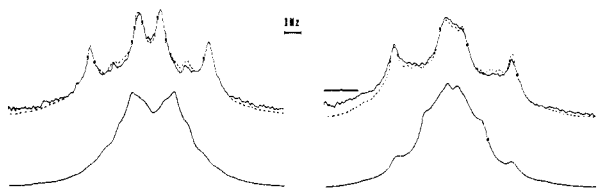


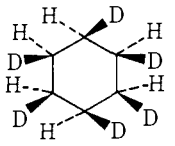
Figure 1. Top (solid line), experimental Fourier transform ^1H {D} NMR spectrum of I at −100° (the region indicated by the asterisk is affected by a nearby spinning side-band of the cyclopentane peak); top (dotted line), calculated and convoluted[7] ^1H {D} spectrum for *all-cis*-cyclohexane-d_6 (II); bottom: calculated and convoluted ^1H {D} spectrum of III.

isomer. As reported earlier,[3] the only compositional isomer we detect in this hydrogenation is $C_6D_6H_6$[5] (I). The ^1H NMR spectrum of I, with deuterons decoupled, is a single line at room temperature, in agreement with a structure of the type $(CHD)_6$, and shows that CH_2 groups are not present to a significant extent.[6] Much more information can be obtained at low temperatures under conditions that ring inversion is slow on the NMR time scale. Figure 1 shows the Fourier transform $^1H\{D\}$ spectrum of I in a CS_2 solution,[7] and a theoretical spectrum calculated for *all-cis*-cyclohexane-*1,2,3,4,5,6*-d_6 (II) with $\nu_{a,e}$ = 120.0 and $^3J_{ae}$ = 3.62, $^4J_{ee}$ = 1.90 and $^4J_{aa}$ = −0.30, and $^5J_{ae}$ = 0 Hz.[8] These parameters agree with chemical shifts and coupling constants found in other partially deuterated cyclohexanes at low temperatures,[8] with the exception of $^4J_{aa}$, which has not been determined before. A poor fit of the axial proton band shape occurs if $^4J_{aa}$ is zero or positive and a negative value is expected.[9] The agreement between the observed and calculated spectra is very good.

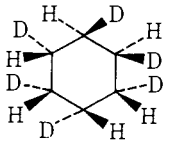
We have also calculated the spectrum (Figure 1) of *cis,cis,trans,cis,trans*-cyclohexane-*1,2,3,4,5,6*-d_6 (III) with the parameters given above and $^3J_{ee}$ = 3.0, $^3J_{aa}$ = 13.2, and $^4J_{ae}$ = $^5J_{aa}$ = 0 Hz.[8] If the hydrogenation proceeds through addition of pairs of hydrogen atoms in a cis-1,2 fashion with the formation of free $C_6D_6H_2$ and $C_6D_6H_4$ as intermediates, 25% of II and 75% of III should be produced, provided that secondary isotopes effects are negligible as is likely. Comparisons of the observed spectrum with sums of the spectra of II and III in various proportions show that the fits of the calculated to the observed spectra become progressively worse as the amount of III increases and that there must be less than 10% (and probably less than 5%) of III in the reduction product. The purity of the C_6D_6 reagent was 99.6 ± 0.1%; accordingly, there should be ~2.4% cyclohexane-d_5 in our product. Because the resonances of this compound are rather well spread out, this $C_6D_5H_7$ impurity has very little effect upon the simulated spectrum.

The pervasive facial hydrogen addition to arenes in the η^3-$C_3H_5Co[P(OCH_3)_3]_3$ system demands that certain stereochemical and qualitative features be accommodated in any viable outline of the intimate mechanism of the hydrogenation reaction. First and foremost, the arene once bound to the cobalt[10] must rarely leave until the sixth hydrogen atom is transferred. Secondly, a relatively fixed orientation of the ring must be maintained through the sequential hydrogen addition.[11,12] The ring must remain largely in a plane perpendicular to the C_6 centroid-cobalt axis. We defer speculation about the detailed geometric and electronic character of the intermediates until our synthesis of intermediates or models thereof is completed, but a reaction sequence previously presented by us[1] demands this stereochemical feature.

This unique reaction for stereospecific deuterium labeling of cyclohexane derivatives should be extendable to polynuclear aromatic hydrocarbons. In fact, naphthalene is hydrogenated in the presence of this cobalt catalyst to decalin. Careful GC-MS analysis of the product decalin against standard *cis*- and *trans*-decalin showed evidence only for the presence of the cis isomer. Clearly the gross stereochemical feature of the reaction with mononuclear arenes is established. Extensions to other polynuclear arenes are being made.



