syn-anti DUALITY IN E2 REACTIONS: THE EFFECTS OF LEAVING GROUP AND BASE ASSOCIATION IN THE COMPETING PATHWAYS*

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Operation of the associated and the dissociated form of potassium tert-butoxide base has been investigated in bimolecular elimination of six 5-decyl derivatives (*I*; X = $N^{(+)}(CH_3)_3$, F, Cl, Br, I, OTs) in several solvents. Using the potassium ion-complexing agent *IV* as a diagnostic tool, limiting solvents have been selected which secure a prevalent operation for either of the two alternative base forms in the reaction. For the two limiting solvents (benzene and dimethyl sulphoxide) quantitative contributions of the competing *syn*- and *anti*-elimination pathways to the *trans*- and *cis*-5-decene formation have been evaluated in the reaction of five 5-decyl derivatives (*I*; X = $N^{(+)}(CH_3)_3$, F, Cl, Br, OTs) with the aid of the corresponding deuterium labelled (*erythro*- and *threo*-6-D) analogues. The effect of leaving group and base association in the individual (*syn* and *anti*) processes could thus be independently examined. Novel informations on the detailed transition state geometries in the two pathways have been drawn from the study. The long-standing problem concerning the *syn-anti* duality and the divergent stereoselectivity of the competing pathways can be plausibly interpreted on these grounds.

The studies reported over the past decade from this as well as other Laboratories have revealed that E2 reactions represent a much more difficult mechanistic problem than it was previously anticipated. Contrary to the original assumption that the elimination proceeds uniformly by a single (*anti*-) mechanistic pathway, a participation of two stereochemically different (*syn*- and *anti*-) mechanisms has been demonstrated in the reaction, the evidence covering now a wide range[3-5] of structures and reaction conditions examined. Moreover, a simultaneous operation of different ionic forms (dissociated and associated) of the participating base has been established[6-10] in a number of the reactions, including those performed in some common[6,7,9] solvents. Evidence has been obtained that the different forms of base lead usually to different[2,7,9] elimination results introducing thus further mechanistic inhomogeneity in the E2 reactions.

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These findings clearly necessitate a thorough reexamination of structural as well as environmental effects in the reaction. Obviously, a meaningful understanding of these effects may be attained only when the effects on the individual participating pathways (induced by homogeneous base forms) are separately examined. Approaches towards solution of the complex problem will be the subject of this and the forthcoming papers.

In this paper, we shall examine the effect of leaving group on the *syn*- and the *anti*-pathway in the elimination of five 5-decyl derivatives *I* (X = $\overset{(+)}{N}(CH_3)_3$, OTs, F, Cl, Br) induced, separately, by the dissociated and the associated forms of potassium tert-butoxide base (Scheme 1).

$$\underset{I}{C_4H_9CHXCH_2C_4H_9} \xrightarrow[\text{solvent}]{\text{tert-}C_4H_9OK} \underset{\textit{cis}\text{- and }\textit{trans}\text{-}II}{C_4H_9CH{=}CHC_4H_9} + \underset{\textit{cis}\text{- and }\textit{trans}\text{-}III}{C_3H_7CH{=}CHC_5H_{11}}$$

SCHEME 1

Towards these ends, we have surveyed first the course of the reaction of the derivatives *I* with potassium tert-butoxide in four solvents differing greatly in their capability for ion association (benzene, tert-butanol, dimethylformamide and dimethyl sulphoxide). Employing the potassium ion complexing agent[11], dicyclohexyl-18--crown-6-ether (*IV*), as a diagnostic tool[7], we have selected the limiting conditions which secure a prevalent operation for either of the two extreme (dissociated and associated) forms of the tert-butoxide base in the examined reactions. For the limiting conditions, we have next quantitatively determined the contributions of the *syn*- and *anti*-pathways to the overall reaction. The procedure consisted of the evaluation of deuterium contents in the *cis*- and *trans*-5-decene isomers (*cis*- and *trans-II*) resulting from the eliminations of the appropriately deuterium labelled analogues of the derivatives *I* (*erythro*- and *threo*-[6-D]-*I*). The labelled trimethylammonio and the tosyloxy derivatives *I* (X = $\overset{(+)}{N}(CH_3)_3$ and OTs), together with some pertinent results, were already available from the previous work[12]. The unlabelled as well as the labelled (*erythro*- and *threo*-6-D) halides *I* (X = F, Cl, Br) were prepared (Scheme 2) by the known stereospecific[13–19] reactions (with inversion of configuration) from the corresponding hydroxy compounds (*I*, *threo*- and *erythro*-[6-D]-*I*, respectively; X = OH).

$$\text{[6-H(D)]-}I\ (X = OH) \xrightarrow[(C_2H_5)_2O]{(C_2H_5)_2NCF_2CHFCl} \text{[6-H(D)]-}I\ (X = F)$$

$$\text{[6-H(D)]-}I\ (X = OH) \xrightarrow[CCl_4]{CCl_4\,(C_6H_5)_3P} \text{[6-H(D)]-}I\ (X = Cl)$$

$$\text{[6-H(D)]-}I\ (X = OH) \xrightarrow[HCON(CH_3)_2]{(C_6H_5)_3PBr_2} \text{[6-H(D)]-}I\ (X = Br)$$

SCHEME 2

The determination of the deuterium contents in the olefins *cis-II* and *trans-II*, subsequent calculation of the *syn*- and *anti*-contributions to their formation as well as the correction for operation of the isotope effect has been performed by the procedures described by us previously[12]. On these grounds, the contributions of the *syn*- and *anti*-pathways in the reactions of the unlabelled derivatives *I* have been allocated. Accordingly, the effects of leaving group and base association in the competing pathways could be independently considered.

EXPERIMENTAL

5-Fluorodecane (*I*; X = F)

5-Decanol (20 g; 0·13 mol) in ether (30 ml) was added dropwise to the stirred solution of 1,1,2-trifluoro-2-chlorotriethylamine[20] (35 g; 0·2 mol) in ether (50 ml). After 24 h standing at room temperature, the mixture was decomposed by water (70 ml), the ethereal layer was separated, washed with water, dried over magnesium sulphate and the solvent taken down. The oily residue was placed on a column with alumina (II; 150 g) and eluted with pentane (500 ml) affording a mixture of the required fluoride and olefinic by-products. The mixture was treated with formic acid (200 ml) and hydrogen peroxide (30%; 40 ml) under stirring (10 h), diluted with water (2·5 l) extracted with pentane and the pentane layer filtered through a column of alumina (II; 100 g). The work-up afforded the pure product in 50% yield; b.p. 80°C/11 Torr. For $C_{10}H_{21}F$ (160·2) calculated: 74·94% C, 13·21% H; found: 75·24% C, 12·94% H.

erythro- and *threo*-[6-D]-*I* (X = F): Prepared analogously from the corresponding deuterium labelled alcohols[12] (*threo*- and *erythro*-[6-D]-*I* (X = OH), respectively).

