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Carbon-13 Nuclear Magnetic Resonance Study of Canthin-6-one Alkaloids

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The carbon-13 nuclear magnetic resonance chemical shift assignments for several canthin-6-one alkaloids isolated from *Ailanthus altissima* SWINGLE and *Picrasma quassioides* BENNET, made on the basis of two-dimensional ^{13}C–^{1}H chemical shift correlation, ^{13}C–^{1}H heteronuclear couplings, and long-range selective ^{1}H decoupling experiments, are reported.

Keywords——^{13}C-NMR; canthin-6-one alkaloid; chemical shift assignment; carbon–proton coupling; long-range selective proton decoupling experiment

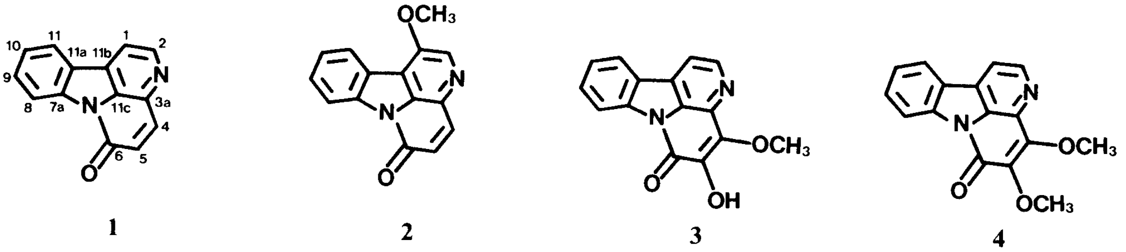
Introduction

Canthin-6-one alkaloids occur plentifully in many plants of Simaroubaceae and Rutaceae.[1] However, no carbon-13 nuclear magnetic resonance (^{13}C-NMR) study of canthin-6-one alkaloids has yet been done, even though such information would be useful in structural elucidation. The proton nuclear magnetic resonance (^{1}H-NMR) spectra of canthin-6-one alkaloids provide only limited information regarding slight structure variations in the canthin-6-one molecule due to overlapping or obscured signals. We have now found that ^{13}C-NMR is more useful than ^{1}H-NMR for the structural elucidation of canthin-6-one alkaloids.

We report here the ^{13}C-NMR spectra of four canthin-6-one alkaloids conclusively analyzed with the aid of carbon–proton chemical shift correlation, high-resolution proton-coupled ^{13}C spectra, and long-range selective proton decoupling (LSPD) experiments.

Experimental

Canthin-6-one (**1**) and 1-methoxycanthin-6-one (**2**) were obtained from *Ailanthus altissima* SWINGLE (Simaroubaceae).[2] 5-Hydroxy-4-methoxycanthin-6-one (**3**), and 4,5-dimethoxycanthin-6-one (**4**) were obtained from *Picrasma quassioides* BENNET (Simaroubaceae).[3] ^{1}H-NMR, ^{13}C-NMR spectra and heteronuclear ^{13}C–^{1}H couplings were recorded with a JEOL GX-400 NMR spectrometer (^{1}H 400 MHz and ^{13}C 100 MHz), the samples being observed in a 5 mm dual-tuned $^{1}H/^{13}C$ probe at *ca.* 22 °C. ^{13}C-NMR Spectra were measured for 0.3—0.5 M solutions in chloroform-*d* (**1** and **4**), chloroform-*d*–methanol-d_4 (95 : 5) (**2**), and dimethylsulfoxide-d_6 (**3**) with tetramethylsilane as an internal standard. The two-dimensional experiment on **1** was done on a JEOL GX-400 spectrometer using a 0.7 M solution of **1** in chloroform-*d*. The spectral width in the F2 domain was 5140 Hz and that in the F1 domain was 960 Hz for **1**. Total data collection for **1** required less than 15 h for the 2048 × 256 data point matrix.



1 **2** **3** **4**

Chart 1

Results and Discussion

^{1}H-NMR Spectra

Since identification of individual carbon resonances involved ^{13}C–^{1}H shift correlation, it was desirable to examine exactly the ^{1}H-NMR spectra of these alkaloids. We have achieved the complete assignment for canthin-6-one alkaloids, given in Table I, based primarily on the standard chemical shift, multiplicity, coupling constant, and double resonance considerations.

