Increasing the Time Resolution of Dynamic Nuclear Magnetic Resonance Spectroscopy through the Use of Lanthanide Shift Reagents

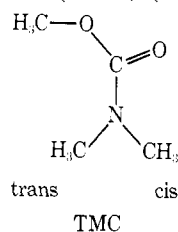**Stephen R. Tanny, Miles Pickering, and Charles S. Springer, Jr.***

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Abstract: A method for increasing the time resolution of dynamic nmr spectroscopy is described. This technique involves using a lanthanide shift reagent to cause a continuous change of the nmr time scale through the exchange sensitive region, while the rates of the observed processes remain constant. The method is illustrated and tested with the interaction of trimethyl carbamate (TMC, $(H_3C)_2NC(O)OCH_3$) with tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III) in CCl_4 at 27°. The free energy of activation of the isomerization of TMC (which cannot be studied by proton nmr in CCl_4 solution alone) is easily obtained. It is found to be 15.5 ± 0.1 kcal/mol, in excellent agreement with a literature value determined in $CDCl_3$ solution. In addition, the free energy of activation for isomerization of TMC bound to the metal chelate is found to be considerably increased. This is reasonable in terms of both electronic and steric factors.

Dynamic nuclear magnetic resonance (dnmr) spectroscopy has been extremely useful in the study of relatively rapid molecular motions and reactions.[1] Two problems which have plagued the application of this technique involve the magnitude of the *difference* of the resonance frequencies of exchanging nuclei in the absence of exchange $(\Delta\nu_\infty)$.[1d] First, small values of $\Delta\nu_\infty$ frequently cause limited or inaccessible temperature ranges which are amenable to kinetic measurements and, at best, yield only inaccurate rate data. Second, accidental degeneracy $(\Delta\nu_\infty = 0)$ precludes any dnmr experiment. We wish to report some of our experiments with lanthanide shift reagents (LSR)[2] which reveal a method of alleviating both of these problems.

Almost all dnmr experiments have been carried out by varying the rate(s) of the observed reaction(s) (through changes in the temperature or concentrations of reactants) while keeping the $\Delta\nu_\infty$ (or $\Delta\nu_\infty$'s) constant (by operating at a constant H_0 field strength). In principle, one should be able to gain similar information by varying $\Delta\nu_\infty$ while keeping the rate of reaction constant (*i.e.*, at constant temperature and/or concentration).[1d] This can be done conveniently (*i.e.*, without using a number of spectrometers of different field strengths) in favorable cases through the use of the lanthanide induced shift (LIS).

Trimethyl carbamate (TMC, $(H_3C)_2NC(O)OCH_3$) is

H₃C—O
\
C=O
/
N
/ \
H₃C   CH₃

trans   cis

TMC

a substrate particularly well suited to illustrate and test this principle. It is known that there is hindered rotation about the carbonyl carbon–nitrogen bond; the nonequivalence of the cis and trans N–CH₃ resonances has been observed in 10 mol % solution in $CDCl_3$ below $-23°$.[3,4] However, the $\Delta\nu_\infty$ observed at these temperatures is quite small (0.030 ppm,[3] 0.032 ppm[4]) thereby reducing the precision of the activation parameters derived from a traditional dnmr study.[3] In 25% solutions in CH_2Cl_2 or toluene, no splitting of the N–CH₃ resonance is seen, even at $-46°$ (60 MHz).[5] Neither is splitting observed at ambient probe temperature in CCl_4 solution at 60 MHz.[5,6] This situation must arise because, in CCl_4 solution, the isomerization rate has been increased and/or $\Delta\nu_\infty$ has been reduced (perhaps to zero) at the ambient probe temperature.

Carbamates do interact with LSR in labile solution equilibria in nonaqueous solvents.[7,8] Bauman has shown that, while TMC interacts with tris(2,2,6,6-tetramethyl-3,5-heptanedionato)europium(III) (Eu(thd)₃) trimethyl thiocarbamate $((H_3C)_2NC(S)OCH_3)$ does not.[7] This indicates that the LSR is coordinated by the carbonyl oxygen of TMC and not by the ester oxygen or the nitrogen.

Figure 1 depicts examples of the proton nmr spectrum of TMC in CCl_4 for different values of the mole ratio (ρ) of the LSR, tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionato)europium(III) (Eu(fod)₃·$(OH_2)_x$, where $x < 1/2$).[9] The usual downfield shift of all the resonances, as more of the substrate associates with the paramagnetic europium chelate,[2]

(1) (a) W. E. Stewart and T. H. Siddall, *Chem. Rev.*, **70**, 517 (1970); (b) H. Kessler, *Angew. Chem., Int. Ed. Engl.*, **9**, 219 (1970); (c) G. Binsch, *Top. Stereochem.*, **3**, 97 (1968); (d) M. Saunders, *Magn. Resonance Biol. Syst., Proc. Int. Conf., 1966*, **9**, 85 (1967).

