Alkaloids of *Daphnandra* Species. Part XI.[1] Some Dibenzo-*p*-dioxin-type Biscoclaurine Alkaloids from an Unnamed Species. The Structure of Micranthine

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Micranthine has been shown to have the trilobine-type structure (VII). The new alkaloids *O*-methylmicranthine (IV), its diastereoisomer telobine (VI), and *ON*-dimethylmicranthine (III) have been isolated from an unnamed species from northern New South Wales, together with the known alkaloids nortenuipine and fangchinoline.

THE taxonomy of the family Monimiaceae is at present under review, as a result of which it is expected that several new *Daphnandra* species will be established. We have examined a bark specimen collected from a tree growing in the Whian Whian State Forest, New South Wales, provisionally identified as specimen Dt-7, which has yielded five biscoclaurine alkaloids, including nortenuipine [2] and fangchinoline.[3] The major alkaloid, provisionally named base *a*, resembled trilobine [4] (I) in its mass spectrum,[5] in giving a positive dibenzodioxin

[1] Part X, I. R. C. Bick and W. I. Taylor, *J. Chem. Soc.* (*C*), 1971, 3779.

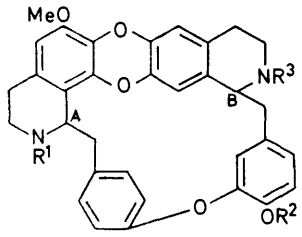
[2] I. R. C. Bick, W. I. Taylor, and A. R. Todd, *J. Chem. Soc.*, 1953, 695; I. R. C. Bick, J. Harley-Mason, and M. J. Vernengo, *Anales Asoc. quim. argentina*, 1963, **5**, 135.

[3] C.-K. Chuang, C.-Y. Hsing, Y.-S. Kao, and K.-J. Chang, *Ber.*, 1939, **72**, 519; C.-Y. Hsing and C.-H. Chang, *Sci. Sinica*, 1958, **7**, 59.

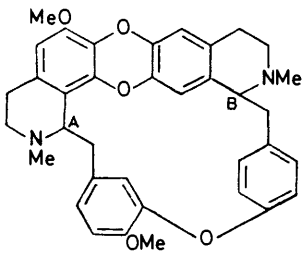
[4] Y. Inubushi and K. Nomura, *Tetrahedron Letters*, 1962, 1133; Y. Inubushi, K. Nomura, and M Miyawaki, *Yakugaku Zasshi*, 1963, **83**, 282; M. Tomita and H. Furukawa, *ibid.*, 1963, **83**, 760; 1964, **84**, 1027.

[5] J. Baldas, Q. N. Porter, I. R. C. Bick, and M. J. Vernengo, *Tetrahedron Letters*, 1966, 2059; J. Baldas, I. R. C. Bick, T. Ibuka, R. S. Kapil, and Q. N. Porter, *J.C.S. Perkin I*, 1972, 592.

test,[6,7] and in having one *N*-methyl and two methoxy-groups (n.m.r.); the presence of a secondary amino-group was confirmed by the appearance of a second methylimino-signal after *N*-methylation.[8]



(I) $R^1=H, R^2=R^3=Me$; A = B = *S*
(II) $R^1=R^2=R^3=Me$; A = B = *S*
(III) $R^1=R^2=R^3=Me$; A = B = *R*
(IV) $R^3=H, R^1=R^2=Me$; A = B = *R*
(V) $R^1=R^2=R^3=Me$; A = *S*, B = *R*
(VI) $R^3=H, R^1=R^2=Me$, A = *S*, B = *R*
(VII) $R^2=R^3=H, R^1=Me$; A = B = *R*



(VIII) A = *R*, B = *S*
(IX) A = *S*, B = *S*

The *N*-methyl derivative of base *a* proved identical with a minor component of the bark extract. It had mass and n.m.r. spectra identical with those of isotrilobine[4] (II) and the same m.p., but its specific rotation was of opposite sign; it is thus the (*R*,*R*)-enantiomer (III), which has been synthesised as its picrate[9] with a reported m.p. and specific rotation in accord with those found for *N*-methyl base *a* picrate. However, the n.m.r. spectra of base *a* and trilobine, while similar, are not identical, and differ particularly in their *N*-methyl resonances: trilobine shows a three-proton singlet at τ 7·55 and base *a* a similar signal at τ 7·42; isotrilobine and *N*-methyl base *a* each show two singlets at τ 7·58 and 7·42. Base *a* thus has structure (IV), isomeric with that of trilobine, with an *R*,*R*-configuration and with the secondary amino- and methylimino-groups of the latter interchanged.

