TRANSITION DIPOLE INTERACTION IN POLYPEPTIDES: AB INITIO CALCULATION OF TRANSITION DIPOLE PARAMETERS *

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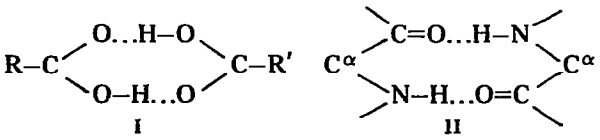
Received 22 March 1984

Ab initio calculations of dipole moment derivatives of a model system of N-methylacetamide hydrogen-bonded to two formamide molecules give values for amide I and amide II transition dipole moments consistent with those derived from observed band splittings in the spectra of polypeptides. Transition dipole coupling thus provides a reasonable mechanism for explaining these splittings.

1. Introduction

Observed splittings in the amide I and amide II modes of polypeptides have been attributed to interactions between peptide groups in the structural repeat [1]. However, the proposed couplings [1], through the intramolecular covalent force field and the intermolecular hydrogen bonds, were found from normal-mode calculations [2–4] to be inadequate in accounting for the observed splittings. It was shown [5,6] that when transition dipole interaction or coupling (TDC) is also included, a reasonable and consistent explanation of these splittings can be obtained. The transition dipole parameters derived from β-sheet spectra [3,4] have been successful in explaining splittings in α-helix [7], 3_1-helix [8], and 3_{10}-helix [9] polypeptides as well as in small peptide molecules [10–12]. This body of results provides compelling support for the presence of such an interaction mechanism in polypeptide systems.

Bosi and Zerbi (BZ) [13], however, have suggested on the basis of a CNDO calculation on formaldehyde that the magnitudes of the dipole moment derivatives required are unreasonably large. These authors then proposed [14] that in hydrogen-bonded acid dimers (I) dynamical charge transfer occurs during vibration, leading to interactions between the CO groups. While we agree that such a charge-transfer mechanism may be important in these and similar structures [15], we think that the effect will be much smaller in the larger hydrogen-bonded rings involving polypeptides with trans CONH groups (II).



I

II

As part of attempts to account for infrared intensities in peptides and polypeptides, we have recently calculated by ab initio Hartree–Fock procedures the dipole moment derivatives of the peptide group in N-methylacetamide (NMA); this was done for an isolated NMA molecule and for a model of NMA hydrogen bonded to two formamide molecules. Full details of our calculations and results on intensities will be given in a forthcoming paper [16]. We wish to discuss here those results that bear directly on TDC in polypeptides. We show that the conclusions of BZ are not relevant to polypeptide systems, and that the TDC parameters that our group has used are in good agreement with our ab initio results and with experimental data on intensities. Before discussing these results, we give a more careful treatment of the TDC formalism than has been presented in earlier papers in order to show clearly the meaning of the parameters involved.

* This paper is No. 25 in a series on "Vibrational Analysis of Peptides, Polypeptides, and Proteins", of which ref. [9] is No. 24.

0 009-2614/84/$ 03.00

2. Theory

The transition dipole–transition dipole interaction energy between two molecules A and B is given by [17]

$$V_{dd} = |\Delta\boldsymbol{\mu}^A||\Delta\boldsymbol{\mu}^B| X_{AB} , \quad (1)$$

where the transition dipole moment $\Delta\boldsymbol{\mu} = \langle 1|\boldsymbol{\mu}|0\rangle$, and the geometrical factor

$$X_{AB} = (\hat{e}_A \cdot \hat{e}_B - 3\hat{e}_A \cdot \boldsymbol{r}_{AB}\, \hat{e}_B \cdot \boldsymbol{r}_{AB})/r_{AB}^3 ,$$

$\hat{e}$ being the direction of the transition moment and r_{AB} the distance between the centers of the dipoles. Making the usual expansion of $\boldsymbol{\mu}$ in terms of the normal coordinates Q (assuming electrical harmonicity), $\boldsymbol{\mu} = \boldsymbol{\mu}_0 + \Sigma_i (\partial\boldsymbol{\mu}/\partial Q_i) Q_i$, and using harmonic oscillator wavefunctions, we get for the αth transition,

$$\Delta\boldsymbol{\mu} = (h/8\pi^2 c\nu_\alpha)^{1/2}\, \partial\boldsymbol{\mu}/\partial Q_\alpha$$
$$= (4.1058/\nu_\alpha^{1/2})\, \partial\boldsymbol{\mu}/\partial Q_\alpha \text{ D} , \quad (2)$$

