vacuo. The residue was worked with ether, and filtered. This gave 1.1 g. of crude adduct product, m.p.[6] 230° unsharp, dec., and with previous softening. Three recrystallizations from dilute acetic acid gave 0.57 g. of III, m.p. 244–246.5° dec., $\lambda_{max}^{abs.\ alc.}$ none (possible maximum at 267 mμ, ε 500), $[\alpha]^{26}D$ +124°, $[\alpha]^{26}_{Hg}$ +190° (19 mg. in 2 ml. of chloroform solution, 1-dm. semi-micro tube, gave αD +1.18°, α_{Hg} +1.80°), $\alpha_{Hg}/\alpha D$ 1.53, [M]D +326.

Anal.[7] Calcd. for $C_{25}H_{28}O_6$ (424.47): C, 70.74; H, 6.65. Found: C, 70.52; H, 6.83.

Maleic Anhydride Adduct (IV) of $\Delta^{5,7,9(11)}$-Pregnatriene-3β-ol-20-one Acetate.—A mixture of 3.0 g. of $\Delta^{5,7,9(11)}$-pregnatriene-3β-ol-20-one acetate (II), 1.2 g. of maleic anhydride and 150 ml. of xylene was refluxed for 19.5 hours. The product was worked up as above, wt. 3 g., m.p. 263–264°, dec. above m.p. Recrystallization from acetic acid gave 2.53 g. of IV, m.p. 264–265° dec. above m.p. From the mother liquors there was obtained an additional 100 mg. of IV, m.p. 263° dec. above m.p.; $[\alpha]^{25}D$ +117°, $[\alpha]^{25}_{Hg}$ +151° (22.1 mg. in 2 ml. of chloroform solution, 1-dm. semi-micro tube, gave αD +1.29°, α_{Hg} +1.67°), α_{Hg}/α_D 1.29, [M]D +529.

Anal. Calcd. for $C_{27}H_{32}O_6$ (452.53): C, 71.66; H, 7.13. Found: C, 71.48; H, 7.10.

Pyrolysis of the Maleic Anhydride Adduct (IV) of $\Delta^{5,7,9(11)}$-Pregnatriene-3β-ol-20-one Acetate.—Compound IV (0.5 g.) was pyrolyzed and evaporatively distilled in the following manner. A pressure of 0.18 mm. was maintained. The material was heated for about 5 hours from room temperature to 313°. The solid sublimate which appeared at 220°, became considerable at 250°. The sublimate was slurried with ether, and the insoluble starting material (IV) was removed by filtration; wt. 0.20 g., m.p. 261–264° dec. The ether filtrate was washed with water, dried, and concentrated. The solution was allowed to stand at room temperature overnight. During this time a very small amount of material was deposited as a film on the walls of the flask. It was separated by decantation. The ether decantate was concentrated with simultaneous addition of methanol until all of the ether was removed. Addition of water gave 60 mg. of impure II. Recrystallization from dilute methanol gave pure II, wt. 20 mg., m.p. 143–144°, $\lambda_{max}^{abs.\ alc.}$ 312, 324 and 339 mμ, ε 10800, 12200, 7600, respectively.

(6) All melting points are uncorrected and were determined with uncalibrated Anschütz thermometers.

(7) We are indebted to Messrs. Louis M. Brancone, Samuel M. Modes and Edward B. Ruffing, Jr., for the microanalytical data.

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The Reaction of Benzylmagnesium Chloride and Dibenzylmagnesium with Pyridine

BY ROBERT A. BENKESER AND DEXTER S. HOLTON

In 1932 Bergmann and Rosenthal[1] reported that dibenzylmagnesium reacts with pyridine to form 2-benzylpyridine. In 1946 Veer and Goldschmidt[2] disputed this work and claimed that 4-benzylpyridine is formed exclusively and not the 2-isomer. The picrates of both of these isomers have about the same melting point (140–142°), and hence care must be exercised in identifying them.

Since the reaction of quinoline with dibenzylmagnesium is reported to yield largely the 2-isomer,[1,3] it seemed likely that pyridine should give at least a mixture of the 2- and 4-benzyl isomers and not exclusively one or the other as claimed by the previous workers.[1,2] This was actually found to be the case although the 4-isomer was formed in larger amounts. The addition of dioxane to the Grignard solution did not seem to alter the ratio of the isomers; however, its presence did greatly increase the over-all yield of the benzylpyridines. This is in keeping with the observations made on quinoline.[3]

The 2- and 4-benzylpyridines were separated by carefully fractionating them through an efficient column. Mixed melting points of the picrates of these isomers and those obtained from authentic 2- and 4-benzylpyridine prepared by the method of Crook and McElvain[4] completed the identification.

Experimental

Authentic 2- and 4-Benzylpyridine.—The method used for preparing these compounds was essentially that described by Crook and McElvain.[4] The reaction product was fractionated through a Todd column with a vacuum jacketed 5-mm. wire spiral. Approximately 25.5 g. of the 2-isomer was collected boiling 275–278°[5a] at 753 mm., $n^{20.5}D$ 1.5792[5a]; d^{20}_4 1.055,[5b] and 5.1 g. of the 4-isomer boiling 284–287°[5a] at 753 mm., $n^{20.5}D$ 1.5810; d^{20}_4 1.062.[5b]

A picrate of the 2-benzylpyridine prepared in the usual manner melted at 141–142° (lit. 141.5–142°[2]). A picrate of the 4-isomer melted at 140.5–141° (lit. 141–142°[2]). A mixed melting point was depressed to 115–118°.