Another minor alkaloid, base *b*, was eventually separated from base *a* through their *N*-acetyl derivatives. Base *b* gave a positive dibenzo-*p*-dioxin test, and proved to be isomeric with base *a*, with virtually the same mass spectrum. However, the n.m.r. spectra of the two bases and their respective *N*-acetyl and *N*-methyl derivatives (Table) were significantly different, which indicated that *N*-methyl base *b* might be a diastereoisomer of isotrilobine (II) and *N*-methyl base *a* (III), or might be a structural isomer of type (VIII) with a different arrangement of ether linkages between the two benzyl groups.

The type of structural variation represented by structure (VIII) is common throughout the biscoclaurine series, and although neither (VIII) nor its diastereoisomer (IX) occur naturally, both have been synthesised.[10] Their n.m.r. spectra are generally similar to that of *N*-methyl base *b*, but the three spectra are different in detail (Table), and the m.p.s and specific rotations

Characteristic peaks from the n.m.r. spectra of some dibenzo-*p*-dioxin alkaloids [τ ($CDCl_3$)]

		High-field singlets	OMe	NMe
(II)	Isotrilobine	3·70, 3·87	6·03, 6·15	7·40, 7·60
(III)	*ON*-Dimethyl-micranthine (*N*-Methyl base *a*)	3·70, 3·87	6·04, 6·16	7·41, 7·60
(V)	*N*-Methyltelobine (*N*-Methyl base *b*)	3·51, 4·02	6·07, 6·11	7·43, 7·49
(VIII)	Structural analogue of isotrilobine	3·28, 3·73	6·04, 6·17	7·36, 7·72
(IX)	Structural analogue of isotrilobine	3·73, 4·58	6·02, 6·17	7·33, 7·85

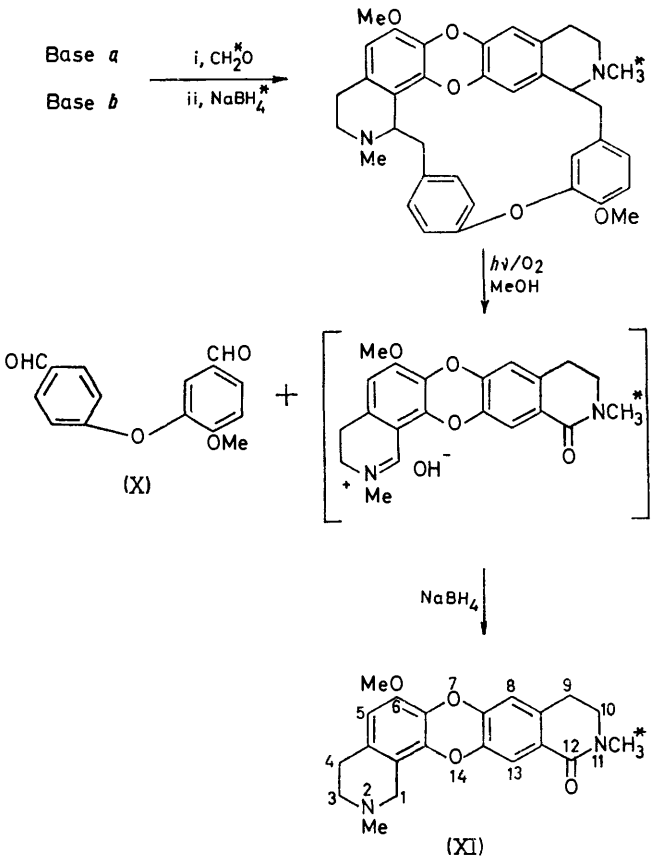
reported for (VIII) and (IX) are at variance with those of *N*-methyl base *b*. We conclude that *N*-methyl base *b* is a diastereoisomer rather than a structural isomer of (II) and (III); one such diastereoisomer (V), whose reported m.p. and specific rotation agree with those of *N*-methyl base *b*, has been synthesised,[11] and although we have not been able to make a direct comparison between the two compounds, we believe them to be identical.

