464. *Carbon–Sulphur Fission in Thioethers. Part V.* The Structural Factors Leading to either Carbanion–Sulphenium Fission or Benzoyl Elimination in (α-Benzoylmethylthio)acetic Acids by the Action of Alkalis.*

By Youssef Iskander and Rasmy Tewfik.

Thioethers Ph·CO·CXX′·S·CX″X‴·CO_2H readily undergo alkaline hydrolysis with carbanion–sulphenium fission when X″ and X‴ are hydrogen or phenyl, but not when they are methyl, showing the polar rather than the steric effect of these groups to be important.

The Teich–Curtin mechanism, based on proton abstraction from the X″ or X‴ positions, cannot apply when both are phenyl. When X″ and/or X‴ are methyl and X and/or X′ are phenyl, the benzoyl group is eliminated owing to resonance stabilisation of the anion formed; this does not occur when X or X′ is hydrogen or methyl.

Thioethers (sulphides), RSZ, are normally very stable towards acids or alkalis, but if R is strongly electron-releasing, the thioether undergoes acidic hydrolysis with carbonium–sulphide fission of the conjugate acid $R-\overset{+}{S}H-Z$, giving ROH and ZSH. On the other hand, when R is electron-withdrawing, the thioether undergoes alkaline fission, giving RH and Z·S·OH,[1] which can be called carbanion–sulphenium fission. Thioethers of the latter type, having the general formula Ph·CO·CXX′·S·CX″X‴·CO_2H were investigated by the authors [2] who found either C–S or CO–C fission according to the natures of the X's.

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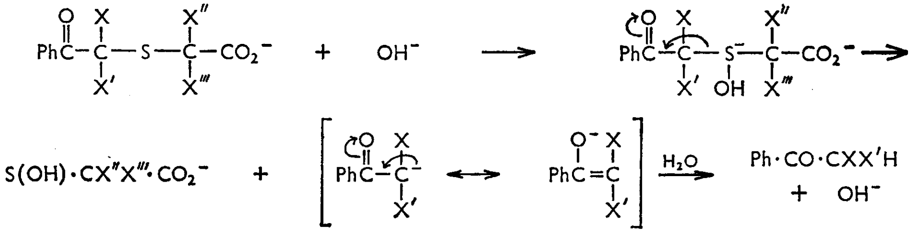
* Part IV, Iskander and Riad, *J.*, 1961, 223.

[1] Iskander, *J.*, 1948, 1549.

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

The explanation given,[1,2] based on that of Behaghel and his co-workers,[3,4] was that, as the hydroxyl ion approaches the sulphur atom, made deficient in electrons by the electron-attractive influence of the carbonyl group, the negative charge imposed on the sulphur atom causes separation of the Ph·CO·CXX′$^-$ anion which receives a hydrogen from a water molecule and regenerates a hydroxyl ion:



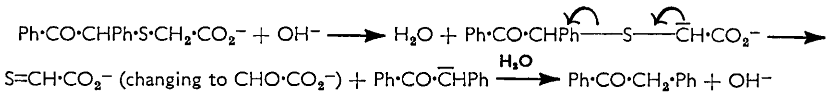
$$\mathrm{PhC({=}O){-}CXX'{-}S{-}CX''X'''{-}CO_2^-} + \mathrm{OH^-} \longrightarrow \mathrm{PhC({=}O){-}CXX'{-}\overset{-}{S}(OH){-}CX''X'''{-}CO_2^-} \longrightarrow$$

$$\mathrm{S(OH)\cdot CX''X'''\cdot CO_2^-} + \left[\mathrm{PhC({=}O){-}\overset{-}{C}XX'} \longleftrightarrow \mathrm{PhC(O^-){=}CXX'}\right] \xrightarrow{\mathrm{H_2O}} \mathrm{Ph\cdot CO\cdot CXX'H} + \mathrm{OH^-}$$

When X″, X‴ = H, $\mathrm{S(OH)\cdot CH_2\cdot CO_2^-}$ changes to $\mathrm{CHO\cdot CO_2^-}$.