II



III

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(5) Within the limits of the GC mass spectrometric analysis.
(6) The isotope chemical shift effect is expected to be on the order of 0.015 ppm or 3.8 Hz at 251 MHz (H. Batiz-Hernandez and R. A. Bernheim, *Prog. Nucl. Magn. Reson. Spectrosc.*, **3**, 63 (1967). Thus, a single line would not be expected if both CHD and CH_2 groups are present.
(7) A small amount of cyclopentane was included in the sample to provide a line shape for convolution of theoretical spectra. The cyclopentane line had half-, quarter-, and eighth-height widths at −100° of 0.56, 1.5, and 2.5 Hz, respectively. An extra Lorentzian broadening of 0.17 Hz was also used in the calculations to take into account the finite rate of ring inversion in I and the fact that the decoupling was not quite complete.
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(10) More precisely, once the first hydrogen atom is transferred to the arene.
(11) At least to the point that the fifth hydrogen atom is transferred to the ring.

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Geminal and Vicinal ^{13}C–^{13}C Coupling Constants of 85% ^{13}C-Enriched Amino Acids

Sir:

During the last few years, the carbon-carbon coupling constants have been widely investigated,[1-10] most of the couplings observed being the single bonded $^1J_{C-C}$ type. This kind of coupling can reflect the hybridization state of the bonding orbitals and the electronegativity of the substituents of a molecule. Some recent studies[6,7] have shown that the geminal, $^2J_{C-C}$, and vicinal, $^3J_{C-C}$, exist. In general

Table I. $^{13}C-^{13}C$ Coupling Constants[a] Obtained from Amino Acids Enriched to 85% in ^{13}C

Amino acids	pH	$^1J_{0-\alpha}$	$^1J_{\alpha-\beta}$	$^1J_{\beta-\gamma_1}$ ($^1J_{\beta-\gamma_2}$)	$^1J_{\gamma-\delta}$	$^1J_{\delta-\epsilon}$	$^2J_{C-C}$	$^3J_{0-\gamma_1}$ ($^3J_{0-\gamma_2}$)	$^3J_{\alpha-\delta}$	$^3J_{\beta-\epsilon}$
Valine	11.2	53.1	33.6	35.1 (35.2)				2.4 (1.0)		
Threonine	0.7	58.8	36.3	37.5			$^2J_{\alpha-\gamma}$	2.3		
Aspartic	6.5	53.8	36.6	50.6			1.3	3.3		
Glutamic	0.9	59.6	33.6	35.9	53.8			1.5	3.4	
Pyroglutamic	1.0	59.9	29.3	32.5	45.0			1.1	7.5	
Lysine	7.0	53.6	34.2	34.5	34.0	35.4		~0.6	4.3	4.7
Arginine	7.6	53.4	33.7	34.1	35.8			~0.5	4.8	~0.5
Histidine	0.8	59.8	34.6	$^1J_{\beta-5}$ 51.0	$^1J_{4-5}$ 74.5		$^2J_{\beta-4}$ 5.9			
Tyrosine	11.3	53.2	33.0	$^1J_{\beta-1}$ 33.7	$^1J_{1-2}$ ($^1J_{1-6}$) 57.5	$^1J_{2-3}$ ($^1J_{5-6}$) 58.0	$^1J_{3-4}$ ($^1J_{4-5}$) 60.5	$^3J_{1-4}$ 7.6		

[a] The maximum error is 0.3 Hz.

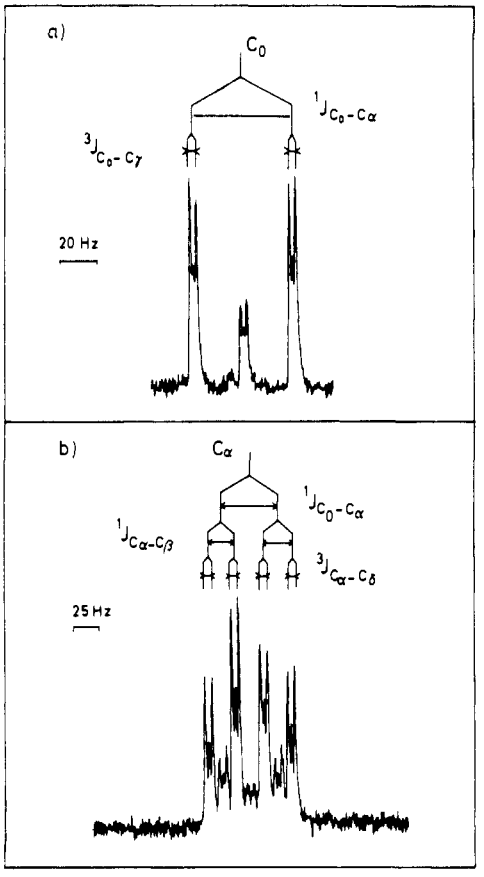

Figure 1. ^{13}C NMR spectrum of (a) the carbonyl carbon of aspartic acid (0.1 *M*, pH 6.0) and (b) C_α of pyroglutamic acid (0.15 *M*, pH 1.0). The bridges above these spectra indicate only the main multiplets.

