

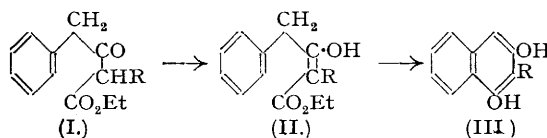
20. *Syntheses in the Naphthalene Series. Part I. 1:3-Dihydroxynaphthalenes.*

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Ethyl γ -phenylacetoacetate was prepared by hydrolysis of ethyl α -phenylacetylacetoacetate and converted into 1:3-dihydroxynaphthalene by the action of concentrated sulphuric acid at room temperature. Its α -alkyl derivatives, prepared by alkylation, were similarly converted into the corresponding dihydroxynaphthalenes.

METZNER has shown (*Annalen*, 1897, **298**, 383) that ethyl phenylacetylmalonate (I, R = CO₂Et) gives 2-carbethoxy-1:3-dihydroxynaphthalene (III, R = CO₂Et), but ethyl γ -phenylacetoacetate (I, R = H) yields an unstable β -keto-acid, by the action of sulphuric acid at room temperature. However, ethyl $\alpha\gamma$ -diphenyl-

acetoacetate (I, R = Ph) has been converted by Volhard (*Annalen*, 1897, **296**, 14) into 1:3-dihydroxy-2-phenylnaphthalene (III, R = Ph) by the action of cold sulphuric acid.



We have confirmed the results of Metzner and Volhard regarding the formation of dihydroxynaphthalenes, but have also succeeded in converting ethyl γ -phenylacetoacetate into 1:3-dihydroxynaphthalene by the action of sulphuric acid at room temperature. Further, the α -methyl-, -ethyl-, -propyl-, -isopropyl-, -butyl-, -isobutyl-, and -isoamyl derivatives, prepared by the action of alkyl halides on the sodio-derivative of the ester in absolute alcohol, have been converted into the corresponding 1:3-dihydroxynaphthalenes, the yields varying from 50 to 70%. The isopropyl, isobutyl, and isoamyl derivatives were not obtained analytically pure, but their diacetates gave analyses conforming to the formulæ assigned. None of the cyclisation experiments gave a β -keto-acid, but in most cases the dihydroxynaphthalenes were accompanied by the ketones which would arise by decarboxylation of such acids. We obtained γ -4-nitrophenylacetoacetic acid by the action of sulphuric acid on its ethyl ester, which failed to give the corresponding dihydroxynaphthalene.

Ethyl γ -phenylacetoacetate was prepared by hydrolysis of ethyl γ -phenylacetylacetoacetate (Sonn and Litten, *Ber.*, 1933, **66**, 1515). Its alkyl derivatives were shown to be α -substituted by hydrolysis, *e.g.*, of ethyl γ -phenyl- α -methylacetoacetate (I, R = Me) to benzyl ethyl ketone. Dimethylation gave ethyl γ -phenyl- α -dimethylacetoacetate, which yielded benzyl isopropyl ketone on hydrolysis. β -Benzoylpropionic acid was not cyclised by the action of cold sulphuric acid, although some of its α -benzylidene derivatives were shown by Ohmaki (*A.*, II, 1939, 370) to give 1-phenylnaphthalene-3-carboxylic acids by the action of sulphuric acid in methanol.

The method here described appears to be the only one by which 1:3-dihydroxynaphthalenes can be prepared directly. Auger (*Bull. Soc. chim.*, 1890, **3**, 128) reported the isolation of a dimethyl-1:3-dihydroxynaphthalene by the action of methylalmonyl chloride on *m*-xylene in presence of aluminium chloride, but assigned to it two alternative formulæ, namely, 1:3-dihydroxy-2:6- or -2:8-dimethylnaphthalene.

EXPERIMENTAL.

Ethyl γ -Phenyl- α -methylacetoacetate.—This was prepared by the action of methyl iodide (1.2 mols.; 30 g.) on the sodio-derivative formed by addition of an absolute alcoholic solution of sodium (4.6 g.) to ethyl γ -phenylacetoacetate (41 g.). The reaction was complete after 3 hours' heating; alcohol was then distilled, and the ester extracted with ether and distilled. The fraction (35 g.), b. p. 176–178°/18 mm., gave a plum colour with ferric chloride (Found: C, 70.7; H, 7.3. $C_{13}H_{16}O_3$ requires C, 70.9; H, 7.3%). Hydrolysis of the ester gave benzyl ethyl ketone, identified as the semicarbazone, m. p. 154° (cf. Ludlam, *J.*, 1902, **81**, 1189; Tiffeneau and Fourneau, *Compt. rend.*, 1908, **146**, 699) (Found: C, 64.4; H, 7.3. Calc.: C, 64.4; H, 7.3%).