The methyl groups in the X″ and X‴ positions release electrons to the sulphur atom and thus hinder the approach of the hydroxyl ions.

Teich and Curtin,[5] however, have proposed that the hydroxyl ion abstracts a proton from the X″ and X‴ positions to form an anion which decomposes to the same final products:



$$\mathrm{Ph\cdot CO\cdot CHPh\cdot S\cdot CH_2\cdot CO_2^-} + \mathrm{OH^-} \longrightarrow \mathrm{H_2O} + \mathrm{Ph\cdot CO\cdot CHPh{-}S{-}\bar{C}H\cdot CO_2^-} \longrightarrow$$

$$\mathrm{S{=}CH\cdot CO_2^-}\ (\text{changing to } \mathrm{CHO\cdot CO_2^-}) + \mathrm{Ph\cdot CO\cdot \bar{C}HPh} \xrightarrow{\mathrm{H_2O}} \mathrm{Ph\cdot CO\cdot CH_2\cdot Ph} + \mathrm{OH^-}$$

They attributed the ease of this proton abstraction to the possibility of expansion of the sulphur valency shell; therefore, in absence of these hydrogen atoms no C–S fission should occur.

The present work was aimed at clarification of three main points: (*a*) Whether our mechanism or Teich and Curtin's is the more probable, by studying cases where both X″ and X‴ are not hydrogen. (*b*) Whether the steric or the polar effects of groups X″ and X‴ cause retardation; they were thus replaced by phenyl which has about the same steric effect but has also $-I \pm T$ effects. (*c*) The influence of methyl and phenyl groups in the X and X′ positions. Table 1 combines results for the present compounds with those previously investigated, and indicates the position(s) of bond fission in the compounds R–S–Z (the standard time of the hydrolysis is 30 min.). The compounds will be discussed in groups.

(I) The (benzoylmethylthio)-acids ($\mathrm{Ph\cdot CO\cdot CH_2\cdot S\cdot CX''X'''\cdot CO_2H}$) (column I). Where X″ and X‴ were phenyl the compound (IE) has undergone 90% of C–S fission, in contrast to the case (ID) where X″ and X‴ were methyl, in which only a trace of C–S fission has occurred. This result indicates: (i) that the absence of hydrogens in X″ and X‴ positions does not stop C–S fission, showing that the Teich–Curtin mechanism is not applicable in this case; (ii) and that the ease of C–S fission of the compound (IE) where X″ and X‴ are phenyl indicates the relative unimportance of steric effects. The phenyl and the methyl groups must have opposite polar effects in these cases. The electron-withdrawing phenyl facilitates approach of hydroxyl ions, while the methyl does not. (iii) The reaction cannot proceed by the S_N1 mechanism, which the methyl groups would have favoured. The "benzoyl" fission did not occur at all in this series of compounds.

(II) The (α-benzoylethylthio)- and (α-benzoylbenzylthio)-acids, $\mathrm{Ph\cdot CO\cdot CXX'\cdot S\cdot CX''X'''\cdot CO_2H}$ (X = H, X′ = Me or Ph). All the (α-benzoylethylthio)-acids (column II) underwent C–S fission, except where X″ and X‴ were both methyl

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[3] Behaghel and Schneider, *Ber.*, 1935, **68**, 1588.
[4] Behaghel and Ratz, *Ber.*, 1939, **72**, 1257.
[5] Teich and Curtin, *J. Amer. Chem. Soc.*, 1950, **72**, 2481.

(IID) when no reaction occurred. When they were phenyl (IIE), C–S fission was nearly complete, confirming again that it is the polar nature rather than the steric effect of groups in these positions that controls the reaction. Compound (II′D) underwent a complete " benzoyl fission " with the separation of a substituted benzyl anion.[2]

TABLE 1. *Modes of fission of compounds* RSZ.

