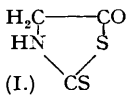
123. *Studies in the Azole Series. Part XXV. The Action of Bases on 2-Thio-5-thiazolidone.*

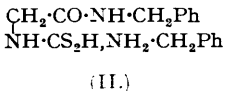
By A. H. Cook and A. L. Levy.

2-Thio-5-thiazolidone (I) reacts vigorously with primary and secondary bases to give salts of the corresponding *N*-dithiocarboxyglycine amides (*e.g.*, II). In the presence of aqueous acids these are recyclised to (I), but with anhydrous acids afford carbon disulphide and the corresponding glycine amide salts. Triethylamine or aqueous alkali causes dimerisation of (I) to a derivative of diaminoacetone, whereas pyridine and alcohols effect polymerisation to polyglycines of low molecular weight.

In Part III (Cook, Heilbron, and Levy, *J.*, 1948, 201) a synthesis of the novel 2-thio-5-thiazolidone (I) by the action of acids on salts of carbamylmethyldithiocarbamic acid was described. The present communication is concerned with a study of the action of bases on this compound (I).



(I.)



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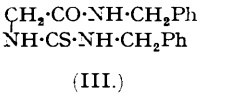
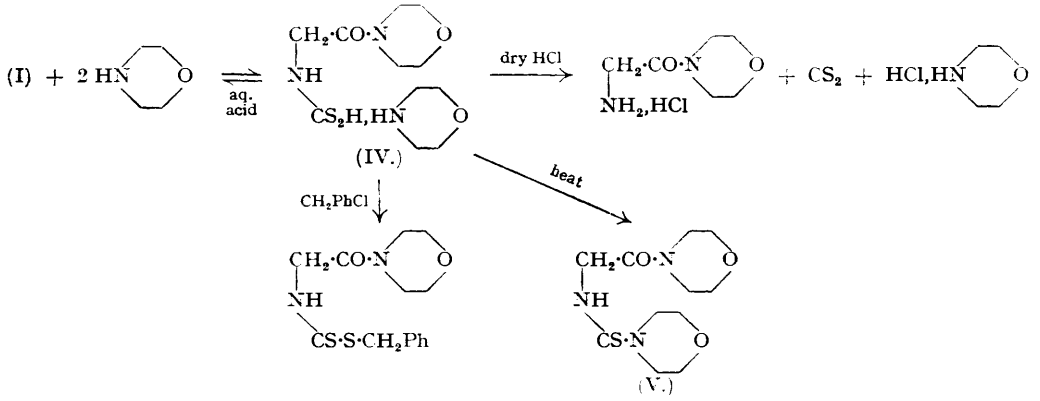


(III.)

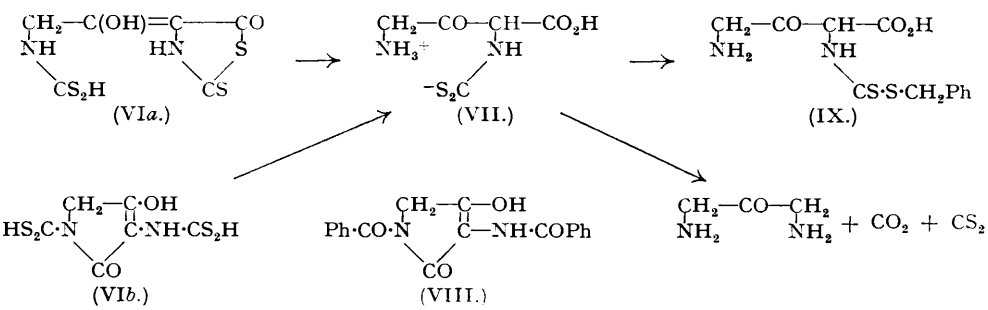
When (I) was treated with benzylamine in ether at 0°, the product rapidly separated as a gum, which was presumably benzylammonium *N*-(*N'*-benzylcarbamylmethyl)dithiocarbamate (II), since it readily regenerated (I) on acidification. Dissolved in benzylamine, however, and gently warmed, (I) yielded the crystalline thiourea (III), identical with that described earlier (Cook, Harris, Heilbron, and Shaw, *J.*, 1948, 1058). It will be recalled (Cook, Harris, Heilbron, and Shaw, *loc. cit.*) that relatively minor changes in the experimental conditions gave either (III) or benzyl *N*-(*N'*-benzylcarbamidomethyl)dithiocarbamate, when 2-benzylthio-5-thiazolinone was treated with benzylamine.



