Stereochemistry of Elimination Reactions of 2-Chloro-1-phenylpropane in Different Solvent–Base Systems

By **Sergio Alunni, Enrico Baciocchi,* Rosario Nicoletti,** and **Marco Tingoli,** Dipartimento de Chimica, Università di Perugia, 06100 Perugia, Italy, and Istituto Chimico, Università di Roma, 00180 Roma, Italy

The stereochemistry of β-elimination from DL-*erythro*- (I) and DL-*threo*-2-chloro-1-deuterio-1-phenyl propane (II) promoted by a variety of solvent–base combinations has been investigated. Elimination from (I) occurs by an *anti*-mechanism in EtOH–EtONa and in Bu^{t}OH–Bu^{t}OK–crown ether, whereas a small amount of *syn*-elimination (<6%) is observed in Bu^{t}OH–Bu^{t}OK. *anti*-Stereochemistry is always observed for eliminations from (II).

As shown in previous studies [1,2] the geometrical orientation in the elimination reactions from β-phenyl activated substrates depends on the nature of the leaving group and of the solvent–base system in a different way than the geometrical orientation in the corresponding eliminations from non-activated substrates. Thus, in the reactions of 1-benzylethyl halides in EtOH–EtONa [1] the *highest trans* : *cis* 1-phenylpropene ratio has been observed when the leaving group is fluoride; in contrast fluoride is the leaving group which produces the *smallest trans* : *cis* ratio in the eliminations from 1-methylpentyl and 1-methylbutyl halides.[3,4] Moreover, the *trans* : *cis* ratio for the elimination from 2-chloro-1-phenylpropane decreases when the solvent–base system is changed from Bu^{t}OH–Bu^{t}OK to EtOH–EtONa and when the base is crown-ether complexed Bu^{t}OK.[2] Opposite trends have been found with non-activated alkyl halides for identical structural modifications of the solvent–base system.

The intervention of a *syn*-elimination mechanism could reasonably explain the results of the elimination reactions of 1-benzylethyl halides since high *trans* : *cis* ratios are characteristic of a *syn*-mechanism; [5] moreover this mechanism appears to be favoured by associated bases in low dielectric constant solvents,[5] and an increase of the *trans* : *cis* ratio in passing from EtOH–EtONa to Bu^{t}OH–Bu^{t}OK is therefore expected.

In order to acquire information in this respect a study of the stereochemistry of the eliminations from DL-*erythro*- (I) and DL-*threo*-2-chloro-1-deuterio-1-phenylpropane (II) in a variety of base–solvent combinations was undertaken.

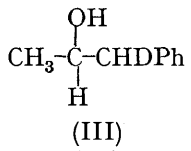
RESULTS AND DISCUSSION

DL-*erythro*- (III) and DL-*threo*-1-deuterio-1-phenylpropan-2-ol (IV) were obtained by deuterioboration of

[1] S. Alunni and E. Baciocchi, *Tetrahedron Letters*, 1973, 205.
[2] S. Alunni, E. Baciocchi, R. Ruzziconi, and M. Tingoli, *J. Org. Chem.*, 1974, **39**, 3299.
[3] R. A. Bartsch and J. F. Bunnett, *J. Amer. Chem. Soc.*, 1968, **90**, 408.
[4] W. H. Saunders, jun., S. F. Fahrenholtz, E. A. Caress, J. P. Lowe, and M. Schreiber, *J. Amer. Chem. Soc.*, 1965, **87**, 3401.
[5] J. Závada, M. Pánková, M. Svoboda, and M. Schlosser, *J.C.S. Chem. Comm.*, 1973, 168, and references therein.

cis- and *trans*-1-phenylpropene, respectively. The yields were very low (≤10%) since the main product in both cases, was 2-deuterio-1-phenylpropan-1-ol.

The reactions of (III) and (IV) with CCl_4 and PPh_3 [6]



(III)
(IV)

gave the inverted chlorides (II) and (I) respectively. Analysis, by mass spectrometry, of these diastereoisomeric compounds revealed that (I) and (II) contained 5 and 5.5%, respectively, of undeuteriated 2-chloro-1-phenylpropane.

