arginine (XI) in 60 ml. of warm 5:1 methanol-water mixture was cooled to room temperature and hydrogenated overnight at room temperature and 40 p.s.i. using 2.5 g. of 10% palladium-on-carbon catalyst. After removal of the catalyst, the solvent was evaporated *in vacuo* and the residue was dissolved in 50 ml. of water and the solution lyophilized. The residue, weighing 1.30 g., was dissolved in 12 ml. of hot methanol whereupon crystallization occurred. The crystalline methylene-L-asparaginyl-L-arginine·CH_3OH (XII) weighed 1.13 g. (72%) and showed m.p. 160–165° dec., R_f^{MPW} 0.29 (N). A 250-mg. sample of this product was dissolved in 1 ml. of water and diluted with 1 ml. of isopropyl alcohol. Seeding and addition of 3 ml. of methanol gave 177 mg. of crystalline material, m.p. 163–165°, $[\alpha]_D^{23}$ −31° (*c*, 1 in 0.1*N* hydrochloric acid). A sample was dried at 78° for 2 hr. at *ca.* 0.1 mm. over Drierite for analysis. NMR spectrum on this sample showed the presence of 1 mole of methanol.

Anal. Calcd. for $C_{12}H_{24}N_6O_5$: C, 43.36; H, 7.28; N, 25.29. Found: C, 43.16; H, 7.26; N, 25.40.

Attempted conversion of XII *to* L-*asparaginyl*-L-*arginine.* A solution of 600 mg. of dimedone was prepared in 50 ml. of hot water and a solution of 600 mg. of XII in *ca.* 3 ml. of water was added to it. The mixture was heated 1.5 hr. and put in the refrigerator. The dimedoneformaldehyde adduct, weighing 413 mg. (71%), was collected on a filter and the filtrate was lyophilized. The residue, after extraction with three 50-ml. portions of hot ethyl acetate, weighed 698 mg. and showed R_f^{MPW} 0.29–0.38 (N); L-arginine·HCl, R_f^{MPW} 0.32–0.48 (N). Further precipitations from methanol–ethyl acetate gave multicomponent products which were not further characterized.

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New Synthesis of 18-Hydroxy-17-methoxy-15,16,17,18,19,20-hexadehydroyohimbane Hydrochloride

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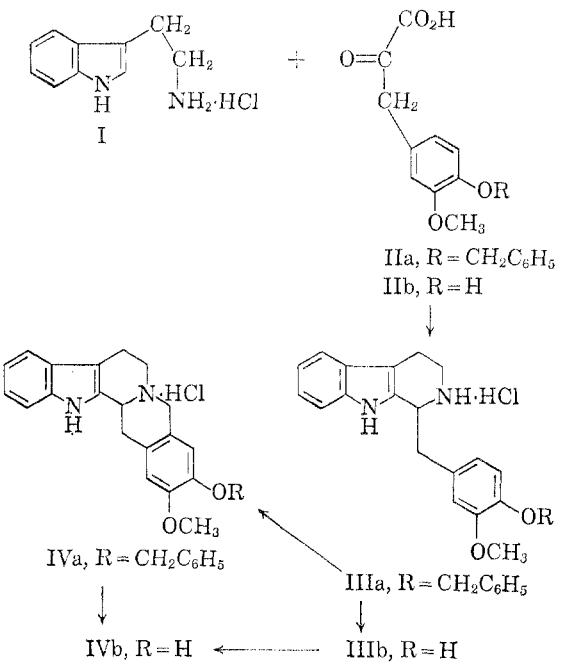
Synthesis of 18-hydroxy-17-methoxy-15,16,17,-18,19,20-hexadehydroyohimbane hydrochloride (IVb), which contains the pentacyclic ring system of reserpine, deserpidine, and related compounds, was accomplished as early as 1938.[1] Since then, other investigators[2–4] have reported the preparation of this substance and related compounds.

Preparation of IVb is usually accomplished by condensing tryptamine (I) with 4-hydroxy-3-methoxyphenylpyruvic acid (IIb). The product, 1 - (4 - hydroxy - 3 - methoxybenzyl) - 1,2,3,4-tetrahydro-β-carboline hydrochloride (IIIb), is then cyclized with formaldehyde to obtain IVb. The preparation of IIIb by this method, while satisfactory on a small scale, did not lend itself to large scale work. The difficulty appeared to be the lack of stability of IIb. Douglas and Gulland[5] have previously commented on the instability of IIb.