Morpholine, selected as a model secondary amine, was found to react rapidly and exothermally with (I) in ether, acetone, or ethanol to give the *morpholinium* salt of *N*-dithiocarboxy-

glycine morpholide (IV) in a yield of 87%. This structure was confirmed by shaking (IV) with benzyl chloride in ether–water, whereupon the S-*benzyl* ester was produced. Under more vigorous conditions, however, or when (IV) was heated in methanol, hydrogen sulphide was lost and the substituted *thiourea* (V) was produced. (IV) was reconverted into (I) in 84% yield by dissolution in water and acidification with hydrochloric acid, so that the synthesis of the thiothiazolidone is by no means confined to simple carbamylalkyldithiocarbamates. Indeed, the morpholide (IV) appeared to undergo cyclisation even more readily than the simple amide. When (IV) was treated with dry hydrogen chloride in chloroform, however, another reaction took place, carbon disulphide, morpholine hydrochloride, and *glycine morpholide hydrochloride* being produced. When 3-acetyl-2-thio-5-thiazolidone (Cook, Heilbron, and Levy, *loc. cit.*) (the location of the acetyl group in the 3-position is not proven though it is supported by the low melting point of the compound) was treated with morpholine in acetone, (IV) was once again produced; the acetyl group was also detached by rapid treatment with warm concentrated hydrochloric acid, (I) being isolated.

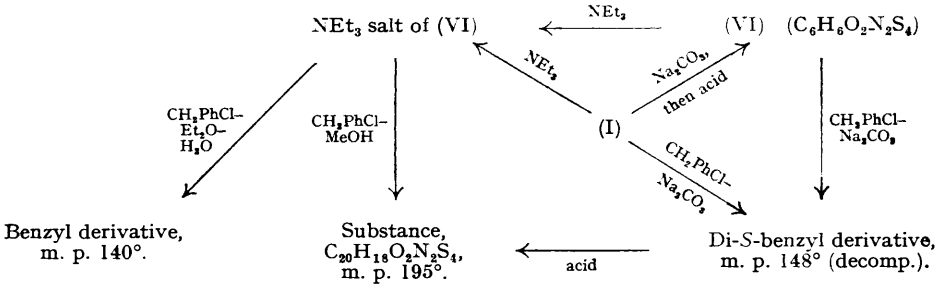
When 2-thio-5-thiazolidone (I) was treated with triethylamine in acetone, a crystalline *salt* rapidly separated which seemed from its composition to be the triethylamine salt of (I). On acidification in water, however, it gave a labile yellow isomeride of (I), which for reasons which will now be developed is regarded as a *dimeride*, $C_6H_6O_2N_2S_4$ (VI). This substance was soluble in sodium hydrogen carbonate and gave a dark green colour with ferric chloride. The same compound was produced, to the extent of about 60%, by keeping (I) overnight in sodium hydroxide or carbonate solution, and acidifying the solution; the remaining 40% was converted into sodium carboxymethyldithiocarbamate, which decomposed to give glycine and carbon disulphide on acidification. The dimeride was freely soluble in cold acetone, methanol, or ethanol, but after a few minutes these solutions deposited colourless needles of a compound, $C_5H_8O_3N_2S_2$ (VII), which was soluble in sodium hydroxide though no longer soluble in sodium hydrogen carbonate, and gave a deep green colour, rapidly becoming purple, with ferric chloride. It afforded a reddish-purple colour with the ninhydrin reagent, was insoluble in common solvents, and melted with decomposition about 200°. Inspection of the empirical formula shows that loss of carbon disulphide and addition of the elements of water had occurred in this reaction. The compound (VII) was most conveniently prepared by dissolving the triethylamine salt of (VI) in acetic acid, whereupon it separated almost immediately in 75% yield. An important clue to the nature of these compounds was provided by acid hydrolysis of (VII), which very readily gave carbon disulphide, carbon dioxide, and 1 : 3-diaminoacetone (isolated as its *dipicrate*). The dimeride (VI) also yielded these products when boiled for a short while with 2N-hydrochloric acid, but a sulphur-containing *substance* isomeric with (VII), but of unknown structure, was formed in addition. The last-mentioned substance gave no diaminoacetone on further hydrolysis, and therefore represents an alternative path of decomposition.



