Using secondary alpha deuterium kinetic isotope effects to determine the stereochemistry of an E2 reaction; the stereochemistry of the E2 reaction of 1-chloro-2-phenylethane with potassium *tert*-butoxide in *tert*-butyl alcohol

Peter James Smith, David A.J. Crowe, and Kenneth Charles Westaway

Abstract: Isotopic labelling studies have shown that the E2 reaction of 1-chloro-2-phenylethane with potassium *tert*-butoxide in *tert*-butyl alcohol occurs via an anti-periplanar stereochemistry. This demonstrates that the different secondary alpha deuterium kinetic isotope effects found for the high and low base concentrations and in the presence of 18-crown-6 ether are because of changes in transition state structure that occur when the form of the reacting base changes rather than to a change in the stereochemistry of the reaction.

Key words: E2 reaction, stereochemistry, secondary alpha deuterium kinetic isotope effects, transition state.

Résumé : Des études de marquage isotopique ont permis de démontrer que la réaction E2 du 1-chloro-2-phényléthane avec *tert*-butylate de potassium dans l'alcool *tert*-butylique se produit avec une stéréochimie antipériplanaire. Cette observation démontre que les divers effets isotopiques cinétiques secondaires du deutérium en alpha qui ont été observés à des concentrations élevées et faibles de base et en présence de l'éther 6-couronne-18 sont dus à des changements dans la structure de l'état de transition qui se produisent lorsqu'il se produit un changement dans la forme de la base qui réagit plutôt que la stéréochimie de la réaction.

Mots clés : réaction E2, stéréochimie, effets isotopiques cinétiques secondaires du deutérium en alpha, état de transition.

[Traduit par la Rédaction]

Introduction

The stereochemistry of E2 elimination reactions has been investigated for some time (1–5). An E2 reaction can occur with an anti-periplanar (the dihedral angle between the abstracted β-hydrogen and the leaving group is 180°, Fig. l*a*) or a syn-periplanar (the dihedral angle between the leaving group and abstracted β-hydrogen is 0°, Fig. l*b*) stereochemistry. Although theoretical calculations (3, 6) indicate that the anti-periplanar stereochemistry is favoured, not all E2 reactions follow the anti-periplanar pathway. For example, syn-periplanar E2 reactions are observed in rigid cyclic systems where a β-hydrogen and the leaving group are coplanar (2, 7). Syn-periplanar E2 eliminations are also observed when the less rigid, but rotationally restricted, 1,2-dihaloacenaphthalenes (8) and 2,3-dihalo-2,3-dihydrobenzofurans (9) react with alkoxide ions.

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P.J. Smith and D.A.J. Crowe. Department of Chemistry, University of Saskatchewan, Saskatoon, SK S7N 0W0, Canada. **K.C. Westaway.**[1] Department of Chemistry and Biochemistry, Laurentian University, Sudbury, ON P3E 2C6, Canada.

[1]Corresponding author (fax: (705) 675-4844; e-mail: kwestawa@nickel.laurentian.ca).

Changes in the form of the abstracting base can also affect the stereochemistry of an E2 reaction. Bartsch and Zavada (5) state that alkoxide ions exist as dissociated ions, ion pairs, several different complex ions, or ion-pair aggregates connected by a series of equilibria (eq. [1]).

The amount of association increases as (*i*) the cation is made smaller, i.e., going from cesium to lithium; (*ii*) the alkoxide ion is made larger, i.e., the base is changed from methoxide ion to *tert*-butoxide ion; and (*iii*) when a less polar solvent is used and the strength of the base is increased, e.g., the solvent is changed from ethanol to *tert*-butyl alcohol (10–12). Surprisingly, 18-crown-6 ether does not affect the degree of association (13), although a 1:1 K^+–18-crown-6 ether complex does form in potassium *tert*-butoxide – *tert*-butyl alcohol (l4). Zavada et al. (15) found a greater percentage of syn-periplanar dehydrohalogenation of 5-decyl halides with the associated base (potassium *tert*-butoxide in benzene) than when the base was the dissociated ion (potassium *tert*-butoxide in *tert*-butyl alcohol). Bartsch and Lee (2) also found the amount of syn-elimination from *endo*-2-bicyclo[2.2.1]heptyl bromide and 2,4,6-triisopropylbenzenesulfonate was significantly higher with the associated base (potassium *tert*-butoxide in triglyme) than when 18-crown-6 ether was present. The higher proportion of syn-elimination with the associated base may occur because the counter ion in the associated base stabilizes the partial charge on the leaving group in the syn-periplanar E2 transition state (Fig. 2).

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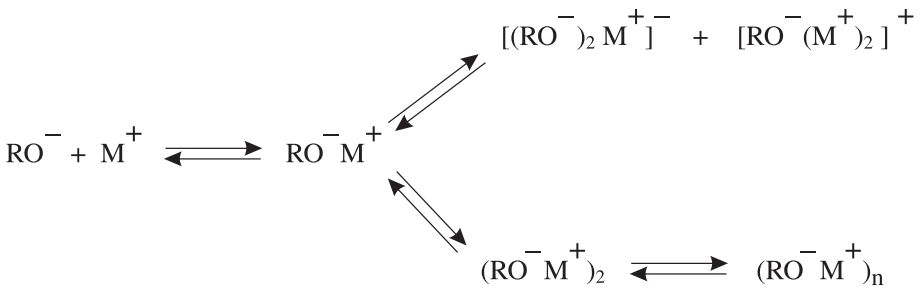
[1] 

Zavada et al. (15) also reported that the amount of syn-elimination increased as the electronegativity of the leaving group increased from bromo to fluoro in the E2 reactions of 5-decyl halides. Several workers (16–18) have suggested that Elcb-like E2 reactions (with poor leaving groups) occur with the syn-periplanar stereochemistry rather than the anti-periplanar stereochemistry that is found for E2 reactions, which have good leaving groups and central transition states.

