of X in 6 ml. of 3% acetic acid was treated with 4 ml. of 36% formaldehyde solution and 0.8 g. of solid sodium bicarbonate. The mixture was warmed on the steam bath for 15 minutes, then cooled. A thick, gummy material separated from the aqueous solution. It was washed several times with water and dissolved in benzene. The benzene solution was washed twice with water and evaporated. The thick, oily residue was dissolved in 5 ml. of 3*N* hydrochloric acid, and the solution was heated on the steam bath for 15 minutes. The solution was cooled, diluted with water, extracted with ether, made basic with ammonium hydroxide, and extracted with chloroform. The extract was dried and evaporated to yield 460 mg. of thick, pale yellow oil. Examination of the product by gas-phase chromatography (¾% SE-30 column, 177°) showed that it consisted of approximately 1 part of unreacted secondary amine (retention time 5.15 minutes) and 2 parts of another compound with the same retention time as the product obtained by degradation (7.9 minutes). The two compounds were separated by Hinsberg's method through reaction with *p*-toluenesulfonyl chloride. The final product was distilled at 140°/0.01 mm. to yield 196 mg. of colorless oil. The infrared spectra (carbon tetrachloride solution and liquid film) of this material were identical with the spectra of the degradation product of powellane.

Anal. Calcd. for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; neut. equiv., 273. Found: C, 74.77; H, 8.58; neut. equiv., 280.

The *picrate* was obtained as rectangular plates m.p. 209–212°, after recrystallization from chloroform-ethanol. The infrared spectrum (KBr) was identical with that of the picrate of IX (R = OCH_3) obtained by the degradation of powellane.

Anal. Calcd. for $C_{23}H_{26}N_4O_9$: C, 54.97; H, 5.22; N, 11.15. Found: C, 54.68; H, 5.11; N, 11.06.

BETHESDA 14, MD.

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, UNIVERSITY OF ADELAIDE, AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF LOUISVILLE]

Synthetical Experiments Related to the Indole Alkaloids. II.[1a] The Synthesis of Hexadehydroyohimbane

D. R. LILJEGREN AND K. T. POTTS[1b]

Received July 28, 1961

Lithium aluminum hydride reduction of 2-(2-3′-indolyl-2-oxoethyl)isoquinolinium iodide (III), obtained from 3-acetylindole, isoquinoline, and iodine, gave directly 5,7,8,13,13b,14-hexahydrobenz[*g*]indolo[2,3-*a*]quinolizine (II), hexadehydroyohimbane. This is the simplest and most direct method of obtaining the yohimbine ring skeleton.

Interest in the synthesis of alkaloids of the indole group has been very intense over the last few years, and many notable successes have been achieved, especially the synthesis of reserpine,[2] strychnine,[3] and yohimbine,[4] and more recently a simulated biogenetic route to the strychnine-type ring skeleton.[5] The early methods of synthesis used in this field have been thoroughly discussed in *The Alkaloids*.[6] Our approach to the synthesis of the yohimbine ring skeleton has been developed in two stages. In part I of this series known methods were evaluated, and in a new method an intermediate 2-(2-3′-indolylethyl)isoquinolinium iodide (I) was reduced with lithium aluminum hydride to hexadehydroyohimbane (II) in good yield. Alstonilinol[7] has since been synthesized by this method and apart from an application to the berberine group[8] no others have been reported.

We now wish to report a more direct route to the yohimbine ring skeleton. An isoquinolinium salt that is capable of undergoing reduction and ring closure to the quinolizine is still the key intermediate, and the pentacyclic base is available from indole itself in three steps. Use is made of the two different ways in which 3-acetylindole can react. It possesses normal ketonic properties, readily forming a phenylhydrazone,[9] an oxime,[10] a thiosemicarbazone,[11] and a Mannich base with paraformaldehyde and dimethylamine hydrochloride.[12a] As it is analogous to acetophenone, it should condense with iodine and a tertiary organic base forming the corresponding salt, a reaction that is general for a methyl ketone group directly attached to an aromatic nucleus.[13]

(1) (a) K. T. Potts and Sir Robert Robinson, *J. Chem. Soc.*, 2675 (1955) is regarded as Part I in this series; see also D. R. Liljegren and K. T. Potts, *Proc. Chem. Soc.*, 340 (1960); (b) Department of Chemistry, University of Louisville, Ky.

