Natural Abundance ^{13}C–^{13}C Coupling Constants for Carbon Connectivity Pattern Determination and N.M.R. Spectral Analysis: Patchoulol

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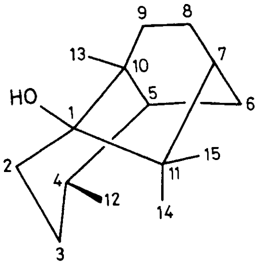
Summary Unambiguous ^{13}C n.m.r. spectral analysis has been accomplished and the carbon connectivity pattern established for patchoulol (**1**) by the determination of all one-bond carbon–carbon coupling constants at natural abundance.

THE potential of using one-bond carbon–carbon coupling constants for unequivocal spectral analysis of compounds of known constitution or for structural investigation of new substances has been recognized for a long time. However, ^{13}C–^{13}C couplings without enrichment have not been used for such purposes in natural product chemistry. We report here the carbon-13 n.m.r. spectral analysis of patchoulol (**1**)[1] (m.p. 55—56 °C), the most important odour component of the oil from *Pogostemon cablin*,[2] based only on the observed carbon–carbon couplings at natural abundance and on the unsymmetrical distribution of the satellite signals due to AX or AB systems. The study has been carried out without the help of any model compound.

The observation of carbon–carbon couplings requires the presence of two ^{13}C isotopes in the same molecule. At natural abundance there is approximately 1 such a molecule out of 10^4. In proton-decoupled ^{13}C n.m.r. spectra the resonances due to these species appear as weak doublet-type satellites superimposed on the signals of molecules containing only one ^{13}C isotope. As a consequence of the very low natural abundance of species with three ^{13}C spins in the same molecule the spectra of interest are always of the AX or AB type.

The proton-decoupled natural abundance ^{13}C Fourier transform (F.t.) n.m.r. spectrum of the chromatographically homogeneous (**1**) was recorded at 25·16 MHz with a Varian



(1)

XL-100-15 spectrometer equipped with a Varian 620/L-100 computer operated with the MOS-E disk system (no quadrature detection was applied). A 12 mm o.d. tube was used containing 3 g of (**1**) and 0·3 ml of C_6D_6, at a temperature of 60 °C. For the measurement of the ^{13}C—^{13}C couplings the spectrum was accumulated for 6 h. The number of data points was 32 K with a frequency range of 1600 Hz giving a digital resolution of 0·1 Hz/point. The sample tube was rotated slowly (10 Hz) in order to avoid interference of the satellites with spinning side bands whose intensity was comparable with that of the satellites. Resolution enhancement was applied using the Gaussian multiplication technique.[3] After this operation the width at 0·55% height of the strong central lines, due to molecules containing only one ^{13}C isotope, was only 4—5 Hz and 2 Hz for proton-bearing and quaternary carbon atoms respectively. In a preliminary experiment carbon-13 spin–lattice relaxation times were measured for (**1**). From the relatively long T_1 values (Table) the required very sharp resonances both for the central lines and for the satellites were predicted.

A simple analysis of the spectral data, fully supported by the computer program CABSA written recently for such investigations,[4] is given in the Table. Inspection of the results provides unequivocal proof for the carbon connectivity pattern, for the ^{13}C—^{13}C coupling constants, and for the signal assignments. Distinction between C-14 and C-15 is arbitrary. A precise spectral analysis based on chemical

TABLE

^{13}C N.m.r. spectral data for patchoulol (**1**) (25·16 MHz).

Carbon	δ[a]	T_1/s[b]	Line frequency /Hz[h]	Coupled with carbon	One-bond coupling constant /Hz	TOTAL /mm[c]	*L*/mm[d]	*H*/mm[e]	*r*[f]	*J*/Δ*f*
C-1	75·1	23·0	1890·55	C-2	38·2	191·0	97·2	93·8		
				C-10	35·4	177·0	90·2	86·8	1·0386	0·0379
				C-11	35·4	177·0	90·3	86·7	1·0414	0·0406
C-2	33·0	1·7	836·38	C-1	38·2	191·0	93·8	97·2	1·0369	0·0362
				C-3	32·5	162·5	93·8	68·7	1·3653	0·3164
C-3	29·0	1·7	733·67	C-2	32·5	162·5	68·7	93·8		
				C-4[g]	33·4	167·0	136·5	30·5		2·1287
C-4	28·4	3·1	717·98	C-3[g]	33·4	167·0	30·5	136.5		
				C-5	33·0	165·0	79·0	86·0		
				C-12	36·0	180·0	96·6	83·4		
C-5	44·0	3·3	1111·63	C-4	33·0	165·0	86·0	79·0	1·0873	0·0838
				C-6	32·6	163·0	84·2	78·8	1·0638	0·0670
				C-10	33·3	166·5	92·0	74·5	1·2354	0·2130
C-6	24·7	1·4	624·73	C-5	32·6	163·0	78·8	84·2		
				C-7	33·0	165·0	78·9	86·1		
C-7	39·6	2·9	999·07	C-6	33·0	165·0	86·1	78·9	1·0920	0·0882
				C-8	33·0	165·0	86·2	78·8	1·0937	0·0897
				C-11[g]	32·9	164·5	36·0	128·5		1·6458
C-8	24·9	1·7	631·16	C-7	33·0	165·0	78·8	86·2		
				C-9	31·8	159·0	67·8	91·2		
C-9	29·1	1·5	737·14	C-8	31·8	159·0	91·2	67·8	1·3441	0·3001
				C-10	33·8	169·0	78·0	91·0		
C-10	37·8	16·5	955·27	C-1	35·4	177·0	87·0	90·0		
				C-5	33·3	166·5	74·5	92·0		
				C-9	33·8	169·0	91·0	78·0	1·1669	0·1550
				C-13	38·8	194·0	101·4	92·6		
C-11	40·4	17·2	1019·06	C-1	35·4	177·0	86·7	90·3		
				C-7	32·9	164·5	128·5	36·0		
				C-14	36·5	182·5	96·3	86·2		
				C-15	36·5	182·5	95·4	87·1		
C-12	18·7	2·4	474.43	C-4	36·0	180·0	83·4	96·6	1·1587	0·1478
C-13	20·7	2·5	525·41	C-10	38·8	194·0	92·6	101·4	1·0943	0·0903
C-14	27·2	1·4	687·22	C-11	36·5	182·5	86·2	96·3	1·1160	0·1100
C-15	24·4	2·1	619·23	C-11	36·5	182·5	87·1	95·4	1·0955	0·0913