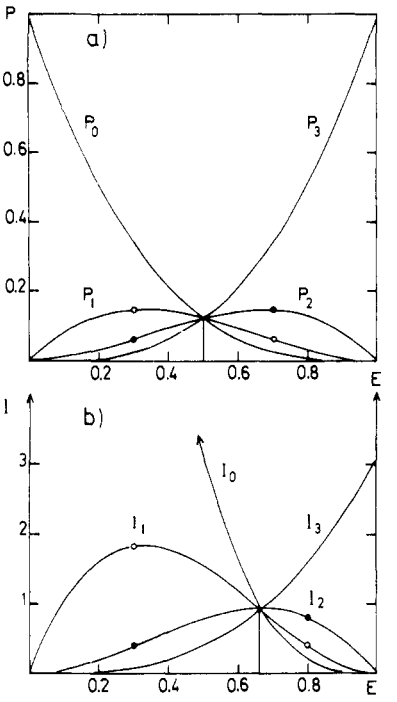

Figure 2. (a) Standardized probabilities and (b) relative intensities of different combinations for the case of one carbon coupled with three others, as a function of enrichment factor E ($0 \leq E \leq 1$). P_n ($n = 3, 2, 1, 0$) is the probability of the combination corresponding to the coupling with n ^{13}C sites, while $3 - n$ others are ^{12}C. There are a total of eight possible combinations: one for the case $n = 3$, three for $n = 2$ or $n = 1$, and one for $n = 0$. $P_3 = E^3$, $P_2 = E^2(1 - E)$, $P_1 = E(1 - E)^2$, and $P_0 = (1 - E)^3$. The spectrum of each combination consists of 8, 4, 2, or 1 peak belonging to $n = 3$, 2, 1, or 0. $I_3 = E^3/8$, $I_2 = E^2(1 - E)/4$, $I_1 = E(1 - E)^2/2$, and $I_0 = (1 - E)^3$. All the probabilities are equal when $E = 50\%$ and the relative intensities of all eight combinations are equivalent when $E = 66.7\%$. The scale of I on Figure 2b was chosen arbitrarily. In all cases the spectra are assumed to be first order.

$^3J_{C-C}$ is slightly higher than $^2J_{C-C}$ and varies with the dihedral angle ϕ. Nevertheless $^2J_{C-C}$ and $^3J_{C-C}$ are relatively small; their values lie between 0 and 5 Hz. Thus it is difficult to observe them if the enrichment factor is low (≤50%) and if the acquisition time is small (≤0.8 sec) when using the Fourier transform mode.

We would like to report here the single bonded, geminal and vicinal $^{13}C-^{13}C$ coupling constants carried out with a series of 85% ^{13}C-enriched amino acids. We think that these coupling data might be useful for theoretical studies to determine a Karplus-type relation correlating the geminal and vicinal $^{13}C-^{13}C$ couplings to the dihedral angles. The results are summarized in Table I.

Uniformly ^{13}C labeled amino acids were prepared by biosynthesis from the algae *Sprirulina Maxima*.[9] The ^{13}C NMR spectra were recorded at 25.15 MHz on a Varian XL 100 12 WG spectrometer. The apparatus operated in the pulsed Fourier transform mode associated to a 16 K 620f computer which allowed an acquisition time of 4 sec for a 1000-Hz spectral width (resolution = 0.25 Hz). Proton decoupling was obtained with a Varian Gyrocode spin decoupler. Neither sensitivity enhancement nor resolution enhancement was used in any of the spectra. The enriched amino acids dissolved in D_2O were run in the concentration range of 0.05 → 0.15 *M*. Figure 1a shows the C_0 spectrum of aspartic acid, a typical spectrum of one carbon (C_0) coupled with two others (C_α, C_γ). It consists of nine peaks in-

stead of three as generally observed for the terminal carbon. Although the extra splitting is small, only a few hertz, this could not be due to the incomplete proton noise decoupling, since, under the same experimental conditions, this phenomenon has not been observed in other compounds such as alanine and serine (pH 11). In addition the number of peaks and their relative intensities of the C_0 multiplet agree with theoretical predictions for the case of one carbon coupled with two others.[9] Figure 1b shows the C_α spectrum of pyroglutamic acid, a case of one carbon coupled with three others. Since the enrichment factor is lower than 100%, there are in all $2^3 = 8$ possible combinations of different ^{13}C or ^{12}C sites giving rise to a multiplet of $3^3 = 27$ peaks! The combination probabilities and their relative intensities as a function of enrichment factor E are plotted in Figure 2. We note that in the case of one carbon coupled with two[9] or three carbons, the intensities of different combinations are comparable when $E = 67\%$. Below this value, the main peaks decrease quickly and will be masked by the increased intensity of peaks due to other submultiplets. This probably explains why Sogn et al.[10] even using an intrinsic resolution of 0.12 Hz did not observe the geminal and vicinal couplings with 45% ^{13}C-enriched amino acids. In our previous papers[8,9] the chosen conditions (1.25 Hz of intrinsic resolution) did not allow, even with a ^{13}C-enrichment ratio of 85%, the good observation of these couplings.