(2) R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey, and R. W. Kierstead, *Tetrahedron*, **2**, 1 (1958).

(3) R. B. Woodward, M. P. Cava, W. D. Ollis, A. Hunger, H. U. Daeniker, and K. Schenker, *J. Am. Chem. Soc.*, **76**, 4749 (1954).

(4) E. E. Van Tamelen, M. Shamma, A. W. Burgstahler, J. Wolinsky, R. Tann, and P. E. Aldrich, *J. Am. Chem. Soc.*, **80**, 5006 (1958).

(5) E. E. Van Tamelen, L. J. Dolby, and R. G. Lawton, *Tetrahedron Letters*, No. 19, 30–35 (1960).

(6) L. Marion, *The Alkaloids*, Academic Press, New York, 1952; J. E. Saxton, Vol. 7, Ch. 10, 1960.

(7) R. C. Elderfield and B. A. Fischer, *J. Org. Chem.*, **23**, 949 (1958).

(8) J. W. Huffman and E. G. Miller, *J. Org. Chem.*, **25**, 90 (1960).

(9) B. Oddo and L. Sessa, *Gazz. chim. ital.*, **41**, 234 (1911).

(10) Ramart-Lucas and M. Roch, *Compt. rend.*, **232**, 843 (1951).

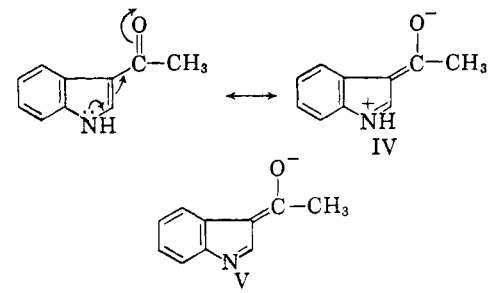
(11) G. Tsatsas, *Compt. rend.*, **235**, 175 (1952).

(12) (a) J. Szmuszkovicz, *J. Am. Chem. Soc.*, **82**, 1180 (1960); (b) J. Thesing, *Chem. Ber.*, **87**, 507 (1954).

(13) L. C. King, *J. Am. Chem. Soc.*, **66**, 894 (1944); L. C. King, M. McWhirter, and D. M. Barton, *J. Am. Chem. Soc.*, **67**, 2089 (1945), and other papers up to 1958; see also F. Kröhnke, *Angew. Chem.*, **65**, 605 (1953).

3-Acetylindole condensed with isoquinoline, and with other similar tertiary bases, forming 2-(2-3′-indolyl-2-oxoethyl)isoquinolinium iodide (III) in practically quantitative yield. Exchange of the iodide anion for a perchlorate anion can readily be effected with 50% aqueous perchloric acid. This type of substituted indole containing a quaternary pyridine nucleus has been prepared previously by the Grignard method from various indolylmagnesium iodides and iodoacetyl chloride and condensation of the resulting 3-indolyliodomethyl ketone with pyridine.[14] Unsatisfactory yields are obtained in both these steps.

