N,N'-Di-*n*-butyl-*p*-phenylenediamine

By John V. Capinjola

This compound was prepared by essentially the same procedure as that described by Michaelis, Schubert and Granick[1] for the preparation of the corresponding methyl derivative.

Twenty-five grams of N,N'-di-*p*-toluenesulfonyl-*p*-phenylenediamine, obtained by the reaction of *p*-phenylenediamine with *p*-toluenesulfonyl chloride, was dissolved in dilute (3%) sodium hydroxide solution and treated with 55 g. of *n*-butyl sulfate. The mixture was heated under reflux for several hours, after which the alkylated product was isolated in the usual manner; yield 47%; recrystallized from methyl alcohol, m.p. 132–132.5°.

Anal. Calcd. for $C_{28}H_{36}O_4N_2S_2$: S, 12.14. Found: S, 12.19.

N,N'-Di-*n*-butyl-*p*-phenylenediamine was obtained by hydrolysis of 13.5 g. of the above compound at 90° with a mixture of 20 ml. of glacial acetic acid and 40 ml. of concentrated sulfuric acid; yield 91%. Treatment with activated carbon followed by sublimation *in vacuo* at 100° produced colorless crystals, m.p. 53.2–53.8°.

The identity of the product was confirmed by analysis of the dihydrochloride salt.

Anal. Calcd. for $C_{14}H_{26}N_2Cl_2$: Cl, 24.21. Found: Cl, 24.15.

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[1] Michaelis, Schubert and Granick, This Journal, 61, 1989 (1939).

Ethyl Corporation
Research Laboratories
Detroit, Michigan

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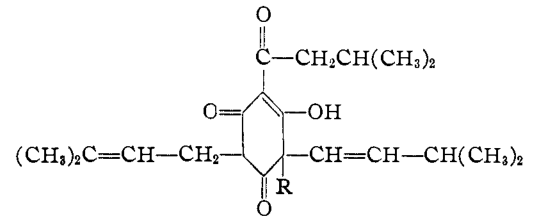
The Synthesis and Absorption Spectra of Some Analogs of Humulon[1]

By Tod W. Campbell and Galvin M. Coppinger

Humulon (I) and lupulon (II) are two substances isolated from hops (*Humulus lupulus*)

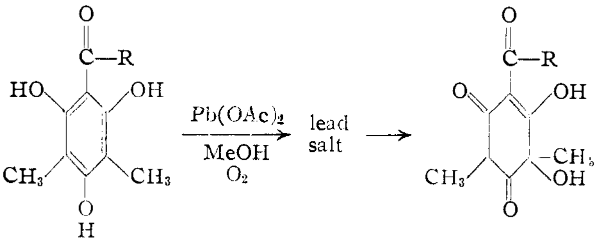


I, R = —OH
II, R = —CH=CH—CH(CH₃)₂

whose structures were elucidated by Wieland and Wollmer and their co-workers.[2]

In view of the recent interest in humulon and lupulon as antibiotics and tuberculostatic agents,[3] two analogs of humulon have been prepared, and their spectra compared with that of humulon. The similarity of the spectra is added confirmation for the structure of humulon itself, which has yet to be synthesized.

They were synthesized by acylating dimethylphloroglucinol by the Hoesch method[4] to give dimethylacylphloroglucinol (III). A methanol solution of this substance, in the presence of lead acetate, readily absorbed oxygen to give an insoluble lead salt (IV),[2] which was then decomposed with sulfuric acid to give (V), acyl-3,5-dimethyl-2,3-dihydroxy-4,6-diketocyclohexene-1.



