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Magnetic Circular Dichroism Studies XXXII*

CNDO Calculations of the Magnetic Circular Dichroism Spectra of 7- and 9-Methyladenine

Robert E. Linder, Hannah Weiler-Feilchenfeld**, Günter Barth,
Edward Bunnenberg, and Carl Djerassi
Department of Chemistry, Stanford University, Stanford, USA

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CNDO calculations of the MCD spectra of 7- and 9-methyladenine have been carried out in two approximations. A minor modification of the CNDO/S method of Jaffé and coworkers shows an improvement over Jaffé's parameterization with respect to band separations and the signs of the MCD B terms, but is not applicable to $n \rightarrow \pi^*$ transitions.

Key words: Magnetic circular dichroism spectra – 7-methyladenine – 9-methyladenine

1. Introduction

The electronic structure of purine and pyrimidine nucleotides, essential components of nucleic acids, has been extensively studied by many workers and has been reviewed by Pullman and Pullman [30]. In particular, the electronic spectra of the isolated nucleic acid bases have received considerable attention, often in connection with SCF calculations of the Pariser-Pople-Parr type. Because of the semi-empirical nature of these calculations and the concomitant freedom to choose parameters for each "different" type of atom, it is desirable that an all-valence electron procedure of the CNDO type be utilized. Furthermore, since the electronic absorption spectra of the bases often consist of overlapping bands, a more subtle property, such as the magnetic circular dichroism (MCD) spectra [9, 14, 38, 39], is useful. Of the bases, we chose 7- and 9-methyladenine for spectral calculations because their MCD spectra are detailed and vary on changing the site of methylation.

Several previous calculations of the electronic absorption spectra of adenine and 9-methyladenine have been performed, mostly in the framework of the Pariser-Pople-Parr (PPP) π-SCF-LCAO-CI theory [1, 3–5, 15, 19, 20, 25, 36] and also using CNDO wave functions [16, 17]. Both the PPP [24, 33] and CNDO [22, 23, 32] theories have been used in conjunction with Stephens' theory [35], to calculate MCD spectra. We report here the MCD spectra of 7- and 9-methyladenine as well as CNDO calculations of these spectra. As will be seen apparently subtle changes in calculational procedure lead to dramatic differences in the results.

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[**] On leave from the Institute of Chemistry, Hebrew University, Jerusalem, Israel.

2. Experimental

The MCD spectra were run on a Jasco Model ORD-UV 5 spectropolarimeter which has been modified for circular dichroism measurements and fitted with a superconducting magnet built by Lockheed Palo Alto Research Laboratories (Model OSCM 103). The absorption spectra were run on a Cary 14 spectrophotometer. The spectra were measured at room temperature (~20° C) in triply distilled water, pH 6.8 or in 0.1 *N* HCl. The samples were obtained from Cyclo Chemical Co. and were used as received. The *B* values were obtained by planimeter integration using the approximate formula

$$B = \frac{1}{-33.53\,\lambda_{\max}} \int [\theta]_M \, d\lambda$$

where $[\theta]_M$ is in units of deg cm^2 dmol^{-1} G^{-1}.

When positive and negative *B* terms overlapped in the spectra, the baseline was taken as the boundary and no attempt was made to correct for overlap. Hence these reported *B* values are minimum values. When *B* terms of the same sign overlapped in the spectra, we estimated, by extrapolation of the larger *B* term, the correction for overlap.

3. Theoretical Methods

The MCD spectrum of a molecule which does not have a three-fold or higher symmetry axis may be described [35] by,

$$\frac{[\theta]_M}{\nu} = -33.53 \sum_J B_{AJ} \, f_0(\nu, \nu_{AJ})$$

where $f_0(\nu, \nu_{AJ})$ is a normalized shape factor and where

$$\begin{aligned} B_{AJ} = \sum_{K \neq A,J} \Bigg\{ & \frac{\langle J|\mu|K\rangle}{E_K - E_J} \cdot \langle A|m|J\rangle \times \langle K|m|A\rangle \\ & + \frac{\langle K|\mu|A\rangle}{E_K - E_A} \cdot \langle A|m|J\rangle \times \langle J|m|K\rangle \Bigg\} \\ & + \frac{\langle J|\mu|A\rangle}{E_J - E_A} \cdot \langle A|m|J\rangle \times [\langle J|m|J\rangle - \langle A|m|A\rangle] \,. \end{aligned} \tag{2}$$

Since Eq. 2 has been discussed in detail elsewhere [22–24, 32, 33, 35], we now proceed to the methods of generating the state wave functions.