In order to locate the secondary amino-group of base *b*, a photo-oxidative degradation[12,13] of *N*-methyl base *b*, which had been partially deuteriated in the methylimino-group, was carried out (Scheme). One product was identical with authentic 4-methoxy-3,4′-oxydibenzaldehyde (X),[7,14] and the other was reduced to the amino-lactam (XI). The same products [(X) and (XI)] were obtained by a parallel series of reactions on the correspondingly deuteriated *N*-methyl base *a*, thus confirming the close structural relationship between bases *a* and *b*, which evidently extends to the positions of the *N*-methyl and secondary amino-groups. Base *b* is thus a diastereoisomer of base *a* and has structure (VI).

Although compounds (III), (IV), and (VI) are the first bases of the trilobine type reported from a *Daphnandra* species, one of the earliest isolated from this genus, micranthine,[15] had the dibenzo-*p*-dioxin structure (XII) assigned to it.[7] Since the plant from which it was obtained, *D. micrantha* Benth., also grows in the same

[6] H. Kondo and M. Tomita, *J. Pharm. Soc. Japan*, 1932, **52**, 139; M. Tomita, *ibid.*, p. 147; 1933, **53**, 138.
[7] I. R. C. Bick and A. R. Todd, *J. Chem. Soc.*, 1950, 1606.
[8] S. Kubota, T. Masui, E. Fujita, and S. M. Kupchan, *J. Org. Chem.*, 1966, **31**, 516.
[9] M. Tomita and F. Furukawa, *Yakugaku Zasshi*, 1963, **83**, 676.
[10] M. Tomita, Y. Inubushi, and M. Kozuka, *Pharm. Bull.* (*Japan*), 1953, **1**, 360; Y. Inubushi, *ibid.*, 1954, **2**, 1.
[11] Y. Inubushi and M. Kozuka, *Pharm. Bull.* (*Japan*), 1954, **2**, 215.
[12] I. R. C. Bick, J. B. Bremner, and P. Wiriyachitra, *Tetrahedron Letters*, 1971, 4795.
[13] I. R. C. Bick, J. B. Bremner, H. M. Leow, and P. Wiriyachitra, *Tetrahedron Letters*, 1972, 33.
[14] F. von Bruchhausen and P. H. Gericke, *Arch. Pharm.*, 1931, **269**, 115.
[15] F. L. Pyman, *J. Chem. Soc.*, 1914, 1679.

area of northern New South Wales, and since the taxonomic studies had suggested it was subject to variation, we have made a fresh study of micranthine to



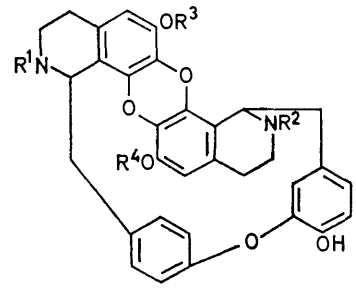
SCHEME Compounds with H* may contain varying amounts of deuterium

see whether it also has a trilobine-type structure. Previous samples of *D. micrantha* from different regions of northern New South Wales and southern Queensland had shown variation in alkaloid content: in the original material studied by Pyman,[15] micranthine was a minor constituent, the major alkaloids being daphnandrine and daphnoline; subsequent specimens [7,16] contained mainly micranthine with little or none of the other two alkaloids.

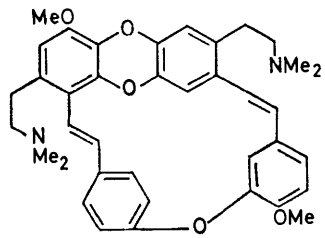
An extract of bark of *D. micrantha* from Whian Whian State Forest yielded micranthine as the major alkaloid, identical in all comparative tests with Pyman's [15] original sample. It was accompanied by base *a* and *N*-methyl base *a*, and several other alkaloids in amounts too small for adequate purification and structural investigation, but no trace of daphnandrine or daphnoline was detected.

