utes and then allowed to sit at room temperature until the reaction was complete. For the reaction of 2-methyl-5-isopropylbenzaldehyde this entailed two days; for the 3-methyl-6-isopropylbenzaldehyde this entailed two weeks. We judged the reaction complete when the contents of the reaction vessels, stoppered after heating, appeared as a solid mass of crystals, with no visible liquid phase. From 7 g. of 2-methyl-5-isopropylbenzaldehyde and 1.3 g. of acetone was obtained 4.6 g., 61%, of bis-(2-methyl-5-isopropylbenzal)-acetone, m. p. 93.5–94.5°.

Anal. Calcd. for $C_{25}H_{30}O$: C, 86.6; H, 8.72. Found: C, 86.4; H, 8.69.

From the same quantities of 3-methyl-6-isopropylbenzaldehyde and acetone was obtained 4.5 g., 60%, of bis-(3-methyl-6-isopropylbenzal)-acetone, m. p. 95–96°.

Anal. Calcd. for $C_{25}H_{30}O$: C, 86.6; H, 8.72. Found: C, 86.3; H, 8.70.

Preparation of Substituted Mandelic Acids.—Using the same molar quantities of material and following in detail the procedure described by Fieser for the preparation of mandelic acid,[12] from 10 g. of the bisulfite compound of 2-methyl-5-isopropylbenzaldehyde was obtained 2.44 g., 36%, of (2-methyl-5-isopropylphenyl)-glycolic acid, m. p. 124–125°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.2; H, 7.69; neut. equiv., 208. Found: C, 69.1; H, 7.68; neut. equiv., 206.8.

In like manner from 10 g. of the bisulfite compound of 3-methyl-6-isopropylbenzaldehyde was obtained 0.8 g., 12%, of (3-methyl-6-isopropylphenyl)-glycolic acid, m. p. 139–140°.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.2; H, 7.69; neut. equiv., 208. Found: C, 69.4; H, 7.83; neut. equiv., 208.9.

Reaction of the Aldehydes with Sodium Bisulfite.—A solution of 2.16 g., 0.0133 mole, of each aldehyde in 50 ml. of ether was placed in a glass bottle and 100 ml. of saturated aqueous sodium bisulfite was added to each bottle. The bisulfite solution was from the same stock solution. The bottles were stoppered and strapped together on the same shaking machine. At the end of four hours shaking 2.036 g., 57.4%, of the addition compound of 2-methyl-5-isopropylbenzaldehyde had precipitated. Further shaking for a total of twenty-four hours produced no additional precipitate. At the end of four hours 1.635, 46.1%, of the addition compound of 3-methyl-6-isopropylbenzaldehyde had precipitated. At the end of seven hours a total of 1.794 g., 51.1%, and at the end of twenty-two hours, a total of 1.976 g., 55%, had precipitated. No further precipitation occurred on an additional two hours shaking. At each time interval mentioned above, shaking was interrupted and the precipitate was filtered at the water pump. The precipitate was washed with ether and the ether solution of the aldehyde restored to its original volume by adding the washings and any additional ether necessary. Shaking was then resumed. The precipitate collected was dried and weighed.

Cannizzaro Reaction.—From 10 g. of 2-methyl-5-isopropylbenzaldehyde treated according to a standard procedure (the reaction mixture was allowed to sit for forty-eight hours[13]) was obtained 3 g., 57%, of 2-methyl-5-isopropylbenzoic acid, m. p. and mixed m. p. with authentic sample[1] 70–71°, and 5.1 g. of material, b. p. 137–138° (20 mm.). This proved to be a mixture of alcohol and unreacted aldehyde, since it gave positive fuchsin aldehyde test and reacted with 3,5-dinitrobenzoyl chloride to give an ester,[14] m. p. 74–75°.

Anal. Calcd. for $C_{18}H_{18}O_6N_2$: N, 7.81. Found: N, 7.66.

When 10 g. of the 3-methyl-6-isopropylbenzaldehyde was treated as above, less than 0.1 g. of acid was obtained and 8.9 g. of unreacted aldehyde was recovered. The reaction was repeated and the reaction mixture heated at 100° with mechanical stirring for one week. From this reaction was obtained 0.8 g., 12%, of 3-methyl-6-isopropylbenzoic acid, m. p. and mixed m. p. with authentic sample[1] 84–85°. In addition to the acid, 2.5 g. of material, b. p. 131–134° (20 mm.), was isolated. When treated with 3,5-dinitrobenzoyl chloride[14] and steam distilled to remove unreacted aldehyde, the ester of the 3-methyl-6-isopropylbenzyl alcohol, m. p. 76.5–78°, was obtained.