III IV V

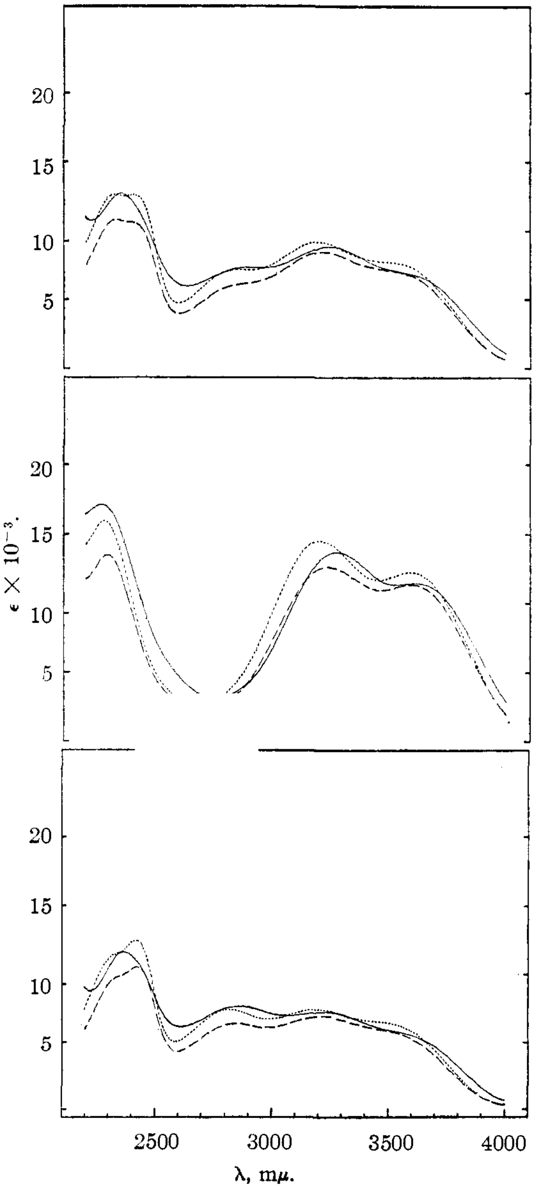


Fig. 1.—Absorption spectra: top, neutral; middle, basic; bottom, acidic; ——, humulon; — —, butyro-3,5-dimethyl-2,3-dihydroxy-4,6-diketocyclohexene-1; . . . aceto-3,5-dimethyl-2,3-dihydroxy-4,6-diketocyclohexene-1.

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[1] Article not copyrighted.

[2] H. Wieland, *Ber.*, 58, 2012; 102 (1925); H. Wieland and E. Martz, *ibid.*, 59, 2352 (1926); W. Wollmer, *Ber.*, 49, 780 (1916); 58, 672 (1925).

[3] (a) Y. C. Chin, A. A. Andersen, H. Hamilton, G. Alderton and J. C. Lewis, *Soc. Expt. Biol. Med. Proce.*, 70, 158 (1949); (b) J. C. Lewis, *et al.*, AIC 231, Western Regional Research Laboratory, Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture.

[4] P. E. Spoerri and A. S. DuBois, *Org. Reactions*, 5, 387 (1949).

Experimental Part

1,3-Dimethylphloroglucinol was prepared from trinitro-*m*-xylene.[5]

Acylation of 1,3-dimethylphloroglucinol was carried out after the method employed by Karrer.[6] Dimethylphloroacetophenone, m.p. 221–222°. *Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 61.4; H, 6.18. Found: C, 60.9; H, 6.19. Dimethylphlorobutyrophenone, m.p. 140°. *Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 64.4; H, 7.20. Found: C, 64.2; H, 7.29.

Air Oxidation of Dimethylacylphloroglucinol.—One mole of phlorophenone was dissolved in twenty times its weight of methanol, and a solution of one mole of lead acetate in an equal volume of methanol was added. This solution on agitation in an atmosphere of oxygen absorbed one mole of oxygen rapidly with evolution of heat and production of a yellow precipitate. After one hour, the precipitate was filtered off, washed with methanol, and decomposed by shaking with excess aqueous 6 *N* sulfuric acid and ether. The ether layer was separated, dried and evaporated. The residue was recrystallized once from aqueous methanol. The two compounds prepared were nicely crystalline light yellow solids, obtained in 30–50% yields, based on the acyldimethylphloroglucinol. Butyro-3,5-dimethyl-2,3-dihydroxy-4,6-diketocyclohexene-1, m.p. 104.5–105.0. *Anal.* Calcd. for $C_{12}H_{16}O_4$: C, 56.7; H, 5.70. Found: C, 56.7; H, 5.81. Aceto-3,5-dimethyl-2,3-dihydroxy-4,6-diketocyclohexene-1, m.p. 150.5–151.5. *Anal.* Calcd. for $C_{10}H_{12}O_4$: C, 60.0; H, 6.67. Found: C, 60.0; H, 6.74.

Absorption Spectra.—The spectra of the two synthetic analogs are shown in Fig. 1, compared with the spectrum of humulon itself.

Acknowledgments.—We wish to thank Dr. John Carson for a sample of humulon and Miss Geraldine Secor and Mrs. Mary Kilpatrick for the carbon–hydrogen analyses reported here.

WESTERN REGIONAL RESEARCH LABORATORY[7]
ALBANY, CALIF. RECEIVED SEPTEMBER 12, 1950

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(5) H. Weidel and F. Wenzel, *Monatsh.*, **19**, 249 (1898).

