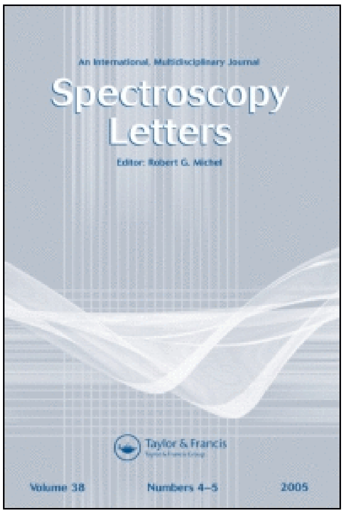

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Two Dimensional NMR Study of Some Natural Coumarins

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TWO DIMENSIONAL NMR STUDY OF SOME NATURAL COUMARINS

Key Words: Coumarin, NMR, HETCOR, *Diosmeae*, *Rutinae*

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ABSTRACT

Two dimensional HETCOR and long range HETCOR experiments have been performed on the natural coumarins hopeyhopin, dehydrogeijerin, 6-methoxy-7-(3′,3′-dimethylallyloxy)-coumarin, puberulin, oxypeucedanin and isoimperatorin which allowed complete ^{1}H and ^{13}C spectral assignments to be made.

INTRODUCTION

Recently ^{13}C data on some natural coumarins and coumarin derivatives[1] have been reported. In the course of our phytochemical studies on the *Diosmeae* and *Rutinae* (sub-family *Rutoideae*) of Southern Africa we have isolated and identified a number of coumarin structures.[2,3] We report here ^1H and ^{13}C chemical shifts for the compounds hopeyhopin (**1**), dehydrogeijerin (**2**), 6-methoxy-7-(3′,3′-dimethylallyloxy)-coumarin (**3**), puberulin (**4**), oxypeucedanin (**5**) and isoimperatorin (**6**). Two dimensional n.m.r. techniques have been used to make unambiguous assignments. The structures of these compounds are given in Fig. 1.

RESULTS AND DISCUSSION

The proton spectrum of hopeyhopin(1) is shown in Fig. 2. The assignments of protons 3, 4, 5 and 8 follow from standard chemical shift arguments but are confirmed by ^1H-^{13}C correlations. The H-2′ resonance is virtually coincident with the OMe resonance as shown by an enlargment of this spectral region, but also by the cross peaks shown in the HETCOR[4] spectrum.

The ^{13}C spectrum of **1** is shown in Fig. 2. The assignment of protonated carbons followed directly from the HETCOR experiment (Fig. 2). Note that in general there is a linear relationship between the proton and carbon chemical shifts. This relationship, however, can only be used for assignment when there is a large difference in chemical shift. For example H-8 is downfield of H-3 while C-8 is upfield of C-3. Similarly the order of H-4, H-5 and C-4, C-5 chemical shifts are not as expected.

In order to assign the quaternary carbons the long range HETCOR[5] (J_{CH} = 6 Hz) pulse sequence was used (Fig. 3). While some of the one bond correlations are still present many three bond C-H correlations are now apparent. H-5 shows cross peaks with C-5, C-4 and C-1′, H-4 is correlated