^{13}C-NMR Spectra

The resulting assignments along with the ^{13}C chemical shifts are presented in Table II and ^{13}C–^{1}H coupling constants in Tables III and IV. The ^{13}C–^{1}H shift correlation of canthin-6-one (**1**) is presented as a contour plot in Fig. 1. Figure 1 shows very clear assignment of tertiary carbon resonances. The resonances of quaternary carbons and carbonyl carbon were assigned based on the change in splitting patterns in the LSPD experiments.

Canthin-6-one (1)

The proton coupled ^{13}C-NMR spectrum of **1** is shown in Fig. 2. In the LSPD experiments, irradiation of either the H-1 proton at 7.59 ppm or the H-4 proton at 7.77 ppm reduced the triplet signal at 130.91 ppm to a doublet, revealing three-bond couplings among

TABLE I. ^{1}H-NMR Spectral Data[a] for Compounds **1**–**4**

Proton	**1**	**2**	**3**	**4**
1	7.59 (d, $J=5.0$)		7.98 (d, $J=5.0$)	7.47 (d, $J=5.0$)
2	8.58 (d, $J=5.0$)	8.43 (s)	8.71 (d, $J=5.0$)	8.54 (d, $J=5.0$)
4	7.77 (d, $J=9.7$)	7.91 (d, $J=9.7$)		
5	6.75 (d, $J=9.7$)	6.81 (d, $J=9.7$)		
8	8.28 (d, $J=7.7$)	8.60 (d, $J=7.7$)	8.38 (d, $J=7.7$)	8.16 (d, $J=7.7$)
9	7.45 (t, $J=7.7$)	7.62 (t, $J=7.7$)	7.67 (t, $J=7.7$)	7.37 (t, $J=7.7$)
10	7.28 (t, $J=7.7$)	7.47 (t, $J=7.7$)	7.49 (t, $J=7.7$)	7.19 (t, $J=7.7$)
11	7.73 (d, $J=7.7$)	8.12 (d, $J=7.7$)	8.14 (d, $J=7.7$)	7.54 (d, $J=7.7$)
1-OCH$_3$		4.23 (s)		
4-OCH$_3$			4.28 (s)	4.40 (s)
5-OCH$_3$				4.04 (s)
5-OH			5.77 (s)[b]	

a) Solvent: **1**, **2**, and **4** in CDCl$_3$ and **3** in DMSO-d_6. Coupling constant in Hz. *b*) Disappeared with D$_2$O.

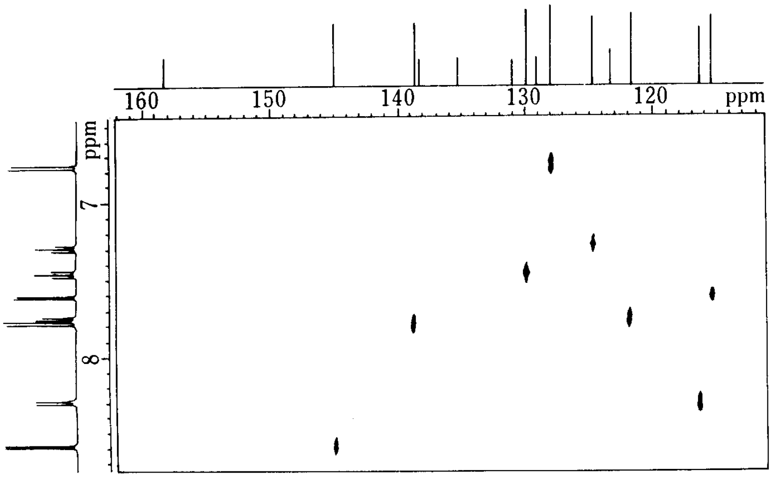


Fig. 1. Contour Plots of Two-Dimensional Carbon–Proton Chemical Shift Correlation Spectra for Canthin-6-one (**1**)

