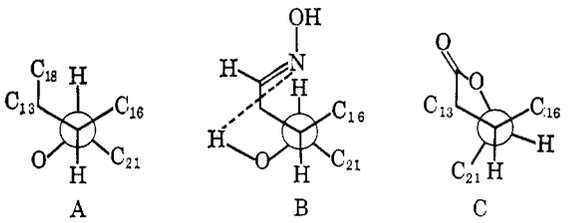
in the staggered form, and between C-21 and the 17α-hydrogen and/or the 20α-hydroxyl group and C-16 when the dihedral angle decreases to 120° in the eclipsed form.

Of special interest is 18-oximino-20α-hydroxypregn-4-en-3-one[7] in which $J_{17\alpha\text{-H},20\beta\text{-H}}$ decreases to 3.5 cps (dihedral angle 130°), presumably owing to hydrogen bonding between the 20α-hydroxyl proton and the oximino nitrogen atom. This is confirmed by the downfield shift of the hydroxyl hydrogen to 208 cps from the normal chemical shift of about 96 cps in this series of compounds. The identity of this peak was demonstrated by exchange with D_2O which also exchanged with the oxime hydroxyl group at 554 cps. The same phenomenon has been observed for *syn*-19-oximino-5α-androstane-2β,3α,17β-triol 3,17-diacetate by Kwok and Wolff.[12] The nmr spectrum of 18-oximino-20β-hydroxypregn-4-en-one[8] also indicates hydrogen bonding between the hydroxyl and oximino groups. The coupling values in the 20β-hydroxy series, however, are less subject to variation by different substituents. This probably is due not only to the rather stable staggered conformation (Chart III), but also to the formation of a hydrogen bond without altering the geometry of the conformation shown in Chart III. The distance between the hydroxyl oxygen and C-18 is about 2.8 A for the 20β-hydroxy compound (Chart IIA) and about 3.5 A for the 20α-hydroxy compound (Chart IA) as measured by models.

CHART III

CONFORMATIONS OF 20β-OXYGENATED PREGNANE DERIVATIVES



Experimental Section

Materials.—Compounds **1–4**, **7**, **8**, **11**, and **12** were obtained by literature methods as indicated, or by modifications of these methods. Compounds **5**, **6**, **9**, and **10** were obtained as part of another investigation.[13]

Nmr Spectra.—Spectra were obtained on a Varian HA-100 instrument on samples in deuteriochloroform or benzene solution using tetramethylsilane as internal standard.

(12) R. Kwok and M. E. Wolff, *Chem. Ind.* (London), 1194 (1962).
(13) H. Lee and M. E. Wolff, in preparation.

A Convenient Synthesis of Dihydrojasmone[1]

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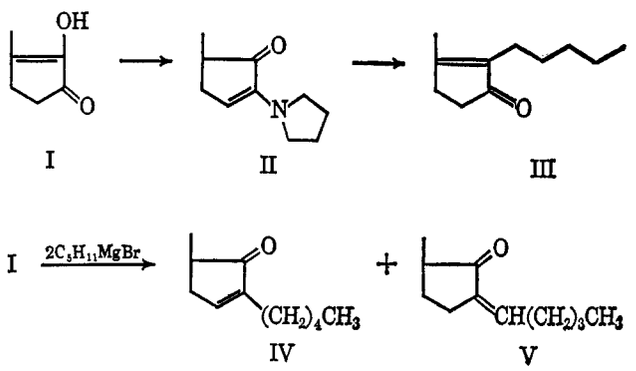
The primary odorous principle of jasmine flowers is jasmone which is 3-methyl-2-(2-*cis*-pentenyl)cyclopent-2-en-1-one.[2,3] This material is very expensive because it is found only in small quantities in nature. Although several syntheses of jasmone have been recorded[4,5] it cannot be considered an economical perfumery material.

Dihydrojasmone (III) is closely related to jasmone both in structure and odor and is useful in perfumery.[6] Dihydrojasmone has been synthesized by several cyclization procedures but in either low yield or purity or both.[7]

Recently, a synthesis starting with 3-methylcyclopent-2-en-2-ol-1-one, a material readily available from both natural and synthetic sources has been described by Erickson and Collins.[8] In this process the C-1 keto group was protected as a ketal while the C-2 keto group was treated with Grignard reagents. The protection required three steps and resulted in an over-all yield of 40%.

In our process, 3-methylcyclopent-2-en-2-ol-1-one (I, Scheme I) was treated with pyrrolidine in boiling benzene to give a 95% yield of 2-N-pyrrolidino-5-methylcyclopent-2-en-1-one (II). Treatment of (II) with *n*-amylmagnesium bromide, followed by hydrolysis and dehydration, gave dihydrojasmone (III) in 68% yield.