(2) For reviews of studies and uses of LSR see: (a) R. von Ammon and R. D. Fischer, *Angew. Chem., Int. Ed. Engl.*, **11**, 675 (1972); (b) R. E. Sievers, M. F. Richardson, and C. S. Springer, submitted for publication.

(3) P. T. Inglefield and S. Kaplan, *Can. J. Chem.*, **50**, 1594 (1972).

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(6) A. E. Lemire and J. C. Thompson, *Can. J. Chem.*, **48**, 824 (1970).

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(9) For details of the preparation, use as LSR, and difficulty in drying of the Ln(fod)₃·$(OH_2)_x$ chelates, see: (a) C. S. Springer, D. W. Meek, and R. E. Sievers, *Inorg. Chem.*, **6**, 1105 (1967); (b) R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, **93**, 1522 (1971); (c) A. H. Bruder, S. R. Tanny, H. A. Rockefeller, and C. S. Springer, submitted for publication.
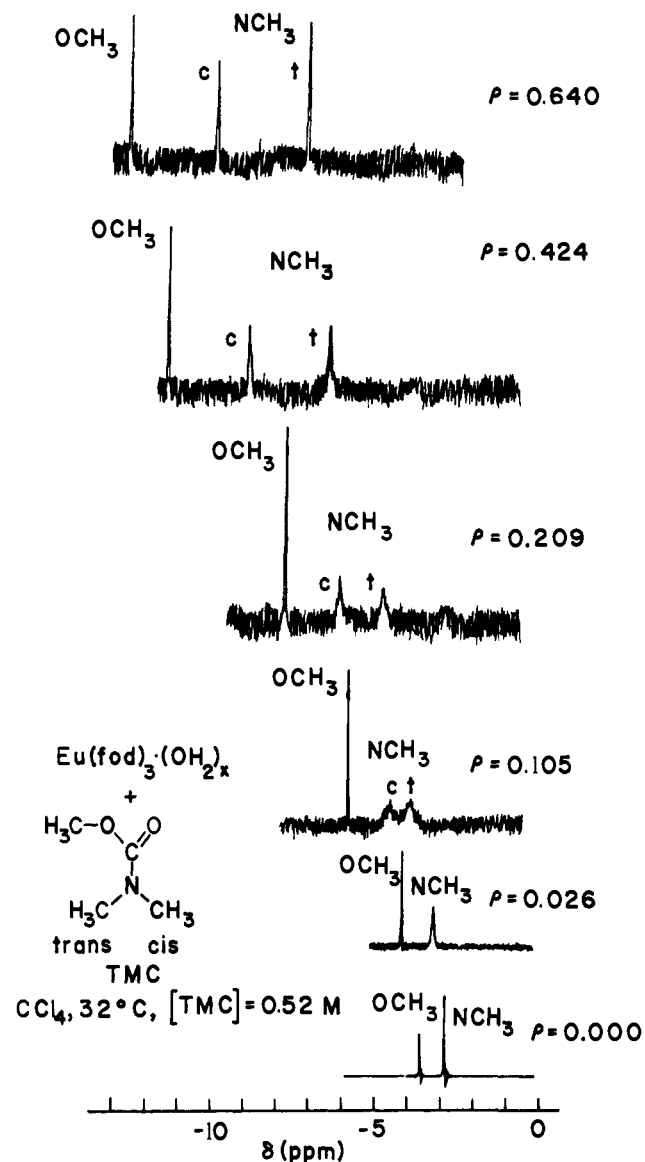
Figure 1. The proton nmr spectrum of TMC in CCl_4 with varying mole ratios (ρ) of Eu(fod)$_3 \cdot$(OH$_2$)$_x$ ($x < 1/2$). [TMC] = 0.52 ± 0.02 M, $T = 32°$. The spectrum was recorded with differing values of the spectrum amplitude setting for different values of ρ.

is observed. The NCH_3 resonance, which is a single sharp peak with twice the area of the OCH_3 rseonance in the diamagnetic CCl_4 solution[5,6] ($\rho = 0$), is broadened and then split into two peaks as more LSR is added. The NCH_3 resonance shifted further downfield is assigned to the cis NCH_3 group because of its closer proximity to the site of complexation.[8] A most important observation is that the NCH_3 resonances *resharpen after their splitting*, and after ρ reaches approximately 0.5, three equally sharp resonances are observed.[10] This is a clear indication that chemical exchange is affecting the shape of the resonance lines. A smaller, steady increase in line width of all peaks with ρ is caused by the paramagnetic ion. This is more clearly seen in Figure 2 where the line widths (full width at half-height) of all the resonances are plotted as a function of ρ. The OCH_3 group, which

