41. *Carbon–Sulphur Fission in Thioethers. Part IV.*[1] *The Mechanism of Base-catalysed Elimination from 4-Nitrophenethylthio-derivatives of Acetic, Propionic, and Related Acids.*

By Youssef Iskander and Youssef Riad.

The action of dilute alkali on acids $O_2N\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot SZ$ gives 4-nitrostyrene in amounts varying according to the nature of Z and the concentration of alkali. At higher concentrations of alkali (8 equiv., 1·25M) the α-proton-extraction was much faster than elimination of SZ^- from the conjugate base, and accordingly brown-red acids containing nitrogen and sulphur became the main products. Increase in the electronegativity of the sulphur by the introduction of phenyl groups into Z resulted in complete, probably *E*2, elimination, unaccompanied by the formation of brown-red acids. Partial reversibility of the first stage was confirmed in one example by showing that deuterium in the solvent became incorporated in the starting material recovered after partial reaction.

Eliminations, having second-order kinetics, generally have the *E*2 mechanism. The *ElcB* mechanism predicted by Skell and Hauser[2] and discussed by Ingold[3] has been sought by examining reaction in a deuterated solvent and determining deuterium in the starting material recovered after partial reaction. This method, applied to phenethyl bromide, showed no evidence for incorporation of deuterium.

In acids of the type $O_2N\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot S\cdot CRR'\cdot CO_2H$, the *p*-nitro-group is expected to facilitate proton-removal from the α-CH_2 group, and the $S\cdot CRR'\cdot CO_2H$ substituent should be liberated as an anion much less readily than is, for example, the bromide ion from p-$O_2N\cdot C_6H_4\cdot\overset{-}{C}H\cdot CH_2Br$. The action of bases on these compounds has therefore been examined, to see whether this system is suitable for observation of the *ElcB* mechanism (equations 1, 2 with $v_{-1} > v_2$) (cf. ref. 4):

$$\mathrm{OH^- + O_2N\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot S\cdot CRR'\cdot CO_2^-} \underset{v_{-1}}{\overset{v_1}{\rightleftharpoons}} \mathrm{O_2N\cdot C_6H_4\cdot\overset{-}{C}H\cdot CH_2\cdot S\cdot CRR'\cdot CO_2^- + H_2O} \quad . \quad (1)$$

$$\mathrm{O_2N\cdot C_6H_4\cdot\overset{-}{C}H\cdot CH_2\cdot S\cdot CRR'\cdot CO_2^-} \xrightarrow{v_2} \mathrm{O_2N\cdot C_6H_4\cdot CH{:}CH_2 + {}^-S\cdot CRR'\cdot CO_2^-} \quad . \quad . \quad . \quad . \quad (2)$$

Experimental

β-4-*Nitrophenethylthiopropionic Acid.*—4-Nitrophenethyl chloride (5 g.) in alcohol (70 ml.) was treated with a solution of β-mercaptopropionic acid (2·9 g.) and sodium hydrogen carbonate (4·8 g.) in water (20 ml.). The mixture was boiled for 1 hr., cooled, and diluted with water. After removal of turbidity by extraction with ether, acidification gave the *acid* (5·7 g.), m. p. 63—65° (from benzene–light petroleum) (Found: C, 51·6; H, 4·8; N, 5·3; S, 12·9. $C_{11}H_{13}NO_4S$ requires C, 51·8; H, 5·1; N, 5·5; S, 12·5%).

A neutral aqueous solution of the acid, after being boiled for 1 hr., gave only a slight odour of 4-nitrostyrene. In the presence of a slight excess of sodium hydrogen carbonate the same result was obtained. Acidification in these experiments liberated the original acid.