	R	I	II	II′	III	III′
		Ph·CO·CH$_2$–	Ph·CO·CHMe–	Ph·CO·CHPh–	Ph·CO·CMe$_2$–	Ph·CO·CPh$_2$–
	–S–Z					
A	–S·CH$_2$·CO$_2$H	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ [6]	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ [4]	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ [3] 3·5 min.	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$	$\text{CO}\overset{\downarrow}{\text{—}}\text{C}\overset{\downarrow}{\text{—}}\text{S}$ [7] 20% 80%
B	–S·CHMe·CO$_2$H	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ [2]	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$	$\text{CO}\overset{\downarrow}{\text{—}}\text{C}\overset{\downarrow}{\text{—}}\text{S}$ [2] 20% 80%	—	$\text{CO}\overset{\downarrow}{\text{—}}\text{C—S}$ [2]
C	–S·CHPh·CO$_2$H	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$	—	—
D	–S·CMe$_2$·CO$_2$H	CO—C—S [2] Trace	CO—C—S Unchanged	$\text{CO}\overset{\downarrow}{\text{—}}\text{C—S}$ [2]	—	$\text{CO}\overset{\downarrow}{\text{—}}\text{C—S}$ [2]
E	–S·CPh$_2$·CO$_2$H	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ 90%	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ 90%	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$	—	—
F	–S·(CH$_2$)$_2$·CO$_2$H	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ [2] 40%	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ 30%	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ [7] 15% 20 min.	$\text{CO—C}\overset{\downarrow}{\text{—}}\text{S}$ 30%	$\text{CO}\overset{\downarrow}{\text{—}}\text{C—S}$ [7]
		X = X′ = H	X = H, X′ = Me	X = H, X′ = Ph	X = X′ = Me	X = X′ = Ph

(III) The (α-benzoylisopropylthio)- and (α-benzoyldiphenylmethylthio)-acids (X and X′ = Me or Ph). When X″ and X‴ were hydrogen and X and X′ methyls (IIIA), C–S fission was complete. Lengthening the acid chain (IIIF) decreased the fission to 30% but there was no benzoyl fission. The corresponding compounds having phenyl in the X and X′ positions undergo " benzoyl " fission to the extent 20% (III′A) and 100% (III′F). This difference is presumably due to the influence of the phenyl groups that stabilise the anion containing two of them. The second phenyl group in the III′ series, compared with the series II′, favours the benzoyl fission.

EXPERIMENTAL

α-(*Ethoxythiocarbonylthio*)-α-*phenylacetic acid*, Ph·CH(S·CS·OEt)·CO$_2$H, was prepared as described for the analogous isobutyric acids,[8] from α-bromo-α-phenylacetic acid (21·5 g.) and potassium ethyl xanthate (30 g.). It crystallised from carbon tetrachloride in prisms, m. p. 95—96° in almost quantitative yield (Found: C, 51·8; H, 4·8; S, 24·9. $C_{11}H_{12}O_3S_2$ requires C, 51·6; H, 4·7; S, 25·0%).

α-Mercapto-α-phenylacetic acid [9] was obtained as described for α-mercaptoisobutyric acid,[8a] from the above acid. It distilled at 145°/4 mm. (yield 44%). It formed a disulphide, m. p. 218°, identical with an authentic specimen.

α-(*Benzoylmethylthio*)-α-*phenylacetic* (IC) and -αα-*diphenylacetic* (IE), α-(α-*benzoylbenzylthio*)-α-*phenylacetic* (II′C) and -αα-*diphenylacetic* (II′E), and α-*benzylthio*-α-*phenylacetic* (IVC) and -αα-*diphenylacetic* (IVE) *acid* were prepared from the corresponding chloride and the substituted mercaptoacetic acid.

α-(α-*Benzoylethylthio*)-*propionic* (IIB), -α-*methylpropionic* (IID), -*phenylacetic* (IIC), and

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[6] Holmberg, *Arkiv Kemi Min. Geol.*, 1936, **12**, *A*, No. 9; *Chem. Zentr.*, 1936, I, 4564.

