[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, HEBREW UNIVERSITY]

# Synthesis of 8-Bromo-1-Methylnaphthalene from *o*-Bromoacetophenone

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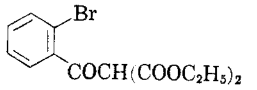
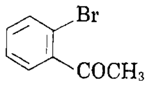
*o*-Bromoacetophenone, for which a new synthesis is described, has been converted by condensation with ethyl cyano acetate, hydrogenation, hydrolysis, and decarboxylation into β-(*o*-bromophenyl)butyric acid (VIII). Arndt-Eistert reaction converted this acid into γ-(*o*-bromophenyl)valeric acid (IX) which was cyclized to 4-methyl-5-bromo-1-tetralone (X). From this, 8-bromo-1-methylnaphthalene was prepared.

8-Bromo-1-methylnaphthalene has been synthesized by Fieser and Seligman[1] from 1,8-diaminonaphthalene by a three-step procedure and with an over-all yield of 21%. Another synthesis reported starts with 8-methyl-1-naphthylamine, which is not an easily available substance.[2] In the course of a study of reactions of *o*-bromoacetophenone (II) a new synthesis for the above compound has been elaborated.

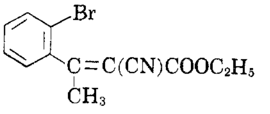
For the preparation of the starting material (II), three methods have been described: the Sandmeyer reaction of *o*-aminoacetophenone,[3,4] the reaction of *o*-bromobenzonitrile with methylmagnesium iodide,[5,6] and the reaction of *o*-bromobenzoyl chloride with diazomethane.[7] In the present study, the method used by Walker and Hauser[8] for the preparation of *o*-nitro- and *o*-chloroacetophenones has given advantageous results (92% yield). *o*-Bromobenzoyl chloride was condensed with diethyl malonate and the diethyl *o*-bromobenzoylmalonate (I) hydrolyzed. The condensation of *o*-bromoacetophenone (II) with ethyl cyanoacetate in the presence of ammonium acetate[9] as catalyst gave an 86% yield of ethyl α-cyano-β-(*o*-bromophenyl)crotonate (III), which showed considerable resistance to hydrolysis. Alkali in aqueous Cellosolve eliminated the carbethoxy group and gave a 71% yield of β-(*o*-bromophenyl)-crotononitrile (IV), whilst with hydrobromic acid in glacial acetic acid a 70% yield of the crude dicarboxylic acid (V) was obtained. The purification of this product was accompanied by serious losses of material.



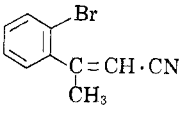
I



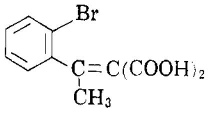
II



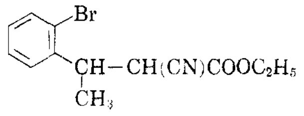
III



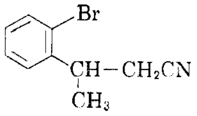
IV



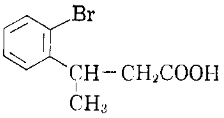
V



VI



VII



VIII

Better results were achieved after the hydrogenation of the double bond in III which gave ethyl β-(*o*-bromophenyl)-α-cyanobutyrate (VI) in 85% yield. It has not been established whether this oily product is sterically homogeneous or not. Its treatment with hydrobromic acid in glacial acetic acid gave mixtures of the nitrile VII and the acid VIII; the nitrile, which is formed first, hydrolyzes only with difficulty. Another method for the preparation of the key substance of the synthesis, the acid VIII, consists in the transformation of VI into the diethyl ester of the dicarboxylic acid by means of alcoholic hydrogen chloride, hydrolysis of the ester with methanolic potassium hydroxide,

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[1] L. F. Fieser and A. Seligman, *J. Am. Chem. Soc.*, **61**, 136 (1939).

[2] Vesely, F. Stursa, H. Olejnicek, and E. Rein, *Collection Czechoslov. Chem. Commun.*, 2, 145 (1930) [*Chem. Abstr.*, **24**, 3008 (1930)].

[3] J. Meisenheimer, *et al.*, *Ann.*, **446**, 219 (1926).

[4] L. A. Elson, C. A. Gibson, and J. D. A. Johnson, *J. Chem. Soc.*, 1128 (1930).

[5] W. Borsche and W. Scriba, *Ann.*, **541**, 283 (1939).

