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Polyisopropylbenzenes. V. Acetylation[1]

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The acetylation of four polyisopropylbenzenes, namely, 1,3-di-, 1,4-di-, 1,3,5-tri- and 1,2,4,5-tetra-isopropylbenzenes, with acetic anhydride in presence of aluminum chloride gave the same products in all four cases. Thus 1,3- and 1,4-diisopropylbenzenes gave very similar yields of a hydrocarbon (0.8 and 2.4%, respectively) which was probably cumene, of 4-isopropylacetophenone (I) (11.5 and 15.5%), 2,4-diisopropylacetophenone (II) (54.0 and 51.9%) and 2,4,6-triisopropylacetophenone (IV) (11.5 and 17.1%). The triisopropylbenzene gave II (24.9%) and IV (29.4%) while the tetra- gave II (30.2%) and IV (17.5%). In the last two cases traces of hydrocarbon and of I appeared to be present and about 50% of the total product was an intractable, semi-solid jelly.

The products of acetylation were identified as follows. The oxime from 4-isopropylacetophenone had the literature melting point. Oxidation of 2,4-diisopropylacetophenone gave a mixture of 2,4-diisopropylphenylglyoxylic acid and 2,4-diisopropylbenzoic acid, the latter being identical with specimens prepared[1] from 4-amino and from 4-bromo-1,3-diisopropylbenzene. A test for the presence of any diisopropylacetophenone other than the 2,4- derivative was made on the product from 1,4-diisopropylbenzene by preparing semicarbazones from the distillation fractions next before and next after the range of pure 2,4- derivative but no indication of the presence of any other isomer was obtained. Oxidation of 2,4,6-triisopropylacetophenone gave a glyoxylic acid and then, by thermal decomposition, a triisopropylbenzoic acid with the correct melting point for the 2,4,6-derivative.

Hennion and McLeese have described[2] the acetylation of 1,4-di-*s*-butyl- and 1,4-di-*s*-amylbenzenes with the formation of products claimed to be 2,5-di-*s*-alkylacetophenones. However, examination of the evidence offered for the orientation of these two products reveals that the possibility of isomerization was not excluded. The evidence for the 2,5 assignment of the *s*-alkyl groups in the ketones is (a) terephthalic acid was formed on oxidation and (b) 4-*s*-alkylisophthalic acids were formed on oxidation. Point (a) depends on the *a priori* reasonable, but unproved, assumption that the acyl group rather than one of the alkyl groups is eliminated. Point (b) is of no evidential value as the constitutions of the acids were apparently not verified and, in fact, 4-*s*-butylisophthalic acid, prepared from 2,4-dimethyl-4-*s*-butylbenzene, has been reported[3] as melting at 188° compared with 237–238° given by Hennion and McLeese for their product. There is thus a distinct possibility that these two ketones were actually 2,4-di-*s*-alkylacetophenones.

No product corresponding with the triisopropylacetophenone, m. p. 105.6–106°, reported[4] by Koch and Steinbrink, was obtained under the conditions used in the present work.

Experimental Part

Acetylation Procedure.—A solution of the hydrocarbon (170 g.) in carbon bisulfide (400 ml.) was stirred with coarsely ground aluminum chloride (300 g.) while acetic anhydride (1.15 equivalents) was added in the course of two to three hours at 30–40°. Stirring was continued for two to three hours and the product kept for one to two hours (except in the case of tetraisopropylbenzene, which was allowed to stand for eighteen hours) before decomposing by cautiously adding shaved ice and 50 ml. of 30% hydrochloric acid. The oil layer was washed with water, 10% sodium hydroxide and water and the solvent removed.

Acetylation of 1,3-Diisopropylbenzene.—Fractionation of the crude product (154 g.) *in vacuo* through a 180 × 2.5 cm. bead-packed column gave the following 10-ml. fractions: (1) $n^{30}{}_D$ 1.5078, (2) 1.5112, (3) 1.5097, (4) 1.5087, (5) 1.5077, (6) 1.5069, (7) to (12) 1.5065 ± 0.0001, (13) 1.5058, (14) 5 ml., 1.5052, residue 29.4 g., crystalline. Refractionation of fractions (1) through (5), together with corresponding material from a second preparation gave fairly pure 4-isopropylacetophenone (I) with the following properties: d^{20} 0.9681, dd/dt −0.000819, $n_D{}^{20}$ 1.5206, dn/dt −0.000432. Allen[5] gives d^{15} 0.9753.

Anal. Calcd. for $C_{11}H_{14}O$: C, 81.44; H. 8,70. Found: C, 81.2, 81.3; H, 8.66, 8.85.

Oxime.—White crystals from petroleum ether, m. p. 71.1–71.6°. Allen[5] gives m. p. 70–71° for 4-isopropylacetophenoneoxime.

Anal. Calcd. for $C_{11}H_{15}ON$: C, 74.54; H, 8.53. Found: C, 74.2, 74.3; H, 8.67, 8.42.

