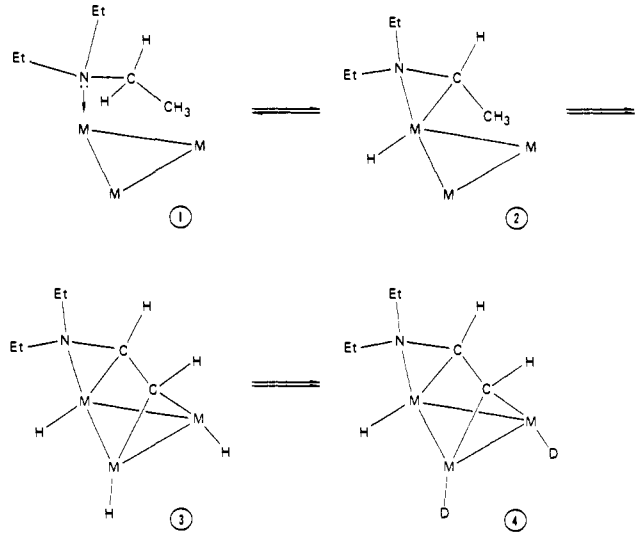
Scheme I



and Deeming and Yin.[14] The methyl group now lies above the plane of the metal triangle and can react with the remaining two metals to produce the insertion product (**3**).[15] If exchange of deuterium for hydrogen (**3** → **4**) is faster at the two metals not bound to nitrogen and the reactions **3** → **2** and **2** → **3** are faster than **2** → **1**, then the major products must be $Et_2NCHDCD_3$ and $Et_2NCH_2CD_3$.

To test this proposed mechanism, we substituted 6.0 mL of $(CH_3CH_2CH_2)_3N$ ($(npr)_3N$) for Et_3N with the expectation that $(npr)_2N$-$CHDCD_2CH_3$ and $(npr)_2NCH_2CD_2CH_3$ would be the major products. After the compound was heated for 20 h under identical conditions, 1.6% d_3 as $(npr)_2CHDCD_2CH_3$ and 0.7% d_2 as $(npr)_2NCH_2CD_2CH_3$ were the only significant deuterated products found.[16] The lower exchange rate as compared with Et_3N is probably the result of increased steric interactions.

This reaction represents one of the few homogeneous catalytic reactions wherein activation of hydrogen at saturated carbon occurs.[6,17] Recently Murahashi et al.[18] have reported the catalytic activation of tertiary alkyl amines by heterogeneous platinum catalysts wherein deuterium exchange experiments indicate metal insertion into the α-carbon–hydrogen bond. This suggests that the present homogeneous catalyst system could be used advantageously for modeling heterogeneous catalytic reactions such as that reported by Murahashi. Moreover, since the experimental data implicates the need for three metal centers (a cluster) during catalysis, then the work described here constitutes validation for Muetterties proposal that homogeneous metal cluster catalysis can be used to model heterogeneous catalytic reactions.[19]

The studies of Deeming[14,15] and Kaesz[13] indicate that this type of homogeneous catalysis reaction may be common to a number of transition metal carbonyl complexes, especially those of group 8.

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(6) While exchange of deuterium for hydrogen at saturated carbons is documented in the literature (see, for example, A. E. Shilov and A. A. Shteinman, *Coord. Chem. Rev.*, **24**, 97 (1977), the present case appears to be without precedent because of the mechanism of exchange and the unique selectivity by which exchange occurs.
(7) Electron impact mass spectra were obtained with an LKB 9000 mass spectrometer equipped with a gas chromatograph. Chemical ionization mass spectra were obtained on a modified Du Pont 21-490B mass spectrometer as described in ref 7b. Replicate mass spectral data are reproducible to better than 0.4% of the base peak (equals 100.0%). All of the quantitative results reported are obtained from averages of three mass spectra, and are corrected for natural abundances of ^{13}C and ^{15}N. (b) P. Price, D. P. Martinsen, R. A. Upham, H. S. Swofford, Jr., and S. E. Buttrill, Jr., *Anal. Chem.*, **47**, 190 (1975).
(8) When H_2O is substituted for D_2O, the catalyst solution actively catalyzes the WGSR with an activity of ~2 mol of H_2 produced per hour per mole of catalyst. A similar solution using 0.1 mmol of $Ru_3(CO)_{12}$ as catalyst has an activity of ~12 mol of H_2 produced per hour per mol of catalyst. The ordering of activities is opposite to those we have observed previously using KOH as base. (See ref 2b,c and 5b.) This suggests that the amine severely affects the mechanism of catalysis of the WGSR for one or both of the catalysts.
(9) A blank reaction run for 20 hr without catalyst produces ~0.5% d_t products.
(10) Note that d_5–d_8 deuterated species are found (<1% of the total exchange products). Of these, the major product is d_8 followed by d_7, which indicates that the d_5–d_8 exchange products result from selective exchange at two ethyl groups.
(11) Deuterium NMR spectra were run on an XL-100-15 FT spectrometer modified for multinuclear operation. $CDCl_3$ is used as internal standard. The relative integration of the CD_3– to the –CHD– is lower than predicted from the mass spectral analyses. This is probably attributable to different T_1 values for $-CD_3$ vs. –CDH–.
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Correlation Time Measurements of Amino Acid Side Chains from ^1H Selective Spin-Lattice Relaxation Rates

