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THE STRUCTURE OF SPIRADINE D

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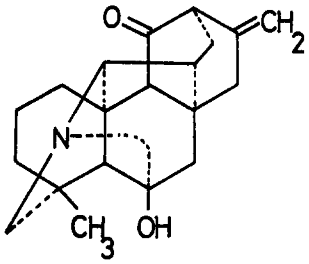
In the previous communication (1) we reported the structure of spiradine A (I) which was isolated from Spiraea japonica L.fil (Japanese name "Shimotsuke"). We could isolate a new alkaloid, spiradine D (m.p. 134 135°), from the same plant.



(I)

In the present communication we wish to report the structure of spiradine D by the chemical correlation between spiradines A and D.

Spiradine D has a molecular formula $C_{22}H_{29}O_2N$ [m/e 339 (M^+); pKa' 9.35 (in 50% MeOH); ν_{max}^{KBr} 1690 (C=O), 1645 and 875 cm^{-1} (double bond); NMR spectrum: 1.44 (s) and 1.47 (s) (total 3H);* 4.22 (1H, s), 4.55 (1H, s) and 4.72 ppm (1H, s)].

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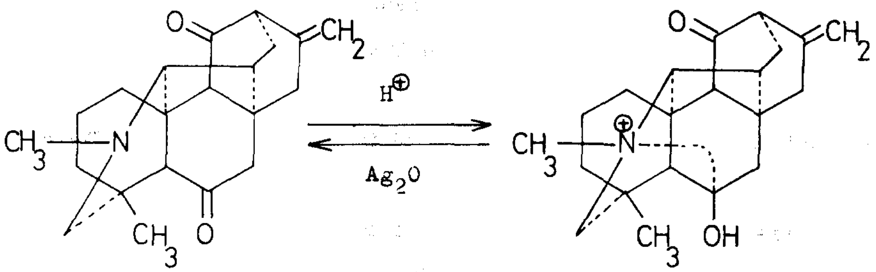
*The appearance of two different methyl singlets (total 3H) must be due to the presence of two kinds of configuration or conformation in the ring G of spiradine D itself. On the basis of the solvent effect, these signals can not be assigned to a secondary methyl group.

Treatment of spiradine D with MeOH-HCl at 0° gave a quaternary salt [m.p. 204-205°, $C_{22}H_{30}O_2NCl\cdot\frac{1}{2}H_2O$; ν_{max}^{KBr} 3480 (OH), 1650 and 870 cm^{-1} (double bond); no ketone band]. This quaternary salt could be reconverted into the original spiradine D by shaking with silver oxide in methanol. The above experiment suggests that spiradine D has a masked amino-ketone group, as shown in Fig. 1 (1, 2).