Smith and Westaway (19) reported that the syn-periplanar E2 elimination from 2-phenylethyldimethylamine oxide had a large secondary alpha deuterium kinetic isotope effect of 1.34, whereas a small secondary alpha deuterium kinetic isotope effect of 1.02 was found for the anti-periplanar E2 reaction of 2-phenylethyltrimethylammonium ion with ethoxide ion in ethanol. Although both reactions had extensive C_β–H and C_α–N bond rupture in their transition states, there is obviously a very different amount of C=C bond formation in the two transition states, i.e., large in the anti-periplanar transition state and small in the syn-periplanar transition state. This led to the suggestion that one might be able to use the magnitude of the secondary alpha deuterium isotope effect to determine the stereochemistry of the E2 elimination reaction. Recently, different secondary alpha deuterium kinetic isotope effects have been found when different concentrations of base (potassium *tert*-butoxide in *tert*-butyl alcohol) were used in the E2 reaction of 1-chloro-2-phenylethane. The different isotope effects could arise because (*i*) the structure of the E2 transition state changes and (or) (*ii*) because the stereochemistry of the reaction changes when different concentrations of base (different bases) are used. This study was undertaken to determine whether the change in the secondary alpha deuterium isotope effect was due to a change in the stereochemistry of the E2 reaction between 1-chloro-2-phenylethane and *tert*-butoxide ion.

Results and discussion

The secondary alpha deuterium kinetic isotope effects observed for the E2 reaction of 1-chloro-2-phenylethane at different base (potassium *tert*-butoxide in *tert*-butyl alcohol) concentrations (eq. [2]) are presented in Table 1. The results show that a smaller secondary alpha deuterium isotope effect of 1.032 ± 0.004 is found for the 1-chloro-2-phenylethane E2 reaction at low base concentrations (between 0.036 and 0.228 M), while a larger isotope effect of 1.050 ± 0.005 is observed at higher concentrations of base (>0.36 M) and at low base concentrations in the presence of 18-crown-6 ether.[2] The 1-chloro-2-phenylethane at low base concentrations were thought to react via the normal anti-periplanar stereochemistry. The larger secondary alpha deuterium kinetic isotope effects found for the E2 reaction of 1-chloro-2-phenylethane at high base concentrations and in the presence of the crown ether could be observed because (*i*) the stereochemistry of the reaction changed to syn-periplanar and (or) (*ii*) the transition state structure changes when the form of the abstracting base changes. At low concentrations of base and in the presence of 18-crown-6 ether, the abstracting base is undoubtedly the free ion. At high concentrations of base, the abstracting base would be one or more of the ion pair, the triple ion, or an ion aggregate. Changing the form of the abstracting base could alter the stereochemistry of the E2 reaction (Fig. 1) and (or) cause a change in the structure of the transition state altering the magnitude of the alpha deuterium kinetic isotope effect. This study was undertaken to determine if the change in the secondary alpha deuterium kinetic isotope effect was due to a change in the stereochemistry of the E2 reaction or due to a change in the structure of the E2 transition state.

The diastereomers of 1-chloro-2-phenyl-1,2-d_2 ethane were synthesized via the scheme shown in Fig. 3. An NMR analysis of the β-bromostyrene showed that the starting material for the synthesis consisted of 75% of the (*E*)-isomer and 25% of the (*Z*)-isomer. A spinning-band distillation of the β-bromostyrene gave samples of isomeric purity ranging from 75 to 88% of the (*E*)-isomer. However, it was not possible to obtain a pure sample of the (*E*)-isomer, so the synthesis was carried out on three different mixtures of β-bromostyrene isomers. These stereospecific syntheses led to the *threo*-(*RS*,*SR*) and *erthyro*-(*SR*,*RS*) 1-chloro-2-phenyl-1,2-d_2 ethanes. The *threo* diastereomers were formed from the (*E*)-isomer of the β-bromostyrene and the *erythro* diastereomers from the (*Z*)-isomer of β-bromostyrene. These mixtures of diastereomers were reacted at both low and high concentrations of base, i.e., where the different secondary al-

[2] $$C_6H_5CH_2CL_2\text{-}Cl + (CH_3)_3CO^- \xrightarrow{(CH_3)_3COH} C_6H_5CH{=}CL_2 + (CH_3)_3COH + Cl^-$$

$$L = H, D$$

[2] A student t-test showed that the secondary alpha deuterium kinetic isotope effects at "high base" concentrations and in the presence of 18-crown-6 ether are different from those at the "low base" concentrations at the 99% confidence level.

