The Synthesis of 1,3-Thiazine-2,4-dithiones by the Reaction of Carbon Disulfide with Cyclic Ketones or Their Ketimines

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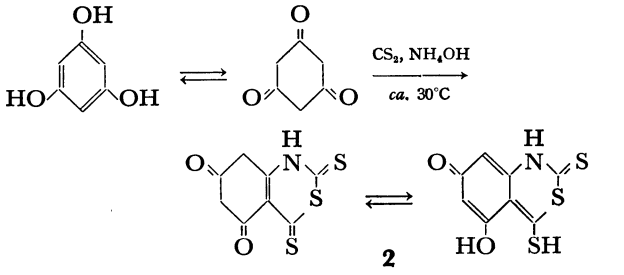
Cyclohexanone, 4-methylcyclohexanone, and phloroglucinol, when treated with carbon disulfide in the presence of triethylamine and aqueous ammonia, gave the respective 3,1-benzothiazine-2(1*H*),4-dithiones. Glutazines and 2-iminocyclopentanedithiocarboxylic acid underwent this reaction without ammonia.

We have previously shown that cyclohexanone, in the presence of sodium amide, reacts with carbon disulfide to give a small amount of 5,6,7,8-tetrahydro-3,1-benzothiazine-2(1*H*),4-dithione in addition to the major product, 5,6,7,8-tetrahydro-spiro[2*H*-3,1-benzothiazine-2,1'-cyclohexane]-4(1*H*)-thione.[1]

Concerning 1,3-thiazine-2,4-dithiones, there have also been a few reports.[2-4]

We wish now to report a method of preparing the thiazinedithiones, involving the treatment of ketones or ketimines with carbon disulfide, in the presence of triethylamine, and also aqueous ammonia if needed.



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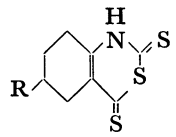
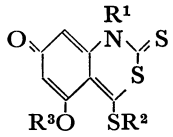
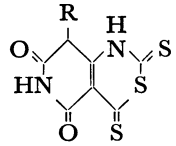


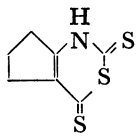
1a, R=H
1b, R=Me



2a, $R^1=R^2=Me$, $R^3=H$
2b, $R^1=R^2=R^3=Me$
2c, $R^1=COCH_3$, $R^2=R^3=H$



3a, R=H
3b, R=Me
3c, R=Et



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Cyclohexanone, 4-methylcyclohexanone, phloroglucinol, glutazine, and 3-substituted glutazines, in this reaction, afforded the expected thiazinedithiones or their tautomers—**1a**, **1b**, **2**, and **3a**—**c**, in yields ranging from 16 to 85%. Other ketones were reluctant to undergo this reaction. 2-Iminocyclopentanedithiocarboxylic acid,[5] on treatment with carbon disulfide and triethylamine, naturally gave 1,5,6,7-tetrahydrocyclopenta[*d*][1,3]thiazine-2,4-dithione (**4**), but 3-substituted 2-iminocyclopentanedithiocarboxylic acids did not undergo this reaction.

The structures were identified on the basis of their IR, UV, NMR, and mass spectra, together with elemental analyses and chemical reactions. Structure **2** was assigned on the basis of the following spectral data. The IR spectrum had an imino group band near 3260 cm^{-1}. The mass spectrum had the parent peak together with the most intense one, which corresponds to the elimination of the mercapto group from the molecular ion. On methylation or acetylation, the imino group band disappeared from both the IR and NMR spectra. Instead, the two doublets due to the two protons at 6- and 8-C of Compound **2** turned into two double doublets in the NMR spectrum of the acetyl derivative of this compound because of the restricted rotation of the acetyl group (in hexadeuteroacetone). These facts, together with the slightly broadened singlet corresponding to *ca.* two protons at τ −3.17 in the NMR spectrum of **2** (in heptadeuterodimethylformamide), led us to assign this structure: 1,7-dihydro-5-hydroxy-4-mercapto-7-oxo-3,1-benzothiazine-2-thione.

Experimental

The melting points, the appearances, the solvent of recrystallization, and the results of elemental analyses are all listed in Table 1.

