Carbon-13 Nuclear Magnetic Resonance Spectroscopy of Naturally Occurring Substances. I. A Direct Analysis of Nonprotonated Carbon Centers

Sir:

Progress in structure elucidation and synthesis of organic substances usually has accompanied advances in organic functional group analysis. We herewith wish to describe a method of direct analysis of the least functionalized site, the quaternary carbon center, and other nonprotonated carbon positions of complex organic compounds based on natural-abundance ^{13}C high-resolution nuclear magnetic resonance spectroscopy using a noise off-resonance decoupling technique.[1,2] It has enabled us to determine the number of quaternary carbon units in a hydrocarbon framework, tertiary carbinols in polyfunctional systems, and disubstituted olefinic centers in a polyunsaturated material.[3]

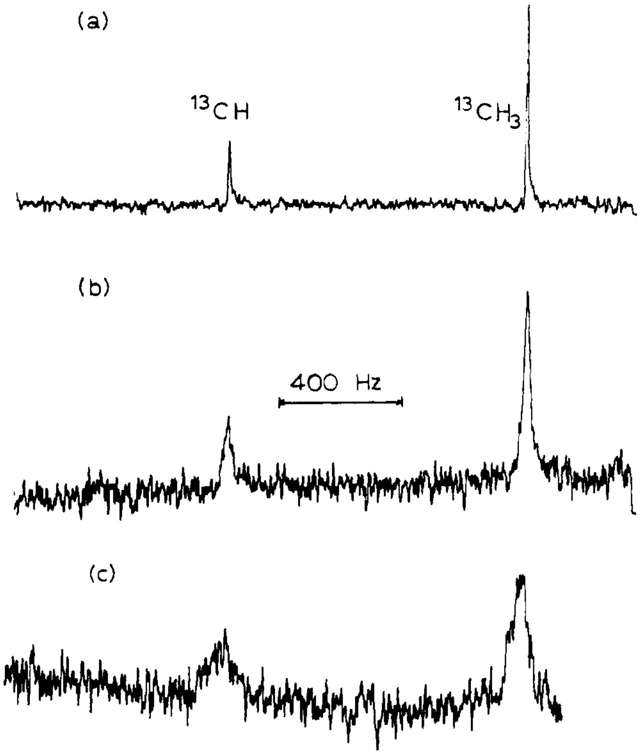

Figure 1. Carbon-13 nmr spectra (15.074 MHz) of liquid $HC(OCH_3)_3$ under conditions of noise decoupling holding the noise-modulated side band at (a) 59.950687 MHz (9 scans), (b) 59.950267 MHz (17 scans), and (c) 59.949876 MHz (35 scans). The noise band width in each case was 300 Hz.

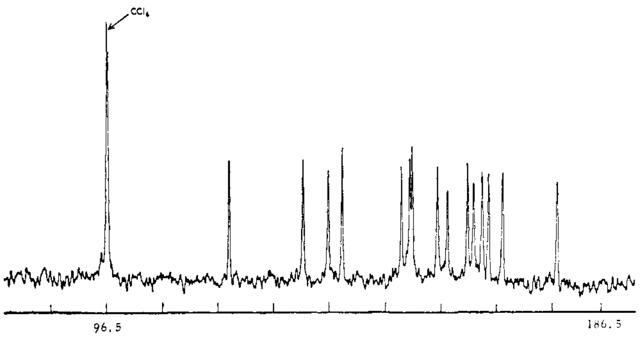

Figure 2. Carbon-13 nmr spectrum (15.074 MHz) of a carbon tetrachloride solution of cedrol (**2**) under noise resonance decoupling conditions after 65 scans; parts per million from CS_2.

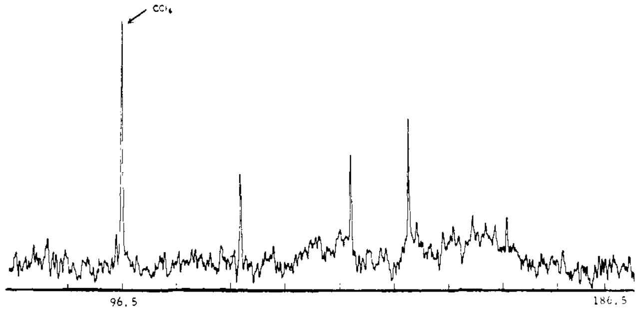

Figure 3. Carbon-13 nmr spectrum (15.074 MHz) of the solution used in Figure 2 under noise off-resonance decoupling conditions after 32 scans; in parts per million from CS_2. The noise-modulated side band was set *ca.* 800 Hz upfield that of Figure 2.