Ethyl γ -Phenyl- α -dimethylacetoacetate.—Prepared by further methylation of the above ester in the same manner, this distilled at 180°/22 mm., gave no colour with ferric chloride, and did not add bromine. In these properties it is identical with the ester prepared by Blaise (*Compt. rend.*, 1901, **132**, 480) by the action of phenylacetonitrile on the zinc complex of ethyl α -bromoisobutyrate (Found: C, 71.6; H, 7.7. Calc. for $C_{14}H_{18}O_3$: C, 71.7; H, 7.7%). Treatment of the ester with cold sulphuric acid gave neither a β -keto-acid nor a cyclic compound; the chief product was benzyl isopropyl ketone.

α -Alkylated γ -Phenylacetoacetic Esters.—The following compounds were prepared in the same way as the α -methyl compound: *a*-ethyl, a pale yellow oil, b. p. 160°/6 mm., which gave a plum colour with ferric chloride (Found: C, 71.7; H, 7.3. $C_{14}H_{18}O_3$ requires C, 71.7; H, 7.7%); *a*-propyl, b. p. 164°/6 mm., which gave a plum colour with ferric chloride (Found: C, 72.5; H, 7.9. $C_{15}H_{20}O_3$ requires C, 72.5; H, 8.1%); *a*-isopropyl, b. p. 158°/6 mm. (Found: C, 72.6; H, 7.8%); *a*-butyl, b. p. 172–174°/7 mm., which gave a violet-red colour with ferric chloride (Found: C, 73.1; H, 8.1. $C_{16}H_{22}O_3$ requires C, 73.3; H, 8.45%); *a*-isobutyl, b. p. 172–174°/7 mm. (Found: C, 73.1; H, 8.2%); *a*-isoamyl, b. p. 152°/2 mm., which gave a violet-red colour with ferric chloride (Found: C, 73.8; H, 8.6. $C_{17}H_{24}O_3$ requires C, 73.9; H, 8.8%).

1:3-Dihydroxynaphthalene.—Ice-cold concentrated sulphuric acid (15 c.c.) was gradually added to ethyl γ -phenylacetoacetate (5 g.), and the red solution kept overnight at room temperature and then poured on ice. The yellowish sticky mass obtained was extracted with ether, and the extract shaken with sodium bicarbonate and with 2% sodium hydroxide solution. The bicarbonate extract gave traces of phenylacetic acid and the red alkaline solution gave a reddish-brown oil. This was extracted with ether and the residue recovered from the ethereal solution was treated with cold light petroleum until it solidified; it then crystallised from chloroform in plates, m. p. 118–120° (Found: C, 75.2; H, 5.0. Calc. for $C_{10}H_8O_2$: C, 75.0; H, 5.0%). It gave a diacetate, m. p. 56° (cf. Metzner, *loc. cit.*). The first neutral ethereal extract gave traces of benzyl methyl ketone, identified in the form of its semicarbazone.

1:3-Dihydroxy-2-methylnaphthalene.—This was prepared by dissolving ethyl γ -phenyl- α -methylacetoacetate (10 g.) in cold concentrated sulphuric acid (30 c.c.), and keeping the red solution at room temperature for 24 hours. When the solution was poured on ice, a crystalline orange solid (about 6 g.) was obtained, which formed prisms, m. p. 139°, from benzene and needles, m. p. 139–140°, from water saturated with sulphur dioxide (Found: C, 75.7; H, 5.8. $C_{11}H_{10}O_2$ requires C, 75.8; H, 5.8%). It gave a reddish colour with ferric chloride, and on treatment with acetic anhydride and fused sodium acetate it gave a diacetate, which crystallised from methanol in prisms, m. p. 118° (Found: C, 69.8; H, 5.5. $C_{15}H_{14}O_4$ requires C, 69.7; H, 5.5%).

1:3-Dihydroxy-2-ethylnaphthalene.—The cyclisation of ethyl γ -phenyl- α -ethylacetoacetate (7 g.) was effected by concentrated sulphuric acid (25 c.c.). The product which separated on ice treatment was extracted with 2% sodium hydroxide solution. Addition of hydrochloric acid to the red alkaline solution gave an orange solid (4.2 g.), which crystallised from benzene in needles, m. p. 126–128° (Found: C, 76.6; H, 6.3. $C_{12}H_{12}O_2$ requires C, 76.6; H, 6.3%). The

diacetate crystallised from dilute methanol in white plates, m. p. 82° (Found : C, 70.6; H, 5.8. $C_{16}H_{16}O_4$ requires C, 70.6; H, 5.9%).

1 : 3-*Dihydroxy-2-propylnaphthalene*.—Obtained by the action of cold sulphuric acid (20 c.c.) on ethyl γ -phenyl- α -propylacetoacetate (5 g.) and isolated in the usual manner, this crystallised from light petroleum in orange needles, m. p. 103°, which became reddish on keeping (Found : C, 76.8; H, 6.7. $C_{15}H_{14}O_2$ requires C, 77.1; H, 6.9%). The *diacetate* crystallised from light petroleum in needles, m. p. 75° (Found : C, 71.2; H, 6.3. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3%).

1 : 3-*Dihydroxy-2-isopropylnaphthalene*.—This was prepared from ethyl γ -phenyl- α -isopropylacetoacetate in the usual manner but was not obtained analytically pure. On treatment with acetic anhydride and pyridine, it gave a *diacetate*, which crystallised from dilute methanol in prisms, m. p. 75° (Found : C, 71.0; H, 6.1. $C_{17}H_{18}O_4$ requires C, 71.3; H, 6.3%).