As we desired a large quantity of IVb, it was necessary to find a suitable modification of this sequence. Covering the phenolic function with a group which could be removed later suggested itself, and it seemed likely that the benzyl group might satisfactorily serve this function.



Vanillin, therefore, was converted to its *O*-benzyl derivative, and then into an azlactone. Hydrolysis of the latter with barium hydroxide gave the desired 4-benzyloxy-3-methoxyphenylpyruvic acid (IIa).

Tryptamine (I) and IIa gave 1-(4-benzyloxy-3-methoxybenzyl) - 1,2,3,4 - tetrahydro - β - carboline hydrochloride (IIIa) in good yields, irrespective of the quantities used. Debenzylation of IIIa led to IIIb and the latter was cyclized to the desired IVb, or IIIa could first be cyclized to IVa, and then debenzylated to give IVb.

EXPERIMENTAL[6]

1-(4-Benzyloxy-3-methoxybenzyl)-1,2,3,4-tetrahydro-β-carboline hydrochloride (IIIa).[7] A mixture of 65.5 g. (0.33 mole) of tryptamine hydrochloride[8] and 100 g. (0.33 mole) of

(1) G. Hahn and A. Hansel, *Ber.*, **71**, 2195 (1938).
(2) W. Logemann *et al.*, *Ber.*, **88**, 1952 (1955); **89**, 1043 (1956).
(3) M. Onda and M. Kawanishi, *J. Pharm. Soc. Japan*, **76**, 966 (1956).
(4) T. Nogradi, *Monatsh. Chem.*, **88**, 1093 (1957).
(5) R. Douglas and J. Gulland, *J. Chem. Soc.*, **134**, 2893 (1931).
(6) Microanalyses were carried out by Mr. Elmer Shelberg and his staff of the Abbott Microanalytical Laboratory.
(7) The preferred Chemical Abstracts name for this substance is 1-(4-benzyloxy-3-methoxybenzyl)-1,2,3,4-tetrahydro-9H-pyrido[3,4-b]indole hydrochloride.
(8) M. Freifelder, *J. Am. Chem. Soc.*, **82**, 2386 (1960).

4-benzyloxy-3-methoxyphenylpyruvic acid[5] in 3.5 l. of 1-butanol was heated under reflux for 2 hr. The cooled solution was diluted with 2.0 l. of acetone and chilled. White fluffy needles precipitated and were collected. The product weighed 78 g. (55%) and melted at 223–226°. Recrystallization from glacial acetic acid, or from aqueous ethanol, raised the melting point to 226–227°.

Anal. Calcd. for $C_{26}H_{26}N_2O_2 \cdot HCl$: C, 71.79; H, 6.26; Cl, 8.15. Found: C, 71.76; H, 6.34; Cl, 8.27.

18-Benzyloxy-17-methoxy-15,16,17,18,19,20-hexadehydroyohimbane hydrochloride (IVa). A mixture of 43 g. (0.1 mole) of IIIa and 1.0 l. of 50% ethanol was heated on the steam bath until the solid dissolved. After adding 100 ml. of 36% formaldehyde, the solution was heated on the steam bath for 3 hr. The hot reaction mixture was filtered to remove a yellow solid which was washed with hot 50% ethanol. The product weighed 37 g. (83%) and melted at 265–268°.

Anal. Calcd. for $C_{27}H_{26}N_2O_2 \cdot HCl$: C, 72.55; H, 6.09; Cl, 7.93; N, 6.27; O, 7.16. Found: C, 72.34; H, 6.27; Cl, 7.68; N, 6.07; O, 7.26.

1-(4-Hydroxy-3-methoxybenzyl)-1,2,3,4-tetrahydro-β-carboline hydrochloride (IIIb). A suspension of 2.75 g. (0.005 mole) of IIIa and 0.3 g. 5% palladium on carbon in 100 ml. of 50% ethanol was hydrogenated at 1.7 atm. at 60°. Theoretical uptake occurred in 1 hr., and all of the solid was in solution. The catalyst was removed and the solution was chilled to obtain a solid, m.p. 254–255°. The filtrate was taken to dryness, and the residue was triturated with ether to obtain more product, m.p. 253–254°. The total yield was 1.45 g. (84%). The recorded melting point is 253–254°.[3]

On larger scale runs, it was necessary to extract the catalyst thoroughly with hot 75% ethanol to insure good yields. In a combined workup of four 16-g. (0.0368 mole) runs a 75% yield was obtained.

