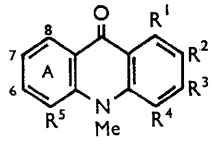
South African Plant Extractives. Part II.[1] Alkaloids of *Teclea natalensis*

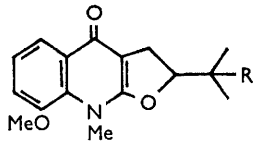
By **K. H. Pegel*** and **Winifred G. Wright**, Department of Chemistry, University of Natal, Durban, South Africa

Evoxanthine, arborinine, and a new alkaloid tecleanthine, $C_{17}H_{15}NO_5$, have been isolated from *Teclea natalensis*; the structure of tecleanthine is indicated.

A NEW alkaloid, tecleanthine (Ia), and two known alkaloids, evoxanthine (Ib) and arborinine (Ic), have been isolated from the bark of *Teclea natalensis* in yields of 0·015, 0·016, and <0·001% respectively. Both evoxanthine and arborinine were identified by comparison of m.p.s and u.v., i.r., and mass spectra with those of authentic samples. Mass measurements of the molecular ion of tecleanthine (*m/e* 313) indicated a molecular formula $C_{17}H_{15}NO_5$. The alkaloid gave a positive



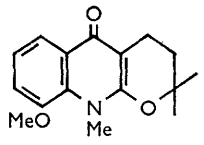
(I)



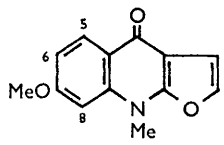
(II)

	R^1	R^2	R^3	R^4	R^5
a;	OMe	O·CH_2·O		H	OMe
b;	OMe	O·CH_2·O		H	H
c;	OH	OMe	OMe	H	H
d;	OH	O·CH_2·O		H	OMe
e;	OMe	O·CH_2·O		OMe	H
f;	OMe	OMe	O·CH_2·O		H
g;	OH	O·CH_2·O		H	H

a; R = OH
b; R = H



(III)



(IV)

methylenedioxy-test,[2] formed a picrate, m.p. 171°, and a picrolonate, m.p. 175—176°. Alcoholic solutions showed a strong blue fluorescence; the fluorescence was replaced by a deep green colour on addition of ferric chloride. The u.v. absorption and the mass fragmentation pattern were both similar to those of evoxanthine, suggesting a 9-acridone structure for the alkaloid.

The n.m.r. spectrum of a solution in deuteriochloroform showed two methoxy-groups [τ 5·88 and 6·20 (each 3H, s)] and one methylimino-group [τ 6·10 (3H, s)]. The latter singlet was shifted more downfield than the methoxy-singlets in trifluoroacetic acid.[3] A singlet at τ 4·01 corresponded to them ethylenedioxy-group. The structure of ring A was indicated by an ABX system: τ 2·00 (1H, q, *J* 6·6 and 3·3 c./sec., 8-H, deshielded by the neighbouring 9-carbonyl group) and 2·81—2·94 (2H, m, 6- and 7-H), showing that there is present an aromatic ring with only three adjacent protons. A singlet signal from another aromatic proton at τ 3·40 must be assigned to the other benzene ring. One methoxy-group was readily hydrolysed to a hydroxy-group with ethanolic hydrochloric acid, to form orange crystals of nortecleanthine (Id), m.p. 207°, insoluble in potassium hydroxide. This is characteristic of the 1-methoxy-group[4] to which the n.m.r. signal at τ 5·88 was assigned; the protons are deshielded by the carbonyl group.