The isolation of diaminoacetone showed that the dimerisation reaction essentially involved attaching the carbonyl grouping of one thiazolone molecule to the active methylene group of another, yielding ultimately a ketone. Thus the simplest expression for the dimeride is the dithiocarbamic acid (VI*a*), which also satisfactorily accommodates all the known facts. Compound (VII) then becomes *γ-amino-α-dithiocarboxyaminoacetoacetic acid betaine*, the structure of which is in keeping with its zwitterionic character and ease of hydrolysis. The dimerisation of (I) recalls a similar change which takes place when 2-phenyloxazolone is treated with Grignard reagents or a mixture of triethylamine and hydrogen cyanide (Cook, Elvidge, Heilbron, and Levy, " The Chemistry of Penicillin," Princeton Univ. Press, 1949, p. 738; Bailey, Baker, and Bradley, *ibid.*). The dimeride in this case has been shown to be " dibenzamidodi-

oxytetrol" (VIII) (Cornforth and Huang, *J.*, 1948, 1958), and so the formally similar expression (VI*b*) should be considered for the dimeride of 2-thio-5-thiazolidone. This alternative expression would not seem to account so well, however, for the addition of water under mild conditions to give (VII).

When (VII) was shaken with benzyl chloride and sodium carbonate solution a mono-*S*-benzyl derivative was obtained, which formed a highly crystalline *hydrochloride*. It was soluble in aqueous sodium hydroxide (though not in aqueous sodium carbonate) and gave an intense colour with the ninhydrin reagent, even in the presence of cupric carbonate, and is therefore formulated as the γ-amino-acid (IX). Under other conditions (I), (VI), and the triethylamine salt of (VI) give altogether three further benzyl *derivatives*; the analyses, solubilities in alkali, and colour reactions do not, however, provide sufficient evidence on which to assign structures to them, but their interrelations are summarised in the following scheme :



Acetylation of (I), (VI), and (VII) in the presence of bases leads to a variety of derivatives dependent on quite small changes in the experimental conditions. The products contain either 2 or 3 acetyl groups, and have all to some extent lost the elements of water. While it is yet too soon to assign individual structures, it is probable from the fact that they do not give ferric chloride colours and do not regenerate the starting materials on hydrolysis, that the products are acetylated thiazoles and oxazoles formed by cyclisation of $-NH\cdot CS_2H$ and $-NH\cdot CO\cdot CH_3$ on to the enolic hydroxyl group of (VI) and (VII). The results are summarised in the table.

		Derivative of (VI) produced.		
Starting material.	Reagent.	No. of Ac groups.	Elements lost.	M. p.
(I)	Ac_2O–NEt_3	3	H_2O	137°
(VI) [a]	Ac_2O + trace of NEt_3			
,, ...	Ac_2O–C_5H_5N	—	—	95
,, ...	Ac_2O–NEt_3	2	CS_2, H_2O	158
NEt_3 derivative [b] of (VI)	Ac_2O			
NEt_3 derivative [c] of (VII)	Ac_2O–NEt_3	3	$2H_2O$	147
,, ,, ,, ...	Ac_2O–C_5H_5N	—	—	173

[a] From (I) by aqueous alkali. [b] From (I) by NEt_3. [c] From (VI) by pyridine or from the NEt_3 derivative of (VI) by AcOH.

Finally, by the action of pyridine on (I), slowly in the cold or rapidly on heating, a *substance* was produced which was insoluble in water and all organic solvents, and soluble only in concentrated hydrochloric acid and aqueous alkalis. Since most of the sulphur had been lost, the material is regarded as a crude polyglycine. It is worth recalling that pyridine rapidly effects the expulsion of carbon dioxide from the analogous anhydrocarboxyamino-acids, with accompanying polymerisation (*inter alia*, Wesseley and Sigmund, *Z. physiol. Chem.*, 1926, **157**, 91). A Van Slyke amino-nitrogen determination indicated a molecular weight of 605 per terminal $-NH_2$, which corresponds to about 9 glycine residues, in fair agreement with the analytical figures, which indicate one atom of sulphur in such a molecule. Insoluble high-melting substances of similar gross composition were also produced by refluxing (I) for a short time in methanol or ethanol, the methoxyl content of a product from the former solvent indicating an average molecular length of 8 glycine residues.