5-Chlorodecane (*I*; X = Cl)

5-Decanol (7·1 g; 0·045 mol) was treated under reflux (15 h) with a solution of triphenylphosphine (25·2 g; 0·096 mol) in tetrachloromethane (100 ml). The mixture was diluted with water (100 ml), the organic layer was separated, dried with magnesium sulphate and the solvent was taken down. The residue was extracted with pentane (100 ml), the pentane extract was concentrated and placed on a column of alumina (II; 100 g). The pentane eluate (400 ml) consisted of the required product and olefinic by-products; the latter were separated by treatment of the mixture with performic acid under the conditions described above for the fluoride. It was obtained 4·9 g (62%) of the pure chloride, b.p. 98°C/12 Torr. For $C_{10}H_{21}Cl$ (176·7) calculated: 67·95% C, 11·97% H; found: 68·28% C, 11·94% H.

erythro- and *threo*-[6-D]-*I* (X = Cl): Prepared analogously from the appropriately labelled alcohols[12] (*threo*- and *erythro*-[6-D]-*I*; X = OH, respectively).

5-Bromodecane (*I*; X = Br)

Bromine (8·0 g; 0·05 mol) was added to a stirred solution of 5-decanol (8·0 g; 0·05 mol) and triphenylphosphine (14·6 g; 0·056 mol) in dimethylformamide (80 ml) at −15°C. After additional standing for 15 min at −2°C, the mixture was treated with water (1 l) and pentane (200 ml). The pentane layer was filtrated, washed with water, dried with sodium sulphate and the solvent taken down. The residue was placed on a column of alumina (II; 300 g) and eluted with pentane

(800 ml). Fractional distillation from a Hickmann flask afforded 4·5 g (41%) of the pure product, b.p. 107°C/27 Torr. For $C_{10}H_{21}Br$ (221·2) calculated: 54·30% C, 9·57% H; found: 54·30% C, 9·62% H.

erythro- and *threo*-[6-D]-*I* (X = Br): Prepared analogously from the *threo-* and *erythro*-[6-D]--labelled 5-decanols, respectively. It is imperative to follow the mild conditions, as described for the parent derivative. A complete loss of stereospecificity (due to epimerization on the $C_{(5)}$ carbon)[19] has been observed in the reaction performed at room temperature (24 h).

5-Iododecane (*I*; X = I)

Iodine (13·0 g; 0·05 mol) was treated under stirring with 5-decanol (7·1 g; 0·045 mol) and triphenylphosphine (13·0 g; 0·05 mol) in dimethylformamide (50 ml). After 48 h standing at room temperature the mixture was worked-up analogously as described for the bromo analogue. It was obtained 1·4 g (10%) of the pure product, b.p. 120°C/13 Torr. For $C_{10}H_{21}I$ (268·2) calculated: 44·78% C, 7·89% H; found: 45·30% C, 7·89% H. Owing to low yields, attempts to prepare the labelled analogues were abandoned.

Elimination Runs

Isomer olefin composition: 0·5—1·0 mmol of the (unlabelled) derivative *I* and a three-fold excess of the alkoxide solution (0·3—0·5M) was heated (Table I) under nitrogen either in sealed tubes or under magnetic stirring in stoppered flasks. (The derivative *I*; X = F, poorly soluble in the solvent

TABLE I
Conditions Employed in the Elimination Runs

Solvent	Molar ratio Base : *IV*	Temperature, °C/Time, h					
		$\overset{(+)}{N}(CH_3)_3$	OTs	F[a]	Cl	Br	I
$(CH_3)_2SO$	1 : 0	25/2	25/2	40/2	25/2	25/2	25/2
	1 : 1	25/2	25/2	40/2	25/2	25/2	25/2
$HCON(CH_3)_2$	1 : 0	25/2	25/2	40/2	25/2	25/2	25/2
	1 : 1	25/2	25/2	25/100	25/2	25/2	25/2
tert-C_4H_9OH	1 : 0	80/20	110/10	130/40	120/30	110/10	110/10
	1 : 1	80/20	100/5	120/20	110/10	100/4	100/4
C_6H_6	1 : 0	25/10	120/20	130/40	120/20	120/20	120/20
	1 : 1	25/2	80/2	100/20	100/2	80/2	80/2

[a] The reaction was incomplete under the conditions indicated. Isomerization (according to control experiments) precluded to use more forcing conditions. In the preparative runs with labelled reactants, the unreacted fluoride was separated from the olefins on the silver nitrate–alumina column by elution with pure pentane, thereafter the *trans-* and *cis*-olefins were eluted by pentane containing 1% and 3% of ether, respectively.

dimethylformamide and dimethyl sulphoxide.) The contents were transferred into a separatory funnel, acidified with an excess of 1M hydrochloric acid, the olefins taken up in pentane (5 ml) and analysed by gas-chromatography.

Deuterium distribution: The deuterium labelled reactants (10–30 mmol) were eliminated analogously as described for the parent compound. The resulting mixture of olefins was separated into the *trans*- and *cis*-olefin fractions on a column of alumina coated with silver nitrate (30%). The individual olefin fractions were subjected to ozonolysis followed by reduction with lithium aluminium hydride. The resulting alcoholic mixtures (1-butanol, 1-pentanol and 1-hexanol) were separated by preparative gas chromatography. Experimental details were reported previously[12]. The deuterium contents in the individual olefin fractions and in the resulting 1-pentanol were determined mass spectroscopically. The results are summarized in Table II.

RESULTS AND DISCUSSION

Competition between Associated and Dissociated Form of Potassium tert-Butoxide in the Elimination

Ion-pairing of potassium tert-butoxide occurs pronouncedly in majority of organic solvents (Eq. (*A*)). The associated form

$$\underset{a}{\text{tert-C}_4\text{H}_9\overset{(-)}{\text{O}}} + \overset{(+)}{\text{K}} \rightleftharpoons \underset{b}{(\text{tert-C}_4\text{H}_9\overset{(-)(+)}{\text{O}}\text{K})_n}\,; \quad n \geqq 1 \qquad (A)$$

b prevails greatly in solvents of low polarity[21–23] (such as benzene or tert-butanol) and is present, non-negligibly (at 0·1–1·0M overall base concentration), even in very polar solvents renowned for their ion-separating ability[6,24] (dimethylformamide and dimethyl sulphoxide). Despite a lower basicity (due to the proximity of counterion), the associated form has been demonstrated to be able of competition[6,7,9] with the dissociated base *a* in E2 reactions in proportions which depend on ion-separating ability of the solvent[7] and on other[6,8,9] factors controlling the equilibrium. Significantly, however, also the reactant and its propensity to be eliminated by the alternative base form has been shown[2,22,25] to play a role in the competition. Accordingly, an *a priori* prediction that the dissociated and the associated base form will generally prevail in elimination performed respectively in the solvent with very high ion-dissociating and very high ion-associating capacity would not be fully warranted.