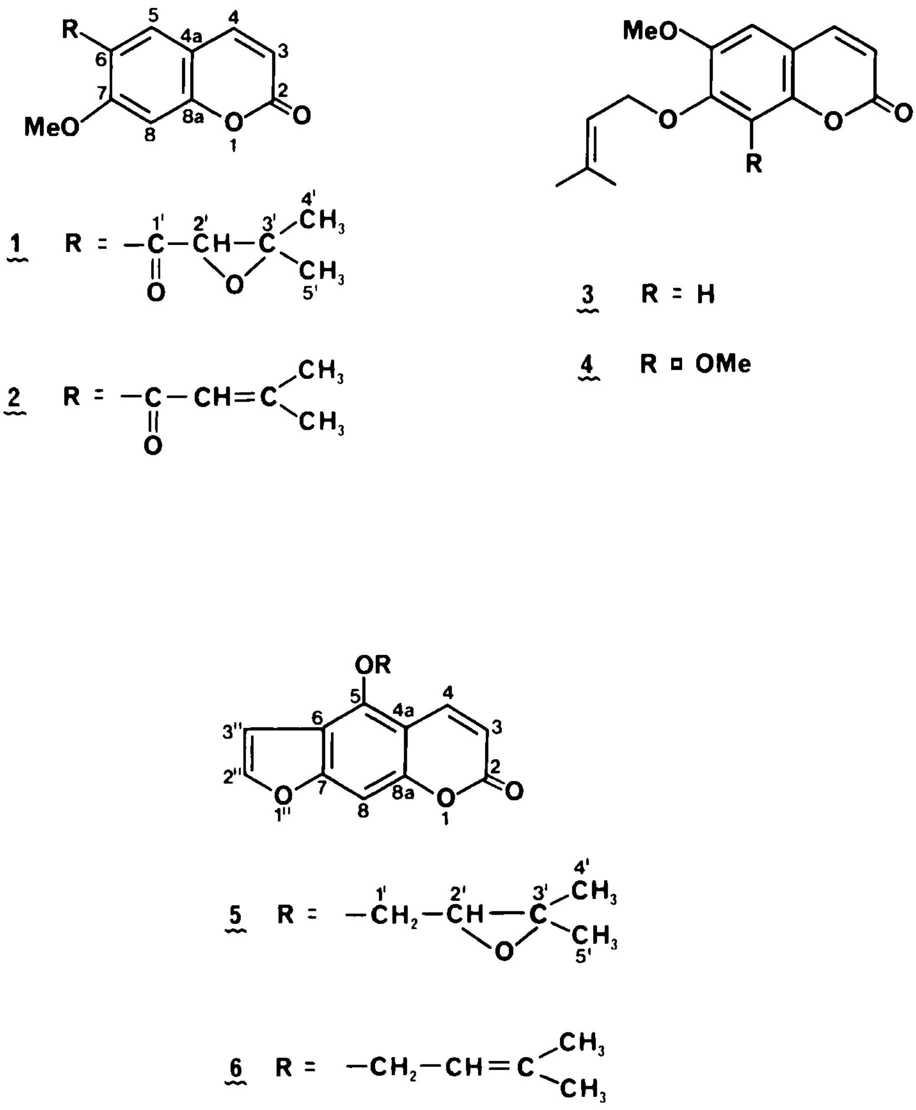

FIG. 1. Structures of compounds 1-6.

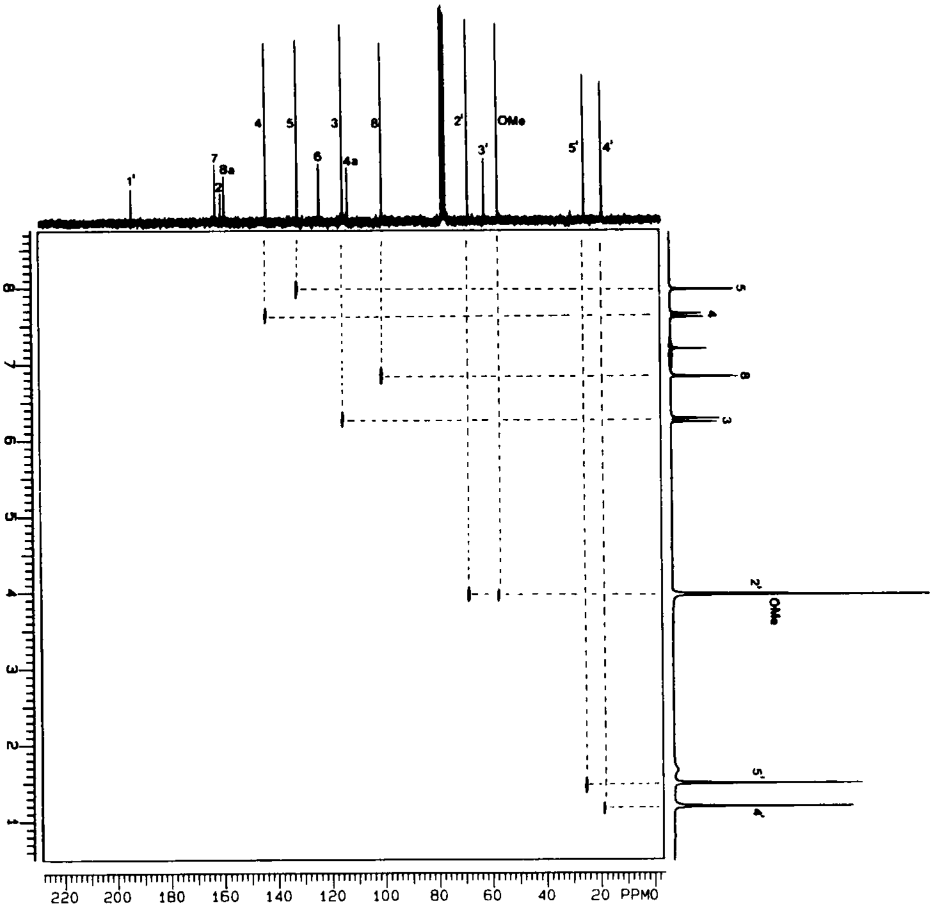

FIG. 2. Two dimensional heteronuclear shift correlated spectrum (HETCOR) of 1 using $J_{C,H}$ = 140 Hz.

