465. *Carbon–Sulphur Fission in Thioethers. Part VI.* The Structural Factors Leading to either Carbanion–Sulphenium Fission or α-Proton Extraction in* p-*Nitrophenylmethylthio-acids.*

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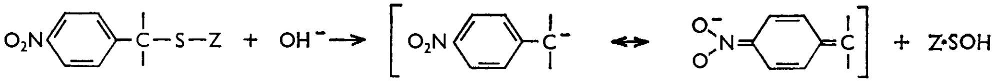
Alkaline hydrolysis of thioethers p-$O_2N{\cdot}C_6H_4{\cdot}CXX'{\cdot}S{\cdot}CX''X'''{\cdot}CO_2H$ and p-$O_2N{\cdot}C_6H_4{\cdot}CX(S{\cdot}CX''X'''{\cdot}CO_2H)_2$ has been investigated. Carbanion–sulphenium fission occurred with all the compounds in series I, II, and III, and with some of the compounds in series IV and VI (see Table).

The mechanism of the formation of *p*-azoxybenzaldehyde and *p*-azoxybenzophenone is discussed.

Whilst *p*-nitrobenzylthiosalicylic acid is rapidly hydrolysed the oxygen analogue is unchanged.

Thioethers (sulphides), p-$O_2N{\cdot}C_6H_4{\cdot}CHX{\cdot}SZ$ and p-$O_2N{\cdot}C_6H_4{\cdot}CX(S{\cdot}CH_2{\cdot}CO_2H)_2$ (X = H or Ph; for Z, cf. Table 1) have been prepared and their sensitivities towards alkalis investigated.[1,2,3,4] Most of these compounds underwent carbanion–sulphenium fission, while the corresponding unnitrated or *m*-nitro-derivatives were recovered unchanged. All the retarding factors, which are increased length of Z or presence of one or two substituted methyl groups in it,[2,4] failed to prevent fission, but in the case of the compound (VA) [3] (cf. Table 1) the second thio-acid group did stop it, although (VIA) underwent fission readily. This difference was attributed to the possibility of *aci*-formation (α-proton-extraction) in (VA), which prevented the C–S fission:



The present work was concerned with the following points: (i) the introduction of further retarding factors in the above structures until the C–S fission is either stopped or

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* Part V, preceding paper.

[1] Schönberg and Iskander, *J.*, 1942, 90.

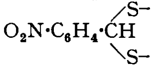
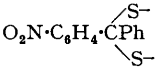
[2] Iskander and Riad, *J.*, 1951, 2054.

[3] Iskander and Salama, *J.*, 1951, 2058.

[4] Iskander and Tewfik, *J.*, 1951, 2050.

exceeded by the α-proton-extraction, so as to find out the structural conditions favouring the predominance of one process over the other. (ii) An investigation of the mechanism of the transformation of the *p*-nitrobenzyl and *p*-nitrodiphenylmethyl anion in aqueous alkaline solution into the corresponding azoxy-compounds, by trapping any intermediate. (iii) Finding out whether sulphur is essential for this type of fission or if it can be extended to the C–O link.

TABLE 1. *Products of the hydrolysis of the thioethers* $O_2N{\cdot}C_6H_4{\cdot}CXX'{\cdot}SZ$ and $O_2N{\cdot}C_6H_4{\cdot}CX(SZ)_2$ *with boiling* 5% *aqueous sodium hydroxide for* 5 *minutes.*

		A	B	C	D
	Z =	$-CH_2{\cdot}CO_2H$	$-CH_2{\cdot}CH_2{\cdot}CO_2H$	$-CHMe{\cdot}CO_2H$	$-CMe_2{\cdot}CO_2H$
I	$O_2N{\cdot}C_6H_4{\cdot}CH_2{\cdot}S-$ ...	azoxy- [1]	azoxy- [1]	azoxy- [2]	azoxy- [2]
II	$O_2N{\cdot}C_6H_4{\cdot}CHPh{\cdot}S-$	azoxy- [3]	azoxy-	azoxy-	azoxy-
III	$(O_2N{\cdot}C_6H_4)_2CH{\cdot}S-$ ...	azoxy- (?)	azoxy- (?)	—	—
IV	$O_2N{\cdot}C_6H_4{\cdot}CPh_2{\cdot}S-$	methane deriv.[1]	unchanged [4]	methane deriv.[4]	unchanged [4]
V	 $O_2N{\cdot}C_6H_4{\cdot}CH(S-)_2$ ...	brown-red acid [3]	brown-red acid	brown-red acid	unchanged
VI	 $O_2N{\cdot}C_6H_4{\cdot}CPh(S-)_2$ ...	azoxy- [3]	unchanged	—	—