where the unperturbed frequency ν_α is in cm^{-1} and $\partial\boldsymbol{\mu}/\partial Q_\alpha$ in D Å^{-1} $\text{u}^{-1/2}$ (u = atomic mass unit). To first order in perturbation theory, we may neglect interaction between different normal modes on A and B. Hence, for the αth mode, the frequency shift due to V_{dd} is

$$\Delta\nu_\alpha = V_{dd}/hc = 5034(\Delta\boldsymbol{\mu})^2 X_{AB}^\alpha$$
$$= (84862/\nu_\alpha)(\partial\boldsymbol{\mu}/\partial Q_\alpha)^2 X_{AB}^\alpha \text{ cm}^{-1} , \quad (3)$$

when X_{AB}^α is in Å^{-3}. The dipole moment $\boldsymbol{\mu}$ can also be expanded in terms of the internal coordinates S: $\boldsymbol{\mu} = \boldsymbol{\mu}_0 + \Sigma_i (\partial\boldsymbol{\mu}/\partial S_i) S_i$. Then, using the relation $S_i = \Sigma_j L_{ij} Q_j$, where $\mathbf{L}$ is the eigenvector matrix,

$$\partial\boldsymbol{\mu}/\partial Q_\alpha = \sum_i (\partial\boldsymbol{\mu}/\partial S_i) L_{i\alpha} . \quad (4)$$

Substituting (4) into (3), we see that in the S basis, we need to sum over terms in $|\partial\boldsymbol{\mu}/\partial S_i||\partial\boldsymbol{\mu}/\partial S_j|$ even when we do not consider interactions between different normal modes.

Classically, a dipole–dipole interaction energy is given as $V_{dd} = |\boldsymbol{\mu}^A||\boldsymbol{\mu}^B| X_{AB}$, where $\boldsymbol{\mu}$ appears in place of the transition moment $\Delta\boldsymbol{\mu}$. V_{dd} is introduced as an additional (non-bonded) term in the total potential energy of the system, $V_T = V_M + V_{dd}$, where V_M is the usual intramolecular energy due to bond stretches and angle bends. During vibrational motion, V_{dd} gives rise to a restoring force; like V_M it can therefore be expanded in terms of Q or S to obtain the force constants to be used in a normal coordinate calculation using the GF method. These force constants are, in the Q basis,

$$f_{\alpha\alpha} = (\partial\boldsymbol{\mu}/\partial Q_\alpha)^2 X_{AB}^\alpha (0.1) \text{ mdyne } \text{Å}^{-1} \text{ u}^{-1} \quad (5)$$

and, in the S basis,

$$f_{ij} = |\partial\boldsymbol{\mu}/\partial S_i||\partial\boldsymbol{\mu}/\partial S_j| X_{ij} (0.1) \text{ mdyne } \text{Å}^{-1} , \quad (6)$$

where X_{ij} is given in terms of the directions and positions of the derivatives $\partial\boldsymbol{\mu}/\partial S_i$ and $\partial\boldsymbol{\mu}/\partial S_j$. In general, cross-terms in (6) such as $|\partial\boldsymbol{\mu}/\partial r_{CO}||\partial\boldsymbol{\mu}/\partial r_{CN}|$ are needed just as cross-terms are in V_M. The frequency shifts in the presence of V_{dd} can be calculated by diagonalizing the $\mathbf{F}_T$ matrix or by perturbation using the Jacobian matrix elements $\Delta\nu/\Delta F$:

$$\Delta\nu_\alpha = (848619/\nu_\alpha) f_{\alpha\alpha} \text{ cm}^{-1} , \quad (7)$$

$$\Delta\nu_\alpha = (848619/\nu_\alpha) \sum_{ij} L_{i\alpha} L_{j\alpha} f_{ij} \text{ cm}^{-1} . \quad (8)$$

These expressions follow from the relation $\mathbf{A} = \tilde{\mathbf{L}}\mathbf{F}\mathbf{L}$, i.e. $4\pi^2 c^2 \nu_\alpha^2 = \Sigma_{ij} L_{i\alpha} L_{j\alpha} F_{ij}$.

