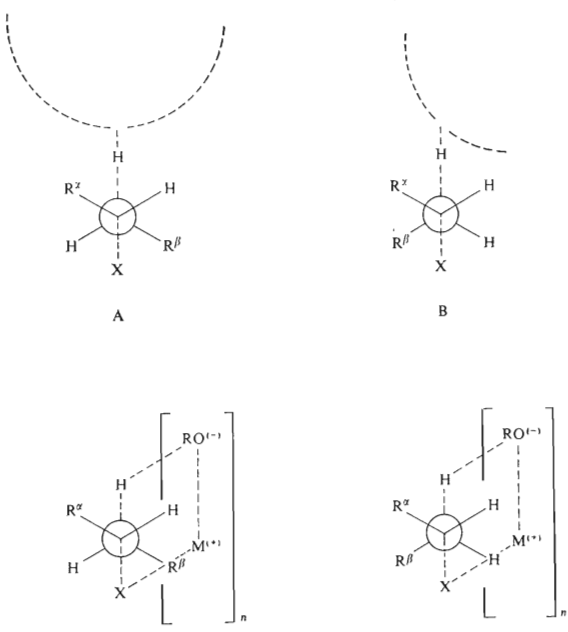
trans-IV/*cis-IV* Ratios in tert-C_4H_9OK–tert-C_4H_9OH Promoted *anti*-Elimination from Tosylates *II*: The Effect of 18-Crown-6-ether and Alkyl Substitution

R	*trans-IV*/*cis-IV* Ratios	
	Crown absent[a]	Crown present[b]
CH_3	0·38 (2·7)[c]	2·29
C_2H_5	0·42 (4·7)[c]	3·12
n-C_3H_7	0·36 (2·9)[c]	2·08
iso-C_3H_7	0·75 (24·0)[c]	35·6
tert-C_4H_9	0·90 (54·5)[c]	54·5

[a] From ref.[15]. [b] tert-C_4H_9OK/crown ratio 1 : 1. [c] Values from tert-C_4H_9OK promoted elimination in dimethylformamide; ref.[15].

Models explaining divergent stereoselectivities of the associated and disociated alkoxide species: The divergent stereoselectivities of the two alternative base species attracted a considerable attention[8-16] in the recent years. While there is a general agreement that *trans*-stereoselectivity of the dissociated species originates simply from a prevalence of eclipsing effects in the reaction, *cis*-stereoselectivity of the associated base continues to be a subject of controversial views.

According to Bartsch[3,10], the associated alkoxide base is a clump aggregate of ion pairs which has exceedingly large steric dimensions. Steric interference between the "outsized" associated base and alkyl substituents in substrate destabilizes selectively transition state leading to *trans*-alkenes; in the transition state for *cis*-alkenes it is postulated that the interference can be avoided by tilting out the base to that side where only hydrogens are placed (Scheme 2; *A* and *B*, respectively).



SCHEME 2

In a contrast, we and Schlosser suggested[12] that the associated alkoxide base can be a sterically modest ion pair monomer. Because of the propensity of metal cations for coordination, it is proposed that the ion-paired species in low polar solvents tends to a cyclic transition state (Scheme 2; *C* and *D*; $n = 1$). Such a cyclic transition state should be energetically favourable, because, as the metal counterion helps to weaken the C_α—X bond, the incipient $\overset{(+)}{M}\cdots\overset{(-)}{X}$ interaction will destabilize the tert-$\overset{(-)}{C_4H_9O}\cdots\overset{(+)}{M}$ ion pair, thus making the tert-C_4H_9O portion more effective as base. For

TABLE VI

trans-III/*cis-III* Ratios in tert-C_4H_9OK–tert-C_4H_9OH Promoted *anti*-Elimination from Tosylates *I*: The Effect of 18-Crown-6-ether and Alkyl Substitution

R	*trans-III*/*cis-III* Ratios	
	Crown absent[a]	Crown present[b]
H	0·34 (2·9)[c]	2·24
CH_3	0·44 (3·9)[c]	2·92
C_2H_5	0·36 (3·4)[c]	2·23
n-C_3H_7	0·37 (3·7)[c]	2·57
iso-C_3H_7	0·21 (2·0)[c]	1·84
tert-C_4H_9	0·22 (0·57)[c]	0·57

[a] From ref.[15]. [b] tert-C_4H_9OK/crown ratio 1 : 1. [c] Values from tert-C_4H_9OK promoted elimination in dimethylformamide; ref.[15].

