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1,2,3,4-Tetrahydro-2-hydroxy-α-methyl-1-naphthylideneacetic Acid γ-Lactone from the Condensation of β-Tetralone with Methyl α-Chloropropionate

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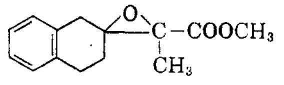
An attempted Darzens glycidic ester synthesis with β-tetralone and methyl α-chloropropionate yielded 1,2,3,4-tetrahydro-2-hydroxy-α-methyl-1-naphthylideneacetic acid γ-lactone (II) as the only readily-isolable product. The structure of II was proved by dehydrogenation to 2-hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone which was synthesized for comparison by an alternative route. Reduction of II yielded a new isomer of 1,2,3,4-tetrahydro-2-hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone (III) which could be isomerized to a known isomer. Configurations are proposed for the three known isomers of III.

For a study in progress in this laboratory, we required various 1-substituted 1-(β-naphthyl)-ethanes and we considered, briefly, the possibility of using the glycidic ester I as an intermediate in their preparation. To this end, we attempted a Darzens condensation between β-tetralone and methyl α-chloropropionate. The only readily-isolable product of the reaction, however, was not I but a lactone, the structure proof for which, along with ancillary observations on some structures derived therefrom, constitutes the subject of this paper. Some of the transformations involved are summarized in Fig. 1.



I

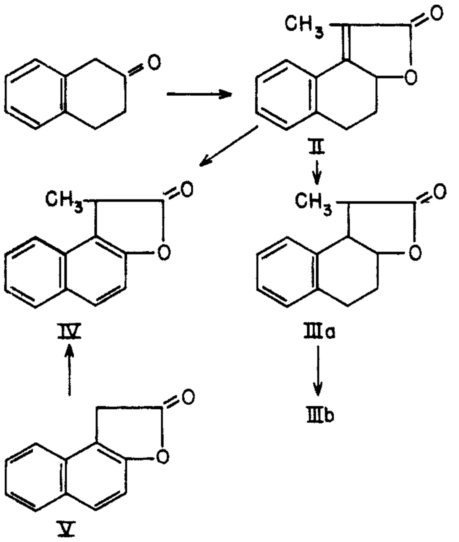


Fig. 1. Some reactions deriving from the condensation of β-tetralone with methyl α-chloropropionate

With sodium hydride as the condensing agent and benzene as the solvent, reaction between β-tetralone and methyl α-chloropropionate occurred readily, and there was isolated a crystalline substance, m.p. 153–154.5°, which obviously was not I. This substance had the elemental composition $C_{13}H_{12}O_2$, was neutral, but dissolved in hot alkali to yield a saponification equivalent of 196; within experimental error of that implied by its empirical formula. In the infrared, it exhibited carbonyl absorption at 1731 cm.$^{-1}$ and intense absorption at 1648 cm.$^{-1}$ which suggested carbonyl-conjugated unsaturation.[1] It possessed an ultraviolet spectrum remarkably similar to that of *trans*-cinnamic acid, with λ_{max} 272 mμ and λ_{min} 235 mμ. It readily added one mole of hydrogen to form a liquid dihydro derivative (IIIa) which exhibited carbonyl absorption in the infrared at 1756 cm.$^{-1}$ and possessed the ultraviolet spectrum of a simple benzene chromophore with λ_{max} 265 and 272 mμ, λ_{min} 238 and 269 mμ. On the bases of these observations and mechanistic consideration, the condensation product was tentatively identified as 1,2,3,4-tetrahydro-2-hydroxy-α-methyl-1-naphthylideneacetic acid γ-lactone (II).

When the condensation product was dehydrogenated with sulfur, there was obtained a compound, m.p. 121–124°, whose properties were in accord with the structure IV expected. It had the correct empirical formula, exhibited the high-frequency carbonyl absorption (1790 cm.$^{-1}$) associated with β,γ-unsaturated γ-lactones,[2] and possessed an ultraviolet spectrum similar to that of β-naphthol, with λ_{max} 227.5, 270.0, 280.0, 291.5, 315.0, 324.0, and 330.0 mμ. This compound proved to be identical with that prepared by methylation of the known[3,4] 2-hydroxy-1-naphthaleneacetic

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(1) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, John Wiley and Sons, Inc., New York, N. Y., 1958, p. 42.

(2) Ref. 1, p. 187.

(3) M. Julia and M. Baillarge, *Bull. soc. chim. France*, 640 (1953).

(4) D. S. Tarbell and B. Wargotz, *J. Am. Chem. Soc.*, 76, 5761 (1954).

acid γ-lactone (V), making unambiguous the structural assignments II and IV.