Anal. Calcd. for $C_{18}H_{18}O_6N_2$: N, 7.81. Found: N, 7.63.

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[12] Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Co., Boston, Mass., 1941, p. 94.

[13] Robertson, "Laboratory Practice of Organic Chemistry," The Macmillan Company, New York, N. Y., 1943, p. 279.

[14] McElvain, "The Characterization of Organic Compounds," The Macmillan Company, New York, N. Y., 1945, p. 193.

Alkylation of Thiophene by Propylene and Isobutylene

By Walter M. Kutz and B. B. Corson

In view of the publication of Appleby, Sartor, Lee and Kapranos,[1] the compound reported by us[2] as probably being 2-*t*-butylthiophene was further examined. Comparison of its infrared spectrum with the spectrograms of the 2- and 3-isomers reported by Appleby and co-workers definitely showed the presence of the 3-isomer. The spectrum of our sample was also examined by those investigators. Their estimate of the content of the 3-isomer was about 30%; but owing to uncertainty as to the film thickness used in their characterization of the pure isomers (the original equipment having been replaced), it was not possible to make a quantitative infrared analysis. The estimate of the 3-isomer content from refractive index and density values was about 22%.

Inspection of our reported data on isopropylthiophene disclosed a typographical error. The density (d^{20}_{4}) of this product, prepared from propylene and isopropyl alcohol, was 0.9684 and 0.9687, respectively, instead of the reported values of 0.9884 and 0.9887. Our refractive index and density values fall between the values reported by Appleby and associates for the 2- and 3-isopropylthiophene isomers. Assuming linear blending relationship in these values, our product contained 78.5% of the 2-isomer and 21.5% of the 3-isomer according to refractive index, and 73.5% of the 2-isomer and 26.5% of the 3-isomer according to density, or an average of 76% of the 2-isomer and 24% of the 3-isomer as compared with 59% of the 2-isomer and 41% of the 3-isomer reported by Appleby and co-workers. This difference in product composition could well be due to the difference in the alkylation catalysts employed—"solid phosphoric acid" by Appleby, *et al.*, and "Filtrol" by us.

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[1] Appleby, Sartor, Lee and Kapranos, This Journal, **70**, 1552 (1948).

[2] Kutz and Corson, *ibid.*, **68**, 1477 (1946).

Evidently the chemical proof of structure[2] of our isopropylthiophene (based on the oxime and *p*-nitrophenylhydrazone of 2-isopropyl-5-acetylthiophene[3]) accounted for only the major component (*ca.* 75%) of the mixture.

[3] Scheibler and Schmidt, *Ber.*, **54**, 139 (1921).

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The Apparent Ionization Constants of Acethydrazide and Glycylhydrazide

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In considering the reactions of glycylhydrazide with nitrous acid[2] the apparent ionization constants of acethydrazide and glycylhydrazide have been determined at 24 ± 1° and 25 ± 2°, respectively. With the former compound potentiometric titration of approximately 0.1 formal solutions, which were also 0.05, 0.10 or 0.20 formal in sodium chloride, with standard hydrochloric acid indicated that pK'_A was independent of the ionic strength over the range studied and had a value of 3.24 for the reaction

$$[CH_3CONHNH_3]^+ \rightleftarrows CH_3CONHNH_2 + [H]^+$$

The titration data for glycylhydrazide, obtained as described below, were evaluated by the method of Britten[3] because preliminary calculations indicated that the two constants were not sufficiently separated to permit evaluation on the basis of assumed non-interaction. pK'_{A_1} was found to have a value of 2.38 and pK'_{A_2} a value of 7.69. From these data and those available for other derivatives of glycine[4] it is not unreasonable to assume that $pK_{A_1} = 2.38$ for the reaction