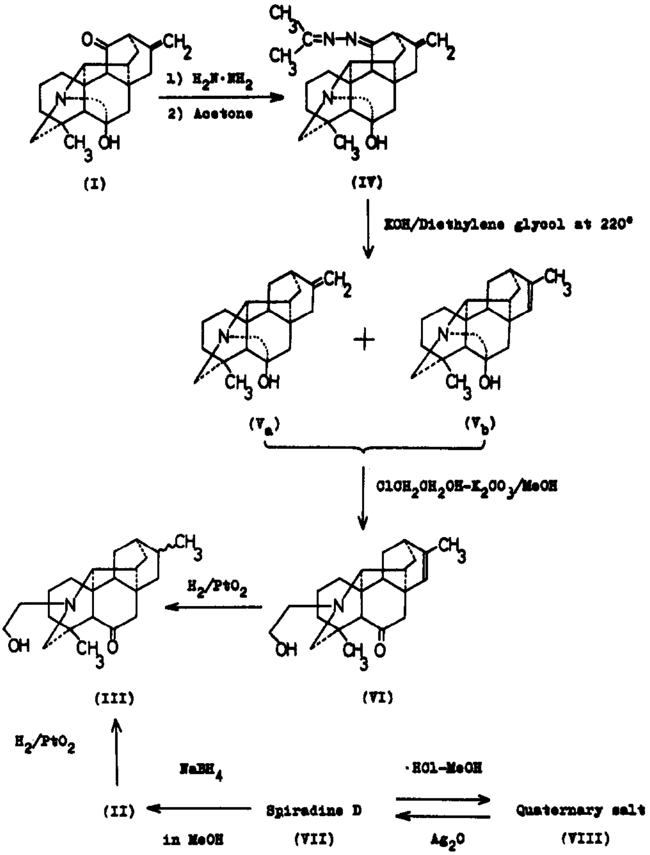
Fig. 1



The presence of a carbinolamine-ether system N-C-O-C in spiradine D was shown by the following fact: spiradine D was reduced by sodium borohydride in methanol to give a hydroxy derivative (II) [m.p. 143-144°; $C_{22}H_{31}O_2N$; ν_{max}^{KBr} 3560 (OH), 1670 (C=O), 1670 and 870 cm^{-1} (double bond); NMR spectrum: 1.54 (3H, s), 4.51 (1H, q, $J_1 = 5$ c.p.s. and $J_2 = 2$ c.p.s.) and 4.69 ppm (1H, q, $J_1 = 5$ c.p.s. and $J_2 = 2$ c.p.s.)] without loss of oxygen (3). Catalytic hydrogenation of II in ethanol afforded a dihydro derivative (III) [m.p. 141-142°; $C_{22}H_{33}O_2N$; ν_{max}^{KBr} 3560 (OH) and 1670 cm^{-1} (C=O)]. The NMR spectrum of III shows a new doublet at 0.96 ppm (3H, d, J=6 c.p.s.) indicating the presence of an exo-cyclic methylene group in spiradine D.

From a series of above-described chemical reactions, the correlation of spiradine D to spiradine A was planned so as to establish the structure of spiradine D and it has been achieved as follows.

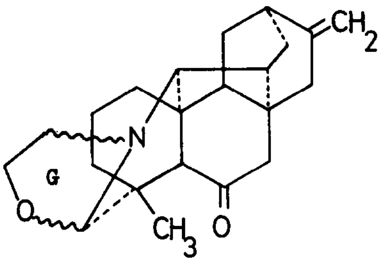
When heated with anhydrous hydrazine in diethylene glycol at 180° and then treated with excess amounts of acetone at 20°, spiradine A gave an azine (IV) [m.p. 253-254°; $C_{23}H_{31}ON_3$; ν_{max}^{KBr} 3080 (OH), 1640 (C=N) and 870 cm^{-1} (double bond); NMR spectrum: 1.36 (3H, s), 1.37 (3H, s), 2.00 (3H,



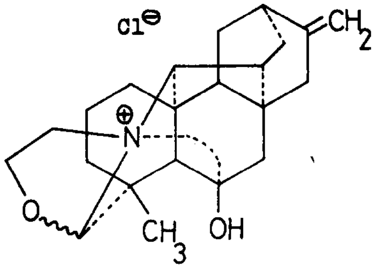
s), 4.66 (1H, s) and 4.90 ppm (1H, s)] in 65% yield. Wolff-Kishner reduction of IV gave a mixture of V_a and V_b [$C_{20}H_{27}ON$, m/e 297 (M^+); ν_{max}^{KBr} 3100 (OH) and 1650 cm^{-1}; no ketone band] in 31% yield (4). When the above mixture was refluxed with the mixture of freshly-distilled ethylene chlorohydrin and methanol (1:1) in the presence of anhydrous potassium carbonate, N-β-hydroxyethyl derivative (VI) [m.p. 155-156°; $C_{22}H_{31}O_2N$; ν_{max}^{KBr} 3560 (OH) and 1670 cm^{-1} (C=O); NMR spectrum: 1.54 (3H, s), 1.78 (3H, d, J = 2 c.p.s.) and 5.29 ppm (1H, t, J = 2 c.p.s.)] was obtained in crystalline state (73% yield). Catalytic hydrogenation of VI in ethanol afforded a dihydro derivative, which was identical with III by the mixed melting point, IR and mass spectra.

In the NMR spectrum of spiradine D the signal at 4.22 ppm (1H, s) is due to a proton attached to the carbon atom bearing the carbinolamine-ether linkage.

Accordingly, the structure of spiradine D and its quaternary salt should have VII and VIII, respectively.



(VII)



(VIII)

All m.ps are uncorrected. Satisfactory analyses were obtained for all new compounds described herein. The chemical shifts of all NMR spectra are given in ppm from an internal TMS standard using $CDCl_3$ as a solvent (s = singlet, d = doublet, t = triplet and q = quartet).

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(4) We could not separate V_a or V_b from the reaction mixture as a pure compound. IR and mass spectra of the mixture of V_a and V_b are recorded.