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AN ASSESSMENT OF THE USE OF PROTON-^{13}C SATELLITE AND PROTON-^{12}C RELAXATION STUDIES FOR THE ISOLATION OF INTRA- AND INTERMOLECULAR CONTRIBUTIONS TO T$_1$ FOR ORGANIC MOLECULES

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Abstract—It is proposed that spin-lattice relaxation studies of hydrogen bound to ^{12}C and of hydrogen bound to the corresponding natural abundance ^{13}C can be combined with ^{13}C{^{1}H} nuclear Overhauser measurements to isolate the intra- and intermolecular contributions to proton relaxation times for certain classes of organic compounds. The proposals are illustrated by measurements on benzene, 1, 3, 5-trimethylbenzene and 1, 4-dioxan.

Fundamental studies of proton spin-lattice relaxation times (T_1) necessitate the separation of the intra- and intermolecular contributions to the measured values.[1] This can be achieved by dilution studies involving either the perdeuterated analogue of the compound of interest[2,3] or solvents containing no, or ineffective, dipolar nuclei.[1] In either case extrapolation to infinite dilution enables the intramolecular term $T_{1\,intra}$, to be determined. However, these approaches suffer from several disadvantages. Both are time consuming, the first may be costly and neither can provide a value for T_{1intra} that applies to other sample concentrations or for other solvents. Evidently, there is a need for a method that will provide both T_{1intra} and T_{1inter}, the intermolecular term, for a single sample.

Because of the low (1.1%) natural abundance of ^{13}C the familiar proton satellite spectra that it gives rise to creates the possibility of conducting T_1 studies under conditions corresponding to that of the ^{12}C molecule at low concentration. However, because of the high concentration of hydrogen, principally in the ^{12}C molecules, the proton satellite T_1 must contain both intra- and intermolecular contributions. Nevertheless, in certain circumstances the unique identity afforded hydrogen attached to ^{13}C can result in it having a different relaxation rate from that of the corresponding hydrogen bound to ^{12}C. This difference can be used to identify T_{1intra} and T_{1inter}.

In order to simplify matters the relaxation rates for hydrogen in a pure compound will be considered. Considering one magnetically unique hydrogen, i, an extension of the Soloman approach[4,5] yields the rate equation

$$\frac{dI_i}{dt} = -R_i(I_{zi} - I_{0i}) - \sum_{i\neq j} \sigma_{ij}(I_{zj} - I_{0j}) - \sum_{x} \sigma_{ix}(I_{zx} - I_{0x}) \qquad (1)$$

where I is proportional to the integrated intensity of the resonance of the appropriate spin; R_i the total direct relaxation rate of spin i is given[5] by

$$R_i = \sum_{j\neq i} \rho_{ij} + \rho_i^* \qquad (2)$$

where ρ_{ij} is the direct dipolar relaxation between spins i and j, and ρ_i^* is the direct relaxation of i due to other mechanisms not included in $\sum_{j\neq i} \rho_{ij}$ and for present purposes will be considered to arise from intermolecular dipolar interactions. The cross-relaxation terms, σ, are assumed to arise only from dipole-dipole interactions so that[5]

$$\rho_{ij} = 2\sigma_{ij}. \qquad (3)$$

If i in eqn (1) refers to one magnetically unique proton in a ^{12}C molecule the change in its magnetic identity when attached to ^{13}C cannot alter the form of (1) although R_i contains an additional contribution, $\rho_{i^{13}C}$, due to interaction with the ^{13}C dipole.

In order for ^{12}C and ^{13}C bound protons to have substantially different relaxation rates it is necessary for the hydrogen considered to be one of a set of N equivalent spins.

