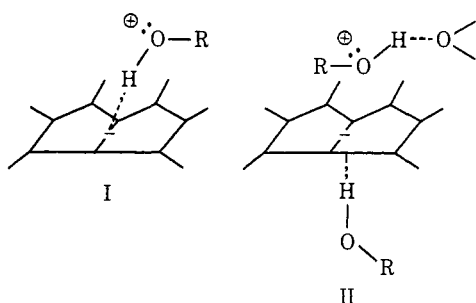


alcohol the new spectrum is fully developed (Figure 1). On addition of 1 equiv of the crown ether to this system, dramatic changes are observed in the spectrum. The rather broad bands in uv and visible regions narrow and red shift to give a separated ion-pair spectrum similar to that observed in aprotic media (Figure 1).

When these titrations are done with THF instead of THP, different phenomena are observed. The originally present bands corresponding to separated ion pairs (Table I) simply increase in intensity on addition of alcohol and no significant broadening or blue shift is apparent.

The above spectra can be most reasonably ascribed to ion pairs since calculated dielectric constants are low (<13) and because the changes observed on addition of crown ether to the THP- n -C₃H₇OH mixture cannot be explained on the basis of free anions.

Assuming that the broadened band near 380 nm in the THP- n -C₃H₇OH system is caused by H bonding, essentially two ion-pair structures can be envisioned,¹⁰ I and II.



Similar structures were first proposed by Cram and Gosser^{2b} in their work on the stereochemistry of substitution reactions at saturated hydrocarbon involving intermediate carbanions of a related type. On collapse of carbanion to hydrocarbon, I leads to retention and II to inversion of configuration. If II represents the structure of such an ion pair, its λ_{\max} should be essentially unaffected by the state of coordination of the cation. The data show that this is not the case. It seems then that H bonding is promoted by cation and takes place "front side." Thus in the presence of powerful cation solvating ethers such as THF and particularly crown ether, the cation-alcohol coordination is disrupted and H bonding is essentially absent. The specificity of this phenomenon is especially obvious with the crown ethers since only 1 equiv is added per ion pair. Competitive H bonding to crown ether is, therefore, impossible owing to the very high alcohol concentration ($\approx 3.5 M$).

The spectroscopic results reported above provide reasonable evidence for H bonding and the role of cations in such bonding in the systems described above and are in substantive agreement with the stereochemical evidence in similar systems.¹¹

(9) Because of partial protonation of carbanion, an isosbestic point cannot be observed in the titration.

(10) Several alcohol molecules may actually be hydrogen bonding the carbanion.

(11) Roitman and Cram, in their studies on electrophilic substitution at saturated carbon involving carbanions as intermediates,^{2a} observe racemization of asymmetric carbon and H-D exchange at about the same rate in the presence of equimolar quantities of base and crown ether, while in the absence of crown ether exchange with retention of configuration occurs. Other work on H-D exchange at asymmetric carbon^{2b} involving ammonium carbanion salts as intermediates indicates exchange occurring with retention.^{2b,c} It is interesting that in solvent systems where retention is observed the spectra of the FD⁻ ion pairs suggest front-side hydrogen bonding.

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T. E. Hogen-Esch

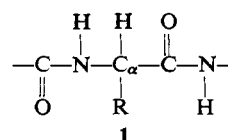
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Conformational Dependence of Vicinal H-N-C-H Coupling Constants in Peptides

Sir:

Recent extensive applications¹⁻⁵ of vicinal H-N-C-H coupling are beginning to complement other types of investigations of polypeptide structures in solution. This technique makes use of some assumed mathematical relationship between the vicinal coupling constant and the dihedral angle ϕ measured about the N-C _{α} bond in the polypeptide backbone **1**.⁶ In most cases



these relationships are of the form^{1-4,9,10}

$${}^3J_{\text{HH}'} = A \cos^2 \theta + B \cos \theta + C \quad (1)$$

which has been shown to provide an adequate representation of vicinal coupling in the H-C-C-H moiety.¹¹⁻¹⁴ In eq 1 θ is the dihedral angle measured

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(6) Two different conventions for the specification of the angle ϕ are in common use.^{7,8} The dihedral angle θ , which is used here, is related to these by $\theta = |\phi - 240^\circ|$ or $\theta = |\phi - 60^\circ|$.

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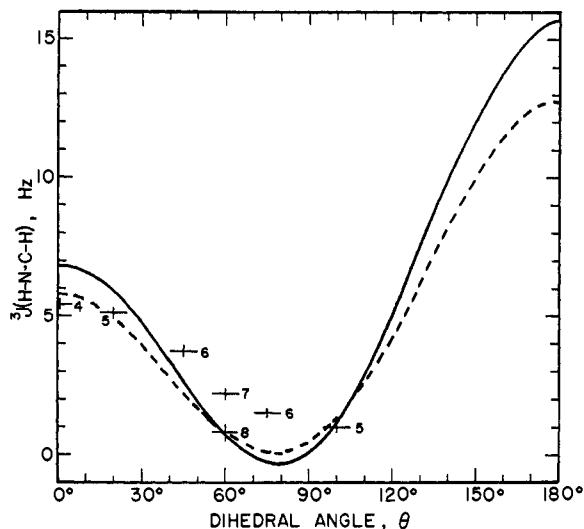


Figure 1. Plots of vicinal H-N-C-H coupling constants in *N*-methylacetamide having the cis arrangement 2 of the amide bond as a function of the dihedral angle θ . The solid curve is a plot of eq 2, whereas the dashed curve is a plot of the semiempirical expression of Thong, *et al.*⁹ Experimental data are plotted for compounds 4-8.

from the plane in which the two C-H bonds are eclipsed.

