A NEW C_{20}-DITERPENE ALKALOID, SPIRASINE III AND THE INTERCONVERSION OF OXAZOLIDINE RING

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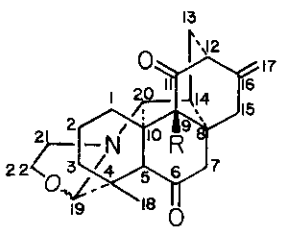
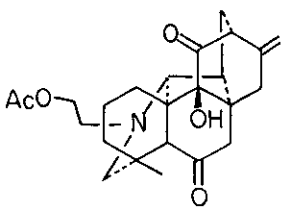
Abstract - The structure of spirasine III (1), a new C_{20}-diterpene alkaloid isolated from Spiraea japonica, was established on the basis of chemical and spectroscopic evidence and confirmed by x-ray crystallography. The interconversion of the epimeric forms of the oxazolidine ring was determined by NMR.

In previous papers[1,2,3] we have reported nine structures of the spirasine series, all C_{20}-diterpene alkaloids, isolated from Spiraea japonica L. f. fortunei (planchon) Rehd. In this paper we wish to present the structural elucidation of a new C_{20}-diterpene alkaloid designated as spirasine III (1), which has an extra C_9-OH group as compared with spiredine (2)[4], the known compound also isolated from the same plant.



(1) R = OH
(2) R = H



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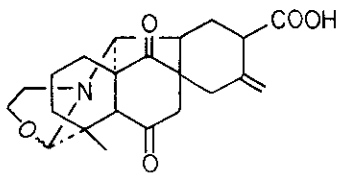


(4)

TABLE 1. ^{13}C NMR spectra of spirasine III (1), spiredine (2), spirasine III salt (6)

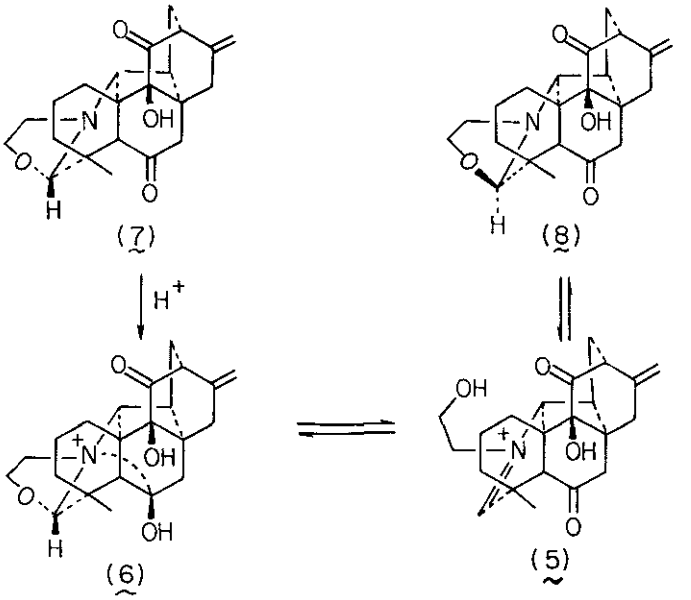
Carbon	1[a]	2[a]	6[b]
1	48.6	49.8 48.9	36.0
2	20.4 18.2	20.3 18.3	17.9
3	32.1 31.9	33.9 32.7	34.2
4	36.6 36.2	36.8 36.7	40.7
5	55.5	61.5	54.5
6	206.9	206.6	106.3
7	45.3 45.1	50.9 50.3	27.0
8	47.3 46.8	43.3 42.1	45.7
9	85.5	64.7	84.4
10	49.0 48.1	47.6 46.7	51.8
11	214.3	210.1	214.5
12	53.2 53.0	53.4 53.3	52.2
13	39.5	39.7	25.3
14	54.9	45.2	39.1
15	29.8 29.5	30.0 29.6	28.9
16	143.6 143.5	143.4 143.2	140.1
17	111.1 110.9	110.3 110.2	114.3
18	30.6 23.3	30.2 23.1	22.6
19	98.0 93.8	97.6 93.3	107.5
20	70.4	73.1 72.5	72.1
21	51.8	52.2	44.4
22	64.8 62.8	64.8 62.8	69.5

Chemical shifts in ppm downfield from TMS, (a) in $CDCl_3$, (b) in CF_3COOD.