Previous work had shown that micranthine had an *N*-methyl, a secondary amino-, a methoxy-, and at least one phenolic hydroxy-group,[7,15] including one in the dibenzyl portion of the molecule.[7] This location is confirmed by the mass spectrum [13] of micranthine, which shows strong doubly- and singly-charged ions at $(M - 212)/2$ and $M - 213$, respectively from double benzylic fission, with loss of hydrogen as well in the latter case.[5] The molecular ion appears at *m/e* 548,[13] at variance with a structure of type (XII), but in accord with a trilobine-type structure. Finally it was found that *O*-methylmicranthine is identical with base *a* (IV), while *ON*-dimethylmicranthine is the (*R*,*R*)-isomer of isotrilobine (II) and identical with *N*-methyl base *a* (III).

Since (XII) has long been accepted as the structure of micranthine, we considered it desirable before proposing (VII) in its place to seek further confirmatory evidence. Firstly, the n.m.r. spectra of micranthine and its *O*-methyl and *ON*-dimethyl derivatives integrate for ten aromatic protons; a structure such as (XII) should have only nine. Furthermore, if *ON*-dimethylmicranthine and isotrilobine are represented by the enantiomeric formulae (III) and (II), respectively, they should give the same product on Hofmann degradation; indeed both



(XII) R^1=H, R^2=Me or *vice versa*
R^3=H, R^4=Me or *vice versa*



(XIII)

give optically inactive methine bases with the same reported m.p. of 115°.[7,17] A methine derived from structure (XII) should have three methoxy-groups and nine aromatic protons, and a molecular weight of 634; micranthine methine in fact has two methoxy-proton resonances and signals for ten aromatic protons in its n.m.r. spectrum, while its mass spectrum shows a molecular ion at *m/e* 604 in accord with structure (XIII).

[16] I. R. C. Bick, F. S. Ewen, and A. R. Todd, *J. Chem. Soc.*, 1949, 2767; I. R. C. Bick, P. S. Clezy, and M. J. Vernengo, *ibid.*, 1960, 4928.
[17] H. Kondo and M. Tomita, *Annalen*, 1932, **497**, 104.

Finally, when *ON*-dimethylmicranthine was oxidatively photolysed as in the Scheme,[13] the amino-lactam product proved to have the formula $C_{21}H_{22}N_2O_4$ corresponding to (XI), and its n.m.r. spectrum showed the presence of one methoxy- and two *N*-methyl groups. One of the latter groups resonates at significantly lower field than the other since it lies in the deshielding zone of the amide carbonyl group; one of the aromatic proton singlets appears at much lower field than the other two for the same reason. When the oxidative photolysis was repeated on *ON*-dimethylmicranthine which had been partially deuteriated [8,18] (Scheme), the product obtained had the same n.m.r. spectrum as before except that the low-field methylimino-peak was reduced to about half intensity, corresponding to a 50% incorporation of deuterium into the methyl group on the lactam nitrogen atom.[13] Structure (XI) for this product is thus confirmed, and in consequence structure (VII) for micranthine, (IV) for *O*-methylmicranthine (the term base *a* being no longer needed), and (III) for *ON*-dimethylmicranthine. In place of the name base *b* for the alkaloid (VI), the first member of a series diastereoisomeric with trilobine, we propose the name telobine.

EXPERIMENTAL

N.m.r. spectra were measured for solutions in deuteriochloroform with tetramethylsilane as internal standard; low-resolution mass spectra were determined on an EAI Quad 300 spectrometer by direct insertion with a source temperature of 250° at 70 eV, and high-resolution mass spectra on an A.E.I. MS 902 spectrometer by direct insertion with a source temperature of 150° at 70 eV. Irradiations were conducted at 25° in an immersion reactor (Hanovia 450 W lamp with a Pyrex filter).