Experimental.

Action of Benzylamine on (I).—2-Thio-5-thiazolidone (1·0 g.) was dissolved in dry ether, and benzylamine (1·61 g., 2 equivs.) added at 0°. A white solid separated at once, which became gummy on exposure to air and afforded (I) on acidification with 2N-hydrochloric acid.

Action of Morpholine on (I).—Morpholine (1·8 g., 2 equivs.) was added to 2-thio-5-thiazolidone (1·3 g.) in acetone (20 c.c.) at 0° during 2 minutes, and the product (2·6 g., 87%), m. p. 127° (decomp.), filtered off after 15 minutes at room temperature. The *morpholinium* salt of *N*-dithiocarboxyglycine-morpholide (IV) recrystallised from aqueous acetone in rectangular prisms, m. p. 142° (decomp.) (Found : C, 43·4; H, 6·4; N, 13·6. $C_{11}H_{21}O_3N_3S_2$ requires C, 43·0; H, 6·8; N, 13·7%), though after crystallisation from hot methanol the m. p. rose to 193°, giving (V). It gave a colourless precipitate with aqueous mercuric chloride, a creamy precipitate (decomp. 100°) with lead acetate, and a pale yellow silver salt which rapidly darkened and was black after 1—2 minutes. The salt (IV) was shaken with excess of benzyl chloride in ether–water for 2·5 hours, whereupon the *benzyl* ester separated; it recrystallised from ethanol in star-like clusters of needles, m. p. 135—136° (Found : C, 54·2; H, 6·1; N, 8·8. $C_{14}H_{18}O_2N_2S_2$ requires C, 54·2; H, 5·8; N, 9·0%). (I) (1·3 g.) was warmed on the steam-bath with morpholine (10 c.c.) for 5 minutes and diluted with acetone to give the substituted *thiourea* (V) (0·7 g.), m. p. 195—196° (decomp.) (after crystallisation from methanol or water) (Found : N, 15·5. $C_{11}H_{19}O_3N_3S$ requires N, 15·4%).

The salt (IV) (2·6 g.) in water (10 c.c.) was treated with concentrated hydrochloric acid (3 c.c.) at 0°, whereupon (I) (0·95 g., 84%) separated immediately. When dissolved in chloroform, however, and treated with dry hydrogen chloride, (IV) gave *glycine morpholide hydrochloride*, m. p. 238°, after evaporation and crystallisation of the residue from ethanol (Found : C, 40·8; H, 7·2; N, 14·9. $C_6H_{13}O_2N_2Cl$ requires C, 39·9; H, 7·2; N, 15·5%). Addition of ether to the filtrate gave morpholine hydrochloride, m. p. 178—179° (after recrystallisation from methanol–ether).

3-Acetyl-2-thio-5-thiazolidone (Cook, Heilbron, and Levy, *loc. cit.*) with morpholine in acetone or ethyl acetate afforded (IV), m. p. 137° (decomp.), when seeded and scratched. When the acetyl derivative was warmed with concentrated hydrochloric acid until dissolved, (I) separated in flakes on cooling, and was identified by its ability to give an intense purple colour with iodine in the presence of sodium acetate and by the characteristic formation of long needles on recrystallisation from benzene.

The Dimerisation of (I).—2-Thio-5-thiazolidone (1·3 g.) in acetone (15 c.c.) was treated with triethylamine (1·0 g., 1 equiv.) under nitrogen, and the resulting *bistriethylamine* salt (1·4 g., 61%), m. p. 133° (decomp.), collected after 20 minutes, washed with acetone to remove a little colour, and analysed directly (Found : C, 46·55; H, 7·9; N, 11·9. $C_6H_6O_2N_2S_4,2C_6H_{15}N$ requires C, 46·1; H, 7·7; N, 11·9%). The yield was not improved by using 2 equivalents of triethylamine. It was soluble in water, methanol, chloroform, or pyridine, insoluble in ethanol, ether, or ethyl acetate, and was best recrystallised from methanol–ethyl acetate. The triethylamine salt was unstable, changing to a black tar when kept overnight, and solutions rapidly developed intense red and purple colours on exposure to air. Treatment with morpholine in chloroform caused separation of the corresponding morpholine salt, m. p. 154° (decomp.).