The technique of noise resonance decoupling, *i.e.*, double resonance with an incoherent radiofrequency field, has been demonstrated to produce simplified ^{13}C nmr spectra revealing only singlets for all carbon units.[4–6] Since residual broadening of the signals is related intimately to the coupling constants, inefficient decoupling, *e.g.*, by application of an oscillating random radiofrequency field of low amplitude or by a shift of the band of decoupling frequencies off the proton resonances, would be expected to affect the signal band widths.[7] In view of the large one-bond $^{13}C-^{1}H$ J values (≥ 120 Hz),[8] protonated carbon centers should respond most strongly. This is exemplified in Figure 1 by the spectra of trimethyl orthoformate decoupled at (a) the center of the proton resonances (the noise resonance decoupling method), (b) *ca.* 400 Hz upfield, and (c) *ca.* 800 Hz upfield (the noise off-resonance decoupling method). Hence the off-resonance procedure should distinguish nonprotonated centers from their protonated neighbors, since the small long-range coupling constants of the former permit effective decoupling of their signals even at off-resonance positions, *cf.* the noise resonance and off-resonance decoupling spectra of cedrol (**2**) (Figures 2 and 3, respectively).[9]

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[1] R. R. Ernst, *J. Chem. Phys.*, **45**, 3845 (1966).

[2] Single-frequency off-resonance proton decoupling of ^{13}C nmr spectra, an alternate method of identification of quaternary carbon sites as well as a procedure for the differentiation of variously substituted carbon centers, has been used extensively for the analysis of a variety of natural products (L. F. Johnson, private communication), steroids, monosaccharides, inositols, and terpenes (J. D. Roberts, private communication), and camphor and related substances (E. Wenkert, A. O. Clouse, D. W. Cochran, and D. Doddrell, manuscript in preparation; P. V. Demarco, D. Doddrell, and E. Wenkert, *Chem. Commun.*, in press).

[3] The method can be applied to many other problems, *e.g.*, the determination of tertiary alcohols and tertiary mercaptans and their derivatives, the substitution pattern of aromatic nuclei, and the distinction, *inter alia*, between aldehydes and ketones, acetals and ketals, and mono- and disubstituted acetylenes, although in many instances such differentiation can be achieved from ^{13}C chemical shift data alone. Unfortunately the chlorine and nitrogen quadrupoles make the method too insensitive for the determination of tertiary chlorides and tertiary carbinylamines.

[4] F. J. Weigert, M. Jautelat, and J. D. Roberts, *Proc. Natl. Acad. Sci. U. S.*, 60, 1152 (1968).

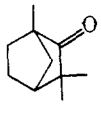
[5] L. D. Hall and L. F. Johnson, *Chem. Commun.*, 509 (1969).

[6] K. Grohmann, J. B. Grutzner, and J. D. Roberts, *Tetrahedron Letters*, 917 (1969).

[7] The residual broadening (b_r, measured in Hz)[1] for almost complete decoupling of albeit an AX spin system at the center of the X resonance is given by $b_r = (2\Delta\omega J_{AX}{}^2)/(\gamma^x H_2)^2$, $2\Delta\omega$ being the noise band width and H_2 the peak amplitude of the oscillating random radiofrequency field.

[8] J. W. Emsley, J. Feeney, and L. H. Sutcliffe, "High Resolution Nuclear Magnetic Resonance Spectroscopy," Vol. 2, Pergamon Press, New York, N. Y., 1966, p 988.

The power of the new method of analysis is illustrated best by the following chemical shift data (ppm) of nonprotonated sites of eight structurally diverse terpenic compounds;[10] quaternary carbons: fenchone (**1**), 138.7, 145.3; cedrol (**2**), 138.1, 148.5; totarol acetate (**3**), 154.5, 159.1; manool (**4a**), 152.5, 158.7; sclareol (**4b**), 153.4, 159.2; retinyl (vitamin A) palmitate (**5**), 158.4; cholesterol (**6**), 150.0, 155.9; friedelin (**7**) (in chloroform), 153.6, 155.9, 157.2, 158.1, 165.3, 167.4; tertiary carbinols: **2**, 118.0; **4a**, 119.3; **4b**, 118.3 (C-8), 119.4 (C-13); disubstituted methylidene moieties: **4a**, 45.2 (C-8); **5**, 54.8, 54.8, 57.1, 64.1.



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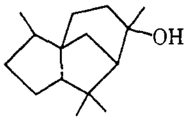

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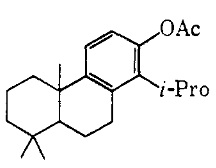

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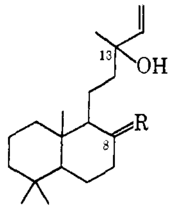
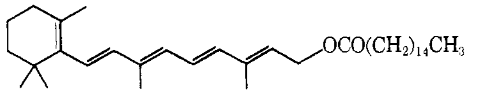


4a, R = CH$_2$
b, R = CH$_3$, OH



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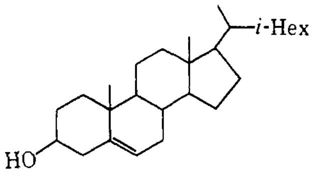

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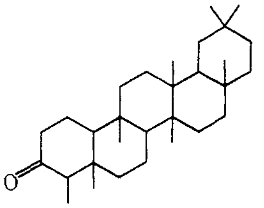

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[9] Natural-abundance ^{13}C nmr spectra were determined by the procedure described by A. O. Clouse, D. Doddrell, S. B. Kahl, and L. J. Todd, *Chem. Commun.*, 729 (1969), at 15.074 MHz. Noise decoupling followed the method of Ernst.[1]

[10] The noise resonance and off-resonance decoupling spectra of carbon tetrachloride solutions showed identical band widths of *ca.* 3 Hz at half-height. Less than 250 scans on a Varian C-1024 time-averaging computer were required. Chemical shifts in ppm, accurate to ±0.4 ppm, are cited relative to carbon disulfide ($\delta_{CS_2} = \delta_{CCl_4} + 96.5 = \delta_{CHCl_3} + 115.2$).