(10) In this case, at low values of ρ, the chelate acid A and the donor substrate D form, almost exclusively, the 1:2 complex AD₂.[9c] Thus, the fraction of substrate bound to A, σ, reaches 1 at $\rho \cong 0.5$. This is not unexpected.[2b]
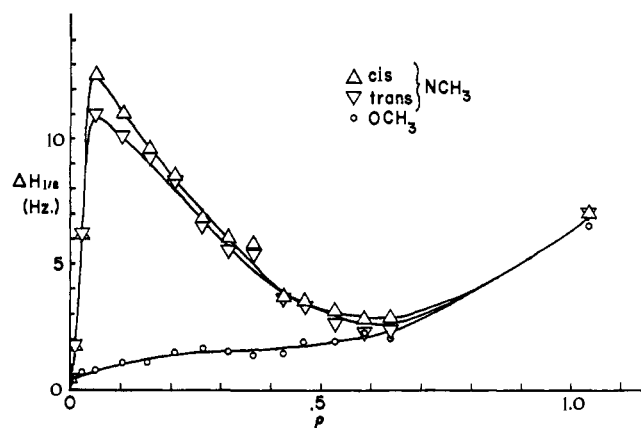

Figure 2. The dependence of the full width at half-height ($\Delta H_{1/2}$) of the proton resonances of TMC on ρ.

undergoes no chemical exchange, shows only the broadening effect of the unpaired metal 4f electrons.[11] The NCH_3 resonances, on the other hand, show a tremendous increase in broadening due to the intramolecular exchange of the N–CH₃ groups between the cis and trans environments. As $\Delta\nu_\infty$ increases toward its value in the LSR:2TMC adduct (3.01 ppm[9c]), however, the line width *decreases* back to that of the OCH_3 resonance. This behavior implies that kinetic information on the process causing the broadening can be obtained from the data gathered *at constant temperature and/or concentration* of substrate.

Cheng and Gutowsky[13] and Beauté, Wolkowski, and Thoai[14] have recently reported the effects of LSR on the coalescence temperatures of the cis and trans N–CH₃ resonances of amides. The former authors calculated the free energy of activation at the coalescence temperature, $\Delta G_c^{\ddagger}$, by the commonly used approximation and reported its dependence on ρ.[13] Although their values of $\Delta G_c^{\ddagger}$ were in good agreement with those obtained by more exact dnmr studies, they noted a slight increase with the coalescence temperature, T_c, which, of course, increases with ρ.[13,14] As noted by Cheng and Gutowsky, it is difficult to interpret this temperature dependence. Besides the temperature dependence of the entropy term in $\Delta G^{\ddagger}$, temperature will affect the association quotient of the LSR:substrate complex and also the paramagnetic broadening of all resonance lines.[13] Perhaps more importantly, the changing values of ρ (necessary to change T_c) mean that different fractions of the substrate are associated with the chelate and that the average rate process observed is being changed (*vide infra*). These problems can be avoided by working at constant temperature as indicated above. Our data for the TMC system at 27° are set out in Table 1.

We have used a computer program, based on the classical modified Bloch equations for uncoupled two-site exchange,[1c] to obtain observed rate constants from the total line-shape analysis of the N–CH₃

(11) The slight maximum in the OCH₃ curve at $\rho \simeq 0.25$ may be a manifestation of the *intermolecular* exchange (of free and complexed TMC) term in the expression for the transverse relaxation time.[12]
(12) J. Reuben and J. S. Leigh, *J. Amer. Chem. Soc.*, **94**, 2789 (1972).
(13) H. N. Cheng and H. S. Gutowsky, *J. Amer. Chem. Soc.*, **94**, 5505 (1972).
(14) C. Beauté, Z. W. Wolkowski, and N. Thoai, *Chem. Commun.*, 700 (1971); see also R. von Ammon, R. D. Fischer, and B. Kanellakopulos, *Chem. Ber.*, **104**, 1072 (1971).

Table I. Proton Nmr Parameters for the Interaction of TMC with $Eu(fod)_3 \cdot (OH_2)_x$ (in CCl_4 with 6% TMS, [TMC] = 0.52 ± 0.02 M, T = 27 ± 2°, $x < {}^1/_2$)