1 : 3-*Dihydroxy-2-butylnaphthalene*.—Prepared by the action of sulphuric acid on ethyl γ -phenyl- α -butylacetoacetate (yield, about 60%) and crystallised from light petroleum, this formed orange needles, m. p. 108—110° (Found : C, 77.6; H, 7.3. $C_{14}H_{16}O_2$ requires C, 77.7; H, 7.4%). The *diacetate* crystallised from methanol in white needles, m. p. 65° (Found : C, 71.6; H, 6.6. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%).

1 : 3-*Dihydroxy-2-isobutylnaphthalene*.—This was prepared by the action of sulphuric acid on ethyl γ -phenyl- α -isobutylacetoacetate. The product, isolated in the usual manner, solidified after treatment with cold light petroleum, but was not obtained analytically pure. The *diacetate* crystallised from light petroleum in prisms, m. p. 135° (Found : C, 72.4; H, 6.7. $C_{18}H_{20}O_4$ requires C, 72.0; H, 6.7%).

1 : 3-*Dihydroxy-2-isoamylnaphthalene*.—Ethyl γ -phenyl- α -isoamylacetoacetate (10 g.) was gradually dissolved in ice-cold sulphuric acid (25 c.c.), the solution kept at room temperature for 24 hours and poured on ice, and the sticky solid extracted with ether. The extract was shaken once with sodium bicarbonate solution and twice with 5% sodium hydroxide solution. The latter alkaline solution gave on acidification a reddish-brown precipitate (6 g.), which crystallised from light petroleum in whitish needles, m. p. 92—93°; these gradually became reddish-brown in the air (Found : C, 77.5, 77.1; H, 7.7, 7.6. $C_{15}H_{18}O_2$ requires C, 78.2; H, 7.9%). The *diacetate*, prepared by heating 1 g. with acetic anhydride (15 c.c.), fused sodium acetate (1 g.), and zinc dust (0.5 g.) for 3 hours on the water-bath, crystallised from light petroleum in white needles, m. p. 79—80° (Found : C, 72.7; H, 7.1. $C_{19}H_{22}O_4$ requires C, 72.6; H, 7.1%). The *dibenzoate*, prepared by the action of benzoyl chloride (1 c.c.) on 1 g. in pyridine (15 c.c.) at 40° for 24 hours, crystallised from methanol in white plates, m. p. 108—109° (Found : C, 79.3; H, 6.1. $C_{23}H_{26}O_4$ requires C, 79.4; H, 6.0%).

1 : 3-*Dihydroxy-2-phenylnaphthalene*.—Prepared by the action of cold sulphuric acid on ethyl $\alpha\gamma$ -diphenylacetoacetate and crystallised from chloroform, this formed plates, m. p. 165° (cf. Volhard, *loc. cit.*). The *diacetate* crystallised from methanol in needles, m. p. 138°.

*2-*Carbethoxy-1 : 3-dihydroxynaphthalene*.—This compound was prepared by the action of sulphuric acid on ethyl phenylacetylmalonate and isolated in the usual manner. It crystallised from methanol in needles, m. p. 85° (cf. Metzner, *loc. cit.*).

Ethyl γ -4-Nitrophenylacetoacetate.—4-Nitrophenylacetyl chloride (1 mol.; 100 g.) was gradually added to the sodio-derivative (1 mol.) of ethyl acetoacetate (65 g.) in dry benzene, the mixture refluxed for 4 hours, and the product isolated and hydrolysed with dilute aqueous ammonia. The liquid was acidified, the product extracted with ether, and, after removal of the precipitated amides and ammonium salts, the extract washed and dried. Removal of ether left a brown oil, which deposited a yellowish solid when kept in the ice-chest for several days. It crystallised from light petroleum in yellowish plates, m. p. 82°, which gave a violet colour with ferric chloride and a reddish-violet colour with aqueous sodium hydroxide (Found : C, 57.5; H, 5.3. $C_{12}H_{13}O_5N$ requires C, 57.4; H, 5.2%). When heated with dilute sulphuric acid, the *ester* gave 4-nitrobenzyl methyl ketone, which crystallised from light petroleum in plates, m. p. 65° (Found : C, 60.5; H, 5.1. Calc. for $C_9H_9O_3N$: C, 60.3; H, 5.1%). When the *ester* was dissolved in cold concentrated sulphuric acid, and the reddish solution kept at room temperature for 3 days, γ -4-nitrophenylacetoacetic acid and a trace of the above ketone were formed. The acid was isolated from a bicarbonate extract of an ethereal solution of the reaction mixture. It crystallised from benzene in needles, m. p. 116° (decomp.), which gave a violet colour with ferric chloride (Found : C, 53.8; H, 4.0. $C_{10}H_9O_5N$ requires C, 53.8; H, 4.0%). The acid decomposed when heated with water; on cooling, 4-nitrobenzyl methyl ketone crystallised.