604. *Eight- and Higher-membered Ring Compounds. Part X.** *Di-, Tri-, and Tetra-thiosalicylides.*

By Wilson Baker, A. S. El-Nawawy, and W. D. Ollis.

Dehydration of thiosalicylic acid gives dithiosalicylide and the hitherto unknown tri- and tetra-thiosalicylides. Alkaline hydrolysis of these compounds regenerates thiosalicylic acid. Di- and tri-thiosalicylides react with benzylamine in boiling benzene to give *N*-benzylthiosalicylamide, which by desulphurisation with Raney nickel gave *N*-benzylbenzamide. When heated with benzylamine an unexpected reaction occurs, the three thiosalicylides each giving *NS*-dibenzylthiosalicylamide.

" Dibenzthiophthene " is shown to be 4′ : 5′-4 : 5-dibenzothiopheno(2′ : 3′-3 : 2)thiophen (VII), because desulphurisation gives dibenzyl and 1 : 2 : 3 : 4-tetraphenyl*cyclo*butane.

The many-membered cyclic anhydro-derivatives of salicylic acid, of three of the cresotic acids, and of thymotic acid, were the subjects of investigations described in Parts II, III, and VI of this series (Baker, Ollis, and Zealley, *J.*, 1951, 201; Baker, Gilbert, Ollis, and Zealley, *J.*, 1951, 209; Baker, Gilbert, and Ollis, *J.*, 1952, 1443). From each of these acids *cis*-di-(8-membered), tri-(12-membered), and tetra-(16-membered)-anhydro-derivatives have been prepared, and in addition, salicylic acid and probably *m*-cresotic acid yielded hexa-(24-membered)-anhydro-compounds. The enquiry has now been extended to thiosalicylic acid, from which only di(thiosalicylide) (I) has previously been

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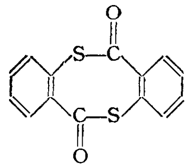
* Part IX, *J.*, 1952, 2991.

prepared (R. Anschütz and Rhodius, *Ber.*, 1914, **47**, 2733), and we find that dehydration can also lead to tri(thiosalicylide) (II), and tetra(thiosalicylide) (III).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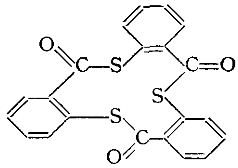
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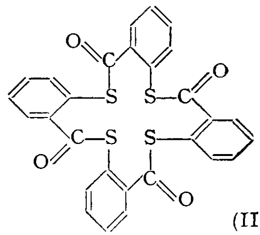
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Although the distillation *in vacuo* of *O*-acetylsalicylic acid gives good yields of *cis*-di- and tri-salicylide (see Part II), the distillation of *S*-acetylthiosalicylic acid gives, according to Anschütz and Rhodius (*loc. cit.*) only a di(thiosalicylide) (I), accompanied by diphenyl disulphide, " dibenzthiophthene," and 9-thioxanthone (the yields of these products are not stated). Repetition of this experiment gave di(thiosalicylide) (5%), diphenyl disulphide (40%), " dibenzthiophthene " (3%) (its structure is discussed below), and traces of 9-thioxanthone and of tetra(thiosalicylide) (III). It has been shown previously that dehydration of salicylic acid yields disalicylide only under mild conditions, and gives increasing amounts of higher salicylides when more vigorous methods are used; these results are in contrast with those obtained by dehydrating thiosalicylic acid, which gives di(thiosalicylide) only under vigorous conditions.

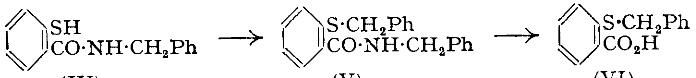
Dehydration of thiosalicylic acid with phosphoric anhydride in toluene or xylene gave di(thiosalicylide) (I) (14—32%), tri(thiosalicylide) (II) (0—15%), and tetra(thiosalicylide) (III) (0—20%) in varying proportions according to the experimental conditions. Increase in the reaction temperature or in the amount of phosphoric anhydride favours the formation of di(thiosalicylide) over the tri- and tetra-compounds; this is contrary to the behaviour of salicylic acid which, under the same conditions, gave the tetramer and hexamer, as well as traces of the trimer. Thiosalicylic acid reacts with phosphorus oxychloride in xylene to give di- and tri-(thiosalicylide) in poor yield. With trifluoroacetic anhydride in xylene thiosalicylic acid gives very small amounts of di-, tri-, and tetra-(thiosalicylide); salicylic acid under these conditions gives small amounts of tetra- and hexa-salicylide.

