Concerning a Case of Apparent Syn Elimination from *erythro*-1,2-Diphenylpropyltrimethylammonium Salts[1]

John K. Borchardt and William H. Saunders, Jr.*

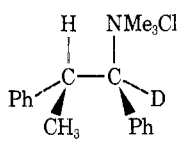
Department of Chemistry, University of Rochester, Rochester, New York 14627

Received July 27, 1973

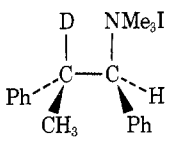
For many years, the E2 transition state was believed to prefer strongly an antiperiplanar orientation of the leaving group and the β hydrogen, except when such an arrangement was sterically prohibited or when the β hydrogen was activated by strongly electron-withdrawing groups.[2] Among the evidence supporting this view was a study by Cram, Greene, and DePuy[3] of eliminations from 1,2-diphenyl-1-propyl derivatives in which the erythro isomer gave *cis*- and the threo isomer *trans*-1,2-diphenylpropene with various bases when the leaving group was chloride, bromide, or trimethylammonium.

One exception was noted: both threo and erythro isomers gave trans olefin when the leaving group was trimethylammonium and the base potassium *tert*-butoxide in *tert*-butyl alcohol. The cis olefin was found to be stable to this base–solvent combination, which means that the erythro isomer formally underwent a syn elimination. The preconception in favor of anti elimination was sufficiently strong at that time, however, that the authors assumed that the reaction involved either epimerization at the α carbon of the reactant, or an ElcB elimination *via* a carbanion which could invert faster than it decomposed to olefin.

To test these hypotheses, we prepared *erythro*-1,2-diphenyl-1-propyl-*1-d*-trimethylammonium chloride (1) and *erythro*-1,2-diphenyl-1-propyl-*2-d*-trimethylammonium iodide (2). The syntheses were adapted from literature pro-



1



2

cedures for undeuterated compounds in the 1,2-diphenyl-1-propyl series, and are described in the Experimental Section. 1 and 2 were treated with potassium *tert*-butoxide in *tert*-butyl alcohol at 35° for one half-life of the elimination reaction. The unreacted material was recovered as the quaternary ammonium bromide[4] in each case, and the nmr spectra of the recovered salts were compared with those of the starting materials. The results are recorded in Table I.

Within the experimental error of several per cent, neither 1 nor 2 had undergone any change in deuterium content. As a further check on this conclusion, undeuterated *erythro*-1,2-diphenyl-1-propyltrimethylammonium iodide was treated with 0.057 *M* potassium *tert*-butoxide in *tert*-butyl-*O-d* alcohol at 35° for one half-life and the unreacted material was recovered.[4] The mass spectrum at 15 eV showed a "parent" peak at *m/e* 240, corresponding to decomposition of the quaternary salt to 1,2-diphenyl-1-propyldimethylamine. The value of [(P + 1)/P] × 100 was found to be 19.56, compared with 19.34 before reaction and 19.07 calculated from natural abundance. There was evidently no deuterium incorporation within experimental error.

As a final control experiment, we tested the stability of a mixture of *cis*- and *trans*-1,2-diphenylpropene to the reaction conditions. While no isomerization is reported in the presence of potassium *tert*-butoxide,[3] no quaternary ammonium salt was present as it would be in an actual reaction mixture. Since quaternary ammonium salt would convert part of the base into the more reactive quaternary ammonium *tert*-butoxide, we repeated the attempted isomerization in the presence of tetra-*n*-butylammonium bromide. No change in the composition of the olefin mixture was detectable by uv spectroscopy after one half-life of the elimination reaction, and there was still no change after nearly 14 half-lives.

Table I
Nmr Spectra of Deuterium-Labeled *erythro*-1,2-Diphenyl-1-propyltrimethylammonium Salts before and after Subjection to Potassium *tert*-Butoxide in *tert*-Butyl Alcohol at 35°[a,b]

Position of deuterium	Group	Position of absorption, δ	Integration Before	Integration After
1	CH_3	1.0	3.00	3.00
	$N(CH_3)_3$	2.0	9.10	9.12
	1-C-D	4.6	0.04	0.03
	2-C-H	3.85	1.05	1.06
	C_6H_5	7.2	(10.0)[c]	(10.0)[c]
2	CH_3	1.0	3.05	3.05
	$N(CH_3)_3$	2.0	9.10	9.12
	1-C-H	4.6	1.00	1.00
	2-C-D	3.85	0.07	0.08[d]
				0.11[d]
				0.07[d,e]
	C_6H_5	7.1	(10.0)[c]	(10.0)[c]

[a] Reactions carried out for one half-life of the elimination reaction (see ref 3) unless otherwise noted. [b] Solvent for nmr spectra was D_2O, and measurements were made on a JEOLCO C-60HL instrument. [c] The peak area for the phenyl peak was taken as exactly 10.0 and the other areas were calculated relative to it. [d] Each figure represents a separate run. [e] Reaction carried out for two half-lives.

