

(-)-N-(3-OXOBUTYL)-CYTISINE, A TOXIC ALKALOID FROM LABURNUM ANAGYROIDES

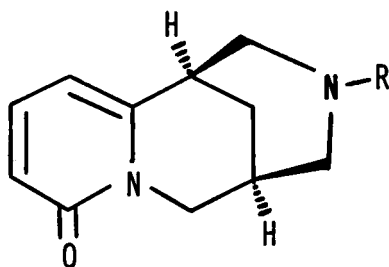
A.I. Gray<sup>1</sup>, M.C. Henman<sup>2</sup> and C.J. Meegan<sup>1</sup>, Department of 1) Pharmacognosy  
2) Pharmacology, School of Pharmacy, Trinity College Dublin, 18 Shrewsbury Rd.,  
Dublin 4, Ireland.

Laburnum anagyroides Med. (Fam. Leguminosae) is a well known poisonous plant which produces quinolizidine alkaloids. The major alkaloid, cytisine (1), has found therapeutic use as a potent respiratory stimulant with activity similar to nicotine (Martindale 1978). We have investigated a sample of dried mature seeds and isolated a toxic quinolizidine alkaloid not previously encountered in L. anagyroides.

A sample (400g) of powdered seeds was defatted with ethyl acetate and extracted with methanol containing 2% NH<sub>4</sub>OH. The concentrated methanol extract was chromatographed on a column of Sigel eluting with ethyl acetate/methanol mixtures yielding (-)-cytisine (1) (585mg), N-methylcytisine (2) (34mg) and (-)-N-(3-oxobutyl)-cytisine (3) (101mg) identified on the basis of m.p., UV, IR, <sup>1</sup>H-NMR, MS and [α]<sub>D</sub>. The structure of N-(3-oxobutyl)-cytisine was confirmed by its synthesis from cytisine and methylvinylketone.

This is the first report of N-(3-oxobutyl)-cytisine from L. anagyroides, it has been previously encountered only in Echinosophora koreensis Nakai (Leguminosae) (Murakoshi, Furuchi et al 1977), and it may be implicated in the biosynthesis of some tetracyclic quinolizidine alkaloids found in many legumes, including L. anagyroides.

(-)-N-(3-oxobutyl)-cytisine (LD<sub>50</sub> 71mg/Kg i.p.) was found to be less toxic than (-)-cytisine (LD<sub>50</sub> 18mg/Kg i.p.) when administered to adult mice intraperitoneally and both compounds caused death after myoclonic convulsions.



(1) R = H

(2) R = CH<sub>3</sub>

(3) R = CH<sub>2</sub>CH<sub>2</sub>C(=O)CH<sub>3</sub>

Martindale's Extra Pharmacopoeia, 27th Edition (1978) p.2010, Pharm. Soc. of Great Britain

Murakoshi, I., Furuchi, K. et al (1977) Phytochemistry 16, 1460-1461