ALKYL STRUCTURE–REACTIVITY RELATIONSHIPS IN *anti*-ELIMINATION OF OPEN-CHAIN TOSYLATES: ON STERIC HINDRANCE TO APPROACH OF ASSOCIATED AND DISSOCIATED TERT-BUTOXIDE BASE*

M.PÁNKOVÁ and J.ZÁVADA

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6

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The dependence of elimination rates on alkyl structure was investigated in *anti*-E2 reaction of two positionally-isomeric series of tosylates, $RCH_2CHOTsC_5H_{11}$ and $RCHOTsCH_2C_5H_{11}$ (R = H, CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7 and tert-C_4H_9), with the associated (in tert-butanol) and with the dissociated (in dimethylformamide) form of potassium tert-butoxide. It is shown that the threshold of alkyl-structure complexity where steric hindrance becomes apparent in the rate pattern is very high, but nonetheless determinable, in the reaction with the associated as well as with the dissociated base. A reconciliation of the current conflicting views concerning the role of base-approach hindrance in preferential formation of *cis*-olefins is proposed on these grounds

In the preceding paper[1] we investigated the relationship between alkyl structure and olefin-isomer distribution in *anti*-E2 reaction of tosylate series *I* and *II* with associated (in tert-butanol) and dissociated (in dimethylformamide) form of potassium tert-butoxide. From comparison of the outcomes obtained for the alternative base forms, steric effects induced by base association in a very wide range of alkyl structures *I* and *II* could be examined.

As a supplement, we have now investigated the relationship between alkyl structure and elimination rates in the same series *I* and *II* (Scheme 1). The rates of formation of individual *cis* and *trans*-alkenes *III* and *IV*, and *cis*- and *trans*-alkenes *IV* and *V* from the positionally-isomeric tosylates *I* and *II*, respectively, have been determined in 0·43M (largely associated) potassium tert-butoxide in tert-butanol and corrected, where necessary[1], for contribution of side (*syn*-E2, E1) elimination processes. The corresponding reaction with the dissociated base in dimethylformamide (which is known[1] to be a clean *anti*-process) has been found to be extremely fast and, accordingly, rate measurement by available routine technique troublesome. As an approximation, we have therefore calculated the relative rates under reasonable simplifying assumptions.

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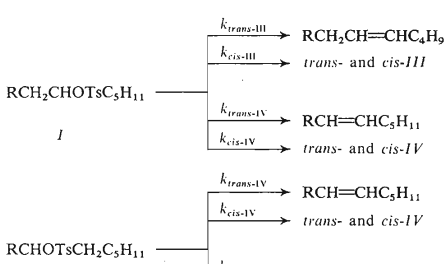


SCHEME 1

Approximate dependence of elimination rates on alkyl structure has thus been obtained for *anti*-E2 process induced by the associated and by the dissociated tert-butoxide base. The controversial[1-11] problem concerning steric hindrance to approach of associated base is discussed on these grounds.

EXPERIMENTAL

The tert-butanol used for the kinetic study was dried by repeated distillation with potassium; the solvent contained less than 0·01% of water. The solution of potassium tert-butoxide in tert-butanol was prepared by dissolving the clean potassium metal in tert-butanol under nitrogen and the concentration was determined titrimetrically[12].

Kinetic procedure: The tosylate (3 mmol) was dissolved in 0·43M solution of potassium tert-butoxide in tert-butanol (30 ml) and distributed into ampoules (2 ml lots). The ampoules were flushed with nitrogen, sealed and placed into the thermostated bath. In appropriate time intervals, the ampoules were withdrawn, cooled down and 1·5 ml aliquots pipetted into solution of acetone (10 ml) and 0·48M hydrochloric acid (1·3 ml). The excess of acid was back-titrated with 0·025M sodium hydroxide.

Determination of product composition: The overall proportion of olefins arising from the individual tosylates was determined gas-chromatographically employing n-propylcyclopentane as the internal standard (Table I). With a sole exception (*II*; R = H), olefins represented the prevalent part of the overall reaction; the remainder was not further analyzed but it consists presumably from products of S_N2 reaction; these are well-documented from previous studies[4,13-15]. Analytic conditions and olefin-isomer distribution (corrected on contribution of *syn*-E2 and E1 processes) were already reported in the preceding paper[1].