Extraction of Bark Sample Dt-7.—Milled bark (5·12 kg) was exhaustively extracted with methanol–chloroform–ammonia (*d* 0·880) (15 : 5 : 1). The extract was concentrated *in vacuo* to a brown tar, a solution of which in glacial acetic acid (1·5 l), was poured in a thin stream with vigorous stirring into water (20 l). A portion of the filtrate (1 l) was basified with ammonia and extracted with chloroform (2 × 500 ml). Phenolic bases were extracted from the chloroform solution with aqueous sodium hydroxide (5%; 2 × 500 ml), from which they were reprecipitated by neutralisation (HCl) then re-extracted with chloroform and finally recovered as a brown solid (0·8 g) after drying (Na_2SO_4) and evaporation of the extract under reduced pressure. The chloroform solution containing the bulk of the alkaloids was dried (Na_2SO_4) and evaporated to dryness *in vacuo*, then the residue was redissolved in benzene (300 ml) and extracted with Claisen's reagent [19] (2 × 200 ml) to remove cryptophenolic alkaloids. The methanolic extract was diluted with water (400 ml), neutralised (HCl), and extracted with chloroform. The chloroform extract was dried (Na_2SO_4) and evaporated to dryness *in vacuo* to a brown residue (4·83 g). The benzene solution containing non-phenolic alkaloids was likewise dried and evaporated to a yellow solid (4·66 g). No pure compound could be isolated from the phenolic fraction; t.l.c. of the cryptophenolic fraction indicated the presence of fangchinoline, nortenuipine, and other bases which could not be obtained pure.

Separation of Non-phenolic Alkaloids.—(*a*) A portion of the crude non-phenolic alkaloid fraction (4·0 g) was chromatographed in benzene on silica gel (800 g) in three columns of successively smaller diameter linked in series. The columns were eluted with benzene, with benzene–chloroform (1 : 1) and chloroform, and with chloroform–methanol containing increasing proportions of methanol. The last eluate was evaporated *in vacuo*, and the residue (0·6 g) was separated into fractions by preparative t.l.c. on silica gel [chloroform–triethylamine (9 : 1) as eluant]. The fraction with R_F 0·5 was further purified by t.l.c. [chloroform–benzene–triethylamine (9 : 9 : 2)]; the band with R_F 0·45 (97 mg) was extracted with chloroform–methanol (1 : 9), the solution was filtered and evaporated, and the residue crystallised from benzene to give base *a*, m.p. 163—165° (decomp.), not depressed on admixture with a sample of O-*methylmicranthine*, $[\alpha]_D^{20}$ −208° ($CHCl_3$) (Found: C, 73·8; H, 6·4; N, 4·6%; M^+, 562. $C_{35}H_{34}N_2O_5,0·5H_2O$ requires C, 73·4; H, 6·3; N, 4·9%. $C_{35}H_{34}N_2O_5$ requires *M*, 562). Base *a* gave an intense blue colour with a mixture of concentrated nitric and sulphuric acids (1 : 9).

(*b*) Another sample of the crude non-phenolic alkaloids (2·0 g) was separated into three fractions by preparative t.l.c. on silica gel with chloroform–triethylamine (9 : 1) as eluant. Fraction A (R_F 0·4—0·6) was subjected to further preparative t.l.c. [chloroform–benzene–triethylamine (9 : 9 : 2) as eluant]. Nortenuipine (R_F 0·55; 30 mg), $[\alpha]_D^{18}$ +235° ($CHCl_3$), identical (m.p. and mixed m.p., mass, n.m.r., and i.r. spectra) with an authentic sample was obtained. Fraction B (R_F 0·65—0·8) was treated similarly to yield fangchinoline (R_F 0·55; 30 mg), $[\alpha]_D^{18}$ +250° ($CHCl_3$), m.p. 237° (decomp.) alone or admixed with an authentic sample; its n.m.r. and mass spectra were also in agreement with those recorded for fangchinoline.[3,5,20] Fraction B also yielded some material of R_F 0·45 (140 mg) which after further preparative t.l.c. in chloroform–benzene–triethylamine gave *N*-methyl base *a* (60 mg), m.p. 210—214° (decomp.), $[\alpha]_D^{19}$ −230° ($CHCl_3$), identical (m.p. and mixed m.p., mass, n.m.r., and i.r. spectra) with a sample obtained by *N*-methylation [8] of base *a*, and with ON-*dimethylmicranthine* (III). The n.m.r. (Table), i.r., and mass spectra also matched those of isotrilobine (II) (Found: C, 71·4; H, 6·2; N, 4·5. $C_{36}H_{36}N_2O_5,0·25CHCl_3$ requires C, 71·8; H, 6·0; N, 4·6%). The picrate had m.p. 189—190°, $[\alpha]_D$ −218° (lit.,[9] m.p. 188—189°, $[\alpha]_D$ −226°). Fraction C (R_F 0·3—0·4) was further purified as for fractions A and B to give a mixture of bases *a* and *b* (1·0 g) which could not be further separated by t.l.c.

