1,2,2,4,4-pentadeuteriocyclobutyl chloride and 1,2,2,3,3-pentadeuteriocyclobutyl chloride in a 1:2 ratio. The rearranged dideuteriomethylene groups are statistically distributed among the 2, 3, and 4 positions as derived by interconversion of bicyclobutonium ion intermediates. There is no rearrangement involving transfer of hydrogen as required if bicyclo[1.1.0]butanes were reaction intermediates in this system. It may well be however that bicyclobutanes are significant intermediates in solvolytic reactions of highly energized cyclopropylcarbinyl and cyclobutyl cationic systems in environments of limited nucleophilicity. It will be of interest to determine if bicyclo[1.1.0]butane and its solvolytic products are formed *via* classical or nonclassical intermediates; upon extension of previous theory,[7] it is probable that bicyclo[1.1.0]butane will be formed from highly energized sources by classical rather than by nonclassical processes.

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The Role of Dipole Interactions in Determining Polypeptide Configurations

Sir:

As a consequence of the planar, *trans* conformation of the peptide linkage,[1,2] the distance between neighboring α-carbon atoms in the polypeptide is fixed within narrow limits, and the chain, shown in Figure 1, may be treated legitimately as a sequence of n_p virtual bonds of length l_p joining the α-carbons.[3] The mutual orientation of each pair of connecting virtual bonds, and hence the spatial configuration of the chain, is determined by the angles of rotation, φ''' and φ', about the two single bonds adjoining the intervening α-carbon. For a given such pair of single bonds, hindrances to rotation about one of the bonds are strongly dependent on the angle of rotation of the other, as is readily verified from molecular models. In contrast to the marked interdependence of rotations for the bonds comprising a given pair, the rotations of one pair are not significantly dependent on the angles of rotation of bonds in neighboring pairs.

A characteristic measure of the unperturbed dimensions[4] of the random polypeptide chain is given by $\langle r^2\rangle_0/n_p l_p^2$, the ratio of the actual mean square end-to-end distance, $\langle r^2\rangle_0$, to the mean square end-to-end distance for the random flight chain of virtual bonds, $n_p l_p^2$. Replacement of the continuous distribution of angles for rotations about the chain single bonds by sets of discrete rotation angles enables one to calculate theoretical values of $\langle r^2\rangle_0/n_p l_p^2$ from bond angles, bond lengths, and rotational potential functions using methods recently developed.[5] Because of the

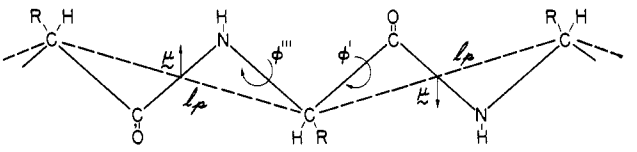

Figure 1. Virtual bonds are shown by dashed lines. Peptide group dipole moment vectors, $\boldsymbol{\mu}$, are depicted as arrows originating at the location of the dipole.

rotational interdependence within the pair of chain bonds adjoining an α-carbon, the potential function adopted must depend jointly on both rotation angles for the pair.

Calculations of $\langle r^2\rangle_0/n_p l_p^2$ based on small inherent sixfold torsional potentials and repulsive van der Waals interactions between nonbonded atoms yielded results smaller by a factor of about three than values estimated from the limited experimental data in the literature.[6] We therefore undertook experiments to determine $\langle r^2\rangle_0$ for poly-β-benzyl-L-aspartate in *m*-cresol at 100°, for poly-L-glutamic acid in aqueous 0.3 *M* sodium phosphate at pH 7.85 and 37°, and for poly-L-lysine hydrobromide in aqueous 1.0 *M* sodium bromide at pH 4.54 and 37°. The mean square end-to-end distances have been calculated from measured intrinsic viscosities, $[\eta]$, and osmotic molecular weights using the familiar relationship[4] $\langle r^2\rangle^{3/2} = [\eta]M/\Phi$, where $\Phi \cong 2.1 \times 10^{21}$ with $[\eta]$ in dl. g.$^{-1}$. Θ-Solvent conditions,[4] under which $\langle r^2\rangle$ assumes its unperturbed value $\langle r^2\rangle_0$, appear to be unattainable for these random polypeptides owing to the preference of the molecules for ordered configurations in poor solvents. The measurements were therefore conducted in the good solvents cited above, and the values of $\langle r^2\rangle$ obtained were corrected to $\langle r^2\rangle_0$ on the basis of measured second virial coefficients.[7,8] The polymers were unfractionated. A Poisson molecular weight distribution ($\bar{M}_w/\bar{M}_n \cong 1$) was assumed for the aspartate and lysine polymers; the most probable distribution ($\bar{M}_w/\bar{M}_n = 2$) was ascribed to the glutamic acid polymer. Errors attributable to departures from these assumed distributions affect the values of $\langle r^2\rangle_0/n_p l_p^2$ by no more than a few per cent.

