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(11) Anal. Calcd for $C_9H_9ClIIrNO_2$: C, 20.88; H, 1.75; Cl, 6.85; I, 24.51; N, 2.71. Found: C, 20.60; H, 1.73; Cl, 6.99; I. 24.70; N, 2.60.
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Alan L. Balch,* Jose R. Yow
Department of Chemistry, University of California
Davis, California 95616
Received August 6, 1979

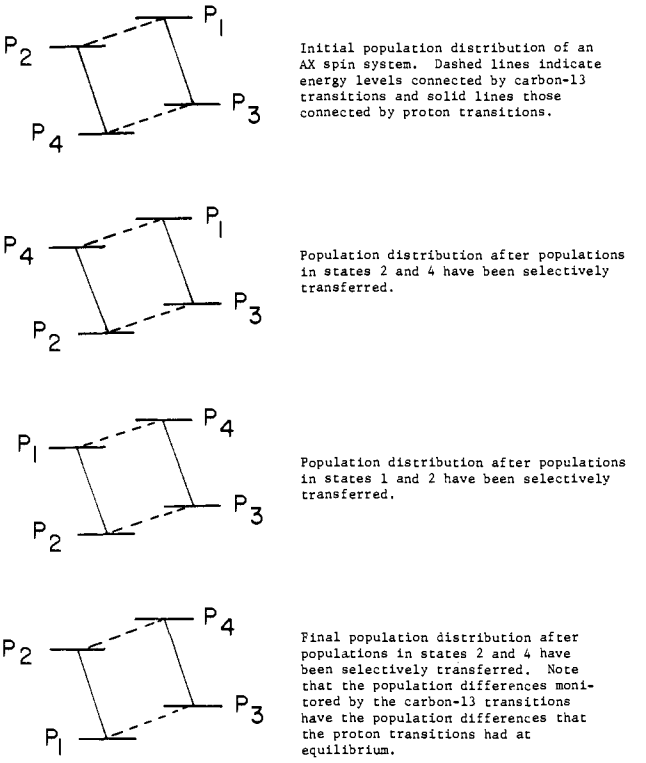

Figure 1. Outline of procedure to obtain proton-enhanced, proton-decoupled spectra. After the population transfers are completed, the population differences are sampled by obtaining a normal carbon-13 spectrum which may be proton decoupled if so desired.

Population Redistribution to Enhance NMR Sensitivity and Allow Decoupling of Low Gyromagnetic Ratio Nuclei

Sir:

The availability of the chemical information present in ^{13}C and ^{15}N NMR spectra of molecules in solution has been restricted by the poor sensitivity of these nuclei. This has motivated several approaches to transfer the relatively large magnetization of protons to nuclei possessing a low gyromagnetic ratio. The transfer of magnetization by cross-polarization (CP) has been quite successful for solids[1,2] and has recently been demonstrated for liquids.[3,4] Selective population transfer (SPT) between energy levels connected by proton transitions has been used to obtain enhanced signals with retention of scalar coupling.[5,6] A new approach to SPT, known as INEPT,[7] is based on the multiplicity and magnitude of the heteronuclear scalar coupling and not on the chemical shifts of the protons as in the standard SPT experiment. While the SPT (and INEPT) procedure increases the amplitude of the signals from the low gyromagnetic ratio nuclei, net magnetization transfer vanishes with both positive and negative signals being observed.[5-7] Consequently, proton decoupling eliminates the signal enhancement.

To realize the advantages of both the signal enhancement of SPT and proton decoupling in a single experiment, the novel scheme outlined in Figure 1 has been developed. A series of population transfers is performed to redistribute the populations of the energy levels.[8] The final population distribution is such that the intensities of the low gyromagnetic ratio nuclei are those of the proton transitions at equilibrium. The total time required for the magnetization transfer depends on the magnitude and multiplicity of the heteronuclear coupling.[7,8] In the case of dioxane, an AX_2 spin system with a scalar coupling constant of 145 Hz, the entire magnetization transfer procedure requires $5/4J$ s, which is <10 ms. Since the signs of the intensities of the low gyromagnetic ratio transitions after the population redistribution are the same, in contrast to an SPT experiment, the free induction decay can be acquired with proton decoupling without loss of signal. Thus, this method is referred to as population redistribution for enhancement with proton decoupling (PREP).

Some typical experimental results for dioxane are shown in Figure 2. Enhancement of the carbon-13 signal by the nuclear Overhauser enhancement (NOE) is shown in Figures 2A and 2B, which compare the proton-coupled spectrum with the NOE-enhanced, decoupled spectrum. The proton-coupled spectrum obtained after the population redistribution procedure is shown in Figure 2C and the proton-decoupled spectrum in Figure 2D. It is noted that the 1:2:1 intensity pattern of the triplet is not observed in the proton-coupled spectrum after the population redistribution procedure as the magnetization transfer is from the protons to the outer energy levels of the carbon-13 transitions.[9-12] The spectra in Figures 2B and 2D were obtained in the same total time. The signal intensity obtained by the PREP method is ~40% greater than that obtained with the NOE. Since PREP is at least competitive with the commonly used NOE method for dioxane, it is of interest to compare the relative merits of the two methods as well as those of CP and SPT (see Table I).