[6] R. E. Lutz, *et al.*, *J. Org. Chem.*, 12, 617 (1947).

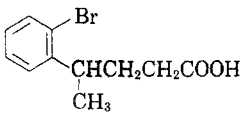
[7] V. Venkateswarlu, *Current Sci.* (*India*), **24**, 155 (1955) [*Chem. Abstr.*, **50**, 4832 (1956)].

[8] H. G. Walker and Ch. R. Hauser, *J. Am. Chem. Soc.*, **68**, 1386 (1946). Similarly *o*-ethylacetophenone has recently been prepared from *o*-ethylbenzoyl chloride by T. Mitsui, M. Kitahara, and T. Nagase, *J. Sci. Research Inst.* (*Tokyo*), **50**, 65 (1956).

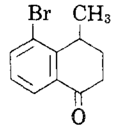
[9] A. C. Cope, C. M. Hoffman, C. Wyckoff, and E. Hardenbergh, *J. Am. Chem. Soc.*, **63**, 3452 (1941).

and decarboxylation of the dicarboxylic acid thus formed.

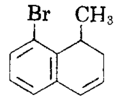
The chloride of the acid VIII was subjected to the Arndt-Eistert reaction, using silver benzoate in triethylamine[10] for the decomposition of the diazoketone. Thus γ-(*o*-bromophenyl)valeric acid (IX) was obtained in quantitative yield; it was characterized by its benzylisothiuronium salt. The acid chloride was cyclized to 4-methyl-5-bromo-1-tetralone (X) by means of aluminum chloride (yield, 75%) and X was reduced by means of aluminum isopropoxide to the corresponding alcohol in 83% yield. Dehydration of the alcohol by azeotropic distillation with toluene in the presence of *p*-toluenesulfonic acid gave a 78% yield of 8-bromo-1-methyl-1,2-dihydronaphthalene (XI).



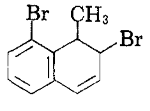
IX



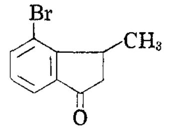
X



XI



XII



XIII

Upon treatment of this compound with *N*-bromosuccinimide, a mixture of the desired 8-bromo-1-methylnaphthalene and of 2,8-dibromo-1-methyl-1,2-dihydronaphthalene (XII) was obtained; the latter is converted into the former by treating it with pyridine, a reaction which also establishes the structure of the compound.[11] The over-all yield of 8-bromo-1-methyl-naphthalene, calculated on II, was 7%. It had the correct melting point and its picrate showed the melting point reported in the literature.

In the course of this investigation the chloride of the acid VIII was also cyclized to 4-bromo-3-methyl-1-hydrindone (XIII) in 80% yield.

## EXPERIMENTAL

*o-Bromoacetophenone* (II). (*a*) The mixture of 150 g. of *o*-bromobenzoic acid and 450 ml. of thionyl chloride was kept at room temperature for 12 hr. and refluxed for 1 hr. Distillation gave 136 g. (83%) of *o*-bromobenzoyl chloride, b.p. 130–132° (20 mm.).

(*b*) In a 3-l. flask, 15 ml. of anhydrous ethanol and 1.5 ml. of carbon tetrachloride was added to 23.7 g. of magnesium turnings. As soon as the reaction started, one added 150 ml. of chlorobenzene and, dropwise, a mixture of 156 g. of diethyl malonate and 60 ml. of ethanol. The temperature was not allowed to rise above 70° during this period. At its end, the mass was heated at 75° for 3 hr., cooled to room temperature and, at a temperature not exceeding 35°, a solution of 127 g. of *o*-bromobenzoyl chloride in 250 ml. of chlorobenzene was added drop by drop. After 12 hr. at room temperature, 200 ml. of 25% sulfuric acid was added, the mixture heated for 1 hr. on the water bath, cooled, and the organic layer separated. The latter was concentrated in the vacuum of the water pump at 100° and the residue refluxed for 7 hr. with a mixture of 200 ml. of glacial acetic acid and 200 ml. of 20% sulfuric acid. The work-up gave 107 g. (92%) of *o*-bromoacetophenone; b.p. 133–135° (20 mm.); semicarbazone, m.p. 177° (lit.: 177°).