The ABX pattern of the aromatic protons in ring A indicates that the second methoxy-group (τ 6·20) is at C-5. The position of the proton τ 3·4 could not be determined by n.m.r., the difference in the chemical shifts for positions 2 and 4 being indistinguishable;[5,6]

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[5] P. L. McDonald and A. V. Robertson, *Austral. J. Chem.*, 1966, **19**, 275.
[6] J. A. Diment, E. Ritchie, and W. C. Taylor, *Austral. J. Chem.*, 1967, **20**, 1719.

thus the methylenedioxy-group could be attached to positions 2 and 3 or 3 and 4. However, a comparison of physical properties with those of evoxanthine, melicopidine (Ie), and melicopine (If) showed the following significant differences. Tecleanthine, evoxanthine, and melicopidine all have an acid-induced shift of +60—73 mμ for a u.v. absorption in the 300 mμ region. Melicopine, differing from melicopidine only in the relationship of the methylenedioxy-group to the nitrogen, shows no shift in acid solution. Melicopine is the only one of these compounds not to give a deep green colour with alcoholic ferric chloride. Tecleanthine and evoxanthine have common significant peaks in the mass spectra at $M-28$, $M-46$, $M-58$, $M-73$, and $M-206$, of the same order of magnitude. These facts favour the structure 1,5-dimethoxy-10-methyl-2,3-methylenedioxy-9-acridone for tecleanthine.

No naturally occurring acridone oxygenated in ring A has been isolated before, but balfouridine (IIa), lunacrine (IIb), and the pyranoquinolone [7] (III), which have the same methoxy-quinolone fragment as tecleanthine, have a similar aromatic proton pattern in the n.m.r. spectra, different from that of isoevolitrine [8] (IV), as shown in the Table. For (Ia) J_{ortho} (6·6 Hz) is surprisingly smaller, and J_{meta} (3·3 Hz) larger than the corresponding coupling constants for compounds (IIa), (IIb), and (III) (Table). This may be a characteristic of acridones monosubstituted with a 5-alkoxy-group in ring A.

	Chemical shift (τ) H *peri* to C=O	Observed splitting (Hz) J_{AX}	J_{BX}	Chemical shift (τ) 2, *ortho* and *meta* to *peri*-H
(Ia)	2·00(q)	6·6	3·3	2·88(m)
(IIa)	1·92(q)	8	2	2·81(m)
(IIb)	1·89(q)	7	2	2·81(m)
(III)	1·97(q)	7	2	2·86(m)
(IV)	1·88(d)	9·5		

The alkaloids arborinine,[9] evoxanthine, melicopidine, and melicopine, which are not substituted in ring A, give a broadened doublet centred at τ 1·77, 1·77, 1·67, and 1·63, respectively for the 8-proton.

Because the i.r., u.v., and n.m.r. data have not been fully recorded for evoxanthine, melicopidine, and melicopine, these values have been included in the Experimetal section.

EXPERIMENTAL

N.m.r. spectra were recorded with a Varian A60 spectrometer. U.v. spectra for solutions in acid were recorded by adding concentrated hydrochloric acid (1 drop) to the solution (3 ml.) and spectra for alkaline solutions by adding 10% sodium hydroxide (1 drop). Mass spectra were measured with an A.E.I. MS9 machine.

Milled, air-dried bark (6 kg.) of *Teclea natalensis* (Sond.) Engl. (Natal Herbarium number NH 51879), was extracted with hexane and benzene, and the solutions were concentrated. The alkaloidal deposits, found by t.l.c. to contain the same substances, were combined, dissolved in chloroform, and passed through an alumina column prepared from a sludge of alumina in benzene. Elution with chloroform gave firstly *tecleanthine* (900 mg.) and secondly evoxanthine (960 mg.); elution with 2% ethanol–chloroform then gave aborinine (29 mg.).