The 2-oxoethylisoquinolinium salt (III) is equivalent to the intermediate I, differing only in the presence of the keto group adjacent to the indole nucleus. These salts are very susceptible to alkaline hydrolysis,[15] and the removal of the keto group requires mild reaction conditions. We found that a second interesting property of 3-acetylindole could be utilized for this purpose. Lithium aluminum hydride reduction of 3-acetylindole readily gives 3-ethylindole[16]; similarly, 3-formylindole gives skatole.[16] These reductions are analogous to the reduction of an amide to an amine that occurs with this reagent.[17] The low carbonyl absorption frequency of 3-acetylindole in Nujol [ν_{CO} 1617 cm.$^{-1}$ (6.18 μ); *cf.* ν_{CO} aromatic ketone 1700–1680 cm.$^{-1}$ (5.88–5.95 μ); ν_{CO} aliphatic ketone 1725–1705 cm.$^{-1}$ (5.74–5.85 μ)] is due mainly to intermolecular hydrogen bonding,[18] as is shown by the accompanying data, and though there must be a certain contribution to the resonance hybrid from the dipolar form[12] IV, it is not sufficient to deprive the carbonyl group of its ketonic properties (see above) nor appreciably affect the absorption of the carbonyl group. However, in solution in the presence of lithium aluminum hydride, the conjugate base V of 3-acetylindole is the reactive species that results in hydrogenolysis of the carbonyl group. The absorption of the carbonyl group in the 2-oxoethylisoquinolinium salt (III) occurs at 1642 cm.$^{-1}$ (6.09 μ), and this low value can likewise be attributed to intermolecular hydrogen bonding. The environment of the carbonyl group in III is the same as in 3-acetylindole, and we expected that it would also be readily hydrogenolyzed with lithium aluminum hydride. This did, in fact, occur and by the use of this reagent the removal of the ketone group and the reduction of the —C=N< group of the isoquinolinium moiety were combined in one reaction. Decomposition of the excess of lithium aluminum hydride with water, followed by the addition of mineral acid then effected cyclization to 5,7,8,13,-13b,14-hexahydrobenz[*g*]indolo[2,3-*a*]quinolizine (II).

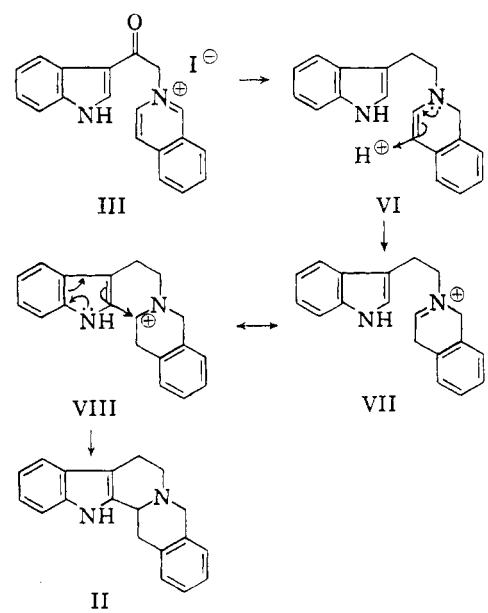


IV

V

ν_{CO} Cm.$^{-1}$		
	Nujol	CCl_4
3-Acetylindole	1617, 1628 (sh)	1669[19a]
	1614	1662 (T.H.F.)[18]
1-Methyl-3-acetylindole	1646	1667[19b]
3,4-Dimethoxyacetophenone	—	1688[19b]

The possible mechanisms of these reactions are extremely interesting. Isoquinolinium salts are readily reduced at room temperature by lithium aluminum hydride,[1,7,20] and it is most likely that the first step was the reduction of this moiety. The nature of the anion does not appear to be critical, as the iodide and perchlorate were reduced in ap-



III VI VIII VII II

(14) G. Sanna, *Gazz. chim. ital.*, **59**, 838 (1929).

(15) S. H. Babcock, F. I. Nakamura, and R. C. Fuson, *J. Am. Chem. Soc.*, **54**, 4407 (1932); F. Kröhnke, *Ber.*, **66**, 604 (1933); G. Hart and K. T. Potts, unpublished work.

(16) E. Leete and L. Marion, *Can. J. Chem.*, **31**, 775 (1953).

(17) A compilation of references may be found in (a) V. M. Micovic and M. Lj. Mihailovic, *Lithium Aluminum Hydride in Organic Chemistry*, Serbian Academy of Sciences, Belgrade, 1955, pp. 58–60; (b) N. G. Gaylord, *Reduction with Complex Metal Hydrides*, Interscience Publishers, Inc., New York, 1956, pp. 544–547.

(18) E. M. Tanner, *Spectrochim. Acta*, **9**, 282 (1957).