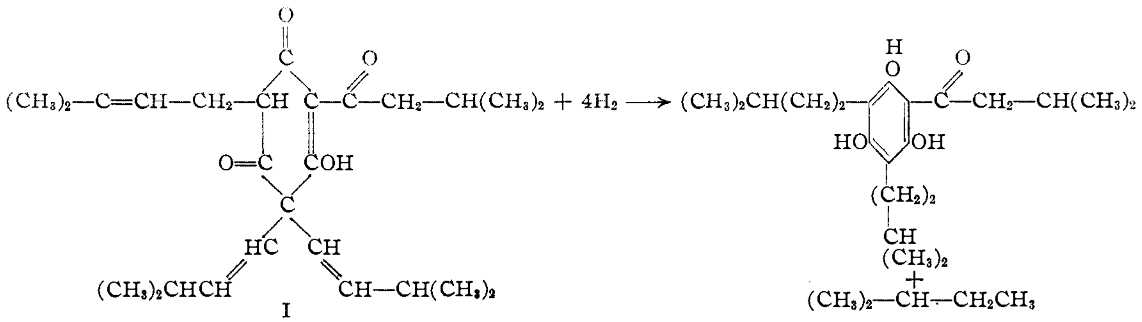
(6) P. Karrer, *Helv. Chim. Acta*, **2**, 473 (1917).

(7) Bureau of Agricultural and Industrial Chemistry, Agricultural Research Administration, U. S. Department of Agriculture.

The Hydrogenation of Lupulone and Humulone

BY J. F. CARSON

In connection with investigations of the antibiotic properties of hop constituents, the hydrogenation of lupulone and humulone has been studied. Wöllmer[1] found that hydrogenation of lupulone (I) in the presence of palladium chloride proceeds according to the equation



I

Wieland[2] observed that humulone, in which one gem isopentenyl group of I is replaced by a tertiary hydroxyl group, under the same conditions absorbed 3 moles of hydrogen and split out isopentane to yield a disubstituted 1,2,3,5-tetrahydroxybenzene derivative.

We have found that hydrogenation of lupulone in methanol in the presence of palladium-on-charcoal or of platinum oxide yields a crystalline compound, hexahydrolupulone. Ultraviolet absorption spectra of the reduced compound show that no significant amounts of phloroglucinol derivatives are formed and that hydrogenolysis does not occur under these conditions.

Hexahydrolupulone has the same characteristic ring structure as lupulone and differs structurally only in that the three exocyclic olefinic double bonds are saturated as is shown by the following evidence: 3.0–3.3 moles of hydrogen are absorbed in reduction in contrast to 3.8–4.0 observed when palladium chloride is the catalyst. The ultraviolet absorption spectrum in alkaline methanol (max. $\epsilon_{\text{molar}} = 20{,}400$ at 3555 Å.) is almost identical with that of lupulone.[3] Potentiometric titration in 80% methanol to *p*H 9.0 gives the neutralization equivalent 419 (calcd., 420.6). Titration of lupulone under the same conditions gives the neut. equivalent 409 (calcd. 414). Both lupulone and the hexahydro derivative have practically superimposable titration curves in 80% methanol with the pk_a (*p*H $^1/_2$ neut.) = 5.8–5.85. Carbon–hydrogen analyses agree closely with hexahydrolupulone.

The difference in the catalysts, palladium chloride and palladium-on-carbon, cannot be explained merely by the presence of hydrochloric acid produced by reduction of the former, since addition of hydrochloric acid to palladium-on-carbon prior to reduction did not alter the course of the reduction. Tetrahydrohumulone, on the other hand, could not be prepared by hydrogenation of humulone in the presence of platinum oxide or palladium-on-carbon. The reduction was always accompanied by appreciable hydrogenolysis of the isopentenyl group and complex mixtures were obtained. Absorption spectra of the hydrogenated solutions showed no evidence of the characteristic absorption of humulone or of tetrahydrohumulone. On exposure to air, the reduced solutions yielded small quantities of the red "humuloquinone"[2] which is also obtained by hydrogenating humulone in the presence of palladium chloride followed by air oxidation.

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(1) W. Wöllmer, *Ber.*, **58**, 675 (1925).

(2) H. Wieland, *ibid.*, **58**, 110 (1925).

(3) J. C. Lewis, *et al.*, Antibacterial Agents from Hops, mimeographed circular of information (A.I.C.-231), Bureau of Agricultural and Industrial Chemistry, U. S. Department of Agriculture, April, 1949.