# Isotope effect studies on elimination reactions. VII. The stereochemistry of elimination from 2-phenylethylammonium ions<sup>1</sup>

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The stereochemistry of the base-promoted elimination reactions of 2-phenylethyltrimethylammonium and 2-phenylethyldimethylanilinium ions has been investigated using both ethoxide ion in ethanol and *t*-butoxide in *t*-butyl alcohol as base-solvent systems. The proton magnetic resonance spectroscopic analysis of the deuterated styrene products formed from the reactions of the *threo*-2-phenylethylammonium-1,2- $d_2$  ions established that elimination proceeds more than 95% by an *anti* process.

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#### Introduction

Base-promoted elimination reactions have generally been considered to proceed most readily via an anti-periplanar transition state. This geometric requirement has been regarded as arising out of the preference for the pair of electrons initially in the H— $C_{\beta}$  bond to act on the  $\alpha$ -carbon from one side, while the leaving group departs from the other side. Such an arrangement of atoms has been assumed in a number of studies, both in our laboratories (1-3) and elsewhere (4-6), in which kinetic isotope effects have been used to determine the effect of changes in substituents, base strength, and solvent on transition state structure in the elimination reactions of 2-arylethylammonium ions. Recently, however, it has been found that the elimination reactions of both open-chain (5, 7-12) and cyclic (13-19) quaternary ammonium ions proceed by a syn process more often than had previously been thought to be the case. Consequently, it seemed desirable to determine whether or not elimination in the 2-arylethylammonium system is in fact an anti process as has been assumed.

In the ground state, the preferred conformation for the 2-phenylethylammonium ion is undoubtedly 1, which places the bulky groups in an *anti* relationship with one another. In order to achieve a transition state in which the departing groups are *anti* and coplanar, the bulky groups must move into staggered positions, conformation 2, resulting in considerable steric retardation. Consequently, a normally less favored transition state geometry, which avoids this strong repulsive



interaction between the two large groups, might be favored.

A study was therefore undertaken of the elimination behavior of 2-phenylethyltrimethylammonium and 2-phenylethyldimethylanilinium ions by determining, by means of proton magnetic resonance (p.m.r.) spectroscopy, the composition and configurations of the  $\beta$ -monodeuterated and  $\alpha,\beta$ -dideuterated styrenes formed from the elimination reactions of *threo*-2-phenylethyltrimethylammonium ion (3) and *threo*-2-phenylethyldimethylanilinium ion (4). The products formed by *syn* and *anti* elimination of these ions are shown in eq. [1].



The stereochemical course of the elimination reactions has been investigated using both ethoxide ion in ethanol and *t*-butoxide ion in *t*-butyl alcohol as the base–solvent systems. The former has been used in our laboratories in most of the kinetic isotope effect studies on quaternary ammonium salt elimination reactions, while the latter has recently been shown (5, 8) to have the

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greater tendency to promote a *syn* elimination process.

The *threo*-2-phenylethyltrimethylammonium-1,2- $d_2$  bromide was obtained by quaternization of *threo*-2-phenylethyldimethylamine formed by nucleophilic displacement on *erythro*-2-phenylethyl-1,2- $d_2$  tosylate by dimethylamine. The tosylate was prepared from the corresponding alcohol which was obtained from *trans*-styrene- $\beta$  $d_1$  by Brown's method of hydroboration (20) using sodium borodeuteride. The *threo*-2-phenylethyldimethylanilinium-1,2- $d_2$  bromide was also prepared from *erythro*-2-phenylethyl-1,2- $d_2$  tosylate through nucleophilic displacement by *N*methylaniline followed by quaternization with methyl bromide.

# Experimental<sup>3</sup>

trans-Styrene- $\beta$ -d<sub>1</sub> The trans-styrene- $\beta$ -d<sub>1</sub> was supplied by Merck, Sharp and Dohme of Canada Limited, Montreal. From the p.m.r. spectrum of this material obtained using a Varian A-60 nuclear magnetic resonance (n.m.r.) spectrometer, as shown in Fig. 2b, and mass spectrometric analysis using a Hitachi Perkin-Elmer RMU-6A mass spectrometer, the isotopic purity of this material was found to be 89.0  $\pm$  0.1%. The remaining 11% was determined to be undeuterated styrene.

## erythro-2-Phenylethanol-1,2-d2

This compound was prepared by the method of Brown and Zweifel (20). Sodium borodeuteride, 3.0 g (0.072 mole) (Merck, Sharp and Dohme), and 2-methyl-2butene, 13.3 g (0.19 mole) (Eastern Chemical Corporation), in diglyme (80 ml) was treated with borontrifluoride etherate, 13.5 g (0.095 mole), in diglyme (30 ml). To the resulting solution, *trans*-styrene- $\beta$ - $d_1$ , 10.0 g (0.095 mole), in diglyme (30 ml) was added and the solution was stirred for 5 h at room temperature. Hydrolysis followed by alkaline oxidation was carried out in the usual manner with the temperature maintained below 45°C. Extraction of the product in ether and isolation by distillation gave 8.6 g (73%) of *erythro*-2-phenylethanol-1,2- $d_2$ , b.p. 72–74°C/1 mm (undeuterated material, b.p. 77–78°C/2 mm).