ρ^a	Trans N-CH₃ $\Delta,^b$ ppm	$\Delta H_{1/2},^c$ Hz	Cis N-CH₃ $\Delta,^b$ ppm	$\Delta H_{1/2},^c$ Hz	OCH₃ $\Delta,^b$ ppm	$\Delta H_{1/2},^{c,d}$ Hz	σ^e	τ_{obsd}, msec	k_{obsd}, sec⁻¹
0	0		0		0	0.38	0		
0.0119	0.16	1.9	0.16	1.8	0.23	0.57	0.0251	10.6	47.3
0.0256	0.30	6.2	0.30	6.2	0.53	0.63	0.055	11.9	41.8
0.0510	0.60	11.0	0.84	12.6	1.21	0.74	0.100	16.7	30.3
0.1048	1.15	10.1	1.84	11.0	2.43	1.01	0.204	20.3	24.6
0.1586	1.73	9.2	2.85	9.6	3.70	1.02	0.309	22.4	22.3
0.2085	2.13	8.3	3.46	8.5	4.54	1.44	0.407	26.3	19.0
0.2642	2.69	6.4	4.44	6.8	5.76	1.60	0.514	34.8	14.4
0.3167	3.09	5.5	5.26	6.0	6.73	1.44	0.618	40.2	12.4
0.3653	3.51	5.6	5.85	5.8	7.57	1.37	0.706	42.0	11.9
0.4238	3.87	3.6	6.43	3.7	8.37	1.45	0.805	67.4	7.42
0.4684	4.21	3.3	7.00	3.6	9.06	1.89	0.873	128.7	3.88
0.5295	4.22	2.6	7.14	3.1	9.21	1.91	0.933	168.9	2.96
0.5842	4.21	2.3	7.16	2.8	9.27	2.25	0.958	383.6	1.30
0.6398	4.06	2.4	7.05	2.9	9.00	2.04	0.974	411.6	1.21

^{a} Mole ratio = (total concn of $Eu(fod)_3 \cdot (OH_2)_x$)/(total concn of TMC). ^{b} $\Delta = \delta_{obsd} = \delta_{diamagn}$, where δ_{obsd} is the observed chemical shift in ppm downfield from TMS and $\delta_{diamagn}$ is the chemical shift in CCl_4 in the absence of the LSR.[2b] $\delta_{diamagn}$ for NCH₃ is 2.86 ppm and for OCH₃ 3.62 ppm.[5,6] ^{c} Full width at half-height. ^{d} Data obtained at $\sim$32°. ^{e} σ = fraction of TMC coordinated to LSR; calculated from the relation $\sigma = ([AD]_{eq} + 2[AD_2]_{eq})/([D]_{eq} + [AD]_{eq} + 2[AD_2]_{eq})$. See the Experimental Section for details.
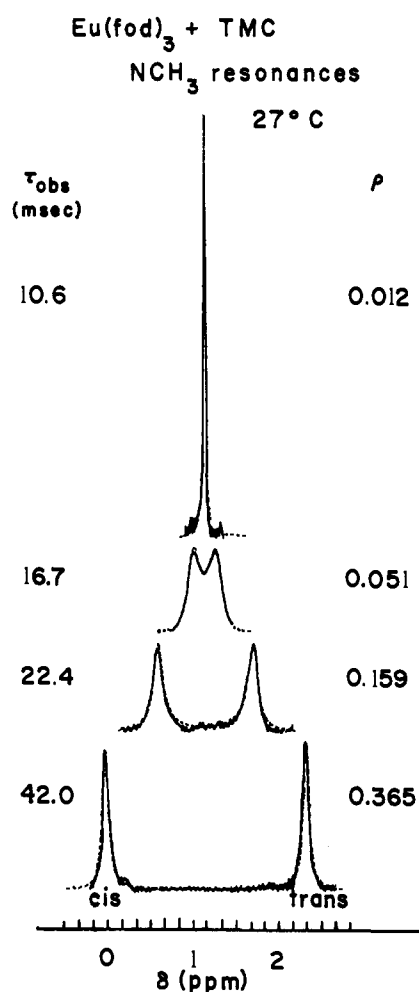
Figure 3. Experimental (—) and calculated (- - -) spectra of the N-CH₃ resonances in TMC with differing values of ρ. The values of τ given are those corresponding to the computer fit.

resonances as a function of ρ. This program requires, as input parameters, the line widths ("effective" T_2 values) and the separation ($\Delta\nu_\infty$) of the exchanging resonances in the absence of exchange. The line width of the nonexchanging OCH₃ resonance at each value of ρ was used to calculate the value of the "effective" T_2 for the NCH₂ resonances in the absence of exchange at that value of ρ ($T_2 = 1/(\pi\Delta H_{1/2})$, $\Delta H_{1/2}$ in Hz). (It can be seen in Figure 2 that the cis NCH₃ resonance, being shifted further, is often slightly broader than the trans NCH₃ resonance. The program used could accommodate peaks of different slow-exchange widths but the differences here were small enough to allow us to ignore this point.) For almost all of the range of ρ values studied, the exchanging peaks were far enough apart that the observed separation $\Delta\nu$ was equal to the observed $\Delta\nu_\infty$ (a distinct advantage of this method). Only for the very smallest mole ratios just above and, of course, just below coalescence ($0.026 < \rho_c < 0.051$, 27°) were estimates of $\Delta\nu_\infty$ necessary. These were made by extrapolation of a $\Delta\nu$ vs. ρ plot.