Action of alkalis. (*a*) The acid (2 g.) was boiled in 5% aqueous sodium hydroxide (50 ml., *ca.* 8 equiv.) for 5 min. Steam-distillation of the deep red solution gave 4-nitrostyrene.[1] Acidification of the alkaline residue gave a brown-red acid (0·64 g.) which on purification by repeated precipitation from sodium hydrogen carbonate solution was obtained as a brown-red infusible powder (Found: C, 59·9; H, 4·5; N, 6·5; S, 9·5%). (*b*) When 1—3 equiv. of alkali were used, some 4-nitrostyrene was formed, but on acidification the residue of the original acid was recovered unchanged.

---

[1] Part III, *J.*, 1951, 2058.

[2] Skell and Hauser, *J. Amer. Chem. Soc.*, 1945, **67**, 1661.

[3] Ingold, "Structure and Mechanism in Organic Chemistry," G. Bell and Sons Ltd., London, 1953, p. 423.

[4] Hanna, Iskander, and (in part) Riad, *J.*, 1961, 217.

α-4-*Nitrophenethylthiopropionic Acid.*—This was prepared similarly from α-mercaptopropionic acid, and had m. p. 85—86° (from benzene–light petroleum) (Found: C, 51·7; H, 4·9; N, 5·4; S, 12·2%). The *acid*, on being boiled with dilute alkali (1—3 equiv.), gave 4-nitrostyrene and unchanged starting material. On being boiled with 5% alkali (8 equiv.) it gave 4-nitrostyrene and a brown-red acid (0·65 g.) (Found: C, 56·8; H, 4·7; N, 6·3; S, 8·1%).

α-*Methyl*-α-(4-*nitrophenethylthio*)*propionic Acid.*—Prepared similarly, this *acid* had m. p. 103—104° (from benzene–light petroleum) (Found: C, 53·8; H, 5·5; N, 5·6; S, 11·2. $C_{12}H_{15}NO_4S$ requires C, 53·5; H, 5·6; N, 5·2; S, 11·9%). When boiled with dilute alkali (1—3 equiv.) it gave *p*-nitrostyrene and unchanged starting material; and with 5% alkali (8 equiv.) it gave 4-nitrostyrene and a brown-red acid (Found: C, 57·1; H, 4·8; N, 5·9; S, 9·4%).

α-4-*Nitrophenethylthio*-αα-*diphenylacetic Acid.*—Prepared similarly from 4-nitrophenethyl chloride and α-mercaptodiphenylacetic acid, this *acid* had m. p. 192° (from ethanol) (Found: C, 67·2; H, 4·9; N, 3·0; S, 7·5. $C_{22}H_{19}NO_4S$ requires C, 67·2; H, 4·8; N, 3·6; S, 8·1%). When it (2·0 g.) was boiled with 5% sodium hydroxide solution (50 ml.) for 5 min., the solution became pale red and on steam-distillation gave 4-nitrostyrene; the alkaline residue gave α-mercaptodiphenylacetic acid.

Estimation of 4-*Nitrostyrene.*—Absolute determination of 4-nitrostyrene could not be carried out, but the following approximate method gave consistent results which established trends in the amount formed in the different experiments. The following is an example. β-4-Nitrophenethylthiopropionic acid (0·20 g.) was dissolved in 0·340N-sodium hydroxide (2·3 ml., one equiv.), made up to 50 ml. with water, and brought to the b. p. in exactly 5 min. Boiling was continued for a further 30 min. The solution was cooled for 2 min., then distilled at a rate of about 1·25 ml./min., so as to collect 30 ml., distilled water being added during this process from a separating funnel so that the volume in the distilling flask remained nearly constant. The whole process took 62·5 min. To the distillate (30 ml.) was added purified acetone (30 ml.) and 2N-sulphuric acid (60 ml.), and the mixture was titrated immediately with 0·1164N-potassium permanganate at laboratory temperature until a faint pink colour persisted for 30 sec. The experiment was repeated with 3·45, 4·60, and 6·90 ml. of the alkali (1·5, 2, and 3 equiv. respectively).