Dicyclohexyl-18-crown-6-ether (*IV*) coordinates[11] strongly potassium ion and converts thus efficiently the associated form of potassium tert-butoxide into separated[7] ions. As we pointed out previously[7], this makes the complexing agent *IV* a very convenient diagnostic tool for the associated base form in E2 reactions: so far as the alternative base forms (dissociated *vs* associated) differ markedly in their elimination outcomes, evidence on the operation of the latter form may be deduced simply from

comparison of the elimination results obtained from the reaction performed respectively in the absence and in the presence of the crown ether *IV*.

We have therefore examined the effect of *IV* on the course of the reaction of six derivatives *I* (X = F, Cl, Br, I, OTs, $\overset{(+)}{N}(CH_3)_3$) with potassium tert-butoxide in four solvents (benzene, tert-butanol, dimethylformamide and dimethyl sulphoxide) differing greatly in their ion-separating ability. The overall *trans*/*cis* olefin ratios (*trans-II* and *trans-III*/*cis-II* and *cis-III*) resulting from the reactions performed in absence and in presence of equimolar amounts of *IV* (in respect to the base) are summarized in Table III.

As Table III shows, very similar results are obtained for all the derivatives *I* which possess a neutral leaving group (X = F, Cl, Br, I, OTs). A very pronounced (*I*; X = Cl, Br, I, OTs) or at least a significant (*I*; X = F) increase in the *trans*/*cis* ratio on addition of the crown ether *IV* is found for the neutral derivatives in the solvents benzene and tert-butanol. A less pronounced effect of *IV* is found for these derivatives in dimethylformamide and the effect is completely absent in dimethyl sulphoxide. A conclusion may be drawn therefore for the neutral derivatives that the associated base operates pronouncedly in the former two solvents (benzene and

TABLE II

Deuterium Isotope Composition Data from Elimination of *erythro*- and *threo*-5-Decyl [6-D]--Halides (*I*; X = F, Cl, Br) with Potassium tert-Butoxide in Dimethyl Sulphoxide and in Benzene

X	Configuration	Solvent	% d_1 [a] *trans*-Fraction		% d_1 [a] *cis*-Fraction	
			$C_{10}H_{20}$ [c]	n-$C_5H_{11}OH$	$C_{10}H_{20}$ [c]	n-$C_5H_{11}OH$
F [b]	*erythro*	$(CH_3)_2SO$	86·4	19·8	95·6	45·3
F [b]	*threo*	$(CH_3)_2SO$	— [d]	48·0	— [d]	— [d]
F [b]	*erythro*	C_6H_6	94·0	45·4	89·3	39·4
F [b]	*threo*	C_6H_6	82·1	19·5	— [d]	— [d]
Cl	*erythro*	$(CH_3)_2SO$	84·6	11·6	99·0	50·0
Cl	*threo*	$(CH_3)_2SO$	100·0	50·0	85·8	21·9
Cl	*erythro*	C_6H_6	88·0	37·2	96·3	47·1
Cl	*threo*	C_6H_6	93·0	39·8	79·1	14·1
Br	*erythro*	$(CH_3)_2SO$	84·6	5·6	100·0	50·0
Br	*threo*	$(CH_3)_2SO$	100·0	50·0	— [d]	— [d]
Br	*erythro*	C_6H_6	81·8	26·4	100·0	— [d]
Br	*threo*	C_6H_6	97·0	46·5	80·4	7·0

[a] Corrected for incomplete labelling of the reactants; [b] the determined values are somewhat less accurate: about 5—10% of isomerization might occur (according to blank experiments) in course of elimination; [c] mixture of 4- and 5-decene; *cf.* ref.[12]; [d] not determined.

tert-butanol) with a very low ion-separating ability and is involved to some extent also in the reactions performed in dimethylformamide. Only for the solvent with the highest ion-separating ability (dimethyl sulphoxide) general absence of the effect convincingly shows that the dissociated base is the sole base form involved in the reaction.

In contrast to the neutral derivatives, a much less pronounced effect of the crown ether *IV* is found for the positively charged analogue *I* ($X = \overset{(+)}{N}(CH_3)_3$). A significant effect of *IV* (a decrease in the *trans*/*cis* ratio) is observed only in the solvent tert-butanol* indicating that the associated base has in some way to be operative in the reaction. Noteworthy, none effect at all is found in the other low polar solvent benzene, which suggests that the dissociated form is in a full control of the expectedly similar reaction.

Admittedly, the absence of the effect of *IV* on the *trans*/*cis* ratios for the quaternary salt (*I*, $X = \overset{(+)}{N}(CH_3)_3$) in benzene does not completely exclude that the associated base is involved in the reaction. Conceivably, both the associated and the dissociated base forms might lead to the same *trans*/*cis* ratios, exploiting however different mechanistic channels (*syn* or *anti*) in the reaction: such a situation holds (*vide infra*) qualitatively for the fluoride *I* and accounts for the substantial lowering (in comparison with the other halides) of the effect of *IV* in Table III. We have, therefore, examined the effect of *IV* on the contribution of *syn*-elimination pathway in the reaction of the quaternary salt *I* in benzene. The results obtained for *trans*-5-decene formation from study of the *erythro*- and *threo*-[6-D]-labelled analogues are summarized in Table IV. No significant effect of the crown ether *IV* on the deuterium isotope distribution is apparent from the data. Practically identical (within limits of experimental error) contributions of the *syn*-pathway are accordingly found in the reaction in the presence as well as in the absence of the complexing agent *IV*. A further support is thus obtained for the suggestion that the associated base form does not operate in the reaction of *I*; $X = \overset{(+)}{N}(CH_3)_3$ in benzene.