Separation of Bases a *and* b via *their* N-*Acetyl Derivatives.*—The mixture of bases from fraction C in chloroform was stirred at 10° while acetic anhydride (1 g) in ether (10 ml) was added dropwise. The solution was stirred for a further 3 h, concentrated *in vacuo*, basified with dilute ammonium hydroxide, and extracted with chloroform. The residue (550 mg) left after removal of the chloroform was separated into three fractions by preparative t.l.c. on silica gel with chloroform–methanol (9 : 1) as eluant. Fraction (i) (R_F 0·5) consisted of unchanged starting material (110 mg). Fraction (ii) (R_F 0·8) gave N-*acetyl*-O-*methylmicranthine* (202 mg) (from chloroform–carbon tetrachloride), m.p. 174—179° (decomp.), $[\alpha]_D^{22}$ −203°

[18] R. A. Olofson and D. M. Zimmerman, *J. Amer. Chem. Soc.*, 1967, **89**, 5057.
[19] L. Claisen, *Annalen*, 1919, **418**, 963.
[20] I. R. C. Bick, J. Harley-Mason, N. Sheppard, and M. I. Vernengo, *J. Chem. Soc.*, 1961, 1896.

($CHCl_3$) (Found: C, 63·6; H, 5·2; N, 4·3%; M^+, 604. $C_{37}H_{36}N_2O_6$,0·67CCl_4 requires C, 64·0; H, 5·2; N, 4·0%. $C_{37}H_{36}N_2O_6$ requires M, 604). Fraction (iii) (R_F 0·7) crystallised from chloroform to give N-*acetyltelobine* (120 mg), m.p. 180—185° (decomp.), $[\alpha]_D^{22}$ +111° ($CHCl_3$), whose mass spectrum closely resembled that of *N*-acetyl-*O*-methylmicranthine (Found: C, 65·4; H, 5·6; N, 3·9. $C_{37}H_{36}N_2O_6$,0·75$CHCl_3$ requires C, 65·3; H, 5·5; N, 4·0%). *N*-Acetyl-*O*-methylmicranthine (200 mg) was hydrolysed by refluxing under nitrogen for 60 h with potassium hydroxide (6 g) in aqueous methanol (90%; 25 ml). The solution was concentrated under reduced pressure, diluted with water, and extracted with chloroform, and the extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo*. From the residue, *O*-methylmicranthine (base *a*) (IV) (R_F 0·5; 90 mg) was obtained together with its unchanged *N*-acetyl derivative (R_F 0·8; 30 mg) by preparative t.l.c. on silica gel with chloroform–methanol (9 : 1) as eluant. *N*-Acetyltelobine from fraction (iii) was hydrolysed and the product separated as for fraction (ii). Some unchanged starting material (32 mg) and *telobine* (base *b*) (VI) (R_F 0·5; 50 mg), m.p. 185—195° (decomp.), $[\alpha]_D^{19}$ +188° ($CHCl_3$) were obtained. Telobine gave an intense blue colour with a mixture of concentrated nitric and sulphuric acids (1 : 9) (Found: C, 69·1; H, 5·7; N, 4·4%; M^+, 562·2452. $C_{35}H_{34}N_2O_5$,0·33CCl_4 requires C, 69·1; H, 5·9; N, 4·6%. $C_{35}H_{34}N_2O_5$ requires M, 562·2486). A sample of telobine was *N*-methylated [8] to give N-*methyltelobine* (V), m.p. 175—180° (decomp.) (from aqueous acetone), $[\alpha]_D^{18}$ +248° ($CHCl_3$) (Found: M^+, 576·2611. $C_{36}H_{36}N_2O_5$ requires M, 576·2624).

