

with an authentic sample of ethyl diphenylacetate gave no depression in the melting point. Identical results were obtained using both 90% and absolute ethanol and varying the time of reflux from 8 to 30 hr.

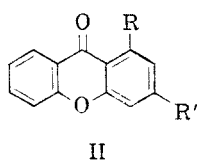
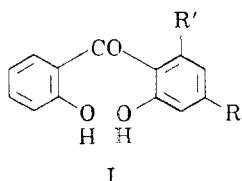
THE CHEMISTRY DEPARTMENT  
UNIVERSITY OF DELAWARE  
NEWARK, DEL.

## 2,2',4- and 2,2',6-Trihydroxybenzophenone

J. S. H. DAVIES,\* F. SCHEINMANN, AND H. SUSCHITZKY

Received July 29, 1957

We have applied Grover, Shah, and Shah's<sup>1</sup> new synthesis of polyhydroxyxanthenes to the preparation of 1-hydroxy-9-xanthenone<sup>2</sup> which is obtained in low yields by the usual methods.<sup>3,4</sup> Condensation of salicylic acid and resorcinol in the presence of anhydrous zinc chloride and phosphoryl chloride yielded a trihydroxybenzophenone. This substance has the same melting point as, and similar solubility properties to, 2,2',6-trihydroxybenzophenone obtained by Michael<sup>3</sup> by fusing the same reactants in the absence of a condensing agent. Michael's compound was assigned the structure of 2,2',6-trihydroxybenzophenone (I; R = H; R' = OH) because it cyclized with zinc chloride to give 1-hydroxy-9-xanthenone (II; R = OH; R' = H).<sup>3,5</sup> Our product, however, could not be made to cyclize with zinc chloride, but gave a quantitative yield of 3-hydroxy-9-xanthenone (II; R = H; R' = OH), when heated with water in a sealed tube at 200–250°. This benzophenone is thus proved to be 2,2',4-trihydroxybenzophenone (I; R = OH; R' = H). Moreover the nonidentity of the two ketones was confirmed by a depression in their melting points and those of their triacetyl derivatives on admixture.



It is, therefore, possible by varying the reaction conditions to obtain either 2,2',4- or 2,2',6-trihydroxybenzophenone from the same reactants. The formation of 2,2',4-trihydroxybenzophenone in the presence of phosphoryl chloride and zinc

chloride is consistent with the findings of Grover, Shah, and Shah<sup>1</sup> who report that under these conditions hydroxybenzoic acids will substitute the resorcinol nucleus in the  $\beta$ -position only.

2,2',4-Trihydroxybenzophenone has been previously mentioned by Atkinson and Heilbron<sup>6</sup> in connection with a by-product isolated from their preparation of 3-hydroxy-9-xanthenone (II; R = H; R' = OH). No structural evidence was, however, given, except that, by drawing attention to its similarity to Michael's compound, the identity of the two substances was implied.

## EXPERIMENTAL<sup>7</sup>

**2,2',4-Trihydroxybenzophenone.** Salicylic acid (5 g.), resorcinol (6 g.), anhydrous zinc chloride (20 g.), and phosphoryl chloride (25 cc.) were heated on a water bath at 75–80° for 2 hr. The deep-red reaction mixture was poured onto crushed ice (400 cc.) containing concentrated hydrochloric acid (25 cc.). A red gum formed on standing and its mother liquor A was decanted off. On triturating the residue with aqueous sodium hydrogen carbonate an orange solid was obtained which yielded on recrystallization from water and from petroleum ether (b.p. 100–120°) 2,2',4-trihydroxybenzophenone, m.p. 133° (0.37 g.) as colorless plates. More ketone (1.85 g.) was obtained from mother liquor A which deposited it as yellow needles on standing for 2 days and by acidification of the sodium hydrogen carbonate extract.

*Anal.* Calcd. for C<sub>13</sub>H<sub>10</sub>O<sub>4</sub>: C, 67.8; H, 4.4. Found: C, 68.1; H, 4.4.

The ketone gives a deep red ferric color in water and dissolves in alkali to form a yellow solution. The triacetate was obtained in the usual way and crystallized from a mixture of ethyl acetate and petroleum ether (b.p. 40–60°) as blunt needles, m.p. 69–70°.

*Anal.* Calcd. for C<sub>19</sub>H<sub>16</sub>O<sub>7</sub>: C, 64.0; H, 4.5. Found: C, 64.0; H, 4.7.

**3-Hydroxy-9-xanthenone.** 2,2',4-Trihydroxybenzophenone (0.4 g.) and water (1.5 cc.) were heated in a sealed tube (50 cc.) for 2.5 hr. at 200–250°. Crude 3-hydroxy-9-xanthenone was obtained in theoretical yield as a yellow crystalline residue, m.p. 238–241°. Recrystallization from aqueous ethanol yielded the xanthenone as white needles, m.p. 242° (Atkinson and Heilbron<sup>6</sup> give m.p. 246°).