Evaluation of the rate data: The rate constants of the overall process (E2 + S_N2), k^{tot}, were evaluated from the equation $k^{tot} = 2{\cdot}303/t(b-a) \,.\, \log a(b-x)/b(a-x)$ where a and b are the initial concentrations (in mol l^{-1}) of the tosylate and the base, respectively, and x is the fraction reacted in the time t (in s). Two independent sets of measurements were made for

each tosylate, the difference being usually less than 7%. The average values are summarized in Table I. Although the plot of $\log a(b - x) : b(a - x)$ was invariantly linear at least up to 70% conversion, the obtained values of k^{tot} have to be viewed as pseudo-constants owing to base association (the concentration b determined titrimetrically does not correspond to the actual concentration of the probably oligomeric[16,17] associated base) and also owing to the inaccuracy introduced, in two instances (*II*; R = iso-C_3H_7, tert-C_4H_9) by the competition between second-order (E2) and first-order (E1) processes. For discussion of such a complication see ref.[15,16].

The overall rate constants of E2 process, k_E, were calculated from the equation $k_{E2} = k^{tot}$ . . % E2/100. The obtained values (Table I) were further dissected into the partial rate constants of individual *cis*- and *trans*-alkene formation and corrected on contribution of side (*syn*-E2) process using the data reported in the preceding paper[1].

RESULTS AND DISCUSSION

Table II summarizes the dependence of elimination rates on alkyl structure for *anti*-E2 reaction of tosylates *I* with associated potassium tert-butoxide in tert-butanol. The corresponding dependence determined for the positionally-isomeric tosylates *II* is summarized in Table III.

As we suggested already on basis of the preceding olefin-isomer composition study[1], formation of individual isomers from the two series may be influenced by several steric and polar factors depending on R. Accordingly, before we enter a detailed examination of steric hindrace to approach of the associated base, which is the major

TABLE I

Reaction of Tosylates $RCH_2CHOTsC_5H_{11}$ and $RCHOTsCH_2C_5H_{11}$ in 0·43M Potassium Tert-Butoxide in Tert-Butanol at 80·7°C: Overall Rates (k^{tot} and k_{E2}) and Overall Composition (% E2)

R	$RCH_2CHOTsC_5H_{11}$ (*I*)			$RCHOTsCH_2C_5H_{11}$ (*II*)		
	$10^5 k^{tot}$	% E2[a]	$10^5 k_{E2}$[b]	$10^5 k^{tot}$	% E2[a]	$10^5 k_{E2}$[b]
H	162	79	128	455	2·1	9·5
CH_3	83·8	88	73·8	189	79·0	149
C_2H_5	55·7	90	50·1	84·3	91·0	77·0
n-C_3H_7	56·9	87	49·5	46·2	82·0	37·9
iso-C_3H_7	29·4	100	29·4	24·5[c]	70·0[d]	17·2[e]
tert-C_4H_9	26·5	100	26·5	4·8[c]	16·0[d]	0·78[e]

[a] Unless otherwise indicated, the remainder consists mainly of the corresponding tert-butyl ethers; for minor by-products see ref.[13]; [b] *anti* and *syn*; [c] E2 + E1; [d] the remainder consists of E1-products; *cf.* ref.[1]; [e] corrected on contribution of E1 component by procedure described by Colter and McKelvey (ref.[15]).

target of the present study, we have first to outline how the other (steric and polar) factors affect the rates of the olefin formation.

Alkyl–alkyl interactions: Evidently, steric interactions between alkyls on C_α and C_β influence only the *cis*-isomer formation (eclipsing effect). A very small decrease of rate with increasing bulk of R is found in the process *I* → *cis-III* (Table II), where the variable R group is separated from C_α by a methylene unit ($R^\alpha = CH_2R$, $R^\beta =$ = n-C_4H_9). On the other hand, a very pronounced decrease of rates is found in the processes *I* → *cis-IV* (Table II) and *II* → *cis-IV* (Table III), which may be taken

TABLE II

Partial Rate Constants of *anti*-Elimination of Tosylates *I*, $RCH_2CHOTsC_5H_{11}$, in 0·43M Potassium Tert-butoxide–Tert-Butanol Solution at 80·7°C

R	10^5k_{E2}	$RCH_2CH{=}CHC_4H_9$ (*III*)		$RCH{=}CHC_5H_{11}$ (*IV*)	
		10^5k_{trans}	10^5k_{cis}	10^5k_{trans}	10^5k_{cis}
H	128	6·3	18·6	103·1	
CH_3	73·8	5·6	13·3	17·0	37·6
C_2H_5	50·1	6·0	16·8	8·1	19·2
n-C_3H_7	49·5	6·7	18·0	6·7	18·0
iso-C_3H_7	28·2[a]	3·3	16·2	3·4	5·3
tert-C_4H_9	23·6[a]	2·8	12·7	7·4	0·8

[a] Corrected on the contribution of *syn*-pathway to the *trans-III* alkene formation; *cf.* ref.[1].

