2.3, and 1.0 cps), 0.87 (19-Me), and 0.80 ppm (18-Me); ORD 352 (−3250) and 297 mμ (+6700); CD 331 mμ (−7760).

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.06; H, 9.15.

Testosterone Acetate (21). A.—Acetylation of **testosterone 20** in the usual way gave **21**: mp 141–142°; $[\alpha]_D$ +96.2°.

B.—The bromo ketone **22** (300 mg) was dehydrobrominated with Li_2CO_3 (180 mg) in DMF (4 ml) to give the enone **21** (221 mg; mp 136–138°, mmp 138–140°; $[\alpha]_D$ +93.1°), whose tlc showed a faint spot of the enone **3**, besides a main spot of **21**.

Epoxidation of the Enone 1.—To a solution of the enone **1** (600 mg) in MeOH (20 ml) and CH_2Cl_2 (6 ml) was added 30% H_2O_2 (1.8 ml) and 4 *N* NaOH (0.9 ml) at 0°, and the reaction mixture was kept in an ice chest at 3° for 48 hr. Dilution with water and extraction with CH_2Cl_2 gave a product (423 mg; mp 167–174°), which on recrystallization from EtOH afforded 297 mg (47%) of **17β-acetoxy-2α,3α-epoxy-5α-androstan-1-one (24)**: mp 177–178°; $[\alpha]_D$ +20.6°; nmr, δ 3.43 ($C_{3\beta}$-H, m), 3.13 ($C_{2\beta}$-H, d, J = 3.5 cps), 1.01 (19-Me), and 0.78 ppm (18-Me); ORD 342 (−2110) and 298 mμ (+3670); CD 321 mμ (−4080).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.41; H, 8.74.

The residue after separation of the α isomer **24** showed, in addition to the signals which are due to the α isomer, a doublet at 3.21 ppm (J = 5 cps) and a singlet at 1.22 ppm, ascribable to the presence of the β isomer **25**. The aqueous solution, after extraction of the neutral component, was acidified with dilute HCl, extracted with CH_2Cl_2, esterified with CH_2N_2, and separated by preparative tlc to afford an ester (145 mg, 20%).

Epoxidation of the Enone 4.—A solution of the enone **4** (507 mg) in CH_2Cl_2 (5 ml) and MeOH (10 ml) was treated with 30% H_2O_2 (1.5 ml) and 4 *N* NaOH (0.75 ml) at 0°. Working up as mentioned above gave 494 mg of a neutral product, which on recrystallization from ether afforded 319 mg (60%) of **17β-acetoxy-2α,3α-epoxy-5α-androstan-4-one (26)**: mp 123–125°; $[\alpha]_D$ +9.0°; nmr, δ 3.50 ($C_{2\beta}$-H, m), 3.23 ($C_{3\beta}$-H, d, J = 3.8 cps), 0.76 (19-Me), and 0.79 ppm (18-Me); ORD 324 (−1850), 314 (−1620), and 280 mμ (+3060); CD 307 (−2850) and 300 mμ (−3020).

Anal. Calcd for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 73.02; H, 8.71.

The 2β,3β-epoxy-4-one **27** was detected by the additional signals (multiplet at 3.05 and singlet at 1.10 ppm) in the nmr spectrum of the residue after separation of the α isomer. An acidic component (30 mg) was isolated but resisted purification, even as a methyl ester as shown by a multiplicity of spots on tlc.

Registry No.—**1**, 6199-40-2; **2**, 68-61-1; **4**, 65-01-0; **6**, 5846-70-8; **10**, 16801-95-9; **11**, 16801-96-0; **12**, 16801-97-1; **13**, 16801-98-2; **14**, 16801-85-7; **15**, 16801-86-8; **17**, 1236-50-6; **18**, 16801-88-0; **19**, 2311-73-1; **21**, 1045-69-8; **22**, 16801-91-5; **23**, 1242-08-6; **24**, 16801-93-7; **26**, 16801-94-8.

The Alkaloids of *Tabernaemontana crassa*. Crassanine, a New Oxindole Alkaloid

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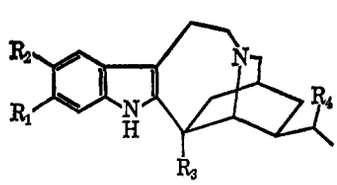
As part of an extended chemotaxonomic study of the genus *Tabernaemontana* (Apocynaceae),[1] we now describe the results of a study of the alkaloids of the African species, *Tabernaemontana crassa* Benth.