[11] Public Health Service Predoctoral Fellow, 1967–present.

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Flash Vacuum Pyrolysis. VI. Cyclobutadieneiron Tricarbonyl[1]

Sir:

The discovery of stable cyclobutadiene transition metal complexes[2] has naturally led to attempts to generate and characterize the free organic ligand. For example, Pettit and coworkers[3a,b] have concluded that free cyclobutadiene (**1**) is generated by the oxidation of cyclobutadieneiron tricarbonyl (**2**) on the basis of its dimerization and reactions with dienophiles. They also reported results suggesting that **1** had a finite lifetime in the gas phase and in the condensed phase at −196°. Flash photolysis of **2** generates transients having *m/e* 52 and 104 and lifetimes of 1–2 and 20 msec, respectively, at 0.010–0.250 Torr.[3c] More recently, the pyrolysis of **2** has been reported[4] to give **1** "as a stable compound" which could be distilled from a cold surface at −105° into a mass spectrometer.

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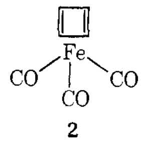

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Here we report on our investigation of the flash vacuum pyrolysis (FVP) of **2**. On the basis of these results and those recently reported on the FVP of photo-α-pyrone,[1] we conclude that the only detectable C$_4$H$_4$ thermal product from **2** is vinylacetylene. Moreover, we believe that the data of Li and McGee[4a,b] are more consistent with a similar assignment.

2 was first pyrolyzed at low pressures ($\sim$1 μ) and short contact times ($\sim$1 msec) in a tubular oven coupled to the ionization chamber of a mass spectrometer.[5] Significant decomposition occurred at about 450° giving major thermal fragments at *m/e* 52, 28, and 26, moderately intense signals at *m/e* 54 (C$_4$H$_6$) and 78 (C$_6$H$_6$), and minor signals at *m/e* 104 (C$_8$H$_8$) and 80 (C$_6$H$_8$). The thermal fragments maximized at temperatures between 560 and 700° except for that having *m/e* 26 which maximized at about 1000°: AP[6] (*m/e*, oven temperature); 9.8 eV (52, 700°), 11.5 eV (26, 900°), 9.4 eV (54, 700°), 9.7 eV (78, 560°), 8.6 eV (104, 560°). These appearance potentials can be compared with the independently determined ionization potentials for vinylacetylene (9.9 eV), acetylene (11.4 eV),[7] butadiene (9.2 eV),[7] benzene (9.7 eV), and cyclooctatetraene (8.4 eV). Radical titration experiments with methyl radicals generated by copyrolysis of ethyl nitrite led only to minor signals at *m/e* 67 and 68 and no new signals at *m/e* 66 and 82.

The thermal products were ultimately identified by the FVP of **2** at 560° and *ca.* 50 μ in the apparatus previously described,[8] where the pyrolysate was rapidly quenched on the surface of a large liquid nitrogen dewar closely coupled to the tubular oven. The products were isolated by distillation into a small vacuum manifold

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[1] Part V: E. Hedaya, R. D. Miller, D. W. McNeil, P. F. D'Angelo, and P. Schissel, *J. Amer. Chem. Soc.*, **91**, 1875 (1969).

[2] For a review see: M. P. Cava and M. J. Mitchell, "Cyclobutadiene and Related Compounds," Academic Press, New York, N. Y., 1967.

[3] (a) L. Watts, J. D. Fitzpatrick, and R. Pettit, *J. Amer. Chem. Soc.*, **87**, 3253 (1965); (b) R. Pettit, *Pure Appl. Chem.*, **17**, 253 (1969); (c) W. J. R. Tyerman, M. Kato, P. Kebarle, S. Masamune, O. P. Strausz, and H. E. Gunning, *Chem. Commun.*, 497 (1967).

[4] (a) H. A. McGee, Jr., Abstracts, 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1969, PHYS-061; (b) P. H. Li and H. A. McGee, Jr., *Chem. Commun.*, 592 (1969); (c) *Chem. Eng. News*, 47, 51 (April 21, 1969).

[5] P. Schissel, D. J. McAdoo, E. Hedaya, and D. W. McNeil, *J. Chem. Phys.*, **49**, 5061 (1968).

[6] AP, appearance potential; IP, ionization potential.

[7] F. H. Field and J. L. Franklin, "Electron Impact Phenomena," Academic Press, New York, N. Y., 1957.

[8] E. Hedaya and D. W. McNeil, *J. Amer. Chem. Soc.*, **89**, 4213 (1967).