5,6,7,8-Tetrahydro-3,1-benzothiazine-2(1H),4-dithione (1a). To a mixture of cyclohexanone (20 g), triethylamine (60 g), and aqueous 28% ammonia (40 ml), carbon disulfide (38 g) was added dropwise under cooling to 10 °C and vigorous stirring. The stirring was then continued for an additional 20 hr. A fairly viscous reaction mixture was acidified with dilute hydrochloric acid at 0 °C, and then a small quantity of ethanol was added to the red viscous oil which was thus separated. The red crystalline solid was dissolved in aqueous 28% ammonia to remove the insoluble material,[6] after which the solution was acidified again to give **1a** (11 g, 26%), which showed no depression of melting point on admixture with an authentic specimen[1] of **1a**.

5,6,7,8-Tetrahydro-6-methyl-3,1-benzothiazine-2(1H),4-dithione (1b). The preparation was the same as that described above (16%).[7] IR (KBr): 3120, 1590, and 1505 cm^{-1}. NMR [$(CD_3)_2SO$]: τ 6.56 (br, 1H), *ca.* 7.4 (m, 4H,) *ca.* 8.2 (m, 3H), and 8.97 ppm (d, 3H).

5,6,7,8-Tetrahydro-5,7-dioxo-3,1-benzothiazine-2(1H),4-dithione (2). A mixture of phloroglucinol dihydrate (5 g), carbon disulfide (12 g), triethylamine (1.5 g), and aqueous 28% ammonia (16 ml) was stirred for 50 hr at 32 °C. The yellow crystals which were then collected and washed with ether were dissolved in water, and the solution was acidified with

Table 1. Properties of thiazinedithiones

Compound	Mp (°C)	Appearance[a]	Recrystal from	Molecular formula	Calcd (%) C	H	N	S	Found (%) C	H	N	S
1b	214—215[b]	Red p	CH_3COCH_3–H_2O	$C_9H_{11}NS_3$	47.12	4.83	6.11	41.93	46.95	4.76	6.06	42.02
2	>300	Yellow n	Dioxane–H_2O	$C_8H_5NO_2S_3$	39.49	2.07	5.76	39.53	39.43	2.08	5.79	39.46
2a	153	Yellow n	CH_3OH	$C_{10}H_9NO_2S_3$	44.26	3.35	5.16	35.44	43.97	3.23	5.18	35.22
2b	71	Yellow n	DMF–H_2O	$C_{11}H_{11}NO_2S_3$	46.29	3.89	4.91	33.70	46.02	3.81	4.79	33.75
2c	199	Yellow n	DMF–H_2O	$C_{10}H_7NO_3S_3$	42.09	2.47	4.91	33.69	42.30	2.63	5.08	33.51
3a	>300	Yellow n	DMF	$C_7H_4N_2O_2S_3$	34.41	1.65	11.47	39.36	34.16	1.81	11.46	39.38
3b	>300	Yellow n	DMF	$C_8H_6N_2O_2S_3$	37.19	2.34	10.84	37.23	37.11	2.41	10.56	37.35
3c	>300	Yellow n	DMF	$C_9H_8N_2O_2S_3$	39.69	2.96	10.28	35.32	39.61	2.99	9.99	35.33
4	243—244[b]	Orange p	CH_3COCH_3–H_2O	$C_7H_7NS_3$	41.76	3.50	6.96	47.78	41.99	3.46	6.68	47.97

a) Plates and needles are abbreviated as p and n respectively. b) Decomposition point.

Table 2. Preparation[a] of **3a**—**c** and **4**

	Reactant	Reaction Conditions	Yield (%)
5,6,7,8-Tetrahydro-5,7-dioxopyrido[4,3-*d*]-[1,3]thiazine-2(1*H*),4-dithione (**3a**)	Glutazine[b]	Room temp 24 hr in DMF	60
5,6,7,8-Tetrahydro-8-methyl-5,7-dioxopyrido-[4,3-*d*][1,3]thiazine-2(1*H*),4-dithione (**3b**)	3-Methylglutazine	Room temp 24 hr in DMF	81
8-Ethyl-5,6,7,8-tetrahydro-5,7-dioxopyrido-[4,3-*d*][1,3]thiazine-2(1*H*),4-dithione (**3c**)	3-Ethylglutazine	Room temp 24 hr in DMF	85
1,5,6,7-Tetrahydrocyclopenta[*d*][1,3]thiazine-2,4-dithione (**4**)	2-Iminocyclopentanedithio-carboxylic acid	Room temp 16 hr in DMF	89