*Ethyl α-cyano-β-(o-bromophenyl)crotonate* (III). The mixture of 124 g. of *o*-bromoacetophenone, 72 g. of ethyl cyanoacetate, 130 ml. of benzene, 60 ml. of glacial acetic acid, and 12 g. of ammonium acetate was subjected to azeotropic distillation for 11 hr. Then benzene was added and the product washed with water, sodium bicarbonate, and again water, and dried. The product was an oil, b.p. 175–180° (2.5 mm.); yield, 160 g. (86%).

*Anal.* Calcd. for $C_{13}H_{12}BrNO$: C, 53.1; H, 4.1; Br, 27.2; N, 4.8. Found: C, 53.6; H, 4.3; Br, 27.0; N, 5.2.

*β-(o-Bromophenyl)crotononitrile* (IV). When the solution of 25 g. of the preceding compound in 100 g. of ethylene glycol monomethyl ether was heated for 2.5 hr. with 10.5 g. of potassium hydroxide in 6 ml. of water, no ammonia was liberated. The reaction product was diluted with water and extracted with benzene. The product boiled at 140–145° (5 mm.), 114° (0.4 mm.), and weighed 14 g. (71%).

*Anal.* Calcd. for $C_{10}H_8BrN$: C, 54.1; H, 3.6. Found: C, 54.8; H, 3.8.

*α-(o-Bromophenyl)ethylidene malonic acid* (V). A mixture of 14.5 g. of (III), 30 ml. of glacial acetic acid, and 50 ml. of 48% hydrobromic acid was refluxed for 3 hr. The product was diluted with water, extracted with ether, and the extract treated with a 10% sodium carbonate solution. Acidification of the alkaline solution gave 9.5 g. (70%) of a grey solid which was recrystallized from toluene and melted then at 186°.

*Anal.* Calcd. for $C_{11}H_9O_4Br$: Br, 28.3. Found: Br, 29.0.

*Ethyl β-(o-bromophenyl)-α-cyanobutyrate* (VI). A solution of 10 g. of (III) in 50 ml. of ethanol was hydrogenated in the presence of 100 mg. of platinum oxide. The absorption of the theoretical amount of hydrogen required 16 hr. Distillation gave 8.5 g. (85%) of an oil, b.p. 170° (2.5 mm.).

*Anal.* Calcd. for $C_{12}H_{14}BrNO_2$: C, 52.7; H, 4.8; N, 4.8. Found: C, 53.4; H, 4.7; N, 4.8.

*Acid hydrolysis.* When 5.5 g. of the preceding substance (VI) was refluxed for 8 hr. with a mixture of 30 ml. of glacial acetic acid and 25 ml. of 48% hydrobromic acid, there were obtained, after elimination of the solvent and treatment with 10% sodium carbonate solution, two products: (*a*) an acidic one (3.4 g., 50%) of b.p. 148–150° (0.2 mm.), m.p. 61–62° (from petroleum ether), which was identified as β-(*o*-bromophenyl)-butyric acid (VIII) (see below).

*Anal.* Calcd. for $C_{10}H_{11}BrO_2$: C, 49.4; H, 4.5. Found: C, 49.8; H, 4.4.

(*b*) A neutral one (2.0 g., 31%) of b.p. 118–120° (2 mm.), which according to the analysis and spectrum was β-(*o*-bromophenyl)-butyronitrile (VII).

*Anal.* Calcd. for $C_{10}H_{10}BrN$: N, 6.2. Found: N, 6.2.

The infrared spectrum shows the $C{\equiv}N$ band at 2250 cm.$^{-1}$, in accordance with the observations of Kitson and Griffith.[12]

*Diethyl[α-(o-bromophenyl)ethyl]malonate.* A solution of 35 g. of VI in 150 ml. of anhydrous alcohol was saturated with gaseous hydrogen chloride and, after 12 hr. at room temperature, refluxed for 3.5 hr. in a current of hydrogen chloride. The alcohol was evaporated, the residue was diluted with water and extracted with ether, and the ether solution

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[10] M. S. Newman and P. F. Beal, *J. Am. Chem. Soc.*, **72**, 5163 (1950).

[11] According to K. Ziegler, A. Spaeth, E. Scharf, W. Schumann, and E. Winkelmann [*Ann.*, **551**, 80 (1942)], a tertiary hydrogen atom is generally not attacked by *N*-bromosuccinimide.

[12] R. E. Kitson and N. E. Griffith, *Anal. Chem.*, **24**, 334 (1952).

was distilled to yield 28 g. (70%) of product b.p. 165° (1 mm.).

*Anal.* Calcd. for $C_{15}H_{19}BrO_4$: Br, 23.3. Found: Br, 24.0.