TABLE VII

Ratios of Rate Constants for *cis*-Alkenes Formation in *anti*-Elimination Promoted by Associated and Dissociated Tert-butoxide Base

R^α	$\left(\frac{k^{assoc.}_{I\to cis\text{-}III}}{k^{dissoc.}_{I\to cis\text{-}III}}\right)^a$	R^α	$\left(\frac{k^{assoc.}_{II\to cis\text{-}IV}}{k^{dissoc.}_{II\to cis\text{-}IV}}\right)^a$
CH_3	0·22	CH_3	0·29
C_2H_5	0·29	C_2H_5	0·37
n-C_3H_7	0·35	n-C_3H_7	0·30
iso-C_4H_9	0·47	iso-C_3H_7	1·15
neo-C_5H_{11}	0·45	tert-C_4H_9	1·65

[a] $k^{assoc.}$: second-order rate constant for the *cis*-olefin formation from tert-C_4H_9OK–tert-C_4H_9OH promoted reaction performed at 80·7°C in the absence of crowns, taken from ref.[16]; $k^{dissoc.}$: second-order rate constant for the *cis*-olefin formation from the tert-C_4H_9OK–tert-C_4H_9OH promoted reaction performed at 25·4°C in the presence of 18-crown-6-ether.

steric reasons, however, the cyclic arrangement is easily attainable only in the transition state leading to *cis*-alkenes (*D*); in the formation of *trans*-alkenes (*C*), the cyclic arrangement is opposed by a steric interference between the ion pair and the alkyl portion of the substrate. According to Schlosser[13], linear ion pair oligomers, instead of the monomer ($n = 1$) can be also involved in the cyclic model of *cis*-stereoselective associated base (Scheme 2; *C* and *D*; $n = 2-4$).

Some other models attempting to explain *cis*-stereoselectivity of tert-C_4H_9OK base were proposed in the past two decades[14,20-22]; these, however, can be dismissed from consideration on basis of the previous[9,23,24] evidence.

Effect of 18-*Crown*-6-*ether upon Rate Pattern of* anti-*Elimination from the Homologous Series* I *and* II

There exists a fundamental difference between the clump aggregate and the cyclic model of the associated base which allows an unambiguous distinction by a com-

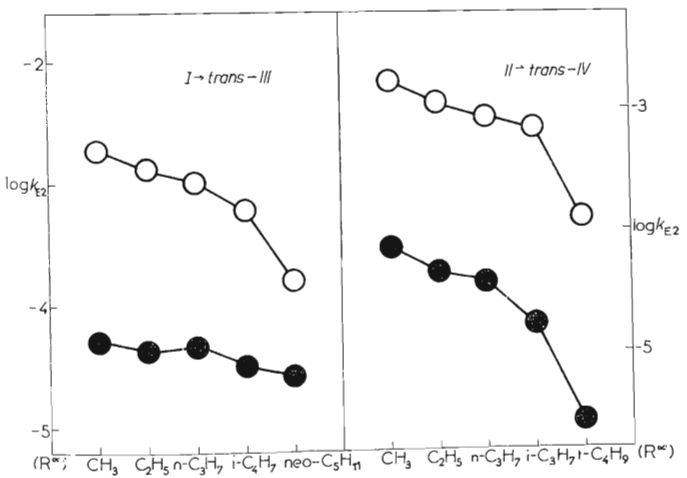


FIG. 1

Effect of the Substituent R$^{\alpha}$ upon Rates of *I* → *trans-III* and *II* → *trans-IV anti*-Elimination

Full circles: reaction with 0·43M tert-C_4H_9OK–C_4H_9OH at 80·7°C in the absence of crowns (from ref.[19]). Empty circles: reaction with 0·23M-tert-C_4H_9OK–tert-C_4H_9OH at 25·4°C in the presence of 18-crown-6-ether (1 : 1).

parison of the rate patterns of *anti*-elimination obtained from the homologous series *I* and *II* in the absence and in the presence of the crown. Specifically, it holds for the elimination pathways *I* → *trans-III* and *II* → *trans-IV*, in which R^{α} (Scheme 2) varies with the variation of the R group ($R^{\alpha} = RCH_2$ and $R^{\alpha} = R$, respectively) whereas R^{β} is a fixed group ($R^{\beta} = n\text{-}C_4H_9$ and $R^{\beta} = n\text{-}C_5H_{11}$, respectively).