Some of the computer-fitted spectra are shown in Figure 3. As can be seen, the fitting is quite acceptable. The preexchange lifetimes, τ_{obsd}, obtained from these fittings are found in Table I. The tabulated first-order rate constants are related to the τ_{obsd} by the equation $k_{obsd} = 1/(2\tau_{obsd})$.

Figure 4 shows a plot of k_{obsd} vs. σ, the saturation fraction (see Table I and the Experimental Section for the calculation of σ). The curve is linear over 90% of the saturation fraction, from $\sim$0.1 to $\sim$1.0, with a small but nonzero slope. Below $\sigma = \sim$0.03, the k_{obsd} values are not accurate because the peaks are coalesced and good values of $\Delta\nu_\infty$ cannot be reliably estimated (vide supra). Thus, it is possible to obtain kinetic information on the constant rate process by varying the nmr time scale through the exchange-sensitive region. This is done by continuously changing the observed $\Delta\nu_\infty$ from zero in the free substrate (obtained by extrapolating $\Delta\nu$ to ρ = 0^s) to 3.01 ppm in the adduct through the operation of the LIS. If the rate of the process observed is truly constant, one must ask why the linear curve in Figure 4 has a nonzero slope. A most reasonable answer is that the observed rate is the weighted average rate of two
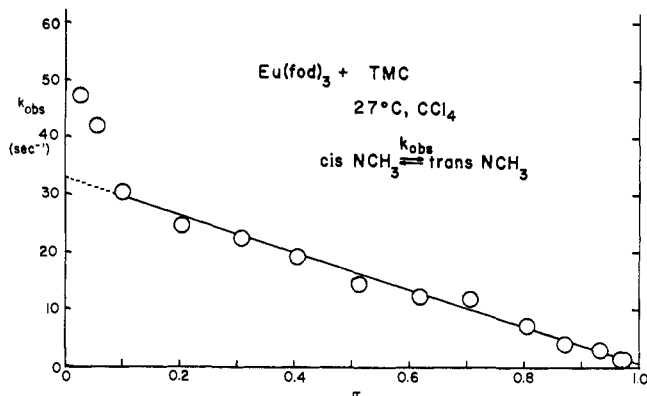
Figure 4. The dependence of the observed rate constant for isomerization of TMC, k_{obsd}, upon the saturation fraction, the fraction of TMC coordinated to Eu(fod)$_3$, σ.

(*or more*) *constant rate processes* whose relative importances are changing with σ.

The weak LSR:2TMC adduct is extremely labile.[2b] The lifetime of the quinoline:Eu(thd)$_3$ adduct under similar conditions has been estimated to be 210 nsec.[12] Although the lifetime of the stronger Ln(fod)$_3$ adduct is expected to be longer,[2b] it is still much shorter than the isomerization lifetime which is on the order of 40 msec (see Table I). The intermolecular exchange is certainly fast on either of the two nmr time scales. Thus, it seems reasonable that the observed rate constant is the weighted average of the rate constant for isomerization of free TMC, k_{free}, and that for complexed TMC, k_{adduct}.[1d]

$$k_{obsd} = (1 - \sigma)k_{free} + \sigma k_{adduct}$$

The value of k_{free} can be found, by extrapolating the linear portion of the curve to $\sigma = 0$, to be 33.0 ± 3.7 sec^{-1} at 27° in CCl$_1$. Employing the standard Eyring equation (with the usual assumption of the transmission coefficient being unity), the free energy of activation for isomerization of uncomplexed TMC, $\Delta G^{\ddagger}_{300}$, is calculated to be 15.5 ± 0.1 kcal/mol. This is in excellent agreement with the value of 15.2 kcal/mol obtained by Inglefield and Kaplan from their total line-shape analysis of the dnmr spectrum of TMC in CDCl$_3$ solution at temperatures near the coalescence (−13°).[3] The values of $\Delta G^{\ddagger}$ for this type of isomerization have been found to be almost temperature and, surprisingly, solvent independent.[1] One might have expected the CCl$_1$ value to be somewhat smaller than the CDCl$_3$ value,[1a] but it seems that the main dnmr problem in CCl$_4$ is caused by the reduction of $\Delta \nu_\infty$. The only other values of $\Delta G^{\ddagger}$ for isomerization of N,N-dimethyl carbamates have been obtained by dnmr methods more approximate than that of Inglefield and Kaplan. Values of 14.4 and 14.5 have been obtained for the O phenyl and O naphthyl derivatives, respectively.[15] A value of 15.9 has been obtained for the O benzyl derivative in both CDCl$_3$ and pyridine.[16]

Thus, we have demonstrated and successfully tested a method of determining rate constants and activation

parameters for processes which cannot be studied under normal, diamagnetic, nmr conditions through the use of the paramagnetic LSR. In this case, in the diamagnetic CCl$_4$ solution, $\Delta \nu_\infty$ is zero at 60 MHz; the isomerization cannot be studied by proton magnetic resonance at any temperature where this is the case. The remaining activation parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$) could be determined by repeating the studies reported above for several different temperatures.