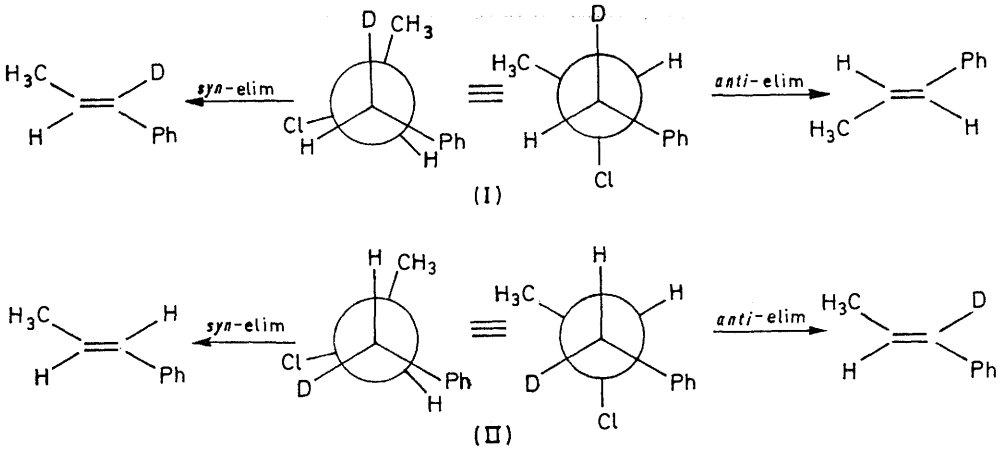
Reactions of (I) and (II) with a variety of bases were carried out in the usual way and the deuterium content of the *trans*-olefin produced was determined by mass spectrometry at low ionizing voltage. As shown in the Scheme the extent of *syn*-elimination may be assessed by the relative amounts of unlabelled and labelled *trans*-1-phenylpropene. Owing to the large *trans* : *cis* ratios generally observed, the amount of *cis*-olefin obtained in these reactions was too small [especially starting from (II)] to enable a satisfactory deuterium analysis for this material.

In MeOH–MeONa a small amount of *trans*-[$^2H_1$]olefin from (I) and *trans*-[$^2H_0$]olefin from (II) was observed. Since an all-*anti*-elimination may be reasonably assumed in this system the above finding was considered to result from the presence of some diastereoisomeric impurity in both (I) and (II). It was thus calculated that (I) was contaminated by 6% of (II) and (II) by 5.5% of (I).

Table 1 reports the values of the *trans* : *cis* olefin ratios obtained in the reactions of (I) and 2-chloro-1-phenylpropane and Table 2 records the observed deuterium content of *trans*-1-phenylpropene in eliminations from (I) and (II) as well as the calculated value (for an all *anti*-elimination), which includes contributions from contaminating diastereoisomeric and unlabelled impurities. *trans* : *cis* Ratios in the reactions of (II) were too high to be measured; thus the calculated values of deuterium content for the olefin from (I) were obtained by assuming that only the *trans*-olefin is produced by (II) present as an impurity.

Results in Table 2 show good agreement between observed and calculated percentages of deuteriated and undeuteriated olefin in eliminations promoted by EtOH–EtONa. Therefore in this solvent–base system a clean *anti*-mechanism of elimination is operating for both (I) and (II). In fact the amount of deuteriated *trans*-olefin is slightly less than expected.

For the reaction of (I) in Bu^tOH–Bu^tOK the amount of deuteriated *trans*-phenylpropene is found to be more than expected; a small (<6%) incursion of a *syn*-mechanism for elimination from (I) in this system is therefore indicated. No *syn*-elimination, in contrast, is observed when (II) reacts with Bu^tOK–Bu^tOH. This clearly depends on the fact that in the reactions of (I)



SCHEME

TABLE 1

trans : *cis*-Olefin ratios in some elimination reactions of DL-*erythro*-2-chloro-1-deuterio-1-phenylpropane and 2-chloro-1-phenylpropane

	trans : *cis*-Phenylpropene		
	erythro-Isomer		Undeuteriated
Base–solvent	Obs.	Corr [b]	chloride [a]
MeONa–MeOH	9.3	8.3	23.5
EtONa–EtONa	7 5	6.7	25.0
Bu^tOK–Bu^tOH	31.6	27.4 [c]	72.0
Bu^tOK–Bu^tOH–crown ether	12.2	10.8	45.0

[a] Ref. 2. [b] Corrected for phenylpropenes from the *threo*-isomer and the unlabelled chloride. [c] Corrected for *syn*-elimination (see text).

