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DECATUR, ILL.

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

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

BY E. C. TAYLOR, JR., JOSEPH WOLINSKY AND HIOK-HUANG LEE

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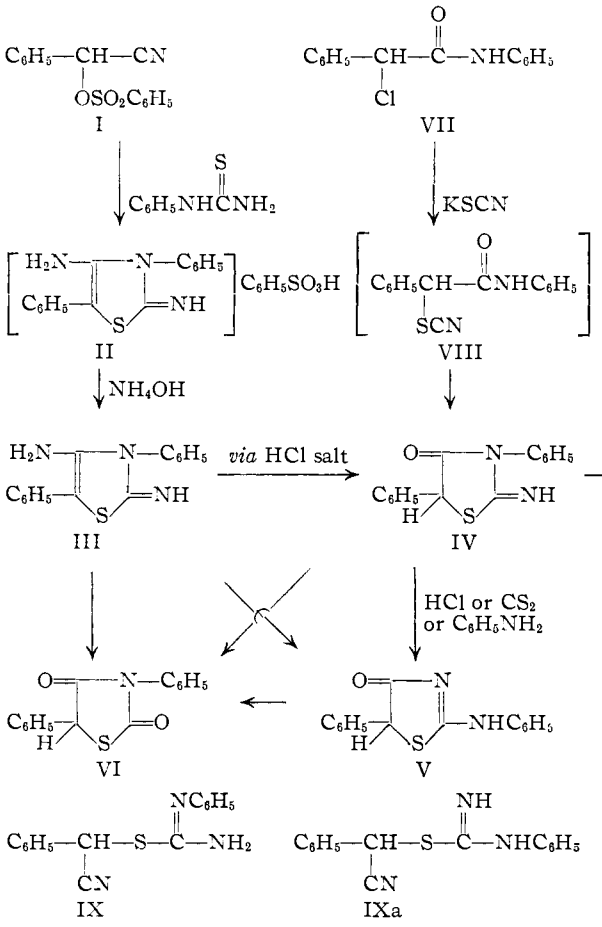
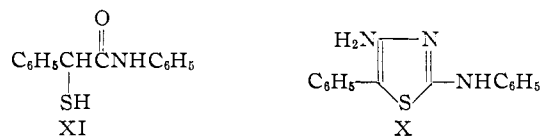
The condensation of α-cyanobenzyl benzenesulfonate (I) with phenylthiourea gave 2(3)-imino-3,5-diphenyl-4-aminothiazoline benzenesulfonate (II). Prolonged heating of the free base III with dilute acid gave 3,5-diphenyl-2,4-thiazolidinedione (VI), while short heating with dilute acid gave 2-anilino-5-phenyl-4(5)-thiazolone (V). Stirring the hydrochloride of III with water gave 2-imino-3,5-diphenyl-4-thiazolidone (IV), the structure of which was established by independent synthesis from α-chloro-α-phenylacetanilide and potassium thiocyanate and by alkaline hydrolysis to α-mercapto-α-phenylacetanilide. IV rearranged to V on heating with acid, carbon disulfide or aniline; V is known to rearrange to VI under hydrolytic conditions. Thus, the observed conversion of III to VI involves hydrolysis with concomitant twofold rearrangement. Similar results were obtained in the condensation of I with alkylthioureas. The significance of the observed rearrangement of IV to V in the interpretation of some reactions of related thiazoles is discussed.

The condensation of benzaldehyde, potassium cyanide and benzenesulfonyl chloride to give α-cyanobenzyl benzenesulfonate (I) and the reaction of this latter compound with thiourea to give 2,4-diamino-5-phenylthiazole has been described recently.[2] As a result of an expanding program on the chemistry of heterocyclic amides and amidines, we became interested in the reactions of 4-aminothiazoles and as a consequence have been led to an investigation of extensions of the above condensation reaction. The reactions of α-cyanobenzyl benzenesulfonate (I) with some aryl and alkylthioureas and some explorations of the chemistry of the products provide the subject for this paper.