The major alkaloid of *T. crassa* proved to be the known ibogamine-type base, conopharyngine (**1**);[2] an amorphous base, which we were unable to completely purify by chromatography, was the second most abundant alkaloid. This latter base, which was assigned the structure of 20-hydroxyconopharyngine (**2**), was purified instead by a new procedure which should be widely applicable for the isolation of related bases.[3] Thus, the reaction of impure **2** with benzyl chloroformate in pyridine afforded the crystalline carbobenzoxy ester **3**, from which pure **2** was readily regenerated by hydrogenolysis in the presence of palladium.

The assigned structure of **2** fully agreed with its spectral properties. Its ultraviolet absorption spectrum was that of a typical 5,6-dimethoxyindole; indeed, it was essentially identical with that of conopharyngine (**1**). In addition, the nmr spectrum of **2** was similar to that of its unmethoxylated analog, heyneanine (**4**),[4] except that the spectrum of **2** clearly showed the presence of the 5,6-dimethoxyindole system in the form of methoxyls at δ 3.78 and 3.86 and a pair of unsplit aromatic protons at 6.71 and 6.83. Furthermore, the mass spectrum of **2** was exactly analogous to the published spectrum of heyneanine (**4**),[4] except that the fragments from **2** containing the indole nucleus were 60 mass units heavier than those from **4** because of two methoxy substituents on the aromatic ring.



1, $R_1 = R_2 = OCH_3$; $R_3 = COOCH_3$; $R_4 = H$
2, $R_1 = R_2 = OCH_3$; $R_3 = COOCH_3$; $R_4 = OH$
3, $R_1 = R_2 = OCH_3$; $R_3 = COOCH_3$; $R_4 = OCO_2CH_2C_6H_5$
4, $R_1 = R_2 = H$; $R_3 = COOCH_3$; $R_4 = OH$
5, $R_1 = R_2 = OCH_3$; $R_3 = R_4 = H$
6, $R_1 = R_2 = OCH_3$; $R_3 = H$; $R_4 = OH$

The structure of **2** was confirmed by its chemical conversion into ibogaline (**5**), using the general degradative scheme which has been employed previously with other 20-hydroxyibogamine-type bases.[5–8] Thus, hydrolysis of the ester function of **2**, followed by decarboxylation, yielded the amorphous 20-hydroxyibogaline (**6**). Reaction of **6** with tosyl chloride in pyridine gave the corresponding quaternary tosylate (**7**) which was reduced directly by lithium aluminum hydride to give ibogaline (**5**). After this work was completed, a preliminary report appeared on the isolation of 20-hydroxyconopharyngine (**2**) from *Conopharyngia jol-*

(1) For the previous report in this series, see M. P. Cava, S. S. Tjoa, Q. A. Ahmed, and A. I. daRocha, *J. Org. Chem.*, **33**, 1055 (1968).

(2) U. Renner, D. A. Prins, and W. G. Stoll, *Helv. Chim. Acta*, **42**, 1572 (1959).

(3) The conversion of the amorphous isovoacristine into its crystalline carbobenzoxy ester has been described by S. K. Mowdood [Ph.D. Dissertation, The Ohio State University, Columbus, Ohio, 1966].

(4) T. R. Govindachari, B. S. Joshi, A. K. Saksena, S. S. Sathe, and N. Viswanathan, *Tetrahedron Lett.*, 3873 (1965).

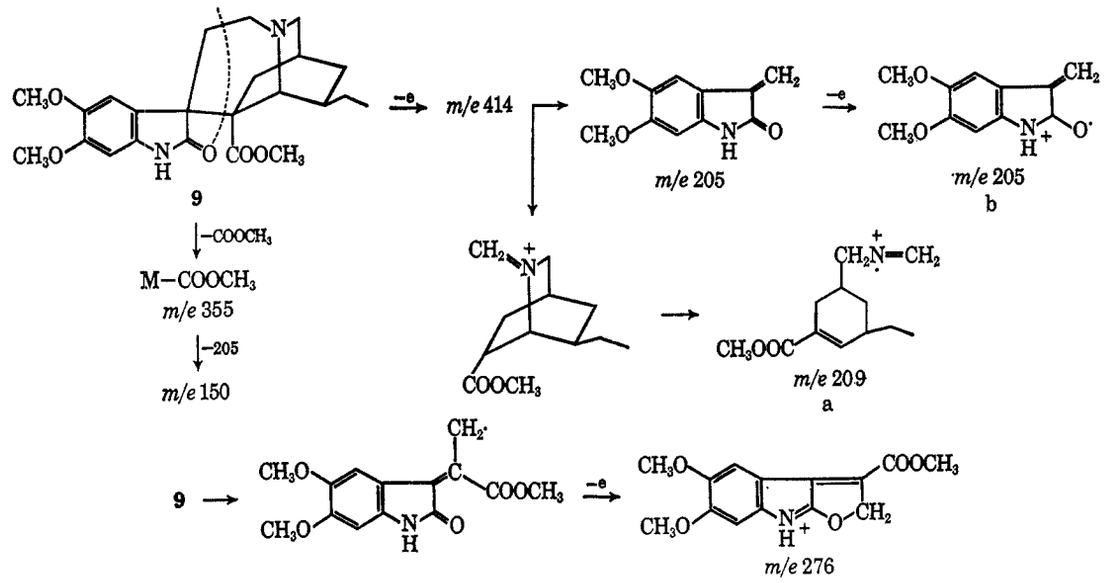
(5) U. Renner and D. A. Prins, *Experientia*, **15**, 456 (1959).

