

# Notes

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## Selected Phenyl-2-methylhexanes

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Of the six possible isomeric alkylbenzenes possessing the 2-methylhexyl group as the alkyl side chain, Francis<sup>1</sup> in his review on the properties of the alkylbenzenes listed two as having been obtained in the pure state. These are 2-phenyl-2-methylhexane, prepared by Huston and coworkers,<sup>2,3</sup> and 2-phenyl-5-methylhexane, prepared by Klages.<sup>4</sup> Two of the four remaining isomers, namely 3-phenyl-2-methylhexane and 3-phenyl-5-methylhexane, were presumably obtained in a ternary mixture with 2-phenyl-5-methylhexane by Huston and Kaye.<sup>3</sup> An examination of the literature since Francis' review has revealed no further reference to the latter two isomers of Huston and Kaye nor any reference to the two remaining unknown isomers, 1-phenyl-5-methylhexane and 1-phenyl-2-methylhexane.

The purpose of the present investigation was to prepare the four "unknown" or unseparated phenyl-2-methylhexanes by unequivocal methods and to determine the physical properties of each. The methods chosen for the preparations are described in the following paragraphs. Each synthesis led in the penultimate step to a ketone which was reduced easily to the desired alkylbenzene<sup>5,6</sup> by the Huang-Minlon modification of the Wolff-Kishner reduction.

1-Phenyl-5-methylhexane was synthesized from malonic ester. The latter was alkylated with isomyl bromide to give ultimately 5-methylhexanoic acid. The acid chloride of the latter was used in the Friedel-Crafts acylation procedure to yield 5-methylhexanophenone.

The synthesis of 1-phenyl-2-methylhexane was attempted initially in a similar fashion. Diethyl methylmalonate, prepared by the methylation of malonic ester according to the procedure of Organic Syntheses,<sup>7</sup> was alkylated with *n*-butyl bromide to

yield 2-methylhexanoic acid. The latter, via the acid chloride and a Friedel-Crafts acylation of benzene, should give the known 2-methylhexanophenone. For this ketone Campbell and co-workers<sup>8</sup> have reported an orange colored 2,4-dinitrophenylhydrazone melting at 74.5–75°. During attempts to establish that the ketone obtained in this work was identical with the ketone of Campbell *et al.*, two 2,4-dinitrophenylhydrazones were isolated. A yellow crystalline one, melting around 78–80°, apparently corresponded to the derivative prepared by the latter workers. The second, crystallizing as thick red needles from acetic acid, melted at 166–168° in comparison to the 2,4-dinitrophenylhydrazone of hexanophenone melting at 168°. It appears, therefore, that the diethyl methylmalonate contained some diethyl malonate and that the hexanophenone came from this source. Pure 2-methylhexanophenone was then made by the excellent one-step synthesis of Campbell *et al.* by alkylating propiophenone on the  $\alpha$ -carbon with *n*-butyl bromide in the presence of sodamide.

The synthesis of 3-phenyl-5-methylhexane started with phenylacetonitrile. Alkylation of the latter with isobutyl bromide in the presence of sodium hydride yielded 2-phenyl-4-methylpentanenitrile, which was forced to react with methyl magnesium bromide at elevated temperatures. The resulting mixture of ketone and unreacted nitrile could not be separated completely with the distillation equipment available. A ketone fraction boiling near 118° at 10 mm. and a presumed nitrile fraction boiling approximately 10 degrees higher were obtained. Both fractions showed the characteristic infrared carbonyl absorption at 3.6 to 3.7 microns, and both gave a strong test for nitrogen by the sodium fusion method. This agrees with the observations of Jullien,<sup>10</sup> who found that he also was unable to separate the ketone and nitrile by distillation, but the ketone could be isolated by the hydrolysis of the nitrile with 80% sulfuric acid. In the present work it was decided that the presence of the nitrile would not interfere with the isolation of the alkylbenzene after the Wolff-Kishner reduction. If the nitrile were not hydrolyzed under the conditions of the reduction, the hydrocarbon would boil so much lower (below 100° at 10 mm.) than the nitrile (above 130° at 10 mm.) that separation should offer no difficulty. On the other hand, if the nitrile were hydrolyzed, the resulting acid would stay in the water

