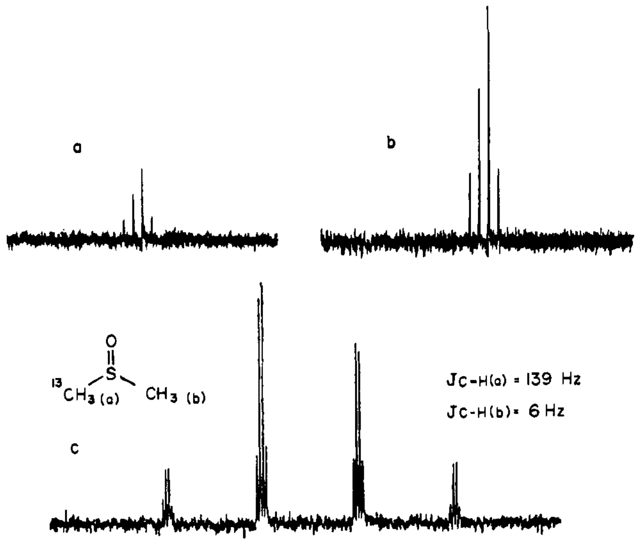

Figure 2. Carbon-13 nmr spectra of dimethyl sulfoxide: (a) no proton irradiation; (b) the apnmr (see text) spectrum; (c) a high-resolution expansion of the apnmr (see text) spectrum.

performed a Fourier transform of the fid to obtain cmr spectra (Figure 2) of a 90% dimethyl sulfoxide–10% hexafluorobenzene solution. With the decoupler power off entirely, Figure 2a was obtained. Alternate power pulsing using the same number of pulse cycles resulted in Figure 2b. The high-resolution spectrum recorded in Figure 2c is an expansion of Figure 2b and demonstrates that even long-range ^{13}C–H coupling returns immediately after decoupling is terminated. *True values of* $J_{^{13}C-H}$ *are obtained.* Off-resonance and single-resonance decoupling frequently distort line shapes and coupling constant values.

A simple application of apnmr resonance to signal assignment can be illustrated by considering the cmr spectra of 2-butanol (not shown). Proton-decoupled, four-resonance signals are observed at −10.4, −23.1, −32.6, and −69.4 ppm *vs.* TMS. The apnmr spectrum shows two quartets (J = 122, 125 Hz), one triplet (J = 120 Hz), and one doublet (J = 134 Hz) allowing immediate assignment of all cmr signals as methyl, methylene, or methine carbons, with, as an additional bonus, the Overhauser enhancement reducing by a factor of 7–9 the time needed to obtain the spectrum. A long-range doublet coupling (not accurately measured) further assigns the resonance at −23.1 ppm to the 1-CH_3 carbon illustrating that in apnmr all spin–spin couplings are available for use to assign signals. The other methyl resonance is a complex multiplet. The several superior features of apnmr lead us to believe it will supersede off resonance methods, especially since instrument modifications required are minimal. When, in addition, lanthanide shift reagents are employed, unequivocal assignment of even ambiguous cmr spectra is simple.[4]

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Carbon Magnetic Resonance. Signal Assignment by Alternately Pulsed Nuclear Magnetic Resonance and Lanthanide-Induced Chemical Shifts

Sir:

Assignment of carbon magnetic resonance (cmr) signals has relied on a variety of complex methods such as nuclear off-resonance irradiation, selective proton decoupling,[1] or deuteration studies. Carbon spectra obtained with the newly developed alternately pulsed nmr (apnmr) experiment[2] together with proton-decoupled spectra determined in the presence of lanthanide shift (lis) reagents,[3] in this case tris(dipivaloylmethanato)europium(III) [Eu(DPM)$_3$], illustrate a convenient, rapid, and unambiguous method of assigning ^{13}C resonances. We demonstrate an application of these two complementary tools by the complete and unequivocal identification of all ^{13}C signals of isoborneol.