A major drawback of the cross-polarization technique for liquids lies in the precision required in matching the Hartman-Hahn condition for efficient magnetization transfer.[3,4] Missetting of the rf fields can lead to a severe loss in signal intensity rather than the anticipated enhancement. The SPT, PREP, and NOE methods are applicable to commercial spectrometers with adequate pulse control. The CP, SPT, and PREP methods all offer certain advantages over the NOE technique in that the pulse recycle time is governed by the proton longitudinal relaxation rate rather than that of the observed nucleus. This can lead to practical enhancements of an order of magnitude or more relative to the NOE method. The CP, SPT, and PREP methods are less dependent on the

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Table I. Comparison of Some Methods Used to Enhance Signals from Low Gyromagnetic Ratio Nuclei in Liquids[a]

method	maximum enhancement	recycle[b] time	enhancement eliminated by decoupling	"maximum" mol wt[c]	suitability to commercial spectrometers[d]
NOE	½	$S T_1$	no	~10 000	all
SPT	1	$^1H T_1$	yes	>10 000	all
CP	1	$^1H T_1$	no	>10 000	none[e]
INEPT	1	$^1H T_1$	yes	>10 000	~1978+
PREP	1	$^1H T_1$	no	>10 000	~1978+

[a] For low gyromagnetic nuclei S in presence of protons. [b] Longest time which typically governs pulse recycle time. [c] Molecular weight for which effect typically decreases to one-half maximum value. This is to be used as a rough estimate in comparison of methods. [d] For multinuclear FT NMR spectrometers. The INEPT and PREP methods require phase shift hardware and a programmable pulse control unit which many post-1978 spectrometers have. [e] An improvement in the CP method, proposed after this article was submitted, may allow CP to be performed on commercial spectrometers.[15]

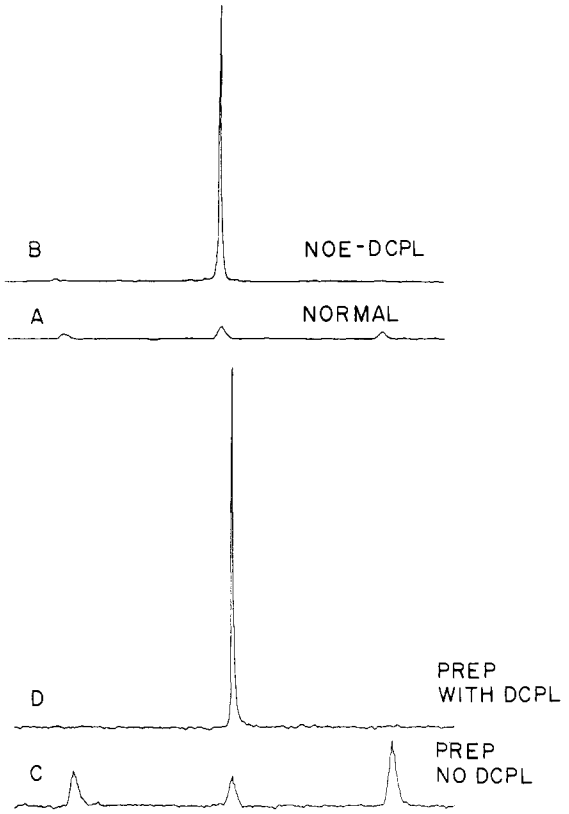

Figure 2. Comparison of NOE and PREP methods. In Figure 2A is the normal proton-coupled spectrum of dioxane (carbon-13 at 50.3 MHz). In Figure 2B is the spectrum obtained using the NOE for signal enhancement; the free induction decay was acquired with proton decoupling. In Figure 2C is the proton-coupled spectrum obtained after population redistribution. The spectrum in Figure 2D is that obtained using PREP and proton decoupling. The signal obtained by the PREP method is ~40% greater than that obtained using the NOE. The pulse recycle time for all of the experiments was 2.2 s. In the PREP experiment with proton decoupling there was a 1-s delay between the termination of signal acquisition and the onset of the magnetization transfer procedure. The spectra were obtained with an XL-200 in the Applications Laboratory of Varian in Palo Alto.

correlation times of the molecule being investigated than the NOE technique and, consequently, may be more applicable to large biological molecules. The NOE, CP, and PREP methods allow proton-decoupled spectra to be obtained in a straightforward fashion.

The major disadvantage of the CP, SPT, and PREP method lies in their dependence on the details of not only the heteronuclear scalar coupling but the homonuclear scalar couplings as well. As a result, for a typical molecule, the enhancement can only be optimized for a single nucleus in a given experiment. A more insidious problem arises from the proton–proton homonuclear couplings which decrease the efficiency of the magnetization transfer in the same manner as the proton-proton couplings disperse the signal in heteronuclear two-dimensional NMR.[13,14]

The dependence of the CP, SPT, and PREP methods on the scalar couplings of a molecule indicates that none of these methods will find widespread use in enhancing the signals of low gyromagnetic ratio nuclei on a routine basis. However, there are many cases in which a spectroscopist wishes to observe only a single nucleus or a few nuclei with similar coupling to protons. In such instances, the PREP method may be advantageous. Also, the PREP method may be useful in obtaining NMR spectra of low gyromagnetic ratio nuclei of biological macromolecules for which the NOE offers very little enhancement.

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Philip H. Bolton, Thomas L. James*
Department of Pharmaceutical Chemistry
School of Pharmacy, University of California
San Francisco, California 94143
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