Tecleanthine (Ia) is a weak base, giving a deep yellow solution in 2N-hydrochloric acid. The alkaloid was purified by crystallisation from ethanol, to give large yellow prisms, m.p. 158°, soluble in ethanol, benzene, acetone, ethyl acetate, and chloroform. Alcoholic solutions had a strong blue fluorescence, becoming deep green on addition of ferric chloride solution (Found: C, 65·3; H, 5·1; N, 4·6%; M^+, 313·0947. $C_{17}H_{15}NO_5$ requires C, 65·2; H, 4·8; N, 4·5%; M^+, 313·0950), *m/e* 313 (M^+, 100%), 285, 270, 267, 255, 240, 239, 224, 212, and 77, $\nu_{max.}$ (KBr) 1635sh, s, 1618s, 1589s, and 1572s cm.$^{-1}$, $\lambda_{max.}$ (EtOH) 220sh, 236, 269, 281sh, 306sh, and 401 mμ (log ε 4·29, 4·23, 4·74, 4·68, 3·83, and 4·05), $\lambda_{max.}$ (EtOH–HCl) 220sh, 240sh, 270, 284, 293, 366, 406, and 453sh mμ (log ε 4·30, 4·33, 4·64, 4·67, 4·76, 4·02, 3·93, and 3·57), $\lambda_{max.}$ (EtOH–NaOH) no change, τ ($CDCl_3$) 6·20 (3H, s, OMe), 6·10 (3H, s, NMe), 5·88 (3H, s, OMe), 4·01 (2H, s, O·CH_2·O), 3·40 (1H, s, Ar), 2·81—2·94 (2H, m, H-6 and -7), and 2·00 (1H, q, H-8, *J* 6·6 and 3·3 c./sec. forming an ABX system with H-6 and -7), τ (CF_3·CO_2H) 5·85 (3H, s, OMe), 5·47 (3H, s, NMe), and 5·40 (3H, s, OMe).

Nortecleanthine (Id).—Tecleanthine (50 mg.) dissolved in conc. hydrochloric acid (0·15 ml.)–ethanol (3 ml.) was heated on a water-bath for 4 hr., and set aside until crystallisation was complete. There was an intermediate formation of gel, which eventually crystallised. The orange crystals of *nortecleanthine*, filtered off and washed with ethanolic hydrochloric acid, then ethanol, were elongated rectangular plates (29·5 mg., 62%), m.p. 207°, not raised by recrystallisation from ethanol. The crystals sublimed from 200°/1 atmos.

The compound was not soluble in potassium hydroxide solution, soluble in chloroform, and very sparingly soluble in ethanol and methanol. It was a very weak base, soluble only in concentrated hydrochloric acid. A deep green colour was produced with alcoholic ferric chloride (Found: M^+, 299·0799. $C_{16}H_{13}NO_5$ requires 299·0794), *m/e* 299 (M^+, 100%), 298, 284, 270, 256, 254, 242, 226, 213, 198, and 77, $\nu_{max.}$ (KBr) 390m, 1547s, 1601s, 1620s, and 1660s cm.$^{-1}$, $\lambda_{max.}$ (EtOH) 208, 222, 240, 269, 290, 318sh, and 413 mμ (log ε 4·36, 4·23, 4·28, 4·65, 4·64, 3·86, and 3·90), $\lambda_{max.}$ (EtOH–NaOH) 232sh, 260, 289, 327, and 422 mμ (log ε 4·28, 4·42, 4·47, 4·01, and 3·68), $\lambda_{max.}$ (EtOH–HCl) no change.

Tecleanthine Picrate.—Tecleanthine in ethanol gave a yellow crystalline precipitate with aqueous picric acid, which gave fine *needles*, m.p. 171° (from ethanol, in which it was very sparingly soluble) (Found: C, 50·8; H, 3·5. $C_{23}H_{18}N_4O_{12}$ requires C, 50·9; H, 3·35%).

Tecleanthine Picrolonate.—Tecleanthine and picrolonic acid were dissolved in methanol and heated. The precipitated picrolonate gave yellow *needles*, m.p. 175—176° (from hot methanol), distilling at 171°/1 atmos. The compound was very sparingly soluble in ethanol, very soluble in acetone (Found: C, 56·0; H, 4·25. $C_{27}H_{23}N_5O_{10}$ requires C, 56·1; H, 4·0%).

Evoxanthine (Ib), crystallised from acetone in yellow needles, m.p. 223°, subliming at 171°/1 atmos. The alcoholic

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solutions showed a strong blue fluorescence, becoming deep green on addition of ferric chloride solution. Mass spectrum *m/e* 283 (M^+, 85%), 255 (100%), 240, 237, 225, 224, 210, 209, 182, and 77, $\lambda_{max.}$ (EtOH) 215sh, 240sh, 275, 303sh, 320sh, 387sh, and 400 mμ (log ε 4·14, 4·11, 4·58, 3·57, 3·41, 3·83, and 3·86), $\lambda_{max.}$ (EtOH–HCl) 240, 267, 283, 346sh, 361, 403, and 430 mμ (log ε 4·26, 4·45, 4·55, 3·83, 4·03, 3·73, and 3·52), $\lambda_{max.}$ (EtOH–NaOH) no change, $\nu_{max.}$ 1568s, 1588s, and 1623 cm.$^{-1}$, τ (Me_2SO) 6·03 (3H, s, OMe), 6·18 (3H, s, NMe), 3·85 (2H, s, O·CH_2·O), 2·52 (3H, m, Ar), and 1·77 (1H, d, Ar).