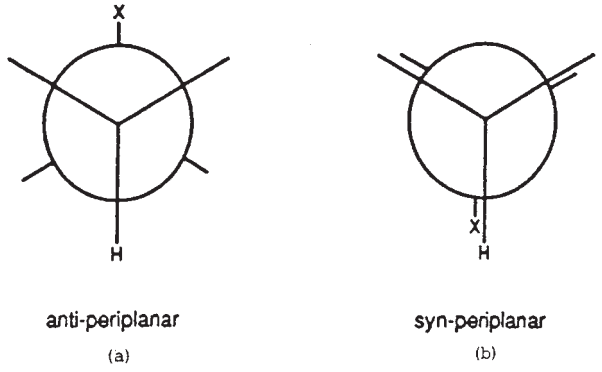
Table 1. The secondary alpha deuterium kinetic isotope effects for the E2 reaction between 1-chloro-2-phenylethane or 1-chloro-2-phenyl-1,1-d_2 ethane and potassium *tert*-butoxide in *tert*-butyl alcohol at 40°C.

[Base] (M)	[18-C-6] (M)	$(k_H/k_D)_\alpha$
0.0364		1.026 ± 0.016[a]
0.0736		1.029 ± 0.005
0.0736		1.034 ± 0.009
0.0832		1.035 ± 0.011
0.100		1.035 ± 0.009
0.2284		1.032 ± 0.009
Avg.		1.032 ± 0.004[b]
0.3640		1.044 ± 0.009
0.3860		1.055 ± 0.006
Avg.		1.050 ± 0.008[b]
0.0118	0.01311	1.056 ± 0.014
0.00662	0.006482	1.047 ± 0.018
0.00627	0.00690	1.047 ± 0.010
Avg.		1.050 ± 0.005[b]

[a]The error in the isotope effects is $1/k_D[(\Delta k_H)^2 + (k_H/k_D)^2 \times (\Delta k_D)^2]^{1/2}$, where Δk_H and Δk_D are the standard deviations for the average rate constants for the reactions of the nondeuterated and deuterated substrates, respectively.

[b]Standard deviation. The student t-test indicated that the secondary alpha deuterium kinetic isotope effects at "high base" concentrations and in the presence of 18-crown-6 are different from those at "low base" concentrations at the 99% confidence level.

Fig. 1. The anti-periplanar (*a*) and syn-perplanar (*b*) stereochemistry for an E2 reaction.



pha deuterium kinetic isotope effects were observed. All the possible E2 products, formed when the different diastereomers of the 1-chloro-2-phenyl-1,2-d_2 ethanes react with *tert*-butoxide ion in *tert*-butyl alcohol, are presented in Fig. 4. The *threo* diastereomers produce compounds I and II when the elimination occurs via the anti-periplanar stereochemistry, whereas compounds III and IV would be formed if the elimination occurred via the syn-periplanar stereochemistry. The *erythro* compounds on the other hand, form products III and IV when the elimination occurs with an anti-periplanar stereochemistry and compounds I and II when it occurs by the syn-periplanar pathway. Thus, if the E2 reaction occurs only via the anti-periplanar pathway, the %(I + II) and the %(III + IV) should be the same as the %(*E*)-isomer and the %(*Z*)-isomer, respectively, in the starting material, i.e., all of

Fig. 2. A syn-periplanar E2 reaction with the counter ion in the ion-pair assisting the removal of the leaving group.

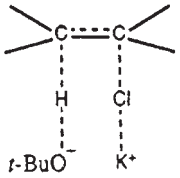
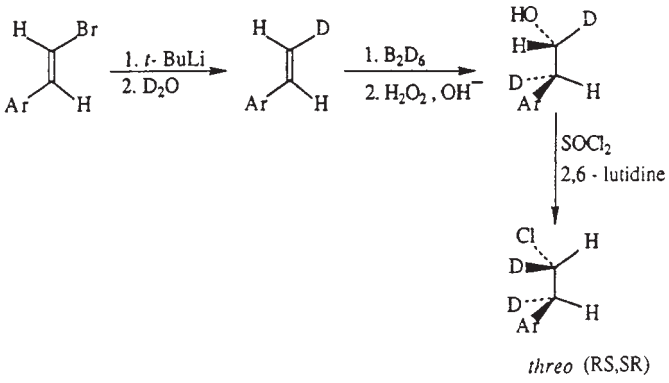


Fig. 3. The stereospecific synthesis of the 1-chloro-2-phenylethane diastereomers.

