FOUR NEW C_{20}-DITERPENE ALKALOIDS, SPIRASINE I, SPIRASINE II, SPIRASINE VII AND SPIRASINE VIII FROM SPIRAEA JAPONICA

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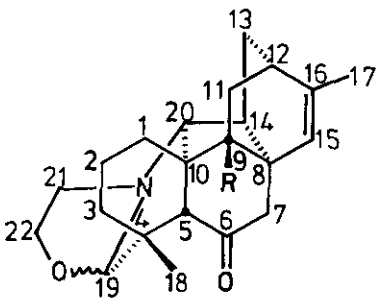
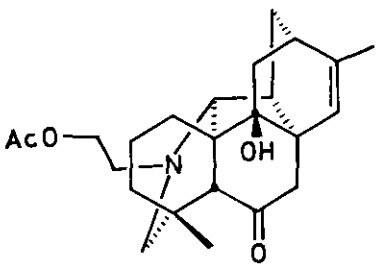
Abstract - The structures of spirasine I (1), spirasine II (2), spirasine VII (3) and spirasine VIII (4), new C_{20}-diterpene alkaloids isolated from Spiraea japonica, were established on the basis of chemical and spectroscopic evidence and confirmed by x-ray crystallography.

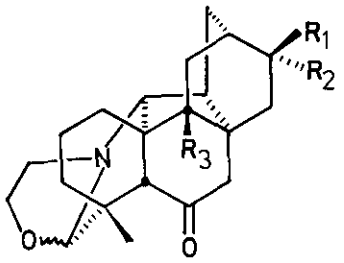
In a previous paper[1] we have reported the structures of spirasine V (7) and spirasine VI (8), two of the fifteen new C_{20}-diterpene alkaloids isolated from Spiraea japonica L. f. var. fortunei (planchon) Rehd. In this paper we wish to present the structural elucidation of four other new alkaloids of this series designated as spirasine I (1), spirasine II (2), spirasine VII (3) and spirasine VIII (4).



(1) R = OH
(6) R = H



(5)



(2) R_1, R_2 = $=CH_2$, R_3 = OH
(3) R_1 = CH_3, R_2 = OH, R_3 = OH
(4) R_1 = OH, R_2 = CH_3, R_3 = OH
(7) R_1 = CH_3, R_2 = OH, R_3 = H
(8) R_1 = OH, R_2 = CH_3, R_3 = H

TABLE 1. ^{13}C NMR spectra of spirasine I (1), spirasine II (2), spirasine VII (3) and spirasine VIII (4)

Carbon	1[a]	2[a]	3[b]	4[b]
1	49.4 49.0	48.7 48.4	49.1 48.6	50.3 49.8
2	20.7 18.6	20.5 18.4	20.6 18.2	21.6 19.4
3	31.6 30.1	32.6 32.3	32.8 31.7	30.5 30.1
4	36.5 35.9	35.7	35.9	36.9 35.9
5	56.1 55.6	55.9 55.4	56.0 55.5	57.2 56.7
6	206.2 ---	209.0 204.0	210.0 205.0	211.5 208.0
7	47.9	48.1 47.9	47.1	49.3 48.0
8	41.0	42.6 42.2	42.5	41.7
9	82.1	78.0 77.8	76.8	78.1
10	47.2 46.5	47.1	48.1 47.5	48.6
11	37.1 36.2	36.8	37.0	37.9 36.5
12	40.0	38.1	38.0	39.0
13	40.6	35.1 34.8	29.1 28.0	29.8 29.2
14	44.4	43.0	41.9	43.1
15	125.0 124.0	29.0 28.2	42.0 39.0	42.8 40.8
16	147.0	150.9 150.7	69.1	70.2
17	19.6	102.8 102.6	30.4	31.3
18	30.5 23.4	29.3 23.4	23.7	24.4
19	97.8 93.9	97.2 93.2	97.2 93.2	98.5 94.3
20	69.9 69.8	70.6	70.6	71.0
21	52.1	51.8	51.9	52.6
22	64.7 62.6	64.2 62.1	64.1 62.1	65.2 63.1

Chemical shifts in ppm downfield from TMS, (a) in $CDCl_3$, (b) in C_5D_5N.

Comparison of ^{13}C NMR data (see table 1) established the spiredine-type skeleton[1,2] for all of the four alkaloids . The presence of an oxazolidine ring was shown by twin signals in ^{1}H as well as ^{13}C NMR, due to the epimeric nature of C-19. The epimers exist in solution in a ratio of approximately 1:1.

Negative Cotton effects at about 290 nm which can be completely quenched upon acidification placed the carbonyl group at C-6, and also established the absolute configuration[1,3] as shown by the respective formulas.