α-Cyanobenzyl benzenesulfonate (I) condensed smoothly in acetone solution with phenylthiourea to give the benzenesulfonic acid salt of 2(3)-imino-3,5-diphenyl-4-aminothiazoline (II). The structure of II (and of the derived free base III) was established as follows. The most likely alternative structures for the condensation product were IX (or IXa) and X (both as the benzenesulfonic acid salts). The open-chain isomer IX (or IXa) was eliminated on the basis of the absence of a cyano band at 2140–2160 cm.$^{-1}$ in the infrared spectrum of the product (Fig. 1A). A decision between II and



X was made as follows: When the condensation product of I and phenylthiourea was dissolved in water and the solution made faintly alkaline with ammonium hydroxide, the free base (III or X) separated. The infrared spectrum of a freshly prepared sample (Fig. 1B) was similar to that of the benzenesulfonate from which it was prepared, indicating, *vide infra*, that no rearrangement had taken place during neutralization. The free base so prepared rapidly turned pink on exposure to air and was destroyed by alkali, but it was converted by short heating with dilute acid to 2-anilino-5-phenyl-4(5)-thiazolone (V) and by prolonged heating with dilute acid to 3,5-diphenyl-2,4-thiazolidinedione (VI), both known compounds. However, when the free base (III or X) was dissolved in dry benzene

(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, September, 1953, Chicago, Ill.

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

and treated with dry hydrogen chloride, a white crystalline hydrochloride separated. When this salt, carefully freed from all traces of excess acid by washing with dry solvent, was suspended in water, 2-imino-3,5-diphenyl-4-thiazolidone (IV) separated. IV rearranged rapidly to 2-anilino-5-phenyl-4(5)-thiazolone (V) when heated with dilute acid, thus explaining our failure to isolate it as an intermediate hydrolysis product between III and V. When the hydrochloride of II was not completely freed of acid before suspension in water, a mixture of IV and V was obtained; when imperfectly dried solvents were employed in the preparation of the hydrochloride, the only product which could be isolated subsequently was V.

The structure of 2-imino-3,5-diphenyl-4-thiazolidone (IV) was established (a) by alkaline hydrolysis to α-mercapto-α-phenylacetanilide (XI) and (b) by independent synthesis from α-chloro-α-phenylacetanilide (VII) and potassium thiocyanate. The infrared spectra of this product and of the hydrolysis product IV were identical (Fig. 1C); the absence of a cyano band at 2140–2160 cm.$^{-1}$ excluded the open-chain isomer VIII which might have been formed from III *via* hydrolytic ring cleavage and which was undoubtedly an intermediate in the conversion of VII to IV.[3] It follows that the initial condensation product of α-cyanobenzyl benzenesulfonate (I) and phenylthiourea must have the structure II.[4] Since it has already been established that 2-anilino-5-phenyl-4(5)-thiazolone (V) rearranges to 3,5-diphenyl-2,4-thiazolidinedione (VI) under hydrolytic conditions,[5] it follows that the observed conversion of II to VI by prolonged heating with dilute acid involves hydrolysis with concomitant twofold rearrangement.

It was found that 2-imino-3,5-diphenyl-4-thiazolidone (IV) could be rearranged to 2-anilino-5-phenyl-4(5)-thiazolone (V) not only with acid but also by heating with carbon disulfide or aniline. The latter reaction is of particular significance since it provides the rationale for the reported synthesis of V from the reaction of ethyl α-thiocyano-α-phenylacetate and aniline.[6,7]