Our data clearly exclude product isomerization, α epimerization of reactant *via* an ylide which can abstract a proton from the bulk solvent, or an ElcB reaction *via* a carbanion which returns appreciably to reactant *via* protonation from the bulk solvent. An ElcB reaction with proton abstraction rate determining still cannot be excluded. Neither can α epimerization, or the reversible ElcB mechanism, if one assumes in each case that reprotonation occurs only from the *tert*-butyl alcohol molecule formed by proton or deuteron abstraction in the first step (internal return[5,6]).

Further narrowing of the possibilities will require additional experimental information. A substantial β-deuterium isotope effect would exclude all possibilities in which cleavage of the β-C–H bond is not rate determining, and appreciable nitrogen isotope effects would exclude all but a concerted elimination or an ElcB process with the second step rate determining. We understand that such studies are under way in another laboratory,[7] and we do not intend to do further work on this system. The data so far are certainly compatible with a syn E2 reaction, a possibility which is rendered still more attractive by numerous recent examples of such eliminations from quaternary ammonium salts.[8-13]

Experimental Section

All melting points and boiling points are uncorrected. Mass spectra were determined on a Hitachi Perkin-Elmer RMU-6E mass spectrometer and nmr spectra on a JEOLCO C-60HL instrument.

***erythro*-1,2-Diphenylpropyltrimethylammonium Chloride.** *threo*-1,2-Diphenylpropyl chloride[14] (0.36 g), trimethylamine (3.7 g), and benzene (5 ml) were heated in a stainless steel reaction tube at 55° for 144 hr. After removal of solvent and excess amine on a rotary evaporator, the crude product was recrystallized three

times from an ethanol–ether mixture to yield 0.19 (33%) of pure product: mp 142° dec; nmr (D_2O) δ 7.1 (multiplet, 10.0 H), 3.85 (quintet, J = 5.0 Hz, 1.08 H), 4.6 (doublet, J = 3.8 Hz, 1.1 H), 2.0 (singlet, 9.0 H), 1.0 (doublet, J = 2.6 Hz, 3.0 H).

erythro-**1,2-Diphenylpropyltrimethylammonium iodide** was prepared by the method of Cram, Greene, and DePuy:[3] mp 212° dec (lit.[3] mp 212–213° dec; nmr (D_2O) δ 7.1 (multiplet, 10.0 H), 3.85 (multiplet, 1.0 H), 4.6 (doublet, J = 3.7 Hz, 1.0 H), 2.0 (singlet, 9.0 H), 1.0 (doublet, J = 2.5 Hz, 3.0 H).

erythro-**1,2-Diphenyl-1-propanol-***1-d* was obtained by reduction of 1,2-diphenylpropanone with lithium aluminum deuteride, following the procedure of Cram and Elhafez[15] for the hydride reduction. After three recrystallizations from ether, 77% of material of mp 49–51° resulted (lit.[15] mp 50–51° for the undeuterated material), 0.93 D atom per molecule by mass spectrometry.

threo-**1,2-Diphenylpropyl-***1-d* **chloride** was prepared from *erythro*-1,2-diphenyl-1-propanol-*1-d* and thionyl chloride as described by Elhafez and Cram.[16]

erythro-**1,2-Diphenylpropyl-***1-d*-**trimethylammonium chloride** was prepared from the reaction of *threo*-1,2-diphenylpropyl-*1-d* chloride with trimethylamine as described above for the undeuterated compound. The product (32% yield) had mp 142–143° dec; nmr (D_2O) δ 7.1 (multiplet, 10.0 H), 3.85 (quartet, J = 5.5 Hz, 1.05 H), 4.6 (doublet, J = 3.7 Hz, 0.04 H), 2.0 (singlet, 9.1 H), 1.0 (doublet, J = 2.5 Hz, 3.0 H).

