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THE SYNTHESIS OF ISOCAMPHORQUINONE

Thomas A. Spencer and Marshall D. Newton
Department of Chemistry, Dartmouth College, Hanover, N. H.

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ISOCAMPHORQUINONE, the "easily resinified" rearrangement product obtained by treatment of camphorquinone with cold fuming sulfuric acid, was recently assigned the structure (I) by Levine.[1] This assignment has now been confirmed by a synthesis involving condensation of ethyl isopropylidenemalonate[2] with ethyl vinyl ketone. When these substances were allowed to react in refluxing methanol containing an equivalent of sodium methoxide for three hours, the sodium salt of 2-methyl-4-isopropenyl-4-carbomethoxy-1,3-cyclohexanedione (II, R=CH_3) precipitated. Acidification of this salt afforded the free diketoester (36% of material with m.p. 125-126°), m.p. 130-130.5°(λ^{EtOH}_{max} 268 mμ, ϵ = 16,000; $\lambda^{CHCl_3}_{max}$ 3.12, 5.80, 6.14

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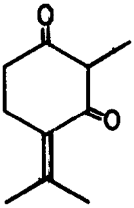
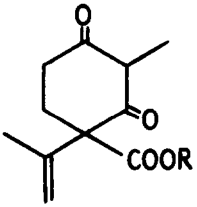
[1] S. G. Levine, *J. Amer. Chem. Soc.* **82**, 2556 (1960). Isocamphorquinone was first reported by O. Manasse and E. Samuel, *Chem. Ber.* **30**, 3157 (1897). These workers (*Chem. Ber.* **35**, 3829 (1902)) proposed 2-hydroxy-3-methyl-6-isopropylidene-2-cyclohexene-1-one as the structure of isocamphorquinone. This "diosphenolene" structure was accepted as correct until the work of Levine. R. H. Reitsema, *J. Amer. Chem. Soc.* **78**, 5022 (1956), has described a different substance which has properties consistent with the "diosphenolene" structure.

[2] Prepared by the method of A. C. Cope and E. M. Hancock, *J. Amer. Chem. Soc.* **60**, 2644 (1938).

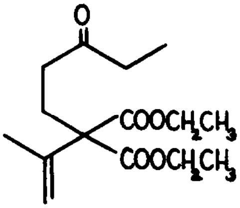
and 10.92 μ; Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.05; H, 6.90.). The corresponding ethyl ester (II, $R=CH_2CH_3$) was obtained as an oil when the reaction was run in ethanol.

Removal of the tertiary carbomethoxy group of II ($R=CH_3$) was effected in excellent yield by treatment with dilute sodium hydroxide solution (room temperature for twenty hours), followed by acidification, whereupon crude isocamphorquinone (92%, m.p. 75-88°) could be isolated directly. After purification by recrystallization from methanol-water[3], this material had m.p. 112-114° (λ_{max}^{EtOH} 293 mμ, ε= 13,000; $\lambda_{max}^{CHCl_3}$ 3.0 (broad), 5.80, 5.94, 6.23 μ). Upon comparison with isocamphorquinone, m.p. 112-114°, prepared by the method of Levine[1], the two samples were found to be identical in all respects, and the mixed melting point was 112-114°.


I



II



III

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[3] Care must be taken in working with isocamphorquinone to prevent the decomposition which presumably accounted for its being termed "easily resinified." Contact with air causes colorless crystalline isocamphorquinone to become yellow and gummy within 24 hours, with an accompanying disappearance of its characteristic 293 mμ absorption band and appearance of a band at 260 mμ.

Isolating the initially-formed Michael adduct (III), b.p. 140-145°/0.35 mm. (n_D^{20} 1.4594; semicarbazone, m.p. 90-91°; Calcd. for $C_{16}H_{27}N_3O_5$: C, 56.29; H, 7.97; N, 12.31. Found: C, 56.09; H, 7.81; N, 12.36), and attempting subsequently to cyclize this purified product proved much less efficacious than the direct formation of II ($R=CH_2CH_3$) by use of more vigorous reaction conditions.

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