Tetrahedron Letters,Vol.22,No.50,pp 5053-5056,1981 0040-4039/81/505053-04$02.00/
Printed in Great Britain

COMPUTER-ASSISTED DETERMINATION OF CARBON CONNECTIVITY PATTERNS BASED ON NATURAL ABUNDANCE ONE-BOND ^{13}C - ^{13}C COUPLING CONSTANTS : TERPENES

GABOR LUKACS*[1] and ANDRAS NESZMELYI*[2]

[1] Institut de Chimie des Substances Naturelles du CNRS, 91190, Gif-sur-Yvette, France and [2] The Central Research Institute for Chemistry of the Hungarian Academy of Sciences, Budapest, Pusztaszeri ut, Hungary.

Summary : With the help of the interactive computer program CABSA the carbon connectivity pattern of representative known terpenes was established by measuring the one-bond ^{13}C - ^{13}C coupling constants in the presence of the signals of molecules containing one ^{13}C isotope.

The determination of one-bond ^{13}C - ^{13}C coupling constants at natural abundance may be of considerable importance for spectral analysis of compounds of known constitution or for structural investigations on new substances. The observation of carbon-carbon couplings requires two ^{13}C isotopes in the same molecule. In proton decoupled ^{13}C nmr spectra the resonances due to these species (1 molecule out of 10^4) appear as weak doublet type satellites unsymmetrically situated on both sides of the strong signals of molecules containing only one ^{13}C isotope. The spectra of interest are always of the AX or AB type as a result of the very low natural abundance of species with three ^{13}C spins.

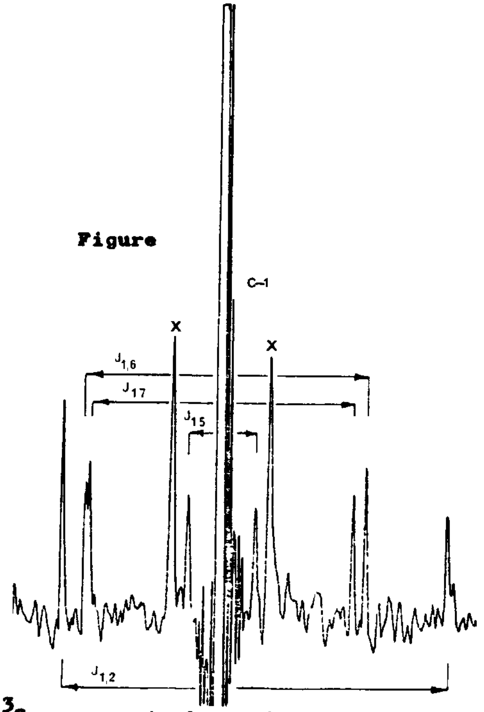
This paper describes the results of an investigation on the measurement without enrichment of the one-bond carbon-carbon coupling constants of representative abundant terpenes. The proton decoupled natural abundance ^{13}C FT nmr spectra of the following four chromatographically homogeneous compounds were recorded at 25.16 MHz : the monoterpenes Carvone (1) and Limonene (2), the sesquiterpene Nootkatone (3) (mp. 37°C) and the diterpene Mannool (4) (mp. 56°C). A Varian XL-100-15 spectrometer equipped with a Varian 620/L-100 computer operated with the MOS-E disk system was used. The spectra were recorded at a temperature of 60°C in 12 mm o.d. tubes containing 2.5 g samples and 0.4 ml C_6D_6. For the measurement of the ^{13}C - ^{13}C couplings the spectra were accumulated for 8 hours. After resolution enhancement with the gaussian multiplication technique[1] 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 carbons respectively. In preliminary experiments carbon-13 spin-lattice relaxation times were measured. On the basis of the relatively long T_1 values (typical NT_1 values of proton bearing ring carbons of the terpenes : 2 sec.) the required very sharp signals for the detection of the ^{13}C - ^{13}C couplings were predicted. On the Figure the spectral section of C-1 of Carvone (1) is represented.

