o-Nitrophenyl acetate is not attacked by boiling water and is slightly volatile with steam.

CHEMICAL LABORATORY OF THE ADMIRALTY
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2-Amino-5-thiazolesulfonic Acid Derivatives

BY H. ELDRIDGE FAITH

For the purpose of bacteriological studies several 2-amino-5-thiazolesulfonic acid derivatives have been made.[1] The intermediate compound used in synthesizing these derivatives was 2-acetamino-5-thiazolesulfonyl chloride, made in 15 to 25% yield by the action of chlorosulfonic acid on 2-acetaminothiazole. The sulfonyl chloride reacted smoothly with several amines in pyridine to form the corresponding 2-acetamino-5-thiazolesulfonamides which were deacetylated by acid hydrolysis. When stirred with sodium sulfite solution, 2-acetamino-5-thiazolesulfonyl chloride was reduced to 2-acetamino-5-mercaptothiazole (VI).

TABLE I

2-AMINO-5-THIAZOLESULFONIC ACID DERIVATIVES

Compound	Name	Decompn. p., °C. (uncor.)	Yield,[a] %	Analytical data,[b] % Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
I	2-Acetamino-5-thiazolesulfonamide	273	52.5	27.12	3.19	18.98	27.12	3.18	18.93
II	2-(2-Amino-5-thiazolesulfonamido)-pyridine	228	65	37.57	3.14	21.86	37.61	3.11	22.13
III	2-(2-Amino-5-thiazolesulfonamido)-pyrimidine	253	39	32.68	2.74	27.22	32.80	2.73	27.29
IV	2-(2-Amino-5-thiazolesulfonamido)-thiazole	235	45	27.47	2.30	21.36	27.37	2.23	21.15
V	*p*-(2-Amino-5-thiazolesulfonamido)-aniline[c]	196	57	39.99	3.73	20.73	39.88	3.81	20.66
VI	2-Acetamino-5-mercaptothiazole	203	73.5	34.46	3.47	16.08	34.37	3.09	15.98

[a] Based on the amount of 2-acetamino-5-thiazolesulfonyl chloride employed. [b] The micro-analyses were performed by Dr. Carl Tiedcke. [c] The intermediate amine used was *p*-aminoacetanilide.

Experimental

2-Amino-5-thiazolesulfonic Acid Derivatives

2-Acetamino-5-thiazolesulfonyl Chloride.—A 15-g. (0.106 mole) portion of 2-acetaminothiazole[2] was heated with 61 g. (0.53 mole) of chlorosulfonic acid at 100° for two hours and fifteen minutes.[3] Then the solution was poured onto 560 g. of ice causing a precipitate to form. The precipitate was filtered off, washed with ice water and dried over sodium hydroxide at reduced pressure. The product weighed 6.2 g. and was used in subsequent reactions without further purification. It decomposed at 220° when inserted in a bath at 200° and decomposed at the same point after crystallizing from acetone. A positive test for chlorine and elemental analyses of the amide derived from the compound indicated that the compound was a 2-acetaminothiazolesulfonyl chloride. Several thiazole studies[4,5,6] have given evidence that the hydrogen in position 5 of a compound like 2-acetaminothiazole would be more active than the one in position 4. This evidence indicated that the sulfonyl chloride was probably in position 5 on the thiazole nucleus.

2-Acetamino-5-thiazolesulfonamide (I).—This derivative was prepared from 5.39 g. of 2-acetamino-5-thiazolesulfonyl chloride in acetone by introducing ammonia with cooling. A yield of 2.6 g. of 2-acetamino-5-thiazolesulfonamide (I) was obtained after crystallizing from dilute ethanol. The sulfonamide group of this compound hydrolyzed rapidly to the sulfonic acid group in the presence of hydrochloric acid or in a solution of hydrogen chloride in 95% ethanol at various concentrations. No conditions were found for selectively hydrolyzing the acetyl group without affecting the sulfonamide portion. No 2-amino-5-thiazolesulfonamide was isolated under conditions of partial hydrolysis of 2-acetamino-5-thiazolesulfonamide.[7]

2-Amino-5-thiazolesulfonamides.—The N^5 substituted sulfonamides (II, III, IV and V) were readily made by heating 2-acetamino-5-thiazolesulfonyl chloride at 60° for one and one-half hours with the appropriate amine in dry pyridine. The pyridine solution was then diluted with water, neutralized with dilute sodium hydroxide and vacuum distilled. The residual acetamino derivative was dissolved in dilute sodium hydroxide solution to remove any alkali-insoluble material, and was then heated with 10% hydrochloric acid to remove the acetyl group. 2-(2-Acetamino-5-sulfonamido)-thiazole (IV) became dark and produced a sulfide odor when subjected to a hydrolysis in hot 2.5 *N* sodium hydroxide. The 2-amino-5-thiazolesulfonamides were purified by crystallization from dilute ethanol.