Extraction of D. micrantha *Bark*.—Ground bark of *D. micrantha* (4 kg) was extracted and non-alkaloidal material removed by acetic acid treatment as for sample Dt-7. The aqueous solutions were combined and basified with ammonia, and the precipitate was centrifuged off and dissolved in the minimum quantity of sulphuric acid (10%). The solution was poured into rapidly stirred water. The filtered solution was again basified and the precipitated alkaloids were centrifuged off, washed with water, and dried (205 g). The basic solution contained water-soluble alkaloids which could not be obtained pure. A portion of the crude alkaloid precipitate (66 g) was dissolved in chloroform (750 ml) and the solution was extracted with aqueous sodium hydroxide (5%). The mixture of phenolic alkaloids (8·1 g) obtained from this solution by neutralisation and extraction with chloroform could not be separated. The solution of crude alkaloids left after removal of phenolic bases was washed with water and evaporated to dryness. The residue was redissolved in benzene and the solution was extracted with Claisen's reagent.[19] The extract containing cryptophenolic alkaloids was diluted with water, neutralised, and extracted with chloroform, then the solution was washed with water, dried (Na_2SO_4), and evaporated. The residue (33·5 g) crystallised from chloroform–methanol containing a little ethyl acetate and was recrystallised from methanol to give needles of micranthine (III), m.p. 193—195° (decomp.), not depressed on admixture with an authentic sample isolated by Pyman.[15] The two samples had the same R_F values on t.l.c. and their i.r., u.v., and mass spectra were identical. Both samples gave a blue colour with a mixture of concentrated sulphuric and nitric acids (Found: C, 72·2; H, 5·6; O, 16·6. Calc. for $C_{34}H_{32}N_2O_5$,H_2O: C, 72·0; H, 6·0; O, 16·9%). The benzene solution of non-phenolic alkaloids was diluted with chloroform, washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue (18·05 g) crystallised from chloroform–light petroleum and was recrystallised from methanol to give *O*-methylmicranthine (IV), m.p. 161—163° (decomp.), not depressed on admixture with a sample made by methylation of micranthine with diazomethane, $[\alpha]_D^{20}$ −204° ($CHCl_3$) (Found: C, 74·7; H, 5·9; O, 14·1; N, 4·9%; M^+, 562. Calc. for $C_{35}H_{34}N_2O_5$: C, 74·7; H, 6·1; O, 14·2; N, 5·0%. Calc. for $C_{35}H_{34}N_2O_5$: M, 562). The mother liquor after crystallisation of *O*-methylmicranthine was submitted to repeated preparative t.l.c. on silica gel [methanol–chloroform (1 : 8) as eluant]. *ON*-Dimethylmicranthine (III) (46 mg) was finally obtained, m.p. 212—214° (decomp.), not depressed on admixture with a sample prepared by *N*-methylation [8] of *O*-methylmicranthine, $[\alpha]_D^{20}$ −239° ($CHCl_3$) (Found: C, 72·3; H, 6·2; N, 4·9%; M^+, 576. Calc. for $C_{36}H_{36}N_2O_5$,H_2O: C, 72·7; H, 6·4; N, 4·7%. Calc. for $C_{36}H_{36}N_2O_5$: M, 576).

T.l.c. of the mother liquors from the crypto- and non-phenolic fractions indicated the presence of small quantities of other bases which could not be separated or identified, but their R_F values did not correspond to those of daphnandrine or daphnoline.

