Anal. Calcd. for $C_{32}H_{48}N_4O_7$ (600.74): C, 63.97; H, 8.05; N, 9.33. Found: C, 64.01; H, 8.16; N, 9.12.

The purified picrate, 140 mg., was taken up in ether and the yellow ethereal solution was washed with three small portions of aqueous ethanolamine[41] (*ca.* 5% v./v. ethanolamine). The combined yellow aqueous extracts were back-washed with two small portions of ether and the combined, colorless ethereal solutions were washed with water, saturated saline solution, dried (magnesium sulfate) and finally evaporated to give 65 mg. of colorless oil which solidified upon standing. Recrystallization from aqueous acetone afforded an analytical sample of 6-aza-5-cholestene (XII), m.p. 94.0–95.5° (Kofler hot-stage), $\lambda_{max}^{ethanol}$ none, $[\alpha]^{25}D$ −73.8; infrared (8% in carbon tetrachloride): no N–H stretching band, 1650 cm.$^{-1}$ ($>C=N$–stretching).

Anal. Calcd. for $C_{26}H_{45}N$ (371.63): C, 84.02; H, 12.21. Found: C, 84.15; H, 12.27.

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[41] L. Goodman, A. Benitez, C. D. Anderson and B. R. Baker, THIS JOURNAL, **80**, 6582 (1958).

[CONTRIBUTION FROM THE MCPHERSON CHEMISTRY LABORATORY OF THE OHIO STATE UNIVERSITY, COLUMBUS 10, OHIO

The Synthesis of 8-Hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene[1]

BY MELVIN S. NEWMAN AND ARLEN B. MEKLER[2]

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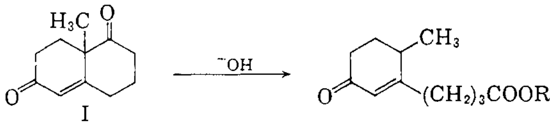
The conversion of 1,6-diketo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (I) to 8-hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene (III) by means of sodium methoxide in methanol is described; III forms a stable copper chelate with ease.

In connection with another problem, we wished to prepare a quantity of methyl γ-(6-methyl-3-keto-1-cyclohexen-1-yl)-butyrate (IIb). Since it was known[3] (and confirmed by us) that treatment of 1,6-diketo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (I) with aqueous alkali affords γ-(6-methyl-3-keto-1-cyclohexen-1-yl)-butyric acid (IIa), we sought to prepare IIb directly from I by treatment with sodium methoxide.

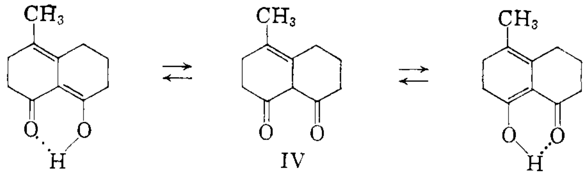


I

IIa, R = H
b, R = CH_3

When Compound I was treated with one equivalent of sodium methoxide in absolute methanol, the expected conversion to IIb was effected only in part. In addition there was obtained in over 90% yield a liquid compound, III, $C_{11}H_{14}O_2$, isomeric to I, which lacked absorption in the 3 and 5–6 μ regions.[4] The new compound absorbed at 233 and 344 mμ (log *E* 4.14 and 3.48, respectively) and formed a copper chelate derivative when treated with cupric acetate.

These facts suggested that III was best represented by the formulas III–IV–V.



III IV V

This formulation was supported by the following findings. Reduction of III with lithium aluminum hydride, followed by aromatization of the reduced product by heating with palladium-on-charcoal, afforded 1-methylnaphthalene in high yield. The lack of infrared absorption in the 5–6 μ region indicates that the diketonic form, IV, is present in minute amount, if at all. A study of the n.m.r. spectrum[5] indicated that either III or V are suitable structures but that it was not possible to distinguish between the two. Similarly, the ultraviolet absorption spectrum was of no aid in distinguishing between the two because of a lack of similar structures for comparison.[6] We believe our compound is best represented by structure 8-hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene (III) since treatment with excess methylmagnesium iodide followed by aromatization yielded almost pure 1,4-dimethylnaphthalene.

The crude product obtained from reaction of III with methylmagnesium iodide afforded a red 2,4-dinitrophenylhydrazone in high, but not exactly determined, yield. The red color indicates that the derivative is that of 5,8-dimethyl-8-hydroxy-1-keto-1,2,3,4,5,6,7,8-octahydronaphthalene (VIII), but no further structure proof was attempted.