2-Acetamino-5-mercaptothiazole (VI).—By the procedure used in reducing *p*-acetaminobenzenesulfonyl chloride to *p*-acetaminobenzenesulfinic acid with sodium sulfite,[8] a 73.5% yield of 2-acetamino-5-mercaptothiazole was obtained from 2-acetamino-5-thiazolesulfonyl chloride. Evidently any 2-acetamino-5-thiazolesulfinic acid formed was reduced immediately to the mercapto derivative. Zinc dust in 95% ethanol at 10° also accomplished this reduction. The compound was soluble in dilute potassium hydroxide and was purified by crystallizing from hot water.

(1) After this work was completed Backer and Buisman published on a similar work which included a description of compounds I, II and IV, *Rec. trav. chim.*, **63**, 228 (1944); *C. A.*, **40**, 2446 (1946).

(2) Jensen and Thornsteinsson, *Dansk Tids. Farm.*, **15**, 41 (1941); *C. A.*, **35**, 5109 (1941).

(3) Heating sodium 2-acetamino-5-thiazolesulfonate with chlorosulfonic acid or with phosphorus pentachloride was not as satisfactory a method of producing the sulfonyl chloride.

(4) Ochiai and Nagazawa, *Ber.*, **72**, 1470 (1939).

(5) Backer and Buisman, *Rec. trav. chim.*, **63**, 226 (1944); *C. A.*, **40**, 2446 (1946).

(6) Erlenmeyer and Kiefer, *Helv. Chim. Acta*, **28**, 985 (1945); *C. A.*, **40**, 1500 (1946).

(7) Since this work was done, Backer and Buisman reported obtaining 2-amino-5-thiazolesulfonamide, *Rec. trav. chim.*, **63**, 228 (1944).

(8) "Organic Syntheses," Coll. Vol. I, p. 7.

RESEARCH DEPARTMENT
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DIVISION OF ALLIED LABORATORIES, INC.
INDIANAPOLIS, INDIANA RECEIVED APRIL 25, 1947

Strength of Aqueous Thiocyanic Acid

BY MEL GORMAN AND JOSEPH CONNELL[1]

In the course of some work on the thiocyanates it became necessary to know the strength of

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aqueous thiocyanic acid. Ostwald's[2] earlier conductivity experiments indicated that this acid is almost as strong as hydrochloric, but more recently Latimer[3] estimated from thermodynamic calculations that it is a weak acid with an ionization constant of approximately 1×10^{-4}. The experiments summarized in Table I prove that thiocyanic acid is a strong acid. The third column gives the pH calculated from the relation, $p\mathrm{H} = -\log (\mathrm{H}^+)$, where (H^+) is the concentration of the hydrogen ion in moles per liter for complete dissociation of the acids. In a private communication Latimer has informed us that soon after he published his book he realized that thiocyanic acid is a strong acid.

Experimental.—Solutions of thiocyanic acid were prepared by mixing equivalent amounts of perchloric acid and potassium thiocyanate solutions. The pH of each thiocyanic acid solution was measured with a commercial model, glass electrode at intervals over a period of thirty minutes. As a check, several solutions of pure perchloric acid having the same concentration as some of the thiocyanic acid solutions were tested likewise. All readings were constant to within 0.02–0.03 pH unit. The temperature was 25°.

TABLE I

Concentration of acid, moles/liter HCNS	$HClO_4$	pH calcd.	HCNS pH obs.	$HClO_4$ pH obs.
0.2506		0.60	0.63	
.1244	0.1244	.91	.94	0.93
.04958		1.30	1.33	
.02513	.02513	1.60	1.63	1.62
.01256	.01256	1.90	1.92	1.91
.00764		2.12	2.15	
.00509		2.29	2.32	
.00188	.00188	2.72	2.72	2.73

(2) W. Ostwald, *J. prakt. Chem.*, **32**, 305 (1885).