With regard to the data in Table I, three remarks are in order. (1) In amino acids with only four carbons (aspartic acid, threonine) or a maximum of four carbons in the principal chain (valine), a vicinal coupling between C_0 and C_γ is observed. $^3J_{C_0-C_\gamma}$ is relatively small, varying from 1.5 to 3.5 Hz. (2) Amino acids with more than four carbons show vicinal coupling clearly between C_α and C_δ while $^3J_{C_0-C_\gamma}$ is lower than 1.5 Hz. $^3J_{C_\alpha-C_\delta}$ is usually higher than $^3J_{C_0-C_\gamma}$, varying from 3.5 to 7.5 Hz. These two remarks would be useful for assignment of terminal and nonprotonated carbons (aspartic, glutamic, pyroglutamic acids). (3) The geminal coupling constant is small ($\leq$1.5 Hz) in the case of saturated amino acids; however, this is not true for histidine where $^2J_{C_\beta-C_4}$ (5.9 Hz) is higher than $^3J_{C-C}$ ($\leq$1.2 Hz). In the case of tyrosine the peaks of aromatic carbons are broad and unresolved, and the geminal coupling constants between these carbons can therefore not be determined.

Doddrell et al.[7] have already given a theoretical curve for alcohols. We now try to establish with experimental data the same correlation. For that, we follow our investigation on selectively enriched rigid peptide molecules which shall give us information on the dihedral angles from the ^{13}C–^{13}C coupling values.

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Hydrogen Bond Cooperativity. The Methanol–Tri-*n*-octylamine System in *n*-Hexadecane

Sir:

Although the concept of a cooperative effect in formation of multiply hydrogen bonded complexes has gained rather wide popularity, there are very few experimental data from which even a roughly quantitative assessment of the magnitude of cooperativity may be extracted. Thermodynamic data which clearly show cooperativity effects are of potential importance in the formulation of improved theories of associated liquids, such as water.

One early suggestion of cooperativity was made by Frank and Wen with relation to their model for the structure of liquid water.[1] The nearest chemical neighbors of water—the lower alcohols—should also possess a degree of cooperativity in forming hydrogen bonded polymers if this effect is of importance. However, the long controversy over alcohol association still does not permit any absolute conclusions to be reached regarding cooperative effects in alcohol self-association.[2] It has been suggested for a number of years that the different OH frequency shifts in the infrared region for alcohol solutions in organic solvents show that the hydrogen bond strength in higher polymers is much more than that in dimers and/or trimers.[3] No previous thermodynamic data for alcohol association using enthalpies from models involving dimer and higher polymers will directly support the qualitative conclusions from frequency shifts.[2] The additional problem of discerning relative proportions of cyclic and acyclic alcohol polymers complicates the interpretation of self-association data.

One method which may be used to limit the possible structure types of hydrogen bonded species is to study the association of alcohols with a single site proton acceptor such as a tertiary amine. The possibility of forming cyclic alcohol–amine complexes is thereby excluded. With the occurrence of only linear complexes, the problem of examining hydrogen bond cooperativity is reduced to that of obtaining accurate values of equilibrium constants and enthalpies for the reactions.

Reagent grade methanol and *n*-hexadecane (Hx) were purified as previously reported.[4] Tri-*n*-octylamine (TNOA) (Aldrich) was purified by two distillations at low pressure through a wiped-film molecular still.

The distribution of methanol between vapor phase and Hx has been reported.[4] New measurements were made for the present study by a slightly different procedure and are fully described in the deposited data.[5] The experimental procedure consists of studying the vapor/solution distribution of MeOH in Hx and in Hx solutions containing added amine. The vapor pressure above these solutions is essentially due only to methanol. Data were taken at two amine concentration levels, ca. 0.07 and 0.18 M, at temperatures of 25, 35, and 45°. The thermostat bath temperature was controlled to ±0.005°. Methanol vapor pressure measurements were made using a Texas Instruments fused quartz precision pressure gage with a minimum resolution of 0.003 Torr absolute.

The basic assumption made is that Henry's law is obeyed by monomeric methanol and other solute species in the concentration range of 0–0.2 M MeOH in Hx. We additionally assume that the amine does not self-associate at the low concentrations used. The vapor pressure–concentration data are presented in Table I (supplementary material).[5]

The monomer methanol molarity in solution may be expressed as

$$C_A = K_D \frac{P_A}{RT}$$