- (1) A. W. Francis, *Chem. Rev.*, **42**, 107 (1948).
- (2) R. C. Huston, W. B. Fox and M. N. Binder, *J. Org. Chem.*, **3**, 251 (1938).
- (3) R. C. Huston and I. A. Kaye, *J. Am. Chem. Soc.*, **64**, 1576 (1942).
- (4) A. Klages, *Ber.*, **35**, 2645 (1902).
- (5) Huang-Minlon, *J. Am. Chem. Soc.*, **68**, 2487 (1946).
- (6) E. Berliner and F. Berliner, *J. Am. Chem. Soc.*, **72**, 222 (1950).
- (7) N. Weiner, *Org. Syntheses, Coll. Vol. II*, 279 (1943).

(8) A. D. Campbell, C. L. Carter and S. N. Slater, *J. Chem. Soc.*, 1741 (1948).

(9) D. P. Evans, *J. Chem. Soc.*, 785 (1936).

(10) P. Jullien, *Bull. soc. chim. France*, [5] **3**, 1347 (1936).

layer (as the sodium salt) during the work up of the hydrolysis mixture and hence would be separated from the hydrocarbon fraction. When the reduction was carried out, part of the nitrile was recovered unchanged and part was hydrolyzed to the acid (as sodium salt). No difficulty was encountered in separating the hydrocarbon.

The starting material for the preparation of 3-phenyl-2-methylhexane was again phenylacetonitrile. Alkylation with isopropyl bromide in the presence of sodamide yielded 2-phenyl-3-methylbutanenitrile, which in turn was treated with ethyl Grignard reagent. Unlike the reaction described above, a much purer ketone could be isolated in this case.

As a result of the work described above, two observations concerning methods of preparation of alkylbenzenes can be made. First, alkylbenzenes of the type of 1-phenyl-2-methylhexane (alternatively it might be named 2-benzylhexane) which have a benzyl group attached to an alkyl chain are made very conveniently by the alkylation of propiophenone or other appropriate alkyl phenyl ketone in the presence of sodamide, followed by a modified Wolff-Kishner reduction. Thus alkylbenzene is produced in two steps from the phenyl ketone. Second, phenylacetonitrile or a nuclear-substituted phenylacetonitrile is alkylated to yield an  $\alpha$ -alkylphenylacetonitrile, the latter is converted into ketones *via* the Grignard reaction, and the ketones thus obtained are reduced readily by the Wolff-Kishner method. Many alkylbenzenes are thus available in three steps from the appropriate phenylacetonitriles. Pure alkylbenzenes free from rearranged products also are available by either of the methods outlined above. Further work is under way in our laboratories toward the preparation of other pure alkylbenzenes.

#### EXPERIMENTAL<sup>11</sup>

**5-Methylhexanoic acid.** From 412.5 g. (2.58 moles) of diethyl malonate, 377.5 g. (2.5 moles) of isoamyl bromide, and sodium ethoxide (from 57.5 g., 2.5 moles of sodium), there was obtained in the usual fashion (essentially as described by Curtius and Sieber<sup>12</sup>) a total of 386 g. (1.67 moles) of diethyl isoamylmalonate distilling at 123–125° (13 mm.),  $n_D^{25}$  1.4229–1.4235, reported b.p. 118–130° (12 mm.),<sup>12</sup>  $n_D^{20}$  1.4255.<sup>13</sup> The foregoing ester was hydrolyzed by refluxing for 5 hr. with 320 g. (5.7 moles) of potassium hydroxide in 320 ml. of water. After the alcohol was distilled off, the aqueous layer was extracted with ether to remove unhydrolyzed ester, and the isoamylmalonic acid was liberated with sulfuric acid. The aqueous acid solution was refluxed for 5 hr. and the oil layer was extracted with benzene. After the low boiling liquids were removed, decarboxylation was completed by

(11) Melting points and boiling points are uncorrected unless otherwise indicated. Analyses by Micro-Tech Laboratories, Skokie, Illinois.

