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DITERPENES FROM *SPIRAEA JAPONICA*

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Key Word Index—*Spiraea japonica var. acuta*; Rosaceae; diterpenes; spiramacetal; spiramadol; spiramilactone C and D.

Abstract—Four new diterpenes, spiramacetal, spiramadol, spiramilactone C and D, were isolated from *Spiraea japonica var. acuta* Their structures were elucidated by chemical and spectral means.

INTRODUCTION

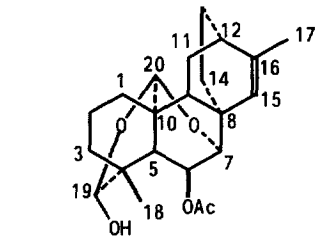
The diterpene alkaloids of *Spiraea japonica* complex, which is distributed mainly in south-west of China, have been studied systematically [1–17]. We isolated and identified some new atisane-type diterpenes from this complex distributed in Yunnan province [11, 17, 18]. Further investigation of the diterpenes has yielded four new components from *Spiraea japonica var. acuta* Yu. We present here spectroscopic and chemical evidence for the structures of spiraminace(**1**), spiramadol(**2**), spiramilactone C(**3**) and D(**4**).

RESULTS AND DISCUSSION

Spiramacetal(**1**) was determined as $C_{22}H_{30}O_5$ on the basis of its HR mass spectrum. The basic skeleton was established by comparing its ^1H NMR and ^{13}C NMR shift values with those of spiraminol (**5**) [11]. Compound **1** showed the presence of two methyl groups [δ_H2.15 and 1.17(each 3H, *s*); δ_C22.7 and 21.1(*q*)], a secondary acetoxyl group[1740 cm^{-1}; δ_H 5.79(1H, *dd*, J=5.3, 1.5 Hz, H-6), 1.75(3H, *s*); δ_C 69.8(*d*,C-6), 169.9(*s*, $\underline{C}OCH_3$), 20.7(*q*, $CO\underline{C}H_3$)], an ether linkage between C-7 and C-20[δ_H 5.69(1H, *s*, H-20), 4.35(1H, *d*, J=5.3 Hz, H-7 β); δ_C 97.3(*d*, C-20), 71.4(*d*, C-7)], acetal group[δ_H 5.79(1H, *s*, H-20); δ_C 97.3(*d*, C-20)], and hemiacetal group[δ_H 5.47(1H, *d*, J=1.6 Hz, H-19); δ_C 95.4(*d*, C-19)]. Unlike spiraminol(**5**), there was no signal of an exo-methylene group for **1**, while a methyl carbon(δC21.1) and tri-substituted double bond were designated as C-15 and C-16, indicated that the migration shift of the exocyclic double bond for **1**. In the ^1H-^1H COSY spectrum of **1**, the signal of the proton at δ5.79(H-6) showed correlation with a proton at δ4.35(H-7), which indicated that an acetoxyl group was located at C-6 as in spiradine F(**6**) [12]. The same coupling constants of δ5.79 and δ4.35 with those of **6** implied the configuration of the acetoxyl group for **1** was β.

Spiramadol(**2**) was assigned as $C_{24}H_{32}O_6$ for its molecular formula on the basis of the HR mass spectrum. In addition to an exo-methylene group[δ_H 4.76, 4.60(each 1H, *d*, J=2 Hz); δ_C 149.9(*s*), 106.6(*t*)], compound **2** showed the presence of two secondary acetoxyl groups[1740, 1250 cm^{-1}; δ_H 2.00, 2.02(each 3H, *s*); 6.00(1H, *dd*, J=9.8, 11.7 Hz, H-6 α), 4.78(1H, *d*, J=9.8 Hz, H-7 β); δ_C 69.1(*d*), 80.8(*d*), 170.4(*s*), 169.9(*s*), 21.3(*q*), 21.1(*q*)], and two aldehyde groups[2730 cm^{-1}; δ_H 9.84(1H, *s*), 9.60(1H, *s*); δ_C 206.0(*d*), 200.0(*d*)]. In the ^1H-^1H COSY spectrum of **2**, the signal at δ6.00 showed correlation with a signal at δ4.78, indicating that two acetoxyl groups were located at C-6 and C-7, respectively. The coupling constant of δ_H 6.00 and 4.78(J=9.8 Hz) implied H-6 and H-7 were situated in the axial-configuration, while the coupling constant of δ_H 6.00(J=11.7 Hz) implied H-6 and H-5 also were situated in the axial-configuration. Since H-5 has the β- configuration, H-6 and H-7 could be designated as α and β, respectively. Unlike spiraminace(**1**) or spiraminol(**5**), compound **2** bears two free-aldehyde groups because there is no free C-7αhydroxyl group in **2**.