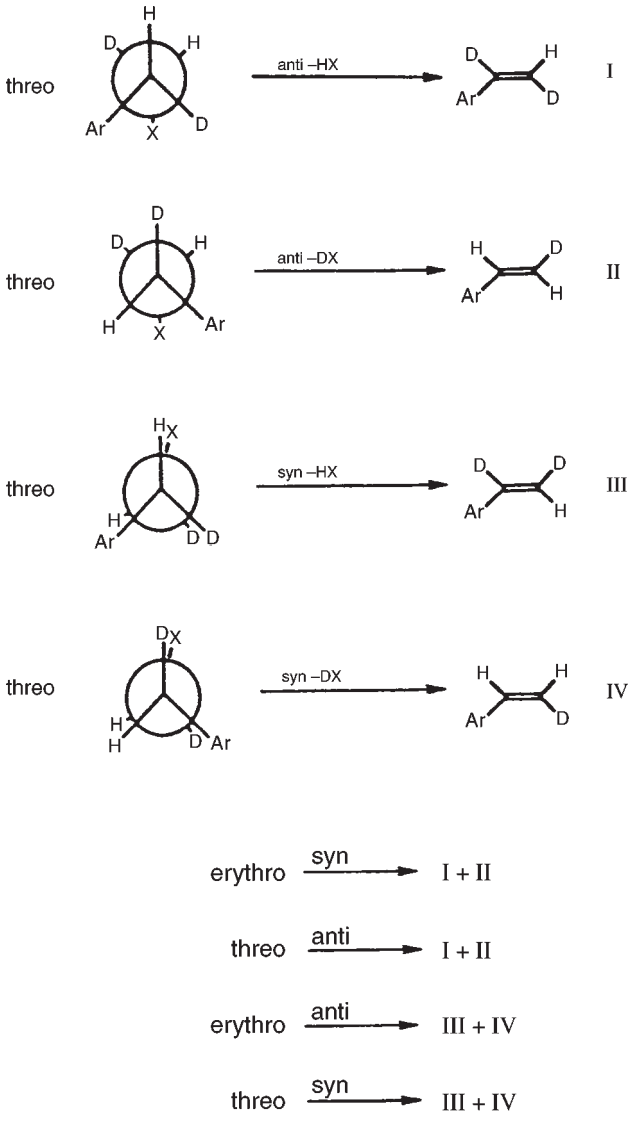


the *threo* isomer (made from the (*E*)-isomer in the synthesis) will form products I and II while the *erthyro* isomers (made from the (*Z*)-isomer in the synthesis) will form products III and IV. If the elimination occurs by the syn-periplanar pathway, the %(I + II) and the %(III + IV) should be opposite the %(*E*)-isomer and the %(*Z*)-isomer, respectively, in the starting material, i.e., the *threo* isomer will only form III and IV while the *erthyro* isomer will produce only I and II. Finally, if the stereochemistry of the elimination reaction is partly syn- and partly anti-, the %(I + II) and the %(III + IV) will be intermediate between the above values.

The stereochemistry of the E2 reactions of the 1-chloro-2-phenyl-1,2-d_2 ethane diastereomers was determined by isolating the products and analyzing them by NMR spectroscopy. The chemical shifts and coupling constants for all of the possible products formed from a syn- and an anti-periplanar elimination are shown in Table 2. The %(I + II) and the %(III + IV) obtained when the 1-chloro-2-phenyl-1,2-d_2 ethane diastereomers were reacted with potassium *tert*-butoxide in *tert*-butyl alcohol concentrations ranging from 0.062–0.23 M (where the secondary alpha deuterium kinetic isotope effect was 1.032) and ranging from 0.36–0.39 M (where the isotope effect was 1.050) are presented in Table 3. The %(I + II) and the %(III + IV) are, within experimental error, identical to the %(*E*)- and %(*Z*)-isomers, respectively, in the starting material in every case. This clearly indicates that (*i*) the E2 reaction of of 1-chloro-2-phenylethane occurs 100% via the anti-periplanar pathway at all concentrations of *tert*-butoxide ion and (*ii*) the change in the secondary alpha deuterium kinetic isotope effect is not due to a change in the stereochemistry of the reaction but must be due to a change in the structure of the E2 transition state.

It is worth noting that the method of determining the stereochemistry of the E2 reactions was tested by reacting

Fig. 4. The E2 products formed from anti- and syn-periplanar elimination of the possible deuterated 1-chloro-2-phenylethane diastereomers.



the 1-chloro-2-phenyl-1,2-d_2 ethane with ethoxide ion in ethanol. These reactions were investigated because they were expected to react via an anti-periplanar stereochemistry. This stereochemistry was expected because (*i*) the substrates are acyclic (3, 6); (*ii*) ion pairing is much less likely in the more polar solvent ethanol than in *tert*-butyl alcohol (10); and (*iii*) because the leaving group in these reactions is at least as good as the trimethylammonium leaving group (16, 18) Bourns and Frosst (20) used to demonstrate that the E2 reaction of 2-phenylethyltrimethylammonium bromide with ethoxide ion in ethanol occurred with an anti-periplanar stereochemistry. The %(I + II) and the %(III + IV) was identical, within experimental error, to the %(*E*)- and the %(*Z*)-isomers, respectively, in the starting material. Thus, the results indicate that this E2 reaction in ethoxide ion and ethanol proceeds with an anti-periplanar stereochemistry and confirm that the stereochemical test is valid.

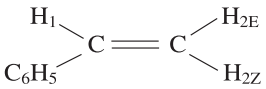
The results clearly show that the E2 reaction of 1-chloro-2-phenylethane with *tert*-butoxide ion in *tert*-butyl alcohol occurs with an anti-periplanar stereochemistry. Therefore, the different secondary alpha deuterium kinetic isotope effects found at different concentrations of base are not due to a change in stereochemistry, but reflect differences in the structure of the E2 transition state. It is also obvious that the change in the secondary alpha deuterium kinetic isotope effect (transition state structure) must result from changes in the form of the reacting base.

