[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF KANSAS]

The Syntheses of 2-Thio-4-arylthiazolines

BY F. B. DAINS AND ORLAND A. KROBER

Previous investigations[1] have shown that the alkyl and aryl thiocyanates in general add thio acids yielding esters of an acyldithiocarbamic acid. Thus benzyl thiocyanate and thiobenzoic acid gave the benzyl ester of benzoyl-dithiocarbamic acid, $C_6H_5CONHCSSCH_2C_6H_5$, and ethyl thiocyanate and thioacetic acid, the corresponding acetyl-ethyldithiocarbamate. In some cases the reaction is not so smooth and decomposition products are formed.

In view of this interesting addition to the SCN grouping, a study has been made of the action of the thio acids on the phenacyl thiocyanates which contained a labile keto grouping, and hence are capable of secondary reactions. Our results show that phenacyl thiocyanate readily adds thiobenzoic acid, yielding the phenacyl ester of benzoyl-dithiocarbamic acid, $C_6H_5CONHCSSCHCOC_6H_5$, which on heating with dilute hydrochloric acid reacts in the enol form, losing benzoic acid and closing the ring with the formation of 2-thio-4-phenylthiazoline.

$$S\text{—}CS\text{—}NHC(C_6H_5)\text{=}CH$$

In the case of thioacetic acid, only the end-product, the thiazoline, could be isolated.

Experimental

The phenacyl thiocyanates are prepared readily by this general procedure.

A mixture of *p*-bromophenacyl chloride (50 g.), potassium thiocyanate (20 g.) and ethanol (100 cc.) was refluxed for two hours or until the sharp odor of the chloride had disappeared completely. Water was then added and the solid product washed free from mineral salts; the *p*-bromophenacyl thiocyanate (I) (m. p. 147°) was purified by crystallization from alcohol.

The following thiocyanates were synthesized for later use: (II) *p*-chloro, (III) *p*-iodo, (IV) *p*-methoxy and (V) *m*-nitrophenacyl thiocyanate.

TABLE I

			M. p., °C.	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found
I	*p*-Bromophenacyl thiocyanate	C_9H_6BrNOS	147			12.50	12.12
II	*p*-Chlorophenacyl thiocyanate	C_9H_6ClNOS	135	6.64	6.74		
III	*p*-Iodophenacyl thiocyanate	C_9H_6INOS	152	4.63	4.48		
IV	*p*-Methoxyphenacyl thiocyanate	$C_{10}H_9NO_2S$	121			15.46	15.56
V	*m*-Nitrophenacyl thiocyanate	$C_9H_6N_2O_3S$	119			14.41	14.27
VI	2-Thio-4-phenylthiazoline	$C_9H_7NS_2$	168	7.25	7.19	33.16	33.34
VII	Benzoyl-phenacyl-dithiocarbamate	$C_{16}H_{13}NO_2S_2$	95	4.44	4.51		
VIII	2-Thio-*p*-chlorophenylthiazoline	$C_9H_6ClNS_2$	199			28.13	28.12
IX	Benzoyl-*p*-chlorophenyldithiocarbamate	$C_{16}H_{12}ClNO_2S_2$	148	4.00	4.53		
X	2-Thio-4-bromophenylthiazoline	$C_9H_6BrNS_2$	214	5.19	5.02		
XI	Benzoyl-*p*-bromophenacyl dithiocarbamate	$C_{16}H_{11}BrNO_2S_2$	158	3.55	3.88		
XII	2-Thio-4-iodophenylthiazoline	$C_9H_6INS_2$	220	4.39	4.44	20.06	20.20
XIII	2-Thio-4-*p*-methoxyphenylthiazoline	$C_{10}H_9ONS_2$	194	6.30	6.28	28.73	28.83
XIV	2-Thio-4-*m*-nitrophenylthiazoline	$C_9H_6N_2O_2S_2$	209	11.77	11.59	26.92	26.86
XV	Benzoyl-*m*-nitrophenacyl dithiocarbamate	$C_{16}H_{12}N_2O_4S_2$	157	7.74	7.87	17.80	18.26
XVI	2-Thio-4,5-diphenylthiazoline	$C_{15}H_{11}NS_2$	214	5.20	5.10	23.84	23.78
XVII	2-Benzylthio-4,5-diphenylthiazoline	$C_{22}H_{17}NS_2$	106	3.90	3.40		
XVIII	2-Thio-4-thiazolidone	$C_3H_3NOS_2$	168	10.53	10.37		

Synthesis of the Thiazolines

2-Thio-4-phenylthiazoline (VI).[2]—Phenacyl thiocyanate (14 g.), thioacetic acid (12 g.) and benzene (60 cc.) were heated for three hours on a steam-bath. After concentrating the solution and cooling, the thiazoline was filtered off and purified from alcohol. The light yellow crystals which were soluble in alkali melted at 168°.

The intermediate acetyl-phenacyldithiocarbamate was not isolated in this or any other case where thioacetic acid was used, but with thiobenzoic acid such intermediate

(1) Chanlaroff, *Ber.*, **15**, 1887 (1882); Wheeler and Merriam, THIS JOURNAL, **23**, 283 (1901); Wheeler, *Am. Chem. J.*, **26**, 345 (1901); Wheeler and Johnson, *ibid.*, **26**, 185 (1901).