a) These compounds were isolated by the acidification of the respective reaction mixtures diluted with water.
b) Glutazine and the 3-substituted glutazines were prepared after Thorpe's method (*J. Chem. Soc.*, **85**, 1726 (1904)).

Table 3. IR and NMR[a] spectra of **3a**—**c** and **4**

Compound	cm^{-1} (KBr)	τ ppm in CD_3SOCD_3
3a	3070, 2915b, 2820b, 1650, 1615, 1575, 1537	4.43 (s, 1H), 4.67 (b, 1H), 7.06 (s, 1H), 7.18 (s, 1H)
3b	3310, 1635, 1605, 1550	−2.00 (br s, 1H), −1.80 (b, 1H), 6.62 (b, 1H), 8.07 (s, 3H) (further, 6.87 (q, 6H), 8.80 (t, 9H))
3c	3150, 1635, 1605, 1550	−0.13 (br s, 1H), 0.17 (b, 1H), 6.60 (b, 1H), 7.43 (q, 2H), 9.07 (t, 3H) (further, 6.87 (q, 6H), 8.83 (t, 9H))
4	3120, 1598, 1515	6.50 (b, 1H), 7.09 (t, 2H), 7.22 (t, 2H), 8.00 (m, 2H)

a) The NMR spectra of **3a**—**c** were obtained by the following conditions: **3a**; in CD_3SOCD_3–C_5D_5N (3: 1), **3b** and **3c**; as triethylammonium salt. (**3a**—**c** Were hardly soluble in most organic solvents and were denatured in dimethyl sulfoxide.)

dilute hydrochloric acid at 0 °C to give **2** (1.7 g, 23%). IR (KBr): 3260br, 1631, 1599, and 1532 cm^{-1}. NMR [$(CD_3)_2NCDO$] τ −3.17 and −3.10 (slightly br s, and br, >2H), 3.23 (d, J=2.4 Hz, 1H), 3.67 ppm (d, J=2.4 Hz, 1H). MS *m/e*: 243, 210, 178, 161, and 117.

Methylation of **2**. By methylation with diazomethane in a usual manner, a mixture of dimethyl and the trimethyl derivative of **2** was obtained. The hot solution which dissolved the mixture in methanol was cooled to separate out the dimethyl derivative of **2** (**2a**, 6%) [IR (KBr): 1620, 1574, and 1536 cm^{-1}; NMR (CF_3COOH): τ 3.11 (s, 2H), 5.91 (s, 3H), and 6.98 ppm (s, 3H); MS *m/e*: 271 and 224]. The solvent was evaporated from the mother liquor of **2a** to give the trimethyl derivative of **2** (**2b**, 28%).

Acetyl Derivative of **2**. To a solution of 2 (1 g) in pyridine, acetyl chloride (0.5 g) was added at 0 °C, after which the mixture was refluxed for 3 hr at 60 °C. The subsequent addition of water to the reaction mixture separated the acetyl derivative of **2** (**2c**) (0.8 g, 68%). IR (KBr): 1778, 1625, and 1530 cm^{-1}. NMR (CD_3COCD_3): τ 3.16 (dd, J=2.4 Hz, 1H), 3.52 (dd, J=2.4 Hz, 1H), 6.98 (s, 1H), 7.13 (s, 1H), and 7.66 ppm (s, 3H).

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6) This material was spiro[2*H*-3,1-benzothiazine-2,1′-cyclohexane]-4(1*H*)-thione, mp 197—198 °C (lit,[1] 197—198 °C).
7) Spiro[2*H*-3,1-benzothiazine-2,1′-(4′-methylcyclohexane)]-4(1*H*)-thione was also obtained, mp 194—194.5 °C (lit,[1] 194—195 °C).