[6] R. G. Weiss and E. J. Snyder, *J. Org. Chem.*, 1970, **35**, 1627; 1971, **36**, 403.

syn-elimination (rupture of a C–H bond) is favoured with respect to *anti*-elimination (breaking of a C–D bond), whereas the reverse situation applies to elimination from (II).

On the same basis nearly complete *anti*-elimination may also be predicted for the reaction of undeuteriated 2-chloro-1-phenylpropane in Bu^{t}OH–Bu^{t}OK since, in this substrate, the *anti*-pathway is not retarded by a kinetic deuterium isotope effect as occurs in (I). Therefore the present results clearly show that the increase of the *trans* : *cis* olefin ratio observed for elimination from 2-chloro-1-phenylpropane in passing from EtOH–EtONa to Bu^{t}OH–Bu^{t}OH[2] can by no means be ascribed to the intervention of a *syn*-mechanism of elimination in the latter solvent–base system.*

It is also interesting to note that the small percentage of *syn*-elimination found for the reaction of (I) in Bu^{t}OH–Bu^{t}OK disappears when the same reaction is carried out in the presence of dicyclohexyl-18-crown-6-ether in agreement with the well recognized importance of ion pair association in favouring *syn*-elimination.[5]

DL-*erythro*-2-Bromo-3-deuteriobutane is different from (I) in that it exhibits all-*anti*-elimination in Bu^{t}OH–Bu^{t}OK.[8] Chloride is a poorer leaving group than bromide and this should favour *syn*-elimination.[9] However also the introduction of a β-phenyl group, probably by increasing the carbanion character of the transition state,[10] may play an important role in this respect.

The *trans* : *cis* ratios obtained in the reactions of the undeuteriated substrate may be divided by those obtained in the reactions of (I) (corrected for the diastereoisomeric and unlabelled impurities and, in the case of the reaction in Bu^{t}OH–Bu^{t}OK, for the contribution of *syn*-elimination which should lead exclusively to the *trans*-olefin) to give the isotope effect for the *anti*-elimination process. The values calculated in the various solvent–base systems are 2.8 (MeOH–MeONa), 3.7 (EtOH–EtONa), 2.6 (Bu^{t}OH–Bu^{t}OK), and 4.2 (Bu^{t}OH–Bu^{t}OK–crown ether). However these values are affected by much uncertainty (±0.6) for the several corrections involved and for errors in the *trans* : *cis* ratios. Therefore the observed variations in the isotope effects are not much larger than experimental errors.

TABLE 2

Deuterium content of *trans*-phenylpropene in some elimination reactions of DL-*erythro*- and DL-*threo*-2-chloro-1-deuterio-1-phenylpropane

	erythro-Isomer				*threo*-Isomer			
	$^2H_0$ (%)		$^2H_1$ (%)		$^2H_0$ (%)		$^2H_1$ (%)	
Base-solvent	Obs.	Calc.[a]	Obs.	Calc.[a]	Obs.	Calc.[b]	Obs.	Calc.[b]
MeONa–MeOH	93.4	93.4	6.6	6.6	9.0	9.0	91.0	91.0
EtONa–EtOH	95.1	93.2	4.9	6.8	8.5	8.7	91.5	91.3
Bu^{t}OK–Bu^{t}OH	88.4	93.8	11.6	6.2	8.3	9.2	91.7	90.8
Bu^{t}OK–Bu^{t}OH–crown ether	96.8	93.5	3.2	6.5				

[a] Calculated allowing for 5% 2-chloro-1-phenylpropane and 6% *threo*-isomer. [b] Calculated allowing for 5.5% 2-chloro-1-phenylpropane and 3.9% *erythro*-isomer.