Norevoxanthine (Ig).—Evoxanthine (50 mg.), dissolved in conc. hydrochloric acid (0·15 ml.)–ethanol (3 ml.) was heated on a water-bath for 2 hr. The resultant orange crystals of norevoxanthine were washed with ethanolic hydrochloric acid and methanol, and recrystallised from dioxan in elongated rectangular plates, m.p. 287°. The demethylation was repeated with an authentic sample of evoxanthine, and the resulting norevoxanthine, after washing with ethanolic hydrochloric acid and methanol, had m.p. 287°, without recrystallisation (31·4 mg., 66%). The crystals were shaken with aqueous sodium carbonate, and the mixture was extracted with chloroform. Concentration of the extract gave diamond-shaped crystals, subliming in diamond and hexagonal shapes at 220°/1 atmos. From 250° both original crystals and sublimate changed to rectangular plates, m.p. 287° (lit.,[10] 274—275°).

A very weak base, the compound was soluble in warm concentrated hydrochloric acid and in hot dioxan, and very sparingly soluble in ethanol, methanol, and chloroform. A deep green colour was produced with alcoholic ferric chloride solution (Found: M^+, 269·0689. Calc. for $C_{15}H_{11}NO_4$: 269·0688), $\nu_{max.}$ (KBr) 370s, 395m, 1548s, 1571s, 1602s, 1627s, and 1665s cm.$^{-1}$, $\lambda_{max.}$ (EtOH) 204, 218, 241, 263sh, 280, 330sh, and 406 mμ (log ε 4·27, 4·18, 4·35, 4·52, 4·66, 3·67, and 3·87), $\lambda_{max.}$ (EtOH–NaOH) 234, 250, 283, 324, and 422 mμ (log ε 4·32, 4·29, 4·56, 3·86, and 3·65), $\lambda_{max.}$ (EtOH–HCl) no change.

Melicopidine (Ie) had $\lambda_{max.}$ (EtOH) 207, 220sh, 257sh, 277, 300sh, and 403 mμ (log ε 4·38, 4·31, 4·44, 4·71, 3·96, and 3·94), $\lambda_{max.}$ (EtOH–HCl) 207, 220sh, 258sh, 277, 293sh, 373, and 406 mμ (log ε 4·32, 4·24, 4·42, 4·67, 4·31, 3·81, and 3·85), $\lambda_{max.}$ (EtOH–NaOH) no change, $\nu_{max.}$ (KBr) 1593s, 1600s, and 1620s cm.$^{-1}$, τ ($CDCl_3$) 6·13 (3H, s, OMe), 6·11 (3H, s, NMe), 5·93 (3H, s, OMe), 3·95 (2H, s, O·CH_2·O), 2·6 (3H, m, Ar), and 1·67 (1H, d, Ar).

Melicopine (If) had $\lambda_{max.}$ (EtOH) 216, 252sh, 271, 302, and 409 mμ (log ε 4·37, 4·49, 4·74, 4·19, and 3·89), $\lambda_{max.}$ (EtOH–HCl) no change, $\lambda_{max.}$ (EtOH–NaOH) no change, $\nu_{max.}$ (KBr) 1572s, 1587s, 1600s, 1615s, and 1635s cm.$^{-1}$, τ ($CDCl_3$) 6·08 (3H, s, NMe), 6·01 (6H, s, 2 × OMe), 3·95 (2H, s, O·CH_2·O), 2·6 (3H, m, Ar), and 1·63 (1H, d, Ar).

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[9/717 *Received, May 2nd,* 1969]

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