The Isolation of Dihydromexicanin E from *Helenium autumnale L.*

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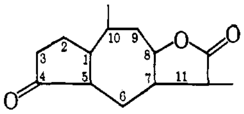
Recently we had occasion to extract a batch of *Helenium autumnale* L. seeking a supply of the sesquiterpene lactone, helenalin, for use in chemical studies.[1] The plants were obtained in late summer, 1963, in the vicinity of Chapel Hill, North Carolina.[2] They were air-dried and 7 kg. of finely ground leaves and stems was extracted in the usual way with methylene chloride.[3] After treatment of an alcoholic solution of the crude extract with aqueous lead acetate, the clarified aqueous alcoholic solution was partially evaporated and extracted with methylene chloride. When attempted crystallization of the dried extract from benzene failed to produce helenalin, as expected, the material was subjected to chromatography in benzene on II–III Activity Woelm neutral alumina. Repeated chromatography of the benzene eluates yielded 14.9 g. of a product which crystallized from ethyl acetate. Repeated crystallization from the same solvent afforded colorless rods, m.p. 133–135°, $[\alpha]^{25}\mathrm{D}$ $-188°$ ($CHCl_3$), $\lambda_{\max}^{\mathrm{EtOH}}$ 222 mμ (ϵ 10,400), $\lambda_{\max}^{\mathrm{NaOH}}$ 242 mμ; ν^{Nujol} 1760 (γ-lactone), 1700, and 1586 (cyclopentenone) cm.$^{-1}$.

The n.m.r. spectrum,[4] τ 7.80 dd (H-2), 6.25 dd (H-3), 4.60 c (H-8), and 1.23 d and 1.13 d (C-10 and C-11 methyl), suggested a norsesquiterpenoid structure.

Anal. Calcd. for $C_{14}H_{18}O_3$; C, 71.77; H, 7.74. Found: C, 71.79; H, 7.84.

Finally, comparison of published data for dihydromexicanin E[5] pointed to the identification of our substance.



Dihydromexicanin E

Through the courtesy of Dr. J. Romo, University of Mexico, Mexico City, Mexico, a sample of dihydromexicanin E was obtained for direct comparison and proved to be identical by the usual criteria. As far as we know, this represents the first isolation of this substance from plant material. It is interesting that no helenalin could be isolated from this sample of *Helenium autumnale* L. inasmuch as it is usually the principal sesquiterpene component.[6]

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[1] R. A. Lucas, S. Rovinski, R. J. Kiesel, L. Dorfman, and H. B. MacPhillamy, *J. Org. Chem.*, **29**, 1549 (1964).

[2] The plant material was collected and identified by H. E. Ahles, Botany Department, University of North Carolina, Chapel Hill, N. C., to whom our thanks are due.

[3] E. P. Clark, *J. Am. Chem. Soc.*, **58**, 1982 (1936).

[4] This was run in deuteriochloroform solution on a Varian A-60 n.m.r. spectrometer using tetramethylsilane as internal reference; multiplets are described: d, doublet; dd, doublet of doublets; c, complex band whose center is given.

[5] A. Romo de Vivar and J. Romo, *J. Am. Chem. Soc.*, **83**, 2326 (1961); J. Romo, A. Romo de Vivar, and W. Herz, *Tetrahedron*, **19**, 2317 (1963).

[6] E. P. Clark, *J. Am. Chem. Soc.*, **58**, 1982 (1936); **61**, 1836 (1939); **62**, 597 (1940).

Bromination of 6-Benzoyl-2,5-diphenyl-2-phenylglyoxoyl-3,4-dihydro-2H-pyran

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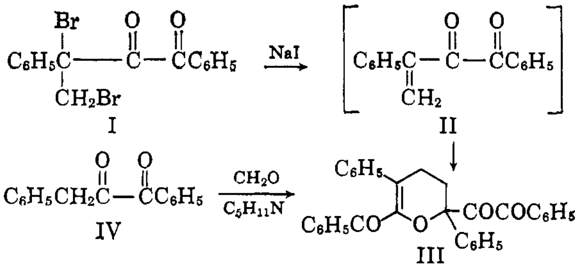
Treatment of 3,4-dibromo-1,3-diphenyl-1,2-butanedione (I) with sodium iodide in acetone previously[2] was reported to produce a dimeric substance which was formulated as 6-benzoyl-2,5-diphenyl-2-phenylglyoxoyl-3,4-dihydro-2H-pyran (III). The structural assignment was based primarily on the elemental analysis,[3] molecular weight of the material, and the analogy to other dimers of similar and proven structure.[3] Presumably III arose *via* the dimerization of 1,3-diphenyl-3-butene-1,2-dione (II) although II could not be isolated. Additional support for this view was obtained by the production of III from the reaction of 1,3-diphenyl-1,2-propanedione (IV) with formaldehyde in the presence of a catalytic amount of piperidine.