2,4-Diisopropylacetophenone-A (IIA).—Refractionation of fractions (6) through (14) together with corresponding material from a second preparation gave 90% of the distillate (fourteen 10 ml. fractions) with $n_D{}^{30}$ 1.5064 ± 0.0001. The middle fractions had d^{20} 0.9417, dd/dt −0.000833, $n_D{}^{20}$ 1.5109, dn/dt −0.000432.

Anal. Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.4, 82.3; H, 9.96, 10.07.

Semicarbazone-A (IIIA).—The crude product was obtained in 93.7% yield, m. p. 192–196°. Crystallization from isopropanol gave large, rectangular tables, m. p. 195.7–196.5°.

Anal. Calcd. for $C_{15}H_{23}ON_3$: C, 68.93; H, 8.87. Found: C, 68.7, 68.9; H, 8.94, 8.93.

Oxidation of 2,4-Diisopropylacetophenone-A (IIA).—2,4-Diisopropylphenylglyoxylic acid (V) and 2,4-diisopropylbenzoic acid (VI).—A mixture of IIA (20 g.), potassium hydroxide (10 g.) and water (1200 ml.) was stirred vigorously at 35–37° while potassium permanganate (32 g.) was added in small portions in the course of one hundred and forty minutes. After a further two hours the color of the permanganate had disappeared. Sulfuric acid (300 ml. of 30%) was added followed by

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[1] Paper IV, THIS JOURNAL, 65, 2441 (1943). Abstracted from a thesis approved by the University of London for the degree of Ph.D.

[2] Hennion and McLeese, *ibid.*, **64**, 2421 (1942).

[3] Nightingale, Radford and Shanholtzer, *ibid.*, **64**, 1662 (1942).

[4] Koch and Steinbrink, *Brennstoff-Chem.*, **19**, 277 (1938).

[5] Allen, "Organic Syntheses," XIV, 1 (1934).

small portions of oxalic acid until the liquid was colorless. A pasty, brown lump separated and was removed, digested with sodium carbonate (10 g.) and water (300 ml.) at 80° for one hour, filtered and the cloudy filtrate extracted with petroleum ether (100 ml.) to remove unchanged ketone. Acidification of the clear aqueous layer with 30% hydrochloric acid gave 11.95 g. of granular white solid. This product from two runs (21.1 g.) was dissolved in a boiling mixture of iso-octane (40 ml.) and benzene (20 ml.) filtered and cooled. The resulting white crystals weighed 8.35 g. and had m. p. 134.3–138.3°. Two crystallizations from benzene gave material with m. p. 140.1–140.8° (V).

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.75; neut. equiv. 234.3. Found: C, 71.5, 71.4; H, 7.84, 7.67; neut. equiv. 233.7, 233.9.

The filtrate from the crude V on evaporation gave 12.6 g. of white solid, m. p. 96–102°. Two crystallizations from 60% ethanol gave white crystals, m. p. 108.7–109.5° (VI), and mixed m. p. with 2,4-diisopropylbenzoic acid[1] made in another way, 108.2–109.0°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80; neut. equiv. 206.3. Found: C, 75.7, 75.6; H, 8.86, 8.93; neut. equiv., 206.7.

2,4,6-Triisopropylacetophenone-B (IVB).—Residues from the first fractionation on crystallization from petroleum ether gave white crystals, m. p. 85.5–86.6°, and mixed m. p. with the A compound (IVA), 85.8–86.6°.

From the distillation curves the yields of the four products were estimated to be (in mole per cent.) hydrocarbon 0.8, I 11.5, IIA 54.0, IVB 11.5.

Acetylation of 1,4-Diisopropylbenzene.—Fractionation of the crude product (184.8 g.) gave the following 10-ml. fractions: (1) n_D^{30} 1.5074, (2) 1.5118, (3) 1.5112, (4) 1.5098, (5) 1.5086, (6) 1.5076, (7) 1.5068, (8) to (14) 1.5065 ± 0.0002, (15) 1.5059, (16) 1.5035, residue 39.0 g., solid.

Semicarbazone (IIIB) of 2,4-Diisopropylacetophenone-B (IIB).—Fraction (10) gave 96.7% of crude derivative, m. p. 191–194°. Crystallization from isopropanol gave material of m. p. 195.9–197.0°, and mixed m. p. with the A compound (IIA), 196.5–197.3°. Semicarbazones from fractions (7) and (15) were obtained in similar yield, with similar crude and pure m. p.'s and showed no depression with the A compound.

Crystallization of the distillation residues from petroleum ether gave white crystals of 2,4,6-triisopropylacetophenone-C (IVC), m. p. 85.7–86.4°, and mixed m. p. with the A compound (IVA), 85.8–86.5°.

The yields in mole per cent. were hydrocarbon 2.4, I 15.5, IIB 51.9, IVC 17.1.