Although the reactive form of the base might be the triple ion or an ion pair aggregate at the highest potassium *tert*-butoxide concentrations (0.3–0.4 M) used in this study, it seems more likely, for two reasons, that the ion pair or a solvated ion pair is the reacting base. Zavada and co-workers (13) reported that the ion pair is the dominant form of the base in 0.1–0.5 M potassium *tert*-butoxide–*tert*-butyl alcohol. This, coupled with the first order dependance of the rate on *tert*-butoxide ion, suggests that the ion pair is the reacting base when the base concentration is 0.3–0.4 M and the larger secondary alpha deuterium kinetic isotope effect is observed.

Conversely, at low base concentrations (<0.23 M) in the absence of 18-crown-6 ether, the reacting base is almost certainly the free ion. However, it seems likely that the reaction does not occur via a simple E2 mechanism under these conditions. Zavada et al. (4) demonstrated that 5-decyl bromide reacts with potassium *tert*-butoxide in *tert*-butyl alcohol by two competing mechanisms; a simple E2 reaction and a reaction where a *free* (dissociated) K^+ ion complexes with the leaving group and provides electrophilic catalysis for its removal (Fig. 5). The reaction was first order in base indicating that the complexing reaction was kinetically indistinguishable from the uncomplexed reaction (21). If the complexing mechanism is operative at low base concentrations, the reaction occurs with a stronger base (the negative charge on the oxygen of the *free tert*-butoxide ion would be greater than that on the oxygen of the ion pair, the reactant at high base concentrations). Also, the low base concentration reaction with the free *tert*-butoxide ion has a better leaving group (the complexed chloride ion leaving group would be a weaker base than the uncomplexed chloride ion). The More O'Ferrall energy surface diagram predicts (*i*) that changing to a better leaving group would not change the amount of C_α–X bond rupture in the transition state but that (*ii*) changing to a stronger base would lead to an E2 transition state with less C_α–X bond rupture. The net effect of these two changes in the reactants should lead to a transition state with less C_α–X bond rupture. This would produce the smaller secondary alpha deuterium kinetic isotope effect that is observed.

Finally, the larger secondary alpha deuterium kinetic isotope effect in the reaction with the crown ether at low base concentrations, suggests that C_α–X bond rupture is more advanced in the transition state when 18-crown-6 ether is used. 18-Crown-6 ether forms a 1:1 complex with potassium ions (13). This means the potassium ion is no longer available to assist in the removal of the leaving group, i.e., that there is a poorer leaving group. Since the More O'Ferrall energy surface diagram suggests that changing to a poorer leaving group leads to a transition state with a longer C_α–X bond, a

Table 2. The NMR spectra of the possible E2 products from (*RS,SR*) *threo*-1-chloro-2-phenyl-1,2-d_2 ethane.



	Chemical shifts (ppm)			Coupling constants (Hz)	
Compound	H_1	H_{2E}	H_{2Z}	$H_{1,2E}$	$H_{1,2Z}$
(*Z*)-Styrene-1,2-d_2 (I)		5.22 (t)		1.7	
(*E*)-Styrene-2-*d* (II)	6.71		5.74 (d)		17.4
(E)-Styrene-1,2-d_2 (III)			5.73 (t)		2.8
(*Z*)-Styrene-2-*d* (IV)	6.71	5.23 (d)		11.0	

Table 3. The product distribution of the E2 reaction between 1-chloro-2-phenyl-1,2-d_2 ethane and potassium *tert*-butoxide in *tert*-butyl alcohol at 40°C.

[Base]	Product distribution (%)				Anti-periplanar
(M)	I	II	III	IV	elimination (I + II) (%)
TEST I: the starting material was 77% (*E*), 23% (*Z*)					
0.430	59.4	19.7	16.6	4.3	79[a]
0.310	63.6	13.6	17.4	5.5	77
0.124	64.5	14.0	18.5	3.0	79
0.103	57.1	20.7	18.2	4.0	78
0.062	60.6	15.2	20.6	3.6	76
Avg.					78 ± 1.3[b]
TEST II: the starting material was 83% (*E*), 17% (*Z*)					
1.035	68.1	15.3	11.7	4.8	83[a]
0.124	70.7	12.6	11.1	5.6	83
Avg.					83 ± 0.0[b]
TEST III: the starting material was 88% (*E*), 12% (*Z*)					
0.865	71.8	16.4	6.1	5.7	88[a]
0.0865	71.1	16.4	7.1	5.4	88
Avg.					88 ± 0.0[b]

[a]The rest of the elimination product is the %(III + IV), i.e., 21% for Test I.
[b]Standard deviation.

larger secondary alpha deuterium kinetic isotope effect would be expected in the 18-crown-6 ether reactions. This is, in fact, what is observed.

Conclusion

Obviously, the magnitude of the secondary alpha deuterium kinetic isotope effects cannot be used to determine the stereochemistry of an E2 reaction. Rather, the changes in the secondary alpha deuterium isotope effect in these E2 reactions are due to changes in the structure of the transition state that occur when the form of the reacting base is altered.

Experimental

General

NMR spectra were determined in solution in chloroform-*d* on a Bruker AM300 instrument. All the chemical shifts are reported in ppm from tetramethylsilane. The UV spectra were measured on a Hewlett Packard HP8451A diode array spectrophotometer. An NMR analysis showed that both the 1, 1-d_2, and the 1,2-d_2 1-chloro-2-phenylethanes were 99% deuterated at the appropriate positions.