In a series of papers [10–13] Del Bene and Jaffé reviewed the inadequacies of the CNDO/2 method for calculating electronic spectra, and reported a new parameterization (CNDO/S). The CNDO/S method, besides reintroducing semi-empirical repulsion integrals and altered β's, is based on reducing the π overlap (in the diatomic bond axis coordinate system [18]) by the factor κ. This was done in order to scale the $\pi \rightarrow \pi^*$ excitation energies with respect to those of the $n \rightarrow \pi^*$ excitations.

The use of the scaling factor, κ, has been criticized on the grounds that rotational invariance is not maintained [37]. However, since the scaling is done in the bond axis coordinate system, this problem does not seem serious. We raise a more fundamental objection.

The value of an off diagonal matrix element of the Hartree-Fock operator is given, in the CNDO approximation [27–29], by

$$F_{\mu\nu} = \tfrac{1}{2} S_{\mu\nu}(\beta^\circ_\mu + \beta^\circ_\nu) - \tfrac{1}{2} P_{\mu\nu}\gamma_{AB}\,.$$

For a given pair of atoms, the first term is non-zero for

$$F_{s,s},\, F_{s,\sigma},\, F_{\sigma,s},\, F_{\pi,\pi},\, \text{and } F_{\pi',\pi'}\,.$$

Scaling down the π overlap integral thus reduces $F_{\pi,\pi}$ and $F_{\pi',\pi'}$. If the atoms have different electronegativities, then diagonalization of F leads to a redistribution in electronic charge and the charge compensation occurs more readily through the s and σ terms. In a planar molecule, either the π or π' orbitals form the AO basis set for the π MO's. Therefore the CNDO/S method allows more electron delocalization through the σ skeleton than the CNDO/2 method. The errors introduced by the CNDO/S procedure are particularly significant when two electrons are donated to the π system by a heteroatom[1].

In order to investigate this point, we tried an admittedly ad hoc procedure. We set the scaling factor, κ, back to unity, as in the CNDO/2 method, and scaled the state energies and all quantities derived from these energies by an adjustable parameter κ' after the CI calculation had been performed. All other semi-empirical parameters remain the same as those used in CNDO/S. Thus, at the SCF stage of the calculation, σ and π delocalizations are nominally in balance. Since this procedure is very similar to CNDO/S, we label it the CNDO/S′ method.

4. Numerical Approximations

The calculational procedure used differs in no significant way from that reported by Del Bene and Jaffé for the CNDO/S procedure [10–13], except for the method of calculating the two center repulsion integrals and the value of κ. The two center repulsion integrals were calculated according to the Nishimoto-Mataga [26] formula, as this formula yielded significantly better results on benzene [6, 32]. When κ is set to one, and the energies scaled after the CI calculation, the results are labeled CNDO/S′. All states involving $\pi \rightarrow \pi^*$ excitations were included in both calculations.

The one and two center electric and magnetic dipole matrix elements were evaluated exactly, assuming that the AO's are Slater orbitals and retaining only nearest neighbor two center integrals. The electric dipole moments were calculated in the dipole length formalism.

For the geometry of 9-methyladenine, we used the values given by Voet and Rich [40] for the heavy atoms, and those of Lai and Marsh [21] for the hydrogens. The methyl group in the 9-position was oriented in such a way that one of its

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[1] In the calculations of Ref. [16], the calculated spectra for pyrrole and furan agree less well with experiment than those for molecules with one π electron per center.

hydrogen atoms was in the plane of the purine skeleton and directed away from the C_8 carbon atom. For 7-methyladenine we were unable to locate experimental data and used a geometry obtained from the preceding one by inverting the five membered ring. Also, the methyl group was rotated so that the hydrogen atom in the plane of the molecule was directed toward the C_8 carbon atom.

Although calculations of MCD *B* terms are in general origin dependent [7, 8, 34], Warnick and Michl [41] have found, for PPP calculations, that "the uncertainty introduced by shifting the origin within the molecule typically is much smaller than that introduced by minor modifications in the calculation". We anticipate our final results by noting that this is almost certainly the case in the present work and we defer further consideration of origin dependence until later.

5. Results and Discussion

The experimental MCD and absorption spectra of 7- and 9-methyladenine in water (pH 6.8) and in 0.1 *N* HCl (pH 1.0) are given in Figs. 1 and 2. Several points are discernible from these spectra. The relatively minor changes on protonation indicate that the bands observed in MCD are $\pi \rightarrow \pi^*$ bands, five being readily