*Anal.* Calcd. for C<sub>13</sub>H<sub>8</sub>O<sub>3</sub>: C, 73.6; H, 3.8. Found: C, 73.8; H, 4.0.

The acetyl derivative had m.p. 156°. Kostanecki and Rutishauser<sup>8</sup> give m.p. 157–158°.

*Anal.* Calcd. for C<sub>15</sub>H<sub>10</sub>O<sub>4</sub>: C, 71.3; H, 4.0. Found: C, 71.1; H, 4.0.

Attempts to cyclize 2,2',4-trihydroxybenzophenone with fused zinc chloride gave only starting material.

**2,2',6-Trihydroxybenzophenone** was prepared as described by Michael.<sup>3</sup> The product crystallizes from petroleum ether (b.p. 100–120°) as white plates, m.p. 134–135° (Michael<sup>3</sup> gives m.p. 133–134°). Its mixed melting point with 2,2',4-trihydroxybenzophenone was depressed.

*Anal.* Calcd. for C<sub>13</sub>H<sub>10</sub>O<sub>4</sub>: C, 67.8; H, 4.4. Found: C, 67.7; H, 4.4.

The triacetate prepared by the acetic anhydride-pyridine method crystallized as blunt needles, m.p. 80–81° from a mixture of ethyl acetate and petroleum ether (b.p. 40–60°).

(6) H. Atkinson and I. M. Heilbron, *J. Chem. Soc.*, 2688 (1926).

(7) All melting points are uncorrected. The analyses were done by Drs. Weiler and Strauss, Oxford.

(8) St. v. Kostanecki and R. Rutishauser, *Ber.*, 25, 1651 (1892).

\* Deceased.

(1) P. K. Grover, G. D. Shah, and R. C. Shah, *Chemistry & Industry*, 62 (1955); *J. Chem. Soc.*, 3982 (1955).

(2) 1-Hydroxy-9-xanthenone was needed for other work: see J. S. H. Davies, F. Scheinmann, and H. Suschitzky, *J. Chem. Soc.*, 2140 (1956).

(3) A. Michael, *Am. Chem. J.*, 5, 81 (1883).

(4) K. S. Pankajamani and T. R. Seshadri, *J. Sci. Ind. Research (India)*, 13B, 396 (1954).

(5) E. Dreher and St. v. Kostanecki, *Ber.*, 26, 71 (1893).

The mixed melting point with 2,2',4-triacetoxybenzophenone was depressed.

Anal. Calcd. for  $C_{19}H_{16}O_7$ : C, 64.0; H, 4.5. Found: C, 64.2; H, 4.3.

*Acknowledgment.* One of us (F.S.) thanks the Governors of the Royal Technical College, Salford, for the award of a Research Demonstratorship.

DEPARTMENT OF PURE AND APPLIED CHEMISTRY  
ROYAL TECHNICAL COLLEGE  
SALFORD, LANCS, ENGLAND

## The Stobbe Condensation on *p*-Methoxy-*m*-methylisobutyrophenone

MILTON D. SOFFER AND ANN DONALDSON<sup>1</sup>

Received August 5, 1957

The substances described were prepared in preliminary experiments directed toward 7-hydroxy-1,6-dimethyl-4-isopropyl-naphthalene whose unambiguous synthesis,<sup>2</sup> serving to confirm the structure of the sesquiterpene copaene,<sup>3</sup> was accomplished while this work was in progress. We therefore wish merely to record the results of these experiments which were discontinued at that time. The products obtained are intermediates in an adaptation of the general "tetralone" scheme developed by Johnson and coworkers.<sup>4</sup> Methyl *o*-cresyl ether readily entered into the Friedel-Crafts reaction with isobutyryl chloride to produce *p*-methoxy-*m*-methylisobutyrophenone. The use of carbon disulfide which gives inferior results with similar phenolic ethers in the reaction with succinic anhydride,<sup>5</sup> gave good yields in the present case. The crystalline acid ester, 3-carbomethoxy-4-(*p*-methoxy-*m*-tolyl)-5-methyl-3-hexenoic acid, was obtained in the Stobbe condensation with dimethyl succinate and sodium hydride. The assignment of the ethylenic linkage to the 3 position is in accord with the infrared absorption spectrum which exhibited in addition to the carboxyl band (5.79  $\mu$ ) the maxima characteristic of the conjugated ester carbonyl and double bond (5.82, 6.11  $\mu$ ).<sup>6</sup> The diacid was also prepared by saponification. Upon recrystallization from hot benzene-petroleum ether a small amount of a lower melting substance was isolated which is apparently the corresponding cyclic anhydride. A similar behavior has been noted for

$\gamma,\gamma$ -di-*p*-methoxyphenylitaconic acid,<sup>7</sup> which is a close electronic and steric analog.