N-*Trideuteriomethylation* [8] *of* O-*Methylmicranthine and of Telobine*.—A solution of *O*-methylmicranthine (1·0 g) in chloroform–methanol (1 : 2; 15 ml) was stirred with dideuterioformaldehyde [18] (0·12 g) at room temperature for 1 h then for 1 h more after addition of more dideuterioformaldehyde (0·05 g), and for a further 2 h after addition of sodium borodeuteride (0·6 g). The residue left after evaporation was basified (aqueous 2% NaOH) and extracted with chloroform, and the extract was washed with water, dried (Na_2SO_4), and evaporated leaving a residue (1·1 g) which was purified by preparative t.l.c. on silica gel [methanol–chloroform (1 : 8) as eluant]. The crystalline product (0·52 g) had an n.m.r. spectrum identical with that of *ON*-dimethylmicranthine (III) (Table) except that the methylimino-proton peak at τ 7·60 was reduced to half intensity. Some *O*-methylmicranthine (0·57 g) was also recovered. Telobine (410 mg) was alkylated similarly to give a colourless product (430 mg) with the same n.m.r. spectrum as *N*-methyltelobine (V) (Table) except that the peak at τ 7·49 was reduced to half intensity.

Oxidative Photolysis of ON-*Dimethylmicranthine* (III).—A solution of *ON*-dimethylmicranthine (0·65 g) in methanol (50 ml; freshly distilled over $NaBH_4$) was irradiated through Pyrex in the presence of oxygen until t.l.c. indicated that most of the starting material had disappeared (18 h). After concentration of the solution *in vacuo*, the products were separated by preparative t.l.c. on silica gel [methanolic chloroform (1 : 12) as eluant]. Fraction (1) (R_F 0·85) crystallised from light petroleum to give 4-methoxy-3,4′-oxydibenzaldehyde (X) as needles (58 mg), m.p. 77—79° alone or in admixture with an authentic sample.[7,12–14] Fraction (2) (149 mg; R_F 0·55) consisted of unchanged starting material. The adsorbent containing fraction (3) (R_F 0·0) was suspended in aqueous methanol (75%) and treated with sodium borohydride (0·5 g). The mixture was stirred for 12 h at room temperature, diluted with water, heated on a water bath for 15 min, then cooled, stirred with chloroform, and filtered. The aqueous methanol layer was extracted with chloroform (50 ml) and the combined chloroform layers were washed with water, dried (Na_2SO_4), and evaporated to dryness. The residue was purified by preparative t.l.c. on silica gel with methanolic

chloroform (1 : 12) as eluant. 1,2,3,4,9,10-*Hexahydro*-6-*methoxy*-2,11-*dimethyl*-p-*dioxino*[2,3-g:5,6-h′]*di-isoquinolin*-12(11H)-*one* (XI) (R_F 0·4; 45 mg) thus obtained had m.p. 99—105°, τ ($CDCl_3$) 2·42 (1H, s, 13-H), 3·30 and 3·70 (each 1H, s, 5- and 8-H), 6·20 (3H, s, MeO), 6·60 (4H, m, 1- and 10-H_2), 6·86 (3H, s, 11-Me), 7·0—7·4 (6H, m, 3-, 4-, and 9-H_2), and 7·52 (3H, s, 2-Me) (Found: C, 61·2; H, 6·8%; M^+, 366·15545. $C_{21}H_{22}N_2O_4$,2·5H_2O requires C, 61·3; H, 6·6%. $C_{21}H_{22}N_2O_4$ requires *M*, 366·15660). The photolysis was repeated on a sample of *ON*-dimethylmicranthine (III) (397 mg) which had been partially deuteriated in one methylimino-group as already described. After irradiation for 22 h and work-up as before, the dialdehyde (X) (26 mg) was isolated, and a sample of the amino-lactam (XI) (25 mg) which had i.r. and n.m.r. spectra closely similar to those of the undeuteriated sample, except that the intensity of the τ 6·86 resonance was reduced to half. A sample of *N*-methyltelobine (V) (408 mg) similarly deuteriated in one methylimino-group was irradiated for 16 h to give the dialdehyde (X) (23 mg) and partially deuteriated amino-lactam (22 mg), identical (i.r., n.m.r., mass spectra) with (XI) obtained by photolysis of the deuteriated sample of (IV).

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