small negative values for 20(α) compounds (*e. g.*, pregnanediol-20(α),21-dione-3,11, $\Delta_1 = -29$) and large positive values for 20(β) compounds (*e. g.*, Reichstein's compounds K, E and U, which are all (17(α),20(β),21 triols, $\Delta_1 = +306$, $+428$, $+308$, respectively). The Δ_1 value (at C_{20}) of the pregnanediol-3(α),20-one-11 3-acetate of Sarett[7] (+91) shows that it is a 20(β) compound, as might be expected from its method of preparation.

Table II shows the Δ_1 values (at C_{20}) for 17(β), 20 diols of the 17-*iso* series. It will be seen that there is no really convincing agreement with the standard Δ_1 values in the 17-*n* series. Since, also, in the comparable case of hydroxyl groups at C_{11} and C_{12} the molecular rotation data are in disagreement with the accepted configurations,[8,9] we feel that the conclusions of Fieser and Fieser regarding the 17-*iso* compounds, although possibly correct, should at present be treated with some reserve.

We are indebted to N. V. Organon, Oss, Holland, for a generous gift of pregnenolone acetate.

Experimental[10]

Allopregnanediol-3(β),20(α) Diacetate.—Allopregnanol-3(β)-one-20 acetate was reduced with sodium and boiling ethanol.[11] The product was acetylated and the acetates chromatographed on alumina. Allopregnanediol-3(β),20(α)-diacetate after repeated crystallization from light petroleum had m.p. 163–165° (reported,[11] 165–168°); $[\alpha]_D$ −0.3° (*c*, 3.3), $[M]_D$ −1°.

Allopregnanediol-3(β),20(α).—The diacetate was hydrolyzed by boiling for two hours with aqueous alcoholic potassium hydroxide. The diol, recrystallized once from ether and once from acetone, had m.p. 218–219° (reported[11] 220–222°) $[\alpha]_D$ +23° (*c*, 0.9), $[M]_D$ + 72°.

Allopregnanediol-3(β),20(β) 3-Acetate.—Δ^5-Pregnenol-3(β)-one-20 acetate was hydrogenated in ether-acetic acid solution using a platinum catalyst until the uptake of hydrogen was complete. The product was recrystallized repeatedly from methanol to give allopregnanediol-3(β),20 (β) 3-acetate, m. p. 168–169°, $[\alpha]_D$ −6° (*c*, 3.6), $[M]_D$ −22° (1-dm. macro-tube).

Anal. Calcd. for $C_{23}H_{38}O_3$: C, 76.2; H, 10.6. Found: C, 76.5; H, 10.5.

Allopregnanediol-3(β),20(β)-diacetate.—The monoacetate was refluxed with acetic anhydride for one hour. The product was chromatographed on alumina and recrystallized from methanol to give the diacetate, m. p. 141–142° (reported[12] 142–143°), $[\alpha]_D$ +22° (c, 5.2), $[M]_D$ +89°.

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[7] Sarett, THIS JOURNAL, **70**, 1690 (1948). By arguments similar to those of Fieser and Fieser, based on the method of formation, Sarett's pregnanetriol-3(α),17,20-one-11 (diacetate m. p. 227–228°) must be 17(α);20(β), and his pregnanetriol-17(α),20,21-dione-3,11 (diacetate, m. p. 212–213°) must be 20(β).

[8] Gallagher, *J. Biol. Chem.*, **162**, 539 (1946).

[9] Wintersteiner, Moore and Reinhardt, *ibid.*, **162**, 707 (1946).

[10] All rotations were determined in $CHCl_3$ solution for the Na_D line at 20–25°. A 0.5 dm. micro-tube was used unless stated to the contrary.

[11] Meystre and Miescher, *Helv. Chim. Acta*, **29**, 33 (1946).

[12] Marker, Kamm, Jones and Oakwood, THIS JOURNAL, **59**, 614 (1937).

Studies in *p*-Cymene. II.[1] The Isomeric Aldehydes Derived from *p*-Cymene

BY CHARLES T. LESTER, RAYMOND E. DONALDSON AND JAMES C. OSWALD[2]

We have prepared the isomeric aldehydes, 2-methyl-5-isopropylbenzaldehyde[3] and 3-methyl-6-isopropylbenzaldehyde,[4] and studied their behavior when subjected to a variety of aldehyde reactions. Our objective was not to realize maximum yields, but to observe what differences, if any, were shown in the reactivities of the isomeric compounds.

Without exception all the experiments reported below indicate that the aldehyde group of 2-methyl-5-isopropylbenzaldehyde is more reactive than the aldehyde group of 3-methyl-6-isopropylbenzaldehyde. This difference is most noticeable in the self-condensation Cannizzaro reaction. The difference in reactivity of the isomeric aldehydes is in agreement with our previous report[1] concerning the saponification rate of the isomeric esters derived from *p*-cymene.

Experimental[4a]

Preparation of 2-Methyl-5-isopropylbenzaldehyde.—*p*-Cymene was converted into 2-methyl-5-isopropylbenzyl chloride[5] in 49% yield. The aldehyde was prepared from the substituted benzyl chloride by the method of Sommelet.[6] This reaction was carried out with 37.5 g. of the chloride and 42 g. of hexamethylenetetramine. The aldehyde was isolated as the bisulfite addition compound; average yield, based on six preparations, 25 g., 65%. Hydrolysis of the bisulfite compound gave the aldehyde, b. p. 125° (20 mm.), in 65% yield. The aldehyde was converted, without modification of standard procedures, into a 2,4-dinitrophenylhydrazone,[7] m. p. 190–191°, and a semicarbazone,[8] m. p. 170–171°.

Preparation of 3-Methyl-6-isopropylbenzaldehyde.—The aldehyde was prepared from 3-bromo-*p*-cymene[9] according to the procedure of Smith and Nichols.[10] From the Grignard reagent prepared from 63.9 g. of 3-bromo-*p*-cymene was obtained (average of eight preparations) 21.6 g., 27% yield, of the aldehyde bisulfite compound. Hydrolysis of the bisulfite compound gave a 60% yield of the aldehyde, b. p. 123° (20 mm.). Attempts to prepare a 2,4-dinitrophenylhydrazone[7] and a semicarbazone[8] by the usual procedures were unsuccessful. However, when the aldehyde and proper reagents were heated in a boiling water-bath for one hour, a 2,4-dinitrophenylhydrazone, m. p. 192–193°, and a semicarbazone, m. p. 177–178° were obtained.

Reaction of the Aldehydes with Acetone.—The aldehydes were treated with the same molar quantities of reagents as described by Porter and Stewart[11] for benzaldehyde. Each reaction mixture was refluxed for five min-

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[1] Lester and Bailey, THIS JOURNAL, **38**, 375 (1946).

[2] Present address: Georgia State Department of Agriculture, Atlanta, Georgia.

[3] Verley, *Bull. soc. chim.*, [3] **17**, 906 (1897).

[4] Blum-Bergmann, *J. Chem. Soc.*, **1**, 1930 (1935).

[4a] All melting points are uncorrected.

[5] Whittleston, THIS JOURNAL, **59**, 825 (1937).

[6] Sommelet, *Compt. rend.*, **157**, 852 (1913).

[7] Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 143.

[8] Shriner and Fuson, *ibid.*, p. 142.

[9] Fileti and Crosa, *Gazz. chim. ital.*, **16**, 292 (1886).

[10] Smith and Nichols, *J. Org. Chem.*, **6**, 489 (1941).

[11] Porter and Stewart, "Organic Chemistry for the Laboratory," Ginn and Co., Boston, Mass., 1943, p. 103.

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).