of benzylpyridines of 42 g. (32%) of which approximately 20% is the 2-isomer and 80% the 4-isomer.

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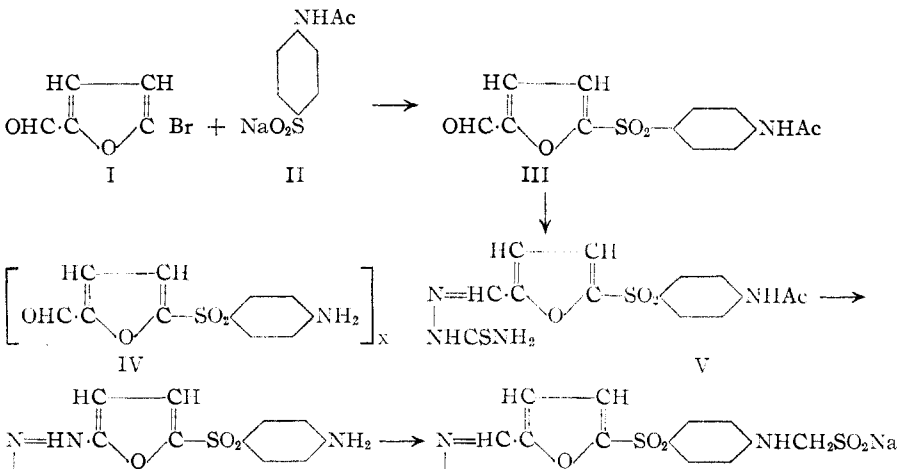
5-Sulfanilyl-2-furaldehyde Thiosemicarbazone

BY HUGO BAUER

5-Sulfanilyl-2-furaldehyde thiosemicarbazone was synthesized as a compound representing a combination of the sulfone and thiosemicarbazone groupings. Similar compounds derived from methyl, ethyl and *n*-propyl sulfonylbenzaldehydes have been reported in the literature.[1] Furaldehyde was chosen for its stability and the reactivity of its 5-bromo derivative,[2] whose preparation was improved by the use of N-bromosuccinimide as the brominating agent (Wohl–Ziegler reaction). Condensation of 5-bromofuraldehyde (I) with sodium acetaminobenzenesulfinate (II) yielded 5-acetylsulfanilyl-2-furaldehyde (III). The deacetylation of the amino group could not be performed satisfactorily by the conventional acid hydrolysis. By this procedure a partially polymerized substance was obtained the analysis of which agreed with 5-sulfanilyl-2-furaldehyde (IV). However, after condensation of III with thiosemicarbazide, deacetylation proceeded smoothly in alkaline medium, yielding 5-sulfanilyl-2-furaldehyde thiosemicarbazone (VI). The solubility in water of this compound was too low for practical purposes. To obtain a more soluble product, VI was condensed with sodium formaldehyde sulfoxylate.[3] The resulting compound VII had a solubility of 0.4% in water at 23°.



Experimental

5-Bromo-2-furaldehyde (I).—The reported[2] yield of 34% was raised to 68% by the use of N-bromosuccinimide as the brominating agent. The melting point of 81.5–82° was the same as reported in the literature.

Sodium *p*-Acetaminobenzenesulfinate (II).—Instead of the procedure described by Ferry, Buck and Baltzly[4] for the preparation of the sodium salt of *p*-acetaminobenzenesulfinic acid, the following procedure was applied to advantage. The sulfinic acid[5] (59.7 g., 0.30 mole) was suspended in 600 cc. of 95% ethanol and dissolved by the addition of 30 cc. of 10 *N* sodium hydroxide. In case there was a residue, the solution was filtered immediately. The sodium salt began to crystallize after a few minutes. To complete the precipitation, about 300 cc. of ether was added and the mixture kept in the cold room overnight. The yield was 58–65 g. (75–84%). This product contained two moles of water of crystallization, which could be removed by drying *in vacuo* at 100°.

Anal. Calcd. for $C_6H_8NNaO_5S \cdot 2H_2O$: H_2O, 14.0. Found: H_2O, 14.4.

5-Acetylsulfanilyl-2-furaldehyde (III).—A mixture of 51.4 g. (0.2 mole) of the dihydrate of II, 35 g. (0.2 mole) of bromofuraldehyde (I) and 150 cc. of ethylene glycol monoethyl ether was refluxed in an oil-bath for 45 minutes. Addition of 250 cc. of water to the cooled solution produced a light colored crystalline precipitate which was collected, washed with water and dried in a desiccator. The yield was 47–51 g. (80–87%). Recrystallization from ethanol gave a product melting at 172–173°.