Treatment of III with 1 equiv. of bromine in dry carbon tetrachloride provided hydrogen bromide and a yellow solid (V, $C_{32}H_{22}O_4$) in 74.6% yield. The same substance could be generated from III using excess bromine or N-bromosuccinimide.

The ultraviolet spectrum of V, $\lambda_{\max}$ 250 mμ (ϵ 30,550), 357 (16,500), indicated considerable unsaturation; however, no tractable hydrogenation product could be obtained. Although oxidation of V with periodic acid or ozone provided no information as to the nature of V, treatment of the substance with alkaline hydrogen peroxide provided 2 equiv. of benzoic acid and a high melting acid (VI, $C_{18}H_{14}O_4$).

The dibasic nature of VI was confirmed by the formation of a dimethyl ester (VII) when VI was treated with excess diazomethane. Hydrogenation of VII provided a mixture of diastereoisomers. Decarboxylation of VI was accomplished smoothly using a copper–quinoline catalyst at 220°. Chromatography of the product provided *trans*-1,4-diphenyl-1,3-butadiene (VIII), identical in all respects with an authentic sample. On the basis of these conversions, the bromination product (V) can be formulated as 1,3,6,8-tetraphenylocta-3,5-diene-1,2,7,8-tetraone.

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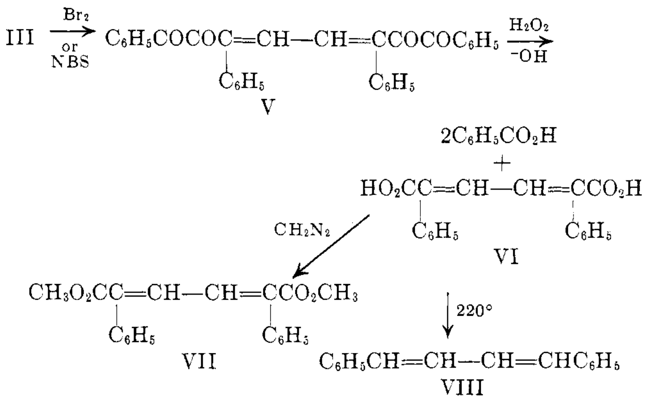
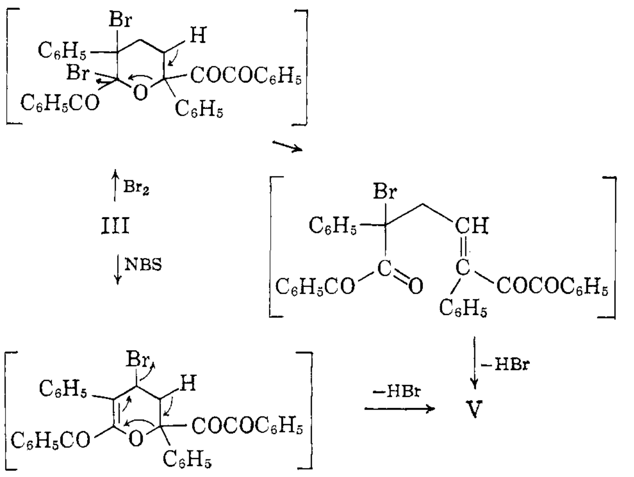
[1] Abstracted in part from a dissertation by R. L. Smith submitted to the University of North Carolina in partial fulfillment of the requirements for the Ph.D. degree, June, 1962.

[2] C. L. Stevens and R. G. Hiskey, *J. Org. Chem.*, **24**, 32 (1959).

[3] K. Alder and E. Ruden, *Ber.*, **74**, 920 (1941); C. Mannich, *ibid.*, **74**, 557 (1941); H. Fiesselmann and F. Meisel, *ibid.*, **89**, 657 (1956).



The formation of V from III may be rationalized by several pathways. One possibility would involve the following scheme. The isolation of V from III provides definite evidence for the previous assignment of III.



Experimental[4]

Preparation of 6-Benzoyl-2,5-diphenyl-2-phenylglyoxoyl-3,4-dihydro-2H-pyran (III).—To 18.2 g. (0.081 mole) of 1,3-diphenyl-1,2-propanedione[5] in 80 ml. of methanol was added 25 ml. (0.29 mole) of 37% formalin solution. The mixture was heated to reflux and 0.5 ml. of piperidine in 10 ml. of methanol was added in 5 min. The solution was refluxed 3 hr., poured into water, and extracted with methylene chloride. The organic extract was washed with successive portions of dilute sulfuric acid, 5% sodium bicarbonate solution, and water. Removal of the solvent provided a yellow oil which was heated 10 hr. at 95°. The oil was then triturated with methanol and yielded a yellow solid which was recrystallized from a benzene-*n*-heptane mixture to afford 2.1 g. (11.5%) of dense yellow prisms, m.p. 132–134°. A mixture melting with a sample of III obtained[2] from I melted at 132–134°.