Calculations of vicinal H-N-C-H coupling constants were performed for the model compound *N*-methylacetamide by means of self-consistent perturbation theory¹⁵ in the semiempirical INDO (intermediate neglect of differential overlap) approximation¹⁶ of self-consistent-field molecular orbital theory. Since the proton positions for this molecule were not specified in the X-ray study,¹⁷ molecular geometries for both the cis and trans *N*-methylacetamide were based on the values proposed for the cis amide peptide linkage by Ramachandran and Venkatachalam.¹⁸ All calculations were performed on a Control Data Corp. 6400 digital computer.

Calculated values of $^3J(\text{H-N-C-H})$ for the cis (2) and trans (3) orientations of the amide bond, which



were obtained at 30° intervals of the dihedral angle, are entered in Table I. The calculated values in the table can be reproduced to within 0.05 Hz by the expressions

$$^3J(\text{H-N-C-H}) = 11.27 \cos^2 \theta - 4.32 \cos \theta + 0.01 \text{ Hz} \quad (2)$$

$$^3J(\text{H-N-C-H}) = 12.06 \cos^2 \theta - 4.48 \cos \theta + 0.01 \text{ Hz} \quad (3)$$

for the cis and trans arrangements of the amide bond, respectively. Equations 2 and 3 are plotted (solid

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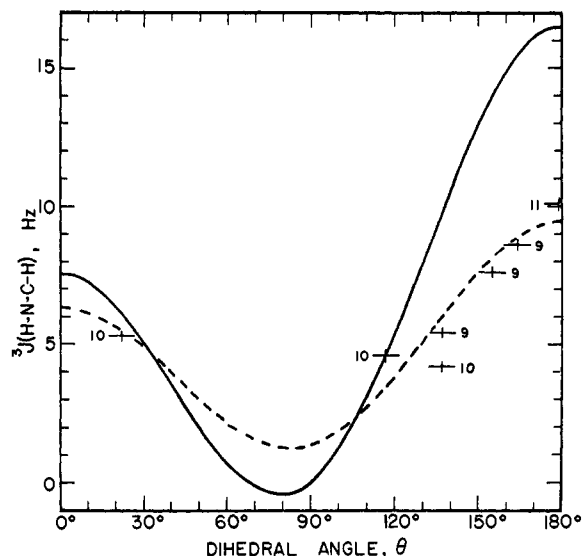


Figure 2. A plot of vicinal H-N-C-H coupling constants in *N*-methylacetamide as a function of dihedral angle for the trans arrangement of the amide bond. The solid curve is a plot of eq 3 and the dashed curve conforms to the semiempirical expression of Ramachandran, *et al.*¹⁸ Experimental data are for the ornithine (9) and glycine (10) residues of alumichrome.²³ Dihedral angles are those from the related compound ferrichrome A.²⁴ Experimental data are plotted also for the cyclotrisarcosyl-L-alanyl (11).²⁵

Table I. Calculated Vicinal H-N-C-H Coupling Constants at 30° Intervals of the Dihedral Angle θ for the Cis (2) and Trans (3) Orientations of the Amide Bond in *N*-Methylacetamide

Dihedral angle, θ , deg	$^3J(\text{H-N-C-H})$, Hz Cis	$^3J(\text{H-N-C-H})$, Hz Trans
0	6.856	7.553
30	4.695	5.166
60	0.712	0.788
90	0.014	-0.042
120	4.937	5.270
150	12.219	13.010
180	15.704	16.592

lines) as a function of the dihedral angle θ in Figures 1 and 2, respectively. The slight difference between the coupling constants for the cis and trans arrangements of the amide bond reflects a conformation dependent substituent effect, and provides a theoretical justification for the empirical assumption that a single expression should be adequate to describe both types of coupling constants.^{1-5,9-10}

The trans arrangement 3 of the amide bond is the most stable one for *N*-methylacetamide at room temperature.¹⁹⁻²¹ If it is assumed that the hydrogens of the methyl group occupy discrete rotational states with one of the methyl protons trans to the N-H proton, then the calculated average coupling constants for the cis (2) and trans (3) molecules are 5.7 and 6.1 Hz, respectively. With the same assumptions, but with values from the empirical curve in Figure 2, the values would both be 3.9 Hz. The experimental values for *cis*- and *trans*-*N*-methylacetamide are 5.3 and 4.8 Hz, respectively.^{19,20}