(12) T. Curtius and W. Sieber, *J. prakt. chem.*, [2] 125, 156 (1930).

(13) I. Heilbron, *Dictionary of Organic Compounds*, Revised Edition, Oxford University Press, New York, 1953, Vol. III, pp. 58 and 61.

heating the resulting oil to about 200° until the evolution of carbon dioxide ceased. Distillation through a 12 in. Vigreux column gave 146 g. (1.12 moles, 44.8% based on sodium) of 5-methylhexanoic acid, b.p. 110–116° (16 mm.),  $n_D^{25}$  1.4202–1.4206, reported<sup>13</sup> b.p. 108–110° (14 mm.),  $n_D^{19}$  1.4209.

**5-Methylhexanophenone.** To the above 5-methylhexanoic acid was added dropwise 157 g. (a 20% excess) of thionyl chloride. The mixture was refluxed for 2.5 hr. Distillation gave 145 g. (0.977 mole) of acid chloride boiling at 76–82° (34 mm.). The Friedel-Crafts acylation of benzene was carried out essentially as described<sup>9</sup> for a similar acylation by adding a solution of 83 g. (0.56 mole) of the acid chloride in 500 ml. of anhydrous thiophene-free benzene to 115 g. (0.937 mole) of anhydrous aluminum chloride in 150 ml. of benzene. Distillation of the product fraction through the Vigreux column gave 84 g. (0.44 mole, 79%) of ketone boiling at 148–151° (17 mm.),  $n_D^{25}$  1.5050–1.5060, reported<sup>14</sup> b.p. 145–148° (18 mm.),  $n_D^{26}$  1.5067.

**1-Phenyl-5-methylhexane.** To a solution of 400 ml. of diethylene glycol, 50 g. (0.9 mole) of potassium hydroxide and 50 ml. of 85% hydrazine hydrate<sup>15</sup> was added 84 g. (0.44 mole) of the above ketone. The solution was refluxed for an hour, the water and excess hydrazine hydrate were distilled out until the temperature reached 190°, and the solution was then refluxed an additional 3 hr. After the reaction mixture was worked up in the usual way, distillation through a Vigreux column gave the hydrocarbon boiling at 110–115° (mostly 111–112°) at 17 mm. Redistillation from metallic sodium through the Vigreux column gave five fractions. The three middle fractions, b.p. 111–114° (17 mm.), possessed a constant  $n_D^{20}$  1.4850,  $n_D^{25}$  1.4828 and amounted to 55 g. *Fraction 3*, taken as the pure hydrocarbon, had a micro b.p. 238.3° (735 mm.) corr. and  $d_4^{20}$  0.8547,  $d_4^{25}$  0.8509.

*Anal.* Calcd. for C<sub>13</sub>H<sub>20</sub>: C, 88.56; H, 11.44. Found: C, 88.62; H, 11.44.

The diacetamino derivative, prepared by nitrating the alkylbenzene at 50° or above and then proceeding in the usual fashion, had a m.p. 206.5–207° corr. (from ethanol).

*Anal.* Calcd. for C<sub>17</sub>H<sub>26</sub>N<sub>2</sub>O<sub>2</sub>: N, 9.65. Found: N, 9.68.