A referee has pointed out that some amides undergo self-association in nonpolar solvents. The equilibrium quotient for dimerization of N,N'-dimethylformamide (DMF) in CCl$_4$ is ~ 1 M^{-1} at 36°.[17] This causes temperature and concentration dependencies, in diamagnetic solutions, of the $\Delta \nu_\infty$ observed because of hindered rotation. These dependencies must be taken into account if accurate kinetic parameters for the isomerization are to be obtained from conventional dnmr techniques.[18,19] The parameters so obtained pertain to the equilibrium mixture of monomer and oligomers and are thus weighted averages.[19] The values for the monomer and oligomers must not be very different, however,[19] because excellent linear Arrhenius plots are obtained.[1a]

Since the self-association seems to occur because of the polar nature of these solutes[17] implied by resonance form II, the carbamates would be expected to

I   II
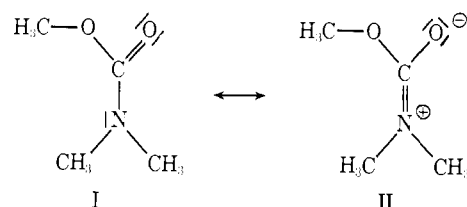
associate to a smaller degree than the amides and thus this would be less of a problem. If TMC had a dimerization quotient of ~ 1 M^{-1} in CCl$_4$ at 27°, $\sim 38\%$ of the TMC would be dimerized at the concentration employed in this study. If the LSR dnmr method described here were carried out at several temperatures, as suggested above, the set of k_{free} values so obtained would have the same complications due to oligomerization as those obtained by conventional dnmr techniques on the amides, except probably to a lesser degree. As noted, these effects do not seem to be noticeable in the Arrhenius plots of the amides and would probably also not be a problem for the carbamates. The operational problems of the temperature and concentration dependencies of $\Delta \nu$ will, of course, be corrected for implicitly by the method of obtaining $\Delta \nu_\infty$ in the LSR dnmr technique. This is another advantage of this approach.

Extrapolating the k_{obsd} vs. σ curve to $\sigma = 1$, gives a rate constant for isomerization of complexed TMC, k_{adduct}, of 0.5 ± 3.7 sec^{-1} at 27° (see Figure 4). A rate constant of 0.5 sec^{-1} corresponds to a free energy of activation, $\Delta G^{\ddagger}_{300}$, of 18.0 kcal/mol. However, k_{adduct} is zero within experimental error and the only definitive statement which can be made is that complexation of TMC to Eu(fod)$_3 \cdot$(OH$_2$)$_x$ retards the process of isomerization. This is to be expected for both elec-

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tronic and steric reasons. Coordination through the carbonyl oxygen would lead to increased double bond character in the carbonyl carbon–nitrogen bond due to relative stabilization of resonance form II.[20] Protonation of amides at the carbonyl oxygen has been found to increase the barrier to isomerization.[1a,21] Substrate molecules have been found to be quite crowded in the LSR adducts which have been studied by X-ray crystallography.[2b] This would almost certainly lead to some steric hindrance to substrate isomerization in the adduct complex. Therefore, the increase in the activation free energy or the complete hindrance of the isomerization seems quite reasonable. This is the most likely source of the increase in $\Delta G_c{}^{\pm}$ with ρ observed by Cheng and Gutowsky for the isomerization of amides.[13] In the method described in this paper, extrapolation to $\sigma = 0$ or 1 ensures that the activation parameters measured are those corresponding to the rate process of the free or complexed substrate, respectively.[22]

The isomerization studied in this paper is a "diastereotopomerization" reaction in the nomenclature of Kessler.[1b] That is, it involves the exchange of diastereotopic methyl groups. The "isomers" are "degenerate" ("topomers"[1b]). When the two N substituents are different, real diastereomers are, of course, obtained. Interactions with LSR have been found to change the isomer ratios of diastereomeric amides.[20,23] Diastereomerization reactions could be studied by the method described in this paper by simply using continuously changing relative site populations as input parameters to the line-shape program. Our program can accommodate such a situation.

A comparison should be made of the dnmr technique described here to the elegant method of Saunders and Yamada for measuring the extremely rapid inversion of amines.[1d,24] These authors have shown that increasing the extent of protonation of an amine (by increasing [H$^+$]) continuously increases its lifetime in one or the other pyramidal form because the quaternary ion cannot invert. Thus, the lifetime can eventually be made long on the nmr time scale. Line-shape analysis of the spectrum as a function of pH can yield rate data. Extrapolation allows the determination of the rate of inversion of the free unprotonated amine.

Both techniques involve the use of acid dnmr reagents although the organic soluble Lewis acid LSR should be more generally useful. More importantly, the proton acts as a dnmr reagent primarily by hindering the reaction and only very slightly or not at all by changing the nmr time scale. The LSR, on the other hand, acts primarily by changing the time scale (i.e.,

acts as a shift reagent) and only incidentally, in this case, by hindering the reaction.