azoxy- = 4,4′-diformylazoxybenzene (from the I series) or 4,4′-dibenzoylazoxybenzene (from the II and VI series).
azoxy- (?) = the azoxy-compounds formed are unidentified.

Table 1 combines the results of the present work with previous work. The unnitrated and the *m*-nitro-compounds are not included since they are all stable to alkalis.

The products of the action of alkali on these compounds were the result of any of the following processes: (*a*) Carbanion–sulphenium fission in which the liberated carbanion has extracted a hydrogen from the solvent to give the methane derivative. This occurs when no α-hydrogen is present (series IV):

$$O_2N{\cdot}C_6H_4{\cdot}CPh_2^- + H_2O \longrightarrow O_2N{\cdot}C_6H_4{\cdot}CHPh_2 + OH^-$$

(*b*) Carbanion–sulphenium fission in which the anion has rearranged to give an azoxy-structure (series I, II, III, and the compound VIA):

$$2(O_2N{\cdot}C_6H_4{\cdot}\bar{C}HX) \longrightarrow X{\cdot}CO{\cdot}C_6H_4{\cdot}NO{=}N{\cdot}C_6H_4{\cdot}COX$$

Compound (VIB), however, is recovered unchanged.

(*c*) Retardation of the C–S fission and, in presence of an α-hydrogen atom (series V), proton-extraction leads to the formation of brown-red acids of unknown structure, still having the nitrogen and the sulphur:

$$O_2NC_6H_4{\cdot}CH(SZ)_2 + OH^- \longrightarrow H_2O + [O_2N{\cdot}C_6H_4{\cdot}\bar{C}(SZ)_2] \longrightarrow \text{Brown-red acid}$$

Compound (VD), however, is recovered unchanged.

Discussion.—(i) In series (I) and (II) of Table 1, the introduction of two methyl groups in Z did not prevent C–S fission, thus providing additional evidence against the Teich–Curtin mechanism.[5]

The compounds (IIIA and B) are interesting because their solutions in sodium hydrogen carbonate are dark red, and in cold sodium hydroxide deep wine-red, which on warming change to brown with the precipitation of yellow products expected to have the azoxy-structure (or a more complicated form of it) similar to those of series (I) and (II). The wine-red colour of the acids in solution is presumably that of the readily formed anion:

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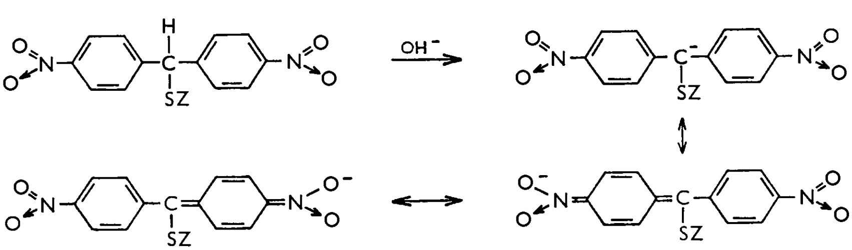
[5] Iskander and Tewfik, preceding paper.