Di-, tri-, and tetra-(thiosalicylide) are readily hydrolysed to thiosalicylic acid by 5% ethanolic sodium hydroxide, but are relatively stable towards acid hydrolysis, and they are unchanged by phosphorus oxychloride in boiling xylene (cf. conversion of di- and trisalicylide into tetra- and hexa-salicylides under these conditions; Part II, *loc. cit.*). Both di- and tri-(thiosalicylide) separate from benzene with solvent of crystallisation which is not present in stoicheiometric amount; these complexes are presumably clathrates (cf. tetra-*m*- and tri-*p*-cresotide, Part III, and tri-*o*-thymotide, Part VI).

The dipole moment of di(thiosalicylide) (6·39 D) shows that it possesses the *cis* (or " trough ") rather than the centro-symmetrical *trans* (or " chair ") constellation (cf. *cis*-disalicylide, the *cis*-dicresotides, and *cis*-dithymotide, which have dipole moments varying from 6·26 to 6·74 D; Edgerley and Sutton, *J.*, 1951, 1069, and unpublished observation by Dr. L. E. Sutton and Mr. M. F. Saxby, Oxford—see Part VI, *loc. cit.*). The dipole moment of tri(thiosalicylide) (1·54 ± 0·02 D) shows that it probably has a constellation similar to that proposed for trisalicylide (Edgerley and Sutton, *loc. cit.*).

Di- and tri-(thiosalicylide) react normally with benzylamine in boiling benzene to give *N*-benzylthiosalicylamide (IV), and this amide is reduced by Raney nickel to *N*-benzylbenzamide. All three thiosalicylides, however, react abnormally with benzylamine at the boiling point giving *NS*-dibenzylthiosalicylamide (V), the structure of which follows from the facts that (*a*) alkaline hydrolysis gives *S*-benzylthiosalicylic acid (VI), (*b*) desulphurisation with Raney nickel gives *N*-benzylbenzamide and some dibenzyl, (*c*) it may be synthesised by benzylation of *N*-benzylthiosalicylamide (IV) by benzyl chloride and potassium carbonate in acetone or by boiling benzylamine alone. The amide (IV) is clearly an intermediate in the formation of (V) from the thiosalicylides. When boiled with benzylamine, thiosalicylic acid gave a mixture of (IV) and (V).

"*Dibenzthiophthene.*"—This substance, $C_{14}H_8S_2$, isolated in small (3%) yield from the products of distillation of *S*-acetylthiosalicylic acid (Anschütz and Rhodius, *loc. cit.*), is obtained in 16% yield along with di(thiosalicylide) by heating thiosalicylic acid with phosphoric anhydride in tetralin. Anschütz and Rhodius suggested two formulæ for this compound, *viz.* : (VII) and (VIII); and (VII) is now shown to be correct by desulphurisation with Raney nickel. With a freshly prepared specimen of Raney nickel in ethanol it gave 1 : 2 : 3 : 4-tetraphenyl*cyclo*butane (IX) but with Raney nickel which had been kept for three months it gave a mixture of tetraphenyl*cyclo*butane and dibenzyl. When methanol was used as solvent, Raney nickel, either freshly prepared or aged, gave dibenzyl. Both results prove that the benzene rings are united by a C_2 bridge, thus excluding structure (VIII), and it may be observed that only 4′ : 5′-4 : 5-dibenzothiopheno(2′ : 3′-3 : 2)thiophen (VII) contains the carbon skeleton of *two* thiosalicylic acid units. A diradical, •CHPh–CHPh• is probably involved in the formation of tetraphenyl*cyclo*butane and of dibenzyl by the desulphurisation of (VII) (see Kenner, Lythgoe, and Todd, *J.*, 1948, 961). Stilbene is not an intermediate in the reaction of (VII) with Raney nickel, as it gives neither dibenzyl nor 1 : 2 : 3 : 4-tetraphenyl*cyclo*butane under these conditions.