TABLE III

Partial Rate Constants of *anti*-Elimination of Tosylates *II*, $RCHOTsCH_2C_5H_{11}$, in 0·43M Potassium Tert-Butoxide–Tert-Butanol Solution at 80·7°C

R	$RCH{=}CHC_5H_{11}$ (*IV*)			$R^1R^2C{=}CHC_6H_{13}$ (*V*)	
	10^5k_{E2}	10^5k_{trans}	10^5k_{cis}	10^5k_{trans}	10^5k_{cis}
H	9·5	9·5		—	—
CH_3	149·0	8·2	21·6	119·2	
C_2H_5	77·0	5·8	13·9	17·9	39·1
n-C_3H_7	37·9	4·6	12·9	6·2	14·2
iso-C_3H_7	16·5[a]	1·8	2·3	12·4	
tert-C_4H_9	0·6[a]	0·27	0·33	—	—

[a] Corrected on the contribution of *syn*-pathway to the *trans-IV* alkene formation; *cf.* ref.[1].

to reflect increasing weight of the repulsive interaction between alkyls (R^α = n-C_5H_{11}, R^β = R and R^α = R, R^β = n-C_5H_{11}, respectively). The circumstance that the overall spread of rates in the latter two processes is very similar (47 and 65, respectively) suggests that polar effects are only of a secondary importance in the reaction (*vide infra*).

Alkyl–tosyloxy interactions: No unambiguous evidence concerning the interaction between R and tosyloxy group can be drawn from the rate data in Tables II and III. However, on basis of the detailed analysis from the preceding paper we may suggest that the interaction is reponsible for lowering the rate of the *I* → *trans-III* process observed in the reaction of the sterically most demanding homologues (*I*; R = iso-C_3H_7 and R = tert-C_4H_9); *cf.* Scheme 3 in ref.[1].

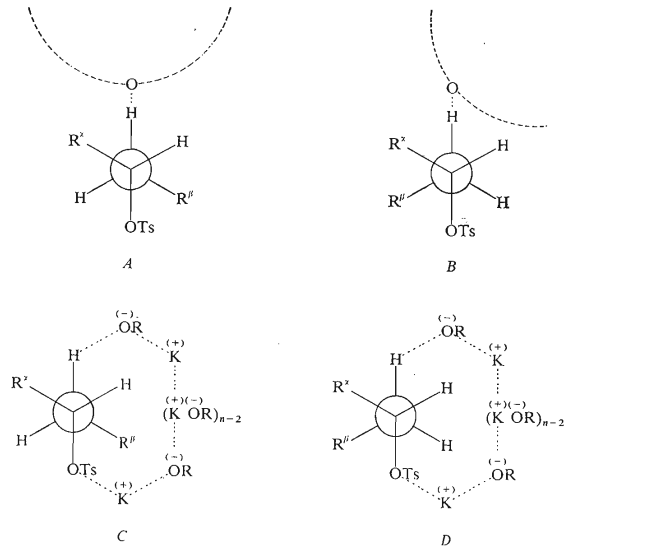
Polar effects: As we already suggested[1], position of transition state in the Elcb-like – E2-central – El-like spectrum may change in *anti*-elimination of tosylates *I* and *II* with variation of the substituent R. A gradual shift from Elcb-like – E2-central region towards the El-like side was predicted to occur with increasing steric bulk of the group R. The present rate data are in a reasonable agreement with this suggestion. A continuous decrease of rates of the *I* → *trans-IV* process (Table II) occurs on going from R = CH_3 to R = iso-C_3H_7, in accord with operation of inductive effect of R on C_β expected in the Elcb-like – E2-central region of transition states. However, a sudden increase of rate of this process results from further branching of R (R = tert-C_4H_9), which may suggest that the process is already taken out of the sphere of influence of the inductive effect and that it proceeds in the El-like region. Similar situation may be found also in the *II* → *V* process (Table III); here, increase of rate is introduced already by isopropyl group (*II*; R = iso-C_3H_7).

On Steric Hindrance to Base Approach

It has been proposed that extremely low *trans-cis* ratios generally observed in *anti*-elimination of aliphatic reactants with associated alkoxide base originate from selective hindrance to base approach in *trans*-olefin formation. Two different models were devised for such a hindrance assuming either a collinear[9] (Scheme 2*A*,*B*) or a non-linear[2,3] (Scheme 2*C*,*D*) approach of the base to the C_β—H bond.