to C-5, C-4 and C-8a, H-8 is correlated to C-8 and C-6, while H-3 is correlated to C-4a, C-3 and C-2. In addition correlation between OMe and C-7 and H-2′ and C-1′ confirms the assignment of the other carbon resonances. Reversal of any of the proton assignments would lead to an inconsistent set of ^{13}C assignments.

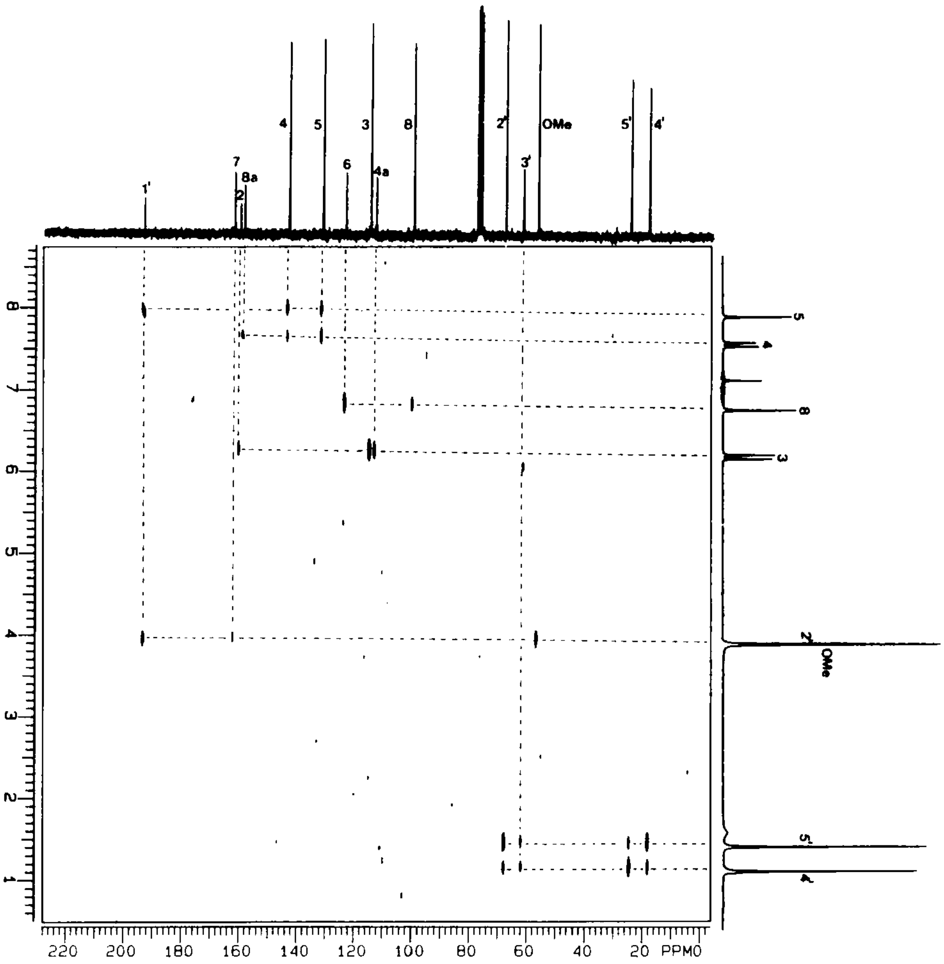

FIG. 3. Two dimensional long range HETCOR spectrum of 1, $J_{C,H}$ = 6 Hz.

TABLE 1

^{13}C N.M.R. Chemical Shifts for Compounds **1** - **6**.