Preparation of reagents

1-Chloro-2-phenylethane

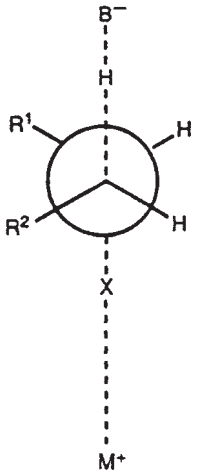
2-Phenylethanol was prepared using the method of Amundsen and Nelson (22). Ethyl phenylacetate (5.9 g, 0.036 mol) in anhyd ether (10 mL) was added slowly to a stirred mixture of lithium aluminum hydride (1.4 g, 0.038 mol) in anhyd ether (60 mL). The mixture was heated at reflux for 7 h and allowed to cool. Sulphuric acid (10%, 50 mL) was added slowly. The organic layer was separated, washed with water, dried over anhyd magnesium sulphate, and the ether removed on a rotary evaporator. The 2-phenylethanol was used in the next step without further purification. ^{1}H NMR δ 7.22–7.38 (m, 5H), 3.86 (t, J = 6.6 Hz, 2H), 2.87 (t, J = 6.6 Hz, 2H), 1.39 (br s, 1H).

The 1-chloro-2-phenylethane was prepared by adding a mixture of 2-phenylethanol (1 g, 0.0082 mol) and 2,6-lutidine (0.9 g, 0.0082 mol) dropwise to a stirred solution of thionyl chloride (1.2 g, 0.010 mol) in toluene (2 mL). Two drops of water were added to break up the solid that formed and the reaction was stirred for 30 min at 40°C. Cold water was added slowly and the toluene separated as an upper layer. The toluene layer was washed successively with water, 10% sodium bicarbonate solution, and water, then dried over anhyd sodium sulphate and the solvent removed on a rotary evaporator. Distillation gave 1.0 g (0.0071 mol, 87%) of 1-chloro-2-phenylethane bp 47–50°C, 1.5 mm Hg (lit. (23) 34°C, 1 mm of Hg). ^{1}H NMR δ 7.20–7.35 (m, 5H), 3.71 (t, J = 7.5 Hz, 2H), 3.06 (t, J = 7.5 Hz, 2H).

1-Chloro-2-phenyl-1,2-d_2 *ethane diastereomers*

*(*E*)-Styrene-*β*-*d*:* (*E*)-Styrene-β-*d* was prepared using the method described by Tao and Saunders (24). (*E*)-β-Bromostyrene (Aldrich) (1.0 g, 5.5 mmol) in dry ether (7 mL) (heated at reflux over and distilled from sodium) was cooled to –78°C and *tert*-butyl lithium in pentane (1.7 M, 4.9 mL) (Aldrich) was added slowly. The mixture was stirred for 30 min at –78°C, then deuterium oxide (>99.9% d_2) (0.22 g, 11 mmol) was added dropwise with stirring. The reaction mixture was warmed to room temperature and water (10 mL) was added. The organic layer was separated and the aqueous layer was extracted once with

Fig. 5. An anti-periplanar E2 elimination from a free *tert*-butoxide ion and a metal-complexed leaving group.



ether. The combined organic layers were dried over anhyd magnesium sulphate and the solvent was removed on a rotary evaporator at room temperature. The crude yield of (*E*)-styrene-β-*d* was 0.56 g (96%). If the product was not used immediately, it was stored as an ether solution to minimize isomerization and (or) polymerization.

NMR spectroscopy showed that the β-bromostyrene consisted of 75% of the (*E*)-isomer, the rest being (Z). Several attempts to separate the isomers were made, spinning-band distillation being the most successful. Several batches of styrene-β-*d* were made, with degrees of isomeric purity ranging from 75 to 88% of the (*E*)-isomer. In each case, the isomeric constitution of the styrene-β-*d* determined by NMR was the same as that of the β-bromostyrene used for the synthesis.

erythro-*2-Phenyl-1,2*-d_2 *ethanol:* The procedure used by Dohner and Saunders (25) was followed. Deuteroborane, generated by the addition of boron trifluoride etherate (4.75 mL, 0.029 mol) to a solution of sodium borodeuteride (>98% d_4) (0.921 g, 0.022 mol) in tetrahydrofuran (200 mL) at 0°C, was added dropwise to (*E*)-styrene-β-*d* (0.56 g, 0.005 mol) in tetrahydrofuran (5 mL) in a 50 mL three-necked round-bottom flask equipped with a nitrogen inlet, a nitrogen outlet, and a dropping funnel. After the reaction mixture had been stirred for 3 h at room temperature, water (0.8 mL), sodium hydroxide (4 mL, 3 M), and hydrogen peroxide (4 mL of a 30% solution) were added. This mixture was stirred for 4 h and then extracted with ether (3 × 30 mL). The combined ether extracts were washed with an aqueous ferrous sulphate solution, then with water, and dried over anhyd magnesium sulphate. Evaporation of the ether and distillation at 49–50°C at 1.5 mm yielded 0.55 g (88%) of the product. ^{1}H NMR δ 7.22–7.38 (m, 5H), 3.84 (d, J = 4.5 Hz, 1H), 2.85 (d, J = 4.5 Hz, 1H), 1.39 (br s, 1H).

threo-*1-Chloro-2-phenyl-1,2*-d_2 *ethane:* This was prepared from *erythro*-2-phenyl-1,2-d_2 ethanol using the method and quantities described for 1-chloro-2-phenylethane.[3] ^{1}H NMR δ 7.20–7.35 (m, 5H), 3.71 (m, 1H), 3.06 (d, 1H). ^{13}C NMR δ 138.0, 128.8, 128.6, 126.9, 44.6 (t, J = 23 Hz), 38.8 (t, J = 20 Hz).