18-Hydroxy-17-methoxy-15,16,17,18,19,20-hexadehydroyohimbane hydrochloride (IVb).[9] A suspension of 44.7 g. (0.1 mole) of IVa and 7.5 g. of 5% palladium on carbon in 250 ml. of dimethylformamide was hydrogenated at 2 atm. at about 70°. When hydrogen uptake was complete (8–15 hours) product had begun to precipitate. The product was dissolved by heating to boiling with addition of 65 ml. of dimethylformamide and 360 ml. of water. The hot solution was filtered to remove the catalyst, and the filtrate chilled to obtain 26 g. (73%) of bright yellow solid melting at 277–279°. Recorded melting points are 254–256°,[1] 256–257°,[3] and 254–256°.[4]

Anal. Calcd. for $C_{20}H_{20}N_2O_2 \cdot HCl$: C, 67.31; H, 5.93; Cl, 9.93; N, 7.85; O, 8.96. Found: C, 67.27; H, 5.82; Cl, 10.00; N, 7.87; O, 9.27.

Consensation of IIIb with formaldehyde as described previously[1,3,4] gave a bright yellow solid, m.p. 277–279°, identical in every respect with the material described above. Although the melting point varied somewhat with the rate of heating, and also on whether an oil bath or metal block was used, pure material was never observed to melt below 270°.

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(9) The preferred *Chemical Abstracts* name for this compound is 5,7,8,13,13b,14-hexahydro-2-methoxybenz[g]-indolo[2,3-a]quinolizin-3-ol hydrochloride.

Spectral Studies on Flavonoid Compounds. III. Polyhydroxychalcones

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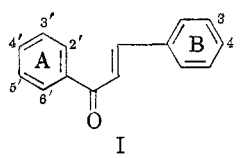
The ultraviolet spectra of most of the known, naturally occurring, hydroxylated chalcone (I) derivatives have been reported.[2] However, as an aid in the identification of new pigments, the spectra of a number of additional hydroxychalcones in neutral and in alkaline solutions are presented in this note.



I

The spectra of twenty-five hydroxychalcones are collected in Table I. These chalcones absorb strongly in the 300–400 mμ region and less strongly in the 220–270 mμ region. In alcoholic sodium ethylate solution the long wave-length band of those chalcones which contain a free hydroxyl group in the 4- position undergoes a bathochromic shift of 70–90 mμ and a considerable *increase* in its intensity (Table I; compounds I–II). This spectral shift is sufficiently characteristic of the 4-hydroxychalcones to be used as evidence for the the presence of this grouping in chalcones. The alkali spectrum of the natural chalcone, xanthohumol (II), reported by Verzele and his co-workers,[3] provides a good example of this shift.

Chalcones which contain a free 4'-hydroxyl *and* either a free 2'-hydroxyl or an alkylated or glycosidated 4-hydroxyl show a bathochromic shift of only 40–50 mμ in sodium ethylate (Table I; compounds 12–18). On the other hand, when the 2'- and 4- positions are unsubstituted, 4'-hydroxychalcones give a bathochromic shift of 65–70 mμ in sodium ethylate (Table I; compounds 19, 20). This shift is easily distinguished from that given by the 4-hydroxychalcones, however, since it is accompanied by a considerable *decrease* in the intensity of the long wave-length band. The difference is illustrated by the spectra of 4-hydroxychalcone and 4'-hydroxychalcone (Fig. 1). The influence of a 2'-hydroxy group on the alkali spectrum of a 4'-hydroxychalcone is probably to be attributed to chelation with the carbonyl group, while the influence of a 4-alkoxy group may be accounted for by assuming a cross-conjugation effect similar to that proposed by Geissman and Harborne[4] for hydroxyaurones.

(1) (a) Western Regional Research Laboratory, Albany, Calif.[1c]; (b) Fruit and Vegetable Chemistry Laboratory, Pasadena, Calif.[1c]; (c) Laboratories of the Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) For examples, see J. B. Harborne and T. A. Geissman, *J. Am. Chem. Soc.*, **78**, 829 (1956); T. A. Geissman, J. B. Harborne, and M. K. Seikel, *J. Amer. Chem. Soc.*, **78**, 825 (1956); T. A. Geissman, *Modern Methods of Plant Analysis*, Vol. 3, eds. K. Paech and M. V. Tracey, Springer-Verlag, 1955, p. 450.

(3) M. Verzele, J. Stockx, F. Fontijin, and M. Anteunis, *Bull. Soc. Chim. Belg.*, **66**, 452 (1957).

(4) T. A. Geissman and J. B. Harborne, *J. Am. Chem. Soc.*, **78**, 832 (1956).