Sir:

Correlation times are routinely evaluated from ^{13}C T_1 measurements,[1-4] but few determinations using ^1H T_1 techniques exist.[5] Here we report correlation times derived from ^1H and ^{13}C relaxation times in both concentrated and dilute solution of *N*-acetyl-D(*allo*)-isoleucine (**1**). This method is generally applicable to all molecules having a known geminal, or otherwise defined, interproton distance and has the advantage of applying to dilute solutions (in any solvent) or to molecules of greater molecular weight or complexity. It is not even necessary that the molecule have a determined crystal structure; the interproton distance could be derived from dihedral scalar coupling constants and the appropriate Karplus curve.

Many mechanisms, m, can determine proton relaxation pathways and, generally, if $R_1^i = 1/T_1^i$,

$$R_1 = \sum_{i,m} R_{1m}{}^i \qquad (1)$$

In the extreme narrowing limit for the intramolecular dipole–dipole interactions of a proton, i, and all neighboring protons, j,

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$$R_1^i = \sum_{j \neq i} R_1^{ij} \quad (2)$$

where

$$R_1^{ij} = [\gamma_H{}^4 h^2][d_{ij}]^{-6}[\tau_c{}^{ij}] \quad (3)$$

To account for cross-relaxation which occurs during nonselective ^1H T_1 measurements we can write[6]

$$R_1^i(NS) = R_1^i + \sum_{j \neq i} \sigma_{ij} \quad (4)$$

Freeman and co-workers[7] have shown that R_1^i can be measured in the initial rate approximation[7] with the 180° − τ − 90° sequence provided that the 180° pulse is selective (e.g., 10 ms in our experiments) and that, in the extreme narrowing limit,[8] $[R_1^i(NS)/R_1^i] = 1.5$.

In a thoroughly dried and deoxygenated 2×10^{-2} M sample of **1** in Me_2SO-d_6 this ratio was 1.5 for both H-γ_1 and H-γ_2 showing that their relaxation was entirely intramolecular dipole–dipole. Double selective excitation experiments[9] of H-γ_1 and H-γ_2 gave all the experimental data to determine $\sigma_{\gamma_1\gamma_2}$ $\sigma_{\gamma_2\gamma_1}$ from the equations

$$R_1^{\gamma_1}(\gamma_1,\gamma_2) = R_1^{\gamma_1} + \sigma_{\gamma_1\gamma_2}$$

and

$$R_1^{\gamma_2}(\gamma_1,\gamma_2) = R_1^{\gamma_2} + \sigma_{\gamma_2\gamma_1}$$

Here the $R_1^{\gamma}(\gamma_1\gamma_2)$ and R_1^{γ} terms were obtained by double selective and monoselective experiments, respectively. In accordance with theory $\sigma_{\gamma_1\gamma_2} = \sigma_{\gamma_2\gamma_1}$ with a value of 0.290 ± 0.010 s^{-1}. By writing $2\sigma_{\gamma_1\gamma_2} = R_1^{\gamma_1\gamma_2} = \gamma_H{}^4 h^2 (d_{\gamma_1\gamma_2})^{-6}$. $(\tau_c{}^{\gamma_1\gamma_2})$ and assuming $d_{\gamma_1\gamma_2}$ = 1.8 Å, $\tau_c{}^{\gamma_1\gamma_2} = (3.4 \pm 0.2) \times 10^{-11}$ s.

