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Triethylamine-promoted Elimination from (*R*,*R*)-PhCHORCHClCO$_2$Me (R = MeCO, PhCO, 4-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$, MeSO$_2$ and 4-MeC$_6$H$_4$SO$_2$) in Various Solvents†

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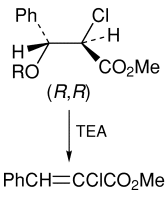
The rates and stereochemistry of elimination from a number of (*R*,*R*)-PhCHORCHClCO$_2$Me (R = MeCO, PhCO, 4-MeC$_6$H$_4$, 4-MeOC$_6$H$_4$, MeSO$_2$ and 4-MeC$_6$H$_4$SO$_2$) with triethylamine in tetrahydrofuran, acetone, methanol, dimethylformamide and acetonitrile as solvents led to the conclusion that the elimination process occurs through an (E1cB)$_I$ mechanism.

Kinetic results, together with stereochemical evidence, obtained from the triethylamine-promoted dehydroacetoxylation from methyl (*R*,*R*)-2-chloro-3-acetoxy-3-phenylpropanoate (**1**) in methanol have been interpreted as proceeding *via* an E1cB process of the irreversible type.[1] We report here an examination of the response of the elimination to the effect of substitution of the acetyl–methyl portion (**1**) by some aromatic groups as well as the behaviour of some related compounds.



	R
1	MeCO
2	PhCO
3	4-MeC$_6$H$_4$CO
4	4-MeOC$_6$H$_4$CO
5	MeSO$_2$
6	4-MeC$_6$H$_4$SO$_2$

To obtain further information about these eliminations, the effect of solvents of different dielectric constants upon both the kinetic and the stereochemical behaviour of the eliminations was also analysed.

According to the structural analogy between methyl (*R*,*R*)-2-chloro-3-acetoxy-3-phenylpropanoate (**1**) and compounds **2**, **3** and **4**, it seems not unreasonable to assume the involvement of a carbanionic species in the methanolic triethylamine (TEA)-induced elimination from the latter substrates. Support for this suggestion is found in a comparison of the data recorded in Table 1, which indicates that the variation in reactivity along the series **1–4** is qualitatively consistent with that expected on the grounds of the different stabilizing effects of the electron-withdrawing 3-substituent on the rate-determining 2-carbanion formation.[1–3] Moreover, from examination of the rate coefficient values (Table 1) it follows that the relative degree of reactivity of these compounds is associated with the change in the dielectric constant of the solvent, which again is in accordance with the view that the rate-controlling stage involves an anionic species.[4–6] However, the sensitivity of the reaction rates to the solvent change appears to be less pronounced with an increase in the inductive stabilising influence exerted by the 3-substituent on the carbanion. A likely explanation for this might lie in the assumption that the anion stabilisation through electrostatic solvation should become weaker as the electron-attracting power of the 3-substituent dissipates the degree of negative charge concentration.

Although the structural characteristics of substrates **5** and **6** are not strictly analogous to those of the remaining compounds, the kinetic evidence (Table 1) seems to suggest that the previous considerations also apply to them. As regards the stereochemical outcome of the outcome of the reactions, the results arising from those carried out in the less polar solvents (tetrahydrofuran and acetone respectively) show that all the substrates afford, exclusively, the thermodynamically more stable olefin (*Z*), which argues in favour of a carbanionic process.‡ As to methanol (MeOH), dimethylformamide (DMF) and acetonitrile (AN) the stereospecificity of the eliminations in these solvents appears to depend on both the nature of the 3-substituent and the polarity of the reaction medium. The data in Table 2 reveal that the product ratio *Z*:*E* decreases with increasing dielectric constant of the solvent. This effect is comparable to that reported for the TEA-mediated elimination from (*R*,*R*)-PhCHORCHClCO$_2$Me (R = Ac, CH$_2$ClCO, CHCl$_2$CO and CCl$_3$CO), which was rationalised in terms of a polar solvent-induced increase of the population of the rotational

Table 1 Kinetic data[a] for elimination from (*R*,*R*)-PhCHORCHClCO$_2$Me[b] with TEA[c] in various solvents at 30 °C

