concentrations of metal ion the rates of solvolysis are leveling off.

The enhanced rate of solvolysis as a function of cation concentration strongly suggests that the solvolysis results from the formation of a dissociable complex between geranyl PP or chrysanthemyl PP and a divalent cation. From the dissociation constants of Mg geranyl PP and Mn geranyl PP, one can calculate that at 1 mM metal ion concentration essentially all of the geranyl PP exists as the monometal salt.[15] Yet, at this concentration the rate of solvolysis of the allylic pyrophosphate is not significantly above control values. Consequently, the formation and decomposition of another, most likely M_2-geranyl PP rather than M_1-geranyl PP, must be responsible for the enhanced solvolysis we have observed. The shape and position of the two curves are very similar. Thus the fivefold greater rate observed with Mn^{2+} could be attributed to the stability of the metal ion allylic pyrophosphate complex rather than to a difference is dissociation constants. The dissociation constants for the formation of M_2-geranyl PP can be estimated from the curves graphed in Figure 1 and are ~0.7 M.

The requirement for a second divalent cation for promotion of the solvolysis of an allylic PP is of particular interest since we have shown that two metal ions are bound per catalytic site of prenyltransferase when substrate is present.[3] Since the divalent cations are required for catalysis by prenyltransferase, we would like to postulate that the two metals bound with the allylic substrate serve to ionize this substrate and in so doing initiate the catalytic sequence of prenyltransferase and that one of the functions of the enzyme is to properly orient the metals and allylic pyrophosphate in the catalytic site.

The demonstration that the rate of chrysanthemyl PP solvolysis is enhanced by a divalent cation strengthens the suggestion that enzymes that use cyclopropylcarbinyl PP systems as substrates (phytoene and squalene synthetases) also proceed by a reaction mechanism that is initiated by ionization.[17,18]

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Selenium-77 Relaxation Time Studies. Considerations Regarding Direct Observation of Selenium Resonances in Biological Systems

Sir:

Selenium has for a number of years attracted biological interest, most notably for the selenosis that adversely affects livestock and its implication as a carcinogen. More recently it has been linked to the metabolism of vitamin E and the prevention of liver necrosis.[1] Its importance has prompted us to consider selenium NMR as a probe for investigating its role in these biological systems. Appealing features of ^{77}Se NMR are the pronounced sensitivity of the nuclear shielding to the chemical environment (the established shift range is over 1500 ppm)[2] and the stereospecificity of the coupling constants.[3] The technique therefore has great potential to afford valuable new information to supplement the present knowledge of this essential nutrient.

The low natural abundance (7.5%) and relative NMR sensitivity (6.97×10^{-3} that of the proton) of the ^{77}Se isotope combined with the concentration problems which one generally must be concerned with in biological applications pose significant experimental difficulties. These problems can be minimized by the use of Fourier transform (FT) NMR through which substantial gains in the signal-to-noise ratio over conventional NMR may be realized.[4] To take full advantage of the FT method a knowledge of the inherent spin-lattice relaxation time, T_1, of the selenium nucleus is desirable since it influences the time duration of the experiments (via the recycle time between pulses).[5] The T_1s also provide valuable information concerning molecular dynamics. In general, several mechanisms are known to contribute to the relaxation of spin ½ nuclei and the possible variation in the magnitude of T_1 is considerable,[5b,6] but there is no information to date relative to selenium-77. Accordingly, we have initiated a study of ^{77}Se spin-lattice relaxation in some model compounds.[7]

All samples were degassed by a series of freeze–pump–thaw cycles before sealing under dynamic high vacuum. The T_1 and nuclear Overhauser effect (NOE) enhancements were determined in a standard manner.[6a,8,9] The select group of compounds investigated ($(CH_3)_2Se$, CH_3SeH, $(CH_3)_2Se_2$, $(C_6H_5)_2Se_2$, and $(C_6H_5CH_2)_2Se_2$) are representative of the three most common chemical environments in which selenium is expected to be found in biological systems.