Spiramilactone C(**3**) was assigned the molecular formula $C_{20}H_{28}O_4$ by the HR mass spectrum. Compound **3** showed the presence of an exo-methylene group[δ_H 5.34, 5.12(each 1H, *d*, J=1.5 Hz, H_2-17); δ_C 155.4(*s*), 1 09.9(*t*)], a methyl group[δ_H 1.28(3H, *s*, H_3-18); δ_C 23.6(*q*)], two secondary OH groups[3400 cm^{-1}; δ_H 4.17(1H, *br.s*, H-15β), 3.87(1H, *dd*, J=4.0, 11.4 Hz, H-7β); δ_C 77.4(*d*), 81.1(*d*)], and a lactone moiety[1740 cm^{-1}; δ_H 4.94(1H, *dd*, J=2.0, 12.1 Hz, H-20), 4.26(1H, *d*, J=12.1Hz, H-20); δ_C 74.1(*t*), 175.7(*s*)]. Compound **3** and spiramilactone(**7**) [18] have the same molecular skeleton and functional groups. The difference between **3** and **7** is the position of carbonyl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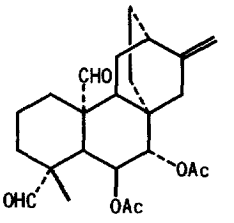
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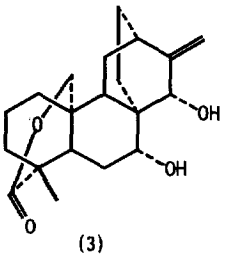
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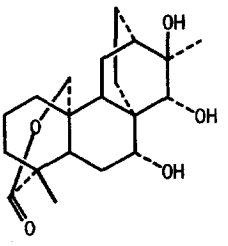
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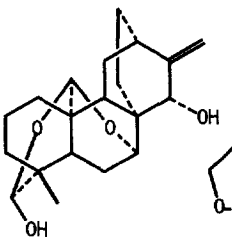
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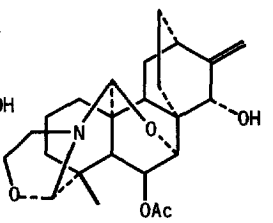
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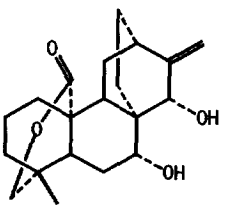
(7)

groups. The downfield shift of the C-18 methyl group(δ_H 1.28) of **3** indicated its carbonyl group is located at C-19. The intramolecular Cannizzaro reaction of spiraminol(**5**) gave **3** and **7**, confirming the structure of **3**.

Spiramilactone D(**4**) has the molecular formula $C_{28}H_{30}O_5$ and showed the same skeleton and functional groups as **3** except for an exo-methylene group by comparing their NMR spectra. The signals of a tertiary carbon[δ_C 70.3(*s*)] and a methyl carbon[δ_H 1.47(3H, *s*); δ_C 31.0(*q*)] indicated **4** was derived from **3** by hydroxylation at the exocyclic double bond, and the configuration of C-16 was designated as R comparing with spiramine P(**7**) [17].

EXPERIMENTAL

General.

Mps: uncorr. IR spectra were measured as KBr pellets, optical rotation in $CHCl_3$. ^1H and ^{13}C NMR and 2D NMR spectra were recorded in pyridine-d_5 using TMS as int. standard. EIMS were measured at 70 eV.