(3) W. Latimer, "Oxidation Potentials," Prentice-Hall, Inc., New York, N. Y., 1938, p. 128.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF SAN FRANCISCO
SAN FRANCISCO 17, CALIFORNIA RECEIVED JUNE 10, 1947

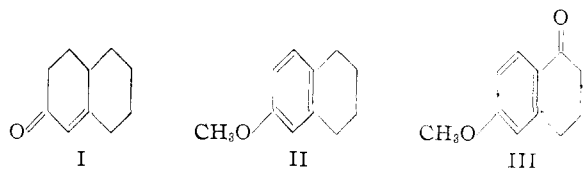
A Synthesis of 6-Methoxytetralin

BY JAMES H. HUNTER AND ALAN H. NATHAN

Concurrently with other studies which have resulted in a satisfactory method[1] for the production of 6-methoxytetralone-1 (III) in relatively large amounts, a synthesis of this compound from cyclohexanone was developed.

In the procedure of Thomas and Nathan,[1] the ultimate step involves the oxidation of 6-methoxytetralin (II) to the ketone (III). The new method described herein for the preparation of (II) was investigated as an alternative to that used,[1] but was abandoned in view of the unfavorable yields.

Since aromatization of α,β-cyclohexenones to phenols is an established but comparatively little used reaction,[2] it was of considerable interest to ascertain whether partial aromatization could be applied to an α,β-unsaturated bicyclic ketone such as I.



I II III

2-Keto-2,3,4,5,6,7,8,10-octahydronaphthalene (I) was prepared from cyclohexanone through 2-carbethoxycyclohexanone[3] according to the procedure of Du Feu, McQuillin and Robinson.[4] Extension of the classical method[5] of bromination and subsequent dehydrobromination to the ketoperhydronaphthalene (I) was unpromising; however, selective dehydrogenation with sulfur[6] or palladinized charcoal[7] according to procedures which have been used for aromatization of monocyclic unsatured ketones yielded a phenolic product. Methylation of this crude product gave 6-methoxy-tetralin (II)[8] in approximately 30% yield.

Oxidation of II with chromic anhydride according to the method of Burnop, Elliot and Linstead[9] yielded 6-methoxytetralone-1 (III), identified by mixed melting point with an authentic specimen.[1]

Experimental[10]

6-Methoxytetralin.—A mixture of 7.5 g. (0.05 mole) of 2-keto-2,3,4,5,6,7,8,10-octahydronaphthalene[4] and 1.5 g. (0.05 mole) of sublimed sulfur was heated under reflux for one hour at a bath temperature up to 220°; during the early stages of heating brisk boiling occurred and hydrogen sulfide was evolved. The mixture was cooled and transferred to a small Claisen flask. Distillation gave 6.0 g. of yellowish oil, b. p. 130–160° at 11 mm. The distillate was dissolved in ether, extracted twice with dilute sodium hydroxide solution, and once with water. Carbon dioxide was bubbled into the alkaline fraction until precipitation of the oily phenolic material was complete. The oil was extracted with ether, dried over magnesium sulfate and the solvent removed; yield, 3.87 g.

The crude phenol was dissolved in 35 ml. of 10% sodium hydroxide solution, and 6 ml. of dimethyl sulfate added dropwise with mechanical stirring. After stirring for one and one-half hours, the product was extracted with ether, the ethereal extract washed with water, dried over magnesium sulfate and the solvent removed. Distillation of the residue gave 2.69 g. (33%) of 6-methoxytetralin boiling at 127–129° at 11 mm.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.04; H, 8.67.

RESEARCH LABORATORIES
THE UPJOHN CO.
KALAMAZOO, MICHIGAN RECEIVED APRIL 5, 1947

(1) Thomas and Nathan, in press.

(2) Horning, *Chem. Rev.*, **33**, 89 (1943).

(3) Kotz and Michels, *Ann.*, **350**, 210 (1906).

(4) Du Feu, McQuillin and Robinson, *J. Chem. Soc.*, 53 (1937).

(5) Knoevenagel, *Ann.*, **281**, 98 (1894); *Ber.*, **26**, 1951 (1893); *Ann.*, **288**, 339, 346 (1895).

(6) Horning, THIS JOURNAL, **67**, 1421 (1945).

(7) Smith and Rouault, *ibid.*, **65**, 631 (1943).

(8) Schroeter, *Ann.*, **426**, 83 (1922).

(9) Burnop, Elliot and Linstead, *J. Chem. Soc.*, 727 (1940).

(10) Details for the preparation of 6-methoxytetralin (II) only are described since adequate directions for all other compounds involved are recorded in the literature.