2-Phenylpropionaldehyde-*2-d* was obtained by refluxing with stirring a mixture of 54 g (0.40 mol) of 2-phenylpropionaldehyde and 40 g (2.0 mol) of deuterium oxide containing a few drops of 40% sodium deuteroxide in deuterium oxide. The aldehyde was recovered and the process was repeated twice. The final product contained 0.97 D atom per molecule by mass spectroscopy.

threo-**1,2-Diphenylpropanol-***2-d* was obtained by the reaction of 2-phenylpropionaldehyde-*2-d* with phenylmagnesium bromide and recrystallization of the *p*-nitrobenzoate of the product 16 times from ethyl acetate [final *p*-nitrobenzoate mp 143–144° (lit.[15] mp 143–144°)], followed by saponification to give a viscous, clear oil: bp 136–137° (1.4 mm); $n^{25}D$ 1.5715 (lit.[15] $n^{25}D$ 1.5718); nmr ($CDCl_3$) δ 1.02 (doublet, J = 5.0 Hz, 3.0 H), 2.25 (broad singlet, 1.1 H), 3.05 (multiplet, 0.9 H), 4.65 (doublet, J = 3.5 Hz, 0.9 H), 7.10 (multiplet, 10.0 H).

threo-**1,2-Diphenylpropyl-***2-d p*-**bromobenzenesulfonate** was obtained as previously described for the undeuterated compound.[17] It was kept in dry benzene because it decomposes in the neat state.[17]

erythro-**1,2-Diphenylpropyl-***2-d*-**dimethylamine** was obtained from *threo*-1,2-diphenylpropyl-*2-d p*-bromobenzenesulfonate and dimethylamine as described for the undeuterated compound.[3] Its mass spectrum indicated 0.97 D atom per molecule; nmr ($CDCl_3$) δ 7.1 (multiplet, 10.0 H), 4.75 (doublet, J = 0.8 Hz, 1.0 H), 3.4 (multiplet, 0.07 H), 2.1 (singlet, 6.0 H), 1.40 (doublet, J = 0.9 Hz, 3.0 H).

erythro-**1,2-Diphenylpropyl-***2-d*-**trimethylammonium iodide** was obtained from *erythro*-1,2-diphenylpropyl-*2-d*-dimethylamine and methyl iodide by the procedure for the undeuterated compound:[3] mp 212–213° dec; nmr (D_2O) δ 7.1 (multiplet, 10.0 H), 3.85 (multiplet, 0.07), 4.6 (doublet, J = 0.8 Hz, 1.0 H), 2.0 (singlet, 9.0 H), 1.0 (doublet, J = 0.9 Hz, 3.0 H).

Recovery of 1,2-Diphenylpropyltrimethylammonium Salts after Partial Reaction. The reactions were carried out with 5.3 × 10^{-4} M *erythro*-1,2-diphenylpropyltrimethylammonium salt, appropriately deuterated, in 0.057 M potassium *tert*-butoxide in *tert*-butyl alcohol at 35° for one half-life (5.8 hr). The mixture was chilled and worked up by the procedure used by Smith and Bourns[4] to recover 2-phenylethyltrimethylammonium bromide. Two recrystallizations of the crude material from ethanol–ether yielded crystals of 1,2-diphenylpropyltrimethylammonium bromide.

Stability of 1,2-Diphenyl-1-propene to Reaction Conditions. A 2.41 × 10^{-3} M solution of α-methylstilbene [Pfaltz and Bauer, Inc., λ_{max} 274 nm (lit.[15] 274 nm for trans isomer)] in *tert*-butyl alcohol was photolyzed for 3 hr in a Kimax test tube with a medium-pressure mercury lamp, using a potassium dichromate filter solution to isolate the 313-nm line. The resulting material was diluted 1:25 with 95% ethanol and the uv spectrum was determined. λ_{max} 264 nm, no shoulder near 255 nm (9-methylphenanthrene). For the cis olefin, λ_{max} 260 nm is reported;[18] so the photoisomerized mixture appears to contain an excess of cis over trans olefin. The photostationary state is reported to have a cis/trans ratio of 2.6 at 313 nm.[19] In contrast, the trans isomer predominates by at least 50:1 at equilibrium.

A solution containing the photoisomerized olefin mixture (4.82 × 10^{-4} M), potassium *tert*-butoxide (0.3 M), and tetra-*n*-butylammonium bromide (8 × 10^{-3} M) was placed in a bath at 30°. Samples were taken after 2 hr and 27 hr and diluted 1:5 with 95% ethanol, and the uv spectra were determined. For both samples λ_{max} 265–266 nm was observed, indistinguishable within experimental error from λ_{max} for the starting material. The half-life of the elimination reaction of 4.82 × 10^{-4} M 1,2-diphenylpropyltrimethylammonium iodide in 0.3 M potassium *tert*-butoxide can be calculated from the reported rate constant[3] at 30° to be 2 hr.