Plant material

Roots of *Spiraea japonica var. acuta* Yu were collected in Li-Jiang, Yunnan Province of China in July 1993, and identified by Dr. Hang Sun, a botanist of Kunming Institute of Botany, Chinese Academy of Sciences, where the voucher specimen is deposited (No. 8018).

Extraction and isolation

Powdered dried roots(5 kg) were extracted with 95% EtOH at room temp. After removal of solvent by evapn, the combined extracts were dissolved in 3% HCl and filtered. The HCl soln was extracted with benzene-petrol(1:1) and made basic with NaOH soln(PH11) and extracted with $CHCl_3$. Evapn of $CHCl_3$ gave 35 g of a basic fr.(0.7%). The fr.(35 g) was chromatographed on a silica gel column eluting with petrol-Me_2CO-Et_2NH (50:1:0.5 to 50:5:4) to give 4 diterpenes and 8 alkaloids.

Spiramacetal (**1**) (20 mg, 0.0004%) as needles (petrol-$CHCl_3$), mp 148–150° $[\alpha]_D$-75 ($CHCl_3$, *c* 0.5). HRMS: obsd 374.2117 for $C_{22}H_{30}O_5$, calc. 374.2093. EIMS *m/z* (rel. int.) 374[M]+, 328(55), 314(10), 240(100). IR $\nu KBr_{max}cm^{-1}$: 3400, 2880, 1740, 1380, 1240, 1020, 890; ^1H NMR(400 Hz): δ6.00(1H, *s*, H-15), 5.79(1H, *dd*, J=5.3, 1.5 Hz, H-6 α), 5.69(1H, *s*, H-20), 5.47(1H, *d*, J=1.6 Hz, H-19), 4.35(1H, *d*, J=5.3 Hz, H-7 β), 2.15(3H, *s*, H_3-17), 1.75(3H, *s*, H_3-22), 1.17(3H, *s*, H_3-18). ^{13}C NMR: Table 1.

Spiramadol(**2**) (20 mg, 0.0004%) as needles (petrol-$CHCl_3$), mp 208–210° $[\alpha]_D$-19 ($CHCl_3$, *c* 0.67). HRMS(F_{AB}): obsd 417.2247 for $C_{24}H_{32}O_6$, calc. 417.2277. EIMS *m/z* (rel. int.) 416[M]+, 399(20), 370(5), 356(40). IR $\nu KBr_{max}cm^{-1}$: 2990, 2730, 1740, 1710, 1640, 1020, 990, 750; ^1H NMR(400 Hz): δ9.84(1H, *s*, H-19), 9.60(1H, *s*, H-20), 6.00(1H, *dd*, J=9.8, 11.7 Hz, H-6α), 4.78(1H, *d*, J=9.8 Hz, H-7β), 4.76, 4.60(each 1H, *d*, J=2 Hz, H2-17), 2.02(3H, *s*, H3-24), 2.00(3H, *s*, H3-22), 1.06(3H, *s*, H3-18). ^{13}C NMR: Table 1.

Spiramilactone C(**3**) (15 mg, 0.0003%) as needles (petrol-$CHCl_3$), mp 172–174° $[\alpha]_D$-50 ($CHCl_3$, *c* 0.38). HRMS: obsd 332.1986 for $C_{20}H_{28}O_4$, calc. 332.1988.