A characteristic ratio of 9 ± 1 was found for all three polymers. Previously published results for poly-γ-benzyl-L-glutamate[6] yield a value in the same range. The experimental result is much larger than the value of 1.93 calculated assuming free rotation about the single bonds adjoining the α-carbons.[3,9] Thus, the same value of $\langle r^2\rangle_0/n_p l_p^2$ holds within experimental error for the four systems studied, marked differences in solvents and in amino acid side chains notwithstanding. It would appear that specific interactions between side chains, between side chains and backbone, or between polymer and solvent exert little effect on the unperturbed dimensions of these four molecules.

Further efforts to rationalize the experimental unperturbed dimensions in terms of the chain struc-

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ture through reasonable variations of the torsional and van der Waals potentials failed to reduce appreciably the discrepancy noted above. The polar character of the polypeptide molecule suggested investigation of the influence on the chain configuration of dipolar interactions between peptide units. The charge distribution within the peptide groups has been expressed by associating with each such group a point dipole moment vector of magnitude 3.7 D. This vector, shown as μ in Figure 1, is located in the plane of the peptide unit at the midpoint of the peptide bond. It makes an angle of 56° with this bond and points in the N–H direction. The assigned magnitude is consistent with the observed dipole moments of a number of alkyl amides[10]; the orientation specified above is suggested by the sum of peptide group bond moments[11] and supported by the observed dipole moment vector in formamide.[12] If the dielectric constant is assigned the value 3.5, then differences in nearest neighbor interaction energies as large as 3 kcal./mole occur for sets of discrete rotation angles which are not excluded by steric repulsions. Energy differences of this magnitude make decisive contributions to the rotational potential function. Calculations of the characteristic ratio carried out using rotational potentials which include the dipole–dipole contributions to the energy are in satisfactory agreement with the experimental results quoted above.

The strong influence of dipole interactions on the unperturbed polypeptide coil dimensions suggests that similar effects may play an important role in ordered polypeptide configurations as well. We have accordingly calculated the total dipole interaction energy for a peptide unit within and at the ends of α-helical sequences. Interactions between helix and coil units are ignored while those between peptide dipoles in the helix separated by more than 20 units in the chain sequence are found to be negligible. If the effective dielectric constant is again chosen to be 3.5, a peptide unit buried in a long α-helical sequence experiences a favorable dipole interaction energy of about -1.2 kcal./mole. This value does not, however, represent the net dipole contribution to the Zimm and Bragg[13] helix stability parameter, s, which must be estimated with reference to the average dipole energy for the random coil. Preliminary calculations suggest that dipole interactions are particularly important with respect to the parameter σ characterizing helix–coil junctions. These results will be included in a paper in preparation.

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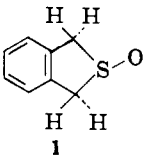
Dimeric Structure of a Sulfoxide

Sir:

Extensive current interest in the stereochemistry of sulfoxides has concerned various configurational equilibrations of this group. Recent communications[1] which have reported the inversion of configuration of the sulfoxide group by acid catalysis[1a,b] and by thermal isomerization[1c,d] prompt us to report an interesting and related observation made with the sulfoxide **1**, 2-thiaindan 2-oxide.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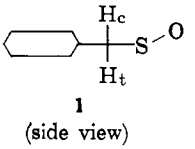
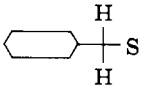

1 (side view)

It had occurred to us that this compound might be well suited to nuclear magnetic resonance studies of the inversion of the sulfoxide group. This system (**1**) should possess two types of n.m.r.-distinguishable methylenic hydrogens, the pairs *cis* and *trans* (H_c and H_t) to the oxygen of the sulfoxide group, which should yield a proton resonance "quartet"—actually two doublets, 2(AB).[2] It was conceived that under the proper conditions of temperature and acidity, rapid inversion of the sulfur–oxygen bond might be obtained producing a symmetrical environment for the methylenic hydrogens and a singlet n.m.r. signal.

The spectrum (Figure 1) at room temperature of the methylenic hydrogens of 2-thiaindan 2-oxide does consist of a quartet, which may be contrasted with the singlet signals obtained from the analogous but symmetrical systems of 2-thiaindan (**2**) and 2-thiaindan 2,2-dioxide (**3**). The quarter was observed to coalesce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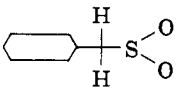
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to a singlet at room temperature in the presence of a 50% solution of deuterated trifluoroacetic acid in deuterium oxide. However, the interesting observation we wish to discuss here concerns a purely thermal effect on the methylenic n.m.r. signal of **1**.

N.m.r. spectra of **1** were obtained at temperatures ranging from $-50°$ to $+200°$. It was expected that at sufficiently elevated temperatures a purely thermal inversion of sulfoxide might occur and be revealed by coalescence of the methylene quartet. This coalescence was not observed, but conversely the splitting appeared more pronounced at 200°. Most startling of all, *the signal was observed to coalesce at low temperatures*, yielding finally a single sharp peak at $-37°$. These results suggested to us the possibility of some type of association between sulfoxide molecules.[3] Indeed,

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