**2-Methylhexanophenone.** To a sodamide [prepared from 11.5 g. (0.5 mole) of sodium by the procedure of Hancock and Cope<sup>16</sup>] suspension 67 g. (0.5 mole) of propiophenone was added dropwise with stirring. After 30 min. of stirring, 77 g. (0.56 mole) of *n*-butyl bromide was added dropwise, and the mixture was heated on the steam bath an additional 1.5 hr. and then permitted to stand overnight. The oil layer was washed with 300 ml. of water, the wash water was extracted with benzene, and the combined organic layers were again washed with water. The benzene was removed and the residual oil was fractionated through a 12 in. glass helices packed column at 2 mm. pressure. After a forerun of 12 g. distilling up to 107°, there was obtained a total of 69 g. (0.363 mole, 72.5%) of 2-methylhexanophenone, b.p. 107–110°,  $n_D^{25}$  1.5048–1.5058, reported b.p. 133–138° (15 mm.),<sup>8</sup> 109–110° (3 mm.),<sup>16</sup>  $n_D^{20}$  1.5070.<sup>16</sup> The 2,4-dinitrophenylhydrazones melted at 74.5–76°, reported<sup>8</sup> 74.5–75°.

**1-Phenyl-2-methylhexane.** Wolff-Kishner reduction of 67 g. (0.35 mole) of the above ketone was carried out by the Huang-Minlon procedure as described above. Fractionation of the product layer through a 12 in. Fenske-type column at 6 mm. gave 39 g. (0.22 mole, 63%) of product distilling at 97–100°,  $n_D^{25}$  1.4833–1.4840. Redistillation from sodium metal through an 8 in. packed column at 10 mm. gave the following: *Fraction 1*, 1.2 g., b.p. 99–101°,  $n_D^{25}$  1.4832; *Fractions 2–6*, 27.7 g., b.p. 101–102.5°, each with constant  $n_D^{20}$

(14) W. M. Lauer and M. A. Spielman, *J. Am. Chem. Soc.*, 55, 4923 (1933).

(15) E. M. Hancock and A. C. Cope, *Org. Syntheses*, 25, 25 (1945).

(16) T. I. Temnikova, A. K. Petryaeva and S. S. Skorokhodov, *Zhur. Obshchei Khim.*, 25, 1575 (1955); *Chem. Abstr.*, 50, 4891 (1956).

1.4852,  $n_D^{25}$  1.4832. *Fraction 4*, taken as the pure alkylbenzene, had micro b.p. 233.5° (735 mm.) corr., and  $d_4^{20}$  0.8558,  $d_4^{25}$  0.8521.

Anal. Calcd. for  $C_{13}H_{20}$ : C, 88.56; H, 11.44. Found: C, 88.48; H, 11.36.

The diacetamino derivative (from ethanol) had a m.p. 193–193.8° corr.

Anal. Calcd. for  $C_{17}H_{26}N_2O_2$ : N, 9.65. Found: N, 9.85.

*2-Phenyl-4-methylpentanenitrile*. To a suspension of 24.4 g. (1.017 moles) of sodium hydride in 200 ml. of anhydrous toluene contained in a 1-l. three-necked flask equipped with a stirrer, condenser, thermometer, dropping funnel, and necessary drying tubes, there was added all at once a mixture of 122 g. (1.043 moles) of phenylacetone nitrile and 150 g. (1.095 moles) of pure isobutyl bromide (b.p. 90.5–91°). The reaction flask was heated by a mantle to 65°, at which temperature the reaction started. The mantle was removed and the flask was cooled as necessary by means of a dry ice-cooled kerosene bath in order to keep the reaction from becoming too vigorous. The main vigor of the reaction was spent in 0.5 hr. The reaction mixture was refluxed an additional 5 hr. and permitted to stand over night.