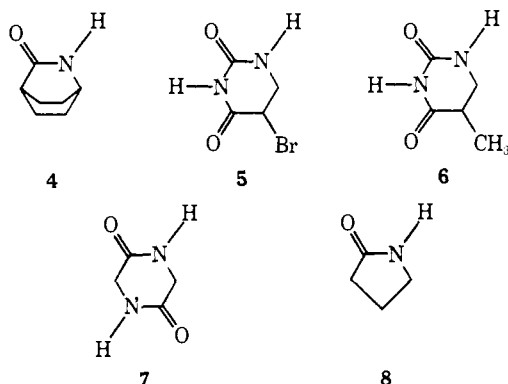
In general, for simple cyclic molecules with the cis

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amide linkage there is less conformational ambiguity than for those with the trans amide linkage because the symmetry of the molecule limits the number of allowable conformations. Experimental values of the vicinal H-N-C-H coupling constants for the compounds isoquinolidone (**4**),^{3,9} 5-bromodihydrouracil (**5**),²² dihydrothymine (**6**),³ diketopiperazine (**7**),³ and pyrrolidone (**8**)⁹ are plotted in Figure 1 for estimated values



of the dihedral angles. Nominal errors of $\pm 5^\circ$ were assumed for these angles which were based on symmetry or X-ray studies.^{3,9} Except in the region of large values of the dihedral angles, which are conformationally inaccessible for the cis amide linkage, there is generally good agreement of calculated and experimental results. The dashed curve in Figure 1 is the one of Thong, *et al.*,⁹ which was inferred from the experimental data points.

Experimental data for comparison with the theoretical results for molecules having the trans-amide linkage are based on nmr and X-ray data for cyclic hexapeptides and a tetrapeptide. However, in some cases the interpretations of the nmr data may be confused by the possibility that the conformational details in solution are different from those in the solid.^{4f} As a consequence, it is reasonable to expect that the experimental vicinal coupling constant data can reflect more motional averaging than would be expected for the simple compounds 4-8, which have the cis-amide linkage. Coupling constant data in Figure 2 are from the cyclic hexapeptide alumichrome.²³ This is an aluminum analog of ferrichrome A for which X-ray structural data are available.²⁴ From a space-filling model of the cyclic tetrapeptide cyclotrisarcosyl-L-alanyl²⁵ (point 11 in Figure 2), the dihedral angle must be near 180° . Therefore, the disparities between the experimental and theoretical results in Figure 2 for angles greater than about 130° must partially reflect an overestimation of the theoretical formulation. The situation is probably analogous to that for vicinal H-C-C-H coupling for which experimental values are most invariably less than 12 Hz,¹⁴ whereas the theoretical values^{26,27} for the trans orientation are closer

to the experimental value of about 18 Hz, which is estimated for ethane.²⁸

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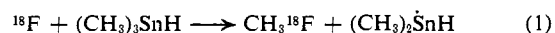
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Formation of Methyl Fluoride by Fluorine Atom Cleavage of Tin-Carbon Bonds in Trimethyltin Hydride and Tetramethyltin

Sir:

Fluorine atoms react directly with $(\text{CH}_3)_3\text{SnH}$ and $(\text{CH}_3)_4\text{Sn}$ in our experiments to cleave the Sn-C bond with the formation of methyl fluoride, as illustrated in (1). The ^{18}F atoms were formed in an energetic state



by the $^{19}\text{F}(n,2n)^{18}\text{F}$ fast neutron nuclear reaction in gaseous SF_6 and are thermalized by multiple collisions with the SF_6 which is present in excess.¹⁻⁷ When $(\text{CH}_3)_3\text{SnH}$ or $(\text{CH}_3)_4\text{Sn}$ is added in low mole fraction, the product CH_3^{18}F can be isolated and measured by radio gas chromatography with yields of about 5.6 and 8.3%, respectively, of the total ^{18}F . By analogy with other systems, most of the remaining ^{18}F atoms can be assumed to react by H atom abstraction to form H^{18}F .^{3,4} Molecules of H^{18}F so formed would have reacted with the glass sample container walls prior to chromatography and were not measured in these experiments. No attempt has yet been made to search for nonvolatile products from displacement on tin [*e.g.*, $(\text{CH}_3)_2\text{SnH}^{18}\text{F}$ or $(\text{CH}_3)_3\text{Sn}^{18}\text{F}$]. Many macroscopic problems for such systems—such as the corrosive nature of HF and disposal of the heat generated by the exothermicity of its formation—are avoided by the use of tracer levels of atomic fluorine (approximately 10^7 atoms of ^{18}F per experiment). All of the samples have been irradiated at the approximate temperature (10°) of the target area in the fast neutron generator used for formation of ^{18}F atoms.

When ^{18}F atoms are initially formed in an energetic state, a finite possibility exists that any particular reaction might have been initiated by the attack of a still-energetic ^{18}F atom. The probability of such *hot* reactions should be approximately proportional to the mole fraction of substrate $(\text{CH}_3)_3\text{SnH}$ or $(\text{CH}_3)_4\text{Sn}$, mixed with the SF_6 . In these experiments, however, the

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