#### erythro-2-Phenylethyl-1,2-d2 p-Toluenesulfonate

The tosylate was prepared by the general procedure of Tipson (21). Treatment of *erythro*-2-phenylethanol-1,2- $d_2$ , 8.6 g (0.069 mole), with *p*-toluenesulfonyl chloride, 16.4 g (0.086 mole), in dry pyridine (100 ml) gave the *p*-toluene-sulfonate, 14 g (73%), m.p. 38–39°C (undeuterated material, m.p. 37.4–38°C (4); mixed m.p. 37.5–38.5°C).

## threo-Dimethyl-2-phenylethylamine-1,2-d2

The preparation of this material was performed by treating the *erythro*-2-phenylethyl-1,2- $d_2$  *p*-toluenesulfonate, 6.05 g (0.0217 mole), with anhydrous dimethylamine, 2.0 g (0.0453 mole), in anhydrous ether (4). Workup of the reaction mixture gave 1.5 g (46%) of the product, b.p. 106°C/20 mm (lit. (4) b.p. 111°C/20 mm). Mass spectrometric analysis showed 0.89 atoms of deuterium on the  $\alpha$ -carbon atom and 0.98 atoms of deuterium on the  $\beta$ -carbon atom.

## threo-2-Phenylethyltrimethylammonium-1,2-d2 Bromide

This compound was prepared by treating the tertiary amine, 1.3 g (0.0086 mole), with methyl bromide, 2 g (0.021 mole), in nitromethane (25 ml). The product was recrystallized from ethanol – ether to yield 1.9 g (90%), m.p. 238–238.5°C (undeuterated material, (4) m.p. 238–239.5°C).

## threo-N,N-Methyl-2-phenylethylaniline-1,2-d2

A solution of *erythro*-2-phenylethyl-1,2- $d_2$  *p*-toluenesulfonate, 8 g (0.0287 mole), and methylaniline, 3.4 g (0.0317 mole), in nitromethane (8 ml) was swept with dry nitrogen for 30 min. The flask was then stoppered securely and the reaction mixture was heated on the steam bath for 9 h. The nitromethane was removed under reduced pressure and then water (30 ml) and ether (20 ml) were added. The resulting solution was treated with sodium carbonate (3 g) and extracted with four 20 ml portions of ether. The combined ether layers were dried, evaporated under reduced pressure, and distilled to yield 3.5 g (57%) of the tertiary amine, b.p. 118–122°C/0.4 mm (undeuterated material, b.p. 133°C/1 mm).

[1]

<sup>&</sup>lt;sup>3</sup>All melting points are corrected.

threo-2-Phenylethyldimethylanilinium-1,2-d<sub>2</sub> Bromide

Quaternization was carried out in the usual manner to yield 3.3 g (65%), m.p.  $166-167^{\circ}C$  (undeuterated material, m.p.  $167-168^{\circ}C$ ; mixed m.p.  $166-167^{\circ}C$ ).

Anal. Calcd. for  $C_{16}H_{18}D_2NBr$ : C, 62.34; H + D, 7.20; N, 4.55. Found: C, 62.24; H + D, 7.04; N, 4.51.

## Materials for Elimination Reactions

Anhydrous ethanol was prepared by the method of Lund and Bjerrum (22). Anhydrous *t*-butyl alcohol was obtained by distilling Baker Reagent Grade material twice from sodium The standard solutions of alkoxides were obtained by dissolving the clean metal in the alcohol under a nitrogen atmosphere. Standardization of the alkoxide solutions was carried out just before use.

#### Elimination Reactions

The reactions were carried out in 50 ml volumetric flasks in a thermostatted bath at 60°C as described by Saunders and Williams (23). An accurately weighed amount (ca. 45 mmole) of the desired quaternary ammonium salt was dissolved in anhydrous alcohol (24 ml) in the reaction vessel and placed in the bath. After equilibration at the reaction temperature, an aliquot of standardized alkoxide solution was added to the reaction vessel and the solution made up to the standard volume with the addition of a little alcohol. After the reaction had proceeded for at least 20 half-lives, the solution was mixed with water (75 ml) and extracted with four 25 ml portions of pentane. The combined pentane layers were then washed with several aliquots of water and dried over anhydrous sodium sulfate. For reactions of the anilinium salt, it was necessary to extract the dimethylaniline out of the pentane layer with two 20 ml portions of 10% hydrochloric acid.



FIG. 1. Calculated signal patterns for the ethylenic protons of styrene and deuterated styrenes (24).



FIG. 2. Proton magnetic resonance spectra at 60 MHz of ethylenic protons for (a) styrene; (b) trans-styrene- $\beta$ -d<sub>1</sub> supplied by MSD; (c) styrene products from reactions.

After the pentane had been removed by fractionation through a 6 in. column of glass helices, the residue styrene products were analyzed by n.m.r. spectroscopy using Varian A-60 and T-60 n.m.r. spectrometers.