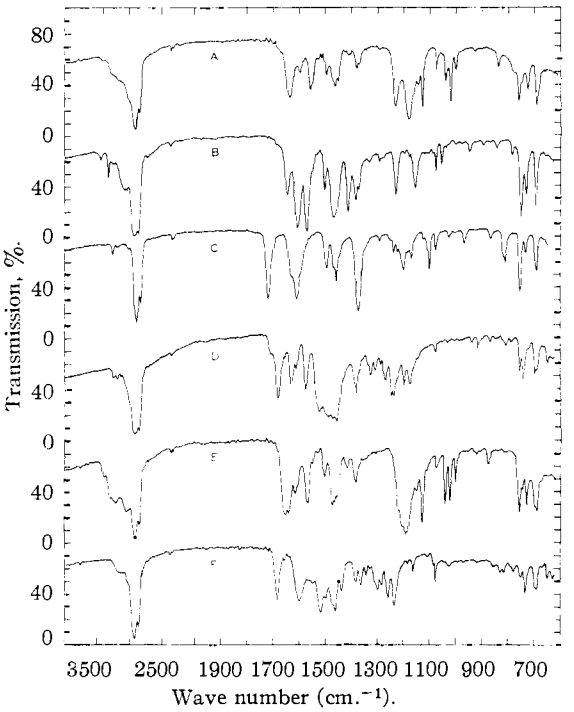
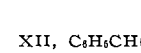


Fig. 1.—Curve A, 2(3)-imino-3,5-diphenyl-4-aminothiazoline benzenesulfonate (II); curve B, 2(3)-imino-3,5-diphenyl-4-aminothiazoline (III); curve C, 2-imino-3,5-diphenyl-4-thiazolidone (IV); curve D, 2-anilino-5-phenyl-4(5)-thiazolone (V); curve E, 2(3)-imino-3-benzyl-4-amino-5-phenylthiazoline benzenesulfonate (XIII); curve F, 2-benzylamino-5-phenyl-4(5)-thiazolone (XIV).

The condensation of α-cyanobenzyl benzenesulfonate (I) with alkylthioureas followed a similar course. I and isopropylthiourea gave an oil which could not be induced to crystallize,[4] but which yielded 2-isopropylamino-5-phenyl-4(5)-thiazolone on mild acid hydrolysis and 3-isopropyl-5-phenyl-2,4-thiazolidinedione on more vigorous acid hydrolysis. I and benzylthiourea gave the benzenesulfonic acid salt of 2(3)-imino-3-benzyl-4-amino-5-phenylthiazoline (XIII) which was readily converted to 2-benzylamino-5-phenyl-4(5)-thiazolone (XIV) on mild acid hydrolysis. All attempts to isolate 2-imino-3-benzyl-5-phenyl-4-thiazolidone (XV), the hydrolysis intermediate corresponding to IV, were unsuccessful. An attempt to synthesize XV by the condensation of α-chloro-α-phenyl-N-benzylacetamide (XVI) with potassium thiocyanate gave α-thiocyano-α-phenyl-N-benzylacetamide (XVII) rather than the cyclized product XV. Treatment of XVII either with sodium ethoxide or dilute hydrochloric acid resulted in cyclization *with concurrent rearrangement* to give 2-benzylamino-5-phenyl-4(5)-thiazolone (XIV).

The influence of substituents on the propensity for cyclization of N-substituted α-thiocyano-α-phenylacetamides is noteworthy; whereas the N-phenyl derivative VIII could not be isolated because of spontaneous cyclization to IV, the N-benzylam-

(3) The absence of a cyano band in the infrared spectrum also serves to eliminate the isomeric cyanobenzylthiocarbamide structure



XII, $C_6H_5CH(CN)SCNHC_6H_5$, which might have been expected from the reaction of α-chloro-α-phenylacetanilide and potassum thiocyanate above on the basis of recent work on the isomerization of thiocyanoacetamide (W. Davies and J. A. Maclaren, *J. Chem. Soc.*, 2595 (1951)).