In the collinear model advocated by Bartsch[9], it is assumed that severe interactions between the associated (probably oligomeric[16,17]) base and R^α can be avoided in *cis*-alkene formation by tilting the base to that side of reactant where only hydrogens are placed (Scheme 2*B*); in *trans*-alkene formation such a tilting is prohibited by R^β (Scheme 2*A*). In the non-linear model advocated by Schlosser[2,3,16] and us[3,10,11], it has been postulated that attractive interactions between cation of the associated base and oxygens of the tosyloxy group necessitate a non-linear approach of the base (Scheme 2*C*,*D*); in the pseudocyclic arrangement, the base approach

is again unhindered in *cis*-alkene formation, but it is opposed in the *trans*-isomer formation* by the substituent R^{β}.



SCHEME 2

A closer consideration of the alternative Schemes suggests that a distinguishment between the collinear and non-linear model could be made from examining the rate pattern of the processes *I* → *trans-III* and *II* → *trans-IV*. In both the processes R^{β} remains constant within the homologous series *I* and *II* (R^{β} = n-C_4H_9 and n-C_5H_{11}, respectively), whereas R^{α} varies with variation of R (R^{α} = RCH_2 and R, respectively). Accordingly, a pronounced increase of the base-approach hindrance with increasing bulk of R would be expected on basis of the collinear model leading correspondingly to a decrease of the elimination rates. On the other hand, independence of the rates on R would be expected on basis of the non-linear model,

* It is assumed that oxygens of tosyloxy group in *trans*-alkene formation are placed *syn* to $R^{\prime\beta}$; *cf.* refs[1,4].

because the steric hindrance, which is now induced mainly by R^{β} should remain within the two series practically unchanged.

As Table II shows, a rather small decrease of rates (by a factor of about 2–3) occurs in the process *I* → *trans-III* on going from the least to the most bulky R. A very pronounced decrease (by a factor of 40) is found (Table III) in the process *II* → *trans-IV*, providing thus apparently a support for the collinear model.

However, objections can be raised against drawing immediate conclusion from the rate data. As we already pointed out, interactions between R and tosyloxy group may also be responsible for the rate decrease in the process *I* → *trans-III*. Even more importantly, polar influence of R may affect the rates of *II* → *trans-IV* process. Namely, while hyperconjugative contribution of R can be assumed negligibly small in Elcb-like region of transition states, it might be very important[18–21] in the E2-central – El-like region and cause, eventually the observed decrease of rates with successive branching of R (three hydrogens are available for hyperconjugation when R = CH_3, two when R = C_2H_5, but only one when R = iso-C_3H_7 and none when R = tert-C_4H_9). For appreciation of the actual importance of the two factors, it would be very desirable to have corresponding rate data for the reaction of tosylates *I* and *II* with the dissociated tert-butoxide base. On basis of previous results[1,11], we expect that operation of steric and polar factors, except for base-approach hin-

TABLE IV

Relative Rates of *anti*-E2 Reaction of Tosylates *I*, $RCH_2CHOTsC_5H_{11}$, with Dissociated Tert-Butoxide Base Calculated under Simplifying Assumptions

R	$RCH_2CH{=}CHC_4H_9$ (*III*)		$RCH{=}CHC_5H_{11}$ (*IV*)	
	$k_{trans-III}$[b]	$k_{cis-III}$[a]	$k_{trans-IV}$[c]	k_{cis-IV}[c]
H	54	18·6	191	
CH_3	52	13·4	115	35
C_2H_5	57	16·8	75	17
n-C_3H_7	67	18·0	66	18
iso-C_3H_7	32	16·2	28	4·1
tert-C_4H_9	7·3	12·7	32·5	0·75

[a] Rates determined for the corresponding process in the reaction with the associated base (Table II); it is assumed that dependence of $k_{cis-III}$ on R is not influenced by base association; [b] calculated from the expression $k_{trans-III} = k_{cis-III}$ (% *trans-III*/% *cis-III*), where % *trans-III* and % *cis-III* are proportions of the particular isomers in the reaction with the dissociated base in dimethylformamide (Table V in ref.[1]); [c] calculated analogously as indicated in the footnote[b].

drance, should be qualitatively similar in the reaction with the associated as well as with the dissociated base. Assuming that steric hindrance to approach of the associated base has to be much greater than for the dissociated form, the role of the other effects could be better estimated from the rate data for the latter reaction.