Molecular formulas of both spirasine I and II were determined as $C_{22}H_{29}NO_3$ by high resolution MS. Spirasine I had mp 244~246°C, IR (KBr) 1680 cm^{-1}, $[\alpha]_D^{21}$ -131° (c 1.1, $CHCl_3$), CD $\Delta\varepsilon$ -2.38 (292 nm, EtOH). An endocyclic double bond was evident by δ_H 5.29 (1H, br s) and 1.86 (3H, s, 17-CH_3) as well as δ_C 147.0 (s), 125.0 (d) and 19.6 (q). The hydroxyl group (IR 3400 cm^{-1}) at C-9 was supported by δ_C 82.1 (s) and biogenetic considerations[4].

Reduction of spirasine I (1) with $NaBH_4$ opened the oxazolidine ring to give a dihydro derivative $C_{22}H_{31}NO_3$, mp 254~256°C which was treated with acetic anhydride in pyridine to give the acetyl derivative 5, $C_{24}H_{33}NO_4$. Here the acetylated carbinylic methylene resonated at δ_H 4.32 as a triplet, as expected.

The structure of spirasine I (1) was confirmed by x-ray diffraction analysis which will be reported elsewhere. The crystal used for analysis was found to consist of only one epimer with 19 (S) configuration. However, rapid equilibration to the epimeric mixture takes place upon dissolution in $CDCl_3$ as evidenced by ^{1}H NMR.

Spirasine II (2) had mp 208~209°C, IR (KBr) 3460 (OH), 1680 (C=O), 3080, 1650, 890 ($C=CH_2$) cm^{-1}. The signals of δ_C 150.9 (s) and 102.8 (t) and δ_H 4.52, 4.62 confirmed the presence of the exocyclic methylene group. By comparison of ^{13}C NMR data with spirasine I (1), the structure of spirasine II can be ascertained as 2.

The high resolution MS of both spirasine VII (3) and spirasine VIII (4) established the same molecular formula $C_{22}H_{31}NO_4$. Spirasine VII had mp 191~193°C, IR (KBr) 3440, 3340 (OH), 1680 (C=O) cm^{-1}, $[\alpha]_D^{28}$ -78.0° (c 1.3, $CHCl_3$), CD $\Delta\varepsilon$ -2.2 (291 nm, EtOH). Similar to the case of spirasine I (1) and II (2), one of the hydroxyl groups can be assigned at C-9, supported by the signal at δ_C 76.8 (s). The other hydroxyl group shouled be at C-16, with a corresponding signal at δ_C 69.1 (s). Comparison of ^{13}C NMR data with established structures of spirasine I (1) and spirasine VI (8)[1] also strongly support these assignments.

Spirasine VIII (4) had mp 207~209°C, $[\alpha]_D^{28}$ -57.0° (c 1.0, $CHCl_3$), IR (KBr) 3480, 3320 (OH), 1680 (C=O) cm^{-1}, CD $\Delta\varepsilon$ -2.0 (292 nm, EtOH). It is isomeric at C-16 with

spirasine VII, as has been the case with spirasine V (7) and spirasine VI (8). The assignments of 16 α- and 16 β-OH for spirasine VII (3) and VIII (4), respectively, followed by the differences[1] in $\Delta\varepsilon$ values and δ_c values of C_{11} and C_{13}. Here the α- OH group at C-16 makes a more negative contribution to $\Delta\varepsilon$.

As an intercorrelation, spirasine VII (3) was dissolved in acetic acid containing $HClO_4$ and allowed to stand overnight at room temperature, giving the dehydration product spirasine I (1), along with some spirasine VIII (4), the C-16 isomerization product. Spirasine VIII behaved similarly.

Oxymercuration-demercuration (successive treatments with $Hg(OAc)_2$ and $NaBH_4$)[5] of spirasine I (1) afforded a hydration product which was identified (Rf, IR and MS) as spirasine VII (3). It is of interest that the isomeric spirasine VIII (4) with a 16 β-OH was not formed in this reaction. This behavior can be attributed to the presence of the 9 β-OH group which directed the attack of the mercuric ion on the β-face. The directive role of the 9 β-OH group was convincingly demonstrated by compound 6, a dehydration product of spirasine V (7). Under the same conditions, compound 6 led to the formation of both spirasine V (7) and VI (8) in a ratio of approximately 1:1, thus showing a complete loss of stereoselectivity in the absence of the 9 β-OH group.

The content of total alkaloids in the root was found to be about 0.8%. The isolated yields of spirasine I, II, VII and VIII were, respectively, 6.7, 1.3, 1.7 and 3.4% in the crude alkaloids.

REFERENCES AND NOTES

1. F. Sun, X. T. Liang, D. Q. Yu, C. F. Xu and J. Clardy, Tetrahedron lett., 1986, 27, 275.
2. F. P. Wang, Org. Chem. (China), 1982, 3, 161.
3. F. Sun and D. Q. Yu, Org. Chem. (China), 1985, 5, 395.
4. The structure of spirasine III with a hydroxyl group at C-9 in the same plant had been elucidated by x-ray crystallopraphy, in preparation.
5. H. C. Brown and P. Jr. Geoghegan, J. Amer. Chem. Soc., 1967, 89, 1522.

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