$$[H_3NCH_2CONHNH_3]^{++} \rightleftarrows [H_3NCH_2CONHNH_2]^+ + [H]^+$$

and $pK'_{A_2} = 7.69$ for the reaction

$$[H_3NCH_2CONHNH_2]^+ \rightleftarrows H_2NCH_2CONHNH_2 + [H]^+$$

since the ionization constants of all the simpler α-amino acid esters and amides are in the neighborhood of $pK'_A = 7.7$.[4] The greater acidity of the hydrazinium group in the doubly protonated glycylhydrazide relative to the singly protonated acethydrazide appears to be a logical consequence of the presence of the positively charged ammonium group in the former compound though the difference ($\Delta pK = 0.86$) is only approximately one-half of that obtaining in the case of $[CH_3CH_2CH_2NH_3]^+ - [NH_3CH_2CH_2CH_2NH_3]^{++}$ ($\Delta pK = 10.6 - (8.6 + 0.3) = 1.7$) if 0.3 is added to the observed pK'_{A_1} of the latter species to correct for a statistical factor of two.[5]

Experimental

Reagents.—Acethydrazide, prepared from redistilled ethyl acetate and 85% hydrazine[6] was recrystallized twice from an ether–chloroform mixture and dried over potassium hydroxide. Glycylhydrazide was prepared essentially as described by Curtius and Levy,[2] the product recrystallized as described above and dried over phosphorus pentoxide.

Procedure.—Solutions were prepared which were approximately 0.10 formal in acethydrazide or 0.05 formal in glycylhydrazide and 0.05, 0.10 or 0.20 formal in sodium chloride. Five-ml. aliquots of these solutions were titrated with standard 0.10 normal hydrochloric acid using a Beckman Model G *p*H meter equipped with a Beckman type E glass electrode. In every case the *p*H meter was calibrated against a standard buffer solution before a titration.

Results.—With acethydrazide five determinations using solutions 0.20 formal in sodium chloride gave a value for pK'_A for the first half of the titration curve of 3.21 ± 0.10; five determinations using solutions 0.10 formal in sodium chloride a value of 3.25 ± 0.10; and three determinations with solutions 0.05 formal in sodium chloride a value 3.23 ± 0.05. The average of all determinations was 3.24. With glycylhydrazide the following values were obtained for pK'_{A_1} and pK'_{A_2} in the order named: with 0.2 formal sodium chloride 2.38 and 7.68, 2.36 and 7.68; with 0.1 formal sodium chloride 2.42 and 7.68, 2.40 and 7.73; and with 0.05 formal sodium chloride 2.36 and 7.69; 2.38 and 7.67. The average of all of the above was pK'_{A_1} 2.38 and $pK'_{A_2} = 7.69$.

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[1] Present address: Department of Chemistry, University of California at Los Angeles.

[2] T. Curtius and L. Levy, *J. prakt. Chem.*, **70**, 89 (1904).

[3] H. T. S. Britten, "Hydrogen Ions," 3rd edition, Vol. I, Van Nostrand, New York, N. Y., 1943, pp. 197–200.

[4] E. J. Cohn and J. T. Edsall, "Proteins, Amino Acids and Peptides," Reinhold Publ. Corp., New York, N. Y., 1943.

[5] The authors are indebted to Dr. J. T. Edsall for bringing this relation to their attention.

[6] T. Curtius and T. S. Hoffman, *J. prakt. Chem.*, **53**, 513 (1896).

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The Preparation of 2-Nitro-3,4-xylenol

BY GEORGE P. MUELLER AND WALTER S. PELTON[1]

A need for 2-nitro-3,4-xylenol, for which no preparation has been described, prompted its synthesis in this Laboratory. The method selected was the sulfonation of 3,4-xylenol in the 6-position and nitration in the 2-position, followed by desulfonation. The well-known exchange of nitro- for sulfo-group during nitration of phenolsulfonic acids occurred here, and some 2,6-dinitro-3,4-xylenol was always formed. However, by varying the temperature and the amounts of nitric and sulfuric acids used, conditions were found which permitted yields of 40% to be obtained.

It was observed that the 2,6-dinitro-3,4-xylenol, m.p. 125–126°[2] separating during nitration carried 2-nitro-3,4-xylenol with it to form a molecular compound, m.p. 67–68°. The presence of 2-nitro-3,4-xylenol here indicates that the reaction conditions bring about nitration and some desulfonation without introducing a second

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[1] This note was taken from the thesis submitted by Walter S. Pelton to the Committee on Graduate Study of the University of Tennessee in partial fulfillment of the requirements for the M.S. degree.

[2] Datta and Varma, THIS JOURNAL, **41**, 2039 (1919).