Anal. Calcd. for $C_{13}H_{11}NO_5S$: C, 53.23; H, 3.78; N, 4.78. Found: C, 53.21; H, 3.90; N, 4.70.

Deacetylation of III by heating with hydrochloric acid (sp. gr. 1.12) afforded a compound of no definite melting point in 74% yield. The presence of a free amino group could be shown by diazotization and coupling. The analysis agreed with the formula of 5-sulfanilyl-2-furaldehyde (IV).

Anal. Calcd. for $C_{11}H_9NO_4S$: C, 52.58; H, 3.61; S, 12.76. Found: C, 52.50; H, 4.20; S, 12.72.

5-Acetylsulfanilyl-2-furaldehyde Thiosemicarbazone (V).—To a solution of 29.3 g. (0.1 mole) of III in 500 cc. of hot 95% ethanol, a solution of 9.1 g. (0.1 mole) of thiosemicarbazide in 50 cc. of 2 *N* hydrochloric acid was added. Pale yellow crystals (34 g., 94%) of the thiosemicarbazone separated. They melted with decomposition at 240–242°.

Anal. Calcd. for $C_{14}H_{14}N_4O_4S_2$: C, 45.89; H, 3.85; S, 17.50. Found: C, 45.98; H, 4.00; S, 17.53.

5-Sulfanilyl-2-furaldehyde Thiosemicarbazone (VI).—Compound V (18.32 g., 0.05 mole) was heated on the steam-bath with 100 cc. (0.5 mole) of 5 *N* sodium hydroxide solution for 15 minutes. Upon cooling the clear brown solution a sodium salt separated which was dissolved by the addition of an equal volume of water. The mixture was acidified to litmus paper by the addition of about 225 cc. of 2 *N* hydrochloric acid. The cream-colored crystalline precipitate obtained was collected, washed with water and dried in a desiccator. This material (16.1 g., 91%) contained 1.5 moles of water of crystallization (Calcd.: H_2O, 7.69. Found: H_2O, 7.63). When heated in a melting point tube, it frothed at 140° with loss of water, then decomposed at 199–200°. From 75% ethanol pale yellow anhydrous blades were obtained which decomposed at 207°.

(1) (a) R. Behnisch, F. Mietzsch and H. Schmidt, *Am. Rev. Tuberc.*, **61**, 1 (1950); (b) E. Hoggarth, A. R. Martin, N. E. Storey and E. H. P. Young, *Brit. J. Pharmacol.*, **4**, 248 (1949); (c) R. Donovick, F. Pansy, G. Stryker and J. Bernstein, *J. Bact.*, **59**, 667 (1950); J. Bernstein, H. L. Yale, K. Losee, M. Holsing, J. Martins and W. A. Lott, THIS JOURNAL, **73**, 906 (1951).

(2) H. Gilman and G. F. Wright, *ibid.*, **52**, 1170 (1930).

(3) (a) H. Bauer, *ibid.*, **61**, 617 (1939); (b) G. W. Raiziss, L. W. Clemence and M. Freifelder, *J. Am. Pharm. Assoc., Sci. Ed.*, **33**, 43 (1944).

(4) "Organic Syntheses," **22**, 31 (1942.)

(5) "Organic Syntheses," Coll. Vol. I, Second ed., John Wiley and Sons, Inc., New York, N. Y., 1941, p. 7.

Anal. Calcd. for $C_{12}H_{12}N_4O_3S_2$: C, 44.43; H, 3.73; S, 19.77. Found: C, 44.36; H, 3.84; S, 19.87.

The presence of a free amino group was shown by diazotization and coupling with F-salt to form a deep red dye.

Condensation Product of Sodium Formaldehyde Sulfoxylate with 5-Sulfanilyl-2-furaldehyde Thiosemicarbazone (VII).—The condensation product was prepared in 93% yield, using the procedure of Raiziss.[3b] Recrystallization of 21.5 g. of the product from 300 cc. of boiling water with the addition of 1 g. of sodium bicarbonate yielded 14.4 g. of colorless crystals. The solubility in water at 23° was about 0.4%.

Anal. Calcd. for $C_{13}H_{13}N_4NaO_5S_3 \cdot 1/2H_2O$: C, 36.02; H, 3.26; N, 12.93; Na, 5.31; S, 22.19; H_2O, 2.08. Found: C, 35.97; H, 3.51; N, 13.10; Na, 4.96; S, 21.35; H_2O, 2.29.

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5-Methyl-2-cyclohexenone

BY JEAN P. BLANCHARD AND HARLAN L. GOERING

In connection with synthetic work now in progress, large quantities of 5-methyl-2-cyclohexenone (IV) were required. We have found that this compound can be conveniently synthesized from the readily available 5-methyl-1,3-cyclohexanedione[1] by a scheme which parallels that of Frank and Hall[2] for the preparation of 5-isopropyl-2-cyclohexenone.