In the first instance one nucleus, S, out of N_s equivalent spins will be considered the subject of the measurements so that $N_s - 1$ nuclei, labelled D, will be detected simultaneously but not the subject. The other molecules in the bulk sample will be considered to contain solvent nuclei, X. The rate equation for the subject ^{12}C bound nucleus is

$$\frac{dI_s}{dt} = -R_s(I_{zs} - I_{0s}) - \sum_{N_s-1} \sigma_{sD}(I_{zD} - I_{0D}) - \sum_{x} \sigma_{sx}(I_{zx} - I_{0x}) \qquad (4).$$

Because $I_{zD} = I_{zs}$ and $I_{0D} = I_{0s}$ eqn (4) reduces to

$$\frac{dI_s}{dt} = -\left(R_s + \sum_{N_s-1} \sigma_{sD}\right)\left(I_{zs} - I_{0s}\right) - \sum_{x} \sigma_{sx}(I_{zx} - I_{0x}). \qquad (5)$$

There are of course N_s equations of the type (5) but because each acts independently at the nuclear level only one need be considered. Nevertheless, because the individual values of I are proportional to the total integrated signal intensities, the latter may be used with eqn (5).

For inversion recovery, or progressive saturation, experiments for systems having bi-exponential recovery rates corresponding to eqn (5) it has been shown that semi-logarithm plots of $(I_{zs} - I_{0s})$ vs t for the initial recovery data yield adequately accurate values of the relaxation rate.[6,7] The experimental relaxation rate R_{ss} may thus be determined and evaluated through eqn (6)

$$R_{ss} = R_s + \sum_{N_s - 1} \sigma_{sD} = 3/2\rho_{intra} + \rho_{inter} \tag{6}$$

If the same nucleus S is considered attached to ^{13}C this is now located in a system with $N_s - 1$ non-equivalent spins (N). Consequently, the analogue of eqn (4) is

$$\begin{aligned}\frac{dI_s}{dt} = &- R_s'(I_{zs} - I_{0s}) - \sum_{N_s - 1} \sigma_{sN}(I_{zN} - I_{oN}) \\ &- \sum_x \sigma_{sx}(I_{zx} - I_{ox}) - \sigma_{sc}(I_{zc} - I_{oc})\end{aligned} \tag{7}$$

with the additional final term being due to the effects of the ^{13}C nucleus. By applying a saturating rf field at the position of the ^{12}C-bound proton resonance not only are the satellite spectra reduced to two single resonances but $I_{zN} = I_{zx} = 0$. Consequently, eqn (7) reduces to

$$\begin{aligned}\frac{dI_s}{dt} = &- R_s'(I_{zs} - U_{os}) \sum_{N_s - 1} \sigma_{sN} I_{0N} \\ &+ \sum_x \sigma_{sx} I_{0x} - \sigma_{sc}(I_{zc} - I_{0c})\end{aligned} \tag{8}$$

and R_s' can be obtained from the initial part of a conventional semi-logarithm plot of the appropriate data. However R_s' is now given by

$$R_s' = \rho_{intra}' + \rho_{inter} \tag{9}$$

where

$$\rho_{intra}' = \rho_{intra} + \rho_{HC}. \tag{10}$$

Provided ρ_{HC} can be determined, eqns (6) and (9) can be used to obtain ρ_{intra} and ρ_{inter}.

It is possible to estimate ρ_{HC} from $^{13}C-\{^1H\}$nOe studies, because the observed

$$\sum_{N_S} \rho_{CH} = T_{1DD}^{C-1} = T_{1obs}^{C-1} \frac{\eta}{1.988} \tag{11}$$

^{13}C relaxation time T_{1obs}^{C} is related to its dipole-dipole component and the nOe, η, by eqn (11).[5,8] Implicit in this is the usual assumption that solvent contributions to ^{13}C relaxation times and nOe's are negligible.[8,9] It should be noted that eqn (11) yields $\sum\limits_{N_s} \rho_{CH}$ and not the required ρ_{CH}. However, the percentage of $\sum\limits_{N_s} \rho_{CH}$ attributable to ρ_{CH} can be estimated using the classical eqn (12).[8]

$$T_{1DD}^{C-1} = \hbar^2 \gamma_{^{13}C}^2 \gamma_{^1H}^2 \sum_{N_s} r_{CH}^{-6} \tau_c \tag{12}$$

for which, in the present context, only values for the H–C distances r_{CH} are required.