The NMR parameters for the series of compounds are shown in Table I. For all compounds an Arrhenius plot of the observed relaxation rate, R_1*, vs. the reciprocal temperature exhibited a negative slope. The linearity of these plots (Figure 1) along with the lack of a Se-{^1H} NOE enhancement points

Table I. ^{77}Se NMR Parameters of Some Organoselenium Compounds[a]

Compd	Temp, °C	T_1^{OBS}, s[b]	T_1^{DD}, s[c]	E_a^{SR}, kcal/mol[d]	Chemical shift, ppm[e]	$\Delta\nu_{1/2}$, Hz[f]	$^nJ_{SeH}$, Hz $n=1$	$^nJ_{SeH}$, Hz $n=2$
$(CH_3)_2Se$	−60	24.4	626	−1.8	0	0.5		10.0
	32	7.5						
C_2H_5SeH	−60	9.5	248	−2.2	38.7	0.7	43.0	
	40	1.6						
CH_3SeH	−55	4.3	112	−1.6	−130.3	0.5	43.0	10.0
	40	1.4						
$(C_6H_5CH_2Se)_2$	18	31	809	−0.7	411.5	1.4		14.4
	55	27						
$(C_6H_5Se)_2$	0	31	809					
	45	20		−1.7	480.6	1.1		
$(CH_3Se)_2$	0	13	339	−1.4	280.6	1.0		12.7
	45	9						

[a] Measurements at 19.1 MHz in $CDCl_3$ solvent. [b] Inversion-recovery pulse sequence. Estimated error <10%. [c] Within experimental error (±10%) no NOE was observed for any of the compounds. The reported values are based on an arbitrary NOE of 0.10 and therefore represent lower limits for T_1^{DD}. [d] Spin-rotation activation energy obtained from the slopes of the Arrhenius plots. [e] A positive chemical shift is deshielded with respect to Me_2Se. [f] Half-height line width.

to the fact that a single mechanism, spin rotation (SR),[10] dominates the relaxation of selenium-77 in these compounds.[5b,6a]

The importance of spin-rotation relaxation is not surprising in light of the large chemical shift range for ^{77}Se.[11] The absence of a measurable NOE can be explained principally in terms of the spacial orientation of the nuclei. The dipole-dipole (DD) mechanism has the approximate form

$$R_1^{DD} \propto \alpha(\gamma^2_{Se}\gamma^2_H/r^6_{SeH})\tau_c \qquad (1)$$

where τ_c is the reorientation correlation time of the Se-H vector, r_{Se-H} is the internuclear separation, and the γs are the respective gyromagnetic ratios.[5b,6a] The relatively long Se-H distances (2.53 Å in dimethyl selenide,[12] with similar values expected for the diselenides and the alkyl portions of the selenols) and the inverse sixth power dependence of R_1^{DD} on this distance mitigate against an efficient dipolar interaction. Even the directly bound protons of the selenols are too far removed (1.44 Å in C_2H_5SeH)[13] to contribute significantly. A comparison with the 1.09-Å C-H bond distance indicates that a 9.3-fold reduction in R_1^{DD} per bound proton is expected for selenium-77 relative to carbon-13. A similar reduction has been noted in ^{29}Si studies of silicones for some molecules containing direct Si-H bonds.[14] A further reduction in R_1^{DD} relative to carbon-13 follows from the smaller gyromagnetic ratio of selenium-77 ($\gamma^2_{Se}/\gamma^2_C = 0.57$).

Chemical-shift anisotropy relaxation may be ruled out from the temperature dependencies of the R_1s.[5b,6b] The possibility of a scalar coupling mechanism, which could result from intermolecular exchange of the selenol protons,[5b,6b] is unlikely in view of the complete retention of the Se-H spin-spin coupling, and the sharpness and high-field shift of the selenol protons (δ −0.6 ppm in $CDCl_3$ relative to TMS).