The annexed Table shows the detailed results.

Formation of 4-*nitrostyrene from acids* $O_2N\cdot C_6H_4\cdot CH_2\cdot CH_2\cdot SZ$.

		Oxidisable product formed (expressed in ml. of 0·1164N-KMnO₄)			
Group Z	Starting material (g.)	NaOH 1·0 equiv.	NaOH 1·5 equiv.	NaOH 2·0 equiv.	NaOH 3·0 equiv.
$CH_2\cdot CO_2H$	0·1890	0·18	1·95	3·24	5·48
$CHMe\cdot CO_2H$	0·2000	0·12	1·70	3·14	5·18
$CMe_2\cdot CO_2H$	0·2109	0·07	1·30	2·80	4·14
$CH_2\cdot CH_2\cdot CO_2H$	0·2000	0·27	1·65	2·47	4·18
$CPh_2\cdot CO_2H$	0·3082	0·37	1·88	2·94	4·86

Reaction in Deuterium Oxide.—α-4-Nitrophenethylthioacetic acid [1] (0·11 g.) was dissolved in 99·5% deuterium oxide (10 ml.) containing sodium hydroxide (0·0365 g., 2 equiv.). The mixture was boiled for 1 hr., cooled, and acidified. Some unchanged acid was liberated; crystallised from aqueous ethanol, this had m. p. 85°. Comparison of the infrared spectrum of the recovered acid with that of the original sample showed the presence of new bands, as well as the shift of others to longer wavelengths. Attempts to prepare a synthetic sample of the deuterated acid of known deuterium content failed (see below), but other related compounds were prepared and investigated for comparison. Starting from [α-^{2}H]toluene gave the compounds shown in the Table by standard methods. The chlorination, (*a*)→(*b*), is assumed to give a product containing 66% of deuterium in the side-chain, and accordingly compounds (*e*), (*f*), and (*g*) are considered to have the same percentage of side-chain deuterium. Acid-hydrolysis of the nitriles (*f*) and (*g*), and reduction of the nitrile (*f*) by sodium and ethanol, followed by nitration of the resulting amine to obtain 4-nitrophenethylamine hydrochloride (*i*), gave products having infrared spectra identical with those of the appropriate undeuterated materials. So hydrogen–deuterium exchange, probably activated by the cyano-group, must have occurred during the reduction or the hydrolysis of the nitriles.

The Table summarises the important clear changes in infrared spectra[5] [determined in Nujol, except that (*d*) and (*f*) were examined in CCl$_4$]. New bands and band shifts appearing for the acid (*h*) (recovered from the reaction mixture described above after partial reaction) are present also in the spectra of other α-deuterated compounds; the band at 7·7 μ, which is the clearest new one in this spectrum, is present also in the spectra of compounds (*a*), (*d*), (*e*), and (*f*). Similarly the shift from 12·6 to *ca.* 12·9 μ is probably attributable to a band at 12·7 μ in the spectrum of compound (*e*), and may also be responsible for the increased strength of the similar band for (*a*) and for the shifts with (*b*) and (*c*). The band at 13·5 μ for the acid (*h*) is found in a similar region for compounds (*a*) and (*e*), and might have caused the shifts for compounds (*b*) and (*c*). It is concluded that compound (*h*) contained deuterium incorporated in the α-position to the phenyl group.