Bromination of 6-Benzoyl-2,5-diphenyl-2-phenylglyoxoyl-3,4-dihydro-2H-pyran (III).—Treatment of 2.0 g. (4.2 mmoles) of III in 100 ml. of refluxing dry carbon tetrachloride with 1.0 g. (6.25 mmoles) of bromine in 50 ml. of carbon tetrachloride provided 1.47 g. (74.6%) of yellow needles, m.p. 166–167° after recrystallization from a benzene-*n*-heptane mixture, lit.[2] m.p. 162–163°.

Anal. Calcd. for $C_{32}H_{22}O_4$: C, 81.68; H, 4.71. Found: C, 81.51; H, 4.62.

When 0.60 g. (1.28 mmoles) of III was treated with a solution of 0.23 g. (1.28 mmoles) of N-bromosuccinimide in carbon tetrachloride containing a trace of benzoyl peroxide, hydrogen bromide was evolved copiously. Purification of the resulting solid provided 0.42 g. (70.0%) of V.

Oxidation of V with Alkaline Hydrogen Peroxide.—A solution of 2.0 g. (4.3 mmoles) of V in 35 ml. of purified dioxane was treated with 5 ml. of 30% hydrogen peroxide. To this solution was added 2.3 ml. of 20% sodium hydroxide solution. The addition was carried out drop-wise over a 30-min. period. The solution was stirred overnight, the solvent removed, and the residue was dissolved in water. Acidification of the aqueous solution provided 1.87 g. (85%) of acidic material. Sublimation of the resulting solid afforded 0.97 g. of benzoic acid and 0.90 g. of an acid melting above 300°. The high melting acid (VI) exhibited a maximum at 316 mμ (ε 20,250).

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.45; H, 4.79. Found: C, 73.28; H, 4.61.

A 0.90-g. (0.30 mmole) sample of VI was suspended in 25 ml. of dry ether and treated with excess diazomethane solution. Filtration and removal of the solvent afforded 0.85 g. (88.1%) of solid ester. Recrystallization from a benzene–petroleum ether mixture gave VII as needles, m.p. 178–179°; λ_{max} 321 mμ (ε 18,750).

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.52; H, 5.63. Found: C, 74.47; H, 5.64

Hydrogenation of 1,4-Dicarbomethoxy-1,4-diphenyl-1,3-butadiene (VII).—A solution containing 0.15 g. (0.47 mmole) of VII in 30 ml. of ethyl acetate consumed 23.0 ml. of hydrogen when stirred at room temperature and atmospheric pressure with 0.10 g. of 10% palladium-on-charcoal catalyst. Recrystallization of the resulting solid from *n*-heptane provided dense prisms melting indefinitely from 95–112°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.59; H, 6.80. Found: C, 73.88; H, 6.67.

Decarboxylation of 1,4-Dicarboxy-1,4-diphenyl-1,3-butadiene (V).—To 0.60 g. (2.05 mmole) of V was added 0.125 g.-atom of copper powder and 5 ml. of quinoline. The mixture was heated at 220° for 6 hr., diluted with ether, and filtered; the quinoline was removed by extraction with dilute hydrochloric acid. The ether extract was washed with sodium bicarbonate and water. Removal of the solvent provided a yellow oil which was dissolved in petroleum ether and chromatographed on neutral alumina. Elution with petroleum ether provided 0.275 g. of colorless solid, m.p. 145–149°. Recrystallization from benzene–ethanol afforded colorless crystals of VIII, m.p. 152–153°. A mixture melting point with an authentic sample[6] of VIII was not depressed.

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[4] Melting points are uncorrected. Elemental analysis were by Spang Microanalytical Laboratory, Ann Arbor, Mich., and Micro-Tech Laboratories, Skokie, Ill.

[5] H. Fiesselmann and J. Ribka, *Ber.*, **89**, 27 (1956).

[6] B. B. Corson, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 229.

Overreduction of Naphthalenic Diethers

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The Birch reaction is a standard method for converting aromatic ethers into unsaturated alicyclic ketones.[1] The reduction of di- and tetrahydronaphthalenic *monoethers* is a basic step in many schemes for the total synthesis of terpenes and steroids. In contrast, the conversion of naphthalenic *diethers* into bicyclic ketones has been almost ignored; to date only 2,6-dimethoxynaphthalene, 2,6-diethoxynaphthalene, and 1,5-dimethoxynaphthalene are known to be reducible in sodium–liquid ammonia solution in the presence of ethanol.[2] Both 2,6-diethers afford the expected 2,6-dialkoxy-1,4,5,8-tetrahydronaphthalenes

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[1] For a comprehensive review of this entire field, see H. Smith, "Organic Reactions in Liquid Ammonia," John Wiley and Sons, Inc., New York, N. Y., 1963, pp. 245–279.

[2] M. Kocor and W. Kotlarek, *Bull. Acad. Polon. Sci. Ser. Sci. Chim.*, **9**, 507 (1961).