*[α-(o-Bromophenyl)ethyl]malonic acid.* A mixture of 10.3 g. of the foregoing ester, 5 g. of potassium hydroxide, 5 g. of methanol, and 5 g. of water was heated at 100° for 30 min. The methanol was distilled off and the remaining clear aqueous solution acidified. Trituration of the product with carbon tetrachloride and recrystallization from toluene gave 5 g. (63%) of the desired acid, m.p. 156–157°.

*Anal.* Calcd. for $C_{11}H_{11}BrO_4$: Br, 27.9. Found: Br, 27.5.

*β-(o-Bromophenyl)butyric acid* (VIII). When the malonic acid (4.55 g.) was heated at 180–185° for 30 min., it gave the acid (VIII) (yield 2.2 g., 57%). The acid crystallized only slowly and showed a m.p. of 61–62°. It was identified by a well-defined *benzylisothiuronium salt* of m.p. 136–137°.

*Anal.* Calcd. for $C_{18}H_{21}BrN_2O_2S$: C, 52.9; H, 5.1; N, 6.9. Found: C, 53.5; H, 5.9; N, 6.7. Infrared spectrum of the acid (KBr pellet): $\nu_{c=o}$ 1700 cm.$^{-1}$

The *chloride* (31.5 g., 91%) was obtained when the acid (32 g.) and thionyl chloride (100 ml.) were kept at room temperature for 12 hr. and refluxed for 1 hr.; b.p. 118–120° (0.9 mm.).

*Anilide,* from a mixture of benzene and ligroin, m.p. 97–98°.

*Anal.* Calcd. for $C_{16}H_{16}BrNO$: C, 60.4; H, 5.0; N, 4.4; Br, 24.1. Found: C, 60.7; H, 5.2; N, 4.4; Br, 24.6.

*p-Toluidide,* from a mixture of benzene and ligroin, m.p. 106°.

*Anal.* Calcd. for $C_{17}H_{18}BrNO$: N, 4.2; Br, 25.2. Found: N, 4.3; Br, 25.2.

*γ-(o-Bromophenyl)valeric acid* (IX). To an ethereal solution of 5.5 g. of diazomethane, 10.5 g. of the acid chloride of VIII was added, dropwise, and with stirring. After 12 hr. at room temperature, the ether was removed *in vacuo* and the oily residue taken up in 75 ml. of anhydrous methanol. To the solution was added gradually 1 g. of silver benzoate in 10 ml. of triethylamine and the mixture was refluxed, after 30 min., for 1 hr. The filtered solution was refluxed for 5 hr. with a solution of 10 g. of potassium hydroxide in 10 ml. of water, and the methanol was distilled off. The residue was then taken up with water and ether and the aqueous layer acidified. The acid (IX) was an oil which boils at 153° (0.2 mm.). Yield, 10.5 g. (quantitative).

*Anal.* Calcd. for $C_{11}H_{13}O_2Br$: C, 51.4; H, 5.1. Found: C, 50.8; H, 4.9. Infrared spectrum: $\nu_{c=o}$ 1700 cm.$^{-1}$

The acid gave a well-defined *benzylisothiuronium salt,* which crystallized from aqueous dioxane and melted at 135°. Its melting point is depressed by admixture of the analogous derivative of (VIII).

*Anal.* Calcd. for $C_{19}H_{23}BrN_2O_2S$: N, 6.6. Found: N, 6.9.

The *chloride* (8 g., 83%), was obtained from the acid (9 g.) as described above; b.p. 133–135°/0.3 mm.

*Anilide,* from benzene-ligroin, m.p. 85–86°.

*Anal.* Calcd. for $C_{17}H_{18}BrNO$: N, 4.2. Found: N, 4.0.

*p-Toluidide,* from benzene-ligroin, m.p. 89–90°.

*Anal.* Calcd. for $C_{18}H_{20}BrNO$: N, 4.1. Found: N, 4.1.

*5-Bromo-4-methyl-1-tetralone* (X). To an ice-cold solution of 6.5 g. of the chloride of X in 50 ml. of carbon disulfide, 3 g. of aluminum chloride was added with stirring, during 30 min. The stirring was continued for 4 hr. at 0°, and the mixture was kept at room temperature for 12 hr. and decomposed with ice and concentrated hydrochloric acid. B.p. 160–163° (5 mm.); yield, 4.3 g. (75%).