It follows from these results that the associated base form is much more preferred in the reactions of neutral derivatives than in the reaction of the quaternary salt. A reasonable explanation for the difference may be given in terms of the Eq. (*B*):

$$[\overset{(+)}{R}\overset{(-)}{N}(CH_3)_3Cl] + [\text{tert-}C_4H_9\overset{(-)}{O}\,\overset{(+)}{K}] \rightleftharpoons [\text{tert-}C_4H_9\overset{(-)}{O}\,\overset{(+)}{R}N(CH_3)_3] +$$

$$+ [\overset{(+)}{K}\,\overset{(-)}{Cl}] \rightleftharpoons \text{tert-}C_4H_9\overset{(-)}{O} + \overset{(+)}{R}N(CH_3)_3 \qquad (B)$$

* An analogous effect of *IV* in reaction of 3-hexyltrimethylammonium iodide performed in the same base–solvent combination is apparent from ref.[25]; see, however, ref.[26].

Metathesis occurs (Eq. (*B*)) between the quaternary salt and the associated form of potassium tert-butoxide. Owing to weak attractive interactions between the bulky counterions in $[\text{tert-}C_4H_9O^{(-)}\ R\overset{(+)}{N}(CH_3)_3]$, a higher equilibrium concentration of the dissociated tert-butoxide base is attained allowing a more extensive operation of this particular form in the elimination of the quaternary salt.

TABLE III

The Effect of Solvent and the Crown Ether *IV* on the Overall *trans*/*cis* Ratios (*trans-II* and *trans-III*/*cis-II* and *cis-III*) in the Elimination of the Derivatives *I*

Solvent	Base : *IV* molar ratio	*trans*/*cis* Olefin ratio					
		F	Cl	Br	I	OTs	$\overset{(+)}{N}(CH_3)_3$
C_6H_6	1 : 0	4·88	1·21	0·81	1·32	0·85	27·6
	1 : 1	5·73	2·51	3·10	3·55	2·17	27·6
tert-C_4H_9OH	1 : 0	4·80	1·29	1·24	1·78	0·32	2·12
	1 : 1	5·73	6·24	5·94	7·28	2·55	1·86
$HCON(CH_3)_2$	1 : 0	5·25	6·70	6·70	7·70	3·25	6·14
	1 : 1	4·40	6·70	6·15	7·70	3·25	6·14
$(CH_3)_2SO$	1 : 0	4·55	6·04	6·70	6·46	3·17	4·00
	1 : 1	4·55	6·04	6·70	6·46	3·17	4·00

TABLE IV

The Effect of the Crown Ether *IV* on the Deuterium Isotope Distribution in the Formation of *trans*-5-Decene from *erythro*- and *threo*-[6-D]-*I*, $X = \overset{(+)}{N}(CH_3)_3$ in Benzene

Reactant	Base : *IV* molar ratio	% d_1 in		% *syn*
		4- and 5-decene[a]	1-pentanol[b]	
erythro-[6-D]	1 : 0	99·0	49·5	99·0
erythro-[6-D]	1 : 1	98·8	49·5	99·0
threo-[6-D]	1 : 0	79·9	11·8	76·4
threo-[6-D]	1 : 1	79·2	13·1	73·8

[a] The separated mixture of the *trans*-isomers; [b] from ozonolysis of the *trans*-olefin mixture.

Hydrogen Bonding and Reactivity of the Alternative Base Forms

An intriguing question remains to be settled in this context, namely why the prevalent operation of the dissociated base form, which we have established for the reaction of the quaternary salt *I* ($X = \overset{(+)}{N}(CH_3)_3$) in the aprotic solvents dimethyl sulphoxide, dimethylformamide and benzene, does not hold also in the protic solvent tert-butanol. According to conductivity studies[27], association of ions is more favoured in benzene than in tert-butanol; in spite of this, the associated base participates, for the quaternary salt, not in the former (more advantageous) but in the latter (less advantageous) solvent. It appears therefore that other factors, than the ion-separating ability or solvent alone, have also to be in control of the competition between the alternative base forms in the reactions.

Hydrogen bonding may influence considerably relative reactivity of the alternative base forms. As we found, the reaction rates of alkyl halides with the associated tert-butoxide base (*i.e.*, in absence of *IV*) are very similar in the aprotic benzene and in the protic tert-butanol. However, a rate difference of several orders ($10^3 - 10^4$) between the two solvents was found in the reaction with the dissociated tert-butoxide form (*i.e.*, in presence of *IV*), the elimination being much slower in the protic solvent tert-butanol. A conclusion may be drawn from these observations that hydrogen bonding is not important in the associated base form, but that it decreases, very pronouncedly, reactivity of the dissociated form. Although the dissociated tert-butoxide is still more reactive in tert-butanol than the associated form, the lowered difference ($\sim 10^1$) already allows the associated base to take part in the competition.

Interestingly, the levelling out of reactivities of the competing base forms may also account for the recent observation by Saunders[25] that the associated form of alkali metal phenoxides operates prominently in elimination of quaternary ammonium salts performed in an efficiently ion-separating solvent mixture dimethyl sulphoxide–tert-butanol–phenol. Phenol is an extremely strong hydrogen bonding agent. It has been pointed out by Cram[28] for carbanion reactions that the associated potassium phenoxide is in actual fact a stronger base than the dissociated form hydrogen-bonded by the conjugate acid.

Homogeneity of tert-Butoxide Base in Extreme Solvents

A homogeneous base form (dissociated tert-butoxide) has been convincingly established in the preceding sections for the E2 reactions of all derivatives *I* ($X = \overset{(+)}{N}(CH_3)_3$, F, Cl, Br, I, OTs) in the dipolar solvent dimethyl sulphoxide. The other (associated) tert-butoxide form has been proved to operate, for the neutral derivatives *I* (X = F, Cl, Br, I, OTs), in the low polar solvents benzene and tert-butanol. However, no distinction could be made from the evidence whether the associated base alone, or

together with the dissociated form, is involved in the reactions. Bartsch and his coworkers[9] demonstrated in a study of related derivatives that competition of both the tert-butoxide forms occurs in the solvent tert-butanol. Accordingly, it may be expected to hold also for the solvent benzene. Nonetheless, the following results will show that in benzene the contributions of the dissociated base form both in the *syn*- and in the *anti*-elimination component cannot be large.

The Effect of Leaving Group and Base Association on the Proportions of the syn- *and the* anti-*Elimination Pathways*

Quantitative contributions of the *syn*- and the *anti*-pathway in elimination of the unlabelled derivatives *I* are obtained by the procedure outlined earlier in this paper. The data for the reaction of five derivatives *I* (X = $\overset{(+)}{N}(CH_3)$, F, Cl, Br, OTs) with potassium tert-butoxide in two extreme aprotic solvents (benzene and dimethyl sulphoxide) are summarized in Table V.

