Structure and Synthesis of Permethylnarciprimine

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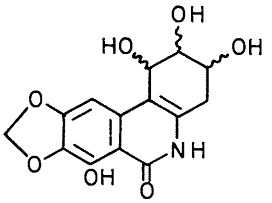
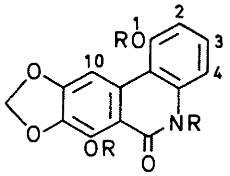
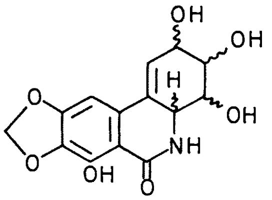
Summary Assignment of structure (VI) to permethylnarciprimine proves structures (III) and (IV) for narciclasine and narciprimine, respectively.



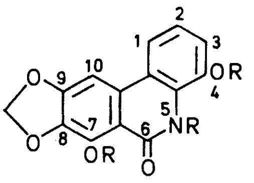
(I)



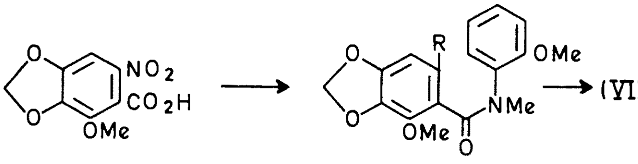
(II) R = H
(V) R = Me



(III)



(IV) R = H
(VI) R = Me



(VII)

(VIII) R = NO$_2$
(IX) R = NH$_2$

STRUCTURES (I) and (II), respectively, have been suggested[1] for narciclasine and narciprimine, both extracted from daffodil bulbs and from other Amaryllidaceae.[2] Narciclasine, which is strongly antimitotic, is identical with lycoricidinol, extracted from *Lycoris radiata*, for which Okamoto[3] has suggested the structure (III); narciprimine is identical with arolycoricidinol, for which the structure (IV) has been suggested.[3] The transformation of narciclasine into narciprimine and of lycoricidinol into arolycoricidinol has been described[1,3] by treatment with aqueous or alcoholic hydrochloric acid.

We have transformed narciprimine into permethylnarciprimine $C_{17}H_{15}O_5N$ [(V) or (VI)] by treatment with Me_2SO_4 in acetone. The product, m.p. 198° (from MeOH), has a blue fluorescence. M.s.: m/e (M^+) 313, i.r. (Nujol): 1645 cm^{-1}; u.v. (EtOH): $\lambda_{\max}$ 348 (log ϵ 3·72), 334 (3·78), 298 (4·09), 275 (4·29), and 248 nm (4·75); n.m.r. (perdeuterioacetone, 60 MHz, Jeol C-60H): δ 3·67 (s, NMe), 3·93 (s, OMe), 3·98 (s, OMe), 6·18 (sl. broad.s, methylenedioxy), 7·63 (s, 10-H), and 6·8—7·8 (complex pattern, 3 Ar-H); ($CDCl_3$): δ 3·85, 3·91, 4·12 (s, NMe and two OMe), 6·09 (s, methylene, dioxy), 7·37 (s, 10-H), 6·97 (dd, J_{AB} 7·5, J 2·25 Hz, H_A)-7·18 (t, $J_{AB} = J_{BX} =$ 7·5 Hz, H_B), and 7·63 (dd, J_{AX} 2·25, J_{BX} 7·5 Hz, H_X). The ABX pattern of three vicinal aromatic protons is the same as that observed in narciprimine;[1] the possibility of *O*-methylation of the amide is ruled out by the signal at δ 3·67 observed for NMe (perdeuterioacetone).

Total synthesis of (VI) has been achieved as follows. 2-Nitrocroweacic acid[4] (VII) has been converted into the acid chloride and condensed with *N*-methyl-*o*-anisidine; the resulting product (VIII) has been reduced catalytically to (IX) and the latter subjected to Pschorr cyclisation. By chromatography of the complex mixture we have isolated a product, m.p. 198°, identical (i.r., u.v., n.m.r., m.s., t.l.c., mixed m.p.) with permethylnarciprimine of natural origin.

This result confirms that permethylnarciprimine has the structure (VI). Hence the structures of narciprimine and narciclasine are (IV) and (III), respectively.

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[2] F. Piozzi, M. L. Marino, C. Fuganti, and A. Di Martino, *Phytochemistry*, 1969, **8**, 1745.
[3] T. Okamoto, Y. Torii, and Y. Isogai, *Chem. and Pharm. Bull.* (*Japan*), 1968, **16**, 1860.
[4] A. F. Wagner and F. A. Kuehl, U.S. Pat. 3,000,902; *Chem. Abs.*, 1962, **56**, 1399.