Registry No.—**1**, 42879-24-3; **2**, 42879-25-4; *erythro*-1,2-diphenylpropyltrimethylammonium chloride, 42879-26-5; *threo*-1,2-diphenylpropyl chloride, 7693-88-1; trimethylamine, 75-50-3; *erythro*-1,2-diphenylpropyltrimethylammonium iodide, 42879-28-7; *threo*-1,2-diphenylpropanol-*2-d*, 42879-29-8; *erythro*-1,2-diphenylpropyl-*2-d*-dimethylamine, 42879-30-1; *threo*-1,2-diphenylpropyl-*2-d p*-bromobenzenesulfonate, 42879-31-2.

References and Notes

(1) This work was supported by the National Science Foundation.
(2) See, for example, W. H. Saunders, Jr., in "The Chemistry of Alkenes," S. Patai, Ed., Wiley Intercience, New York, N. Y., 1964, Chapter 2.
(3) D. J. Cram, F. D. Greene, and C. H. DePuy, *J. Amer. Chem. Soc.*, **78**, 790 (1956).
(4) P. J. Smith and A. N. Bourns, *Can. J. Chem.*, **48**, 12 (1970).
(5) D. J. Cram, D. A. Scott, and W. D. Nielsen, *J. Amer. Chem. Soc.*, **83**, 3696 (1961).
(6) A. Streitweiser, J., W. C. Langworthy, and D. E. Van Sickle, *J. Amer. Chem. Soc.*, **84**, 251 (1962).
(7) A. C. Frosst and A. N. Bourns, private communication.
(8) J. Závada and J. Sicher, *Collect. Czech. Chem. Commun.*, **32**, 3701 (1967).
(9) J. Sicher and J. Závada, *Collect. Czech. Chem. Commun.*, **33**, 1278 (1968).
(10) J. Sicher, J. Závada, and M. Pánková, *Collect. Czech. Chem. Commun.*, **36**, 3140 (1971).
(11) D. S. Bailey and W. H. Saunders, Jr., *J. Amer. Chem. Soc.*, **92**, 6904 (1970).
(12) M. P. Cooke, Jr., andJ L. Coke, *J. Amer. Chem. Soc.*, **90**, 5556 (1968).
(13) More complete references are given in a recent review: J. Sicher, *Angew. Chem.*, **84**, 177 (1972); *Angew Chem., Int. Ed. Engl.*, **11**, 200 (1972).
(14) F. A. A. Elhafez and D. J. Cram, *J. Amer. Chem. Soc.*, **75**, 339 (1953).
(15) D. J. Cram and F. A. A. Elhafez, *J. Amer. Chem. Soc.*, **75**, 5828 (1952).
(16) F. A. A. Elhafez and D. Cram, *J. Amer. Chem. Soc.*, **75**, 339 (1953).
(17) D. J. Cram and F. A. A. Elhafez, *J. Amer. Chem. Soc.*, **74**, 5851 (1952).
(18) V. J. Traynelis, W. L. Hergenrother, J. L. Livingston, and J a. Valicenti, *J. Org. Chem.*, **27**, 2377 (1962).
(19) G. S. Hammond, J. Saltiel, A. A. Lamola, N. J. Turro, J. S. Bradshaw, D. O Cowan, R. C. Counsell, V. Vogt, and J. C. Dalton, *J. Amer. Chem. Soc.*, **86**, 3197 (1964).

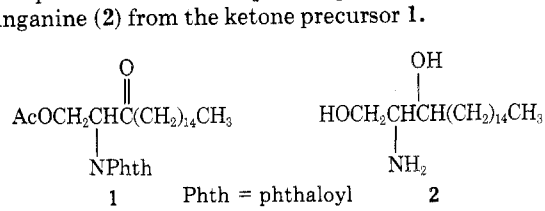
Stereospecific Synthesis of D-*threo*-Sphinganine

Howard Newman

Infectious Disease Therapy Section, Lederle Laboratories, American Cyanamid Company, Pearl River, New York 10965

Received August 16, 1973

In the course of our studies on the synthesis of sphingolipid bases[1,2] we have uncovered a very interesting case of stereoelectronic control on the course of a reduction, which permits the stereospecific preparation of D-*threo*-sphinganine (**2**) from the ketone precursor **1**.



1 Phth = phthaloyl **2**

Heretofore, **2** has been available only by resolution of the DL mixture which was, in turn, obtained by separation