TABLE V

Contributions of *syn*- and *anti*-Elimination in the *trans*- and *cis*-5-Decene Formation from the Derivatives *I* (X = $\overset{(+)}{N}(CH_3)_3$, F, Cl, Br, OTs) in Benzene and in Dimethyl Sulphoxide

X	*trans*-5-Decene		*cis*-5-Decene		Overall
	% *syn*	% *anti*	% *syn*	% *anti*	% *syn*
			Benzene		
$\overset{(+)}{N}(CH_3)_3$	91·6[a]	8·4[a]	18·0	82·0[a]	84·2[a]
F	88·0[b]	12·0[b]	20·0[c,d]	80·0[c,d]	76·4
Cl	65·0[b]	35·0[b]	11·0[e]	89·0[e]	40·6
Br	33·0[b]	67·0[b]	4·0[e]	96·0[e]	17·0
OTs	27·0[a]	73·0[a]	6·6[a]	93·4[a]	16·0[a]
			Dimethyl sulphoxide		
$\overset{(+)}{N}(CH_3)_3$	93·6[a]	6·6[a]	6·0[a]	94·0[a]	75·9[a]
F	11·0[b]	89·0[b]	20·0[c,d]	80·0[c,d]	12·6
Cl	6·0[b]	94·0[b]	15·0[e]	85·0[e]	6·6
Br	2·5[b]	97·5[b]	0·0[f]	100·0[f]	3·0
OTs[g]	3·7[a]	96·3[a]	5·8[a]	94·2	4·2[a]

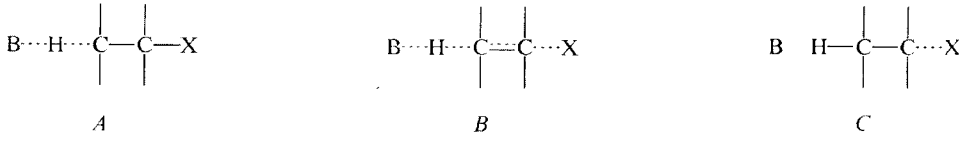
[a] The value from ref.[12]; [b] calculated from the data of Table II using Eq. (*5*) in ref.[12]; [c] a less accurate value, *cf.* footnote *b* in Table II; [d] calculated from the data of Table II using Eq. (*6*) in ref.[12]; [e] calculated from the data in Table II using Eq. (*4*) in ref.[12]; [f] approximate values from the data in Table II; [g] the values found for dimethylformamide.

As Table V shows, both the *syn*- and the *anti*-pathway operate, side by side, in all the reactions examined and participate in the *trans*- as well as in the *cis*-5-decene formation. The pronounced effect of leaving group and of solvent, as well, on the *syn-anti* competition is immediately apparent from the data.

Let us examine first the effect of leaving group. A gradual and very clear-cut increase of the *syn*-proportion is found in both the extreme solvents with changing the leaving group in order $OTs \sim Br < Cl < F < \overset{(+)}{N}(CH_3)_3$ No meaningful correlation accordingly exists between the observed trend and steric bulk of the leaving groups ($F \leqq Cl \leqq Br < OTs < \overset{(+)}{N}(CH_3)_3$). The earlier proposal by Saunders[29] that steric bulk of leaving group plays the major role in promotion of the *syn*-pathway may therefore be definitely abandoned. This question we discussed already in detail in our preliminary communication[2]. Supporting evidence in favour of our arguments has been reported[30] meanwhile from the original advocates of the steric theory and the point does not require at present further comments.

On the other hand, a very reasonable correlation may be found between the proportions of *syn*-elimination and polar characteristics of the leaving groups examined. Thus, energy required for the leaving group displacement increases usually[5] in order $OTs \sim Br < Cl < F < \overset{(+)}{N}(CH_3)_3$, in a complete agreement with the observations in Table V. Also, electron-withdrawing power of the leaving groups is known to follow a similar order[31,32]: $Br < Cl < F < OTs < \overset{(+)}{N}(CH_3)_3$.

A very plausible rationalization for the correlations may be given in terms of the theory of variable E2 transition state[33]. According to the theory, the process of a loosening of the C_β—H and C_α—X bonds, although concerted in E2 reactions, need not keep in pace with one other, or exactly balance in the transition state. Depending on polar influences, either C_β—H or C_α—X bond loosening may more progress initially and decline thus from the strictly synchronous form of the transition state *B* towards an E1cb-like form *A* or an E1-like form *C* (Scheme 3). A gradual shift



A *B* *C*

SCHEME 3

towards the E1cb-like form is predicted (and also amply experimentally verified) to ensue[31] from increasing, concurrently, the electron-withdrawing power and the energy of displacement of the leaving group. Accordingly, it may be inferred from

the above correlations that a near-proportionality* has to exist between the propensity of the derivatives *I* to *syn*-elimination and the relative progress made in the C_β—H bond loosening in the transition state.

Significantly, precisely such a situation as it has now been found was predicted by Ingold on theoretical grounds. In his analysis[35], Ingold dissected, conceptually, E2 reactions into an electrophilic substitution (S_E) at C_β with C_α as the attacking electrophile, and a nucleophilic substitution (S_N) at C_α with C_β as the attacking nucleophile. Considering possible stereochemical outcomes of the two concerted processes, Ingold suggested that, for E2 reactions where the bond changes are coupled to near-simultaneity (form *B* in the Scheme 3), the nucleophilic substitution (S_N) will proceed with inversion while the electrophilic component (S_E) will retain configuration, enforcing thus an antiperiplanar arrangement of the departing groups (*anti*-elimination; *cf.* Scheme 4*a*). On the other hand, for less coupled E2 processes Ingold predicted that "if proton transfer is extensive enough in the E2 transition state, the involved electrophilic, as well as the nucleophilic substitution coupled with it, might involve inversion. This would produce *syn*-periplanar stereospecifity ..." (*syn*-elimination; *cf.* Scheme 4b). An excellent confirmation of the theory is thus provided by the present results. A less unambiguous support to the theory we afforded previously[36,37] in examining the effect of base strength on the *syn-anti* contributions in elimination of quaternary ammonium salts.