The formation of II by reaction of β-tetralone and methyl α-chloropropionate may be rationalized as outlined in Fig. 2 with the first step, *alkylation* of β-tetralone at the 1-position by methyl α-chloropropionate, defining the unexpected course of the reaction. Although formation of the 1-enolate from β-tetralone should be facile, we had anticipated little difficulty from side reactions involving this enolate ion since β-tetralone has been successfully employed as the ketone component in a Reformatsky condensation.[5] Obviously, however, II was derived from just such a reaction and, surprisingly, the reaction involved alkylation by the secondary (although activated) chloride function rather than acylation by the methyl ester function. The remaining steps in the sequence of Fig. 2 are straightforward and require only a catalytic amount of base which was present as sodium hydride and sodium methoxide. VII would be formed by *O*-acylation of the enolate ion derived from the 1-position of VI, and would be converted to II by simple prototropy.

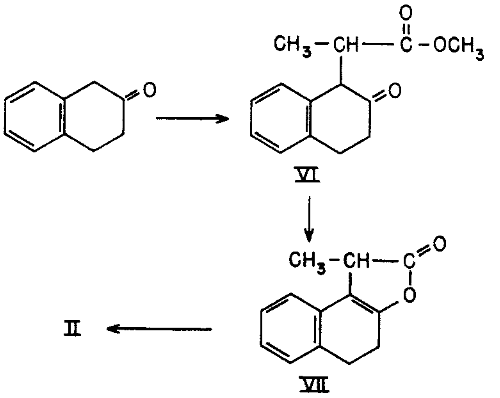

Fig. 2. A possible reaction path for the condensation of β-tetralone with methyl α-chloropropionate

As noted above, hydrogenation of II produced a liquid dihydro derivative IIIa which must be formulated as a 1,2,3,4-tetrahydro-2-hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone. Of the four racemates possible with this structure, two have been described[6]; IIIb, m.p. 121–121.5°, and IIIc, m.p. 152.5–153.5°. Although the configurations of the methyl groups were in doubt, the assignments of a *cis* ring fusion to IIIb and a *trans* ring fusion to IIIc were certainly correct. When our γ-lactone IIIa was treated with sodium ethoxide in ethanol it was converted into an isomeric γ-lactone, m.p. 118.0–119.5°, apparently the γ-lactone IIIb described by the previous workers.[6] The assumptions that hydrogenation of II involved *cis*-addition of hydrogen to the less hindered side of the double bond and that the all-*cis* isomer of III is less stable than the alternative *cis*-fused isomer lead to the configurations IIIa and IIIb as represented in Fig. 3. On the assumption that the acid treatment utilized for the isomerization of IIIc to IIIb[6] did not affect configuration at the position α to the acyl function,[7] the configuration of IIIc is that represented in Fig. 3.

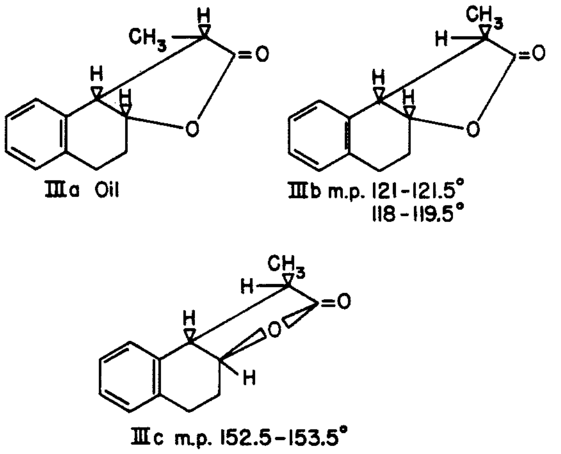

Fig. 3. Configurations of the three known 1,2,3,4-tetrahydro-2-hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactones

Preparation of lactone V has been described in the literature,[3] but we employed a more direct route which is recorded in the Experimental section. Methylation of lactone V was not quantitative. In addition to the desired methyl lactone IV, we obtained comparable quantities of unchanged V and the dimethyl lactone VIII, 1,2,3,4-tetrahydro-2-hydroxy-α,α-dimethyl-1-naphthaleneacetic acid γ-lactone.

The yield of lactone II from the condensation of β-tetralone and methyl α-chloropropionate was not high, and it is possible that a significant quantity of the desired glycidic ester I was present in the reaction mixture. However, isolation of I, if present, appeared to be a difficult task not readily amenable to large-scale operations, and we abandoned this approach to the preparation of 1-substituted-1-(β-naphthyl)ethanes.