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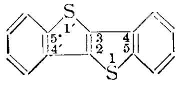

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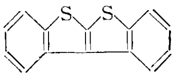

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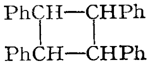

(IX)

EXPERIMENTAL

M. p.s are uncorrected. Molecular weights were determined with a Menzies–Wright apparatus as described in Part II (*J.*, 1951, 208). Analyses are by Drs. Weiler and Strauss, Oxford, and by Mr. W. M. Eno, Bristol.

Dehydration of Thiosalicylic Acid.—(*a*) *Phosphoric anhydride in toluene.* cis-*Di*(*thiosalicylide*) (I), *tri*(*thiosalicylide*) (II), *and tetra*(*thiosalicylide*) (III). Thiosalicylic acid (15 g.) and phosphoric anhydride (45 g.) were heated under reflux in dry toluene (200 c.c.) for 5·5 hours; after cooling, the solid cake on the surface was separated and triturated with hot chloroform. The combined toluene and chloroform solutions were washed with aqueous 5% sodium hydrogen carbonate, dried, and evaporated under diminished pressure. The residue was fractionally crystallised from benzene, and the two components, which both contain benzene of crystallisation, separated by handpicking; this is facilitated by the fact that di(thiosalicylide) rapidly loses its benzene of crystallisation at room temperature and the crystals become opaque. The *cis*-di(thiosalicylide) (II) (1·9 g., 14%) was recrystallised from benzene, giving the *benzene* complex as large, thick parallelograms (Found : loss in wt. when a freshly prepared specimen was kept at 100°, 13·5%. $C_{14}H_8O_2S_2,0{\cdot}55C_6H_6$ requires C_6H_6, 13·6%).

Crystallisation from chloroform gave unsolvated *cis*-di(thiosalicylide) as irregular, thick rhombs, m. p. 176—177° [Anschütz and Rhodius, *loc. cit.*, gave m. p. 175° (rapid heating); the two m. p.s mentioned by them were not verified] (Found : C, 61·3; H, 3·1; S, 23·25%; *M*, ebullioscopic in benzene, 293; *M*, ebullioscopic in chloroform, 282. Calc. for $C_{14}H_8O_2S_2$: C, 61·7; H, 2·9; S, 23·5%; *M*, 272).

The *tri*(*thiosalicylide*) (II) (2·0 g., 15%) separated from benzene in long, colourless prisms containing solvent of crystallisation (Found : loss in wt. at 100° of a freshly prepared specimen, 12·2%. $C_{21}H_{12}O_3S_3,0{\cdot}725C_6H_6$ requires C_6H_6, 12·2%). Crystallisation from chloroform or dioxan gave unsolvated tri(thiosalicylide), m. p. 257—258° (Found : C, 61·8; H, 2·7; S, 23·7%; *M*, ebullioscopic in benzene, 416; *M*, ebullioscopic in chloroform, 420. $C_{21}H_{12}O_3S_3$ requires C, 61·7; H, 2·9; S, 23·5%; *M*, 408).

The solid (3·1 g.; m. p. 248—250°) which separated from the cooled reaction mixture and was insoluble in hot chloroform (see above) was crystallised several times from dioxan–chloroform and finally from dioxan, giving *tetra*(*thiosalicylide*) (2·6 g., 20%) as long needles, m. p.

288—290° (rapid heating) (Found: C, 61·7; H, 3·7; S, 22·9%; *M*, ebullioscopic in benzene, 556; *M*, ebullioscopic in chloroform, 554. $C_{24}H_{16}O_4S_4$ requires C, 61·7; H, 2·9; S, 23·5%; *M*, 544). Small amounts of tri(thiosalicylide) were also isolated during these crystallisations. Tetra(thiosalicylide) is only slightly soluble in benzene but is very easily soluble in dioxan and chloroform.

