(b) **With Sodium Ethoxide.**—A mixture of 2.0 g. of α-thiocyano-α-phenyl-N-benzylacetamide (XVII) in sodium ethoxide (prepared by dissolving 0.2 g. of sodium in 25 ml. of absolute ethanol) was heated under reflux for 15 minutes. Addition of dilute (1:2) hydrochloric acid precipitated a gummy solid which was washed well with water and then dissolved in chloroform. The chloroform solution was dried over anhydrous sodium sulfate and concentrated to a small volume; addition of cyclohexane caused the separation of a colorless, powdery solid; yield 0.89 g. (45%), m.p. 173–176°. Recrystallization from chloroform–cyclohexane raised the melting point to 184–185°. Admixture with an authentic sample of 2-benzylamino-5-phenyl-4(5)-thiazolone gave no depression in melting point.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Reaction of α-Cyanobenzyl Benzenesulfonate with Dithiocarbamates[1a,b]

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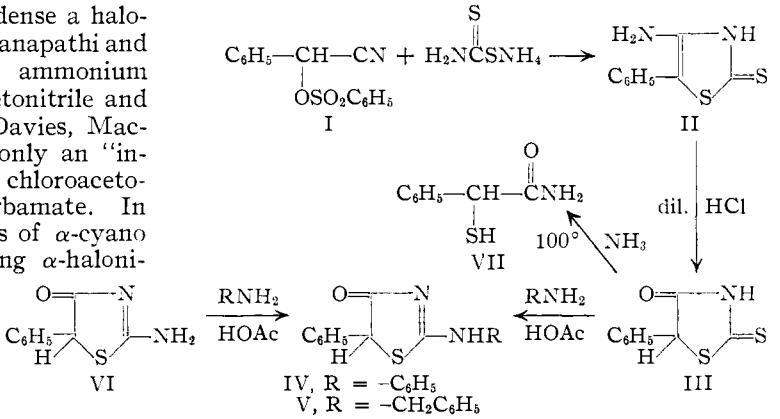
The condensation of α-cyanobenzyl benzenesulfonate with dithiocarbamates has been shown to give derivatives of 4-amino-5-phenyl-2(3)-thiazolinethione. Some reactions of the latter compounds have been described.

The only reported attempts to condense a halonitrile with a dithiocarbamate are by Ganapathi and Venkataraman,[2] who obtained only ammonium chloride and ammonia from chloroacetonitrile and ammonium dithiocarbamate, and by Davies, Maclaren and Wilkinson,[3] who obtained only an "indefinite, sulfur-containing liquid" from chloroacetonitrile and ammonium benzyldithiocarbamate. In view of the similarity of the reactions of α-cyano alkyl sulfonates and the corresponding α-halonitriles[4,5] and the established advantages of the former in a number of condensation reactions, it seemed desirable to investigate the condensation of α-cyanoalkyl sulfonates with dithiocarbamates in the hope that a convenient route to 4-amino-2(3)-thiazolinethiones might result.



α-Cyanobenzyl benzenesulfonate (I),[4] selected because of its ease of formation and established reactivity,[4,5] reacted with ammonium dithiocarbamate in absolute ethanol to give, after treatment of the reaction solution with dry hydrogen chloride, the crystalline hydrochloride of 4-amino-5-phenyl-2(3)-thiazolinethione (II). The rapid decomposition of the free base on exposure to air parallels the observed sensitivity of other 4-aminothiazoles.[3–5] As expected, the 4-amino group was readily hydrolyzed with dilute acid[3–7] to give 5-phenyl-4-keto-2 thiazolidinethione (III) in quantitative yield. This synthesis of III is superior both in yield and in convenience to the previously described procedure from diethyl α-bromo-α-phenylmalonate and potassium thiocyanate, followed by treatment of the resulting diethyl α-thiocyano-α-phenylmalonate with thioacetic acid.[8]

I also condensed readily with ammonium phenyldithiocarbamate to give 4-amino-3,5-diphenyl-2(3)-thiazolonethione (VIII) as the free base. The remarkable stability of VIII is in striking contrast to the usual instability of 4-aminothiazoles; it could be sublimed unchanged, was stable to light and air and could be recrystallized repeatedly from 95% ethanol without any evidence of decomposition or hydrolysis. The structure of VIII was confirmed (a) by an examination of its infrared spectrum, where the absence of a —C≡N band excludes the isomeric open-chain structure X, and (b) by acid hydrolysis to 3,5-diphenyl-4-keto-2-thiazolidinethione (IX).