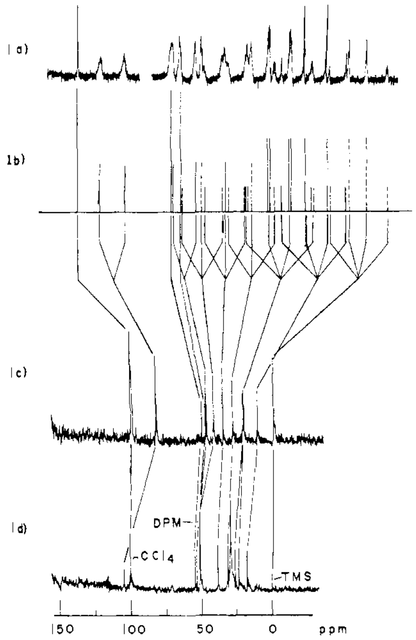

Figure 1. Carbon magnetic resonance spectra of isoborneol: (a) the alternately pulsed nmr spectrum (scale expanded); (b) a histogram of the apnmr spectrum, some lines dashed for clarity; (c) the cmr spectrum of 1.0 M isoborneol; (d) a lanthanide-shifted cmr spectrum of isoborneol (1.0 M + 523 mg of Eu(DPM)$_3$).

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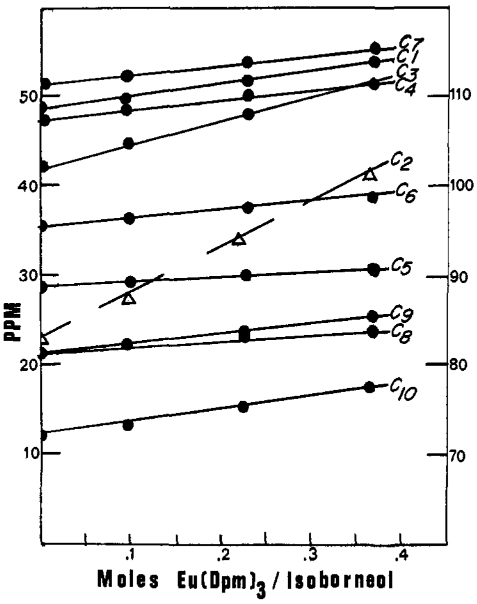


Figure 2. A plot of cmr chemical shifts of 1.0 *M* isoborneol at several concentrations of added Eu(DPM)$_3$: ●, refer to 0–60-ppm scale; △, refer to 60–120-ppm scale.

The ^{13}C apnmr spectrum of isoborneol (Figure 1a) was obtained by a method previously described[2] using a Bruker HFX-10 nmr spectrometer with ^{19}F stabilization, ^{1}H decoupling, and ^{13}C observation frequencies of 84, 90, and 22.6 MHz, respectively. On inspection, the spectrum appears as numerous envelopes of overlapping lines some of which may be immediately identified with the tetramethylsilane (TMS) quartet and, from isoborneol, one well-defined and two superimposed quartets (J = 126 Hz), three methylene triplets (J = 136 Hz), two methine doublets (J = 150 Hz), and two broad signals attributed to the quaternary carbons. Figure 1b is a histogram of the apnmr spectrum. The precise cmr shifts measured for all ten atoms obtained from the entirely proton-decoupled spectrum (Figure 1c) are recorded in Table I. Shift assignments agree with those proposed independently by Lippma, *et al.*, and Schneider and Bremser, except for interchanging C-1 and -7. One of these studies[4a] was performed in CS$_2$ solvent, while the other[4b] referenced signals to CS$_2$ but did not specify the solvent. Small shift differences from our data, likely due to solvent choice, are noted.

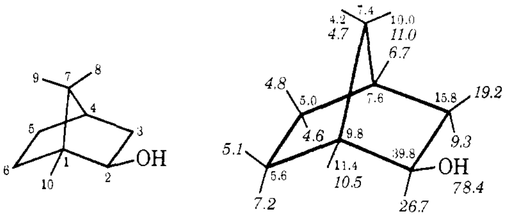
Table I. ^{13}C Chemical Shifts for Isoborneol (1 *M* in CCl$_4$)[a]

C-1	48.5	C-6	35.6
C-2	83.0	C-7	51.2
C-3	42.4	C-8	21.1
C-4	47.4	C-9	21.5
C-5	28.8	C-10	11.9

[a] All shifts downfield from TMS.

