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THE ALKALOIDS OBTAINED FROM SPIRAEA JAPONICA L.fil

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Several alkaloids were first isolated in 1964 from Spiraea japonica L.fil by Molodozhnikov et al (1). We have examined alkaloidal components of the same plant (Japanese name "Shimotsuke") and could isolate ten new alkaloids.

In the present communication, we wish to report the structures of three new alkaloids: spiradine A (m.p. 281-282°), B (m.p. 259-260°) and C (m.p. 248-249°).

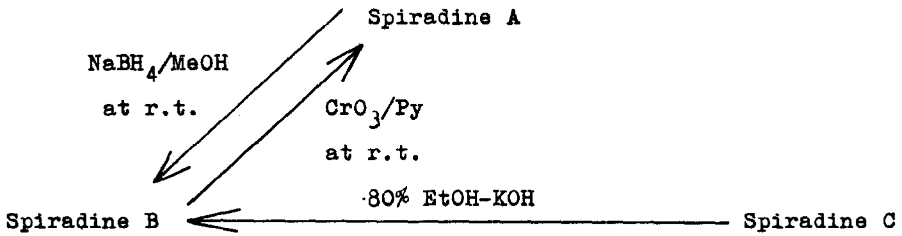
Spiradine A ($C_{20}H_{25}O_2N$): m/e 311 (M^+); pKa' 8.35 (in 50% MeOH); ν_{max}^{KBr} 3100 (OH), 1710 (C=O) and 1655 cm^{-1} (double bond).

Spiradine B ($C_{20}H_{27}O_2N$): m/e 313 (M^+); pKa' 9.54 (in 66% MeOH); ν_{max}^{KBr} 3250 br (OH) and 1655 cm^{-1} (double bond).

Spiradine C ($C_{22}H_{29}O_3N$): m/e 355 (M^+); pKa' 9.02 (in 66% MeOH); ν_{max}^{KBr} 3200 (OH), 1730, 1240 (OAc) and 1655 cm^{-1} (double bond).

The relationship among these alkaloids was established by the following chemical reactions, as shown in Fig. 1.

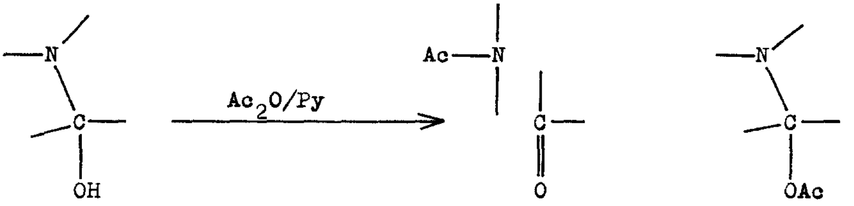
Fig. 1



The NMR spectrum of spiradine A shows the presence of a tertiary methyl group (3H, singlet at 1.33 ppm) and an endo-methylene group (2H, near singlet at 4.73 and 4.87 ppm). The presence of the latter was also supported by the catalytic hydrogenation of spiradine A in ethanol, which afforded a dihydrospiradine A, m.p. 291-292° ($C_{20}H_{27}O_2N$). In its NMR spectrum, dihydro derivative has a secondary methyl signal at 0.93 ppm (3H, $J=5$ cps) instead of two signals at 4.73 and 4.87 ppm in spiradine A.

When treated with acetic anhydride in pyridine, spiradine A afforded two mono-acetate, N-acetate (m.p. 173-175° ; $C_{22}H_{27}O_3N$; ν_{max}^{KBr} 1710 (C=O), 1690 (C=O) and 1630 cm^{-1} (N-Ac and double bond); no hydroxyl band; NMR spectrum: 1.16 (3H, s), 2.07 (3H, s), 4.70 (1H, s) and 4.89 ppm (1H, s)) and O-acetate (m.p. 215-216° ; $C_{22}H_{27}O_3N$; ν_{max}^{KBr} 1735 (OAc), 1705 (C=O), 1635 (double bond) and 1250 cm^{-1}; no hydroxyl band; NMR spectrum: 1.04 (3H, s), 2.00 (3H, s), 4.68 (1H, s) and 4.84 ppm (1H, s); no proton attached to the carbon atom bearing acetoxyl group). The IR spectrum of the former indicates the formation of another new carbonyl group in addition to N-acetyl group. The above result indicates the presence of an alcamine group (I), as shown in Fig. 2. (2).

Fig. 2

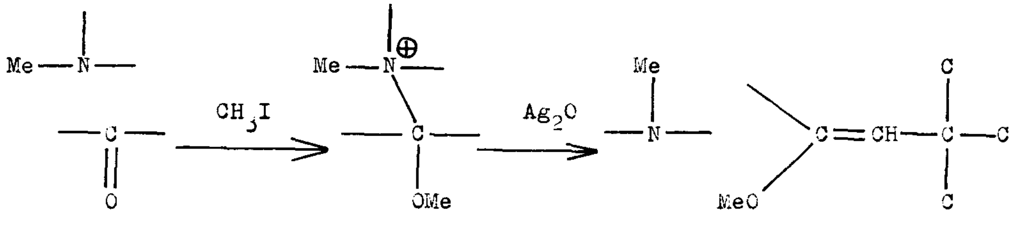


(I) N-acetate O-acetate

When treated with methyl iodide in methanol, spiradine A afforded a methiodide (Dec.>330° ; $C_{20}H_{25}O_2N \cdot CH_3I$; ν_{max}^{KBr} 3190, 1710 and 1640 cm^{-1}), which was shaked with silver oxide in 50% aqueous methanol to give a N-methyl diketone (II) (m.p. 167° ; $C_{21}H_{27}O_2N$; ν_{max}^{KBr} 2800, 1710, 1690 and 1650 cm^{-1}). The N-methyl diketone was heated with methyl iodide at 100° (in a sealed tube) followed by