When a solution of crude III was refluxed in xylene solution for 36 hours, a small amount of 8-keto-4-methyl-5,6,7,8-tetrahydro-1-naphthol (VI) was produced. This result, however, was not always obtained as all samples of crude III did not yield VI on similar treatment. Reduction of VI afforded 4-methyl-5,6,7,8-tetrahydro-1-naphthol[7] (VII).

The conversion of I to III (etc.), an intramolecular transacylation, by sodium methoxide is readily explained as shown.

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[1] This work is taken from the Ph.D. Thesis of A.B.M., Ohio State University, 1959.

[2] Holder of a Charles F. Kettering Foundation Fellowship, 1956–1957, U. S. Industrial Co. Fellowship, 1957–1958, and Allied Chemical Co. Fellowship, 1958–1959. This work was also supported in part by funds donated to the Chemistry Department by the E. I. du Pont de Nemours Co.

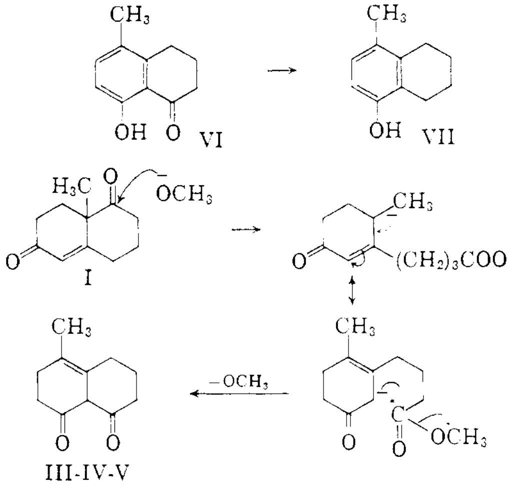
[3] N. L. Wendler, H. L. Slates and M. Tishler, THIS JOURNAL, **73**, 3816 (1951).

[4] On treatment with sodium methoxide, IIb, prepared by acid-catalyzed esterification of IIa, affords III in high yield.

[5] We thank Dr. G. V. D. Tiers of the Minnesota Mining and Manufacturing Co., St. Paul, Minn., for this determination and interpretation of the result.

[6] The only other 1,8-diketohydronaphthalene structure known to us is 1,8-diketodecahydronaphthalene (also undoubtedly completely enolized); see H. Stetter and U. Milbers, *Ber.*, **91**, 977 (1958).

[7] R. B. Woodward and T. Singh, THIS JOURNAL, **72**, 494 (1950). We thank Dr. Woodward for sending us a sample which proved identical to VII.



The product is present as an anion which on acidification is converted into III (IV, V). Interestingly, if the cooled reaction mixture is treated with only a small amount of water, it is possible to isolate III as a solid sodium salt which can be dissolved in warm water. On treatment with dilute acid III is formed.

Experimental[8,9]

2-Methyl-1,3-cyclohexanedione.—A freshly prepared solution of 432 g. (10.8 moles) of sodium hydroxide, 1500 ml. of water and 990 g. (9.0 moles) of resorcinol was placed in a 3-l. hydrogenation bomb together with 180 g. of finely powdered Raney nickel catalyst.[10] The hydrogenation was carried out under 1800 lb. of hydrogen for 12 hours without the application of external heating. The temperature was adjusted to 50° and the reaction was continued until a total of 9.0 moles of hydrogen had been absorbed. After cooling to room temperature, the catalyst was removed by filtration and washed with two 200-ml. portions of water. The filtrate and washings were transferred to a 5-l. round-bottomed flask and treated with 150 ml. of concentrated hydrochloric acid (for partial neutralization), 650 ml. of dioxane and 1500 g. (9.5 moles) of methyl iodide. The reaction mixture was refluxed for 14 hours, allowed to cool, and the dione which crystallized was collected by filtration. The mother liquors were concentrated *in vacuo* to one-half of the original volume and then cooled in an ice–salt-bath to yield additional dione. The total yield of the dione, m.p. 200–203° dec., was 700 g. (61%).

4-Diethylamino-2-butanone.—To 115 g. (1.08 moles) of diethylamine, 100 g. (1.17 moles) of methyl vinyl ketone[11] was added dropwise with stirring over a 1-hour period, maintaining the temperature of the reaction mixture below 0° by means of an ice–salt-bath. After the addition was completed, the cooling bath was removed and the stirring was continued for 7 hours, while the temperature was allowed to rise to 25–30°. The reaction mixture was fractionally distilled through a 10-inch packed column topped with a total condensation partial take-off head to yield 150 g. (73%) of colorless 4-diethylamino-2-butanone, b.p. 69–73° (16 mm.). Redistillation of the liquid collected in the Dry Ice–acetone trap yielded 31 g. more of the desired Mannich base. The total yield was 181 g. (88%).