CABSA[2], (Connectivity by AB Satellite Analysis), a recently developed computer program for the determination of matching satellite pairs, affords unambiguous proof for the carbon connectivity pattern, for the carbon signal assignments and for the ^{13}C - ^{13}C coupling constants (Tables). As the experiments were carried out at a relatively low magnetic field strong AB effects were observed in the spectra studied. In three cases [(1) C-4/C-5 J/Δf 2.8075 ; (3) C-8/C-9 J/Δf 1.3827 and (4) C-10/C-1 J/Δf 1.8062] , only the intense inner satellites of the strong AB systems were detected, the very weak outer satellites were hidden in the spectral noise. However, the ^{13}C - ^{13}C coupling constants could be calculated from the inner satellites f_2 and f_3 using the following formula derived from AB rules[3] :

$$J = \frac{1}{2}\left[\frac{\Delta f^2}{f_2 - f_3} - (f_2 - f_3)\right]$$

A considerable advantage of this method of nmr spectral analysis, based on the measurement of one-bond carbon-carbon coupling constants, over other techniques is that carbon signals of the same off-resonance multiplicity can be specifically attributed even though they appear very close to one another.

Figure



^{13}C nmr spectral section of C-1 of (1) The intense peak arises from the species of one carbon-13 isotope.The four AB doublets represent molecules with two ^{13}C isotopes.x designates spinning side bands.

On the basis of an early ^{13}C nmr spectral analysis of limonene (2) the signals at 31.3 and 31.0 ppm were assigned respectively to C-3 and C-6[4]. From the determination of the one-bond ^{13}C - ^{13}C coupling constants and the corresponding satellite distributions the reverse assignment proved to be correct[5]. With respect to C-3 and C-6, the C-4 signal comes at about 10.5 ppm lower field while C-5 appears at higher field by 2.6 or 2.9 ppm. As a consequence, C-6 should be the signal which exhibits a strong AB system, having its outer satellite downfield while C-3 should show a much weaker AB pattern, having its outer satellite upfield as indicated in the detailed ^{13}C nmr spectral data of Table 1.

Inspection of the Tables reveals remarkable differences in the coupling constants between the corresponding bonds of (1), (2) and (3) where sp^2 hybridized sites are involved. These differences reflect conjugation and substitution effects. In the α,β-unsaturated carbonyl system of (1) and (3) large two-bond couplings through the ketone could be also measured (Figure). It is also of interest to note that in the case of mannool (4) the coupling constants

TABLE 1

Detailed ^{13}C NMR spectral data for Limonene (2) (25.16 MHz)

Carbon	Chemical Shift (ppm) (TMS=0) 25°C	Line Frequency (Hz) 60°C	Coupled with carbon	One-bond coupling constant (Hz)	Total[a] (mm)	L[b] (mm)	H[b] (mm)	r[c]	J/Δf
C-1	133 3	3344.67	C-2	72.9	364 5	203.8	160.7		
			C-6	39.6	198.0	99.8	98.2		
			C-7	43 8	219.0	110.4	108.6		
C-2	121.2	3040 48	C-1	72 9	364.5	160 7	203.8	1.2680	0 2397
			C-3	40.9	204.5	103 2	101.3	1.0180	0.0181
C-3	31.0	778.17	C-2	40 9	204 5	101.3	103.2		
			C-4	33.3	166.5	78.0	88.5	1.1370	0.1288
C-4	41.6	1036.70	C-3	33 3	166.5	88.5	78.0		
			C-5	33.0	165 0	86.5	78.5		
			C-8	42 2	211 0	104.7	106.3	1.0156	0.0155
C-5	28.4	705.43	C-4	33.0	165.0	78.5	86.5	1.1050	0.0996
			C-6	33.9	169 5	64.0	105.0		
C-6	31.3	771.00	C-1	39.6	198.0	98 2	99.8	1 0160	0.0154
			C-5	33.8	169 0	105.0	64 0	1.6405	0.5155
C-7	23.6	584.56	C-1	43.8	219.0	108 6	110.4	1.0160	0.0159
C-8	149.6	3756.72	C-4	42.2	211.0	106 3	104.7		
			C-9	72.5	362.5	187.6	171.9		
			C-10	41.9	209.5	105.4	104.1		
C-9	108.9	2730.60	C-8	72.5	362.5	171.9	187.6	1.0730	0.0707
C-10	20.8	516.00	C-8	41.9	209 5	104.1	105.4	1.0130	0.0129