Potassium tert-*butoxide in* tert-*butyl alcohol*

tert-Butyl alcohol was dried over 3 Å molecular sieve beads for at least 24 h, then refluxed over and distilled from powdered 3 Å molecular sieves under a dry nitrogen atmosphere (26). Sufficient potassium (typically, 8 g of potassium in 1 to 2 g chunks) was added to dry *tert*-butyl alcohol (200 mL) through which dry, high purity nitrogen was being bubbled. The mixture was left until all the potassium had reacted. The base solution was stored under dry nitrogen in the refrigerator and aliquots were removed under dry nitrogen and diluted with dry *tert*-butyl alcohol for kinetic studies. When the base had been diluted for kinetic studies, its concentration was determined by titrating it in CO_2-free distilled water with 0.01 N sulphuric acid (BDH Volumetric) to a bromocresol green endpoint. A blank sample containing only CO_2-free distilled water and indicator normally reached the end point with the first drop of sulphuric acid. Although every attempt was made to keep the potassium *tert*-butoxide solution free of air and water, some of the *tert*-butoxide ion was inevitably destroyed by reaction with water or carbon dioxide. Thus, second order rate constants measured with different batches of the base were not reproducible to better than ±10%.

Kinetic measurements

Two different methods were used. For reactions where the base concentration was 0.01 M or less, the reaction was carried out and monitored in a 1 cm cuvette in the spectrophotometer cell. Because of the significant absorption of *tert*-butoxide ion in the 200–250 nm range at base concentrations >0.01 M, the reactions were carried out in a constant temperature bath and aliquots of the reaction mixture were quenched before measurement of the spectrum. All the rate constants were measured under pseudo first-order conditions with the base being at least twenty times more concentrated than the substrate in the reaction mixture. No attempt was made to control the ionic strength.

Water-bath method

The potassium *tert*-butoxide solution was made by pipetting the required volume of the stock (1 M) base solution into a dry 200 mL volumetric flask and making up the volume with dry *tert*-butyl alcohol. Approximately 22 mL of this solution was transferred into each, of up to seven, 25 mL dry, volumetric reaction vessels fitted with serum caps. The solutions were temperature equilibrated in the constant temperature bath for at least 30 min and filled up to the mark with the base solution. To one of the reaction ves-

[3] A referee expressed concern about the formation of a phenonium ion, which would alter the stereochemistry of this step of the synthesis. This reaction was done in toluene and since phenonium ions have only been found in good ionizing solvents such as HOAc or formic acid, (27) it is difficult to envisage it forming it this reaction. More important, the phenonium ion intermediate can be ruled out because there was no evidence of the rearranged product when this reaction was used in the synthesis of the 1-chloro-2-phenyl-1,1-d_2 ethane that was to measure the secondary alpha deuterium KIE. A referee also questioned the stereochemistry of the chlorosulfite ester reaction. However, March (28) reports that this reaction proceeds with inversion of configuration.

sels was added 1 mL of temperature-equilibrated dry *tert*-butyl alcohol and the solution was titrated to determine the base concentration.

The reactions were started by adding 1 mL of a temperature equilibrated solution of the substrate (approximately 5×10^{-5} M, but accurately known) in dry *tert*-butyl alcohol to the reaction vessel with a calibrated syringe. At intervals of several minutes, 1 mL aliquots of the reaction mixture were withdrawn with a syringe and quenched in 20 mL of the appropriate concentration of hydrochloric acid in distilled 95% ethanol. The quenched aliquot was diluted to 25 mL with 95% ethanol and the UV spectrum was recorded. Best results were obtained by measuring against a reference sample of ethanol or quenching solution, subtracting the absorbance at a point on the baseline of the product spectrum from the absorbance at λ_{max} for the product. Ten aliquots were normally taken from each vessel over two half-lives.

After ten or more half-lives, samples were taken and quenched to obtain a value for the product absorbance when the reaction was complete (OD_∞). The pseudo first-order rate constant was obtained from the slope of the plot of ln ($OD_\infty - OD_t$) vs time (t).

Cuvette method

The base solution was prepared by diluting the stock base solution using the method described above. If required, 18-crown-6 was first weighed into a 50 mL volumetric flask and 3 mL of the base solution were pipetted into each of seven oven dried cuvettes with tightly fitting stoppers. The cuvettes were left in the thermostated cell holder in the spectrophotometer for at least 20 min to allow them to reach thermal equilibrium. One cell was used as the reference. The reactions were started by adding between 5–10 μL of substrate solution (typically 5×10^{-3} M in *tert*-butyl alcohol) to the cuvette using a syringe and inverting the cuvette several times to ensure mixing.