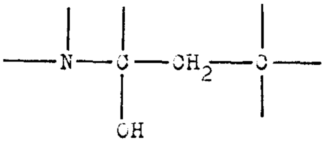
Hofmann degradation to give a degradation product (III) (m.p. 130-132°; $C_{22}H_{29}O_2N$; ν_{max}^{KBr} 1700, 1655 cm^{-1} (strong band; $>C{=}C<_{OMe}$ and endo-methylene group); NMR spectrum: 0.98 (3H, s), 2.22 (3H, s), 3.39 (3H, s), 4.44 (1H, s), 4.65 (1H, s) and 4.83 ppm (1H, s)) in 53% yield. The new NMR signal at 4.44 ppm (1H, s) is due to a proton attached to the new double bond. (See Fig. 3)

Fig. 3



(II) (III)

Accordingly, spiradine A should have a partial structure (IV).

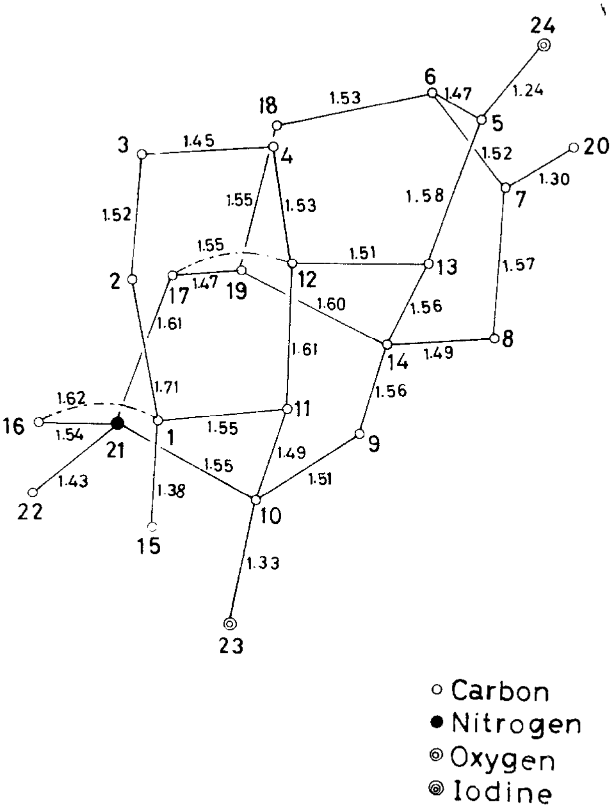


(IV)

Spiradine A methiodide (orthorhombic) crystallises in space group $P2_12_12_1$ with a = 14.04 Å, b = 15.88 Å, c = 8.55 Å; V = 1906 $Å^3$; D_m = 1.579 $g \cdot cm^{-3}$; D_c = 1.580 $g \cdot cm^{-3}$ and Z = 4.

Using multiple film technique and a standard scale, relative intensities were estimated on the equi-inclination Weissenberg photographs taken with Ni-filtered Cu-K_α radiation and rotated about b and c axes. From these intensities 1768 independent structure factors in the absolute scale were derived by Wilson's method. The position of the iodine atom was determined from the sharppened Patterson function and those of other atoms were found through the three-dimensional minimum function as well as heavy atom methods. These atomic coordinates were then refined by the successive applications of the three-dimensional Fourier synthesis and the least squares method. The R factor thus obtained is 16.26% without non-observed data. Furthermore, the absolute configuration of spiradine A was also determined by the anomalous dispersion of iodine atom (Cu-K_α radiation, $\lambda = 1.5418$ Å). The molecular shape viewed along the c axis is shown in Fig. 4. The spectral and chemical data are in agreement with the present result of X-ray analysis of spiradine A (V). Accordingly, VI and VII should be given to spiradines B and C, respectively.

Fig. 4



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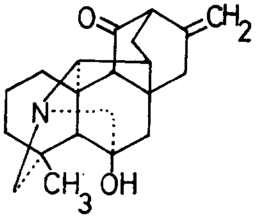
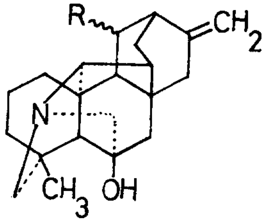


(V)



(VI) R=OH

(VII) R=OAc

Studies are now in progress to transform spiradine A into the other minor alkaloids.

All m.ps are uncorrected. Satisfactory analyses were obtained for all new compounds described herein. Chemical shifts of all NMR spectra are given in ppm from an internal TMS standard using CDCl$_3$ as a solvent. The calculations were performed on the NEAC-2206 electronic computer using our own programs.

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REFERENCES

(1) V. I. Frolova, A. I. Ban'kovskii, A. D. Kuzovkov and M. M. Molodozhnikov, Med. Prom. S.S.S.R. 18 (1), 19-21 (1964).

(2) T. Okamoto, M. Natsume, H. Zenda and S. Kamata, Chem. Pharm. Bull. (Tokyo), 10, 886 (1962).