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SYNTHESIS OF TWO PYRROLIDINE ALKALOIDS, PERIPENTADENINE AND DINORPERIPENTADENINE

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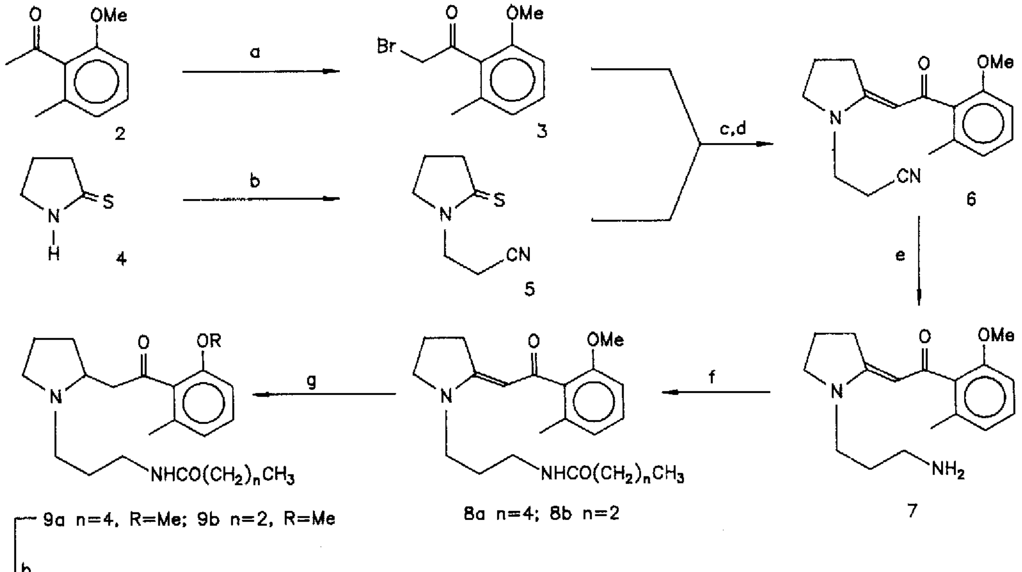
Summary. The alkaloids peripentadenine (1a) and dinorperipentadenine (1b) were obtained in a synthesis having as key features a sulphide contraction and the chemoselective reduction of vinylogous amides (6) and (8).

The title alkaloids, (1a) and (1b), have recently been isolated from *Peripentadenia mearsii* (C.T. White) L.C. Smith, an elaeocarpaceous tree of the rain forests of north Queensland[1]. The 2-phenacylpyrrolidine units in these alkaloids are reminiscent of the 2-acylmethylpyrrolidine structures found in several simple N-methylpyrrolidine alkaloids we previously synthesised[2] by a route involving sulphide contraction[3], but compounds (1) are rather more challenging targets for synthesis because of the additional functionality in the substituents on nitrogen. In view of current interest in generalised approaches to alkaloid synthesis[4], we wish to report preliminary details of syntheses of (1a) and (1b) as further examples of our own generalised synthetic route[2,5] to alkaloids (below, **Scheme**).



Scheme. (a) $(C_4H_7NO)_3.HBr_3$, THF; (b) $H_2C{=}CHCN$, THF, NaOH (cat.); (c) No solvent, R.T.; (d) PPh_3, NEt_3, MeCN; (e) Ni-Aℓ, NaOH, EtOH; (f) RCOCℓ, pyridine; (g) $LiAℓH_4$, THF, 0° (h) BBr_3, $CH_2Cℓ_2$.

The phenacyl bromide (3) required for the sulphide contraction step was prepared (59%)[6], along with the 1,1-dibrominated compound (20%), by treating the aryl methyl ketone (2)[7] with pyrrolidinone hydrotribromide in tetrahydrofuran. N-Cyanoethylpyrrolidine-2-thione (5) was obtained (97%) by hydroxide-catalysed conjugate addition of pyrrolidine-2-thione (4) to acrylonitrile, a method we have routinely used for attaching conjugated electrophiles to nitrogen in ambident thioimidate anions[5]. Compounds (3) and (5) combined at room temperature to form a salt that underwent smooth sulphide contraction in acetonitrile with triphenylphosphine and triethylamine to give vinylogous amide (6) (88%).

Of specific interest in this report are two chemoselective reductions. Model studies with the unsubstituted aroyl analogue of (6) showed that our previous best method[2] for reducing the C=C bond of the acylated enamine ($LiA\ell H_4$, ether, 0°C) gave erratic results; hydride, acting as base, induced partial removal of the cyanoethyl chain by reversing the conjugate addition. The problem was solved by reducing the nitrile group of (6) first by hydrogenation over activated nickel, formed *in situ* by treating nickel - aluminium alloy with sodium hydroxide in ethanol. The unstable amine (7) (*ca*. 92%) was immediately acylated with hexanoyl or butanoyl chloride to give amides (8a) and (8b) (43% and 65% respectively). $LiA\ell H_4$ then chemoselectively reduced the C=C bond in these compounds at 0°C, giving the O-methylated alkaloids (9a) and (9b) (71% and 55% respectively). The ^1H and ^{13}C n.m.r. spectra of these compounds agree with those published by Bick and co-workers[1]. The syntheses were completed with some difficulty by demethylating (9a) and (9b) with boron tribromide to give peripentadenine (1a) (19%) and dinorperipentadenine (1b) (46%)[8].

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8. We thank the Foundation for Research Development and the University of the Witwatersrand for financial support, Mrs S Heiss and Dr L Carlton (Wits) for n.m.r. spectra, and the C.S.I.R. (Pretoria) for mass spectra and microanalyses.

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