The correlation time for the C^{γ}–H vectors was determined from ^{13}C T_1 measurements to be $\tau_c{}^{CH} = 6.5 \times 10^{-11}$ s, a value appreciably slower than $\tau_c{}^{\gamma_1\gamma_2}$. Since the ^{13}C T_1 sample had a concentration 40 times that of the −H T_1 sample, this discrepancy is to be attributable to viscosity and/or intermolecular effects. The fact that $\tau_c{}^{\gamma_1\gamma_2}$ for the ^{13}C T_1 sample was (5.8 ± 0.3) × 10^{-11} s, a value close to $\tau_c{}^{H\text{-}\gamma} = (6.5 \pm 0.5) \times 10^{-11}$ s, indicates that intermolecular effects are no larger than the experimental error.

(1) By combining nonselective and mono- and diselective excitation T_1 values and known geminal ^1H–^1H distances, τ_c can be calculated. This technique is generally applicable to simple and complex molecules, including amino acid side chains in peptides and proteins. (2) Measurements of τ_c are made at low concentrations and are significantly faster than those at the high concentrations typical of ^{13}C measurements. The two protons involved in these measurements should exhibit first-order coupling. (3) Extention of this method to nongeminal protons is possible, e.g., distances derived from dihedral scalar coupling constants and Karplus curves.

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Ultraviolet Resonance Raman Study of Oxytyrosinase. Comparison with Oxyhemocyanins

Sir:

Tyrosinase and hemocyanin are metalloproteins which contain an EPR-nondetectable binuclear copper active site often classified together with the binuclear sites in laccase, ascorbate oxidase, and ceruloplasmin as type 3 copper.[1] Both proteins interact with molecular oxygen: hemocyanin[2] functions as the oxygen carrier for molluscs and arthropods, whereas tyrosinase[3] utilizes oxygen in the hydroxylation of monophenols and the dehydrogenation of *o*-diphenols. Resonance Raman spectroscopy has been used to study the active site structure and mode of oxygen binding for various oxyhemocyanins. This communication reports the results of parallel studies on oxytyrosinase.

Oxytyrosinase is produced by the reaction of either mushroom[4] (*Agaricus bispora*) or *Neurospora crassa*[5,6] tyrosinase with hydrogen peroxide in the presence of oxygen. This protein derivative has an absorption spectrum remarkably similar to that of oxyhemocyanin (hemocyanin, $\epsilon_{345\ nm}$ 20 000 M^{-1} cm^{-1}, ϵ_{570} 1000; oxytyrosinase, ϵ_{345} 18 000, ϵ_{600} 1000) and has been postulated[4] to be a catalytic intermediate in the biological functioning of tyrosinase. Initial resonance Raman studies[7] on oxyhemocyanin (*Cancer magister*) used visible excitation frequencies (457.9–647.1 nm) and revealed an enhanced vibration at 744 cm^{-1} assignable to O–O stretching on the basis of its $^{18}O_2$ isotope shift. The frequency of the O–O stretch indicates that oxygen is bound as peroxide. More recent resonance Raman studies[8] on *Busycon canaliculatum* and *Limulus polyphemus* oxyhemocyanin involved UV excitation (351.1 and 363.8 nm). These spectra exhibit a cluster of bands in the metal–ligand region which have been tentatively assigned as copper–imidazole stretches and a remnant of the 742-cm^{-1} O–O stretch. Parallel resonance Raman studies were undertaken to investigate the increased reactivity of the bound oxygen in oxytyrosinase as compared to that in oxyhemocyanin.

Tyrosinase from *Neurospora crassa* wild-type strain was purified[9] by salt fractionation and a combination of ion-exchange and hydroxylapatite chromatography and stored as microcrystals in 20 mM sodium phosphate buffer, pH 6.8. Raman samples were prepared by dissolving the microcrystals in 20 mM sodium phosphate, 0.5 M sodium chloride, pH 6.8 buffer to a final concentration of 10–20 mg/mL (0.5–1.0 mM in copper). Approximately 30% of the dissolved tyrosinase was in the oxy form. Conversion of the resting protein to oxytyrosinase was accomplished by the addition of a 1.2–1.5 molar excess of H_2O_2 or a 5-fold molar excess of NH_2OH·HCl in the presence of oxygen. Oxytyrosinase containing $^{18}O_2$ (Stohler Isotope Chemicals) was prepared by repeated evacuation and

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