Spirasine III (1), $C_{22}H_{27}NO_4$ (M^+ 369.1858, calc. 369.1940), mp 210~212 °C, $[\alpha]_D^{21}$ -9.0° (c 1.1, $CHCl_3$), showed the presence of an exocyclic methylene group (δ_C 143.6, 143.5, s; 111.1, 110.9, t) and a methyl group (δ_H 1.53, 1.49, total 3H, s), characteristic of a C_{20}-diterpene alkaloid. The twin signals are due to the epimeric nature[2] of the oxazolidine ring at C-19. The presence of the C_{11}-carbonyl group was evidenced by an absorption maximum at 310 nm (log ε 1.66) for the β,γ-unsaturated ketone, and a positive Cotton effect at 318 nm (Δε +4.05) in the CD spectrum. The other carbonyl group was located at C-6 because of the negative Cotton effect at

278 nm ($\Delta\varepsilon$ -0.87), which can be completely quenched upon acidification[5]. Reduction of spirasine III (1) with $NaBH_4$ gave a dihydro derivative, $C_{22}H_{29}NO_4$, mp 180-182 °C, which was treated with acetic anhydride in pyridine to give the acetyl derivative (3), $C_{24}H_{31}NO_5$. In agreement with the ring-opened structure, here the acetylated carbinolic methylene resonated at δ_H 4.17 as a triplet. The IR spectrum of spirasine III (1) exhibited the absorption of a hydroxyl (3545 cm^{-1}), which may be reasonaly placed at C-9 or C-5 to account for the signal at δ_c 85.5 (s). Oxidation of spirasine III (1) with periodate afforded a cleavage product, $C_{22}H_{27}NO_5$ (385.1889 by high resolution MS) (4). The IR spectrum of 4 showed a typical Cyclopentanone absorption[6] at 1759 cm^{-1} to be expected with structure 1 having a hydroxyl group at C-9. ^{13}C NMR spectral data of spirasine III are found to be in agreement with its postulated structure 1 when comparison was made with that of the known compound spiredine (2) (see table 1). The structure (1) was confirmed later by x-ray crystallography[7].

Although the oxazolidine-containing spirasines exist as a single epimer with the 19 (S) configuration in the solid state, such as spirasine V[2] and spirasine I[3], by x-ray crystallography, fast equilibration occurs in solution to form a pair of C-19 epimers, displaying a pair of signals at about δ_H 4.2 (19 R) and 3.7 (19 S) in an approximate ratio of 1:1. Upon acidification, there are two possibilities for salt formation, one is the open chain immonium (5), and the other is the carbinolamine type (6). Both forms are by nature configurationally homogeneous. This is obviously true for the sp^2-trigonal C-19 of 5, and the C-19 R epimeric alternative for 6 (with C-19 S) has prohibitively high strain. The equilibrium between the salts was found to be changeable with solvents. ^{13}C NMR of the salt in methanol showed it to be predominantly in the form of 6 as evidenced by the δ_c 105 (s) of C-6. The form of 5, however, must have had at least transient existence in order to mediate the conversion of 19 (S) to 19 (R), leading to the ultimate formation of exclusively 6. In aqueous medium, the existence of 5 as a minor isomer was detected by the methine signal at δ_c 185, which could also be seen in trifluoroacetic acid solution[8,9]. Equilibration in solution between the C-19 epimers can be completely suppressed by complete removal of the protonated form like 5. Thus dissolution of the powdered crystals of spirasine III into CCl_4 (containing triethylamine) leaves the C-19 S epimer intact as shown by ^1H NMR.



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