(6) M. P. Cava, S. K. Mowdood, and J. L. Beal, *Chem. Ind.* (London), 2064 (1965).

(7) T. R. Govindachari, B. S. Joshi, A. K. Saksena, S. S. Sathe, and N. Viswanathan, *Chem. Commun.*, 97 (1966).

(8) S. M. Kupchan, J. M. Cassady, and S. A. Telang, *Tetrahedron Lett.*, 1251 (1966).

SCHEME I



CRASSANINE

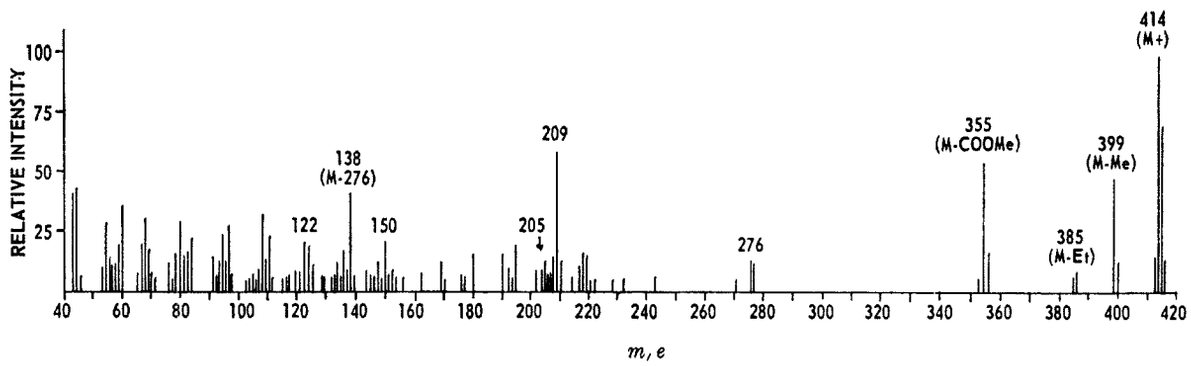
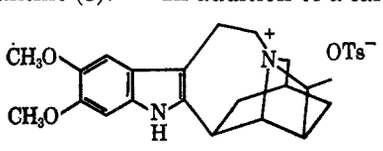


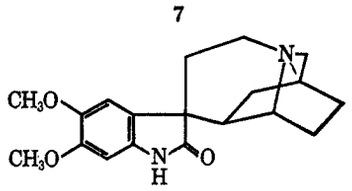
Figure 1.

lyana and *C. durissima*, and on its structure proof, using methods similar to those just described.[9]

The least abundant base isolated from *T. crassa* was a new crystalline alkaloid, crassanine, mp 190–191°, which was isomeric (M^+ 414) with 20-hydroxyconopharyngine (**2**). The infrared spectrum of crassanine indicated the presence of two carbonyl groups (1739 and 1709 cm^{-1}). Its ultraviolet absorption spectrum (see Experimental Section) was different from that of a 5,6-dimethoxyindole, but was very similar to that of known 5,6-dimethoxyoxindole alkaloids such as kisantine (**8**).[10] In addition to a carbomethoxy methyl at δ 3.47, the nmr spectrum of crassanine reveals two aromatic methoxyls at δ 3.83, single unsplit aromatic protons at 6.50 and 7.01, and the low-field oxindole NH at 9.30. The latter values are to be compared with the similar corresponding values (δ 3.9, 6.56, 7.1, and 9.1) recorded for kisantine (**8**).[10] On this basis, crassanine has been assigned structure **9**, which is that of an oxindole corresponding to the indole conopharyngine. At this time, no evidence is available on the configuration at the C-3 spiro carbon. It is interesting to note that a Dreiding model of either of the C-3 epimers of **9** suggests that the carbomethoxy methyl will be somewhat shielded by the aromatic ring, and the carbomethoxy methyl of crassanine does appear, in fact, at the rather shielded position of δ 3.47.