R	THF (7.6[e])	Acetone (Acet) (20.7[e])	MeOH[d] (31.5[e])	DMF (36.7[e])	Acetonitrile (AN) (37.6[e])	k_{AN}/k_{MeOH}	k_{DMF}/k_{Acet}
1 Ac	0.05	0.043	0.104	0.132	0.139	1.34	3.07
2 PhCO	0.05	0.034	0.088	0.113	0.124	1.41	3.32
3 4-MeC$_6$H$_4$CO	0.03	0.029	0.071	0.109	0.120	1.83	3.76
4 4-MeOC$_6$H$_4$CO	0.02	0.021	0.049	0.078	0.111	2.27	3.90
5 MeSO$_2$	0.145	0.805	1.54	1.73	1.92	1.25	2.15
6 4-MeC$_6$H$_4$SO$_2$	0.184	1.41	2.14	2.19	2.36	1.10	1.54

[a]k_2 = dm^3 mol^{-1} min^{-1}. [b][Subst.] = 0.003 mol dm^{-3}. [c][TEA] = 0.06 mol dm^{-3}. [d][TEA] = 0.06 mol dm^{-3}, [TEA–HCl] = 0.03 mol dm^{-3}. [e]Dielectric constant.

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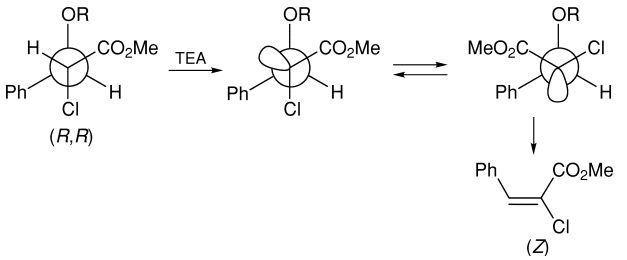
‡The possibility of an *E*2 mechanism for these compounds can be dismissed on the basis that the eliminations afford exclusively or predominantly the *Z* olefin, which is not what should be predicted for a concerted pathway.

conformer of the intermediate carbanion with a geometry closely related to that of the (*E*)-olefin.[1]



On the other hand, the decrease in the proportion of the (*E*)-olefin formed along the series **1**, **5**, **6** in MeOH, DMF and AN, respectively, is qualitatively analogous to the sequence previously found for TEA-induced elimination from methyl (*R,R*)-2-chloro-3-bromo-3-phenylpropanoate with a similar change of solvents.[4] This was interpreted as a function of the ability of the 3-substituent to increase the lifetime of the intermediate and hence to enhance the possibility to attain the appropriate geometry leading to the thermodynamically favoured olefin (*Z*). However, a different trend emerges from comparison of the results arising from compounds **1**, **2**, **3** and **4**, which indicates a negative correlation between the *Z*:*E* ratio and the electron-attracting efficiency of the 3-substituent. If the degree of (*E*)-olefin formation were to reflect only the influence of the factors that seem to govern the rate-controlling pathway, then the sequence of the relative effect of the 3-substituent upon the stereospecificity of the elimination for the whole series of compounds should be comparable to that on the reaction rate. An important factor that possibly influences the final stereochemistry, which should be considered at this stage of the elimination process, is the leaving power of the departing 3-group. Inspection of the data in Table 2 indicates that the stereospecificity of the reactions for the series **1**–**4** increases with decreasing leaving group ability. A justification for this observation could be found in the fact that reluctant leaving groups will allow the intermediate to select the route to the more stable olefin. Thus, the increase in the *Z*-proportion obtained in MeOH, DMF and AN appears to be favoured when the factors that enhance the lifetime of the carbanion are dominant. For the intermediate cases, however, the effect of the solvent polarity seems to be manifested. Therefore, the stereochemical evidence obtained for the elimination of the present series of compounds might partly be accounted for on the grounds of the simultaneous operation of three main factors that govern the product-forming pathway: (i) the carbanion stabilising power of the 3-substituent, (ii) its departing capability, and (iii) the influence of the solvent polarity; the combination of these factors results in the observed stereochemistry.