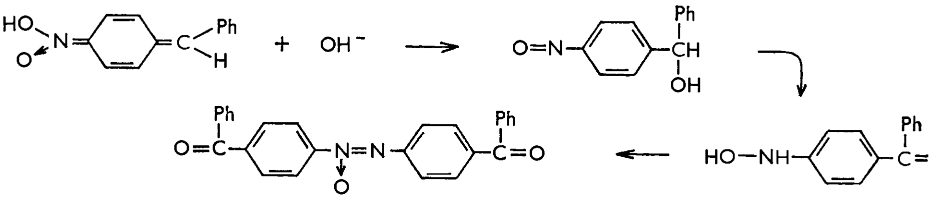


Compounds (VB and C) behaved similar to (VA) previously investigated.[3] They did not undergo C–S fission but changed to brown-red, amorphous, high-melting acids, still containing the nitrogen and sulphur and of unknown structure. Compound (VD), although it has an α-hydrogen atom, was recovered unchanged. It is possible here that the $+I$ effect of the four methyl groups has sufficiently counteracted the labilising influence of the nitro-group on the α-proton.

Compound (VIA) underwent successive C–S fissions,[3] but compound (VIB) was recovered unchanged, thus demonstrating the retarding influence of the length of the acid chain, which could not be detected in series (I, II, and III).

(ii) The azoxy-compounds cannot be formed by direct reduction of the nitro-compounds with sodium sulphide formed in the reaction, since compounds (IVA and C) give sulphide ions but no reduction of the nitro-products occurs, whilst compounds (IB, ID, IIB, and IID) give azoxy-compounds though no sulphide ions are formed. Therefore the azoxy-compounds are probably formed by the rearrangement of the anions resulting from the carbanion–sulphenium fission.

Some support for the mechanism proposed earlier [2] for this transformation was obtained by interrupting the alkaline hydrolysis of the compounds of series (II) before reaction was complete. A compound, m. p. 114—117°, having elementary analysis and properties in agreement with those of 4-nitroso-α-phenylbenzyl alcohol was isolated, though this could not be synthesised. Thus the following reaction sequence may be postulated:



Attempts to prepare the hydroxyamino-compound were not successful, the product being either *p*-aminobenzophenone or 4,4′-dibenzoylazoxybenzene.

(iii) The striking difference between oxygen compounds and their sulphur analogues suggested a comparison of corresponding ethers and thioethers. *p*-Nitrobenzylthiosalicylic acid,[6] when boiled with 5% alkali for 5 min., gave 4,4′-diformylazoxybenzene, whilst the corresponding ether [7] was unchanged by alkali in one hour. The C–S bond fission, therefore, probably occurs by nucleophilic attack by hydroxyl ion on the sulphur atom, which can expand its valency shell whilst oxygen cannot.

EXPERIMENTAL

β-(p-*Nitrodiphenylmethylthio*)*propionic Acid* (IIB).—*p*-Nitrodiphenylmethanol (1 g.) and β-mercaptopropionic acid (0·5 g.) were heated together at 110° while dry hydrogen chloride was passed into the molten mixture for 1·5 hr. Cooling, treatment with sodium hydrogen carbonate solution, removal of turbidity by ether, and acidification gave an *acid* which solidified and separated from benzene–light petroleum in prisms, m. p. 87—89°.

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[6] Apitzsch, *Ber.*, 1913, **46**, 3098.

[7] Lyman and Reid, *J. Amer. Chem. Soc.*, 1929, **51**, 1949.

α-(p-*Nitrodiphenylmethylthio*)-*propionic* (IIC) and -*isobutyric acid* (IID), β-(m-*nitrodiphenylmethylthio*)*propionic acid* (II′B), and α-(m-*nitrodiphenylmethylthio*)-*propionic* (II′C), and -*isobutyric acid* (II′D) were prepared similarly from 1 g. of the alcohol and the equivalent amount (0·5—0·6 g.) of the mercapto-acid, and the products crystallised from benzene–light petroleum; they are recorded in Table 2.

TABLE 2. *Thio-acids.*

Acid	M. p.	Yield (g.)	Found (%) C	H	N	S	Formula	Required (%) C	H	N	S
IIB	87—89°	1·2	60·6	5·0	4·2	9·7	$C_{16}H_{15}O_4NS$	60·6	4·7	4·4	10·1
IIC	104—107	1·2	60·9	5·0	4·2	10·3	$C_{16}H_{15}O_4NS$	60·6	4·7	4·4	10·1
IID	174—175	0·25	61·7	5·2	4·5	9·9	$C_{17}H_{17}O_4NS$	61·6	5·1	4·2	9·7
II′B	97—98	1·2	60·7	4·8	4·6	10·6	$C_{16}H_{15}O_4NS$	60·6	4·7	4·4	10·1
II′C	118—120	1·2	60·7	4·8	4·5	10·3	$C_{16}H_{15}O_4NS$	60·6	4·7	4·4	10·1
II′D	153—155	1·3	61·6	5·0	4·4	9·9	$C_{17}H_{17}O_4NS$	61·6	5·1	4·2	9·7