EXPERIMENTAL[8]

The condensation of β-tetralone with methyl α-chloropropionate. 1,2,3,4-Tetrahydro-2-hydroxy-α-methyl-1-naphthylideneacetic acid γ-lactone (II). To a solution of β-tetralone[9] [14.6 g., 0.100 mole, b.p. 119° (8 mm.)], methyl α-chloropropionate (12.3 g., 0.100 mole) and dry benzene (150 ml.)

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[5] W. G. Dauben and R. Teranishi, *J. Org. Chem.*, 16, 550 (1951).

[6] E. E. van Tamelin, G. Van Zyl, and G. D. Zuidema, *J. Am. Chem. Soc.*, 72, 488 (1950).

[7] This assumption seems warranted in view of the paucity of examples of acid-catalyzed racemizations about asymmetric centers α to ester functions. The same structural assignment follows from consideration of steric interactions in transition states likely for ring closure to the lactone IIIc and, on the basis of steric interactions, appears to be the more stable of the two *trans*-fused isomers.

in a 500-ml. flask which was kept under a nitrogen atmosphere and cooled in an ice bath, was added 50% sodium hydride dispersion in paraffin oil[10] (4.8 g., 0.100 mole). The reaction mixture was stirred magnetically for 3 hr. at 0° and then was permitted to warm to room temperature. When hydrogen evolution had ceased, the reaction mixture was poured into 200 ml. of 0.05*N* hydrochloric acid and the organic layer was separated and dried over magnesium sulfate. After filtration and removal of solvent under reduced pressure, there was obtained an orange paste which was triturated with three 25-ml. portions of petroleum ether (b.p. 60–68°), each portion of petroleum ether being decanted after being cooled to 0°. The solid residue was crystallized from 95% ethanol to give II (6.12 g., 31%) as a light orange solid, m.p. 151–154°. The analytical sample, prepared by recrystallization from ethanol-water and sublimation, was a white solid, m.p. 153.0–154.5°.

Anal. Calcd. for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04; sapon. equiv., 200. Found: C, 77.71; H, 6.05; sapon. equiv., 196.

In the infrared (5% in chloroform), II exhibited absorption at 1731 (lactone carbonyl) and 1648 (carbonyl-conjugated unsaturation) cm.$^{-1}$. In the ultraviolet (95% ethanol), II had λ_{max} 272 (ϵ, 20,800) mμ and λ_{min} 235 (ϵ, 3,200) mμ.

2-Hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone (IV) *from the dehydrogenation of* II. An intimate mixture of II (0.403 g., 2.02 mmoles) and sulfur (0.081 g., 2.53 mmoles) was heated at 240–270° until evolution of gas ceased, and the dark red, gummy residue was then chromatographed on 40 g. of silica gel. There was eluted with 40% methylene chloride in carbon tetrachloride a red solid which, after sublimation and crystallization from *n*-heptane, amounted to 0.119 g., (30%) of IV as white crystals, m.p. 116–121°. This material was identical, by the criteria of mixture melting point and infrared spectral comparison, with the analytical sample of IV described below.

2-Hydroxy-1-naphthaleneacetic acid γ-lactone (V).[3,4] A heterogeneous mixture of 2-methoxy-1-naphthaleneacetonitrile[11] (18.0 g., m.p. 110.5–112.0°) and 48% hydrobromic acid (180 ml.) was heated under reflux for 12 hr. and then cooled and filtered. The precipitate was taken up in benzene (250 ml.), filtered to remove some insoluble red material, washed with three 100-ml. portions of 10% aqueous potassium bicarbonate and dried over magnesium sulfate. After filtration and removal of solvent under reduced pressure, there was obtained a yellow-green solid which was evaporatively distilled and then crystallized from *n*-heptane to yield V (12.6 g., 75%) as white crystals, m.p. 102.5–104.0° (lit.[4] m.p. 103.0–104.5°). In the infrared (5% in chloroform), V exhibited lactone-carbonyl absorption at 1796 cm.$^{-1}$.

Methylation of V. *2-Hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone* (IV) *and 2-hydroxy-α,α-dimethyl-1-naphthaleneacetic acid γ-lactone* (VIII). To a solution of V (3.68 g., 20 mmoles) and methyl iodide (14.0 g., 99 mmoles) in freshly-distilled tetrahydrofuran (100 ml.) contained in a 250 ml. flask under a nitrogen atmosphere and stirred magnetically, was added 50% sodium hydride dispersion in paraffin oil[10] (0.96 g., 20 mmoles). Hydrogen evolution was rapid and complete within 10 min. as the reaction mixture became warm. The reaction mixture was stirred at ambient temperature for 1.5 hr. and then volatile material was removed by evaporation under reduced pressure and the pale-green, pasty residue was chromatographed on 140 g. of silica gel. Fractions A and B were eluted, in order, with 40% methylene chloride in carbon tetrachloride, and fraction C was eluted with 40% carbon tetrachloride in methylene chloride.