When the triethylamine salt was dissolved in water and acidified with concentrated hydrochloric acid at 0°, a yellow gum was precipitated which solidified after a little scratching to give the dimeride (see below). Conversely, the triethylamine or morpholine salt was obtained, when this was treated with the appropriate base in acetone. The *dimeride* (VI) (4·5 g., 64%) was best prepared by keeping (I) (7·0 g.) in 10% sodium hydroxide solution (40 c.c.) overnight under nitrogen and then acidifying the solution at 0° (Found : C, 27·4; H, 2·4; S, 47·7. $C_6H_6O_2N_2S_4$ requires C, 27·1; H, 2·3; S, 48·1%); carbon disulphide was present in the filtrate. The same results were obtained using sodium carbonate solution. Thus secured, the dimeride darkened gradually at >200°, obvious decomposition setting in at >250°. It was soluble in aqueous sodium hydrogen carbonate with effervescence, the solution darkening if exposed to air, and was precipitated unchanged on acidification. It was insoluble in benzene, ethyl acetate, ether, or chloroform, but freely soluble in cold acetone or methanol, and rather less so in ethanol.

When kept for 5—10 minutes, or immediately when boiled or treated with pyridine, the above solutions deposited the *betaine* (VII) which decomposed indefinitely above 200°, was insoluble in all common solvents, and could be recrystallised from a large volume of water in long, colourless needles (Found : C, 29·3; H, 4·2; N, 13·0; S, 30·6. $C_5H_8O_3N_2S_2$ requires C, 28·9; H, 3·9; N, 13·5; S, 30·8%). The compound was soluble in aqueous sodium hydroxide, whence it was reprecipitated by acids, difficultly soluble in sodium carbonate, and insoluble in sodium hydrogen carbonate. The compound was most conveniently prepared by dissolving the triethylamine salt of (VI) (4·2 g.) in acetic acid (25 c.c.) under nitrogen, and collecting the crystals (1·4 g., 75%) after 0·5 hour.

Acid Hydrolyses.—The above compound (VII) (0·5 g.) was heated under reflux with 2N-hydrochloric acid (10 c.c.) for 3 minutes, by which time a clear solution had resulted. Carbon disulphide was observed as oily drops in the condenser, and carbon dioxide was detected with saturated aqueous barium hydroxide in the usual way. Evaporation gave diaminoacetone dihydrochloride which was not readily purified but with picric acid yielded 1 : 3-*diaminoacetone dipicrate* which crystallised from dilute aqueous picric acid in long yellow needles, m. p. 210—215° (decomp.) (Found : C, 31·9; H, 3·0. $C_3H_8ON_2,2C_6H_3O_7N_3,H_2O$ requires C, 31·9; H, 2·9%). The same dipicrate was prepared from authentic diaminoacetone, obtained by hydrolysis of " dibenzamidodioxytetrol " (Rügheimer, *Ber.*, 1888, **21**, 3325). The betaine (VII) was also decomposed by boiling it with water for 15 minutes, but addition of picric acid failed to yield the above picrate in this case.

The dimeride (VI) (1·5 g.) was heated under reflux with 2N-hydrochloric acid (10 c.c.) for 10 minutes, dissolving with vigorous effervescence (carbon dioxide) and production of carbon disulphide. The solution was evaporated, and the yellow gum dissolved in water (8 c.c.), granular prisms (0·5 g.), m. p. 177° (decomp.), being slowly deposited; the filtrate gave diaminoacetone dipicrate (0·25 g.) with picric acid. The above *substance* was recrystallised from water containing a little hydrochloric acid, whence it separated slowly and had m. p. 174° (decomp.) (Found : C, 29·3, 28·6; H, 4·3, 3·7; N, 14·6, 12·5. $C_5H_8O_3N_2S_2$ requires C, 28·9; H, 3·9; N, 13·5%). It was sparingly souble in common solvents, soluble in aqueous sodium hydroxide though not in sodium hydrogen carbonate and was recovered unchanged after being heated for 0·5 hour at 100° with 2N-hydrochloric acid. The dimeride (VI) was transformed in poor yield into (VII) when boiled with water.