1,6-Diketo-8a-methyl-1,2,3,4,6,7,8,8a-octahydronaphthalene (I).—A mixture of 100 g. of 2-methyl-1,3-cyclohexanedione, 40 ml. of triethylamine, 135 g. of 4-diethylamino-3-butanone and 750 ml. of benzene was refluxed on a steam-bath for 18 hours, 30 ml. of water being separated during the course of the reaction by means of a phase-separating head. During the last 3 hours 250 ml. of benzene was distilled. The dark reaction mixture was cooled to room temperature and washed with 800 ml. of 10% hydrochloric acid and then treated in the usual manner. Distillation of the dark-red oil gave 106 g. of a light-yellow oil, b.p. 109–115° (0.05 mm.), and 15 g. of a higher boiling fraction, b.p. 115–150° (0.05 mm.) The lower boiling fraction was cooled in ice until it solidified, triturated with about 40 ml. of ether and filtered to give 66 g. of crystalline I, m.p. 47–48°. An additional 13 g. of I was obtained by diluting the ether filtrate with petroleum ether (b.p. 30–60°) and cooling in ice. An additional 14.1 g. of diketone was obtained from this filtrate by means of oximation. The total yield of I was 93.1 g. (66%).

A sample of I, m.p. 47–48° dec., obtained after two recrystallizations from ether absorbed at 242 mμ (log *E* 4.20) and at 5.82 and 5.98μ.

8-Hydroxy-1-keto-4-methyl-1,2,3,5,6,7-hexahydronaphthalene (III). (A) **From I.**—A solution of 17.80 g. of I and three equivalents of sodium methoxide in 100 ml. of *absolute* methanol[12,13] was refluxed under nitrogen for 4 hours. The cooled reaction mixture was neutralized with hydrogen chloride and treated as usual to yield 16.6 g. (93%) of III, b.p. 105–106° at 0.5 mm. A later experiment[14] showed that if slightly more than one equivalent of sodium methoxide were used, the yield of III was comparable. In some experiments a mixture of III and IIb was obtained. However, this mixture could be treated again with sodium methoxide and converted into III.

Compound III formed a copper chelate in the usual manner. This derivative formed beautiful dark, almost black, shining crystals, the melting point of which varied with the rate of heating in the range 191–215°. This chelate absorbed at 336 mμ (log *E* 4.34).

Anal. Calcd. for $C_{11}H_{14}O_2$: C, 74.2; H, 7.9. Found: C, 73.9; H, 7.9. Calcd. for $C_{22}H_{26}O_4Cu$: C, 63.2; H, 6.3. Found: C, 63.4; H, 6.2.

The 2,4-dinitrophenylhydrazone of III formed dark red elongated prisms, m.p. 213–214° dec.

Anal. Calcd. for $C_{17}H_{18}N_4O_5$: C, 60.4; H, 5.3; N, 16.6. Found: C, 60.5; H, 5.2; N, 16.2.

(B) **From IIb.**—A solution of 20.12 g. of IIb (see below) in 300 ml. of *absolute* methanol containing a slight excess of sodium methoxide was refluxed for 4 hr. under nitrogen. After a conventional workup, III was obtained in 93% yield.

Methyl γ-(6-Methyl-3-keto-1-cyclohexen-1-yl)-butyrate (IIb).—The free acid IIa was obtained from I by treatment with aqueous alcoholic alkali essentially as described.[3] However, we obtained a polymorphic form of IIa, m.p. 55–56°, which was converted into the form reported,[3] m.p. 79–80°, on grinding with the high melting form. The infrared spectra of the two forms were almost, but not quite, identical when measured in potassium bromide. The acid IIa was converted into the methyl ester, IIb, b.p. 92–93° at 0.4 mm., in 93% yield by acid-catalyzed esterification.[14]

Anal. Calcd. for $C_{12}H_{18}O_3$: C, 68.5; H, 8.6. Found: C, 68.4, 68.5; H, 8.6, 8.8. Compound IIb formed a red 2,4-dinitrophenylhydrazone, m.p. 90–91°.

Anal. Calcd. for $C_{18}H_{22}N_4O_6$: C, 55.4; H, 5.7; N, 14.4. Found: C, 55.6; H, 5.8; N, 14.4.