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

[8] (*a*) Biilmann, *Annalen*, 1906, **348**, 129; (*b*) Troeger and Volkmer, *J. prakt. Chem.*, 1904, **70**, 488.

[9] Parravano and Tommasi, *Gazzetta*, 1909, **39**, II, 62; Ulpiani and Ciancarelli, *Atti Accad. Lincei*, 1903, **12**, II, 226.

-diphenylacetic (IIE), β-(α-*benzoylethylthio*)*propionic* (IIF), β-(1-*benzoyl*-1-*methylethylthio*)*propionic* (IIIF), and (1-*benzoyl*-1-*methylethylthio*)*acetic* (IIIA) *acid* were prepared from α-bromopropiophenone or α-bromoisobutyrophenone and the corresponding substituted mercaptoacetic or β-mercaptopropionic acid.

These compounds are recorded in Table 2.

TABLE 2. *Thio-acids.* (*For formulæ see Table* 1.*)

Acid	M. p.	Solvent for crystn.†	Yield (%)	Form	Found (%) C	Found (%) H	Found (%) S	Formula	Required (%) C	Required (%) H	Required (%) S
IC	120—121°	Benzene	87	Needles	67·3	5·0	11·3	$C_{16}H_{14}O_3S$	67·1	4·9	11·2
IE	169	Toluene	85	Prisms	72·6	4·9	8·8	$C_{22}H_{18}O_3S$	72·9	5·0	8·8
II′C	(a) 137	Benzene–Pet	65	Needles	73·5	5·1	8·6				
	(b) 154		15	Needles	73·1	4·7	8·5	$C_{22}H_{18}O_3S$	72·9	5·0	8·8
II′E	152—153	Toluene–Pet	91	Cubes	76·3	5·1	7·1	$C_{28}H_{22}O_3S$	76·7	5·0	7·3
II′B	101—102	Benzene–Pet	45	Prisms	60·3	6·1	13·7	$C_{12}H_{14}O_3S$	60·5	5·9	13·4
IIF	64	CCl_4	90	Prisms	60·3	5·9	13·1	$C_{12}H_{14}O_3S$	60·5	5·9	13·4
IID	85—87	CCl_4	50	Needles	61·9	6·5	12·5	$C_{13}H_{16}O_3S$	61·9	6·4	12·7
IIC				Oil	(equiv., 302)		10·1	$C_{17}H_{16}O_3S$	(equiv., 300)		10·7
IIE	153—154	Toluene–Pet	56	Plates	73·5	5·4	8·3	$C_{23}H_{20}O_3S$	73·4	5·3	8·5
IIA	77—78	Toluene–Pet	79	Prisms	60·6	5·9	13·4	$C_{12}H_{14}O_3S$	60·6	5·9	13·4
IIIF	84	CCl_4	62	Plates	61·8	6·3	12·4	$C_{13}H_{16}O_3S$	61·9	6·4	12·7
IVC	85—86	Benzene–Pet	87	Needles	70·0	5·5	12·3	$C_{15}H_{14}O_2S$	69·8	5·4	12·4
IVE	185	Benzene	95	Plates	75·4	5·3	9·4	$C_{21}H_{18}O_2S$	75·5	5·4	9·6
VC	118—119	Aq. EtOH	26	Prisms	75·1	5·4	9·8	$C_{21}H_{18}O_2S$	75·5	5·4	9·6
VE	196—198	MeOH	73	Cubes	79·1	5·2	7·3	$C_{27}H_{22}O_2S$	79·0	5·4	7·8

Acid	Hydrolysis products (from 2 g.
IC	a (0·7 g.), b (1·1 g.), H_2S.
IE	a (0·05 g.), t (0·85 g.), u (0·2 g.), H_2S.
II′C	d (1·2 g.), b (0·7 g.), H_2S.
II′E	d (0·9 g.), n (0·1 g.), t (0·2 g.), H_2S.
II′B	p (1·1 g.), H_2S.
IIF	p (0·4 g.), u (1·3 g.), H_2S.
IID	All recovered unchanged.
IIC	p (0·8 g.), b (0·8 g.), H_2S.
IIE	p (0·2 g.), t (0·5 g.), u (0·25 g.), H_2S.
IIA	i (1·6 g.), H_2S.
IIIF	i (0·35 g.), u (1·35 g.).