Reaction of Benzylmagnesium Chloride with Pyridine.—In a one-liter three-neck flask fitted with a reflux condenser, stirrer and dropping funnel was placed 24.3 g. (1.0 g. atom) of magnesium turnings and 65 ml. of anhydrous ether. To this was added dropwise and with stirring a solution of 126 g. (1.0 mole) of benzyl chloride in 185 ml. of anhydrous ether. When all the benzyl chloride solution had been added, stirring was continued for 30 minutes. Then 54 g. (0.67 mole) of freshly distilled anhydrous pyridine was added dropwise. A vigorous reaction set in. When all the pyridine had been added, the mixture was refluxed on a steam-cone for 24 hours with constant stirring. After the mixture had cooled it was immersed in an ice-bath, and an ice-cold 20% ammoniun chloride solution was added dropwise to decompose the Grignard complex. The aqueous hydrolyzate was extracted with ether and the ether extracts were in turn treated with 5% sulfuric acid. This acid extract was neutralized with 5% potassium hydroxide and this solution was extracted with ether. These final ether extracts were dried over Drierite, and then the solvent was removed. The residual liquid was distilled through a Claisen head, and the fraction boiling over 100° (15 mm.) was collected. This was then distilled through a Todd column with a vacuum jacketed 5-mm. wire spiral. Approximately 2 g. of the 2-isomer boiling 274–277° at 759 mm. was obtained, $n^{20}D$ 1.5790 and 6 g. of the 4-isomer boiling 277–279° at 759 mm., $n^{20}D$ 1.5810. The over-all yield of benzylpyridines was about 8% of which about 20% was estimated to be the 2-isomer and 80% the 4-isomer. The identity of these isomers was established by mixed melting points with authentic samples of the picrates.

Reaction of Dibenzylmagnesium with Pyridine.—The benzylmagnesium chloride was prepared exactly as described before. Then 150 ml. of freshly purified[6] dioxane was added to the Grignard reagent and the mixture was stirred for 30 minutes. To this suspension was added dropwise 64 g. (0.8 mole) of anhydrous pyridine after which the mixture was refluxed on a steam-cone for 24 hours with constant stirring. The reaction was worked up as described before and the fractionation again was made through the Todd column. Approximately 9 g. of the 2-isomer and 33 g. of the 4-isomer were obtained with identical physical constants as those shown above. This represents a total yield

(1) E. Bergmann and W. Rosenthal, *J. prakt. Chem.*, [2] **135**, 267 (1932).

(2) W. L. C. Veer and St. Goldschmidt, *Rec. trav. chim.*, **65**, 793 (1946).

(3) H. Gilman and G. C. Gainer, THIS JOURNAL, **71**, 2327 (1949).

(4) K. E. Crook and S. M. McElvain, *ibid.*, **52**, 4007 (1930).

(5a) See P. C. Teague, *ibid.*, **69**, 714 (1947); also E. H. Huntress and H. C. Walter, *ibid.*, **70**, 3704 (1948).

(5b) A. Tschitschibabin, *J. Russ. Phys. Chem. Soc.*, **33**, 255 (1901).

(6) L. F. Fieser, "Experiments in Organic Chemistry," D. C. Heath and Co., New York, N. Y., 1941, p. 369.

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

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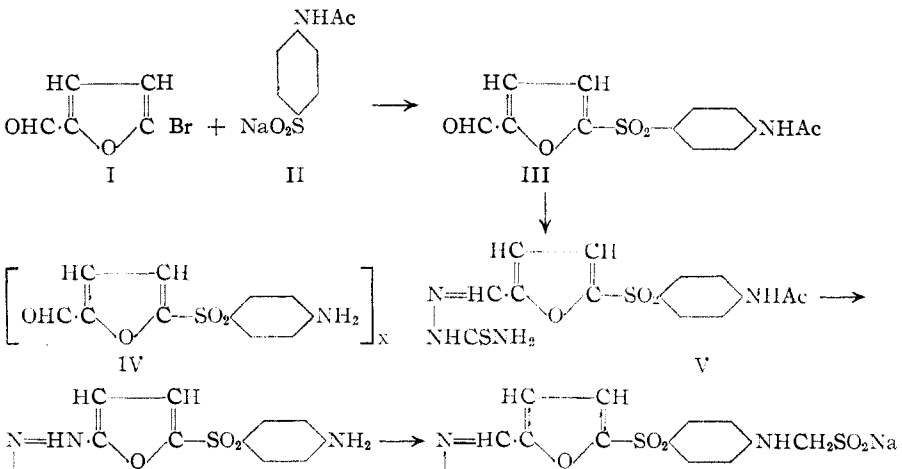
5-Sulfanilyl-2-furaldehyde Thiosemicarbazone

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 $C_8H_8NNaO_3S\cdot 2H_2O$: 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 $C_{13}H_{11}NO_6S$: 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.