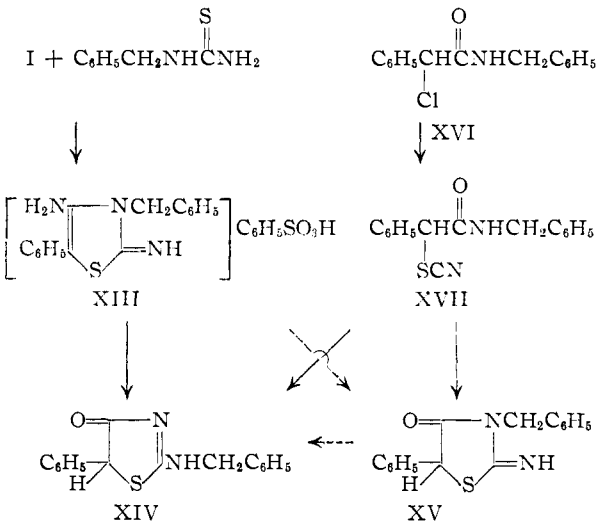
(4) It was suggested by a referee that the selectivity observed in the cyclization of the intermediate amidine IX (or IXa) to II rather than to X recalls the parallel behavior of N-phenylbenzamidine on alkylation, where preference for alkylation on the nitrogen bearing the phenyl group was found to be in the order of 150:1 (F. L. Pyman, *J. Chem. Soc.*, **123**, 367 (1923)). It was also suggested that the failure to obtain a crystalline product from the condensation of α-cyanobenzyl benzenesulfonate (I) and isopropylthiourea (*vide infra*) may have been due to simultaneous formation of 2(3)-imino-3-isopropyl-4-amino-5-phenylthiazoline benzenesulfonate and 2-isopropylamino-4 amino-5-phenylthiazole benzenesulfonate. This view is consistent with the observation of Pyman (ref. above) that alkylation of N-alkylamidines is much less selective than the alkylation of N-aryl amidines. Hydrolysis of the mixtures of benzenesulfonates would, of course, give the single product 2-isopropylamino-5-phenyl-4(5)-thiazolone.

(5) F. A. Eberly and F. B. Dains, THIS JOURNAL, **58**, 2544 (1936).

(6) H. L. Wheeler, *Am. Chem. J.*, **26**, 345 (1901).

(7) The product of the above reaction was originally claimed to be IV, which was reputedly also formed from the reaction of ethyl α-chloro-α-phenylacetate and phenylthiourea (H. L. Wheeler and T. B. Johnson, THIS JOURNAL, **24**, 680 (1902)). The product from both reactions was later shown to be V (ref. 4).

ide XVII could not be cyclized without employing conditions strenuous enough to effect rearrangement of the initially formed cyclization product.



Similarly, α-bromo-α-phenylacetamide and potassium thiocyanate gave α-thiocyano-α-phenylacetamide with no evidence of ring closure.[3] Since the presence of a basic amide grouping prevents cyclization under the reaction conditions, it seems reasonable to assume that the α-thiocyanoamide undergoes cyclization as an anion, the requisite base being thiocyanate ion.

The rapid and irreversible rearrangement represented by the conversions of IV to V and of XIII to XIV has been observed to take place under a variety of conditions and suggests an explanation for a number of reactions of related thiazoles. Thus, the condensations of chloroacetonitrile with phenylthiourea to give 2-anilino-4(5)-thiazolone,[8] of α-chloro-N-(*p*-bromophenyl)-acetamide and potassium thiocyanate to give 2-(*p*-bromoanilino)-4(5)-thiazolone[9] and of phenylmaleimide with phenylthiourea to give 2-anilino-4(5)-thiazoloneacetanilide[10] may all be explained by the assumption that a 2-imino-3-substituted intermediate was first formed which then rearranged under the reaction conditions. It should be pointed out, however, that the tendency toward rearrangement of 3-substituted 2-iminothiazoline derivatives in the absence of acid is markedly dependent on the nature of the substitution in the ring. 2-Imino-3,5-diphenyl-4-thiazolidone (IV) proved to be remarkably stable in the absence of acid. It sublimed unchanged and could be held in the melt under reduced pressure for one hour with only slight decomposition and with no detectable rearrangement. On the other hand, 2-imino-3-phenyl-4-thiazolidone rearranges readily on heating to 2-anilino-4(5)-thiazolone,[11] while 2-imino-3-allyl-4-thiazolidone has been reported to resist rearrangement.[5]

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

(9) F. B. Dains and F. E. Eberly, THIS JOURNAL, **55**, 3859 (1933).