Ethyl alcohol (40 ml.) was cautiously added dropwise, followed by the dropwise addition of water until a total of 200 ml. was added. The oil layer was removed and the water extracted with benzene. The organic phase was washed with dilute acid, water, sodium carbonate solution, and again with water. After filtration through a layer of anhydrous sodium sulfate, the benzene was distilled and the product fractionated through a 12 in. Fenske-type column packed with glass helices. After a forerun of 24 g. consisting largely of recovered phenylacetone nitrile, there was obtained 115 g. (0.666 mole, 65.5%) of product distilling at 130–134° (mostly 132–134°) at 10 mm.,  $n_D^{20}$  1.4990,  $n_D^{25}$  1.4970, reported b.p. 136–138° (15 mm.)<sup>17</sup>  $n_D^{25}$  1.4978–1.4985.<sup>18</sup>

*3-Phenyl-5-methyl-2-hexanone*. To an ethereal solution of methyl magnesium bromide [prepared in the usual manner from 50 g. (2.05 moles) of magnesium] there was added in the course of 2 hr. 175.5 g. (1.014 moles) of 2-phenyl-4-methylpentanenitrile. The solution was refluxed for 5 hr., part of the ether was removed and replaced by toluene, and the reflux continued for several hours at 90°. After hydrolysis of the complex and removal of the solvent, the product was fractionated through a 12 in. Fenske column at 10 mm. pressure. Two main fractions were obtained: *Fraction A*, about 95 g., b.p. 115–122°,  $n_D^{25}$  1.4952–1.4968,  $n_D^{20}$  1.4971–1.4988, shown by sodium fusion to contain nitrogen, was mainly the desired ketone. Schultz *et al.*<sup>19</sup> reported a b.p. 119–124° (14 mm.),  $n_D^{20}$  1.4966 for the ketone prepared by the alkylation of methyl benzyl ketone with isobutyl iodide and powdered sodium hydroxide. *Fraction B*, 46 g., b.p. 124–127°,  $n_D^{25}$  1.4982–1.4894,  $n_D^{20}$  1.5000–1.5011, possessing a strong carbonyl absorption at 3.6  $\mu$ , was nitrile mixed with the desired ketone. Jullien<sup>10</sup> was also unable to separate the ketone and nitrile.

*3-Phenyl-5-methylhexane*. All the fractions obtained immediately above were recombined and treated with 110 ml. of 64% hydrazine hydrate in a solution of 110 g. of potassium hydroxide in 500 ml. of diethylene glycol by the modified Wolff-Kishner procedure.<sup>5,6</sup>

Distillation of the hydrocarbon fraction through the 12 in. Fenske column at 10 mm. gave 67.6 g. of material distilling at 76–96° (mostly 88–90°). A light brown residue,  $n_D^{25}$  1.4960, appeared to be starting nitrile. From the alkaline

diethylene glycol solution there was obtained 32 g. of crude brown crystalline 2-phenyl-4-methylpentanoic acid.

Purification of the hydrocarbon fraction was achieved by shaking repeatedly with ice-cold concentrated sulfuric acid, washing with cold water and sodium carbonate solution. After it dried, thiophene free benzene was added and azeotroped off to remove the final traces of water. The hydrocarbon was then fractionated from 1 g. of sodium metal through the 12 in. Fenske column. The following fractions were collected at 10 mm.: *Fraction 1*, 4.6 g., b.p. 72–77°,  $n_D^{20}$  1.4850, isoamylbenzene [proved by b.p. 197–199° at 752 mm. vs. reported<sup>1</sup> b.p. 196° at 760 mm.,  $n_D^{20}$  1.4847 and by diacetamino derivative, m.p. 216–217° vs. reported<sup>20</sup> m.p. 215–216°. Probably arose by decarboxylation of sodium 2-phenyl-4-methylpentanoate at the high temperatures of the Wolff-Kishner reduction]; *Fractions 2–3*, 5.6 g., b.p. 77–86°; *Fraction 4*, 3.2 g., b.p. 85–88°,  $n_D^{20}$  1.4835,  $n_D^{25}$  1.4818; *Fractions 5–11*, 45.7 g., b.p. 87.5–88.5°,  $n_D^{20}$  1.4832,  $n_D^{25}$  1.4813, b.p. and refractive index identical for all fractions. *Fraction 7*, selected as the pure hydrocarbon, had micro b.p. 216.6° (733 mm.) corr., and  $d_4^{20}$  0.8539,  $d_4^{25}$  0.8501.