Infrared absorption bands and spectral changes attributable to C–D *bonds α to a phenyl group.*

Compound	Wavelength (μ)							
Ph·CH$_2$D (*a*)	4·45		7·7		9·25infl 9·65infl	12·65infl		13·8
p-O$_2$N·C$_6$H$_4$·CH$_2$D (*b*)						12·65 → 12·85		13·5 → 13·6
2,4-(O$_2$N)$_2$C$_6$H$_3$·CH$_2$D (*c*)						12·60 → 12·80		13·0 → 13·2
Ph·CHDCl (*d*)	4·4, 4·6w	5·7	7·7sh	8·3infl		11·1		
p-O$_2$N·C$_6$H$_4$·CHDCl (cf. 3) (*e*)			7·7w	8·3w		11·0	12·7	13·25
Ph·CHD·CN (*f*)	4·7w	5·8	7·85					
p-O$_2$N·C$_6$H$_4$·CHD·CN (*g*)		5·97w		8·25w	10·25w	11·15w		
p-O$_2$N·C$_6$H$_4$·CHD·CH$_2$·S·CH$_2$CO$_2$H (*h*)			7·7		9·55	12·6 → 12·95		13·5

infl = Original band at same wavelength greatly increased in strength; → = Band shifted to slightly longer wavelength; sh = shoulder on the 7·9 μ band; w = weak new band.

It may be noted that the new band at 4·4—4·7 μ, found in the spectra of compounds (*a*), (*d*), and (*f*) which do not contain a nitro-group, is absent from the spectra of the corresponding nitro-compounds.

DISCUSSION

For all the acids investigated, the rate of the elimination was increased by increase in the concentration of alkali up to about 3 equiv. Further increase in the concentration of alkali (to about 8 equiv.) introduced a side reaction involving partial transformation of the acids into resinous brown-red acids containing nitrogen and sulphur in the atomic ratio *ca.* 3 : 2. If the second stage of the reaction (v_2, reaction 2) were faster than the first (v_1, reaction 1), then all the carbanions would have reacted to form the corresponding derivative of styrene, as soon as they had been formed. It is suggested that in the present example the first stage is the faster, and hence the accumulation of the conjugate base, caused by increasing the concentration of alkali, has given an opportunity for the side reaction to occur. The N : S ratio, *ca.* 3 : 2 for the brown-red acids, suggests that every two carbanions have united with one 4-nitrostyrene molecule to give a complex structure. This result was found in each case except for the compound RS·CPh$_2$·CO$_2$H which gave no brown-red acid even at high concentration of alkali, but instead 4-nitrostyrene and thiobenzilic acid. This means that the phenyl groups have increased the electron-attraction towards the sulphur atom, and accordingly the rate of the second stage has increased, leaving no chance for an accumulation of the conjugate base to form the brown-red acid; accordingly, for RS·CPh$_2$·CO$_2$H the elimination seems to proceed by the *E*2 mechanism [reactions (1) and (2), with $v_2 \gg v_1$, $v_2 \gg v_{-1}$], and the case becomes similar to the decomposition of the quaternary ammonium salt *p*-O$_2$N·C$_6$H$_4$·CH$_2$·CH$_2$·NMe$_3$$^+$ to 4-nitrostyrene and trimethylamine.[6]

In all the other cases (cf. Table), the reaction probably proceeds by the *E*lc*B* mechanism;

---

[5] Cf. Turkevich, McKenzie, Friedman, and Spurr, *J. Amer. Chem. Soc.*, 1949, **71**, 4045.

[6] Hughes and Ingold, *Trans. Faraday Soc.*, 1941, **37**, 659.

and it was proved that the first stage of the reaction is reversible (v_2 is much less than v_1 or v_{-1}) by establishing that deuterium from the solvent becomes incorporated in the starting material recovered after partial reaction of $RS{\cdot}CH_2{\cdot}CO_2H$ with dilute alkali.

The authors are grateful to the U.A.R. atomic energy establishment in Cairo for supplying the heavy water, and to Professor F. G. Baddar (A'in Shams University, Cairo) for the infrared curves determined in his laboratory. The authors acknowledge their indebtedness to Professor P. B. D. de la Mare, D.Sc., for his interest and suggestions with respect to the preparation of the manuscript.

CHEMISTRY DEPARTMENT, FACULTY OF SCIENCE,
ALEXANDRIA UNIVERSITY, U.A.R.

[*Received, May* 19*th*, 1960.]