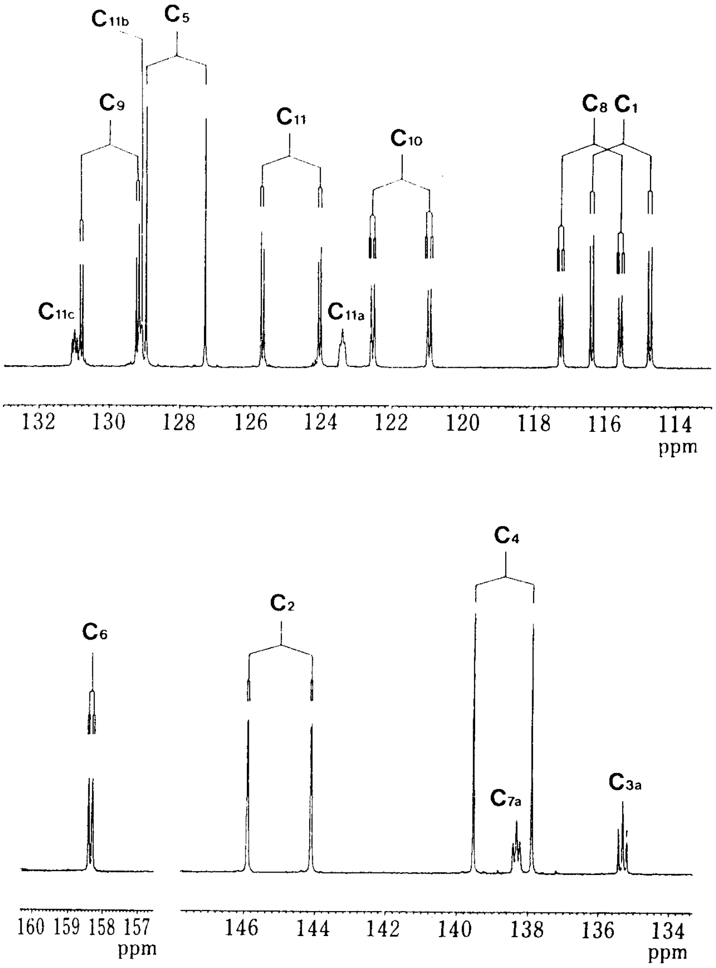


Fig. 2. Proton-Coupled ^{13}C-NMR Spectrum of Canthin-6-one (**1**)

C-11c, H-1, and H-4. Irradiation of either the H-2 proton at 8.58 ppm or the H-5 at 6.75 ppm reduced the triplet signal at 135.23 ppm to a doublet, revealing three-bond couplings among C-3a, H-2, and H-5. At the same time, irradiation of the H-1 or H-2 proton reduced the double doublet signal at 128.99 ppm to a doublet, revealing two-bound coupling between C-11b and H-1 of 3.7 Hz and three-bond coupling between C-11b and H-2 of 8.1 Hz. Irradiation of the H-4 or H-5 proton reduced the double doublet signal at 158.21 ppm to a doublet, revealing two-bond coupling between C-6 and H-4 of 2.2 Hz and three-bond coupling between C-6 and H-5 of 11.0 Hz.

1-Methoxycanthin-6-one (2)

The resonance at 152.23 ppm could be unambiguously assigned to C-1 by irradiating the 1-methoxyl protons at 4.23 ppm. The complex multiplet of C-1 was converted to a clean doublet due to the coupling to the H-2 proton. The doublets of C-11b at 130.18 ppm and C-11c at 130.83 ppm could each be analyzed in terms of three-bond coupling of 8.0 Hz. The assignment was confirmed by irradiation of the H-2 proton at 8.43 ppm, when the signal at 130.18 ppm was reduced from a doublet to a singlet.

The triplet at 128.70 ppm ($^3J_{CH} = 11.0$ Hz) with no one- or two-bond coupling was easily assigned to C-3a, at higher field than in the case of **1** due to the *para*-position effect of the 1-methoxyl substituent. The double doublet of C-6 at 160.21 ppm could be analyzed in terms of two-bond coupling of 2.2 Hz between C-6 and H-5 and three-bond coupling of 11.0 Hz between C-6 and H-4.