It is noteworthy that only a few features of the apnmr spectrum are completely interpretable. The upfield isoborneol methyl group exhibits a single small coupling (J = 3 Hz) in each branch of the quartet, while the other two methyl resonances overlap and contain several long-range coupling constants. We suggest that the upfield methyl signal derives from C-10 and that the observed small coupling arises from a specific interaction[5] with H-4. Explicit assignment of the two remaining signals in the apnmr spectrum is virtually impossible due to the near coincidence of shift values. Identification of the two C–H doublets with C-2 (low field) and C-4 (high field) is obvious from chemical shifts[4] and the magnitude of the ^{13}C–H couplings. The three methylene triplets may be located, but can be specifically assigned only by utilization of elaborate correlation charts constructed from chemical shifts of numerous model compounds.[4] Chemical shifts of the quaternary carbons are equally uncertain.

A proton decoupled ^{13}C spectrum of isoborneol (1 *M* in CCl$_4$, Figure 1c) is dispersed in the presence of Eu(DPM)$_3$ (0.34 *M* in CCl$_4$, Figure 1d). Both carbon and proton downfield pseudocontact shifts from diamagnetic resonance positions measured for a solution with a 1:1 europium–substrate mole ratio are summarized in structure **1**. Proton resonances taken from the literature and/or determined here are italicized.[3b] The graph from which the ^{13}C shifts were determined is presented in Figure 2, while the ^{1}H shifts were measured in a separate experiment. When the europium atom is bonded to isoborneol at a C–O–Eu angle of ~120°, overlaying the C(2)–C(3) bond, and having an O–Eu bond distance of 3.0 Å, proton pseudocontact shifts are nearly proportional to $1/r^3$, where r = Eu–H distance. If corrections for the 3 cos^2 θ − 1 term (θ = O–Eu–H angle) are performed, agreement between observed and calculated shifts is good.[6,7] Furthermore, the spectra resolve ambiguities in the apnmr spectrum. The methyl carbon which exhibits the least lis (4.2 ppm) is revealed as 9-CH$_3$. For the two strongly perturbed methyl signals (10.5 and 11.0 ppm) one was assigned above to C-10, so C-8 remains, accounting for all methyl resonances. The 3-CH$_2$ group shifts 15.8 ppm and is conspicuous. The two other CH$_2$ groups and the two quaternary carbons may be assigned from predicted *vs.* observed values for pseudocontact interactions.[7] Our quaternary carbon assignments differ from those previously made[4] based only on correlation charts. The proximity of C-1 *vs.* C-7 to the alcohol functional group requires that it experience the greater lis, demonstrating the utility of shift reagents in cmr.



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[5] For bicycloheptanes, proton–proton couplings of 1–2 Hz are observed between protons bonded to the two bridgeheads. We anticipate the corresponding ^{13}C–H coupling would be larger. M. Barfield and B. Chakrabarti, *Chem. Rev.*, **69**, 757 (1969).

[6] The location by computation of praseodymium in the borneol molecule has been successful: J. Briggs, F. A. Hart, and G. P. Moss, *Chem. Commun.*, 1506 (1970).

[7] In some preliminary computations, we are able to duplicate cmr data within 10%. This fit assures that even ambiguous cmr resonances (C-1, -7, -8, -10) are correctly assigned: R. E. Davis, private communication.

Comparison of the proton and carbon lanthanide-induced shifts for isoborneol is most informative. A reasonable chemical-shift correspondence between nuclei in similar geometric positions relative to europium evidences that the lis experiment is dominated by a pseudocontact phenomenon governed by an equation of the form[8,9]

$$A = a + \frac{3\cos^2\theta - 1}{3r^3}(g_{\parallel} - g_{\perp})\beta g_N\beta_N \qquad (1)$$

where A is the observed contact shift. When scalar coupling a is small, A is directly proportional to the gyromagnetic ratios of interacting nuclei and is usually referred to as the pseudocontact shift. If A is expressed in field-independent units (parts per million) and if axial symmetry about europium is maintained, then values for all nuclei are predicted and observed to be proportional to $\langle 1/r^3 \rangle$. Deviations between ^{13}C and ^1H shifts in isoborneol would arise from small differences in position relative to europium. This demonstrated effect should be quite general for all similar multinuclear nmr experiments.[8]