(10) D. H. Marrian, *J. Chem. Soc.*, 1797 (1949).

(11) H. L. Wheeler and T. B. Johnson, *Am. Chem. J.*, **28**, 121 (1902).

Experimental[12]

2(3)-Imino-3,5-diphenyl-4-aminothiazoline Benzenesulfonate (II).—A mixture of 11.1 g. (0.073 mole) of phenylthiourea, 20 g. (0.073 mole) of α-cyanobenzyl benzenesulfonate[2] and 50 ml. of acetone (C.P.) was shaken until solution was complete. The reaction was exothermic and the solution turned light yellow. After standing overnight at room temperature, the reaction mixture was diluted with absolute ether until no further precipitation occurred. The solid which was collected by filtration (26.5 g., 85.5%) was recrystallized by solution in a small volume of absolute ethanol and reprecipitation with ether, m.p. 183–185° dec.

Anal. Calcd. for $C_{21}H_{19}N_3O_3S_2$: C, 59.3; H, 4.5; N, 9.9. Found: C, 59.6; H, 4.7; N, 9.9.

2(3)-Imino-3,5-diphenyl-4-aminothiazoline (III).—A mixture of 3.5 g. of 2(3)-imino-3,5-diphenyl-4-aminothiazoline benzenesulfonate (II) and 40 ml. of ammonium hydroxide (1:1) was stirred together for several minutes and the residual solid separated by filtration and washed first with 50 ml. of water, then with two 10-ml. portions of cold absolute ethanol and finally with 25 ml. of cold absolute ether. The infrared spectrum (Fig. 1B) was determined immediately; rapid decomposition to a dark red mass took place on standing at room temperature. On heating, the compound softened at 85° and decomposed rapidly and completely to a dark red liquid at 90°.

2-Anilino-5-phenyl-4(5)-thiazolone (V).—2(3)-Imino-3,5-diphenyl-4-aminothiazoline (III), obtained by the neutralization of 3.5 g. of the benzenesulfonate (II) as described above, was dissolved in 25 ml. of ethanol to which was added 3 ml. of concentrated hydrochloric acid. The solution was boiled for four minutes and then immersed in an ice-bath. Addition of 10% sodium hydroxide to *p*H 8 caused the separation of a solid which was collected by filtration and washed thoroughly with water; yield 1.1 g. (50%), m.p. 175–180°. One recrystallization from ethanol raised the melting point to 191–191.5°. A mixed melting point determination with an authentic sample of 2-anilino-5-phenyl-4(5)-thiazolone[13] showed no depression.

3,5-Diphenyl-2,4-thiazolidinedione (VI).—2(3)-Imino-3,5-diphenyl-4-aminothiazoline (III), obtained by the neutralization of 3.5 g. of the benzenesulfonate (II) as described above, was dissolved in 25 ml. of ethanol containing 3 ml. of dilute hydrochloric acid and the solution was heated under reflux for 30 minutes. Cooling of the reaction mixture resulted in the separation of long, colorless needles which were collected by filtration and recrystallized from dilute ethanol; yield 0.47 g. (21%), m.p. 176°. A mixed melting point determination with an authentic sample of 3,5-diphenyl-2,4-thiazolidinedione[5] showed no depression.

2-Imino-3,5-diphenyl-4-thiazolidone (IV). (a).—2(3)-Imino-3,5-diphenyl-4-aminothiazoline (III), prepared by the neutralization of 3.5 g. of the benzenesulfonate (II) as described above, and carefully dried by washing with cold absolute ethanol followed by anhydrous ether, was dissolved in 30 ml. of dry benzene and dry hydrogen chloride gas passed into the solution until no further precipitation occurred. The resulting white solid was collected by filtration, washed liberally with dry benzene and added to 50 ml. of water. The solid dissolved on stirring, but after ten minutes of additional stirring a small amount of white solid separated. This was separated by filtration and dried in the air, yield 0.10 g. (4.5%), m.p. 156–158° (with decomposition to a purple liquid). Recrystallization from chloroform–cyclohexane raised the decomposition point to 158–159.5°.