The application of TDC is most straightforward in the case of a crystal of small molecule [17]. The dipole moment $\boldsymbol{\mu}$ and its derivatives are then taken to refer to the molecule. For a polymer, $\partial\boldsymbol{\mu}/\partial Q$ or $\partial\boldsymbol{\mu}/\partial S$ can be associated with each repeat unit such as the peptide group in polypeptides. For an oligopeptide it has been found [18] that even the amide I and II modes may not be localized on a particular peptide unit. In such cases, the S basis would be more appropriate than the Q basis.

3. Discussion

The magnitude of the transition-dipole interaction depends on the magnitude of $\partial\boldsymbol{\mu}/\partial Q$ or $\partial\boldsymbol{\mu}/\partial S$. Experimentally, $\partial\boldsymbol{\mu}/\partial Q$ can be obtained from measurements of infrared intensities [19] (N is Avogadro's number):

$$A = (N\pi/3c^2)(\partial\boldsymbol{\mu}/\partial Q)^2$$
$$= 4225.47(\partial\boldsymbol{\mu}/\partial Q)^2 \text{ cm mmole}^{-1} . \quad (9)$$

In addition, $\partial\boldsymbol{\mu}/\partial S$ can be calculated by quantum-mechanical methods [19]. We will now show that the

transition-dipole parameters we have used agree well with both intensity data and the results of our ab initio calculations.

In the poly(glycine I) (PGI) antiparallel rippled sheet structure, it was found [3] that the amide I splittings could be accounted for on the basis of TDC using a transition moment $\Delta\mu$ of 0.348 D oriented at 20° to the CO bond toward the CC^{α} bond. The direction was taken from the results of infrared dichroism measurements [20], and the magnitude was chosen to give the best fit to the frequencies. From (2), using $\nu = 1650\ \mathrm{cm}^{-1}$, we find that the value of $|\partial\mu/\partial Q|$ implied by this $\Delta\mu$ is 3.443 D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}$. This yields an integrated intensity of the amide I band of 50090 cm mmole^{-1}. Chirgadze et al. [21] have measured the amide I intensities for several polypeptides. In the ordered β-forms of these polypeptides, the intensities were in the range 47000–61000 cm mmole^{-1}, while in the random coil forms (which are probably more appropriate for deriving transition-dipole parameters of an individual peptide group) the values were 30000–51000 cm mmole^{-1}.

In our ab initio calculations [16], we computed the dipole-moment derivatives of NMA with respect to the local symmetry coordinates of the peptide unit, i.e. the quantities $\partial\mu/\partial S$. The dipole moment is that of the molecule, and the derivatives are expected to be representative of the peptide group (cf. the group moment model of Snyder [22]). The reliability of our ab initio results is indicated by the computed value of the static moment of NMA, 3.89 D using the 3-21G basis set, compared to an experimental value of 3.71 D [23]. Using the eigenvectors from a recent normal-mode analysis of PGI with a refined force field [24], we calculated the derivatives $\partial\mu/\partial Q$ for the amide I mode using (4). The results for the A_u and B_u symmetry blocks are 3.144 D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}$ (24° to CO) and 3.065 D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}$ (29° to CO), respectively.

Thus, our TDC parameters for amide I are consistent with intensity data and quantum-chemical results. In the case of the amide II transition moment, a $\Delta\mu$ of 0.254 D at 68° to CO was found to fit the observed splittings in PGI [3]. Using $\nu = 1540\ \mathrm{cm}^{-1}$, this $\Delta\mu$ gives a value for $|\partial\mu/\partial Q|$ of 2.428 D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}$. Our ab initio results together with the eigenvectors [24] yield these values for $\partial\mu/\partial Q$: A_u – 2.764 D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}$ (79° to CO) and B_u – 2.617 D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}$ (82° to CO) We note that the orientation of 68° assumed in the TDC calculations [3] was taken from one of a pair of values measured by Sandeman [25]; the other value was 77°, which is in even better agreement with the ab initio results.