[a] In p.p.m. relative to $Me_4Si = 0$. [b] Spin–lattice relaxation time. [c] AB or AX splitting in the spectrum expanded on the scale (10 mm = 2 Hz). [d] Distance between centre and low-field satellite taking into account the isotope shift (10 mm = 2 Hz). [e] Distance between centre and high-field satellite taking into account the isotope shift (10 mm = 2 Hz). [f] *L*/*H* or *H*/*L*. The values of *r* and *J*/Δ*f* are shown only once for all coupling pairs at that nucleus where the values of *L* and *H* could be the more precisely determined from the expanded spectrum. However, *r* was recomputed at the other coupling nuclei as well when *L* and *H* differed from the corresponding values by more than 0·2 Hz. [g] The *J* values were calculated from AB rules[7] (see text). [h] The slight discrepancy between the δ values and the line frequency values (60°C) arises from temperature effects.

shift arguments was considered very difficult. With the method presented, resonance lines appearing very close to one another (0·2 p.p.m.) could be specifically assigned to carbon atoms. As a result of the relatively low magnetic field very strong AB effects were observed. The success of this spectral analysis is based on the unsymmetrical distribution of the satellites on each side of the strong central lines (Table), on the isotope shifts,[5] and on the size of the coupling constants.[6] In two cases (C-3/C-4 $J/\Delta f$ 2·1287 and C-7/C-11 $J/\Delta f$ 1·6458), only the intense inner satellites of the strong AB systems were detected, the very weak outer satellites being hidden in the spectral noise. For such situations the coupling constants were calculated from the inner satellites f_2 and f_3 using equation (1), which is derived from standard AB rules.[7]

$$2J = \Delta f^2/(f_2 - f_3) - (f_2 - f_3) \qquad (1)$$

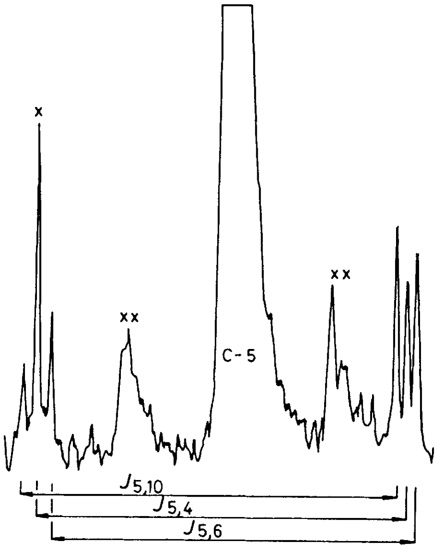


FIGURE 1. Spectral region of C-5 of patchoulol (**1**). The intense peak arises from the species of one carbon-13 isotope. The three AB quartets represent the rare species with two carbon-13 isotopes. C-5 couples only with higher-field signals. Under the satellite signal designated by x there is a peak due to an impurity. The broad signals shown by xx indicate spinning side bands. Very different isotope shifts were measured for the three linkages: C-5/C-4 (0 p.p.m.); C-5/C-6 (−0·032 p.p.m.), and C-5/C-10 (−0·008 p.p.m.).

Figure 1 shows the carbon signal representing C-5 with the corresponding satellites.

Carbon-13 n.m.r. spectral analysis of patchoulol (**1**) was also attempted from a spectrum obtained at 60 °C in C_6D_6 solution at 50·3 MHz with a Varian XL-200 spectrometer using Freeman's 'INADEQUATE' technique[8] (Figure 2). This enabled us to investigate carbon–carbon couplings by suppressing the strong signals from molecules with a single carbon-13 nucleus. Results obtained by this method were in agreement in all but the two strong coupling cases[9] with the data collected at 25·16 MHz. However, the spectral analysis proved to be easier at lower field in view of the much stronger AB effects and the narrower satellite line width. For complex substances the advantages of such investigations at two magnetic fields are considerable.

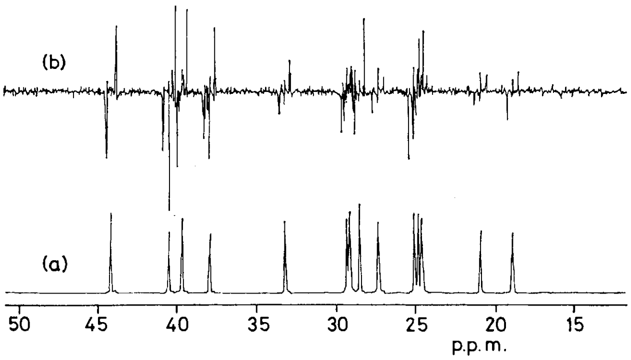


FIGURE 2. (a) The high-field part of the proton-decoupled ^{13}C n.m.r. spectrum of patchoulol (**1**) at 50·3 MHz and (b) the same spectrum obtained using Freeman's 'INADEQUATE technique (ref. 8).

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