	Chemical shift (ppm)					
C	**1**	**2**	**3**	**4**	**5**	**6**
2	159.9	157.4	161.3	160.6	161.0	161.3
3	114.6	113.9	113.0	115.1	113.0	112.5
4	143.1	143.3	143.3	143.5	138.9	139.6
4a	112.7	112.1	111.1	114.4	107.3	107.4
5	131.3	130.3	107.8	103.6	148.3	148.9
6	123.3	128.2	146.4	144.9	114.0	114.1
7	162.0	160.8	151.9	150.7	157.9	158.1
8	99.8	99.6	100.8	143.0	94.7	94.2
8a	158.7	156.7	149.6	141.8	152.4	152.6
1′	193.4	180.0	66.0	70.3	72.2	69.7
2′	67.9	124.8	118.4	120.0	61.0	119.0
3′	61.8	133.8	138.8	139.3	58.3	139.8
4′	24.6	28.1	25.7	25.8	24.5	25.2
5′	18.2	21.4	18.2	17.9	18.9	18.2
2"					145.2	144.9
3"					104.4	105.0
6-OMe			56.1	56.3		
8-OMe				61.7		
7-OMe		52.2				

TABLE 2

^{1}H N.m.r. chemical shifts and coupling constants for compounds 1 - 6.

	Chemical Shift (ppm)					
Proton	1	2	3	4	5	6
3	6.29, *d* (*J*=9.52)	6.30, *d* (*J*=9.53)	6.24, *d* (*J*=10.0)	6.31, *d* (*J*=9.60)	6.22, *d* (*J*=9.8)	6.27, *d* (*J*=9.6)
4	7.67, *d* (*J*=9.68)	7.67, *d* (*J*=9.53)	7.60, *d* (*J*=10.0)	7.58, *d* (*J*=9.40)	8.13, *d* (*J*=9.8)	8.16, *d* (*J*=9.6)
5	8.01	7.74	6.81	6.63		
8	7.23	6.85	6.81		7.09	7.15
1'			4.64, *d* (*J*=6.1)	4.61, *d* (*J*=8.00)	4.61, *dd* (*J*=11, 4.4) 4.44, *dd* (*J*=11, 6.5)	4.91, *d* (*J*=2.8)
2'	4.01	6.61	5.47, *t* (*J*=6.1)	5.55, *t* (*J*=8.00)	3.24, *dd* (*J*=6.5, 4.4)	5.53, *t* (*J*=8.0)
4'	1.52	2.24*	1.76*	1.74*	1.37*	1.78
5'	1.22	2.00*	1.76*	1.68*	1.30*	1.67
2"					7.55, *d* (*J*=2.7)	7.59, *d* (*J*= 2.8)
3"					6.92, *d* (*J*=2.7)	6.94, *d* (*J*= 2.8)
6-OMe			3.88	3.90		
8-OMe				4.00		
7-OMe		3.95				

* Assignments may be reversed.

From the data available it was not possible to assign unambiguously the methyl groups 4′ and 5′. To this end difference nOe spectra[6] were recorded. NOe was detected between H-2′ and both H-4′ and H-5′. However, based on the size of the nOe, H-5′ is *cis* to H-2′ and the assignments are as shown. The final set of chemical shifts and assignments are given in Tables 1 and 2.

In a similar manner complete ^{13}C and ^{1}H n.m.r. assignments of compounds **2** to **6** were made. Compound **5** has been studied before and our assignments are in agreement with the literature.[1] Based on a comparison of structurally related coumarins Patra and Mitra[1] propose that the assignment of C-4a and C-8a be interchanged. Using chemical shift correlations we are able to confirm this proposal.

Inspection of Table 1 reveals that, with the exception of substitution at the 5 position, the chemical shift of C-4, C-3 and C-2 are independent of substitution at the phenyl ring. Substitution at the 5 position results in a 4 ppm, highfield shift, of the C-4 resonance. Similarly the C-4a resonance remains invarient while the C-8a resonance shifts 17 ppm.

EXPERIMENTAL

Ground dried leaves and stems were extracted with petrol (60-80 °C). The solvent was removed under reduced pressure and the residue chromatographed on an alumina column using $CHCl_3$ as solvent. Mixtures of coumarins were separated by preparative TLC (silica gel: solvent C_6H_{12}-EtOAc, 6:4) and recrystallised.

N.m.r spectra were recorded as $CDCl_3$ solutions in 5 mm sample tubes on a Varian VXR200 spectromenter. Chemical shifts are relative to deuterochloroform (δ_H 7.24, δ_C 77.0).

Two dimensional HETCOR spectra were recorded using 128 increments, a sweep width of 11668 Hz and an acquisition time of 0.088 s. The final data matrix of dimensions 2048 x 256 was used with apodization functions RE = 0.005, AF = 0.022 and RE2 = 0.005, AF2 = 0.019 respectively. For the standard HETCOR pulse sequence a C-H coupling of 140 Hz was used, while for the long range HETCOR pulse sequence an additional J_{CH} of 6 Hz was used.

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