Unfortunately, the reaction of tosylates *I* and *II* with dissociated potassium tert-butoxide (in dimethylformamide) is so fast that direct measurement of rates would be very troublesome. To circumvent the unpleasant task, we performed a "peasant" calculation of the rates based on the simplifying assumption that the rate patterns for $I \rightarrow cis\text{-}III$ and $II \rightarrow cis\text{-}IV$ processes in the reaction with the associated and with the dissociated base are, approximately, the same. Then, relative rates of formation of the other isomers can be calculated with aid of the olefin-isomer composition data, reported for the dissociated base in dimethylformamide in the preceding paper[1]. The calculated values are summarized in Tables IV and V.

As the data for $II \rightarrow trans\text{-}IV$ process in Table V show, the overall spread of the calculated rates for the dissociated base is markedly smaller than it was found for the associated form (Table III), a significant decrease (by a factor of about 4) being now apparent only for the most bulky homologue (*IV*; R = tert-C_4H_9). It follows therefore that the very pronounced decrease of rates observed for $II \rightarrow trans\text{-}IV$ process induced by the associated base (Table III) cannot be accounted by the hyperconjugative (or inductive) effect of R; a major part of the decrease had to result from hindrance to approach of the base.

TABLE V

Relative Rates of *anti*-E2 Reaction of Tosylates *II*, $RCHOTsCH_2C_5H_{11}$, with Dissociated Tert-Butoxide Base Calculated under Simplifying Assumptions

R	$RCH{=}CHC_5H_{11}$ (*IV*)		$R^1R^2C{=}CHC_6H_{13}$ (*V*)	
	$k_{trans-IV}$ [b]	k_{cis-IV} [a]	$k_{trans-V}$ [c]	k_{cis-V} [c]
CH_3	58	21·6	201	
C_2H_5	65	13·9	141	44
n-C_3H_7	37·5	12·9	36	13·4
iso-C_3H_7	55	2·3	133	
tert-C_4H_9	15·4	0·3	—	—

[a] Rates determined for the corresponding process in the reaction with the associated base (Table III); it is assumed that dependence of k_{cis-IV} on R is not influenced by base association; [b] calculated from the expression $k_{trans-IV} = k_{cis-IV}$ (% *trans-IV*/% *cis-IV*), where % *trans-IV* and % *cis-IV* are proportions of the particular isomers in the reaction with the dissociated base in dimethylformamide (Table VI in ref.[1]); [c] calculated analogously as indicated in the footnote *b*.

For the process *I* → *trans-III*, on the other hand, the situation seems to be very different. As the data of Table IV show, successive branching of R leads to a decrease of rates of *trans-III* alkene formation which, in actual fact, is greater than it was found for the associated base. In accord with our earlier suggestion (*vide infra*) we may therefore conclude that the interactions between R and tosyloxy group, and not those between R and base, are responsible for the rate decrease in *I* → → *trans-III* process obtained in both the compared reactions.

Summing up, we see that the threshold of alkyl-structure complexity where base approach hindrance becomes apparent in rate pattern is rather high. In the reaction of tosylate series *I* and *II* with the associated base, only two tosylates, *II*; R = iso-$-C_3H_7$ and R = tert-C_4H_9, exhibit a significant slowing-down of rates ascribable to base-approach hindrance.

Justifiably, therefore, we may ask whether steric hindrance to a collinear approach of the associated base does suffice to account for the preferential *cis*-olefin formation which has been found[1] to be a general phenomenon in the reaction, down to the simpliest examples of alkyl structures involved in the series *I* and *II*. When the steep bank in non-bonding energy curve expected for alkyl–base interaction is taken into account, the controlling role of base-approach hindrance postulated in the collinear model (Scheme 2*A*) seems to be, in light of the present results, doubtful. At the same time, a simple acceptance of the alternative (non-linear) model seems to be, owing to the rate-retardation observed (Table III) in the process *II* → *trans-IV*, also difficult.

As a resolution we propose that a supplementation of the collinear model by attractive (electrostatic) interactions between cation of the associated base and the leaving group should be considered. In the collinear model, the attractive interactions can be greatly supported by tilting the base, which is allowed in the arrangement for the *cis*- (Scheme 2*B*), but disallowed (by R^B) in that for the *trans*-alkene (Scheme 2*A*) formation. In accord with our previous[1] arguments, we are inclined to suggest that steric hindrance to tilting the associated base rather than the hindrance to its collinear approach is responsible for the preferential *cis*-olefin formation.

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