This technique should prove quite useful for studying the kinetics of previously unobservable processes because the LSR have been found to interact with a wide range of Lewis basic substrates.[2] A particularly interesting area of application may be the study of fluxional organometallic molecules. Marks and co-workers[25] and Foreman and Leppard[26] have shown that the LSR interact with a large variety of coordinated ligands. Kinetic studies of rapid intermolecular reactions should also be amenable to this method.

It is interesting to speculate on the limits of the magnitudes of rate constants which should be amenable to this technique. The largest values of $\Delta \nu_\infty$ obtainable might be expected to be of the order of 500 Hz.[2] Using the simple formula for the rate constant at coalescence, $k_{\text{coal}} = \pi \Delta \nu_\infty / 2^{1/2}$,[1c] this corresponds to a k_{coal} of $\sim 10^3$ sec^{-1}. At $-23°$, this would correspond to a $\Delta G^{\pm}{}_{250}$ of ~ 11.1 kcal/mol. Thus, one might be able to probe $\Delta G^{\pm}$ values down to ~ 10 kcal/mol in favorable cases.

Experimental Section

Reagents. Commercial "Spectral Grade" CCl$_4$, dried over molecular sieves, was used as the solvent for all solutions. The shift reagent, Eu(fod)$_3\cdot$(OH$_2$)$_x$ ($x < 1/2$) was synthesized according to published procedures.[9a] It was dried for 24 hr at 90° at a pressure of 0.05 mm. For details of the characterization and the difficulty in completely drying this compound, see ref 9a,c. The details of the preparation of trimethyl carbamate will be published elsewhere.[9c] The product was characterized by nmr.[5,6]

Spectral Solutions. The solutions for line-shape analysis were prepared by dilution in nmr tubes of calibrated volumes. The concentration of TMC was kept constant for all samples at 0.52 $\pm$ 0.02 M. Increasing amounts of Eu(fod)$_3$ were added from a stock solution of concentration 0.31 M. Tetramethylsilane (6%) was added for internal lock purposes.

It is obvious from Δ vs. ρ plots [where $\Delta = \delta_{\text{obsd}} - \delta_{\text{diamagn}}$, δ_{obsd} is the observed chemical shift in parts per million downfield from TMS and δ_{diamagn} is the chemical shift in CCl$_4$ in the absence of the LSR;[2b] ρ = (total concentration of Eu(fod)$_3$)/ (total concentration of TMC)], that at low values of ρ, Eu(fod)$_3$ and TMC form, almost exclusively, a 1:2 complex, Eu(fod)$_3\cdot$(TMC)$_2$, via the labile solution equilibrium; Eu(fod)$_3$ + 2TMC $\rightleftarrows$ Eu(fod)$_3\cdot$(TMC)$_2$. The curves level off at $\rho \sim 0.5$.[9c] The fraction of TMC coordinated, the saturation fraction, can be calculated according to the equation

$$\sigma = \frac{[\text{AD}]_{\text{eq}} + 2[\text{AD}_2]_{\text{eq}}}{[\text{D}]_{\text{eq}} + [\text{AD}]_{\text{eq}} + 2[\text{AD}_2]_{\text{eq}}}$$

The equilibrium concentrations of each of the various species present could be estimated quite satisfactorily at each value of ρ by using the equilibrium quotients given for the following competing equilibria: A + D $\rightleftarrows$ AD, K = 1600; AD + D $\rightleftarrows$ AD$_2$, K = 107; A + A $\rightleftarrows$ A$_2$, K = 367; and A$_2$ + A $\rightleftarrows$ A$_3$, K = 12. The latter two equilibrium quotients were determined from best least-squares fits to vapor pressure osmometry data at 37°. The former two were determined using the latter two and the best least-squares fits to the Δ vs. ρ LIS curves at 32°. A detailed description of the computer program which calculates the equilibrium concentrations is given in ref 9c.

Spectroscopy and Computing. Proton (60 MHz) magnetic resonance spectra were obtained on Varian A-60 (32°) and DA-60-IL (27°) analytical spectrometers. The line-shape data were obtained with the latter instrument in the frequency sweep mode. Chemical shifts were calibrated by monitoring the difference frequency between the sweep and manual oscillator (locked on internal TMS) outputs. The ambient probe temperature was determined by thermocouple measurements. The DA-60-IL is interfaced with an

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(21) G. Fraenkel and C. Franconi, *J. Amer. Chem. Soc.*, **82**, 4478 (1960).