SCHEME I



When 3-methylcyclopent-2-en-2-ol-1-one is treated directly with 2 moles of a Grignard reagent followed by hydrolysis and dehydration 1-*n*-amyl-3-methylcyclopent-1(5)-en-2-one (IV) and 1-*n*-pentylidene-3-methylcyclopentan-2-one (V) are formed.[9]

Experimental Section

2-N-Pyrrolidino-5-methylcyclopent-2-en-1-one (II).—A mixture of 56 g (0.5 mole) of 3-methylcyclopent-2-en-2-ol-1-one (I), 42.6 g (0.6 mole) of pyrrolidine, and 500 ml of benzene was refluxed under nitrogen with removal of water for 1 hr. The benzene was removed at 60 mm by heating to 60°. The residue was distilled under nitrogen through a 37-cm column packed with glass halices to give 78 g (95%) of the enamine: bp 85–90° (0.4 mm); $n^{20}D$ 1.5285; λ_{max} 5.90 and 6.20 μ. This material could not be further characterized owing to its instability.

2-*n*-Amyl-3-methylcyclopent-2-en-1-one (III, Dihydrojasmone).—The Grignard reagent was prepared from 113 g of *n*-amyl bromide (0.75 mole), 18 g of magnesium turnings (0.75 g-atom), and 250 ml of dry ether. To this Grignard reagent was added dropwise with constant agitation a solution of 78 g of 2-N-pyr-

(1) Much of this work was presented at the First Middle Atlantic Regional Meeting, Philadelphia, Pa., Feb 3, 1966.
(2) L. Ruzicka and M. Pfeiffer, *Helv. Chim. Acta*, **16**, 1208 (1933).
(3) W. Treff and H. Werner, *Ber.*, **66**, 1521 (1933).
(4) G. Stork and R. Borch, *J. Am. Chem. Soc.*, **86**, 936 (1964).
(5) G. Büchi and H. Wüest, *J. Org. Chem.*, **31**, 977 (1966).
(6) T. F. West, H. J. Strausz, and D. H. R. Barton, "Synthetic Perfumes," Edward Arnold and Co., London, 1959, p 151.
(7) J. H. Amin, *et al.*, *Ind. J. Chem.*, **2**, 14 (1964), and references cited in this article.
(8) J. L. E. Erickson and F. E. Collins, Jr., *J. Org. Chem.*, **30**, 1050 (1965).
(9) J. L. E. Erickson, J. Dorsky, and W. M. Easter, Jr., U. S. Patent 3,137,731 (1964).

rolidino-5-methylcyclopent-2-en-1-one in 250 ml of dry ether. After the addition was complete, the mixture was refluxed for 0.5 hr. The Grignard complex was decomposed by putting it on ice and 15% hydrochloric acid. The mixture was allowed to stand overnight. The organic layer was separated and the water solution extracted with ether. The organic solutions were washed twice with small quantities of saturated salt solution. The ether was removed by distillation and the residue was refluxed with 200 ml of 25% sulfuric acid for 2 hr. The product was steam distilled leaving 1.5 g of residue. The distillate was extracted with ether after saturating with salt. After drying over magnesium sulfate, the solvent was removed by atmospheric distillation. There was produced 60.4 g (73%) of dihydrojasmone: bp 86–93° (2–3 mm); $n^{20}D$ 1.4788; λ_{max} 5.85 and 6.05 μ. The product was 99% pure as determined by vapor phase chromatography.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.33, 79.23; H, 10.49, 10.25.

A New Synthesis of (±)-Yohimbane

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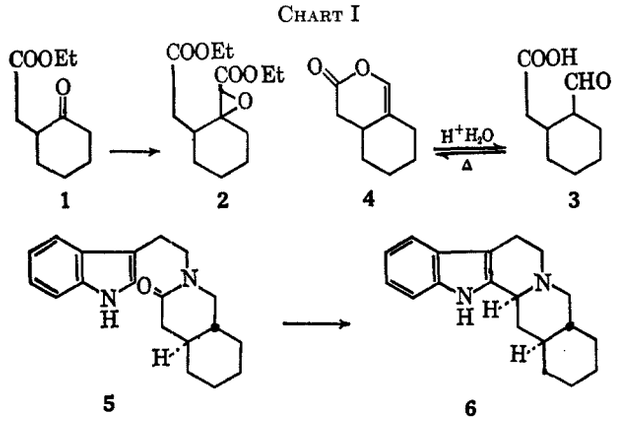
The total synthesis of (±)-yohimbane has already been reported by three groups, E. van Tamelen, *et al.*,[1] S. Corsano and L. Panizzi,[2] and J. Rubinfeld.[3] The goal of our work was not to design a synthesis as a proof of structure of (±)-yohimbane, but one which would lend itself to large-scale preparations of (±)-yohimbane.

For this purpose we have utilized the last two steps of the scheme of van Tamelen as did Rubinfeld.

CHART I



Therefore, more accurately, this paper describes a new preparation of *trans*-octahydro-2-[2-(indol-3-yl)ethyl]-3(2H)-isoquinolinone (**5**).