Anal. Calcd. for  $C_{13}H_{20}$ : C, 88.56; H, 11.44. Found: C, 88.78; H, 11.45.

The diacetamino derivative (from ethanol) melted at 198.8–199.2° corr.

Anal. Calcd. for  $C_{17}H_{26}N_2O_2$ : N, 9.65. Found: N, 9.61.

*2-Phenyl-3-methylbutanenitrile* was prepared by the alkylation of phenylacetone nitrile (117 g., 1.0 mole) with isopropyl bromide (123 g., 1.0 mole) in a manner identical with that used by Hancock and Cope<sup>15</sup> for the preparation of  $\alpha$ -cyclohexylphenylacetone nitrile. Distillation through a 12 in. Fenske-type column at 3 mm. gave 127.5 g. (0.8 mole) of the desired nitrile, b.p. 106–119° (mostly 113–119°),  $n_D^{25}$  1.5038–1.5043, reported<sup>21</sup> b.p. 106° (6 mm.),  $n_D^{25}$  1.5032.

*4-Phenyl-5-methyl-3-hexanone*<sup>10</sup> was prepared by adding 127.5 g. (0.8 mole) of the above ketone in 375 ml. of anhydrous toluene to an ethyl magnesium bromide solution (from 44 g., 1.8 moles of magnesium and 218 g., 2.0 moles of ethyl bromide) in 300 ml. of ether. This solution was refluxed for 12 hr. and worked up in the usual fashion. Fractionation through a 12 in. Fenske-type column at 10 mm. gave 65.0 g. (0.342 mole, 43%) of ketone, b.p. 115–125°,  $n_D^{20}$  1.4968–1.4970. Schultz and Bicking<sup>22</sup> reported a b.p. 118–119° (14 mm.),  $n_D^{25}$  1.4943. The above ketone gave a slight test for nitrogen by the sodium fusion method.

*3-Phenyl-2-methylhexane* was prepared from 65 g. of the above ketone by the modified Wolff-Kishner procedure. Fractionation of the hydrocarbon layer through the 12 in. Fenske column at 10 mm. gave, after a very small forerun, 33.9 g. of product, b.p. 88–91°,  $n_D^{25}$  1.4811–1.4858. After purification by washing with ice cold sulfuric acid, etc., as described before and refractionation at 10 mm. from metallic sodium, the following were obtained: *Fractions 1–2*, 4.3 g., b.p. 87–90.5°,  $n_D^{25}$  1.4860; *Fractions 3–6*, 22.4 g., b.p. 90–91°,  $n_D^{20}$  1.4870–1.4873,  $n_D^{25}$  1.4850–1.4853; *Fraction 7*, 4.3 g., b.p. 89° and falling  $n_D^{20}$  1.4860,  $n_D^{25}$  1.4840. *Fraction 4*, selected as the analytical sample, had a micro b.p. 220.2° (733 mm.) corr.,  $n_D^{20}$  1.4872,  $n_D^{25}$  1.4852,  $d_4^{20}$  0.8609,  $d_4^{25}$  0.8571.

Anal. Calcd. for  $C_{13}H_{20}$ : C, 88.56; H, 11.44. Found: C, 88.58; H, 11.38.

The diacetamino derivative melted at 222.9–223.3° corr.

Anal. Calcd. for  $C_{17}H_{26}N_2O_2$ : N, 9.65. Found: N, 9.67.

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(19) E. M. Schultz, J. B. Bicking, S. Mickey and F. S. Crossley, *J. Am. Chem. Soc.*, 75, 1072 (1953).

(20) V. N. Ipatieff and L. Schmerling, *J. Am. Chem. Soc.*, 60, 1476 (1938).

(21) C. G. Overberger and D. Tanner, *J. Am. Chem. Soc.*, 77, 369 (1955).

(22) E. M. Schultz and J. B. Bicking, *J. Am. Chem. Soc.*, 75, 1128 (1953).