Alkaline Hydrolysis.—The acid (IIB) (3 g.) was boiled with 5% sodium hydroxide solution (75 ml.) for 5 min. The dark brown solution became red with the formation of a yellow-brown sticky mass which solidified (2 g.) and separated from acetic acid in plates, m. p. 200° alone or mixed with authentic 4,4′-dibenzoylazoxybenzene. On acidification of the alkaline filtrate no hydrogen sulphide was evolved but a precipitate was formed which crystallised from hot water in scales, m. p. 155° alone or mixed with authentic ββ′-dithiodipropionic acid. Repetition of the experiment but boiling for 1 min. only, cooling in ice, and dilution with ice-water gave a yellow-brown sticky mass which dissolved completely in warm acetic acid. Precipitation of successive fractions from this solution with water, warming, and then cooling after every addition, gave finally two fractions: (*a*) 4,4′-dibenzoylazoxybenzene; and (*b*) yellow needles, m. p. 114—117° (Found: C, 73·8; H, 5·3; N, 6·4. $C_{13}H_{11}NO_2$ requires C, 73·2; H, 5·2; N, 6·6%). The latter substance gave a positive Liebermann's nitroso-reaction and when boiled with sodium hydroxide solution or acetic acid gave 4,4′-dibenzoylazoxybenzene. It is thought to be 4-*nitroso*-α-*phenylbenzyl alcohol.*

Alkaline hydrolyses of the acids (IIC and D) gave the above products and differ only in that acidification of the alkaline filtrate of (IIC) gave hydrogen sulphide while that of (IID) gave a precipitate, m. p. 197° alone or mixed with αα′-dithiodi-isobutyric acid but no hydrogen sulphide. The acids (II′B, C, and D) were very stable towards boiling alkali.

pp′-*Dinitrodiphenylmethanol.*—This was prepared by Meerwein–Ponndorf–Verley reduction of 4,4′-dinitrobenzophenone (15 g.) with aluminium isopropoxide (33·6 g.) and propan-2-ol (450 ml.). Acidification gave an *alcohol* (14·5 g.) which separated from toluene in pale yellow needles, m. p. 173—174° (Found: C, 57·0; H, 3·6; N, 10·0. $C_{13}H_{10}O_5N_2$ requires C, 56·9; H, 3·6; N, 10·2%).

pp′-*Dinitrodiphenylmethyl Chloride.*—The alcohol (5·5 g.) and phosphorus pentachloride (4·5 g.) were mixed; hydrogen chloride was evolved in the cold. Heating at 140° for 1 hr., cooling, and pouring into ice-water gave a *chloride* (5 g.) that crystallised from carbon tetrachloride in pale yellow plates, m. p. 111—112° (Found: C, 53·0; H, 3·0; N, 9·1; Cl, 11·8. $C_{13}H_9ClN_2O_4$ requires C, 53·3; H, 3·1; N, 9·5; Cl, 12·1%).

(pp′-*Dinitrodiphenylmethylthio*)*acetic Acid* (IIIA).—The above chloride (5 g.) in alcohol (130 ml.) was treated with a solution of mercaptoacetic acid (2 g.) and sodium hydrogen carbonate (3 g.) in water (20 ml.). Distillation of the alcohol, dilution, filtration from a solid 3·5 g.), and acidification gave the *acid* (1·5 g.) which separated from benzene–light petroleum in pale yellow clusters, m. p. 134—136° (Found: C, 51·3; H, 3·3; N, 8·0; S, 9·0. $C_{15}H_{12}N_2O_6S$ requires C, 51·7; H, 3·4; N, 8·05; S, 9·2%).