Acetylation of 1,3,5-Triisopropylbenzene.—The crude product (184.5 g.) was cooled in ice for three days and filtered. Thorough draining gave 45.2 g. (crop 1) of slightly oily, pale yellow crystals. The filtrate, fractionated in the 180-cm. column at 8–10 mm., gave the following 10-ml. fractions: (1) n_D^{30} 1.4941, (2) 1.5046, (3) 1.5054, (4) 1.5053, (5) 1.5047. The residue was then transferred to a Claisen flask and distilled *in vacuo* as long as the distillate showed any tendency to crystallize. The distillate was a viscid oil containing crystals. It was diluted with petroleum ether (10 ml.), cooled in ice for three weeks and filtered, giving 18.2 g. of slightly oily crystals (crop 2). Further distillates were viscid, sticky oils from which no identifiable products could be recovered.

Semicarbazone (IIIC) of 2,4-Diisopropylacetophenone-C (IIC).—Fraction (3) gave a crude semicarbazone, m. p. 191–194.5° (95.9%). This, after crystallization from isopropanol, had m. p. 195.5–196.6° and mixed m. p. with the A compound (IIIA), 196.0–197.2°.

2,4,6-Triisopropylacetophenone-A (IVA).—Recrystallization of combined crops 1 and 2 from 70% ethanol gave white needles, m. p. 86.6–87.1°.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.87; H, 10.64. Found: C, 82.92, 82.90; H, 10.51, 10.44.

Oxidation of 2,4,6-Triisopropylacetophenone-A. 2,4,6-Triisopropylphenylglyoxylic Acid (VII).—IVA (24.7 g.) was oxidized with potassium permanganate (32.0 g.) in 1% aqueous potassium hydroxide (1 liter) at 75° and the product worked up as in the oxidation of IIA. There were obtained 5.65 g. of white solid, m. p. 144.5–148.5° (dec.), and 8.1 g. of unchanged ketone. The white solid from several runs (24.2 g.) was extracted with 100 ml. of cold benzene and filtered leaving 8.95 g. of white powder which, after two crystallizations from isopropanol formed small glittering white crystals which melted with brisk evolution of gas at 195 to 207° depending on the rate of heating.

Anal. Calcd. for $C_{17}H_{24}O_3$: C, 73.88; H, 8.76; neut. equiv., 276.4. Found: C, 73.6, 73.6; H, 9.03, 8.89; neut. equiv., 276.0.

Thermal Decomposition of 2,4,6-Triisopropylphenylglyoxylic Acid (VII).—A test-tube containing 1.983 g. of VII was placed in a bath at 170° and heated at 3° per minute to 229° when all gas evolution had ceased. On cooling, the product was a slightly oily solid weighing 1.728 g. (Loss: Calcd. for CO scission 10.1%, for CO_2 scission 15.9%. Found: 12.9%.) All but a trace of the product dissolved in hot, 10% sodium carbonate solution and the filtrate, acidified with 30% hydrochloric acid, gave 1.63 g. of white solid, m. p. 178–184° and m. p. 185.8–186.8° after two crystallizations from 60% ethanol. Fuson and Horning[6] give m. p. 186–187° for 2,4,6-triisopropylbenzoic acid.

Anal. Calcd. for $C_{16}H_{24}O_2$: neut. equiv., 248.4. Found: neut. equiv., 248.9.

Yields of identifiable acetylation products in mole per cent. were IIC 24.9, IVA 29.4.

Acetylation of 1,2,4,5-Tetraisopropylbenzene.—The crude ketone (195.2 g.) was treated exactly as the product from 1,3,5-triisopropylbenzene. The first crop of crystals weighed 21.5 g. Distillation fractions (10 ml.) were as follows: (1) n_D^{30} 1.5038, (2) 1.5058, (3) 1.5062, (4) 1.5063, (5) 1.5064, (6) 1.5060, (7) 6.8 g., solid.

Semicarbazone of 2,4-Diisopropylacetophenone-D (IIID).—Fraction (4) gave 99.2% of crude derivative, m. p. 191–195°. After crystallization from isopropanol the m. p. was 196.1–196.8° and mixed m. p. with the A compound (IIIA), 196.5–197.3°.

2,4,6-Triisopropylacetophenone-D (IVD).—Crystallization of combined first and second crops from petroleum ether gave white crystals, m. p. 84.8–86.2°, and mixed m. p. 85.0–86.5° with the A compound (IVA).

Yields of identifiable acetylation products in mole per cent. were IID 30.2, IVD 17.5.

Summary

1. The reaction of acetic anhydride in presence of aluminum chloride with 1,3-di- or 1,4-diisopropylbenzene gives the same products in very similar yields. These products have been identified as 2,4-diisopropylacetophenone (main product), and, in decreasing amounts, 2,4,6-triisopropylacetophenone, 4-isopropylacetophenone and a hydrocarbon (probably isopropylbenzene).

2. From both 1,3,5-tri- and 1,2,4,5-tetraisopropylbenzenes there were obtained 2,4,6-triisopropylacetophenone as the main product, some 2,4-diisopropylacetophenone and probably a trace of 4-isopropylacetophenone. A considerable proportion of the product consisted of a viscid jelly from which nothing definite could be obtained.

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[6] Fuson and Horning, THIS JOURNAL, 62, 2962 (1940).