* In compounds (IV) R = CH_2Ph, and in (V) R = $CHPh_2$ (see Table 1). † Pet = light petroleum (b. p. 50—60°). ‡ Key: (a) Acetophenone; (b) benzoylformic acid; (t) tetraphenylsuccinic acid; (d) deoxybenzoin; (p) propiophenone; (i) isobutyrophenone; (n) benzophenone; (u) unchanged acid.

General Methods of Preparation.—The chloride or bromide (0·02 mole), in ethanol or acetone (40 ml.), was treated with the mercapto-acid (0·02 mole) and sodium hydrogen carbonate (0·04 mole) in water (20 ml.), and the mixture boiled for 15—30 min. Cooling, dilution with water, removal of any turbidity by ether, and acidification gave the required acid.

α-(*Diphenylmethylthio*)-α-*phenylacetic acid* (VC) was prepared by heating a mixture of diphenylmethyl bromide (4·7 g.) and α-mercapto-α-phenylacetic acid (1·7 g.) in the dry state at 110° until no more hydrogen bromide was evolved. Extraction with sodium hydrogen carbonate and acidification gave the acid.

α-(*Diphenylmethylthio*)-αα-*diphenylacetic acid* (VE) was prepared from the chloride (2·9 g.) and α-mercapto-αα-diphenylacetic acid (2·4 g.) by the same method.

Many attempts were carried out to prepare the acids (IIIB, C, D, and E) and (III′C and E) by different methods, but all failed; either the original materials were recovered unchanged or the disulphide of the mercapto-acid used was formed and isolated.

The last four acids (IVC, IVE, VC, and VE) in Table 2 were prepared to be used as references for the products of the " benzoyl " fission in the (II′) and (III′) series. They are all stable to boiling alkali.

General Method of Alkaline Hydrolysis.—The acid (2 g.) in 5% sodium hydroxide (50 ml.) was boiled for 30 min. The liberated acetophenone, propiophenone, or isobutyrophenone was removed by ether and identified as its 2,4-dinitrophenylhydrazone. Results are in Table 2; the acids (IVC, IVE, VC, and VE) were unchanged.

In case of the acid (II′C), the deoxybenzoin (isolated by filtration or ether-extraction) had

m. p. and mixed m. p. 58—60°. With acid (II'E) the oil liberated was found to be a mixture of deoxybenzoin and benzophenone which were separated by fractional crystallisation of their semicarbazones.

The alkaline solution left after hydrolysis usually gave hydrogen sulphide on acidification [except in the cases of the acid (IID) (recovered unchanged), and the acid (IIIF) (the products of hydrolysis do no give hydrogen sulphide on decomposition)]; benzoylformic acid separated in the case of acids (IC, IIC, and II'C), and tetraphenylsuccinic acid in that of acids (IE and IIE). Benzoylformic acid was identified as its 2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 196—197°. Tetraphenylsuccinic acid was purified by washing it with boiling toluene and separated from methanol in scales, m. p. 294° (Found: C, 78·9; H, 5·3%; equiv., 209·6. Calc. for $C_{28}H_{22}O_4$: C, 79·6; H, 5·2%; equiv., 211); the mixed m. p. with an authentic specimen was undepressed; the recorded m. p.[10] 260—262° is incorrect.

The authors acknowledge their indebtedness to Professor D. H. Hey, F.R.S., for his interest and suggestions with respect to the preparation of the manuscripts of this and the following two papers.

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[*Received, November* 16*th*, 1960.]

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[10] Bickel, *Ber.*, 1889, **22**, 1538.