5-Hydroxy-4-methoxycanthin-6-one (3)

The two doublets of C-4 at 142.68 ppm and C-5 at 139.60 ppm could be analyzed in terms of three-bond coupling of 4.0 Hz between C-4 and 4-methoxyl protons and two-bond coupling of 2.0 Hz between C-5 and the hydroxyl proton, respectively. The assignments were confirmed by irradiation of the methoxyl protons at 4.28 ppm and the hydroxyl proton at 5.77 ppm, which reduced the appropriate doublet to a singlet. Irradiation of the H-2 proton at 8.71 ppm reduced the doublet signal at 133.46 ppm to a singlet, revealing three-bond coupling between C-3a and H-2. The double doublet of C-11b at 127.96 ppm and the doublet of C-11c at 124.82 ppm could be analyzed in terms of two-bond coupling of 3.5 Hz between C-11b and H-1 and three-bond coupling of 8.0 Hz between C-11b and H-2, and three-bond coupling of 8.0 Hz between C-11c and H-1, respectively. The singlet at 156.27 ppm with no coupling was easily assigned to C-6.

4,5-Dimethoxycanthin-6-one (4)

In the ^{1}H-NMR spectra of **3**, **4**, and 4-hydroxy-5-methoxycanthin-6-one,4) the signal of the 4-methoxyl protons appear at lower field than those of the 5-methoxyl protons. Therefore,

TABLE II. ^{13}C-NMR Spectral Data for Compounds **1**—**4**

Carbon	**1**	**2**	**3**	**4**
1	115.37	152.23	113.70	114.89
2	144.84	130.69	144.11	144.48
3a	135.23	128.70	133.46	132.71
4	138.57	138.69	142.68	152.05
5	127.98	124.61	139.60	139.35
6	158.21	160.21	156.27	157.43
7a	138.24	138.17	137.38	138.22
8	116.29	116.73	115.22	116.24
9	129.84	129.59	129.62	130.01
10	124.69	125.66	124.65	124.59
11	121.61	124.37	122.39	121.78
11a	123.33	123.88	124.20	123.96
11b	128.99	130.18	127.96	129.15
11c	130.91	130.83	124.82	127.61
1-OCH_3		56.70		
4-OCH_3			60.51	61.17
5-OCH_3				61.04

TABLE III. One-Bond ^{13}C–^{1}H Coupling Constants (Hz) for Compounds **1**—**4**

Carbon	**1**	**2**	**3**	**4**
1	165.1		164.0	164.0
2	179.7	178.6	179.0	178.6
4	165.1	164.0		
5	168.0	168.0		
8	168.5	168.7	168.0	168.0
9	162.1	160.0	160.0	160.0
10	162.1	160.0	160.0	160.0
11	162.1	160.0	160.0	160.0
1-OCH_3		145.5		
4-OCH_3			146.5	146.7
5-OCH_3				145.7

TABLE IV. Fine Splitting Patterns and Long-Range ^{13}C–^{1}H Coupling Constants in Compound **1**—**4**