#### **Results and Discussion**

Yoshino *et al.* (24) have calculated the signal patterns for the ethylenic protons of styrene and deuterated styrenes with the results as shown in Fig. 1. The spectra of styrene and the *trans*-styrene- $\beta$ - $d_1$  supplied by Merck, Sharp and Dohme, Figs. 2a and 2b, respectively, were compared with the calculated patterns in order to confirm the signal patterns and the spin-coupling constants. The values determined from the spectra were found to be in complete agreement with the calculated values.

The styrene products recovered from the reactions all gave essentially identical spectra, of which a representative one is shown in Fig. 2c. These spectra were compared with the calculated patterns in order to determine the configurations of the products.

In Fig. 2c, the triplet 2 arises mainly from *trans*-styrene- $\alpha$ ,  $\beta$ - $d_2$ , formula 8, the major product of *anti* elimination, with a small contribution

from styrene- $\alpha$ - $d_1$  (6) the major product resulting from elimination of the isotopic impurity,  $C_6H_5CHDCH_2NR_3$ , in the starting material. The two singlets 4 and 6 arise largely from transstyrene- $\beta$ - $d_1$  (7) the minor product of *anti* elimination, but will include a very small contribution from undeuterated styrene (5) the minor product from the isotopic impurity. The two triplets 8 and 11 also arise largely from *trans*-styrene- $\beta$ - $d_1$  (7), but may include a contribution from *cis*-styrene- $\beta$ -d<sub>1</sub> (9) the minor product of syn elimination. The two small doublets 1 and 3 and the signals 7, 9, 10, and 12 can arise from undeuterated styrene, the minor product resulting from elimination from the isotopic impurity, C<sub>6</sub>H<sub>5</sub>CHDCH<sub>2</sub>NR<sub>3</sub>, in the starting material, and from *cis*-styrene- $\beta$ - $d_1(9)$  the minor product of syn elimination. The sextet 5 can arise from styrene- $\alpha$ - $d_1$  (6) the major product from the isotopic impurity, and from *cis*-styrene- $\alpha$ ,  $\beta$ - $d_2$ (10) the major product of *syn* elimination.

For reaction exclusively by an anti process, the signals 5, 7, 9, 10, and 12 would arise solely from and would account completely for the elimination products, compounds 5 and 6, formed from the 11% isotopic impurity,  $C_6H_5CHDCH_2NR_3$ , in the starting material. In the case of the trimethylammonium derivative, the total contributions of these peaks correspond to 14% of the product for reaction in ethoxide – ethanol and 12% for reaction in t-butoxide - t-butyl alcohol. The corresponding figures for the dimethylanilinium derivative were 12% for reaction in ethoxide - ethanol and 14% for reaction in t-butoxide – t-butyl alcohol. It can be concluded from these results that the amount of syn elimination in these reactions cannot exceed 4-5%.

On the other hand, there are good reasons for believing that the actual amount of syn elimination is much smaller than the n.m.r. data would suggest, at least for the reaction with ethoxide ion in ethanol. In the first place, there is no indication that a larger amount of the syn product is formed using t-butoxide in t-butyl alcohol, despite the fact that the tendency for this mode of elimination has been shown (5, 8) to be much greater in this base-solvent system. Secondly, in all cases, the ratio of the area of signal 5 to the area of the undeuterated styrene signals 7, 9, 10, and 12 is what would be predicted if signal 5 arose solely from styrene- $\alpha$ - $d_1$  (6) the major product from the isotopic impurity, C<sub>6</sub>H<sub>5</sub>CHDCH<sub>2</sub>NR<sub>3</sub>, without any

contribution from *cis*-styrene- $\alpha$ ,  $\beta$ - $d_2$  (10) the major product of syn elimination, and if there was the expected isotope effect for abstraction of hydrogen and deuterium from the  $\beta$ -carbon of the isotopic impurity.

These results show that the base-promoted elimination reactions of 2-phenylethyltrimethylammonium and 2-phenylethyldimethylanilinium ions do indeed proceed mainly, if not almost exclusively, via a transition state in which the departing groups occupy positions anti to one another. As was pointed out earlier, in order for these reactions to proceed via an *anti* elimination, the molecule must rotate about the  $C_{\alpha}$ — $C_{\beta}$  axis bringing the bulky groups into staggered positions and setting up large steric interactions between them. This transition state conformation, although sterically hindered, now has the participating orbitals coplanar. It must be concluded, therefore, that the molecule sacrifices the advantages of the less-encumbered transition state for the *anti*-periplanar transition state.

The observation of almost exclusive anti elimination from the 2-phenylethylammonium salts is consistent with the hypothesis offered by Bailey and Saunders (5) to account for the preference for syn elimination in the formation of transolefins from the reactions of salts of the type  $R^{1}CH_{2}CH(R^{2})N(CH_{3})_{3}$  with bulky bases. In these systems, the  $\beta$ -hydrogen is shielded on both sides by the bulky alkyl groups in the conformation corresponding to 2, mentioned earlier, whereas, in the 2-phenylethyl system, the  $\beta$ hydrogen is readily accessible for attack by base.

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