(2) The compound had been made previously by Miolati by the action of phenacyl bromide on ammonium dithiocarbamate [*Gazz. chim. ital.*, **23**, I, 580 (1893)].

dithiocarbamates were more stable and were obtained in a pure condition.

Action of Thiobenzoic Acid.—Molar quantities of phenacyl thiocyanate and thiobenzoic acid were heated in benzene solution for four hours. The product isolated melted at 95° and corresponded to benzoyl-phenacyl-dithiocarbamate (VII), $C_6H_5CONHCSSCH_2COC_6H_5$, since on heating with dilute hydrochloric acid it gave benzoic acid and the thiazoline (VI), m. p. 168°.

As shown in the table, thiazolines were obtained from thiocyanates I–V, using thioacetic and thiobenzoic acids, but the intermediate dithiocarbamates were isolated only in some cases with thiobenzoic acid.

2-Thio-4,5-diphenylthiazoline (XVI).—Desyl thiocyanate and thioacetic acid gave in good yield this thiazoline (m. p. 214°).

Wheeler and Johnson[3] on treating the desyl thiocyanate with thiobenzoic acid, had isolated an unidentified compound melting at 137°, which was doubtless the benzoyl addition product. Using the same reagents, evidence was obtained of an immediate product melting about 132–133° which went over readily into the diphenylthiazoline (m. p. 214°).

The enol nature of the thiazoline was shown by the formation of a 2-benzyl ether (XVII) when the diphenylthiazoline was treated with benzyl chloride.

Rhodanine. 2-Thio-4-thiazolidone, XVIII.—Diethyl thiocyanomalonate was heated in benzene solution with thiobenzoic acid.[4] On distilling off the benzene, an oil was left which failed to crystallize and had the odor of ethyl benzoate. When this oil was evaporated to dryness with dilute hydrochloric acid, rhodanine was obtained (m. p. 166°). Its identity was proved by analysis and comparison with a synthetic specimen.

(3) Wheeler and Johnson, *Am. Chem. J.*, **26**, 202 (1901).

Summary

This paper describes the syntheses of several substituted aryl thiocyanates and their behavior with thioacetic and thiobenzoic acids. The final products in all cases were 2-thio-4-arylthiazolines, but with thiobenzoic acid the more stable intermediates, benzoyl-phenacyl-dithiocarbamates, were isolated.

(4) Wheeler, *Am. Chem. J.*, **26**, 351 (1911), described the intermediate, the benzoyl-dithiourethan; but did not hydrolyze it. Rhodanine was also obtained by Miolati [*Ann.*, **262**, 62–85 (1891)] from chloroethyl acetate and ammonium dithiocarbamate.

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2,4,6-Trimethyl-β-phenyl- and Benzyl-D-glucosides[1]

BY NELSON K. RICHTMYER

In a previous study on the cleavage of glycosides by catalytic hydrogenation,[2] mention was made of a trimethyl-β-phenylglucoside and a trimethyl-β-benzylglucoside in which the methyl groups were located presumably in the 2,4,6-positions of the glucose chain. The appearance of four recent papers dealing with 2,4,6-trimethylglucose and its derivatives makes a description of the two named glucosides seem desirable at this time.

2,4,6-Trimethyl-D-glucose was obtained first by Haworth and Sedgwick[3] through the hydrolysis of partially methylated glucose and sucrose. The allocation of methoxyl groups was confirmed later by Oldham[4] through a synthesis, the details of which have just been published. Recently, Lake and Peat[5] isolated 2,4,6-trimethylglucose by acid hydrolysis of the corresponding β-methylglucoside which is one of the products resulting from the action of boiling sodium methylate on 4,6-dimethyl-2,3-anhydro-β-methyl-D-mannoside. Barker, Hirst and Jones[6] have separated it from the products arising from incomplete methylation of α-methylglucoside with methyl iodide and thallous hydroxide. Freudenberg and Plankenhorn[7] synthesized it by methylation of 3-benzylglucose, followed by reductive cleavage of the benzyl group and acid hydrolysis of the glycosidic methoxyl group. It is of interest to note also that, from the cell wall of yeast, Zechmeister and Tóth[8] have isolated a glucose polysaccharide, which, after methylation and hydrolysis, furnished this same 2,4,6-trimethylglucose.

Tetraacetyl-β-phenylglucoside is readily accessible through the condensation of phenol with glucose pentaacetate, in the presence of *p*-toluenesulfonic acid as catalyst according to Helferich and Schmitz-Hillebrecht.[9] The incomplete

(1) Publication authorized by the Surgeon General, U. S. Public Health Service.

(2) Richtmyer, THIS JOURNAL, **56**, 1637 (1934).

(3) Haworth and Sedgwick, *J. Chem. Soc.*, 2573 (1926).

(4) Oldham, THIS JOURNAL, **56**, 1360 (1934); Oldham and Oldham, *ibid.*, **61**, 1112 (1939).

(5) Lake and Peat, *J. Chem. Soc.*, 1417 (1938).

(6) Barker, Hirst and Jones, *ibid.*, 1695 (1938).

(7) Freudenberg and Plankenhorn, *Ann.*, **536**, 256 (1938).

(8) Zechmeister and Tóth, *Biochem. Z.*, **270**, 309 (1934).

(9) Helferich and Schmitz-Hillebrecht, *Ber.*, **66**, 380 (1933).