*Anal.* Calcd. for $C_{11}H_{11}BrO$: C, 55.2; H, 4.8. Found: C, 55.6; H, 4.8.

Ultraviolet spectrum (in ethanol): 253 mμ (4.03); 298 mμ (3.26); infrared spectrum $\nu_{c=o}$ 1695 cm.$^{-1}$ (α-tetralone: 1691 cm.$^{-1}$).[13]

*2,4-Dinitrophenylhydrazone,* from butanol, m.p. 225–226°.

*Anal.* Calcd. for $C_{17}H_{15}BrN_4O_4$: C, 48.7; H, 3.6; Br, 19.1. Found: C, 49.2; H, 3.8; Br, 19.2.

*5-Bromo-4-methyl-1-tetralol.* In the usual way, 14.5 g. of the ketone X was reduced with 12.5 g. of aluminum isopropoxide and 70 ml. of isopropyl alcohol. The reduction was complete in 5 hr. After removal of the solvent, the product was treated with dilute hydrochloric acid and extracted with benzene. B.p. 125–130°/2 mm.; yield, 12 g. (83%). Infrared spectrum: $\nu_{O-H}$ 3350 cm.$^{-1}$

*Anal.* Calcd. for $C_{11}H_{13}BrO$: C, 54.8; H, 5.4. Found: C, 54.3; H, 5.4.

*8-Bromo-1-methyl-1,2-dihydronaphthalene* (XI). The solution of 11 g. of 5-bromo-4-methyl-1-tetralol and 0.5 g. of *p*-toluenesulfonic acid in 50 ml. of toluene was subjected to azeotropic distillation. After 5 hr., the solution was washed with water and sodium bicarbonate solution and distilled. B.p. 100–104°/2 mm.; yield, 8 g. (80%).

*Anal.* Calcd. for $C_{11}H_{11}Br$: C, 59.2; H, 4.8. Found: C, 59.1; H, 5.0.

Ultraviolet spectrum (in ethanol); 259 mμ (3.98). This figure conforms with the spectrum of 1,2-dihydronaphthalene [260 mμ (3.96)], as reported by Mousseron and coworkers.[14]

*8-Bromo-1-methylnaphthalene.* The mixture of 2.5 g. of XI, 2 g. of *N*-bromosuccinimide, a few crystals of benzoyl peroxide, and 20 ml. of carbon tetrachloride was refluxed for 2 hr., filtered and subjected to distillation. Two fractions were obtained. (a) B.p. 115–130° (3.5 mm.); 1.5 g. This fraction solidified; recrystallization from methanol gave platelets of the correct m.p. 79–80°.

*Anal.* Calcd. for $C_{11}H_9Br$: C, 59.7; H, 4.1. Found: C, 59.7; H, 4.4. Picrate, m.p. 152–153°.

(b) B.p. 140–150° (3.5 mm.); 0.8 g. According to the analysis and the behavior, this product was 2,8-dibromo-1-methyl-1,2-dihydronaphthalene (XII); it has not been possible to obtain it in analytically pure form.

*Anal.* Calcd. for $C_{11}H_{10}Br_2$: C, 43.7; H, 3.3. Found: C, 42.5; H, 3.2.

When this product was heated for 1 hr. with 5 ml. of pyridine, it gave the above 8-bromo-1-methylnaphthalene, m.p. 79–80°.

*4-Bromo-3-methyl-1-hydrindone* (XIII). To a solution of 6 g. of β-(o-bromophenyl)butyryl chloride in 60 ml. of carbon disulfide, 3.5 g. of aluminum chloride was added with stirring. After 12 hr. at room temperature, the mass was decomposed with ice and concentrated hydrochloric acid and the oily product isolated by distillation. B.p. 140–145° (5 mm.); yield, 4.1 g. (82%).

*Anal.* Calcd. for $C_{10}H_9OBr$: C, 53.3; H, 4.0. Found: C, 53.2; H, 4.4.

*2,4-Dinitrophenylhydrazone,* from butyl acetate, m.p. 267°. Ultraviolet spectrum (in chloroform): 389 mμ (4.33).

*Anal.* Calcd. for $C_{16}H_{13}BrN_4O_4$: C, 47.4; H, 3.2. Found: C, 47.0; H, 2.9.

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(13) E. D. Bergmann and S. Pinchas, *J. chim. phys.*, **49**, 537 (1952).

(14) M. Mousseron, R. Jacqnier, and H. Christol, *Compt. rend.*, **243**, 1532 (1956).