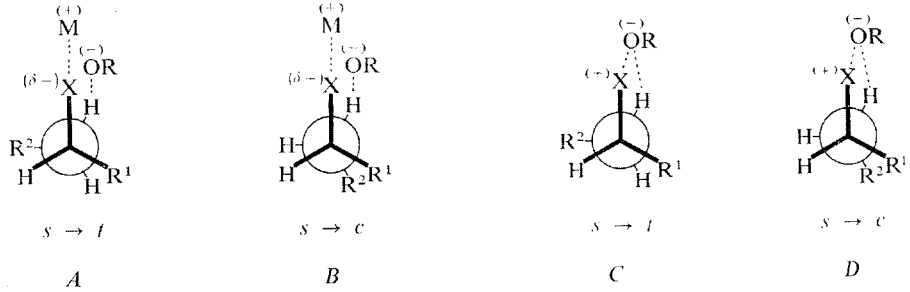
SCHEME 4

Let us examine next the effect of solvent and base on the *syn-anti* competition. As the Table V shows, an increase of the *syn*-proportion results invariantly from changing the very polar solvent dimethyl sulphoxide for the non-polar solvent benzene. Significantly, however, the increase is much greater (5–6 fold) in reaction of the neutral derivatives (*I*; X = F, Cl, Br, OTs), where, as we have already pointed

* For *I* (X = OTs), a higher propensity towards *syn*-elimination would be expected on basis of the correlations. However, difficulties with placing tosyloxy derivatives into the variable E2 transition state scale were noted also by other workers. The explanation proposed by Hoffmann[34] in terms of "near-paradox of Elcb-like eliminations" may be closely relevant to the present problem.

out, the change of solvent is accompanied by a change (dissociated → associated) of the participating base. In elimination of the quaternary derivative *I* (X = $= \overset{(+)}{N}(CH_3)_3$) where the dissociated base prevails in both the extreme solvents, the increase of the *syn*-proportion is only slight. It follows therefore that the change of base rather than that of solvent must play the major role in the examined effect.

Several modes of interactions between base and reactant have to be considered in explanation of the effect. First, as we already pointed out, electrostatic interactions[38] between base and leaving group have to be taken into account. Attractive interactions are expected between potassium counterion of the associated tert-butoxide form and a neutral leaving group with unshared electron pairs, and also between the dissociated base and a positively charged group. On the other hand, repulsive interactions may be expected between the dissociated tert-butoxide form and the leaving groups with unshared electron pairs. For simple geometric reasons, the interactions must be more important in transition states for *syn*- than for the *anti*-pathway. Accordingly, a promotion of the *syn*-pathway by the attractive interactions is expected (Scheme 5*A*, *B*) in reaction of the neutral derivatives *I* (X = F, Cl, Br, OTs) with the associated base form (in benzene) whereas a suppresion of this pathway by repulsive interactions should result for the derivatives in reaction with the dissociated base form in dimethyl sulphoxide, in agreement with the data in Table V. For the quaternary derivative *I* ($X = \overset{(+)}{N}(CH_3)_3$), attractive interactions involving dissociated base should occur (Scheme 5*C*, *D*) in benzene and also in dimethyl sulphoxide and no marked difference between the two extreme solvents should be found, also in accord with Table V.



SCHEME 5

Next, steric (repulsive) interactions between base and the alkyl portion of reactants must be considered. While the dissociated base form usually does not interfere sterically with the reactant, the associated form is expected to interfere[10,38] in the reaction. Because the interactions with alkyls have to be more severe in the sterically more exposed *anti*-pathway, the *syn*-pathway may profit thereby in the competition.

At last, different basicities of the alternative base forms should be taken into account. It has been predicted by Thornton[39,40] and also by Saunders[29] that increase in the C_β—H stretching will ensue in E2 transition state from decreasing the base strength. Accordingly, a shift towards E1cb-like transition state might be expected to occur on going from the dissociated (stronger) tert-butoxide base to the associated (weaker) base form. As we suggested in examining the leaving group effect, such a shift would favour the *syn*-pathway in the competition, in an apparent agreement with the Table V. However, contrary to the prediction, Bunnett[41] and Cram[42] and cowerkers argue that increase, rather than decrease, in base strength shifts E2 transition state towards the E1cb-like side. Importantly, we found for elimination of quaternary salts that proportion of *syn*-elimination increases, significantly, with increasing strenght[36,37] of the participating (presumably dissociated) base, in agreement with the latter suggestion. In this way, it appears to be more justifiable to expect that relative basicities of the alternative tert-butoxide forms act, in actual fact, against the observed trend. Then, the other (aforementioned) factors have to outweight the effect of base strength.

The Effect of Leaving Group and Base Association on the Stereoselectivity in the Competing Pathways

The value of the ratios in which *cis*- and *trans*-isomers arise in bimolecular elimination may serve as a valuable probe in examining the effect of leaving group and base on the transition state geometry. In the present reactions, the ratios for the individual mechanistic pathways are obtained by a simple calculation[12] from the data of Tables II and V. Striking difference are immediately apparent from the Table VI. In the *syn*-pathway, the values of the *trans*/*cis* ratios are invariantly higher than unity. In the *anti*-pathway, on the other hand, the corresponding values are lower than unity in six of the ten reactions examined. The conformational analysis of bimolecular elimination conducted in terms of steric interactions between the adjacent C_α—R and C_β—R alkyl groups predicts that the values of *trans*/*cis* ratios will be greater than unity both in the *anti*- and in the *syn*-pathway. In this way, the *syn*--pathway in our reactions exhibits a "normal" pattern of elimination behaviour and will be therefore examined first.

As Table VI shows for the *syn*-pathway, a qualitatively similar variation of the values is found in both the extreme solvents which suggests that properties of solvent and/or base are in this respect only of a minor importance. Whereas the values for dimethyl sulphoxide may be subject to a considerable experimental error (the *syn*-contributions are in most cases very small; *cf.* Table V), a significant trend is found in benzene. A pronounced increase of the values of the *trans*/*cis* ratios results from changing leaving group in order $OTs < Br < Cl < F < \overset{(+)}{N}(CH_3)_3$, which parallels exactly with the increasing proportion of the *syn*-pathway in the overall reaction

(Table V). We assume that both the trends are of the same origin and reflect a gradual shift in the variable E2-transition state scale towards the E1cb-like side (Scheme 3).

For the *syn*-pathway, a preference in the *trans*- over the *cis*-isomer formation by a factor 3–5 may be expected from relative stabilities of the isomers[12] in a product-like (central) transition state, which agrees well with the values 3·4 and 6·7 found in benzene for the most easily departing leaving groups (X = OTs and Br, respectively). In the reactant (E1cb)-like transition state for the *syn*-pathway, the preference is estimated[43], from energy barriers in butane, to lie between 1·0–2·7 kcal mol^{-1}, which would correspond to *trans*/*cis* ratios 4–50. The ratios now found for the very poor fluoro- and trimethylammonio-leaving groups (21 and 45, respectively) lend a support to the higher estimate.