We now try to reconcile our present results with those of BZ. First, it is important to note that in the above discussion $\partial\mu/\partial Q$ and $\partial\mu/\partial S$ are associated with a peptide group; there is no need to attempt to decompose these group derivatives into bond moment derivatives since we are working in the Q and S bases consistently. BZ obtained a value of 3.3 D $\mathrm{\AA}^{-1}$ for the dipole moment derivative in CH_2O with respect to r_{CO}. However, as they stated clearly, this is essentially the bond moment derivative $\partial\mu_{CO}/\partial r_{CO}$ of a CO bond with sp^2 hybridization at C. To obtain the dipole moment of a peptide group, one needs to sum over the bond moments ($\hat{e}_k$ is a unit vector along the kth bond):

$$\boldsymbol{\mu} = \sum_k \mu_k \hat{e}_k \qquad (10)$$

from which it follows that the derivative of $\boldsymbol{\mu}$ with respect to r_{CO} is [19]

$$\partial\boldsymbol{\mu}/\partial r_{CO} = \sum_k [(\partial\mu_k/\partial r_{CO})\hat{e}_k + \mu_k(\partial\hat{e}_k/\partial r_{CO})] \ . \qquad (11)$$

Except in the overly simplistic zero-order bond moment model [26], $\partial\mu_k/\partial r_{CO} \neq 0$ when $k \neq r_{CO}$. Thus, terms such as $\partial\mu_{CN}/\partial r_{CO}$ contribute to $\partial\boldsymbol{\mu}/\partial r_{CO}$ for a peptide group. Physically, these "cross-terms" arise from the changes in the electronic distribution in the entire peptide group when the CO bond is stretched. Our ab initio results on NMA are: $|\partial\boldsymbol{\mu}/\partial r_{CO}| = 5.58$ D $\mathrm{\AA}^{-1}$ for the free molecule, and $|\partial\boldsymbol{\mu}/\partial r_{CO}| = 6.95$ D $\mathrm{\AA}^{-1}$ when the CO and NH groups participate in hydrogen bonds with formamide molecules. In an earlier paper [6] estimates of $|\partial\boldsymbol{\mu}/\partial r_{CO}|$ of about 10 D $\mathrm{\AA}^{-1}$ were obtained. These values were based on the approximation that in the amide I mode $\partial\boldsymbol{\mu}/\partial Q$ is entirely due to r_{CO}, so that in (4) only the term in $\partial\boldsymbol{\mu}/\partial r_{CO}$ was retained. Using the eigenvector element of about 0.35 $\mathrm{u}^{-1/2}$ [6], one finds $|\partial\boldsymbol{\mu}/\partial r_{CO}| \approx 3.443$ D $\mathrm{\AA}^{-1}$ $\mathrm{u}^{-1/2}/0.35$ $\mathrm{u}^{-1/2} \approx 10$ D $\mathrm{\AA}^{-1}$. Obviously, if other contributions such as $\partial\boldsymbol{\mu}/\partial r_{CN}$ are included, a smaller value of $\partial\boldsymbol{\mu}/\partial r_{CO}$, closer to the ab initio values, can result. It is, of course, possible to set up a scheme for interacting bond moments similar to that for group or molecular moments outlined above. An advantage would be that bond-moment parameters, if reliably determined, may

be more transferable. However, in dealing with polypeptides, all consisting of the basic peptide unit, the group moment model [22], in which $\partial\boldsymbol{\mu}/\partial S$ is the transferred quantity, is clearly adequate and simpler.

Finally, we should consider the problem of where to locate the centers of the transition moments. Previously, the center of $\Delta\boldsymbol{\mu}$ was determined by choosing the best fit to frequency splittings [3]. We are at present examining other procedures. One possibility is a weighting scheme whereby in (4) each contribution $\partial\boldsymbol{\mu}/\partial S_i$ to $\partial\boldsymbol{\mu}/\partial Q_\alpha$ is placed on a bond, atom, or between bonds depending on the definition of S_i, and the resultant position (X, Y, Z) of $\partial\boldsymbol{\mu}/\partial Q_\alpha$ is then given by a weighted sum of the form

$$X \sum_i |(\partial\mu_x/\partial S_i)L_{i\alpha}| = \sum_i |(\partial\mu_x/\partial S_i)L_{i\alpha}|X_i$$

with similar expressions for Y and Z. The location of $\partial\boldsymbol{\mu}/\partial S_i$ can, in turn, be determined by the separate contributions of bond-moment derivatives located on the bonds.

In conclusion, the results of ab initio calculations on a more appropriate model, and a more careful theoretical treatment, confirm that TDC is indeed a reasonable mechanism to explain the splittings in the amide I and amide II modes of polypeptides.

Acknowledgement

This research was supported by National Science Foundation grants PCM-8214064 and DMR-8303610. One of us (TCC) is indebted to the Macromolecular Research Center for postdoctoral fellowship support.

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