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

(b).—A mixture of 4.0 g. (0.0163 mole) of α-chloro-α-phenylacetanilide, 2.0 g. (0.0206 mole) of potassium thiocyanate and 30 ml. of 95% ethanol was heated under reflux on a steam-bath for 40 minutes. The reaction mixture was then evaporated to dryness under reduced pressure, 30 ml. of water added to the residue and the suspended solid separated by filtration and washed thoroughly with water; yield

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

(13) E. C. Taylor, Jr., J. Wolinsky and H. H. Lee, THIS JOURNAL, **76**, 1870 (1954).

2.9 g. (66.5%), m.p. 153–156° (with decomposition to a purple liquid). Recrystallization from chloroform–cyclohexane raised the decomposition point to 158–159.5°.

Comparison of the infrared spectra of the products obtained by methods (a) and (b) showed them to be identical. IV sublimed without change at 150° (0.1 mm.) and was held in the melt for one hour without apparent change at 170° (1 mm.); recrystallization of the melt from chloroform–cyclohexane gave a product identical with the product obtained by (a) and (b) above.

Rearrangement of 2-Imino-3,5-diphenyl-4-thiazolidone (IV) to 2-Anilino-5-phenyl-4(5)-thiazolone (V). (a) With Acid.—A mixture of 0.35 g. of 2-imino-3,5-diphenyl-4-thiazolidone (IV), 3 ml. of dilute hydrochloric acid (1:2) and 25 ml. of ethanol was heated to boiling and then cooled immediately in an ice-bath. Dilute sodium hydroxide (5 *N*) was added dropwise to *p*H 8, and the unreacted starting material (IV) was filtered off (0.065 g.). Concentration of the filtrate under reduced pressure caused the separation of a colorless solid which was separated by filtration and recrystallized from ethanol; yield 0.075 g., m.p. 190–191°. A mixed melting point determination with an authentic sample of 2-anilino-5-phenyl-4(5)-thiazolone (V) showed no depression.

(b) **With Carbon Disulfide.**—A mixture of 4.5 g. of 2-imino-3,5-diphenyl-4-thiazolidone (IV) and 80 ml. of carbon disulfide (C.P.) was heated in an open Pyrex tube in a sealed steel bomb at 180° for six hours. After cooling, the solid pellets were collected by filtration and washed thoroughly with carbon disulfide; yield 1.25 g., m.p. 184–186°. Recrystallization from ethanol raised the melting point to 190–191°; no depression in melting point was observed when this product was mixed with an authentic sample of 2-anilino-5-phenyl-4(5)-thiazolone (V). An additional 0.4 g. of product was obtained by concentration of the filtrates and recrystallization of the residue from benzene–cyclohexane.

(c) **With Aniline.**—A mixture of 1.0 g. of 2-imino-3,5-diphenyl-4-thiazolidone (IV) and 2 ml. of freshly-distilled aniline was heated on a steam-bath for ten hours. Solidification occurred on cooling; the mass was digested thoroughly with cold benzene and filtered; yield 0.63 g., m.p. 190–191°. A mixed melting point determination with an authentic sample of V showed no depression.

α-Mercapto-α-phenylacetanilide (XI).—To a boiling solution of 0.9 g. of 2-imino-3,5-diphenyl-4-thiazolidone (IV) in 25 ml. of ethanol was added 3 ml. of 10% sodium hydroxide and the resulting reddish-brown solution allowed to boil for five minutes. After cooling, the solution was diluted with water to the cloud point and then allowed to stand overnight. The resulting precipitate was filtered, dried and purified by solution in benzene followed by precipitation with petroleum ether; yield 0.22 g., m.p. 245–245.5° dec.

Anal. Calcd. for $C_{14}H_{13}NOS$: C, 69.1; H, 5.4; N, 5.8. Found: C, 69.3; H, 5.1; N, 5.8.