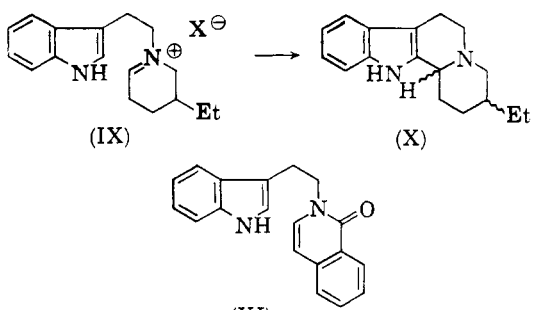
(19) Measurements were made in 3-mm. cells using a Grubb-Parsons Model S4 double-beam spectrometer; (a) saturated solution, (b) concentration of 5 mg./ml. We thank Dr. A. Jones for these precise measurements.

(20) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 960 (1949); ref. 17a, pp. 94–95; ref. 17b, pp. 781–793.

proximately equivalent yields. After the reduction of the carbonyl group, the excess of lithium aluminum hydride was decomposed with water, and mineral acid was added to the reaction mixture. It is thought that ring closure of the intermediate VI occurred at this stage.

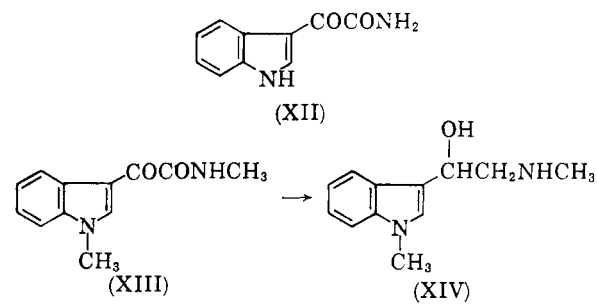
Structure VI represents an α,β-unsaturated amine, an enamine which is a strong base and in the presence of acid is known[21,22] to undergo the structural transformation (VI → VII). The quaternary salt is capable of resonance stabilization (VII ⟷ VIII), and ring closure occurs as shown schematically in VIII.

Under the experimental conditions employed, no decision can be made as to whether mineral acid or lithium aluminum hydride in the role of a Lewis acid acted as the cyclization agent. However, in several experiments where insufficient mineral acid was added to make the solution strongly acid, unstable oily products were associated with the desired quinolizine (II). In contrast to our experience, the cyclization of the intermediate isoquinolinium salt to tetrahydroalstonilinol in the synthesis of alstonilinol[7] was effected without addition of mineral acid, the free base being isolated directly from the reaction mixture. In this case the 6-methoxyl group probably increases the electron density at the α-indole position so that the cyclization is effected by some complex derived from the lithium aluminum hydride. It is interesting to note that in all the other cyclizations of this kind, mineral acid was added at some stage or other. Whichever is the effective cyclization agent, the actual mechanism of the ring closure would be the same. Further evidence in support of the mechanism described above is the cyclization of

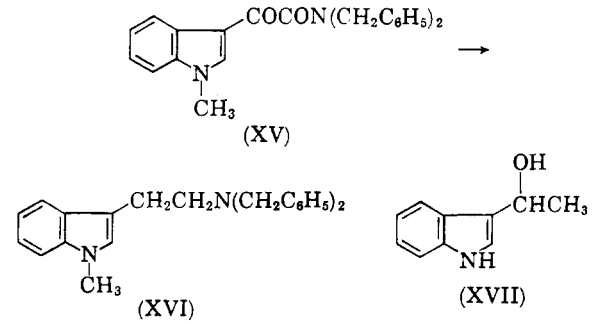


IX to X with mineral acid; dehydrogenation of X gave flavopereirine.[23] Likewise the conversion of XI into II by lithium aluminum hydride reduction, followed by the addition of mineral acid to the reaction mixture, argues in favor of the above mechanism.[24]