The reaction of I with ammonium isopropyldithiocarbamate followed a similar course; however, the initial reaction product, postulated as 3-isopropyl-4-amino-5-phenyl-2(3)-thiazolinethione, proved to be too unstable to isolate and was converted directly by dilute acid hydrolysis to 3-isopropyl-4-keto-5-phenyl-2-thiazolidinethione. It would thus appear that the reaction of α-cyanobenzyl benzenesulfonate with alkyl- and aryldithiocarbamates is general and leads directly to derivatives of 4-amino-5-phenyl-2(3)-thiazolinethione.

By analogy with the reactions of other cyclic thio

(1) (a) Taken in part from theses presented by Joseph Wolinsky and Hiok-Huang Lee to the University of Illinois in partial fulfillment of the degree of Bachelor of Science in Chemistry. (b) Presented before the Division of Organic Chemistry at the 124th National Meeting of the American Chemical Society, Chicago, Ill., September, 1953.

(2) K. Ganapathi and A. Venkataraman, *Proc. Indian Acad. Sci.*, **22A**, 243 (1945).

(3) W. Davies, J. A. Maclaren and L. R. Wilkinson, *J. Chem. Soc.*, 3491 (1950).

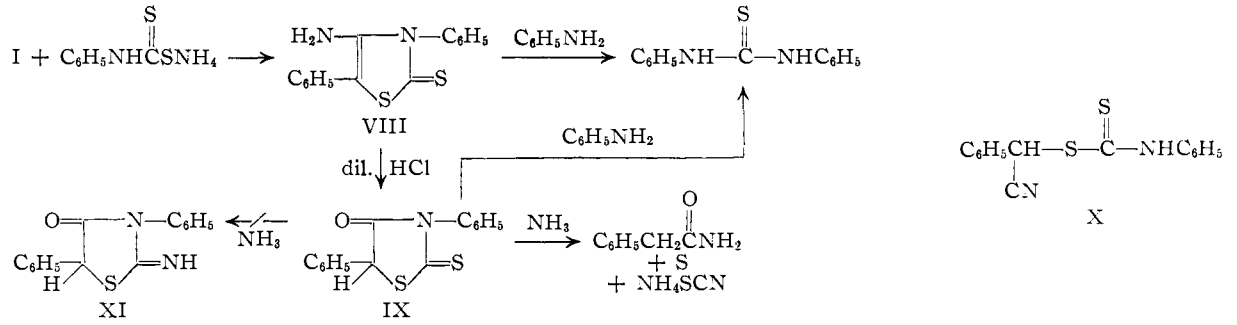
(4) R. M. Dodson and H. W. Turner, THIS JOURNAL, **73**, 4517 (1951).

(5) E. C. Taylor, Jr., J. Wolinsky and H. H. Lee, *ibid.*, **76**, 1866 (1954).

(6) W. Zerweck and M. Schubert, German Patent 729,853; *Chem. Zentr.*, **114**, I, 2035 (1943).

(7) A. H. Land, C. Ziegler and J. M. Sprague, *J. Org. Chem.*, **11**, 617 (1946).

(8) H. L. Wheeler and T. B. Johnson, THIS JOURNAL, **24**, 680 (1902).



amides,[9] it was hoped that the sulfur in the 2-thione group might be replaced by an amino or imino group by heating with amines, and thus lead to a convenient synthesis of 2-alkyl- and 2-arylaminothiazole derivatives. Accordingly, the reactions of III, VIII and IX with several amines were studied. Treatment of III with ammonia in a sealed tube gave only α-phenyl-α-mercaptoacetamide; however, the reaction of III with aniline and with benzylamine in glacial acetic acid gave 2-anilino-5-phenyl-4(5)-thiazolone (IV) and 2-benzylamino-5-phenyl-4(5)-thiazolone (V), respectively.[10] IV and V were formed also by heating 2-amino-5-phenyl-4(5)-thiazolone (VI) with the appropriate amine in glacial acetic acid.[11] These reactions provided convenient routes to authentic samples of IV and V which were required in connection with other work,[5] and constitute a useful preparative route to such 2-substituted aminothiazole derivatives.

The reactions and synthesis of 2-imino-3,5-diphenyl-4-thiazolidone (XI) have been discussed.[5] It was hoped that the ammonolysis of 3,5-diphenyl-4-keto-2-thiazolidinethione (IX) might provide a direct and unequivocal synthesis of XI. However, treatment of IX with ammonia either gave unchanged starting material or, when more strenuous conditions were employed, complete disruption of the molecule to α-phenylacetamide, sulfur and ammonium thiocyanate. Cleavage of the thiazole ring to give *sym*-diphenylthiourea took place when VIII or IX was heated with aniline, recalling the similar observations of Granacher[10d] on the reaction of 3-phenyl-4-keto-2-thiazolidinethione with aniline.