Table 1. ^{13}C NMR data for spiraminace(**1**), spiramadol(**2**), spiramilactone C(**3**) and spiramilactone D(**4**)

Carbon	1	2	3	4
1	34.5(*t*)	42.6(*t*)	40.1(*t*)	53.3(*t*)
2	25.3(*t*)	32.3(*t*)	20.8(*t*)	42.8(*t*)
3	29.8(*t*)	35.4(*t*)	39.9(*t*)	38.2(*t*)
4	37.5(*s*)	53.8(*s*)	42.6(*s*)	47.2(*s*)
5	55.7(*d*)	52.4(*d*)	47.7(*d*)	47.9(*d*)
6	69.8(*d*)	69.1(*d*)	15.3(*d*)	23.0(*d*)
7	71.4(*d*)	80.8(*d*)	81.1(*d*)	82.2(*d*)
8	41.0(*s*)	39.2(*s*)	41.8(*s*)	39.4(*s*)
9	51.5(*d*)	48.9(*d*)	44.8(*d*)	39.3(*d*)
10	35.8(*s*)	47.8(*s*)	36.6(*s*)	34.4(*s*)
11	21.8(*t*)	25.6(*t*)	29.0(*t*)	22.0(*t*)
12	37.5(*d*)	35.9(*d*)	36.2(*d*)	52.7(*d*)
13	20.9(*t*)	22.6(*t*)	28.3(*t*)	21.1(*t*)
14	29.4(*t*)	19.4(*t*)	26.8(*t*)	20.4(*t*)
15	132.2(*d*)	27.3(*t*)	77.4(*d*)	71.0(*d*)
16	139.1(*s*)	149.9(*s*)	155.4(*s*)	70.3(*s*)
17	21.1(*q*)	106.6(*t*)	109.9(*t*)	31.0(*q*)
18	22.7(*q*)	27.4(*q*)	23.6(*q*)	27.0(*q*)
19	95.4(*d*)	206.0(*d*)	175.7(*s*)	174.7(*s*)
20	97.3(*d*)	200.0(*d*)	74.1(*t*)	76.3(*t*)
$\underline{C}OCH_3$	169.9(*s*)	170.4(*s*)		
$CO\underline{C}H_3$	20.7(*q*)	21.3(*q*)		
$\underline{C}OCH_3$	169.9(*s*)			
$CO\underline{C}H_3$	20.4(*q*)			

EIMS *m/z* (rel. int.) 332[M]+, 314(100), 299(30), 286(60), 273(65). IR $\nu KBr_{max}cm^{-1}$: 3400, 2940, 2880, 1740,1240, 1020, 890. ^1H NMR(400 Hz): δ5.34(1H, *d*, J=1.5 Hz, H-17), 4.94(1H, *dd*, J=2.0, 12.1 Hz, H-20), 4.26(1H, *d*, J=12.1 Hz, H-20), 4.17(1H, *br.s*, H-15 β), 3.87(1H, *dd*, J=4.0, 11.4 Hz, H-7β), 5.12(1H, *d*, J=1.4 Hz, H-17), 1.28(3H, *s*, H_3-18). ^{13}C NMR: Table 1.

Spiramilactone D(**4**) (25 mg, 0.0005%) as needles (petrol-$CHCl_3$), mp 225–227°.$[\alpha]_D$-52 ($CHCl_3$, *c* 0.44). HRMS: obsd 350.2090 for $C_{20}H_{30}O_5$, calc. 350.2093. EIMS *m/z* (rel. int.) 350[M]+, 332(43), 314(65), 292(100). IR $\nu KBr_{max}cm^{-1}$: 3420, 2940, 1710, 920, 890; ^1H NMR(400 Hz): δ4.54(1H, *dd*, J=2.0, 11.3 Hz, H-20), 4.04(1H, *d*, J=11.3 Hz, H-20), 4.04(1H, *s*, H-15 β), 3.40(1H, *d*, J=9.0 Hz, H-7β), 1.47(3H, *s*, H_3-17), 1.28(3H, *s*, H_3-18). ^{13}C NMR: Table 1.

Intramolecular Cannizzaro reaction of spiraminol(**5**).

To the soln of KOH(1 g)-MeOH(10 ml) was added 50 mg(0.15 mmol) of **5**. After refluxed 4 hr, solvent was removed by evapn, the residue was extracted with $CHCl_3$. Work-up followed by a short column of silica gel($CHCl_3$–Me_2CO, 5:1) afforded **3**(5 mg, 0.015 mmol) and **7**(10 mg, 0.03 mmol), respectively, which were identified by ^1H NMR, ^{13}C NMR and TLC.

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