Condensation of α-Cyanobenzyl Benzenesulfonate (I) with Isopropylthiourea.—A mixture of 27.3 g. (0.1 mole) of α-cyanobenzyl benzenesulfonate, 11.8 g. (0.1 mole) of isopropylthiourea and 75 ml. of acetone (C.P.) was shaken until solution was complete. The reaction was strongly exothermic. After standing overnight, the reaction solution was diluted with ether. A red oil separated which could not be induced to crystallize satisfactorily.

A portion of the red oil crystallized after standing at room temperature for two months. Purification of the solid by dissolution in ethanol and reprecipitation by addition of ether gave the ammonium salt of benzenesulfonic acid, m.p. 284–287°. The filtrate on evaporation yielded a red oil.

2-Isopropylamino-5-phenyl-4(5)-thiazolone.—A mixture of 20 g. of the above red oil, 10 ml. of dilute hydrochloric acid (1:1) and 30 ml. of ethanol was heated under reflux for 30 minutes. Neutralization of the cooled reaction mixture with 5 *N* sodium hydroxide caused the separation of 8.0 g. (67%) of colorless crystals which were recrystallized from 95% ethanol, m.p. 207.5–208°.

Anal. Calcd. for $C_{12}H_{14}N_2OS$: C, 61.5; H, 6.0; N, 12.0. Found: C, 61.4; H, 6.0; N, 11.9.

3-Isopropyl-5-phenyl-2,4-thiazolidinedione.—A mixture of 5.0 g. of the red oil above, 5 ml. of dilute hydrochloric acid (1:1) and 25 ml. of ethanol was heated under reflux for six hours. Dilution of the reaction mixture with water caused the separation of a solid which was separated by filtration and recrystallized from dilute ethanol; yield 0.55 g. (18%), m.p. 98°.

Anal. Calcd. for $C_{12}H_{13}NO_2S$: C, 61.3; H, 5.6; N, 6.0. Found: C, 61.3; H, 5.7; N, 5.9.

2(3)-Imino-3-benzyl-4-amino-5-phenylthiazoline Benzenesulfonate (XIII).—A mixture of 4.5 g. (0.027 mole) of benzylthiourea, 7.4 g. (0.027 mole) of α-cyanobenzyl benzenesulfonate[2] and 50 ml. of acetone (C.P.) was shaken until solution was complete. After standing overnight at room temperature, the solution was diluted with ether until no further precipitation of solid occurred; yield 9.5 g. (80%), m.p. 204–206°. The material was purified by precipitation from ethanol solution with ether, m.p. 208–209° dec.

Anal. Calcd. for $C_{22}H_{21}N_3O_3S_2$: C, 60.1; H, 4.8; N, 9.6. Found: C, 60.3; H, 5.0; N, 9.8.

2-Benzylamino-5-phenyl-4(5)-thiazolone (XIV).—A mixture of 3.0 g. of 2(3)-imino-3-benzyl-4-amino-5-phenylthiazoline benzenesulfonate (XIII) and 50 ml. of ammonium hydroxide (1:1) was stirred for 15 minutes at room temperature, the solution decanted and the gummy residue washed several times with water. It was then dissolved in 25 ml. of ethanol containing 2 ml. of dilute hydrochloric acid (1:1) and the resulting solution heated under reflux for 15 minutes. The *p*H of the cooled solution was adjusted to 7 by the addition of 5 *N* sodium hydroxide. The solid which separated was collected by filtration (1.3 g.); an additional 0.6 g. was obtained by dilution of the filtrate (total yield 1.9 g., 99%). After three recrystallizations from ethanol, the compound melted at 185–185.5° and gave no depression in melting point when mixed with an authentic sample of 2-benzylamino-5-phenyl-4(5)-thiazolone.[13]

α-Chloro-α-phenyl-N-benzylacetamide (XVI).—To a cooled solution of 28 g. (0.148 mole) of α-chloro-α-phenylacetyl chloride in 90 ml. of dry benzene was added slowly a solution of 32 g. (0.30 mole) of benzylamine in 90 ml. of dry benzene. The mixture was warmed for ten minutes on a water-bath and then extracted with several portions of dilute hydrochloric acid. The benzene solution was then washed twice with water, dried over sodium sulfate and concentrated to a small volume under diminished pressure. Addition of petroleum ether then caused the separation of white crystals; yield 34 g. (89%), m.p. 100–102°. Purification by dissolving in benzene and reprecipitating by the addition of petroleum ether raised the melting point to 109–111°.