The intermediate III may be regarded as containing the structural element of a vinylogous amide and should be reduced with lithium aluminum hydride in a similar fashion to amides.[25] We have found the lithium aluminum hydride reduction of the 3-acylindole system to be more complicated, especially the ind-*N*-methyl compounds, than previously supposed. It has been reported that 1-methyl-3-indolylaldehydes are reduced to the corresponding 1-methyl-3-hydroxymethylindoles,[26] whereas those carbonyl compounds with the indole nitrogen unsubstituted are reduced to the methylene compounds. 3-Indoleglyoxamide (XII) is similarly readily reduced with lithium aluminum hydride to tryptamine,[27] whereas with 1,*N*-dimethyl-3-indolylglyoxamide (XIII) reduction has been reported[28] as stopping at the alcohol stage XIV. However, a later report[29] has claimed the reduction of XV to the corresponding methylene compound XVI. Our results on the reduction of the



ind-*N*-methyl analog of III tend to support this later work, but as yet we have been unable to obtain the free base corresponding to II crystalline,[30] though its infrared spectrum supports the contention that complete reduction and cyclization have occurred. Treatment of II with sodamide and methyl iodide in liquid ammonia is a satisfactory alternative method of obtaining the ind-*N*-methyl compound.



(21) N. J. Leonard and V. W. Gash, *J. Am. Chem. Soc.*, **76**, 2781 (1954).
(22) R. Adams and J. E. Mahan, *J. Am. Chem. Soc.*, **64**, 2588 (1942).
(23) J. Thesing, *Experientia*, **15**, 127 (1959).
(24) C. Ribbens and W. Th. Nauta, *Rec. trav. chim.*, **79**, 854 (1960).
(25) See ref. 17a, pp. 52-60.
(26) E. Leete, *J. Am. Chem. Soc.*, **81**, 6023 (1959).
(27) M. E. Speeter and W. C. Anthony, *J. Am. Chem. Soc.*, **76**, 6208 (1954).
(28) M. E. Speeter, U. S. Patent **2,825,734**; *Chem. Abstr.*, **52**, 12923f (1958).
(29) A. Buzas, C. Hoffmann, and G. Regnier, *Bull. soc. chim.*, 643 (1960).
(30) P. L. Julian and A. Magnani, *J. Am. Chem. Soc.*, **71**, 3207 (1949).

3-Acetylindole on reduction with lithium borohydride in cold tetrahydrofuran solution formed 3-1′-hydroxyethylindole (XVII) in low yield, and this was accompanied by much unchanged starting material. When the reduction was carried out in boiling tetrahydrofuran solution complete hydrogenolysis occurred.[31] This evidence is strong support for the mechanism suggested by Leete and Marion[27] for the hydrogenolysis of this type of acylindole. The elimination of OH^- ion from the intermediate alcohol XVII is greatly facilitated by the conversion of the indole into its conjugate base with lithium aluminum hydride. With the ind-*N*-methyl analog, no such conjugate base can be formed, and the course of the reaction is most likely controlled by the reaction conditions. We are at present investigating the reduction of these ind-*N*-methyl compounds in greater detail.

EXPERIMENTAL[32]

2-(2-3′-Indolyl-2-oxoethyl)isoquinolinium iodide (III). 3-Acetylindole (1.6 g., 0.01 mole) and isoquinoline (3.87 g., 0.03 mole) were warmed together on the water bath to effect solution and iodine (2.5 g., 0.01 mole) added. This mixture was then heated on the steam bath for 45 min. until, when cooled, there was no iodine apparent in the bottom of the flask. At this stage the reaction mixture had set solid. This solid material was washed with a small amount of water to remove isoquinoline and isoquinoline hydroiodide. Trituration with ethanol precipitated the crude iodide, 3.91 g. (94%) as a fawn microcrystalline powder, m.p. 265–268° dec. Crystallization from water yielded the iodide as fine, pale yellow needles, m.p. 270–272° dec.

Anal. Calcd. for $C_{19}H_{15}N_2OI$: C, 55.1; H, 3.7; N, 6.8. Found: C, 54.8; H, 3.8; N, 6.5.

The *perchlorate* was prepared from a hot, aqueous solution of the iodide and 50% perchloric acid. It separated from aqueous dimethylformamide as colorless needles, m.p. 276–277° dec.