Experimental[12]

4-Amino-5-phenyl-2(3)-thiazolinethione Hydrochloride (II).—A mixture of 6.5 g. (0.059 mole) of ammonium dithiocarbamate, 16.1 g. (0.059 mole) of α-cyanobenzyl benzenesulfonate[4] and 25 ml. of absolute ethanol was shaken for ten minutes and then allowed to stand at room temperature for one hour. Addition of ether to the yellow reaction solution caused the separation of ammonium benzenesulfonate (m.p. 285–287°) which was removed by filtration. Dry hydrogen chloride was passed into the filtrate, whereupon the yellow crystalline hydrochloride of 4-amino-5-phenyl-2(3)-thiazolinethione separated; yield 7.3 g. (55%), m.p. 155–159° (with effervescence). The product was purified by reprecipitation from ethanol solution with ether, m.p. 160° (with effervescence). It decomposed rapidly at room temperature but could be stored satisfactorily at 0° over nitrogen.

Anal. Calcd. for $C_9H_8N_2S_2 \cdot HCl$: C, 44.2; H, 3.7; N, 11.4. Found: C, 44.5; H, 3.8; N, 11.3.

5-Phenyl-4-keto-2-thiazolidinethione (III).—A mixture of 1.0 g. of 4-amino-5-phenyl-2(3)-thiazolinethione hydrochloride (II), 20 ml. of 95% ethanol and 1 ml. of concentrated hydrochloric acid was heated under reflux for 15 minutes. Addition of hot water to the reaction solution and cooling caused the crystallization of 0.72 g. (quantitative) of yellow crystals, m.p. 178–180°. Recrystallization from ethanol raised the melting point to 182–183°. The reported melting point for 5-phenyl-4-keto-2-thiazolidinethione is 178–179°.[8]

Anal. Calcd. for $C_9H_7NOS_2$: C, 51.7; H, 3.4; N, 6.7. Found: C, 51.8; H, 3.6; N, 6.4.

4-Amino-3,5-diphenyl-2(3)-thiazolinethione (VIII).—A mixture of 16.1 g. (0.059 mole) of α-cyanobenzyl benzenesulfonate, 11 g. (0.059 mole) of ammonium phenyldithiocarbamate and 100 ml. of absolute ethanol was shaken for five minutes while the initial exothermic reaction subsided. After the reaction mixture had stood at room temperature for five hours, the yellow crystals were separated by filtration and recrystallized from 95% ethanol to give 13 g. (78%), m.p. 203.5–204° dec. Addition of ether to the mother liquor precipitated a small quantity of ammonium benzenesulfonate, m.p. 285–287°.

Anal. Calcd. for $C_{15}H_{12}N_2S_2$: C, 63.3; H, 4.3; N, 9.9. Found: C, 63.4; H, 4.3; N, 10.0.

3,5-Diphenyl-4-keto-2-thiazolidinethione (IX).—To a hot solution of 4.0 g. of 4-amino-3,5-diphenyl-2(3)-thiazolinethione (VIII) in 70 ml. of 95% ethanol was added 5 ml. of concentrated hydrochloric acid. The product started to separate at once, but the mixture was heated under reflux for 15 minutes to ensure complete reaction. Filtration of the hot reaction mixture yielded 2.9 g. (73%) of yellow needles which were recrystallized from aqueous dimethylformamide, m.p. 229.5–230°.

Anal. Calcd. for $C_{15}H_{11}NOS_2$: C, 63.1; H, 3.9; N, 4.9. Found: C, 63.2; H, 3.9; N, 5.0.

3-Isopropyl-4-keto-5-phenyl-2-thiazolidinethione (XI).—A mixture of 11.8 g. (0.043) of α-cyanobenzyl benzenesulfonate, 6.6 g. (0.043 mole) of ammonium isopropyldithiocarbamate and 30 ml. of absolute ethanol was shaken until solution was complete and the initial exothermic reaction had subsided (about 15 minutes). The mixture was then allowed to stand at room temperature for two hours. Addition of ether precipitated some ammonium benzenesulfonate; saturation of the filtrate with dry hydrogen chloride caused the separation of 3.5 g. (28%) of the hydrochloride of 3-isopropyl-4-amino-5-phenyl-2(3)-thiazolinethione. An attempted recrystallization of this material gave 2.4 g. of 3-isopropyl-4-keto-5-phenyl-2-thiazolidinethione (XI), while evaporation of the ether–ethanol filtrate above gave an additional 6.0 g., total yield 8.4 g. (78%). The product was purified by sublimation at 100° (0.5 mm.), m.p. 122.5–124°.