### EXPERIMENTAL<sup>8</sup>

*p*-Methoxy-*m*-methylisobutyrophenone.<sup>9</sup> To a well stirred ice-cooled mixture of 135.8 g. (1.04 moles) of anhydrous aluminum chloride and 160 ml. of dry carbon disulfide, 111 g. (1.04 moles) of carefully fractionated isobutyryl chloride<sup>10</sup> was added slowly, followed by 91.0 g. (0.745 mole) of *o*-methyl cresyl ether. The ether must be added cautiously to keep the copious evolution of gas under control. The mixture was stirred at 0° for 15 hr. and allowed to warm up to room temperature. Following cautious treatment with 400 ml. of ice and water, and 200 ml. of concentrated hydrochloric acid, most of the carbon disulfide was removed at reduced pressure. The product was extracted with ether, washed thoroughly with 5% sodium hydroxide, water, and dried over magnesium sulfate and freed from solvent. The residual oil from two such runs was distilled roughly under nitrogen and fractionated through a five-plate modified Widmer column to give 231 g. (81%) of the colorless ketone, b.p. 110–115° at 0.5 mm., m.p. 22–23°.

The *semicarbazone* was readily obtained in pyridine-methanol, melting at 143–145° after one recrystallization from aqueous methanol, and finally at 144–145°;  $\lambda_{\text{max}}^{\text{Nujol}}$  5.92  $\mu$ .<sup>11</sup>

Anal. Calcd. for  $C_{13}H_{19}O_2N_2$ : C, 62.62; H, 7.68. Found: C, 62.75, 62.70; H, 7.55, 7.55.

The 2,4-dinitrophenylhydrazone crystallized from aqueous methanol in yellow blades, m.p. 151–152°.

3-Carbomethoxy-4-(*p*-methoxy-*m*-tolyl)-5-methyl-3-hexenoic acid. The Stobbe condensation<sup>4</sup> was run in dry benzene using 9.6 g. (0.05 mole) of the foregoing ketone, 26.1 (0.18 mole) of dimethyl succinate, and 2.9 g. (0.12 mole) of granular sodium hydride. The reactants were mixed all at once under dry nitrogen in an apparatus provided for entry and exit of gases and measurement of evolved hydrogen. It was necessary to add a few drops of methanol and to reflux the mixture for a few minutes to induce a steady evolution of hydrogen, which then continued at room temperature for approximately 26 hr.

Excess acetic acid was added cautiously, followed finally by water and ether, and the product was isolated by extraction with a 5% solution of sodium bicarbonate followed by acidification and re-extraction with ether. Drying over magnesium-sulfate and removal of solvent left a semi-crystalline solid, m.p. 95–105° from which one pure stereoisomer was obtained by successive recrystallization from benzene-petroleum ether (b.p. 30–60°), water, and hexane; 3.37 g. (22%); m.p. 120–121°;  $\lambda_{\text{max}}^{\text{Nujol}}$  5.79, 5.82, 6.11  $\mu$ .<sup>11</sup>

Anal. Calcd. for  $C_{18}H_{21}O_5$ : C, 66.65; H, 7.24; neut. equiv., 306.4. Found: C, 66.88, 67.28; H, 7.44, 7.30; neut. equiv., 306.4, 309.0.

In separate experiments in which more methanol was used in priming, or glass marbles were added for pulverizing action,<sup>12</sup> the initial heating period was not required and the

(7) W. S. Johnson and M. W. Miller, *J. Am. Chem. Soc.*, **72**, 511 (1950).

(8) Temperature readings are uncorrected.

(1) From the M.A. thesis of Ann Donaldson, 1949.

(2) L. H. Briggs, N. S. Gill, F. Lyons, and W. I. Taylor, *J. Chem. Soc.*, 1098 (1949).

(3) L. H. Briggs and W. I. Taylor, *J. Chem. Soc.*, 1338 (1947).

(4) W. S. Johnson and G. H. Daub, *Org. Reactions*, VI, 34 (1951); W. S. Johnson and A. R. Jones, *J. Am. Chem. Soc.*, **69**, 792 (1947).

(5) L. F. Fieser and E. B. Hershberg, *J. Am. Chem. Soc.*, **58**, 2314 (1936).

(6) R. S. Rasmussen and R. R. Brattain, *J. Am. Chem. Soc.*, **71**, 1073 (1949).

(9) The orientation of the acyl function is assigned by analogy [cf. reference 5; G. Stadnikoff and A. Baryschewa, *Ber.*, **61**, 1996 (1928); W. P. Campbell and M. D. Soffer, *J. Am. Chem. Soc.*, **64**, 417 (1942)].

(10) R. E. Kent and S. M. McElvain, *Org. Syntheses*, **25**, 58–60 (1941).

(11) We are indebted to Mr. Philip Sadtler of Samuel

(12) N. Green and F. B. LaForge, *J. Am. Chem. Soc.*, **70**, 2287 (1948).