Fraction A, after one crystallization from pentane, amounted to 0.91 g. (21% on lactone V) of *2-hydroxy-α,α-dimethyl-1-naphthaleneacetic acid γ-lactone* (VIII) as long white crystals, m.p. 98–99°. The analytical sample was prepared by recrystallization from pentane and sublimation, m.p. 97–100°, and exhibited lactone-carbonyl absorption in the infrared (5% in chloroform) at 1790 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.30; H, 5.90.

Fraction B, after one crystallization from *n*-heptane, amounted to 0.72 g. (18% on lactone V) of *2-hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone* (IV) as pale orange crystals, m.p. 117–121°. The analytical sample was obtained as stout white crystals, m.p. 121–124°, by two recrystallizations from *n*-heptane followed by sublimation. In the infrared (5% in chloroform), it exhibited lactone-carbonyl absorption at 1790 cm.$^{-1}$ and in the ultraviolet (95% ethanol) it had λ_{max} 227.5 (ϵ, 63,000), 270.0 (ϵ, 3,800), 280.0 (ϵ, 4,800), 291.5 (ϵ, 4,000), 315.0 (ϵ, 1,600), 324.0 (ϵ, 1,500), and 330.0 (ϵ, 1,900) mμ.

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.77; H, 5.09. Found: C, 78.52; H, 5.10.

Fraction C, after one crystallization from *n*-heptane, amounted to 0.87 g. (24% recovery) of the starting lactone V, m.p. 103–104°.

Hydrogenation of II. *1,2,3,4-Tetrahydro-2-hydroxy-α-methyl-1-naphthaleneacetic acid γ-lactone* (IIIa). A solution of II (0.667 g.) in glacial acetic acid (45 ml.) was hydrogenated at atmospheric pressure and 28° in the presence of 10% palladium/charcoal catalyst (0.10 g.). Hydrogen uptake ceased after 20 min. when 101% of theory for saturation of one double bond had been absorbed. The solution was filtered and acetic acid was removed by evaporation on the steam bath at the water aspirator. The residue was evaporatively distilled to yield IIIa (0.600 g., 89%) as a colorless, viscous liquid which exhibited lactone-carbonyl absorption in the infrared (5% in chloroform) at 1756 cm.$^{-1}$ and had, in the ultraviolet (95% ethanol), λ_{max} 265 (ϵ, 390) and 272 (ϵ, 390) mμ and λ_{min} 238 (ϵ, 71) and 269 (ϵ, 250) mμ.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 76.90; H, 6.97.

Isomerization of IIIa *to* IIIb. To a solution of IIIa (0.151 g.) in absolute ethanol (25 ml.) was added 2*M* sodium ethoxide in ethanol (0.20 ml.) and the homogeneous mixture was permitted to remain at room temperature for 19 hr. Ammonium chloride (0.10 g.) was then added and the mixture was evaporated to dryness under reduced pressure. The residue was taken up in boiling benzene (50 ml.), filtered from inorganic salts, and evaporated to dryness under reduced pressure. The pale yellow solid thus obtained was sublimed and then crystallized from methanol-water to yield IIIb (0.100 g., 66%) as long white needles, m.p. 118.5–119.5° (lit.[6] m.p. 121.0–121.5°). The analytical sample was obtained by sublimation, m.p. 118–119.5°, and exhibited lactone-carbonyl absorption in the infrared (5% in chloroform) at 1756 cm.$^{-1}$. In the ultraviolet (95% ethanol), it had λ_{max} 265 (ϵ, 370) and 272 (ϵ, 340) mμ and λ_{min} 237 (ϵ, 60) and 269 (ϵ, 230) mμ.

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.20; H, 6.98. Found: C, 77.35; H, 7.18.

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(8) We are indebted to Mr. William Saschek of this Department for the elemental analyses. Infrared spectra were taken on a Perkin-Elmer Model 21 infrared spectrophotometer and ultraviolet spectra on a Beckman DU spectrophotometer. Melting points were determined on a calibrated Fisher-Johns melting point apparatus.

(9) A. J. Birch, *J. Chem. Soc.*, 430 (1944).

(10) Metal Hydrides Inc.

(11) A. H. Cook, J. Downer, and B. Hornung, *J. Chem. Soc.*, 502 (1941).