Anal. Calcd. for $C_{19}H_{15}N_2O_5Cl$: C, 58.99; H, 4.2; N, 7.2. Found: C, 58.5; H, 4.1; N, 6.7.

1-(2-3′-Indolyl-2-oxoethyl)quinolinium iodide. 3-Acetylindole, quinoline, and iodine were heated together as above. The green-black tar was washed with water (50 ml.) and hot ether (4 × 50 ml.). Ethanol (50 ml.) was added, and after a time a brown powder separated, 1.4 g., m.p. 225–227° dec. Dilution of the mother liquor with petroleum ether (b.p. 40–60°) gave a further 0.8 g. of this product. Crystallization from ethanol (charcoal) and then from water gave 1-(2-3′-indolyl-2-oxoethyl)quinolinium iodide as fine, yellow needles, m.p. 247–249° dec.

Anal. Calcd. for $C_{19}H_{15}N_2OI$: C, 55.1; H, 3.7; N, 6.8. Found: C, 54.8; H, 3.8; N, 6.4.

2-(2-1′-Methyl-3′-indolyl-2-oxoethyl)isoquinolinium iodide. 1-Methyl-3-acetylindole[33] (4.2 g., 0.024 mole) and isoquinoline (9.3 g., 0.027 mole) were warmed together on the water bath. Iodine (6.0 g., 0.024 mole) was added and the mixture heated on the steam bath for 45 min. A little ethanol was added to the cooled melt, and on rubbing the product solidified. Several crystallizations from water yielded the iodide as fine, pale yellow needles (5.8 g., 56%), m.p. 255–256° dec. with previous darkening.

Anal. Calcd. for $C_{20}H_{17}N_2OI$: C, 56.1; H, 4.0; N, 6.5; Found: C, 56.0; H, 3.8; N, 6.5.

The *perchlorate* crystallized from acetone as colorless needles, m.p. 243–244° dec.

Anal. Calcd. for $C_{20}H_{17}N_2O_5Cl$: C, 59.94; H, 4.3; N, 6.99. Found: C, 59.96; H, 4.4; N, 6.7.

1-(2-3′-Indolyl-2-oxoethyl)-3-methylpyridinium iodide. This was prepared as above from 3-acetylindole (1.6 g., 0.01 mole), β-picoline (2.82 g., 0.03 mole), and iodine (2.5 g., 0.01 mole). The yield of crude material was 2.3 g., 64%, m.p. 249–250° dec. and after several crystallizations from water the iodide was obtained as pale pink needles, m.p. 266–267° dec.

Anal. Calcd. for $C_{16}H_{15}N_2OI$: C, 50.8; H, 4.0; N, 7.4. Found: C, 51.2; H, 4.1; N, 6.8.

The *perchlorate* crystallized from water as long, white needles, m.p. 249–250°.

Anal. Calcd. for $C_{16}H_{15}N_2O_5Cl$: C, 54.8; H, 4.3; N 7.99. Found: C, 54.9; H, 4.4; N, 7.8.

3-Ethyl-1-(2-3′-indolyl-2-oxoethyl)-4-methylpyridinium iodide. The use of 3-ethyl-4-methylpyridine in the above condensation gave the corresponding iodide, (2.7 g., 22%) which separated from water as fine, pale fawn needles, m.p. 260–262° dec.

Anal. Calcd. for $C_{18}H_{19}N_2OI$: C, 53.2; H, 4.7; N, 6.9; Found: C, 53.1; H, 4.7; N, 6.6.

The *perchlorate* crystallized from acetone as small, white needles, m.p. 264–265° dec. with previous darkening.

Anal. Calcd. for $C_{18}H_{19}N_2O_5Cl$: C, 57.1; H, 5.1; N, 7.4. Found: C, 57.6; H, 5.3; N, 7.1.