In summary, apnmr supplies ^{13}C spectra with improved sensitivity, while retaining and measuring *all, true* ^{13}C–H coupling constants and directly identifying methyl, methylene, methine, or quaternary carbons. Lis methods apply to cmr and provide spectra which, when compared with proton lis spectra, can facilitate assignment of ^{13}C resonances. In particular, the two nearly equivalent geminal methyl signals and the quaternary carbons of isoborneol were assigned. We further note that selective decoupling of dispersed proton resonances while observing the ^{13}C lis spectrum simplifies measurement of ^{13}C–H coupling constants. The apnmr–lis methods in conjunction are new and most powerful tools for structure determination.

Acknowledgment. The authors acknowledge research support from the Robert A. Welch Foundation.

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(8) Implicit in this statement is that the McConnell relationship (eq 1) holds. Herein, we suggest only that its validity is sufficient to permit use of lis reagents in cmr.

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Rate Processes and Carbon-13 Magnetic Resonance Spectra. Hindered Internal Rotation of *N*,*N*-Dimethyltrichloroacetamide

Sir:

Carbon-13 magnetic resonance (cmr) is a well-established method for determination of molecular structure in solution.[1] However, no studies have as yet been performed to investigate the utility of cmr techniques for study of rates of fast chemical exchange processes although such applications of proton magnetic resonance (pmr) are common.[2] Perhaps the most often and accurately studied exchange reaction is hindered internal rotation about carbon–nitrogen bonds in substituted acid amides.[3] One particular molecule, *N*,*N*-dimethyltrichloroacetamide, has proven most amenable to pmr studies. The presence of only protons participating in chemical exchange allows use of spin-echo as well as high-resolution nmr to determine the energy barrier to internal rotation.[4] This, together with the presence of two carbon atoms exchanging between two chemically different sites, let us initiate this, the first reported cmr study of a kinetic process. We wish to demonstrate that cmr methods are at least as useful as pmr techniques in that nmr signal-shape analysis following the Gutowsky–Holm formulation[5] provides rate constants and activation energies at least as accurately as pmr studies and that, in many cases, cmr studies will prove more accurate than pmr studies.

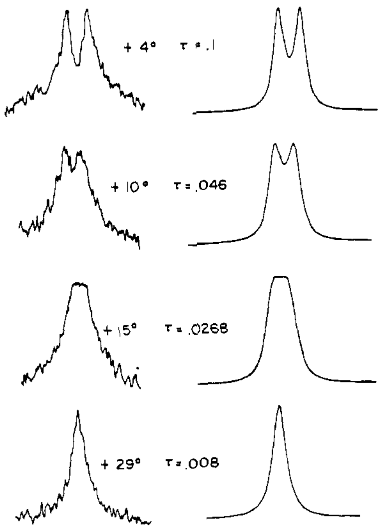

Figure 1. Actual and computer-simulated carbon-13 nmr spectra of the methyl reasonances of *N*,*N*-dimethyltrichloroacetamide at several temperatures (°C). The τ values reported are obtained from computer-simulated signal-shape analysis.

Measurements of ^{13}C spectra were performed operating a Brücker HFX-10 nmr spectrometer at 22.6 MHz using the usual Fourier transform signal enhancement methods[6] in conjunction with broad band proton decoupling.[7] Solutions were 70% DMTCA-30% 1,2-dibromotetrafluoroethane (DFTE), the latter serving as an 84-MHz ^{19}F lock signal. Sample temperature was measured by directly inserting a small thermometer into the 10-mm diameter sample tube spinning in a dewared insert. A thermocouple fixed near the bottom of the freely rotating sample tube serves to regulate a flow of cooled nitrogen gas. Control of temperature was accurate to ±0.5°. A similar 10-mm insert was used for proton measurements at 90 MHz. Our 60-

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