EXPERIMENTAL

Materials.—Purification of solvents and preparation of base–solvent solutions were carried out as previously described.[2] Dicyclohexyl-18-crown-6 ether was prepared following the procedure described by Pederson.[11]

DL-erythro-1-*Deuterio*-1-*phenylpropan*-2-*ol* (III).—This was synthesized by deuterioboration of *cis*-1-phenylpropene [2] followed by oxidation according to standard procedures; [12] however the reaction product contained only 8% of (III), the main product being, as expected, *erythro*-2-deuterio-1-phenylpropan-1-ol. After column chromatography on Silal-13 (eluant light petroleum) a mixture containing 70% of (III) was obtained. Further purification by preparative g.l.c. using a 2 × 0.006 m column of 10% CWX 20M afforded (III) pure by analytical g.l.c., δ (CD_3COCD_3) 1.12 (d, CH_3), 2.74 (m, CHD), 3.41 (d, OH), 3.90 (m, C*H*OH), and 7.20 (m, Ph).

DL-*threo*-1-Deuterio-1-phenylpropan-2-ol (IV) was obtained from *trans*-1-phenylpropene (Fluka) by following the same procedure used for (III). The n.m.r. spectrum of (IV) was identical with that of (III) except that the multiplet due to the CHD proton was centred at δ 2.62.

In an attempt to obtain better yields of (III) and (IV) the oxymercuriation of *cis*- and *trans*-1-phenylpropene, respectively, was carried out. However the stereospecificity of this reaction was low and the product obtained was in both the cases a mixture of (III) and (IV) as shown by the n.m.r. spectra.

DL-*erythro*- (I) and DL-*threo*-2-Chloro-1-phenylpropane (II) were prepared from the reaction of (IV) and (III), respectively, with PPh_3 in CCl_4.[3] The deuterium content was determined by mass spectrometric analysis at 13 eV

* Actually, the *anti*-mechanism has been shown only for the formation of the *trans*-olefin. However this conclusion can be extended also to the formation of the *cis*-olefin since it is well known[7] that the *syn*-mechanism, when present, is more important in the formation of the *trans*- than of the *cis*-olefin.

[7] W. H. Saunders, jun., and A. F. Cockerill, 'Mechanisms of Elimination Reactions,' Wiley-Interscience, New York, 1973, p. 105.

[8] R. A. Bartsch, *J. Amer. Chem. Soc.*, 1971, **93**, 3683.

[9] J. Sicher, *Angew. Chem.*, 1972, 200.

[10] R. A. More O'Ferrall, 'Elimination Reactions in Solution' in The Chemistry of the Carbon–Halogen Bond, Wiley-Interscience, New York, 1973, part 2.

[11] C. J. Pedersen, *J. Amer. Chem. Soc.*, 1967, **89**, 7017.

[12] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, 1960, **82**, 4708.

by the relative intensities of peaks at *m/e* 154 and 155. Compounds (I) and (II) were contaminated by 5.0 and 5.5% respectively of unlabelled material.

Elimination Reactions and Product Analysis.—Reactions were carried out as previously described.[1] The concentrations of the reactants were 0.1—0.8M for the base and *ca.* 0.01M for the chloride. The reaction mixture was poured into water and extracted with n-pentane; most of the solvent was removed under reduced pressure and the *trans*-olefin was analysed by a gas chromatograph (Perkin-Elmer 800) coupled (Bieman separator, home-made device) with a mass spectrometer (A.E.I. MS12). The chromatographic conditions were as follows: column 3 × 0.003 m filled with Chromosorb G coated with 4% OV-17, oven temperature 130°, helium flow rate, *ca.* 25 ml min^{-1}. Mass spectra of effluent peaks were recorded at (nominal) 12 eV (trap current 100 μA), by using mesitylene as reference (M^+ 120). The deuterium content in the olefin was determined by measuring the relative intensities of peaks at *m/e* 118 and 119. Since the two peaks are recorded within 0.2 s, the variation of sample pressure in the source is negligible.

trans : *cis*-Ratios in the elimination from (I) were determined by the procedure previously described.[1]

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