Benzylation Experiments.—Compound (VII) (0·77 g.) was suspended in 2N-sodium carbonate (10 c.c.)

and shaken overnight with benzyl chloride (2 c.c.) and ether (10 c.c.). The insoluble benzyl derivative (0·64 g.), m. p. 180° (decomp.), was recrystallised from 2N-hydrochloric acid as its *hydrochloride*, in colourless needles, m. p. 194—195° (decomp.) (Found: C, 43·8; H, 4·4; N, 8·3; Cl, 11·0. $C_{12}H_{14}O_3N_2S_2$,HCl requires C, 43·1; H, 4·5; N, 8·4; Cl, 10·6%). It was soluble in methanol and insoluble in acetone, and gave a green colour with ferric chloride in methanol. If insufficient acid was present during the recrystallisation, the free base, m. p. 178° (decomp.), separated, insoluble in methanol and hot water, though soluble in hot sodium carbonate solution and cold sodium hydroxide solution. The amino-acid, when heated with ninhydrin and sodium acetate, gave a reddish colour becoming intense green in the presence of cupric carbonate. DL-Alanine gave no colour under these conditions.

2-Thio-5-thiazolidone (I) (5·0 g.) in 2N-sodium carbonate (50 c.c.) was shaken overnight with benzyl chloride (5 c.c.) in ether (30 c.c.) under nitrogen; an insoluble *S*-benzyl derivative (4·0 g.), m. p. 148° (decomp.), was produced. Acidification of the aqueous layer gave *N*-dithiocarbobenzyloxyglycine (1·2 g.), m. p. 164°. The benzyl derivative was soluble in acetone and ethyl acetate, sparingly soluble in cold methanol or ethanol, and insoluble in ether, chloroform, or light petroleum; it decomposed in hot solvents. The same compound (1·2 g.) was produced when (VI) (1·0 g.) in 2N-sodium carbonate (20 c.c.) was shaken with benzyl chloride (1·5 c.c.) in ether for 1·5 hours under nitrogen. In acetone, it gave a deep indigo-blue colour with ferric chloride, extractable into chloroform, which became green with excess of ferric chloride.

When the preceding benzyl derivative was crystallised rapidly from hot acetic acid, a *compound* separated in needles, m. p. 195° (decomp.) (Found: C, 53·9; H, 4·2; N, 6·5; S, 28·3. $C_{20}H_{18}O_2N_2S_4$ requires C, 53·8; H, 4·0; N, 6·3; S, 28·7%). The acidity of the acetic acid was responsible for this change, which was more conveniently effected by adding a few drops of concentrated hydrochloric acid to an acetone solution of the lower-melting benzyl derivative, whereupon the compound, m. p. 195°, was quantitatively precipitated. It was insoluble in common solvents, and gave a deep green colour when warmed with methanolic ferric chloride. Both benzyl derivatives were insoluble in cold 2N-sodium hydroxide, but dissolved on heating, with liberation of toluene-ω-thiol; acidification gave a yellow flocculent precipitate. When the triethylamine salt of (VI) was warmed with benzyl chloride in methanol or chloroform, the benzyl derivative, m. p. 195° (decomp.), rapidly separated. When shaken overnight with benzyl chloride (3 c.c.) in ether (10 c.c.) and water (8 c.c.), however, the triethylamine salt (2·6 g.) yielded a different benzyl derivative (1·9 g.), m. p. 140° (decomp.). This was unaffected by cold dilute acids, but was soluble in cold 2N-sodium hydroxide liberating triethylamine, whereafter acidification afforded a yellow precipitate, m. p. 110° (decomp.) after contracting at 76°.