5,7,8,13,13b,14-Hexahydrobenz[g]indolo[2,3-a]quinolizine (hexadehydroyohimbane) (II). Finely powdered 2-(2-3′-indolyl-2-oxoethyl)isoquinolinium iodide (900 mg.) was added portion-wise to lithium aluminum hydride (500 mg.) in dry tetrahydrofuran (70 ml.), and the mixture heated under reflux for 4.5 hr. The excess of lithium aluminum hydride was decomposed by the careful addition of water, and the reaction mixture then acidified with hydrochloric acid. Evaporation of the tetrahydrofuran left an orange powder which was collected and dried (470 mg., m.p. 275–278°). After crystallization from methanol (charcoal) 5,7,8,13,13b,14-hexahydrobenz[g]indolo[2,3-a]quinolizine hydrochloride separated as fine, colorless needles, m.p. 295–297° dec. (lit.,[1] m.p. 288–289°).

Anal. Calcd. for $C_{19}H_{19}N_2Cl$: C, 73.4; H, 6.2; N, 9.0. Found: C, 73.4; H, 6.5; N, 8.6.

The free base was obtained by the addition of solid sodium hydroxide to a solution of the hydrochloride (80 mg.) in hot water (20 ml.). The precipitated material (76 mg., m.p. 194°) crystallized from aqueous methanol as cream needles, m.p. 193–195° with previous darkening (lit.,[6] m.p. 196–197°).

Anal. Calcd. for $C_{19}H_{18}N_2$: C, 83.2; H, 6.6; N, 10.2. Found: C, 82.9; H, 6.7; N, 9.9.

Both samples had infrared spectra identical with those of authentic specimens.

5,7,8,13,13b,14-Hexahydro-1′-methylbenz[g]indolo[2,3-a]-quinolizine (ind-N-methylhexadehydroyohimbane). Finely powdered hexadehydroyohimbane (450 mg.) was added to a stirred solution of sodamide in liquid ammonia (from 41 mg. of sodium in *ca.* 40 ml. of liquid ammonia). After 5 min. methyl iodide (300 mg.) was added, and the mixture stirred at room temperature until all the ammonia had evaporated. Water was added and the product collected (450 mg., m.p. 121–123°). Crystallization from methanol yielded colorless plates, m.p. 135° (lit.,[30] m.p. 135°).

Anal. Calcd. for $C_{20}H_{20}N_2$: C, 83.3; H, 7.0; N, 9.7. Found: C, 83.6; H, 7.3; N, 9.7.

The picrate formed in ethanol and crystallized from eth-

(31) D. E. Ames, R. E. Bowman, D. D. Evans, and W. A. Jones, *J. Chem. Soc.*, 1984 (1956).

(32) Melting points of samples were determined in capillaries and evaporations were done under reduced pressure on the water bath. Microanalyses were performed by the C.S.I.R.O. Microanalytical Laboratory, Melbourne, Australia.

(33) Y. A. Baskakov and M. N. Melnikov, *Sbornik Statei Obshchet Khim. Akad. Nauk S.S.S.R.*, 1, 712 (1953); *Chem. Abstr.*, 49, 1006d (1955).

anol as small, yellow needles, m.p. 208° dec. (lit.,[1] m.p. 208–209° dec.).

Acknowledgment. D. R. L. acknowledges the award of a Commonwealth Postgraduate Scholarship; we wish to express our thanks to Professor G. M. Badger for his interest in this work.

SOUTH AUSTRALIA
LOUISVILLE 8, KY.

[CONTRIBUTION FROM AVERY LABORATORY, THE UNIVERSITY OF NEBRASKA]

Physical and Chemical Properties of Hydroxyflavones. I. Infrared Absorption Spectra of Monohydroxyflavones and Their *O*-Methyl and *O*-Acetyl Derivatives[1,2]

J. H. LOOKER AND WALTER W. HANNEMAN[3]

Received June 19, 1961

Infrared carbonyl frequencies in appropriate solution(s), and in solid state, are presented for 1,4-pyrone, chromone, 2-methylchromone, flavone, pyromeconic acid, chromonol, and monohydroxy-, monomethoxy-, and monoacetoxyflavones. The spectral data are interpreted as indicating no significant resonance interactions between hydroxyl, or methoxyl, and flavone carbonyl groups. Solid state (potassium bromide disk) spectral data are presented for the fundamental ring systems and for monohydroxy- and monomethoxyflavones in the 3500–2200- and 1650–650-cm.$^{-1}$ regions. Group frequencies are assigned when possible, with emphasis on O—H and C—H stretching bands, in-plane skeletal vibrations, and out-of-plane deformation bands. Bands possibly associated with the pyrone oxide vibration are discussed. Spectral data, especially O—H, C—H, and carbonyl stretching frequencies, of 5-hydroxyflavone and its deuteration product are compared.