(22) It should be noted that as ρ increases, the amount of 1:1 complex, LSR:TMC, present also increases. However, under the conditions of this study, the 1:2 complex strongly dominates the equilibria.[9c] At ρ = 0.5, the amount of *bound* TMC in the 1:1 complex form is still only $\sim 9\%$. The k_{obsd} is, of course, really a weighted average of k_{free}, $k_{1:2\,\text{adduct}}$, and $k_{1:1\,\text{adduct}}$. The k_{adduct} reported is dominated by $k_{1:2\,\text{adduct}}$. In actuality, both $k_{1:2\,\text{adduct}}$ and $k_{1:1\,\text{adduct}}$ are most likely equal and zero.

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IBM 1800 computer. As the spectra were taken, they were directly digitized (up to 1024 points/spectrum) and stored on magnetic tape[27] and punched cards. The data were preprocessed on an IBM 360/67 computer for base-line adjustment and conversion to conventional nmr units. The spectra were analyzed on the 360 with a computer program based on the classical modified Bloch equations for uncoupled two-site exchange.[1c] The search routine for this program is based on that described by Gutowsky, et al.,[18] and has been modified slightly by Professor T. L. Brown and his students at the University of Illinois and ourselves. The program requires, as input parameters, information about the scan, the populations of the two sites, and the line widths ("effective" T_2's) of the two sites and the

(27) E. J. Runde, M.S. Dissertation, State University of New York at Stony Brook, 1970; to be published by E. J. Runde and P. C. Lauterbur.

chemical shift difference ($\Delta\nu_\infty$) in the absence of exchange. The preexchange lifetime, τ, is varied by the program until a best fit is found. The fitted spectra were edited (the large number of points produced a cluttered plot-out) by the 360 and plotted with a Calcomp 1627 plotter by the 1800.

A Probe of Chelated Zinc(II) Environments Using Chlorine-35 Nuclear Magnetic Resonance[1]

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Abstract: Nine zinc chelate systems have been studied by the ^{35}Cl nmr probe method. Bidentate, tridentate, and quadridentate ligand molecules have been included in the study. Molar relaxivities are reported for both 1:1 and 1:2 zinc chelates. This parameter is suitable for characterizing a metal ion environment in terms of the quadrupolar relaxation of ^{35}Cl nuclei that it can produce in 0.5 M NaCl. It is shown that bidentate chelation of Zn^{2+}(aq) can be expected to increase its effectiveness in producing ^{35}Cl relaxation. Tridentate chelation can either increase or decrease the amount of relaxation caused by zinc. The least relaxation is produced when ligand atoms have formal negative charges and large acidity constants. In some instances, Zn(II) which is chelated by four ligand atoms is effective at ^{35}Cl relaxation. This, therefore, does not necessarily represent a coordinately saturated environment. Molar relaxivities for 1:1 and 1:2 chelates usually differed. In these cases it was possible to derive formation constants from the nmr data. These in general are consistent with literature values. In a number of systems hydrolysis-type reactions are readily identified.

There have been a number of reports in which ^{35}Cl nmr has been used to study bound metal ion environments in solution. The method has been called the halide ion probe method and has been described in several places.[2-4] Usually the systems studied have contained bound metal ions in rather poorly defined environments as sensed by halide ions. The experiments were used either to monitor changes in those environments or to derive a more detailed understanding of the actual metal ion binding site. The latter application is difficult because model systems have not been studied. In the work reported here, relatively simple chelate systems are examined whose structures have been previously investigated by other methods. The aim has been to study how Cl$^-$ probe ions interact with these model systems.

It was reported some time ago that the presence of certain metal ions in NaCl solutions increased the observed nmr relaxation rate for ^{35}Cl nuclei. This happens because small concentrations of chloro complexes are formed and these provide centers for quadrupolar relaxation. The relatively few bound ^{35}Cl nuclei have very short relaxation times. The remaining ^{35}Cl are in a rather symmetrical aqueous environment characterized by a relatively long T_2. If chemical exchange is sufficiently rapid, only a single nmr line is observed whose width can be used to infer the properties of the metal ion sites at which Cl$^-$ bind. Nuclear relaxation times and line widths are related by $T_2 = (\pi\Delta\nu)^{-1}$. The full nmr line width at half-maximum, $\Delta\nu$, is given by eq 1 for a particular ^{35}Cl environment[5] and by eq 2 for an exchange averaged line.

$$\Delta\nu_i = (^2/_5\pi)(e^2q_iQ)^2\,\tau_i \qquad (1)$$

$$\Delta\nu_{\text{obsd}} = (^2/_5\pi)(e^2Q)^2\sum_i(f_iq_i{}^2\tau_i) \qquad (2)$$

In the equations, e is the electronic charge, Q is the quadrupole moment for ^{35}Cl, and f is the probability that a ^{35}Cl nucleus will be found at a site of type i. It is assumed that a bound ^{35}Cl nucleus experiences an axially symmetric electric field gradient, q, whose orientation is time dependent and characterized by a correlation time, τ.

(1) This work was performed under the auspices of the U. S. Atomic Energy Commission.
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