Acetylation Experiments.—The bistriethylamine salt of (VI) was warmed with excess of acetic anhydride for a few minutes, cooled, scratched, and diluted with water to give a *diacetyl* derivative, m. p. 157—158°, colourless needles from ethanol (Found: C, 40·5; H, 2·9; N, 10·7; S, 25·5. $C_9H_6O_3N_2S_2$ requires C, 42·2; H, 3·1; N, 10·9; S, 25·0%). The compound was insoluble in cold 2N-sodium hydroxide, dissolving on heating to give a yellow-orange solution, and did not give an insoluble picrate or hydrochloride in benzene. (VI) itself was not acetylated smoothly, though when an equivalent quantity of triethylamine was present, the above acetyl derivative was obtained. With only a trace of triethylamine, however, an acetyl derivative, m. p. 137°, was secured, which appeared to be the same as that obtained from (I) and acetic anhydride–triethylamine (see below). When (VI) was covered with acetic anhydride and a drop of pyridine added, immediate reaction led to the separation of a colourless crystalline mass, m. p. 95° (vigorous decomp.) (after being washed with ethanol). This was clearly of a different character from the other acetyl derivatives mentioned in this section. (VII) dissolved in hot acetic anhydride–pyridine to give an orange solution; dilution with water and crystallisation of the product from aqueous ethanol then gave colourless needles, m. p. 173° (slight decomp.). When (VII) was boiled for a few moments with acetic anhydride–triethylamine, cooled, and diluted with ethanol, a *triacetyl* derivative was obtained which crystallised from ethanol in rosettes of small needles, m. p. 147° (Found: C, 44·8; H, 3·6; N, 9·9; S, 21·7. $C_{11}H_{10}O_4N_2S_2$ requires C, 44·3; H, 3·4; N, 9·4; S, 21·5%). The compound did not yield a picrate in benzene, and was deacetylated with warm 2N-hydrochloric acid to give a product, m. p. 165° (decomp.). 2-Thio-5-thiazolidone (I) was suspended in acetic anhydride; addition of triethylamine caused an exothermic reaction and development of a red colour. After 2 hours, the *triacetyl* derivative was collected and recrystallised from chloroform–ethanol, having m. p. 135—137° (Found: C, 38·6; H, 2·8; N, 8·1; S, 34·3. $C_{12}H_{10}O_4N_2S_4$ requires C, 38·5; H, 2·7; N, 7·5; S, 34·2%). Attempts to recrystallise the material from dilute acetic acid or ethanol led to deacetylation, and the production of a compound, m. p. 198° (decomp.), which was reconverted into the original triacetyl derivative by acetic anhydride–triethylamine. The triacetyl derivative was insoluble in cold 2N-sodium hydroxide, but dissolved on warming.

Polymerisation of (I).—2-Thio-5-thiazolidone (1·0 g.) was kept in the dark in pyridine (10 c.c.) for 18 hours under nitrogen, and the yellow solid (0·45 g.) which had separated, was washed well with pyridine and then with acetone (Found, after drying for 4 hours at 100°/0·1 mm.: C, 38·5; H, 5·1; N, 14·4; S, 6·4%). The substance decomposed indefinitely above 200°, and was insoluble in common solvents, including hot pyridine and acetic acid. It was almost wholly soluble in aqueous sodium hydrogen carbonate, carbonate, or hydroxide, but only a small recovery was obtained on acidification of such solutions. It was soluble in concentrated hydrochloric acid and in hot dilute acid, though almost insoluble in hot water. In another experiment, (I) (0·2 g.) was boiled with pyridine (5 c.c.) for 2—3 minutes under nitrogen, and the polymer filtered off, washed well with pyridine, and dried for 4 hours at 100°/0·1 mm. [Found: C, 38·4; H, 5·5; N, 19·5; S, 5·5; amino-N (Van Slyke; kindly determined by Dr. J. L. Bailey), 2·3%].

2-Thio-5-thiazolidone (0·5 g.) was heated under reflux with methanol (10 c.c.) for a few minutes in nitrogen, and the colourless granular product filtered off and well washed with hot methanol {Found (in 2 different samples, both dried for 3 hours at 80°/0·1 mm.): C, 37·7, 38·7; H, 5·4, 5·5; N, 19·7, 20·0; S, 7·75, 7·6; MeO, 5·8. $C_{18}H_{28}O_9N_8S_2$ (*i.e.*, $HS_2C{\cdot}[NH{\cdot}CH_2{\cdot}CO]_8{\cdot}OMe$) requires C, 38·4; H, 5·0; N, 19·9; S, 11·3; MeO, 5·7%}. Similar results were obtained by using ethanol, though

precipitation was slower. The products were soluble in concentrated hydrochloric acid, and in sodium hydroxide on warming, but could not be suitably recovered by dilution with water or acidification, respectively. They were insoluble in hot pyridine or acetic acid, but readily soluble in formic acid.

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