The ketone **1** was converted to the glycidic ester **2**, hydrolyzed, and decarboxylated to give the aldehyde **3** by a procedure analogous to that described by Johnson[4] for cyclohexanone. The crude acid aldehyde is a mixture of the *cis* and *trans* isomers of **3** and the anhydro actone **4** as shown by the infrared spectrum which shows absorption at 1720 cm^{-1} for the acid and aldehyde carbonyls and 1760 and 1660 cm^{-1} for the lactone carbonyl and double bond. The mixture was refluxed with dilute acid to hydrolyze the lactone and promote the establishment of an equilibrium mixture of the *cis* and *trans* isomers. Although the isomers were not isolated it was assumed that there was a large preponderance of *trans* since *trans*-1,2-dimethylcyclohexane is preferred over the *cis* isomer 20:1 on a thermodynamic basis.[5] Utilizing a procedure for the preparation of berberine derivatives,[6] the aldehyde **3** was condensed with tryptamine, reduced with potassium borohydride, and cyclized with acid to the lactam **5**. Since an authentic sample of **5** was not available for direct comparison we carried through the synthesis of (±)-yohimbane (**6**) which was shown to have an infrared spectrum[7] in chloroform identical with that of yohimbane derived from natural sources.

Since the previous workers in this field had not resolved (±)-yohimbane the unnatural isomer was still unknown. (+)-Yohimbane[8] was obtained from the racemic mixture by using (−)-dibenzoyltartaric acid as the resolving agent.

Experimental Section[9]

Ethyl 1,α-Epoxy-2-(ethoxycarbonylmethyl)cyclohexaneacetate (2).—To a mixture of 630 g of 2-(carboethoxymethyl)cyclohexanone and 420 g of ethyl chloroacetate was added a solution of 384 g of potassium *t*-butoxide in 3.2 l. of *t*-butyl alcohol over a 2-hr interval with cooling such that the temperature was maintained at 0–15°. After the addition had been completed stirring was continued for 2 hr at 0–15° and then 15 hr at room temperature. The solvent was removed *in vacuo* and the residue was treated with an ether–water mixture. The ether layer was washed with saturated sodium bicarbonate solution and water, dried over sodium sulfate, and the solvent was removed. Distillation of the residue gave 572 g (61%) of an oil: bp 128–130° (0.2 mm); $n^{25}D$ 1.4646; ν_{max}^{film} 1740, 1755 cm^{-1}.

Anal. Calcd for $C_{14}H_{22}O_5$: C, 62.20; H, 8.20. Found: C, 62.18; H, 8.11.

2-Formylcyclohexaneacetic Acid (3).—To a solution of 100 g of sodium in 1650 ml of ethanol which had been cooled to 10° was added 590 g of ethyl 1,α-epoxy-2-(ethoxycarbonylmethyl)cyclohexaneacetate. The mixture was cooled to 5° and 91.7 ml of water added dropwise with cooling such that the temperature remained at 0–15°. On standing at room temperature for 15 hr there was deposited 446 g of a crystalline solid, mp >330°. The salt was dissolved in 480 ml of water and 288 ml of hydrochloric acid was added with cooling such that the temperature remained at 10–15°. The solution was extracted with 3.0- and 1.0-l. portions of ether. The combined ether layers were washed with 100 ml of water and dried over sodium sulfate; the solvent was removed. The residue (340 g) and 10 g of copper powder was pyrolyzed at 250° (100 mm) for 5 hr. There was collected 185 g of a mixture, bp 50–192° (100 mm), which was refluxed vigorously with a solution of 73 ml of acetic acid in 1400 ml of water for 10 hr. The mixture was extracted with chloroform. The chloroform layer was dried over sodium sulfate and the solvent was removed. There remained 155 g (43%) of an oil.

A 1.0-g sample of the oil gave 0.65 g (48%) of the semicarbazone as a crystalline solid: mp 172–173.5° dec; ν_{max}^{Nujol} 1773, 1620,

(1) E. E. van Tamelen, M. Shamma, and P. Aldrich, *J. Am. Chem. Soc.*, **78**, 4628 (1956).

(2) S. Corsano and L. Panizzi, *Ann. Chim.* (Rome), **48**, 1025 (1958).

(3) J. Rubinfeld, Ph.D. Thesis, Columbia University, New York, N. Y., 1961.

(4) W. S. Johnson, J. S. Belew, L. J. Chinn, and R. H. Hunt, *J. Am. Chem. Soc.*, **75**, 4995 (1953).

(5) E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 214.

(6) G. Muller and L. Vellu, German Patent 1,143,824 (1963).

(7) Supplied by H. Zinnes of this laboratory.

(8) J. Jost [*Helv. Chim. Acta*, **32**, 1297 (1949)] has reported (−)-yohimbane, mp 206°, $[\alpha]D$ −81° (*c* 0.50, alcohol).

(9) Melting points are corrected. The authors are indebted to Mr. A. Lewis and his associates, to Mr. R. Puchalski for the spectral data, and to Mrs. U. Zeek for analytical determinations.