Infrared spectral data have been invaluable in the investigation of virtually all classes of organic compounds.[4–6] In the flavonoid area, of several investigations already reported, the most extensive, perhaps, have been the studies of Hergert and Kurth,[7] and Shaw and Simpson.[8] Frequency shifts caused by methoxyl groups, and 3- and 5-hydroxyl groups are emphasized by the latter group. Hergert and Kurth present a systematic study of acetophenone derivatives, flavanone, and chalcone, and then interpretations of spectra of several rather complex chalcone, flavanone, and flavone derivatives. The latter include quercetin and three of its derivatives, rutin, and 3,3′,4′,5,8-pentahydroxyflavone and its pentaacetate. Both studies[7,8] emphasize carbonyl absorption.

There is agreement on the following points: (1) Suitable substituents at the 5- and 7- positions of flavanones cause large frequency shifts in the flavanone carbonyl stretching frequencies due to resonance or chelation. (2) The 5-hydroxyl group of flavones is involved in hydrogen bonding. There is no agreement on whether introduction of a 7-methoxyl group onto an unchelated flavone molecule decreases the carbonyl stretching frequency or has no effect.

In the present paper, we report spectral characteristics for the fundamental ring systems 4-pyrone (4*H*-pyran-4-one), chromone, flavone, their 3-hydroxyl derivatives, and for the monohydroxyflavones, their methyl ethers, and their acetates. Of the thirty compounds studied, solution carbonyl frequencies have been listed previously for six (Tables I–III). In addition, partial infrared spectral data for 4-pyrone were reported[9] several years ago. The present work is intended to be sufficiently extensive and systematic that it may serve as a basis for future infrared studies of more complex flavonoid molecules. Certain experimental difficulties must be stressed at the outset, however, notably, the sparing solubility of many flavone derivatives in standard spectral solvents. Inasmuch as carbonyl bands can be located reliably in most instances, somewhat greater emphasis has been placed on this function. However, complete solid state spectra are reported for hydroxy- and methoxy flavones, and interpreted to the extent that appears possible. Certain infrared spectral properties of 5-hydroxyflavone and its deuteration product are discussed.

I. *Carbonyl Absorption.* In Tables I–IV are listed carbonyl absorption bands for the compounds of the present work. In Table I are given bands due to the carbonyl group in 4-pyrone, chromone,

(1) From a portion of the Ph.D. thesis of Walter W. Hanneman, the University of Nebraska, 1958.

(2) This investigation was supported in part by a research grant (E-1703) from the National Institute of Allergic and Infectious Diseases, Public Health Service, and in part by a grant from the University of Nebraska Research Council.

(3) Dow Chemical Fellow, 1956–1957; Public Health Service Research Fellow of the National Institute of Dental Research, 1957–1958.

(4) L. J. Bellamy, *The Infrared Spectra of Complex Molecules*, J. Wiley and Sons, Inc., New York, 1958.

(5) F. A. Miller, *Organic Chemistry*, Vol. 3, H. Gilman, Ed., J. Wiley and Sons, Inc., New York, 1953, pp. 128–158.

(6) A. R. Katritzky, *Quart. Rev. (London)*, **13**, 353 (1959).

(7) H. L. Hergert and E. F. Kurth, *J. Am. Chem. Soc.*, **75**, 1622 (1953).

(8) B. L. Shaw and T. H. Simpson, *J. Chem. Soc.*, 655 (1955).

(9) A. Ross, *Proc. Roy. Soc. (London)*, A **113**, 208 (1926); *Chem. Zentr.*, **1927** I, 2422.