(*b*) *Phosphoric anhydride in xylene.* cis-*Di*(*thiosalicylide*) (I), *tri*(*thiosalicylide*) (II), *and tetra*(*thiosalicylide*) (III). Thiosalicylic acid (20 g.) and phosphoric anhydride (30 g.) were boiled in xylene (250 c.c.) for 4 hours and worked up as in the previous case. The non-acidic product (6·9 g.) was extracted with hot benzene (150 c.c.), and the residue was dissolved in hot dioxan. The benzene extract gave *cis*-di(thiosalicylide) (3·1 g.; m. p. 176—177°) and tri-(thiosalicylide) (1·5 g.; m. p. 257—258°), and the dioxan solution yielded tetra(thiosalicylide) (0·2 g.; m. p. 288—290°).

With 2½ times the amount of phosphoric anhydride and 24 hours' heating the products were "dibenzthiophthene" (0·3 g.) and *cis*-di(thiosalicylide) (2·2 g.). 4 : 5-4′ : 5′-*Dibenzothiopheno*-(2′ : 3′-3 : 2)*thiophen* (VII) separated from glacial acetic acid as thin, colourless flakes, m. p. 209—210° (Anschütz and Rhodius, *loc. cit.*, give m. p. 216°) (Found: C, 70·5; H, 3·6; S, 26·9%; *M*, ebullioscopic in benzene, 237. $C_{14}H_8S_2$ requires C, 70·0; H, 3·3; S, 26·7%; *M*, 240).

Similarly salicylic acid (35 g.), phosphoric anhydride (40 g.), and xylene (250 c.c.) gave, after 2·5 hours' heating, trisalicylide, m. p. 200° (0·5 g., 2%), tetrasalicylide, m. p. 298—300° (5·5 g., 20%), hexasalicylide, m. p. 375° (rapid heating) (3 g., 11%), and unchanged salicylic acid (4 g.).

p-Cresotic acid (10 g.) and phosphoric anhydride (15 g.) in xylene (200 c.c.) gave similarly tri-*p*-cresotide, m. p. 245° (0·9 g.), and tetra-*p*-cresotide, m. p. 347° (decomp.) (2·9 g.).

(*c*) *Phosphoric anhydride in tetralin.* cis-*Di*(*thiosalicylide*) *and dibenzothiophenothiophen.* Thiosalicylic acid (25 g.), boiled with phosphoric anhydride (40 g.) and tetralin (150 c.c.) for 3 hours, gave dibenzothiophenothiophen (3·4 g.) and *cis*-di(thiosalicylide) (4·2 g.); no other thiosalicylide was isolated.

(*d*) *Phosphorus oxychloride in xylene.* cis-*Di*(*thiosalicylide*), *tri*(*thiosalicylide*), *and dibenzothiophenothiophen.* Thiosalicylic acid (84 g.), redistilled phosphorus oxychloride (135 c.c.), and xylene (300 c.c.) were boiled for 8 hours, cooled, and poured into iced water (1·5 l.). The xylene layer, after being washed with aqueous 5% sodium hydrogen carbonate, finally gave a product which was fractionally crystallised from benzene, giving the less soluble dibenzothiophenothiophen (0·5 g.) and a mixture of *cis*-di- and tri-(thiosalicylide) which was separated as before. Recrystallisation gave *cis*-di(thiosalicylide) (2·6 g.; m. p. 176—177°) and tri(thiosalicylide) (0·6 g.; m. p. 257—258°).

(*e*) *Trifluoroacetic anhydride in xylene.* cis-*Di*(*thiosalicylide*), *tri*(*thiosalicylide*), *and tetra*(*thiosalicylide*). Thiosalicylic acid (5 g.), trifluoroacetic anhydride (7 g.; Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2977), and xylene (150 c.c.) were boiled for 1·5 hours and worked up as in previous cases, giving *cis*-di(thiosalicylide) (0·3 g.), tri(thiosalicylide) (0·1 g.), and tetra(thiosalicylide) (0·1 g.); thiosalicylic acid (2·2 g.) was recovered.