Experimental

^{1}H NMR spectra were recorded with a Varian EM 360L instrument. Compound **1** was obtained as described in the literature.[1] The aroyl derivatives **2**, **3** and **4** were prepared by the reaction of methyl (*R,R*)-2-chloro-3-hydroxy-3-phenylpropanoate (7.7 mmol) with the corresponding aroyl chloride (10.5 mmol) in dry pyridine (20 cm^3) at 30 °C. After the reaction was complete (25–30 h) the mixture was poured into a 10% HCO_3Na solution (20 cm^3), extracted with chloroform (3×10 cm^{-3}) and washed with water. The solvent was removed under reduced pressure and the residue purified by recrystallisation from methanol. Analytical data were as follows: *Methyl* (R,R)-2-*chloro*-3-*benzoyloxy*-3-*phenylpropanoate* (Found: C, 63.9; H, 4.8; Cl, 10.2. $C_{17}H_{15}ClO_4$ requires C, 64.1; H, 4.7; Cl, 11.2%); δ (ppm) (CCl_4) 7.85 (2H, m), 7.20 (8H, m), 5.90 (1H, d), 4.34 (1H, d) and 3.38 (3H, s). *Methyl* (R,R)-2-*chloro*-3-(4-*methylbenzoyloxy*)-3-*phenylpropanoate* (Found: C, 65.0, H, 5.2; Cl, 10.4. $C_{18}H_{17}ClO_4$ requires C, 65.0, H, 5.15; Cl, 10.65%); δ (ppm) (CCl_4) 7.72 (2H, d), 7.12 (5H, m), 6.78 (2H, d), 5.88 (1H, d), 4.32 (1H, d), 3.45 (3H, s) and 2.22 (3H, s). *Methyl* (R,R)-2-*chloro*-3-(4-*methoxybenzoyloxy*)-3-*phenylpropanoate* (Found: C, 61.5; H, 4.8; Cl, 10.0. $C_{18}H_{17}ClO_5$ requires C, 2.0; H, 4.9; Cl, 10.2%); δ (ppm) (CCl_4) 7.58 (2H, d), 6.95 (5H, m), 6.48 (2H, d), 5.82 (1H, d), 4.22 (1H, d), 3.35 (3H, s) and 3.27 (3H, s). For the preparation of *Methyl* (R,R)-2-*chloro*-3-*tosyloxy*-3-*phenylpropanoate*, tosyl chloride (13.2 mmol) was slowly added to a solution of methyl (*R,R*)-2-chloro-3-hydroxy-3-phenylpropanoate (11.6 mmol, 36 cm^3) in pyridine–dichloromethane (1:1) at 0 °C. The mixture was stored at 0 °C for 6 days and then worked-up as described for the aroyl derivatives (Found: C, 55.1; H, 4.8; Cl, 9.4. $C_{17}H_{17}ClO_5S$ requires C, 55.4; H, 4.2; Cl, 9.5%); δ (ppm) (CCl_4) 7.22 (2H, d), 7.09 (5H, s), 6.86 (2H, d), 5.48 (1H, d), 4.20 (1H, d), 3.58 (3H, s), 2.24 (3H, s). *Methyl* (R,R)-2-*chloro*-3-*mesyloxy*-3-*phenylpropanoate* was obtained following the procedure described for the tosyl derivative (Found: C, 45.3; H, 4.45; Cl, 12.0. $C_{11}H_{13}ClO_5S$ requires C, 45.1; H, 4.5; Cl, 12.11%); δ (ppm) (CCl_4) 7.15 (5H, m), 5.48 (1H, d), 4.30 (1H, d), 3.58 (3H, s), and 2.08 (3H s).

Kinetic Procedure.—Rates were measured at 30 ± 0.05 °C. The reactions were started by adding a solution of TEA (12 mmol, 100 cm^3) to a solution of the corresponding substrate (0.6 mmol) in the appropriate solvent. In the case of MeOH the basic solution also contained TEA–HCl (6 mmol). The progress of the reaction was checked by quenching aliquots (40 cm^3) in water acidified with hydrochloric acid and extracted with dichloromethane. The worked-up fractions were analysed by ^{1}H NMR integration. The total area corresponding to the aromatic region minus that due to the unreacted material, as estimated from the area under the aliphatic proton signals, gave the area arising from the aromatic protons of the elimination product. Second-order rate constants were obtained in the usual way from those of pseudo-first order.

Product Analysis.—The product compositions were estimated by ^{1}H NMR integration of the areas under the methoxy carbonyl signals for reaction mixtures quenched after eight half-lives.

Table 2 Olefinic product distribution (*Z*:*E*) for the elimination from (*R,R*)-PhCHORCHClCO$_2$Me in various solvents

Compd.	THF	Acetone	MeOH	DMF	AN
1	100:00	100:00	98:02	76:24	63:37
2	100:00	100:00	98:02	81:19	66:34
3	100:00	100:00	100:00	84:16	81:19
4	100:00	100:00	100:00	86:14	85:15
5	100:00	100:00	100:00	97:03	93:07
6	100:00	100:00	100:00	98:02	96:04

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