8-Keto-4-methyl-5,6,7,8-tetrahydro-1-naphthol (VI).—A solution of 1.00 g. of III in 50 ml. of xylene was refluxed for 36 hours. Distillation of the reaction mixture *in vacuo* yielded 0.18 g. (19%) of VI, b.p. 134–135° (0.5 mm.), plus 0.78 g. (78%) of starting diketone.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 75.0; H, 7.0. Found: C, 74.8; H, 7.0.

Subsequent similar runs did not always lead to the formation of VI.

Formation of 1-Methylnaphthalene from III.—A solution of 10.68 g. of III in 60 ml. of anhydrous ether was added dropwise with stirring during one hour to a suspension of

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[8] All melting points uncorrected unless otherwise noted.

[9] All microanalyses by Galbraith Microanalytical Laboratory, Knoxville, Tenn.

[10] "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 181.

[11] The methyl vinyl ketone (technical grade) was used as supplied by Matheson, Coleman and Bell.

[12] If strictly anhydrous conditions were not maintained, more or less of ketoacid IIa was obtained.

[13] Absolute methanol was prepared by refluxing a solution of 5 l. of methanol in which 12 g. of sodium had been dissolved and to which 92 g. of dimethyl phthalate had been added. Distillation afforded absolute methanol.

[14] We are indebted to Mr. S. Ramachandran for these experiments.

3.36 g. of lithium aluminum hydride in 120 ml. of ether. After the addition was completed, the reaction mixture was stirred for 4 hours, and the excess hydride was then destroyed by the addition of wet ether, followed by dilute hydrochloric acid to dissolve the aluminum salts. The organic layer was separated, the aqueous layer extracted with ether and the combined fractions treated in the usual manner. Upon concentration of the ethereal solution there was obtained 7.20 g. (72%) of an oil, b.p. 94–98° (0.15 mm.), which showed infrared absorption at 3.0 and 5.98 μ. Possibly this oil was 8-hydroxy-1-keto-4-methyl-1,2,3,4,5,6,7,8-octahydronaphthalene, but no attempt was made to purify it or determine the structure.

To 7.2 g. of the above oil in a 25-ml. Claisen flask was added 50 mg. of palladium-on-charcoal[15] and the mixture heated to 220–230° for 3 hours. The reaction mixture was then distilled *in vacuo* to yield 4.73 g. (82%) of 1-methylnaphthalene, b.p. 112–114° (14 mm.), which formed a picrate,[16] m.p. 141.5–142.0°, which was undepressed on mixing with an authentic sample.

4-Methyl-5,6,7,8-tetrahydro-1-naphthol (VII).—A mixture of 0.44 g. of VI, 1.3 g. potassium hydroxide, 3 g. of 85% hydrazine monohydrate and 35 ml. of redistilled diethylene glycol was heated. The distillate was removed until the solution temperature reached 196°. The solution was refluxed until the nitrogen evolution had decreased sharply (about 4 hours). The warm reaction mixture was poured on to 50 ml. of ice and 33 ml. of 6 *N* hydrochloric acid. The mixture was then extracted with ether–benzene and the combined organic extracts treated in the usual manner. Concentration of the organic solution yielded 0.369 g. of the tetralol. Recrystallization from petroleum ether (b.p. 30–60°) gave 0.328 g. (81%) of colorless crystals of VII, m.p. 87.5–88.5°.

The X-ray powder diffraction photograph of VII was identical to that of authentic material.[7]

4,8-Dimethyl-8-hydroxy-1-keto-1,2,3,4,5,6,7,8-octahydronaphthalene (VIII).—A solution of 9.4 g. of III in 75 ml. of dry ether was added dropwise with stirring during one hour to 200 ml. of approximately 1.25 *M* methylmagnesium iodide. The reaction mixture was refluxed with stirring for 2 hours, cooled, and then poured onto an ice–hydrochloric acid mixture. The mixture was extracted with ether–benzene and the combined organic fractions treated in the usual manner. Distillation afforded 9.3 g. (89%) of an oil, b.p. 104–105° (1 mm.), which yielded a red 2,4-dinitrophenylhydrazone, m.p. 243–245° dec. For this reason the oil is assumed to have structure VIII with the double bond conjugated to the carbonyl group. However, since no ultraviolet absorption spectral measurements were made, we cannot be sure that in the hydroxy ketone, the double bond was not conjugated.

Anal. Calcd. for $C_{18}H_{22}N_4O_5$: C, 56.5; H, 5.8; N, 16.3. Found: C, 56.7; H, 5.7; N, 16.3.