In the *anti*-pathway, a corresponding shift in the E2-central-E1cb-like transition state scale presumably also occurs, but a comparable preference of the *trans*- over the *cis*-isomer (by a factor 3–7) may be expected on theoretical grounds in the 5-decyl system both for the E2-central as well as for the E1cb-like transition state. In this way, the values 3·2–6·7 now found for the *anti*-pathway in dimethyl sulphoxide agree reasonably with the variable E2 transition state theory. In contrast, however, the values which are lower than unity (*i.e.*, for all the derivatives *I* in benzene and for the quaternary compound *I* (X = $\overset{(+)}{N}(CH_3)_3$) also in dimethyl sulphoxide) are in a complete disagreement with the theory. Other factors than interactions between alkyls accordingly have also to be involved in the latter reaction and to be strong enough to overcome the conformational preference.

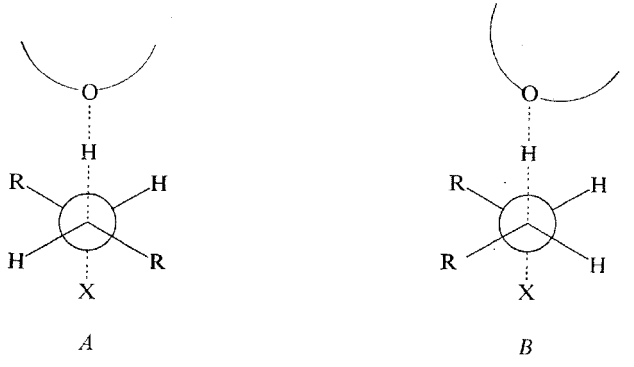
TABLE VI

Stereoselectivities (*trans*/*cis* Olefin Isomer Ratios) in the 5-Decene Formation from the Derivatives *I* (X = $\overset{(+)}{N}(CH_3)_3$, F, Cl, Br, OTs) in Benzene and Dimethyl Sulphoxide

X	Benzene		Dimethyl sulphoxide	
	syn-pathway	*anti*-pathway	*syn*-pathway	*anti*-pathway
$\overset{(+)}{N}(CH_3)_3$	45·7[a]	0·93[a]	62·2[a]	0·28[a]
F	21·5	0·74	2·5	5·1
Cl	7·1	0·48	2·5	6·7
Br	6·7	0·56	≧2·2	6·5
OTs	3·4[a]	0·67[a]	2·0[a,b]	3·2[a,b]

[a] Values from ref.[12]; [b] in dimethylformamide.

Numerous cases of such low *trans*/*cis* ratios have already been found[9,12,29,44–48] in *anti*-elimination. Because the anomaly has been observed originally for compounds with a bulky leaving group (X = OTs, $\overset{(+)}{N}(CH_3)_3$), steric interactions of the leaving group with adjacent alkyls have been invoked to explain[29] the anomaly. However, as the present results show, the anomaly is in benzene a general elimination outcome, entirely independent on the steric bulk of leaving group; accordingly, the steric interactions involved cannot be essential for the anomaly except, perhaps[12,29], for X = $\overset{(+)}{N}(CH_3)_3$).

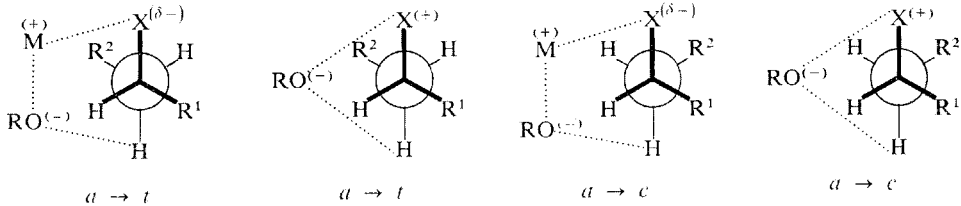


SCHEME 6

Steric bulk of base alone has also been proposed for explanation of the anomaly. Bartsch, from an evidence[9] that low *trans*/*cis* ratios result always in reaction of 2-alkyl bromides and tosylates with the associated tert-butoxide form, but never in the reaction with the dissociated base, reached to the conclusion[10] that severe steric interactions have to exist between the very large associated base (in contrast to the dissociated form) and alkyl portion of the reactant and to be responsible for the anomaly. According to Bartsch's proposal[10] (Scheme 6), the steric destabilization is greater in the transition state for *trans*-isomer formation (*A*) than in that for the *cis*-isomer formation (*B*), because in the latter "the base can be tilted to that side of the developing double bond where only base-hydrogen interactions occur".

Although the Bartsch's explanation would account very well for majority of the results in the Table VI (for *I*; X = F, Cl, Br, OTs) we hesitate to accept it on the following grounds. First, the explanation fails to explain why the sterically less demanding dissociated tert-butoxide base (or methoxide and hydroxide, as well[12]) does suffice to cause the anomaly in reaction with the quaternary (charged) analogues (*e.g.* *I*; X = $\overset{(+)}{N}(CH_3)_3$ in Table VI). Next, on the other side, the explanation fails to explain why neither of the sterically "outsized" dissociated bases so far examined does produce the anomaly in reaction of the derivatives with a neutral leaving

group. Recent results show[49,50], in actual fact, that increasing of steric bulk of dissociated alkoxide base up to the utmost limits of synthetic feasibility does not lead to a decrease but rather to an increase of the values of *trans/cis* ratios in the reaction.



SCHEME 7

Together with Schlosser we proposed another model[38] of base-reactant interactions which is capable to explain why different base forms produce the *trans/cis* anomaly in the elimination of the neutral and the quaternary reactants. From recognition that the low *trans/cis* ratios are found specifically for such base-reactant combinations where attraction may result from interaction between base and leaving group of the reactant (*i.e.*, associated base *vs* neutral group with unshared electron pairs, or dissociated base *vs* positively charged group), we inferred that the attraction may be actually involved in these reactions and induce, eventually in the *anti*-pathway, a non-linear approach of the base to the C_β—H bond (Scheme 7). In a non-linear transition state for *trans*-olefin formation (*A*, *B*) steric interference between base and the alkyl C_α—R (or C_β—R) has to be much stronger than it would be in the linear transition state (Scheme 6*A*); however, in the *cis*-isomer formation the interactions are completely avoided by approaching the base from the unshielded side (Scheme 7*C*, *D*).

In the *syn*-pathway, attraction between base and leaving group does not necessitate the non-linear approach (Scheme 5) and interference between base and alkyls accordingly is not expected to become important.