a. AB or AX splitting in the spectrum (scale 10 mm=2Hz) , b. Distance between center and low or high field satellite taking into account the isotope shift[7] ; c. L/H or H/L The values of r and J/Δf 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.

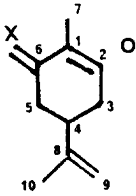
TABLE 2

^{13}C NMR spectral data for terpenes (25.16 MHz)

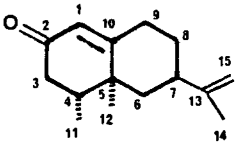
Carbon	Chemical Shift (ppm) TMS=0	Coupled with carbon	coupling constant (Hz)	J/Δf
		Carvone (1)[4]		
C-1	135.4	C-2	66.8	0.3151
		C-6	48 7	0.0311
		C-7	45.8	0.0152
		C-5	11.7	0.0051
C-2	143.3	C-3	39.3	0.0139
C-3	31.4	C-4	33 0	0.1154
C-4	42.8	C-5[b]	33.1	2.8075
C-5	43.3			
C-6	197.3	C-5	40.0	0.0103
C-7	15.7			
C-8	147 1	C-4	42.2	0.0161
C-9	110.4	C-8	72.8	0.0786
C-10	20 4	C-8	42 2	0.0132
		Nootkatone (3)[a]		
C-1	124.9	C-10	64.7	0.0594
		C-3	11.9	0.0057
C-2	196 9	C-1	51 7	0.0286
C-3	42.2	C-2	39.7	0.0102
		C-4	32.0	0.6863
C-4	40.4	C-5	32.0	1.1408
C-5	39.3	C-10	37.6	0.0116
C-6	44.2	C-5	33.8	0.2733
		C-7	33.1	0.3696
C-7	40.6			
C-8	31.9	C-7	33.2	0.1515
		C-9[b]	32.7	1.3827
C-9	32.9			
C-10	168.2	C-9	39.0	0.0114
C-11	14.8	C-4	36.0	0.0560
C-12	16.7	C-5	34.4	0.0605
C-13	149.0	C-7	42 0	0.0154
		C-14	42.0	0.0130
C-14	20.8			
C-15	109.2	C-13	72.4	0.0724

Carbon	Chemical Shift (ppm) TMS=0	Coupled with carbon	One-bond coupling constant (Hz)	J/Δf
		Mannool (4)[6]		
C-1	39.1			
C-2	19.5	C-1	33.8	0 0683
		C-3	33.2	0.0575
C-3	42 4			
C-4	33.5	C-3	34 3	0.1522
		C-5	34.5	0.0614
		C-18	not measurable	
C-5	55.8	C-6	34.4	0.0438
		C-10	33 2	0.0830
C-6	24.5	C-7	32.2	0.0920
C-7	38.5			
C-8	148.1	C-7	39.6	0.0143
		C-9	39.6	0.0174
C-9	57.6	C-10	31 8	0.0715
		C-11	37.3	0.0373
C-10	39.9	C-1[b]	34.3	1.8062
C-11	17.8	C-12	36.2	0.0602
C-12	41.8			
C-13	73.1	C-12	38.0	0.0482
		C-17	39.5	0.0348
C-14	145.6	C-13	46.4	0.0254
C-15	111.3	C-14	70.4	0.0812
C-16	106.7	C-8	72.8	0.0696
C-17	28 0			
C-18	33.7			
C-19	21.8	C-4	35.4	0.1204
C-20	14.5	C-10	36.2	0.0567