The acid (IIIA) (2 g.) was dissolved in 5% sodium hydroxide solution (50 ml.). The deep red solution, on warming, became brown, and after 1 minute's boiling a yellow orange precipitate was formed. After filtration and washing with water, alcohol, and ether, the dry solid (1·5 g.) separated from nitrobenzene–ether as a yellow powder of unknown structure, m. p. >250° (Found: C, 63·9; H, 3·8; N, 8·8%). It is insoluble in molten camphor. Acidification of the alkaline filtrate gave much hydrogen sulphide.

β-(pp′-*Dinitrodiphenylmethylthio*)*propionic Acid* (IIIB).—Prepared in the same way as (IIIA), from the same quantities of chloride and sodium hydrogen carbonate with β-mercaptopropionic acid (2 g.), this acid (1 g.) formed yellow needles, m. p. 148—152° (Found: C, 52·6; H, 4·1; N, 7·7; S, 9·4. $C_{16}H_{14}N_2O_6S$ requires C, 53·0; H. 4·0; N, 8·0; S, 8·8%).

It was hydrolysed in the same way as acid (IIIA). The yellow precipitate (1·5 g.) separated from nitrobenzene–ether as a yellow powder, m. p. >250° (Found: C, 58·3; H, 4·0; N, 20·6%), very different from that obtained from (IIIA) as seen from its analysis. Acidification of the alkaline filtrate gave ββ′-dithiodipropionic acid, m. p. and mixed m. p. 155°.

β- (VB) and α-(p-*Nitrobenzylidenedithio)dipropionic* (VC), α-(p-*nitrobenzylidenedithio)di-(α-methylpropionic)* (VD), β- (V′B) and α-(m-*nitrobenzylidenedithio)dipropionic* (V′C), α-(m-*nitrobenzylidenedithio)di-(α-methylpropionic)* (V′D), β- (V″B) and α-(*benzylidenedithio)dipropionic* (V″C), and α-(*benzylidenedithio)di-(α-methylpropionic acid)* (V″D) were prepared as was (IIB) from the aldehyde (5 g. of benzaldehyde or 7·3 g. of the nitrobenzaldehyde) and the mercapto-acid (10·6 g. of α- or β-mercaptopropionic acid, 11·6 g. α-mercapto-α-methylpropionic acid); they are recorded in Table 3.

TABLE 3. *Dithioacids.*

		Solvent for	Yield	Found (%)					Required (%)			
Acid	M. p.	crystn.	(g.)	C	H	N	S	Formula	C	H	N	S
VB	120—122°	Aq. EtOH	15·5	45·5	4·5	4·0	18·4	$C_{13}H_{15}O_6NS_2$	45·2	4·4	4·1	18·5
VC	116—118	Benzene	15·5	49·95	4·9	3·7	16·6	$C_{13}H_{15}O_6NS_2,\frac{1}{2}C_6H_6$*	50·0	4·7	3·7	16·7
VD	198—199	C_6H_6–EtOH	8·0	48·7	5·1	3·9	16·5	$C_{15}H_{19}O_6NS_2$	48·3	5·1	3·8	17·2
V′B	147—149	,,	15·5	45·6	4·3	4·1	18·6	$C_{13}H_{15}O_6NS_2$	45·2	4·4	4·1	18·5
V′C	Oil	—	—	44·8	4·3	3·9	18·4	$C_{13}H_{15}O_6NS_2$	45·2	4·4	4·1	18·5
V′D	211—213	C_6H_6–EtOH	8·0	48·1	5·3	3·8	17·1	$C_{15}H_{19}O_6NS_2$	48·3	5·1	3·8	17·2
V″B	87—89	Toluene	13·5	52·0	5·5		21·2	$C_{13}H_{16}O_4S_2$	52·0	5·3		21·3
V″C	145—147	Toluene–Pet	13·5	52·5	5·5		21·1	$C_{13}H_{16}O_4S_2$	52·0	5·3		21·3
V″D	165—166	Toluene	14·5	55·1	6·2		19·6	$C_{15}H_{20}O_4S_2$	54·9	6·1		19·5

* The benzene was not completely removed at 100°/vac.