Anal. Calcd. for $C_{12}H_{13}NOS_2$: C, 57.3; H, 5.2; N, 5.6. Found: C, 57.4; H, 5.2; N, 5.7.

(9) See, for example, E. C. Taylor, Jr., and C. K. Cain, THIS JOURNAL, **74**, 1644 (1952), and references cited therein.

(10) For examples of similar replacement reactions in the thiazole series, see (a) reference 3; (b) P. N. Rylander and E. Campaigne, *J. Org. Chem.*, **15**, 249 (1950); (c) C. V. Deliwala and S. Rajagopalan, *Proc. Indian Acad. Sci.*, **31A**, 26 (1950); (d) Ch. Granacher, *Helv. Chim. Acta*, **3**, 152 (1920).

(11) For examples of similar replacement reactions in the thiazole series, see (a) A. E. Dixon, *J. Chem. Soc.*, **71**, 617 (1897); (b) C. C. J. Culvenor, W. Davies, J. A. Maclaren, P. F. Nelson and W. E. Savige, *ibid.*, 2573 (1949); (c) reference 3.

(12) All melting points are corrected. The microanalyses were performed by Mrs. Katherine Pih, Mrs. Esther Fett and Mr. Joseph Nemeth. The infrared absorption spectrum was determined by Miss Helen Miklas.

Reaction of 5-Phenyl-4-keto-2-thiazolidinethione (III) with Ammonia.—A mixture of 2.5 g. of 5-phenyl-4-keto-2-thiazolidinethione (III), 40 ml. of absolute ethanol and 3 ml. of ammonia was sealed in a glass bomb tube and heated at 100° for 12 hours. After cooling, the bomb contents were filtered and the resulting solid recrystallized from aqueous dimethylformamide. The yield of α-mercapto-α-phenylacetamide was 0.88 g. (37%), m.p. 246.5–247° dec.

Anal. Calcd. for C_8H_9NOS: C, 57.5; H, 5.4; N, 8.4. Found: C, 57.9; H, 5.2; N, 8.7.

2-Anilino-5-phenyl-4(5)-thiazolone (IV). (a).—A mixture of 1.2 g. of 5-phenyl-4-keto-2-thiazolidinethione (III), 4 ml. of aniline and 25 ml. of glacial acetic acid was heated under reflux for 12 hours. Cooling and adding a few pieces of ice caused separation of a solid mass which was filtered and added to 100 ml. of boiling water. Decantation of the hot water removed the large amount of acetanilide formed during the reaction. The residual oil was dissolved in 5 ml. of ethanol, from which 0.8 g. (48%) of colorless crystals separated, m.p. 191–191.5°.

(b).—A mixture of 1.5 g. (0.078 mole) of 2-amino-5-phenyl-4(5)-thiazolone (VI),[10b] 0.73 g. (0.078 mole) of aniline and 15 ml. of glacial acetic acid was heated under reflux for two hours. Addition of hot water and cooling caused the separation of 1.4 g. (72%) of white crystals which were recrystallized from ethanol, m.p. 191–191.5°.

Anal. Calcd. for $C_{15}H_{12}N_2OS$: C, 67.1; H, 4.5; N, 10.4. Found: C, 67.4; H, 4.6; N, 10.6.

No depression of melting point was observed upon admixture of the products obtained from (a) and (b) above.

2-Benzylamino-5-phenyl-4(5)-thiazolone (V). (a).—A mixture of 0.5 g. of 5-phenyl-4-keto-2-thiazolidinethione (III), 0.4 ml. of benzylamine and 25 ml. of glacial acetic acid was heated under reflux for 16 hours, 6 ml. of benzylamine added, and the resulting solution allowed to reflux for an additional four hours. Dilution of the reaction mixture with hot water caused the separation of 0.57 g. (77%) of solid which was recrystallized from ethanol, m.p. 185–185.5°.

(b).—A mixture of 1.6 g. of 2-amino-5-phenyl-4(5)-thiazolone (VI),[10b] 2 ml. of benzylamine and 15 ml. of glacial acetic acid was heated under reflux for two hours. Hydrogen sulfide was evolved during the reaction. Addition of hot water to the reaction mixture and cooling caused the crystallization of 0.78 g. (36%) of white crystals which were recrystallized from ethanol, m.p. 185–185.5°.

Anal. Calcd. for $C_{16}H_{14}N_2OS$: C, 68.1; H, 5.0; N, 9.9. Found: C, 68.4; H, 5.0; N, 10.1.