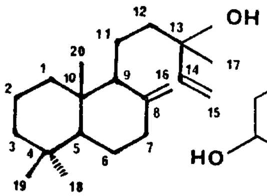
a. An analysis of the ^{13}C nmr spectrum of (3) has not been previously published ; b. These ^{1}J values were calculated from f_2 and f_3 using AB rules[3]. The one-bond coupling constants are shown only once for all coupling pairs at that nucleus where the ^{1}J values could be the more precisely determined from the expanded spectra. The spectral data are presented in a simplified form because of lack of space. The principle of our technique is shown in Table 1.



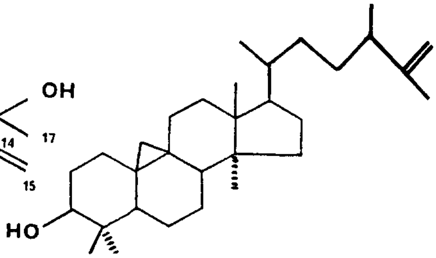
(1) X = O
(2) X = H_2



(3)



(4)



(5)

$J_{9,11}$ and $J_{11,12}$ are larger than those corresponding to other linkages within the cyclohexane rings and formed by sp^3 hybridized carbons.

The determination of the one-bond ^{13}C - ^{13}C coupling constants of the much more complex triterpene cyclolaudenol (5) (mp. 124°C) was also attempted. In view of the large molecular size of this substance, ^{13}C spin-lattice relaxation times for the proton bearing carbons of its backbone were too short at 60°C to insure the required very narrow lines and extremely high signal to noise ratio. The average NT_1 values of the mentioned carbons could be increased to about 1 sec. by preparing a saturated solution of (5) in p.xylene-d_{10} and measuring the spectrum at 110°C. However, in spite of these practically optimal experimental conditions only a few coupling constants could be determined for this highly complex molecule since many satellites were hidden by the strong closely spaced signals of species containing only one ^{13}C isotope. Results on the measurement of the ^{13}C - ^{13}C coupling constants for (5) and for more complex substances with Freeman's "INADEQUATE" technique[8], involving the elimination of the signals due to species with one ^{13}C isotope, will be reported later.

It is obvious that the determination of one-bond ^{13}C - ^{13}C coupling constants will be extremely useful to establish the carbon connectivity pattern of new medium molecular weight abundant materials.

The authors thank Dr. A.F. Thomas, Firmenich, Geneva, for the terpene samples used in this investigation and Miss A. Kmèty for help in writing the program.

REFERENCES

1. A.G. Ferrige and J.C. Lindon, J. Magn. Res., 1978, 31, 337.
2. CABSA (available upon request) has been written in Fortran and implemented to the Varian MOS-E disk system. A. Neszmelyi and G. Lukacs, unpublished results.
3. R.J. Abraham, The Analysis of High Resolution NMR Spectra, Elsevier, 1971.
4. M. Jautelat, J.B. Grutzner and J.D. Roberts, Proc. Nat. Acad. Sci. U.S., 1970, 65, 288.
5. The Varian research group at Zug has reached similar conclusions, W. Ammann, R. Richarz and T. Wirthlin, personal communication.
6. B.L. Buckwalter, I.R. Burfitt, A.A. Nagel, E. Wenkert and F. Näf, Helv. Chim. Acta, 1975, 58, 1567.
7. F.J. Weigert and J.D. Roberts, J. Amer. Chem. Soc., 1972, 94, 6021.
8. A. Bax, R. Freeman and S.P. Kempsell, J. Amer. Chem. Soc., 1980, 102, 4849.

(Received in France 31 August 1981)