Carbon	**1**		**2**		**3**		**4**	
1	dd		m		dd		dd	
	^{2}J (C-1, H-2)	8.8	^{2}J (C-1, H-2)	8.8	^{2}J (C-1, H-2)	8.8	^{2}J (C-1, H-2)	8.8
			^{3}J (C-1, OCH$_3$)	4.0				
2	dd		d		dd		dd	
	^{2}J (C-2, H-1)	2.9			^{2}J (C-2, H-1)	2.4	^{2}J (C-2, H-1)	2.4
3a	t		t		d		d	
	^{3}J (C-3a, H-2)	11.4	^{3}J (C-3a, H-2)	11.0	^{3}J (C-3a, H-2)	12.5	^{3}J (C-3a, H-2)	12.8
	^{3}J (C-3a, H-5)	11.4	^{3}J (C-3a, H-5)	11.0				
4	d		d		q		q	
					^{3}J (C-4, OCH$_3$)	4.0	^{3}J (C-4, OCH$_3$)	4.0
5	d		d		d		q	
					^{2}J (C-5, OH)	2.0	^{3}J (C-5, OCH$_3$)	4.0
6	dd		dd		s		s	
	^{2}J (C-6, H-5)	2.2	^{2}J (C-6, H-5)	2.2				
	^{3}J (C-6, H-4)	11.0	^{3}J (C-6, H-4)	11.0				
7a	t		t		t		t	
	^{3}J (C-7a, H-9)	8.8	^{3}J (C-7a, H-9)	8.8	^{3}J (C-7a, H-9)	8.0	^{3}J (C-7a, H-9)	8.0
	^{3}J (C-7a, H-11)	8.8	^{3}J (C-7a, H-11)	8.8	^{3}J (C-7a, H-11)	8.0	^{3}J (C-7a, H-11)	8.0
8	ddd		ddd		ddd		ddd	
	^{2}J (C-8, H-9)	1.5	^{2}J (C-8, H-9)	1.5	^{2}J (C-8, H-9)	1.5	^{2}J (C-8, H-9)	1.5
	^{3}J (C-8, H-10)	8.1	^{3}J (C-8, H-10)	8.0	^{3}J (C-8, H-10)	8.0	^{3}J (C-8, H-10)	8.0
9	dd		dd		dd		dd	
	^{3}J (C-9, H-11)	8.1	^{3}J (C-9, H-11)	8.0	^{3}J (C-9, H-11)	8.0	^{3}J (C-8, H-11)	8.0
10	dd		dd		dd		dd	
	^{3}J (C-10, H-8)	8.1	^{3}J (C-10, H-8)	8.0	^{3}J (C-10, H-8)	8.0	^{3}J (C-10, H-8)	8.0
11	ddd		ddd		ddd		ddd	
	^{2}J (C-11, H-10)	1.5	^{2}J (C-11, H-10)	1.5	^{2}J (C-11, H-10)	1.5	^{2}J (C-11, H-10)	1.5
	^{3}J (C-11, H-9)	8.1	^{3}J (C-11, H-9)	8.0	^{3}J (C-11, H-9)	8.0	^{3}J (C-11, H-9)	8.0
11a	t		t		t		t	
	^{3}J (C-11a, H-10)	6.0	^{3}J (C-11a, H-10)	6.0	^{3}J (C-11a, H-10)	6.0	^{3}J (C-11a, H-10)	6.0
	^{3}J (C-11a, H-8)	6.0	^{3}J (C-11a, H-8)	6.0	^{3}J (C-11a, H-8)	6.0	^{3}J (C-11a, H-8)	6.0
11b	dd		d		dd		dd	
	^{2}J (C-11b, H-1)	3.7	^{3}J (C-11b, H-2)	8.0	^{2}J (C-11b, H-1)	3.5	^{3}J (C-11b, H-1)	3.5
	^{3}J (C-11b, H-2)	8.1			^{3}J (C-11b, H-2)	8.0	^{3}J (C-11b, H-2)	8.0
11c	t		d		d		d	
	^{3}J (C-11c, H-1)	8.1	^{3}J (C-11c, H-4)	8.0	^{3}J (C-11c, H-1)	8.0	^{3}J (C-11c, H-1)	8.0
	^{3}J (C-11c, H-4)	8.1						
1-OCH$_3$			q					
4-OCH$_3$					q		q	
5-OCH$_3$							q	

the resonances at 152.05 and 139.35 ppm could be unambiguously assigned to C-4 and C-5, respectively, by irradiating the 4-methoxyl protons at 4.40 ppm and the 5-methoxyl protons at 4.04 ppm. The quartet of C-4 and that of C-5 were converted to a singlet. Irradiation of the H-2 proton at 8.54 ppm reduced the doublet signal at 132.71 ppm to a singlet revealing, three-bond coupling between C-3a and H-2. The double doublet of C-11b at 129.15 ppm and the doublet of C-11c at 127.61 ppm could be analyzed in terms of two-bond coupling of 3.5 Hz between C-11b and H-1 and three-bond coupling of 8.0 Hz between C-11b and H-2, and three-bond coupling of 8.0 Hz between C-11c and H-1, respectively. The singlet at 157.43 ppm with no coupling was easily assigned to C-6.

As regards the quaternary carbons 7a and 11a of **1** to **4**, the triplet of 7a could be analyzed in terms of three-bond couplings. The assignment was confirmed by irradiation of

H-9 and H-11 (the triplet was reduced to a doublet). The triplet at 123.96 ppm was assigned to C-11a, which was confirmed by irradiating H-8 and H-10. The triplet collapsed to a clean doublet due to the couplings to H-8 and H-10.

In conclusion, the one-bond carbon coupling constant ($^1J_{CH}$) values of tertiary carbon atoms of **1** to **4** except at the C-2 position were within the range of 160.0—168.7 Hz; however, the ^1J(C-2, H) value of 178.6—179.7 Hz was larger than those of the other carbons because of the neighboring N atom. All of the carbon resonances of canthin-6-one alkaloids were unambiguously assigned.

References and Notes

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