Although the above approached appears attractive because of its simplicity it does have limitations that restrict its applicability. In order to illustrate this, the subject nucleus will again be considered one of a set of N_s equivalent spins in the ^{12}C molecule so that eqns (5) and (6) again apply. If, however, the presence of ^{13}C results in S being one of a set of N_E equivalent spins, E, the appropriate rate equation is

$$\begin{aligned}\frac{dI_s}{dt} = &- R_s''(I_{zs} - I_{0s}) - \sum_{N_E - 1} \sigma_{sE}(I_{ze} - I_{0e}) \\ &- \sum_{N_s - N_E} \sigma_{sN}(I_{zN} - I_{0N}) \\ &- \sum_x \sigma_{sx}(I_{zx} - I_{0x}) - \sigma_{sc}(I_{zc} - I_{0c})\end{aligned} \tag{13}$$

which when the ^{12}C bound proton resonance is saturated reduces to eqn (14)

$$\begin{aligned}\frac{dI_s}{dt} = &- \left(R_s'' + \sum_{N_E - 1} \sigma_{sE}\right)(I_{zs} - I_{0s}) + \sum_{N_S - N_E} \sigma_{sN} I_{0N} \\ &+ \sum_x \sigma_{sx} I_{0x} - \sigma_{sc}(I_{zc} - I_{0c})\end{aligned} \tag{14}$$

for which the measured rate constant R_{ss}'' is

$$R_{ss}'' = R_s'' + \sum_{N_E - 1} \sigma_{sE} = \rho_{HC} + \rho_{intra} + \frac{1}{2} \sum_{E \neq s} \rho_{HH} + \rho_{inter} \tag{15}$$

where $\sum\limits_{E \neq s} \rho_{HH}$ is the total of the direct dipole-dipole effects on S of the remainder of the set of spins E. It follows that the intra- and intermolecular effects can only be separated if $\sum\limits_{E \neq S} \rho_{HH}$ as well as ρ_{HC} can be estimated.

In order to test the above proposals benzene, 1, 3, 5-trimethylbenzene (mesitylene) and 1, 4-dioxan have been studied.

EXPERIMENTAL

Samples of benzene and of 1, 4-dioxan were deoxygenated using the chemical method described elsewhere[10] and sealed, under vacuum, in 5 mm OD tubes. Mesitylene at a mole fraction of 0.6 in CCl_4 was prepared similarly. The sample tubes were placed co-axially in 10 mm tubes containing D_2O as heteronuclear lock. The ^1H and ^{13}C spectra were obtained at 28° ± 0.5°C using a JEOL FX90Q broadband pulse FT nmr spectrometer. The relevant relaxation times were obtained by both inversion recovery and progressive saturation techniques. The proton satellite spectra were obtained by selective homo-nuclear decoupling at the ^{12}C-bound resonance position. Considerable care had to be taken to ensure conditions that resulted in single line satellite resonances without decoupling these from ^{13}C; although the effective removal of the ^{12}C–H resonance alleviated dynamic range problems it proved necessary to obtain a minimum of 20 FID's in order to produce satisfactory satellite spectra.

The $^{13}C-\{^1H\}$ nOe factor was obtained using the gated irradiation technique, which involved waiting $5T_1$ between pulses when using complete irradiation and $10T_1$ between gated pulses.[11]

RESULTS AND DISCUSSION

The ^1H and ^{13}C relaxation times together with the $^{13}C-\{^1H\}$ nOe's for benzene, mesitylene and 1,4-dioxan are recorded in Table 1.