The dipole-dipole and spin-rotation mechanisms have inverse temperature dependencies, with the former being more effective at lower temperatures (τ_c in eq 1 increases).[15] As the data in Table I indicate, however, no appreciable NOE ensues on lowering the temperature, even for the most favorable cases, the selenols. Assuming that the extreme narrowing condition is valid, a maximum NOE of 2.61 for complete ^{1}H-Se dipolar relaxation may be calculated.[6a,16] This value and the observed NOEs allow one to calculate[17] the lower limits for T_1^{DD} shown in Table I assuming that only SR and DD contribute to the relaxation.

The much greater magnitude of the T_1 values for the diselenides is thought to be primarily due to a more restricted motion in these compounds.[5b,6] The importance of size alone can be seen by the decrease in T_1 in the series dibenzyl > diphenyl > dimethyl diselenide. An electronic configuration

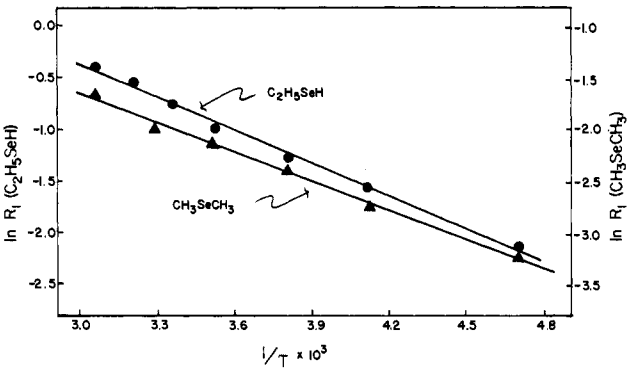

Figure 1. Arrhenius plot of the temperature dependence of the observed relaxation rates ($R_1 = 1/T_1$) of C_2H_5SeH (correlation coefficient −1.00) and $(CH_3)_2Se$ (correlation coefficient −0.99).

peculiar to the Se-Se bond[18] that reduces the spin-rotation coupling constant could also lead to the higher values.[11]

In conclusion, it has been shown that, in three types of organoselenium compounds, the spin-rotation mechanism dominates the spin-lattice relaxation of ^{77}Se and the usual NOE enhancement which is beneficial to ^{13}C NMR studies is relatively insignificant in ^{77}Se NMR. Our initial impetus for these studies was to determine the applicability of ^{77}Se NMR toward the study of biologically important molecules. For small selenium molecules (e.g., an enzyme substrate) interacting with a macromolecule the technique should be readily amenable for both characterization and kinetic studies. Where the selenium nucleus is part of the macromolecule, detection of the ^{77}Se resonance may present a more formidable problem. Here the selenium will for the most part adopt the reorientation time of the macromolecule and the spin-rotation mechanism, which is so effective in shortening the T_1s in the small selenium compounds, will undoubtedly be lost. Although under these conditions the dipole-dipole mechanism should become more effective it was seen to be very ineffective in the small molecules and a considerable enhancement of its efficiency will be required. It is important not to overgeneralize in extrapolating from small systems to macromolecules, however, since other mechanisms not yet observed in the small molecules, such as chemical shift anisotropy, may come into play when the correlation time is greatly increased.[4,19] Also, local motions of the selenium moiety on the surface of the macromolecule may be important. Further studies are currently underway in our laboratories to elucidate ^{77}Se relaxation mechanisms in larger molecules.

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Structure–Energy Correlations for Hydrazine and 2-Tetrazene Oxidation Potentials

Sir:

The tetraalkylhydrazine, hydrazine radical cation redox equilibrium is electrochemically reversible (electron transfer is rapid and the cation radical long lived relative to the time scale of cyclic voltammetry experiments), allowing easy measurement of the thermodynamically significant standard potential, $E°$. $E°$ becomes more positive as it becomes more difficult to remove an electron. $E°$ values measured to ±0.01 V (0.2 kcal/mol) have been reported for a series of tetraalkylhydrazines with a variety of alkyl substituents,[1] giving a set of relative free-energy differences between radical cation and neutral hydrazine. Unlike many reversible redox equilibria, great structural reorganization takes place upon loss of an electron from a hydrazine. Neutral hydrazines have nearly tetrahedral nitrogens,[2] and there is a decided electronic preference for gauche lone pairs, so that, even with rather large alkyl groups, the lone pair–lone pair dihedral angle remains near 90° in the absence of N_1,N_2 bridging.[3] The radical cations are best described as "three electron pi-bonded" structures, and have olefin-like geometries, but the ease of bending at nitrogen is considerably greater than the case of bending at the carbons of an olefin, and the equilibrium geometry is sometimes nonplanar at nitrogen, although activation energies for double nitrogen inversion are quite low.[4] As a consequence of the geometrical change upon electron removal, a hydrazine radical cation has increased R-N_1N_2-R steric interaction relative to that of the neutral hydrazine. When a bulky enough alkyl group is attached to nitrogen, like a *tert*-butyl group, this increase in R-N_1N_2-R strain becomes dominant, and $E°$ increases sharply. Nevertheless, there is a measurable decrease in $E°$ upon *N*-alkyl group homologation, and even upon introduction of α branching by inclusion of isopropyl substituted compounds.[1] For real understanding of the $E°$ values observed for tetraalkylhydrazines, it is necessary to be able to separate the steric and electronic effects observed upon changing alkyl group.

Table I. $E°$ Values (V vs. SCE, in Acetonitrile Containing 0.1 M Sodium Perchlorate) for Some Tetraalkylhydrazines and Tetraalkyl-2-tetrazenes

Substitution	Hydrazine I	2-Tetrazene II
$R_i = CH_3$	0.28[a]	0.41
$R_1 = R_3 = CH_3CH_3$; $R_2 = R_4$ CH_3	0.26[a]	0.36
$R_i = CH_2CH_3$	0.24[a]	0.33
$R_i = CH_2CH_2CH_3$	0.24[a]	0.31
$R_i = CH_2CH_2CH_2CH_3$	0.24[a]	0.30
$R_i = HC(CH_3)_2$		0.23
$R_1 = CH_2Ph$; $R_2 = R_3 = R_4 = CH_3$	0.35	
$R_1 = R_2 = CH_2Ph$; $R_3 = R_4 = CH_3$	0.44	
$R_1 = R_3 = CH_2Ph$; $R_2 = R_4 = CH_3$	0.43	0.51
$R_i = CH_2Ph$	0.60	0.59

[a] From ref 1, where the other saturated alkyl compounds plotted in Figure 1 are also tabulated.

The idea that the electron-releasing effect of alkyl substituents increases with homologation and α branching was expressed quantitatively in terms of σ^* constants by Taft[5] and, as Shorter has pointed out, is rather firmly ingrained in the thinking of organic chemists.[6] The effects are not particularly large, and Ritchie has shown that, for some systems, Taft correlations work as well when σ^* is assigned as zero for simple alkyl groups.[7] Inversions in the σ^*-predicted order are also known, as Brauman and Blair[8] showed for the vapor phase acidity of alkyl alcohols and as Bordwell and coworkers[9] demonstrated in solution for 9-fluorenes with a CH_2, S, or SO_2 interposed between the ring and the alkyl group. The idea that detectable differences in "electronic effects" by different saturated alkyl groups are present in solution at all has been challenged by Charton,[10] who restudied ester and amide hydrolysis data extensively, concluding that the Taft assumption of identical steric effects in acid and base catalyzed ester hydrolysis which led to Taft's σ^* evaluation is frequently wrong, that σ^* values do not reflect differences in electrical effects, but, rather, involve steric factors, and that alkyl groups do not differ significantly in their electrical effects.[10a] We have seen one reply to Charton's arguments which focused on methodology in data treatment.[11]

We report here data indicating that alkyl groups do indeed show a detectable difference in their ability to stabilize dialkylamino radical cations relative to the neutral compounds in solution, and that σ^* does give a useful linear correlation with alkyl electronic effects. For any test of the value of σ^* in quantitatively indicating alkyl group electronic effects, benzyl