The computer-controlled spectrophotometer measured absorbencies for the samples at predetermined intervals over at least two half lives. Rate constants were obtained from between 25–40 data points using either the above OD_∞ method or from Guggenheim plots.

Secondary alpha deuterium kinetic isotope effects

When the water bath method was used to determine the secondary alpha deuterium kinetic isotope effect, the rate constants for six reactions were determined simultaneously in the same constant temperature bath; three reactions used the deuterated substrate and three used the nondeuterated substrate. When the cuvette method was used, the rate was determined for three deuterated and three nondeuterated substrates simultaneously in the thermostated cell holder. The secondary alpha deuterium kinetic isotope effect was obtained by dividing the average rate constants for the nondeuterated and deuterated substrates.

Determination of the elimination stereochemistry

A stock potassium *tert*-butoxide solution was diluted in a volumetric flask with dry *tert*-butyl alcohol, temperature equilibrated in a constant temperature bath, and filled to the mark with dry *tert*-butyl alcohol. This stock solution was at least twenty times more concentrated than the substrate. The required amount (approximately 20 mg) of the 1-choro-2-phenyl-1,2-d_2 ethane diastereomers was weighed into the reaction vessel and temperature equilibrated. The reaction was started by quickly adding the base solution to the reaction vessel. After ten half-lives (>99.9% reaction) the reaction was quenched by adding cold water and the organic products were extracted three times with pentane. After the combined pentane extracts had been washed with water and dried over anhyd magnesium sulphate, the pentane was removed at room temperature in a rotary evaporator. An NMR analysis of the residue in 1 mL of chloroform-*d* gave the composition of the product.

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References

1. H. Matsuda, T. Hamatani, S. Matsubara, and M. Schlosser. Tetrahedron, **44**, 2865 (1988).
2. R.A. Bartsch and J.G. Lee. J. Org. Chem. **55**, 5247 (1990).
3. M.J.S. Dewar and Y.-C. Yuan. J. Am. Chem. Soc. **112**, 2095 (1990).
4. J. Zavada, M. Pankova, and A. Vitek. Coll. Czech. Chem. Commun. **55**, 695 (1990).
5. R.A. Bartsch and J. Zavada. Chem. Rev. **80**, 453 (1980).
6. (*a*) G.A. Stuart and H. Eyring. J. Chem. Ed. **35**, 550 (1958); (*b*) A.F. Thomas and B. William. Tetrahedron Lett. 1309 (1965); (*c*) K. Fukui and H. Fujimoto. Tetrahedron Lett. 4303 (1965).
7. W.H. Saunders, Jr. and A.F. Cockerill. *In* Mechanisms of elimination reactions. Wiley Interscience, New York. 1973.
8. E. Baciocchi, R. Ruzziconi, and G.V. Sebastiani. J. Org. Chem. **47**, 3237 (1982).
9. E. Baciocchi, R. Ruzziconi, and G.V. Sebastiani. J. Am. Chem. Soc. **105**, 6114 (1983).
10. J. H. Exner and E.C. Steiner. J. Am. Chem. Soc. **96**, 1782 (1974).
11. V. Pechanec, O. Kocian, and J. Zavada. Coll. Czech. Chem. Commun. **47**, 3405 (1982).
12. V. Fiandanese, C.V. Maffeo, C. Marchese, and F. Naso. J. Chem. Soc. Perkin Trans. 2, 221 (1975).
13. V. Pechanec, O. Kocian, V. Halaska, M. Pankova, and J. Zavada. Coll. Czech. Chem. Commun. **46**, 2166 (1981).
14. V. Pechanec, O. Kocian, and J. Zavada. Coll. Czech. Chem. Commun. **48**, 1144 (1983).
15. J. Zavada, M. Pankova, and M. Svoboda. Coll. Czech. Chem. Comm. **41**, 3778 (1976).
16. C. Ingold. Proc. Chem. Soc. London, 265 (1962).
17. N.T. Anh. J. Chem. Soc. Chem. Commun. 1089 (1968).
18. D.S. Bailey and W.H. Saunders, Jr. J. Am. Chem. Soc. **92**, 6904 (1970).
19. P.J. Smith and K.C. Westaway. Can. J. Chem. **65**, 2149 (1987).
20. A.N. Bourns and A.C. Frosst. Can. J. Chem. **48**, 133 (1970).
21. J. Zavada, M. Pankova, and A. Vitek. Coll. Czech. Chem. Commun. **46**, 3247 (1981).
22. L.H. Amundsen and L.S. Nelson. J. Am. Chem. Soc. **73**, 242 (1951).
23. R.L. Huang and S. Singh. J. Chem. Soc. 891 (1958).

24. Y.T. Tao and W.H. Saunders, Jr. J. Am. Chem. Soc. **105**, 3183 (1983).
25. B.R. Dohner and W.H. Saunders, Jr. Can. J. Chem. **64**, 1026, (1986).
26. D.R. Burfield and R.H. Smithers. J. Org. Chem. **48**, 2420 (1983).
27. J. March. *In* Advanced organic chemistry: reactions, mechanisms, and structure. 4th ed, John Wiley & Sons, New York. 1992. pp. 317–319.
28. J. March. *In* Advanced organic chemistry: reactions, mechanisms, and structure. 4th ed, John & Sons, New York. 1992. p. 327.