Similarly salicylic acid (5 g.) and trifluoroacetic anhydride (7 g.) in xylene (50 c.c.) gave tetrasalicylide, m. p. 298—300° (15 mg.), and hexasalicylide (10 mg.); salicylic acid (1 g.) was recovered.

Action of Heat on S-*Acetylthiosalicylic Acid.* cis-*Di*(*thiosalicylide, Dibenzothiophenothiophen, and Diphenyl Disulphide* (cf. Anschütz and Rhodius, *loc. cit.*).—*S*-Acetylthiosalicylic acid (20 g.) was heated just above its m. p. (*ca.* 130°) at 22—26 mm. in the apparatus described by Baker, Ollis, and Zealley (Part II, *loc. cit.*) until no more acetic acid distilled. The temperature was raised to 160—170° and the yellow sublimate (7·5 g.) was dissolved in acetic acid. Dibenzothiophenothiophen (0·4 g.; m. p. 209—210°) separated and water was added to the mother-liquors, giving a precipitate (5·5 g.) which was fractionally crystallised from light petroleum (b. p. 40—60°). Recrystallisation of the various fractions from the appropriate solvent gave diphenyl disulphide (4·5 g.; m. p. 60—61°) (lit., m. p. 60°); *cis*-di(thiosalicylide) (0·76 g.; m. p. 176—177°), 9-thioxanthone, m. p. 202—203° (lit., m. p. 207°), and a trace of tetra(thiosalicylide), m. p. 282—284°.

Alkaline Hydrolysis of the Thiosalicylides.—The finely powdered thiosalicylide was boiled with excess of 5% ethanolic sodium hydroxide for 3 hours and evaporated under diminished pressure. Addition of dilute hydrochloric acid and extraction with ether gave thiosalicylic acid, m. p. and mixed m. p. 163—164°, in each case [yields from *cis*-di(thiosalicylide), 68%, tri(thiosalicylide), 70%, and tetra(thiosalicylide), 60%].

N-*Benzylthiosalicylamide* (IV) *and its Desulphurisation.*—Di- or tri-(thiosalicylide) (250 mg.)

and benzylamine (1 c.c.) in benzene (50 c.c.) were boiled in an atmosphere of nitrogen for 7 hours, the benzene evaporated under diminished pressure, and the residue triturated with dilute acid. The solid (350 mg., 79%) was recrystallised from ethanol–water, giving N-*benzylthiosalicylamide* (IV) as needles, m. p. 204—206° (Found: C, 69·1; H, 5·1; N, 5·8; S, 13·8. $C_{14}H_{13}ONS$ requires C, 69·1; H, 5·35; N, 5·8; S, 13·2%).

N-Benzylthiosalicylamide (0·5 g.) and Raney nickel (*ca.* 3 g.) in ethanol (80 c.c.) were boiled for 4 hours and filtered while hot through Filtercel, which was washed twice with hot ethanol (50 c.c.). The ethanol yielded a residue of *N*-benzylbenzamide (0·25 g.; m. p. 100°) which separated from aqueous ethanol as needles, m. p. and mixed m. p. with an authentic specimen, 103—104°.

NS-*Dibenzylthiosalicylamide* (V).—(*a*) *Reaction of the three thiosalicylides with excess of benzylamine.* Each thiosalicylide (0·5 g.), benzylamine (3 c.c.), and a trace of ammonium chloride were boiled for 3 hours, cooled, poured into water and made slightly acid. The resulting oil slowly solidified and was recrystallised from ether, giving NS-*dibenzylthiosalicylamide* (V) as needles, m. p. 97° (Found: C, 75·0; H, 5·75; N, 4·2; S, 9·6%; *M*, ebullioscopic in benzene, 336; *M*, ebullioscopic in chloroform, 317. $C_{21}H_{19}ONS$ requires C, 75·6; H, 5·7; N, 4·2; S, 9·6%; *M*, 333). The yields were *cis*-di- 91%, tri- 90%, and tetra-(thiosalicylide) 79%.