Anal. Calcd. for $C_{15}H_{14}NOCl$: C, 69.7; H, 5.5; N, 5.4. Found: C, 69.4; H, 5.3; N, 5.3.

α-Thiocyano-α-phenyl-N-benzylacetamide (XVII).—A mixture of 7.0 g. (0.027 mole) of α-chloro-α-phenyl-N-benzylacetamide (XVI) 2.8 g. (0.029 mole) of potassium thiocyanate and 40 ml. of 95% ethanol was heated under reflux for four hours on a steam-bath. Evaporation of the reaction solution to dryness and addition of water to the residual solid gave a pink oil which solidified on standing. This solid was separated by filtration and dissolved in chloroform. The chloroform solution was dried over anhydrous sodium sulfate and evaporated to a small volume. Addition of cyclohexane caused the separation of colorless needles; yield 3.8 g. (50%), which were recrystallized from benzene–cyclohexane, m.p. 109°.

Anal. Calcd. for $C_{16}H_{14}N_2OS$: C, 68.1; H, 5.0; N, 9.9. Found: C, 68.4; H, 5.1; N, 9.9.

The infrared spectrum of the product showed a strong C≡N band at 2160 cm.$^{-1}$ indicating that the product had the open-chain structure XVII. XVII underwent no apparent change when subjected to (a) heating under reflux in dry xylene for five hours, (b) heating in the melt for one hour at 130° or (c) heating under reflux in dilute alcoholic hydrochloric acid for ten minutes.

Cyclization of α-Thiocyano-α-phenyl-N-benzylacetamide (XVII). (a) With Acid.—A mixture of 3.0 g. of α-thiocyano-α-phenyl-N-benzylacetamide (XVII), 25 ml. of ethanol and 10 ml. of concentrated hydrochloric acid was heated under reflux for five hours. The cooled solution was neutralized with 5 *N* sodium hydroxide and the resulting solid collected by filtration, dried and recrystallized from chloroform–cyclohexane; yield 1.28 g. (43%), m.p. 185–185.5°. A mixed melting point determination with an authentic sample of 2-benzylamino-5-phenyl-4(5)-thiazolone showed no depression.

(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.

URBANA, ILLINOIS

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

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

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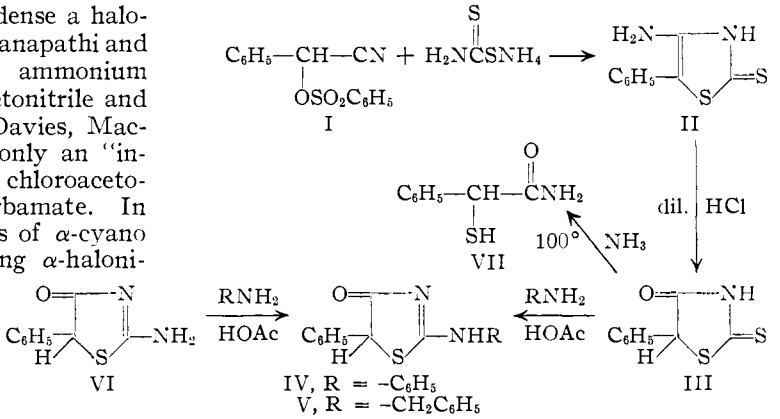
The condensation of α-cyanobenzyl benzenesulfonate with dithiocarbamates has been shown to give derivatives of 4-amino-5-phenyl-2(3)-thiazolinethione. Some reactions of the latter compounds have been described.

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.

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