The acid (VB) (5 g.) dissolved in 5% sodium hydroxide solution (125 ml.) forming a dark red solution. Boiling for 5 min. did not give a precipitate. Acidification precipitated an acid (4·1 g.) and gave a trace of hydrogen sulphide. The precipitated acid was extracted with boiling water from which, on cooling, was precipitated a very small amount of ββ′-dithiodipropionic acid, m. p. 155°. The major product was insoluble in water and most organic solvents, but soluble in alcohol or acetic acid. It was precipitated from alcoholic solution by ether as a brown-red acid, m. p. >250°, insoluble in molten camphor. Its structure is unknown (Found: C, 56·9; H, 4·0; N, 7·8; S, 9·3%).

The acid (VC) was hydrolysed as (VB). No precipitation occurred in the alkaline dark red solution after boiling with the alkali. Acidification gave a little hydrogen sulphide and a brown-red acid which was purified by repeated precipitation from alcohol by ether. It did not melt at 300° (Found: C, 53·2; H, 4·7; N, 5·1; S, 14·9%).

The acid (VD) was recovered after 5 minutes' boiling with alkali. The cold alkaline solution of the acid is light red but, on warming, the red colour deepens and fades again on cooling. The acids (V′B, C, and D) and (V″B, C, and D) also resisted the action of boiling alkali.

β-(*Diphenylmethylenedithio)dipropionic Acid* (VI′B).—Benzophenone (6 g.) was heated with β-mercaptopropionic acid (7 g.) at 110° while dry hydrogen chloride was passed in for 4 hr. The *product* (2 g.), extracted as for (IIB) and crystallised from benzene, had m. p. 140—143° (Found: 60·5; H, 5·7; S, 17·1. $C_{19}H_{20}O_4S_2$ requires C, 60·6; H, 5·3; S, 17·0%).

α-(*Diphenylmethylenedithio)dipropionic Acid* (VI′C).—The above method failed to give this acid but it was prepared from benzophenone dichloride (3 g.) and α-mercaptopropionic acid (3 g.) at 110° (1 hr.). The acid *product* (0·1 g.), extracted as before and crystallised from toluene, had m. p. 168—170° (Found: C, 60·2; H, 5·4; S, 17·3. $C_{19}H_{20}O_4S_2$ requires C, 60·6; H, 5·3; S, 17·0%).

α-(Diphenylmethylenedithio)di-(α-methylpropionic acid) was not formed on use of the methods for (VI′B and C). The acids (VI′B and VI′C) were very stable towards boiling alkali.

β-(p-*Nitrodiphenylmethylenedithio)dipropionic Acid* (VIB).—Prepared from *p*-nitrobenzophenone dichloride (3 g.) and β-mercaptopropionic acid (2·3 g.) as above, this *acid* (2·9 g.) crystallised from benzene–light petroleum and had m. p. 143—145° (Found: C, 54·5; H, 4·8; N, 3·3; S, 15·8. $C_{19}H_{19}NO_6S_2$ requires C, 54·2; H, 4·5; N, 3·3; S, 15·2%).

The acid (1 g.) was dissolved in 5% sodium hydroxide solution (25 ml.). The yellow solution, on warming, changed colour to dark red with the precipitation of a slight amount of a yellow substance containing no sulphur. Acidification of the alkaline filtrate did not give hydrogen sulphide but precipitated the original acid (0·6 g.).

o-4-*Nitrobenzylthiobenzoic Acid.*—Apitzsch[6] did not identify the product of the action of the alkali on this acid. The acid (5 g.) was boiled for 5 min. in 5% sodium hydroxide solution (125 ml.). A yellow precipitate (0·9 g.) was formed which from benzene formed yellow crystals, m. p. 190° alone or mixed with 4,4′-diformylazoxybenzene. Acidification of the alkaline filtrate gave an orange-red substance which, crystallised from dilute acetic acid, had m. p. 298° alone or mixed with 2,2′-dicarboxydiphenyl disulphide.

o-*Carboxyphenyl* 4-*Nitrobenzyl Ether.*[7]—This ether (1 g.) was boiled with 5% sodium hydroxide solution (25 ml.) for 1 hr. On acidification the acid was recovered.

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