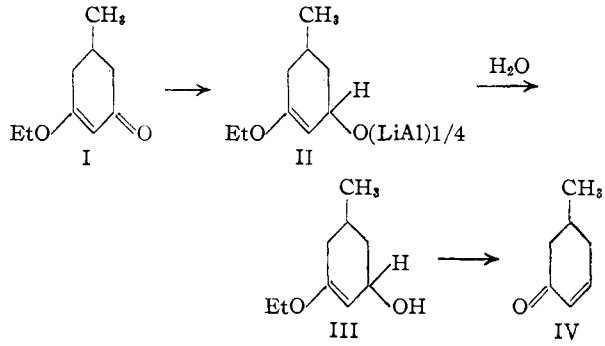
Optically active IV[3,4] as well as the inactive material[5,6] have previously been reported by several workers. In cases where physical properties of IV are reported[4,5] agreement among the earlier workers is satisfactory; however, considerable discrepancies in the melting points of the semicarbazone derivative have been observed.

Inasmuch as the product obtained in the present work has physical properties which differ considerably from the previously described material[4,5] we have investigated the structure of our material. Analysis, ultraviolet absorption, reduction to 3-methylcyclohexanone and method of synthesis provided the necessary evidence for believing the structure to be 5-methyl-2-cyclohexenone.[7] The ultraviolet spectrum was typical for singly substituted α,β-unsaturated ketones,[8] showing a peak at 225.2 mμ (log ϵ 4.0).

In order to clarify the discrepancies between 5-methyl-2-cyclohexenone obtained in our work and the material described in the literature[4,5] we have repeated Godchot's synthesis and indeed obtained the material described by him. This material has not as yet been identified; however, comparison of physical properties and of derivatives clearly showed that the compound is not the alleged 5-methyl-2-cyclohexenone. The Birch synthesis[6] was also investigated and found to give IV in low yield.

In the present synthesis 5-methyl-1,3-cyclohexanedione is converted to the enol ether I, which is subsequently reduced with lithium aluminum hydride to IV.

The conversion of an enol ether of a β-diketone to an α,β-unsaturated ketone by reduction with lithium aluminum hydride has previously been described[2]; however, this method involved an inverse addition and use of an excess of ketone. We have found that the inverse addition is not necessary and indeed gives a poorer conversion than does the general procedure of Nystrom and Brown[9] for the reduction of ketones. The formation of a ketone, IV, from a reduction involving excess lithium aluminum hydride suggests the following reaction path in which the intermediate 1-ethoxy-3-hydroxy-5-methylcyclohexene (III) is converted to IV by hydrolysis to the β-hydroxy ketone followed by dehydration.



Basic[10] as well as acid hydrolysis of the metal alcoholate (II) yields IV.

Experimental[11]

5-Methyl-2-cyclohexenone (IV).—5-Methyl-1,3-cyclohexanedione, m.p. 128–129° (lit.[1,12] 128° and 127°), was prepared in 55% yield from ethyl crotonate and ethyl acetoacetate by a modification of the procedure of Crossley and Renouf.[1] This modification consisted of removal of most of the ethanol by distillation under reduced pressure instead of by azeotropic distillation with water. The dioxime melted at 155.5–157.5° (lit.[13] 155–157°).

5-Methyl-1,3-cyclohexanedione was converted to 3-ethoxy-5-methyl-2-cyclohexenone (I), b.p. *ca.* 83° (0.1 mm.) in 93% yield by the method of Frank and Hall.[2] After crystallization from aqueous acetone it melted at 41–43° (reported for the monohydrate,[12] 42°). The enol ether was converted to IV by lithium aluminum hydride reduction. Best results were obtained by the general procedure of Nystrom and Brown[9] for the reduction of aldehydes and ketones. In this way a 92% yield of IV was obtained, b.p. *ca.* 60° (8 mm.); $n^{25}D$ 1.4739; d^{25}_4 0.947; *MR* calcd. (no exaltation), 31.9; *MR* found, 32.7. Ultraviolet absorption showed a peak at 225.2 mμ (log ϵ 4.0, 0.006 g. per liter of 95% ethanol solution).

Anal. Calcd. for $C_7H_{10}O$: C, 76.32; H, 9.15. Found: C, 76.08; H, 8.99.

The inverse addition method of Frank and Hall[2] gave a

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(6) A. J. Birch, *J. Chem. Soc.*, 1270 (1947).
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(11) All melting points are corrected.
(12) C. Gilling, *J. Chem. Soc.*, **103**, 2029 (1913).
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