Hexahydroimidazo-pyrimidines, a New Class of Alkaloids from ***Alchornea javanensis***

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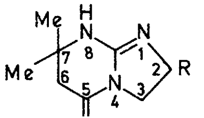
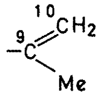
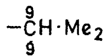
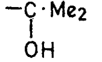
Summary The first naturally-occurring hexahydroimidazo-[1,2-*a*]-pyrimidines, alkaloids (Ia) and (IIIa), and the guanidines (IVa) and (IVb) have been obtained from *Alchornea javanensis* (Bl.) Muell.-Arg.

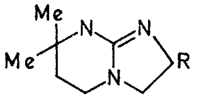
Two hexahydroimidazo-pyrimidine, and two guanidine alkaloids have been isolated from *Alchornea javanensis* (Bl.) Muell.-Arg., a small rain-forest tree of the family Euphorbiaceae. Alchornine, $C_{11}H_{17}N_3O$, m.p. 134—135°; $[\alpha]_D$ + 74° ($CHCl_3$); ν_{max} 1662, 1690 cm.$^{-1}$ (CCl_4); M^+ 207; picrate, m.p. 275—278°, has been shown to be (Ia). The n.m.r. spectrum[†] shows signals at δ 1·26 (s, 7-Me), 1·28 (s, 7-Me), 1·71 (m, with allylic couplings to the 10-CH_2, 9-Me), 2·44 (s, 6-CH_2), 4·84 and 4·98 (multiplets with allylic couplings to 9-Me and 2-H, 10-CH_2), 4·41 (q, $J_{2,3d}$ 9·0, $J_{2,3u}$ 6·0 Hz, 2-H), 3·95 (q, $J_{3d,3u}$ 11·0 Hz, 3-H), 3·53 (q, 3-H), and 6·90 (bs, exchangeable with D_2O, NH). Catalytic reduction over Adams catalyst in ethanol gives dihydroalchornine (Ib), picrate, m.p. 263—267°; M^+ 209; three-proton doublets in n.m.r. spectrum at δ 0·85 and 0·92 (J 7·0 Hz, 9-methyls) and a one proton multiplet at 1·65 (9-H). Alchornine is unaffected by $NaBH_4$ in ethanol at room temp., but with $LiAlH_4$ in tetrahydrofuran under reflux it is converted into (II), picrate m.p. 163—165°; M^+ 193; triplet in n.m.r. spectrum at δ 1·87 (J 6·0 Hz, 6-CH_2), and a triplet at 3·33 (J 6·0 Hz, 5-CH_2). Alchornine on being heated with concentrated hydrochloric acid gives a two component mixture from which has been isolated the major component (Ic), m.p. 79—80°; $[\alpha]_D$ + 67°; M^+ 225; singlets at δ 1·13 and 1·25 (9-methyls), and a broadened singlet at 5·26, exchangeable with D_2O (OH and NH).

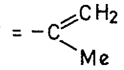


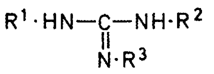
(I) a; R =


b; R =

$-\overset{9}{C}H\cdot Me_2$

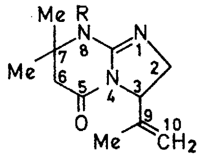
c; R =

$-\overset{9}{\underset{OH}{C}}\cdot Me_2$

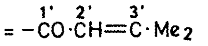


(II) R =



$R^1\cdot HN-\underset{N\cdot R^3}{\underset{\|}{C}}-NH\cdot R^2$

(IV) a; $R^1 = R^2 = Me_2C{=}CH\cdot CH_2-$
$R^3 = H$
b; $R^1 = R^2 = R^3 = Me_2C{=}CH\cdot CH_2-$



(III) a; R =

$-\overset{1'}{C}O\cdot\overset{2'}{C}H{=}\overset{3'}{C}\cdot Me_2$

b; R = H

Alchornidine, $C_{16}H_{23}N_3O_2$, m.p. 96—97°; $[\alpha]_D$ − 18° ($CHCl_3$); M^+ 289, has been shown to be (IIIa). The n.m.r. spectrum has signals at δ 1·19 (s, 7-Me), 1·29 (s, 7-Me), 1·64 (m, with allylic couplings to 10-CH_2, 9-Me), 1·89 (d, J_{allyl} 2·0 Hz, 3′-Me), 2·12 (d, J_{allyl} 2·0 Hz, 3′-Me), 2·25 and 2·43 (AB doublets, J_{AB} 16·0 Hz, 6-CH_2), 4·67 (q, $J_{2u,3}$ 4·2, $J_{2d,3}$ 7·8 Hz, 3-H), 3·88 and 3·82 (multiplets, $J_{2u,2d}$ 11·8 Hz, 2-CH_2), 7·33 (m, 2′-H), and 4·90 (m, 10-CH_2). Hydrolysis of alchornidine in aqueous ethanolic KOH affords 2,2-dimethylacrylic acid and alchornine (Ia), while hydrolysis by heating in aqueous acetic acid affords an isomer, isoalchornine (IIIb), which is converted into alchornine on being warmed with dilute ethanolic NaOH. Isoalchornine (IIIb), m.p. 137—138°; $[\alpha]_D$ − 84° ($CHCl_3$); M^+ 207; has n.m.r. signals at δ 1·30 (s, 7-methyls), 1·71 (m, with allylic

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[†] All n.m.r. spectra were measured at 100 MHz in $CDCl_3$ solution, and chemical shifts are relative to $SiMe_4$. In subscripts, "u" and "d" refer to the upfield and downfield multiplets of non-equivalent methylene protons.

couplings to 10-CH_2, 9-Me), 2·46 (s, 6-CH_2), 3·36 (q, $J_{2u,2d}$ 13·0, $J_{2u,3}$ 5·0 Hz, 2-H), 3·87 (q, $J_{2d,3}$ 10·0 Hz, 2-H), 4·72 (q, 3-H), 4·88 (m, 10-H), 4·93 (m, 10-H), and 4·37 (bs, exchangeable with D_2O, NH). Conversion of (IIIb) into (Ia) occurs by opening the lactam ring at N-4 and recyclization to N-1. The respective structures (Ia) and (IIIb) can be assigned on the basis of the deshielding influence of the 5-oxo-group which leads to a relative downfield shift of the 3-H signal in (IIIb) compared with the 2-H signal in (Ia), and also of the 3-methylene signals in (Ia) compared with the 2-methylene signals in (IIIb).

The other constituents isolated from *A. javanensis* include 2,2-dimethylacrylamide and two new guanidine alkaloids, *N*-1, *N*-2-di-isopentenylguanidine (IVa), M^+ 195; hydrochloride, m.p. 139—141°; acetate, m.p. 218—220°; picrate, m.p. 156—157°; and *N*-1, *N*-2, *N*-3-tri-isopentenylguanidine (IVb), M^+ 263, m.p. (hydrate) 44—46°; hexahydro-derivative, M^+ 269, m.p. (hydrate) 180—181°. The structure of (IVb) has been confirmed by synthesis of the hexahydro-derivative by a known method[1] for the synthesis of *N*-1, *N*-2, *N*-3-trisubstituted guanidines.

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[1] H. Ulrich, J. N. Tilley, and A. A. R. Sayigh, *J. Org. Chem.*, 1964, **29**, 2401.