In the case of benzene the data given in Table 1 were used with eqn (11) to yield a value of 40.75 s for T_{1DD}^{C}. Using the standard molecular geometry for benzene it was deduced that $\rho_{CH} = 0.96\ T_{1DD}^{C-1}$. This, together with

Table 1. ^{12}C and ^{13}C-bound ^{1}H relaxation times and ^{13}C nOe for benzene, mesitylene and 1, 4-dioxan

Compound		T_1/s		
	^{12}C-H	^{13}C-H	^{13}C	η
Benzene	21.0±0.5	14.8±0.24	32.9±1	1.6±0.16
1,4-dioxan	6.6±0.5	5.1±0.5	11.8±0.5	1.8±0.18
Mesitylene	15.0±0.5	5.0±0.5	7.1±0.5	1.96±0.05

the other parameters in Table 1, was used with eqns (6), (9) and (10) to obtain $T_{1intra} = 92.6$s and $T_{1inter} = 27.2$s. Zeidler[12] and also Powles[13] have deduced from studies of C_6H_6 in C_6D_6 that $T_{1intra} = 111$s and $T_{1inter} = 23$s and $T_{1intra} = 87$s and $T_{1inter} = 25$s respectively. It can be seen that these values are consistent with those reported herein.

In the case of mesitylene the presence of the methyl groups contributes an additional exponential contribution to the aryl proton relaxation rates. Consequently, care was taken to ensure that values of the latter were obtained from the initial recovery data. By assuming that $\rho_{CH} = 0.98\ T_{1DD}^{C-1}$ the data in Table 1 can be used to deduce that the aryl hydrogen-aryl hydrogen contribution, ρ_{HH}, to ρ_{intra} is 0.0028 s^{-1}. The high value of 357 s for the corresponding relaxation time is expected because the contributing proton is so remote from the subject nucleus. It should be noted that the other intramolecular relaxation contribution due to the methyl protons cannot be isolated.

In the case of 1, 4-dioxan $2\rho_{CH} = T_{1DD}^{C-1}$ so that the appropriate data in Table 1 yield via eqn (11) $\rho_{HC}^{-1} =$ 26.06 s. Although the value of $\sum_{E\neq S} \rho_{HH}$ required for eqn (15) is not available experimentally, it was estimated using the appropriate form of the Gutowsky–Woessner equation (16)[14]

$$\sum_{E\neq S} \rho_{HH} = \frac{3}{2} \gamma_H{}^4 \hbar^2 r_{HH}^{-6} \tau_c \qquad (16)$$

for adjacent protons; a value of τ_c was deduced according to the Mitchell–Eisner approximation[1]

$$\tau_c = \frac{I}{\mu} \frac{2\eta_v a}{kT} \qquad (17)$$

where I(200.7×10^{-4} g cm^2) is the average moment of inertia of 1, 4-dioxan, μ (44.06 g) its reduced mass, a (deduced to be 2.67 Å from molecular models) its average radius and η_v(1.087 c[16]) its viscosity. In this way ρ_{HH}^{-1} was estimated to be 9.49 s. Using the values of $\sum_{E\neq S} \rho_{HH}$ and ρ_{HC} referred to above together with the other relevant data in Table 1 with eqns (6) and (15) enabled the values of 7.2 s and 83.3 s to be deduced for T_{1intra}† and T_{1inter} respectively.

CONCLUSION

It would appear that, for selected molecules, relaxation studies of ^{13}C and ^{12}C- bound hydrogen, coupled with ^{13}C-{^{1}H} nOE measurements, can be used to isolate the intra- and intermolecular contributions to proton spin-lattice relaxation times. In order to minimize the dependance of the approach on the theoretical estimation of necessary parameters it is important to confine the approach to situations where the presence of ^{13}C differentiates one proton from an otherwise equivalent set of spins. It is likely, therefore, that the approach will only prove of significant value in the analysis of the relaxation times for protons such as those of the aryl hydrogens in symmetrically substituted aromatic compounds. Even in these cases it will prove beneficial to increase the accuracy of the experimentally determined relaxation times and nuclear Overhauser enhancements.

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†$T_{1intra} = (\frac{3}{2}\rho_{intra})^{-1}$ for identical protons attached to ^{12}C.