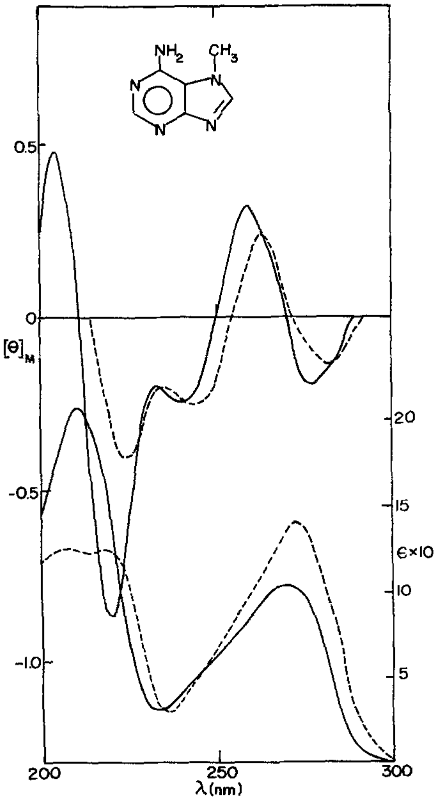

Fig. 1. The MCD and absorption spectra of 7-methyladenine at pH 6.8 (——) and pH 1.0 (– – –)

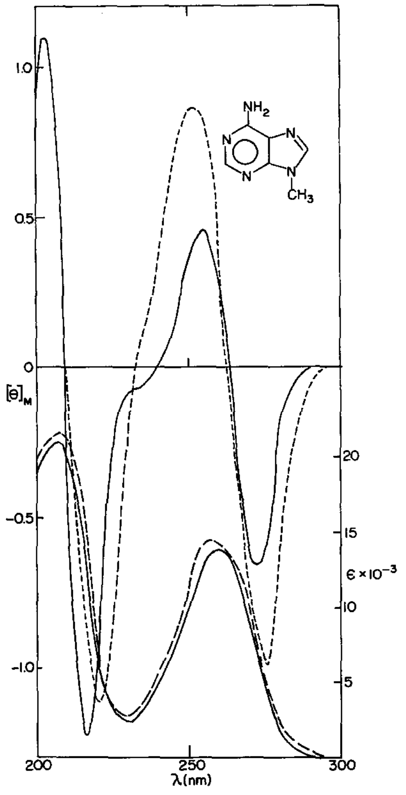

Fig. 2. The MCD and absorption spectra of 9-methyladenine at pH 6.8 (——) and pH 1.0 (– – –)

identifiable in 7-methyladenine and four in 9-methyladenine. The close similarity of the MCD spectra of 9-methyladenine and adenine [39] confirms previous conclusions on the most stable tautomer (9*H*) of adenine [2, 31].

The spectra of 7- and 9-methyladenine also bear a resemblance to each other. The spectra of 7-methyladenine are red shifted about 5 nm with respect to 9-methyladenine. All bands have been altered in intensity, Band III being stronger in 7-methyladenine, and the rest being stronger in 9-methyladenine. The experimental and calculated *B* values, oscillator strengths, and wavelengths are given in Table 1. The experimental wavelengths should be examined with caution because they were taken from the positive and negative maxima of the MCD curves. The corresponding absorption bands, when two *B* terms overlap, can be much closer together and can be accidentally degenerate. For example, the absorption maximum of Band II in 9-methyladenine could be as high as 265 nm.

The CNDO/S method was orginally parameterized to give the energy of the O–O band. Since vibrational structure is not resolved in our spectra, we expect the calculated values to be to the red of the absorption maxima. It is thus surprising that CNDO/S predicts 8 of the 10 bands (in both compounds) to the blue of the

Table 1. Experimental and calculated spectral parameters[a]

	Experimental			CNDO/S			CNDO/S′		
Band[b]	$-B\times10^{-3}$	f	λ_{max}	$-B\times10^{-3}$	f	λ	$-B\times10^{-3}$	f	λ
a) 7-Methyladenine									
I	−0.260	0.23	276	0.559	0.086	281	−1.88	0.223	289
II	0.402		259	−0.973	0.047	242	3.30	0.091	268
III	−0.454		239	2.11	0.096	220	−1.29	0.210	233
IV	−1.466	0.56	220	−3.15	0.623	216	−3.83	0.653	222
V	0.622		204	1.53	0.611	202	3.52	0.290	213
b) 9-Methyladenine									
I	−0.864	0.27	273	−1.04	0.025	275	−5.47	0.216	277
II	0.739		255	1.94	0.285	253	6.75	0.118	269
III	−0.083		233	−0.95	0.167	219	−3.38	0.552	230
IV	−1.776	0.51	216	−1.53	0.582	205	−0.29	0.138	222
V	1.499		202	0.58	0.466	199	3.81	0.459	214

[a] B values are in units of Bohr magneton Debye^2/wavenumber, wavelengths are in nanometers.
[b] See Figs. 1 and 2 for band identification.