In the clump aggregate model, a large difference in the size of the associated and dissociated base is postulated leading to a large difference in R^{α}–base interactions in the formation of *trans*-alkenes (Scheme 2; A). Accordingly, the decrease of rates of *I* → *trans-III* and *II* → *trans-IV* pathways on passing to bulkier substituents R^{α} which is induced[16,25] by increasing R^{α}–base interactions should be much steeper in the absence than in the presence of the crown.

In the cyclic model, on the other hand, the relative dimensions of the associated and dissociated base species are unimportant, as it concerns the R^{α}–base interactions (Scheme 2; C). The variation of elimination rates with R^{α} in the *I* → *trans-III* as well as *II* → *trans-IV* pathways should thus be more or less unaffected by the crown.

Approximate rates of tert-C_4H_9OK – tert-C_4H_9OH promoted *anti*-elimination pathways *I* → *trans-III* and *II* → *trans-IV* determined in the absence and in the presence of 18-crown-6-ether are plotted as function of R^{α} in Fig. 1.

As is immediately apparent, the variation of the elimination rates with R^{α} found in the absence and in the presence of the crown are quite similar. In *I* → *trans-III* pathway, the decrease of rates with increasing size of R^{α} is in actual fact steeper in the presence than in the absence of the crown. In this way, the rate patterns indicate that steric requirements of the associated species by no means exceed those of the dissociated base. It provides a very strong evidence against operation of the clump aggregate model of *cis*-stereoselective alkoxide base.

Previously[16], we attempted to distinguish between the two models from Scheme 2 by an analogous comparison of rate patterns obtained for tert-C_4H_9OK promoted *anti*-elimination *I* → *trans-III* and *II* → *trans-IV* in "base associating" solvent tert-butanol and in "base dissociating" solvent dimethylformamide. Since the reaction in dimethylformamide was too fast for a simple kinetic measurement, we performed a "peasant" calculation of the rates based on a simplifying assumption that the rate patterns for *I* → *cis-III* and *II* → *cis-IV* pathways, respectively induced by the associated (in tert-butanol) and by the dissociated base (in dimethylformamide) are identical.

A comparison of the actual rates determined for tert-C_4H_9OK–tert-C_4H_9OH promoted *anti*-eliminations *I* → *cis-III* and *II* → *cis-IV* in the absence and in the presence of 18-crown-6-ether reveals, however, that there is a distinct difference between the rate patterns for the associated and for the dissociated base. As Table VII shows, the values of $k^{assoc.}/k^{dissoc.}$ ratios rise gradually on passing to bulkier substituents R^{α} in both *I* → *cis-III* and *II* → *cis-IV* pathways. It indicates that rates of the reaction with the associated base are less sensitive to the variation of R^{α}. As a most simple explanation for this pattern of results it could be suggested

that eclipsing effects in the reaction with associated base are weaker than in the reaction with the dissociated base. However, this eventuality seems rather improbable because a previous analysis[9] of this problem led to exactly opposite conclusions.

As another conceivable explanation we suggest that the interaction between associated base and leaving group postulated in the cyclic model (Scheme 2; D) forces a non-linear[11,12] approach of the base to the C_β—H bond. This deviation from collinearity would decrease steric interference between the base and R^α group. Since a linear $C_\beta \cdots H \cdots \overset{(-)}{O}R$ arrangement is anticipated[11] for the dissociated base, stronger steric interactions between the base and R^α group would be expected. Therefore, as the steric requirements of R^α group become large, the *anti* → *cis* process involving associated base species is less affected than that for the dissociated base.

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Translated by the author (J. Z.).