1,4-Dimethylnaphthalene.—A mixture of 9.2 g. of VIII and 50 mg. of palladium-on-charcoal[15] was heated to 220–230° for 4 hours. The reaction mixture was distilled to yield 3.18 g. (43%) of 1,4-dimethylnaphthalene, b.p. 107–110° (1 mm.), which formed a 1,3,5-trinitrobenzene addition compound, m.p. 165–166°, and a picrate, m.p. 143.5–144°, alone and mixed with authentic material.[17]

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[15] The catalyst was supplied by Baker Catalyst Co., Newark, N. J.

[16] G. Darzens, *Compt. rend.*, **183**, 748 (1926), reports a m.p. of 141–142° for the picrate of 1-methylnaphthalene.

[17] M. C. Kloetzel, THIS JOURNAL, **62**, 1708 (1940), reports m.p. 143–144° for the picrate of 1,4-dimethylnaphthalene and m.p. 165–166° for the TNB derivative.

[CONTRIBUTION FROM THE DEPARTMENT OF AGRICULTURAL CHEMISTRY, KYOTO UNIVERSITY, KYOTO, JAPAN]

Electronic Structure and Plant Growth Activity of Substituted 1-Naphthoic Acid Derivatives[1,2]

BY KOICHI KOSHIMIZU, TOSHIO FUJITA AND TETSUO MITSUI

RECEIVED SEPTEMBER 28, 1959

The relationship between plant growth activity of the substituted 1-naphthoic acid derivatives reported in the preceding paper[2] and the reactivity indices of these acids calculated by a molecular orbital method has been discussed. The ability of substituted 1-naphthoic acids to form a molecular complex of a charge-transfer type at the 8-position with plant substrates appears to be a very important factor determining the plant growth activity.

Introduction

The prominent plant growth activity found in certain halogeno-benzoic acids,[3,4] has stimulated many studies of the relationship between chemical structure and growth activity of substituted benzoic acid derivatives.[5–11] Substituted 1-naphthoic acid derivatives have however not been studied so extensively. Studies on substituted naphthoic acids may contribute to an understanding of the structural requirement for growth promoting activity, since these two series, in which a carboxyl group is bound directly to the aromatic ring, seem to be similar in their modes of action.

In the study reported in the preceding paper,[2] 1-naphthoic acid derivatives substituted with a chlorine, bromine, methyl or nitro group in various positions were prepared and their growth activities were measured. The growth activity was intensified by 2- or 8-halo- and 8-methyl substitution, while it was reduced in the other acids, some of them being inactive.

Veldstra and his co-workers[12–15] have affirmed that the action of the growth substance is of physico-chemical nature, the function of the nuclear ring system being considered to be an adsorption to the cellular interface caused by several weak bonds,

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[1] Published as Part XIV of Studies on the Plant Growth Substances. Presented before the monthly meeting of Kansai Branch of the Agricultural Chemical Society of Japan, Kyoto, Sept., 1959.

[2] Part XIII in series: K. Koshimizu, T. Fujita, T. Mitsui and J. Kato, *Bull. Agr. Chem. Soc. Japan*, in press.

[3] P. W. Zimmerman and A. E. Hitchkock, *Contrib. Boyce Thompson Inst.*, **12**, 321, 491, 497 (1942).

[4] J. A. Bentley, *Nature*, **165**, 449 (1950).

[5] K. V. Thimann, *Plant Physiol.*, **27**, 392 (1952).

[6] H. Veldstra, *Rec. trav. chim. Pays-Bas*, **71**, 15 (1952).

[7] H. Veldstra and C. van de Westeringh, *ibid.*, **71**, 318 (1952).

[8] H. Veldstra, "The Chemistry and Mode of Action of Plant Growth Substances," Butterworths Scientific Publications, London, 1955, p. 117.

[9] R. M. Muir and C. Hansch, *Plant Physiol.*, **26**, 369 (1951).

[10] C. Hansch, R. M. Muir and R. L. Metzenberg, *ibid.*, **26**, 812 (1951).

[11] R. M. Muir and C. Hansch, *ibid.*, **28**, 218 (1953).

[12] H. Veldstra, *Enzymol.*, **11**, 97, 137 (1944).

[13] H. Veldstra, *Biochim. Biophys. Acta*, **1**, 364 (1947).

[14] H. Veldstra and H. L. Booij, *ibid.*, **3**, 278 (1949).

[15] H. Veldstra, *Ann. Rev. Plant Physiol.*, **4**, 151 (1953).