No depression in melting point was observed upon admixture of the products formed by methods (a) and (b) above.

Reaction of 3,5-Diphenyl-4-keto-2-thiazolidinethione (IX) with Ammonia.—A mixture of 5.0 g. of 3,5-diphenyl-4-keto-2-thiazolidinethione, 3 ml. of ammonia and 40 ml. of absolute ethanol was heated in a sealed glass bomb tube at 100° for 12 hours. Filtration of the hot bomb contents gave 1.4 g. of unchanged starting material, m.p. 229–230°, while the filtrate on cooling deposited 0.12 g. of monoclinic sulfur, m.p. 116–117°. Evaporation of this filtrate to near dryness under reduced pressure gave a gummy residue which was suspended in hot cyclohexane and filtered to give 1.7 g. of a white solid, m.p. 120–132°. This solid was extracted several times with boiling chloroform, the chloroform extracts concentrated and cyclohexane added to give 0.9 g., of colorless platelets, m.p. 157–158°. The compound was purified by sublimation at 154° (0.5 mm.), m.p. 160–161°. Analysis and a mixed melting point determination showed the compound to be phenylacetamide.

Anal. Calcd. for C_8H_9NO: C, 71.1; H, 6.7; N, 10.4. Found: C, 71.0; H, 6.9; N, 10.4.

The chloroform-insoluble fraction above (0.6 g., m.p. 150–151°) was shown to be ammonium thiocyanate by analysis and a mixed melting point determination.

Anal. Calcd. for NH_4SCN: C, 15.8; H, 5.3; N, 36.8. Found: C, 16.1; H, 5.5; N, 36.9.

Reaction of 3,5-Diphenyl-4-keto-2-thiazolidinethione (IX) with Aniline.—A mixture of 3.0 g. of 3,5-diphenyl-4-keto-2-thiazolidinethione (IX) and 10 ml. of freshly-distilled aniline was heated under reflux for 20 hours. Hydrogen sulfide was evolved slowly during this period. The cooled reaction mixture was diluted with 100 ml. of ether, the resulting solution extracted with dilute hydrochloric acid, and the ethereal layer washed with water, dried and evaporated to give a residual oil which solidified on standing. Recrystallization from dilute ethanol gave 1.3 g. of *sym*-diphenylthiourea, m.p. 150–151°, unchanged upon admixture with an authentic sample. Unchanged starting material and *sym*-diphenylthiourea were obtained when IX and aniline were heated together in ethanol solution.

sym-Diphenylthiourea also was formed when 4-amino-3,5-diphenyl-2(3)-thiazolinethione (VIII) and aniline were heated together for 15 minutes and the reaction mixture worked up as described above.

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Preparation and Identity of Phenylmaleic Acid and Phenylfumaric Acid

BY E. C. TAYLOR, JR., AND E. J. STROJNY[1]

RECEIVED NOVEMBER 16, 1953

Evidence is presented to show that the compound previously reported to be phenylmaleic acid[2] is a half-hydrate of phenylmaleic acid, and that the compound previously reported to be phenylfumaric acid[3] is actually phenylmaleic acid. The properties of authentic phenylfumaric acid are described for the first time. A convenient preparation for both phenylmaleic acid and phenylfumaric acid is described which involves the reaction of benzenediazonium chloride with dimethyl maleate.

A compound which was formed by the mild aqueous hydrolysis of phenylmaleic anhydride and which melted at 100° was described by Alexander[2] in 1890 as phenylmaleic acid. The compound was characterized by elemental analysis and by the fact that on heating at its melting point it was readily reconverted to the anhydride. In 1915, Almstrom[3] reported a compound, m.p. 128–129°, prepared by the alkaline hydrolysis of phenylmaleic anhydride, which was designated as phenylfumaric acid on the basis of elemental analysis, mode of formation and non-identity with the previously described phenylmaleic acid.

The present paper presents evidence to show that the alleged phenylmaleic acid of Alexander is a half-hydrate of phenylmaleic acid and that the alleged phenylfumaric acid described by Almstrom is actually phenylmaleic acid. In addition, the preparation and properties of authentic phenylfumaric acid are described for the first time.

Phenylmaleic anhydride[4] was hydrolyzed with dilute sodium hydroxide to give a compound, m.p. 129–131°, which was described by Alm-

(1) Parke, Davis and Company Fellow, 1952–1954.

(2) H. Alexander, *Ann.*, **258**, 67 (1890).

(3) G. K. Almstrom, *Ber.*, **48**, 2009 (1915).

(4) L. E. Miller, H. B. Staley and D. J. Mann, THIS JOURNAL, **71**, 374 (1949).