7



8

The mass spectrum of crassanine (Figure 1) is in good accord with structure **9**. In common with the corresponding spectrum of kisantine,[10] peaks are observed at M − CH_3 and M − C_2H_5, and the fragments derived from the isoquinuclidine system are observed at *m/e* 122 and 138. Loss of the carbomethoxy function of **9** leads to the strong peak at *m/e* 355. The most significant pair of peaks in the spectrum of **9** are those at *m/e* 209 and 205; these correspond to fragments a and b, the formation of which can be easily rationalized, as shown in Scheme I; the origin of the peaks at *m/e* 150 and 276 is also suggested in this scheme.

(9) C. Hootele, J. Pecher, U. Renner, and R. H. Martin, *Chimia*, **21**, 133 (1967).

(10) W. I. Taylor, *J. Org. Chem.*, **30**, 309 (1965).

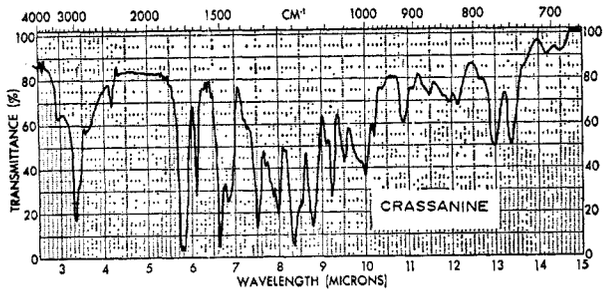


Figure 2.

A number of indole alkaloids have been converted into their oxindole analogs.[11,12] Preliminary attempts to adapt the procedures described in the literature to the transformation of conopharyngine into crassanine have not been successful to date. We plan to continue this investigation when additional supplies of conopharyngine can be obtained.

Experimental Section

Plant Material and Crude Tertiary Bases.—Although *T. crassa* is native to Africa rather than to the South Pacific, the material used in this investigation was collected near the botanical garden in Tahiti in December 1964, by Mr. George Uhe of the Department of Botany, University of Auckland, New Zealand. A voucher specimen (no. 718) has been preserved in Mr. Uhe's personal herbarium. We gratefully acknowledge Mr. Uhe's assistance in collecting and identifying this plant.

The dried and ground plant material (23.75 lb of bark, leaves, twigs, and fruit) was extracted with alcohol in the usual manner. The concentrated extract was refluxed for about 1 hr with ethyl acetate containing 5% concentrated aqueous ammonia. After it had cooled, the ethyl acetate was decanted, and the residue was reextracted until it was free of alkaloids (Mayer's test). The tertiary bases were removed from the combined ethyl acetate extracts by extraction with 5% aqueous H_2SO_4. The acid extract was washed with benzene and made basic with ammonia, and the alkaloids were extracted with chloroform to give 26.5 g of crude tertiary bases after solvent evaporation.

Separation and Characterization of the Tertiary Bases.—A major aliquot (21.4 g) of the crude tertiary bases was dissolved in chloroform (50 ml) and benzene (200 ml) was added. The resulting precipitate (8.0 g) was removed by filtration; it was not further investigated. The filtrate was shaken successively with the following aqueous phases to give, after the usual work-up, the weights of alkaloidal material recorded: (a) 1% NaOH, 0.1 g; (b) pH 5 McIlvain buffer, 0.8 g; (c) pH 4 McIlvain buffer, 2.2 g; and (d) 3.5% HCl, 9.2 g. Additional work described in this paper was carried out with the major 3.5% HCl fraction; thin layer chromatography of the only other major fraction (pH 4) indicated the absence of additional major constituents.

The pH 3.5 fraction (9.2 g) appeared by tlc ($CHCl_3$–CH_3OH on silica gel H) to consist of two major constituents of similar R_f, and one minor constituent. The less polar compound was partially separated by repeated chromatography on alumina (neutral, grade II), the columns being eluted with benzene, followed by benzene–chloroform mixtures. When the pure benzene fractions were evaporated and crystallized from ether, they afforded conopharyngine (1, 4.48 g), mp 133–136° (lit.[1] mp 141–143°). This material was identical (ir and uv spectra) with an authentic sample kindly supplied by Dr. U. Renner (Geigy, A. G., Basel).