Non-Linear Approach of Base and Magnitude of Deuterium Isotope Effects in anti-*Elimination*

Recently, our proposal was questioned by Saunders[51] on grounds of theory of isotope effects. From comparison of theoretical primary deuterium effects, k_H/k_D, calculated for the non-linear transition states, with the values experimentally found in usual

anti-eliminations, the author reached to the conclusion: "In summary, transition state models for *anti*-elimination with the extent of non-linearity of the B—H—C system proposed by Závada and coworkers cannot be made consistent with observed isotope effects unless one assumes that the total bonding to the β-proton is less than half of a normal covalent bond. It seems unlikely that so much bond energy would be sacrificed, so that the models can be probably rejected."

However, we have not overlooked, and we noted it in the proposal, that differences may exist between the predicted and experimental values. Still, it is our contention that the isotope effects which have been observed so far in the reaction are not in variance with our proposal. The objections raised by Saunders make it worthwhile to explain our standpoint in full.

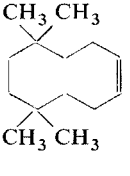
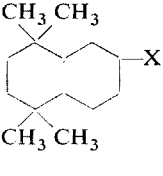
We postulate that attractive interactions between base and leaving group induce a non-linear transition state in a specified group of reactions yielding anomalously low *trans*/*cis* olefin ratios. This by no means implies that we claim a general occurrence of the non-linearity in *anti*-elimination, or that we insist, for the specified category, on the extreme extent of non-linearity as it is visualized in the Scheme 7. On the contrary, it is in line with our reasoning that a deviation from linearity involves a distinct energetic loss. We expect accordingly non-linear transition states only in situations where the attractive interactions or other factors (*e.g.*, C-nucleophilicity in E2C reactions[52]) are involved and may compensate the loss. Even, if strong attractive interactions are involved, non-linearity of transition state need not necessarily be attained, or may be attained only to a smaller extent, for, the geometry of transition state results from a concert of different factors and only sometimes the attractive interactions are allowed to play the prime part. No general agreement between isotope effects observed in *anti*-elimination and those predicted for non-linear transition states can be therefore expected from our proposal, or, to be required for it. Only in the situations, where the *trans*/*cis* anomaly is actually produced, some correlation may be justifiably sought.

As all available experience shows, the anomalously low *trans*/*cis* ratios are encountered almost exceptionless under circumstances where several mechanistic pathways participate in the reaction. This, obviously, renders evaluation of "true" isotope effects for any individual pathway very difficult. Particularly in *trans*-isomer formation, the dichotomy of stereochemical pathways (*syn-anti*) and/or the dichotomy of base (associated or dissociated form) obscures seriously mechanistic significance of the observed isotope effect. In *cis*-isomer formation, however, the complications are presumably less pronounced and the observed isotope effects may be credited, with a due reservation, to have some significance. In several instances[53–55], the values of k_H/k_D for *cis*-olefin formation have been reported in literature. Other values can be provided by evaluation the effect from reported[29,30] data on isomer olefin distribution resulting respectively from appropriately (*threo*-)deuterium labelled and from the unlabelled reactant. It may be seen from the Table VII that none of the

eighteen summarized values of k_H/k_D exceeds significantly the upper theoretical[56] limit (3·9) for the non-linear transition state with the 120° B—H—C angle. Nine of the experimental values lie below the lower theoretical limit (3·0) predicted by O'Ferrall[56] for such a deviation: four of them are clustered between 1·8 – 2·2, which would correspond to the theoretical values 1·4 – 2·3 expected[51,56] for the transition state with 90° deviation from linearity (*cf.* Scheme 7*A*, *C*). It follows therefore clearly from the data that none series discord exists between our proposal and isotope

TABLE VII

Apparent Isotope Effects for *cis*-Olefin Formation from the Reactions where Non-Linear Approach of Base is Expected

cis-Olefin[a]	Reactant	Conditions[b]	k_H/k_D[c]	Ref.
$CH_3CH{=}CHCH_3$	$CH_3CHBrC_2H_5$	tert-C_4H_9OK	3·8	55
$C_2H_5CH{=}CHC_2H_5$	$C_2H_5CHFC_3H_7$	tert-C_4H_9OK	2·1	30
$C_2H_5CH{=}CHC_2H_5$	$C_2H_5\overset{(+)}{C}H(N(CH_3)_3)C_3H_7$	NaOH	2·8	29
		NaOH[d]	3·6	29
		CH_3OK	3·7	29
		n-C_4H_9OK	4·0	29
		tert-C_4H_9OK	2·9	29
		pyrolysis	2·9	29
$CH_3CH{=}CHC_3H_7$	$CH_3\overset{(+)}{C}H(N(CH_3)_3)C_4H_9$	NaOH	2·8	29
		n-C_4H_9OK	3·4	29
		tert-$C_5H_{11}OK$	3·9	29
		pyrolysis	2·9	29
t-$C_4H_9CH_2CH{=}CHC_4H_9$	t-$C_4H_9CH_2CHOTsC_5H_{11}$	tert-C_4H_9OK	2·2	48
		tert-C_4H_9OK[e]	3·3	48
t-$C_4H_9CH_2CH{=}CHC_4H_9$	t-$C_4H_9CH_2\overset{(+)}{C}H(N(CH_3)_3)C_5H_{11}$	CH_3OK	3·6	48
	 X = OTs	tert-C_4H_9OK	1·9	53
	X = OTs	tert-C_4H_9OK[e]	1·8	53
	X = $\overset{(+)}{N}(CH_3)_3$	CH_3OK	3·6	54

[a] Reported cases where proportions of the *cis*-isomer were exceedingly low (<2%) were omitted from the Table; [b] the solvent was the conjugate acid of the base, unless otherwise indicated; [c] calculated by standard procedure[53] from isomer-olefin distribution in the labelled (*threo*) and in the unlabelled derivative; [d] in aqueous dimethyl sulphoxide; [e] in benzene.

effects when a wider* scale of transition states with varying extent of non-linearity is taken into account.

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* *Note added in proof*: As Prof. W. H. Saunders correctly pointed out, the data of Table VII were determined at higher temperatures than it was assumed for the theoretical calculation (25°C) and correction should be therefore made by using the Arrhenius equation: $k_H/k_D = A_H/A_D \exp(\Delta E_a/RT)$. Unfortunately, the correction depends critically on the choice of the value of A_H/A_D. Theoretically, the coefficient is expected to lie between 0·5—1·4, however, experiments show that it may be even lower. If the upper limit is applied in the correction, our conclusion remains essentially unaffected. If the lower limits are used, we obtain values of k_H/k_D which are close to, or are higher than the theoretical maximum for a linear transition state, which might suggest tunneling. It should be stressed that even very high values of k_H/k_D would be compatible with non-linearity of transition state in presence of tunneling.

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