(*b*) *From* N-*benzylthiosalicylamide* (IV) *and benzyl chloride.* The amide (175 mg.), benzyl chloride (1·3 g.), anhydrous potassium carbonate (0·4 g.), and acetone (40 c.c.) were boiled for 2¾ hours, cooled, filtered, and evaporated under diminished pressure. Water was added and chloroform-extraction yielded a solid which was recrystallised from aqueous methanol, giving *NS*-dibenzylsalicylamide (190 mg.), m. p. and mixed m. p. 97—98°.

(*c*) *From* N-*benzylthiosalicylamide* (IV) *and benzylamine.* The amide (250 mg.) and benzylamine (5 c.c.) were boiled for 15 hours, cooled, poured into dilute acid, and extracted with chloroform. This extract yielded *NS*-dibenzylthiosalicylamide (0·3 g.), m. p. and mixed m. p. 97—98° after crystallisation from aqueous methanol.

(*d*) *From thiosalicylic acid and benzylamine.* The acid (2·0 g.), benzylamine (10 c.c.), and a trace of ammonium chloride were boiled for 5 hours, then poured into dilute acid, and the precipitate was washed with warm ether. The ethereal washings yielded the less soluble *N*-benzylthiosalicylamide (1·0 g.), m. p. and mixed m. p. 204—206°, and *NS*-dibenzylthiosalicylamide (1·0 g.), m. p. and mixed m. p. 97°.

Raney Nickel Desulphurisation and Alkaline Hydrolysis of NS-*Dibenzylthiosalicylamide* (V).—The amide (2 g.), Raney nickel (5 g.), and ethanol (80 c.c.) were heated for 5 hours, and after filtration through Filtercel the filtrate yielded a residue (1·1 g.) which was recrystallised from aqueous methanol, giving *N*-benzylbenzamide, m. p. and mixed m. p. 103—104°. From the mother-liquors traces of dibenzyl, m. p. and mixed m. p. 50—51°, were isolated.

NS-Dibenzylthiosalicylamide (0·66 g.) and 10% ethanolic sodium hydroxide (10 c.c.) were boiled for 16 hours, and the ethanol was removed under diminished pressure. After addition of dilute acid the precipitate (0·48 g., 99%), m. p. 178—180°, was sublimed at 150°/13 mm., and recrystallised from ethanol, giving *S*-benzylthiosalicylic acid, m. p. 189° (Found: C, 69·0; H, 5·0; S, 13·0. Calc. for $C_{14}H_{12}O_2S$: C, 68·8; H, 4·9; S, 13·1%) (Apitzsch, *Ber.*, 1913, **46**, 3102, gives m. p. 189°).

Raney Nickel Desulphurisation of Dibenzothiophenothiophen (VII).—(*a*) Dibenzothiophenothiophen (0·06 g.) and Raney nickel (2·0 g.; Brown, *J. Soc. Chem. Ind.*, 1950, **69**, 355) in methanol (30 c.c.) were boiled for 3 hours and worked up as in previous cases. The product was dibenzyl (0·03 g., 66%), m. p. and mixed m. p. 50—51°.

(*b*) Dibenzothiophenothiophen (0·44 g.) and freshly prepared Raney nickel (8 g.) were boiled in ethanol (75 c.c.) for 3·5 hours. The crude product (0·26 g.) was recrystallised from aqueous methanol, giving 1 : 2 : 3 : 4-tetraphenyl*cyclo*butane (IX) (0·18 g., 55%), m. p. 162—163° (Pailer and Müller, *Monatsh.*, 1948, **79**, 615, give m. p. 164—165°). A similar experiment using dibenzothiophenothiophen (0·18 g.) and a specimen of Raney nickel prepared 3 months earlier gave 1 : 2 : 3 : 4-tetraphenyl*cyclo*butane (0·05 g.) and dibenzyl (0·045 g.).

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