On concentration, some of the benzene–chloroform fractions deposited crystals (0.070 g) of the minor base, crassanine (9). Crassanine crystallized from chloroform as colorless plates, mp 190–191°. The physical data for crassanine were as follows: $[\alpha]^{26}D$ +21.4 (*c* 0.013, EtOH); λ_{max}, mμ (log ε), 210 (4.37), 275 (3.68), and 302 (3.55); $\nu_{max}^{CHCl_3}$ 1739 and 1701 cm^{-1}; nmr, δ 9.30 (NH, singlet), 6.50 and 7.01 (aromatic singlets, 1 H each), 3.83 (aromatic OCH_3, singlet, 6 H), and 3.47 (ester OCH_3, singlet, 3 H). See Figure 1 for the mass spectrum of 9. Infrared spectral data is given in Figure 2.

The more polar major, alkaloid was the principal constituent of the benzene–chloroform fractions. This material, 20-hydroxyconopharyngine (2), was obtained in pure form as follows: a sample of crude 2 (0.0988 g) was dissolved in dry pyridine (1.6 ml) and treated with an excess of benzyl chloroformate, work-up in the usual manner, followed by crystallization from methanol, afforded 20-carbobenzoxyconopharyngine (3, 0.0396 g), mp 193°.

Anal. Calcd for $C_{31}H_{36}N_2O_7$: C, 67.87; H, 6.61. Found: C, 68.14, 67.98; H, 6.92, 6.79.

Hydrogenolysis of ester 3 in methanol in the presence of 5% palladium–charcoal gave pure 20-hydroxyconopharyngine (2) as an amorphous glass, tlc of which showed only one clear spot.

The physical data for 20-hydroxyconopharyngine were as follows: $[\alpha]^{26}D$ −36.4 (*c* 1.62, $CHCl_3$); λ_{max}, mμ (log ε), 226 (4.42) and 304 (3.93); $\nu_{max}^{CHCl_3}$, 3521, 1730, and 1639 cm^{-1}; nmr, δ 6.71 and 6.83 (aromatic singlets, 1 H each), 3.86 (aromatic OCH_3, 3 H), 3.78 (aromatic OCH_3, 3 H) 3.70 (ester OCH_3, 3 H) 1.12 δ (CH_3-CH(OH)-, doublet, J = 6). The mass spectrum showed significant peaks at 414 (M^+), 396, 370, 369, 312, 274, 268, 255, 254, 214, 190, 152, 140, 122, 108, and 94.

Degradation of 20-Hydroxyconopharyngine (2) to Ibogaline (5).—Purified base 2 (0.227 g) was hydrolyzed by heating with 20% KOH in methanol. After methanol was removed, the resulting salt was made strongly acid with aqueous HCl and heated on the steam bath for 1 hr to effect decarboxylation. Basification of the solution afforded the amorphous 20-hydroxyibogaline (6, 0.164 g), which was treated with tosyl chloride in pyridine. A portion (0.025 g) of the resulting crude quaternary tosylate (7, 0.063 g) was reduced with $LiAlH_4$ in refluxing tetrahydrofuran to give, after work-up and crystallization, ibogaline (5, 0.003 g), mp 138–142°. This material was identical (mixture melting point and ir spectra) with material prepared from conopharyngine by hydrolysis and decarboxylation.[2]

Registry No.—2, 16790-93-5; 3, 16790-91-3; 9, 16790-92-4.

(11) N. Finch and W. I. Taylor, *J. Amer. Chem. Soc.*, **84**, 3871 (1962).
(12) J. Shavel and H. Zinnes, *ibid.*, **84**, 1320 (1962).

3-Hydroxy- and Alkoxyaryl Derivatives of 1,2-Dithiolium Salts

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Certain 1,2-dithiolium salts have been shown to undergo substitution reactions at the 3 position of the dithiolium ring with nucleophiles such as amines, hydrazines, and the anions of active methylene compounds.[1]

It has now been found that 3-chloro-5-phenyl-1,2-dithiolium perchlorate (1) reacts with relatively unreactive nucleophiles such as hydroxy- and alkoxy-substituted aromatic compounds to give 3-aryl-1,2-dithiolium salts. Benzene derivatives which contain one hydroxy, alkoxy, or thioalkyl group fail to yield aryldithiolium salts when allowed to react with 1. However, the corresponding *meta*-disubstituted benzene derivatives readily react with 1, and naphthalene derivatives containing only one hydroxy group give aryldithiolium salts. These results are similar to many other substitution reactions of strong electrophiles with benzene and naphthalene derivatives of this type.[2]

(1) P. S. Landis, *Chem. Rev.*, **65**, 237 (1965).
(2) *Cf.* M. R. DeMaheas, *Bull. Soc. Chim. Fr.*, 1989 (1962).