Table 2. Calculated π and total charge densities[a]

	Atom										
	1	2	3	4	5	6	7	8	9	10	11
a) 7-Methyladenine											
CNDO/S											
q_π	1.266	0.866	1.203	0.895	1.174	0.860	1.716	0.919	1.218	1.880	1.033
$q_{\sigma+\pi}$	5.278	3.858	5.244	3.838	4.023	3.795	5.081	3.855	5.253	5.201	3.977
CNDO/2											
q_π	1.251	0.906	1.197	0.959	1.144	0.858	1.618	0.943	1.243	1.858	0.981
$q_{\sigma+\pi}$	5.271	3.799	5.277	3.834	4.011	3.726	4.990	3.792	5.323	5.253	3.932
CNDO/S′											
q_π	1.246	0.948	1.169	0.985	1.138	0.904	1.558	1.004	1.218	1.814	1.020
$q_{\sigma+\pi}$	5.252	3.888	5.210	3.879	4.015	3.814	5.002	3.893	5.240	5.169	3.964
b) 9-Methyladenine											
CNDO/S											
q_π	1.278	0.852	1.241	0.920	1.146	0.825	1.200	0.969	1.696	1.871	1.032
$q_{\sigma+\pi}$	5.292	3.844	5.268	3.832	4.021	3.778	5.246	3.880	5.078	5.193	3.976
CNDO/2											
q_π	1.272	0.891	1.204	0.938	1.168	0.847	1.199	0.991	1.618	1.851	0.982
$q_{\sigma+\pi}$	5.294	3.791	5.237	3.781	4.076	3.742	5.250	3.823	5.060	5.250	3.927
CNDO/S′											
q_π	1.258	0.933	1.205	0.987	1.141	0.876	1.205	1.034	1.548	1.801	1.020
$q_{\sigma+\pi}$	5.262	3.878	5.230	3.873	4.018	3.805	5.231	3.910	5.004	5.157	3.964

[a] Atoms 1–9 are the atoms of the purine skeleton. Atom 10 is the amine nitrogen atom and atom 11 is the methyl carbon.

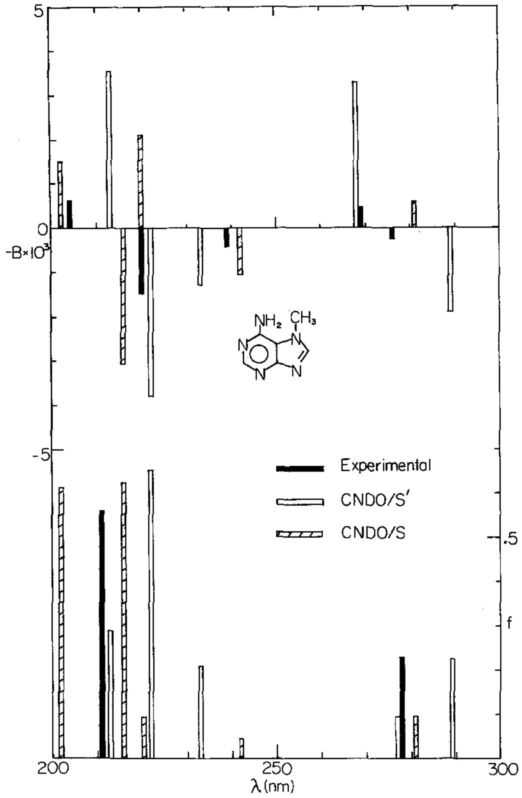

Fig. 3. The calculated (▭, CNDO/S′, ▨, CNDO/S) and experimental (■) MCD and absorption spectra of 7-methyladenine

experimental values. Also, the signs of three of the 10 bands are incorrectly predicted by the CNDO/S method[2]. The scaling factor in the CNDO/S′ calculation ($\kappa' = 0.65$) was chosen empirically, thus negating comparison of the O–O band calculations. However, the splitting pattern (see Figs. 3 and 4) is much more nearly reproduced by CNDO/S′ than by CNDO/S. The signs of all ten MCD bands are correctly predicted by CNDO/S′.

Table 2 shows the σ and π Mulliken atomic populations in the ZDO approximation for three calculational methods, CNDO/S, CNDO/2, and CNDO/S′. Generally speaking, the π charge densities are most uniform in the CNDO/S′ calculation, less so in CNDO/2, and least in CNDO/S, apparently reflecting a decrease in π delocalization in that order. Most notably, the π charge density on the atoms which donate two electrons to the π system increases by 0.07–0.16 e in the same sequence. It is also of interest to note that the σ changes overcompensate for this effect.

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[2] In CNDO/S calculations on both 7- and 9-methyladenine in which we included several $\sigma \rightarrow \pi^*$ and $\sigma \rightarrow \sigma^*$ states, the predicted spectra did not change sign. Some intensity variation ($< 20\%$) was noted.

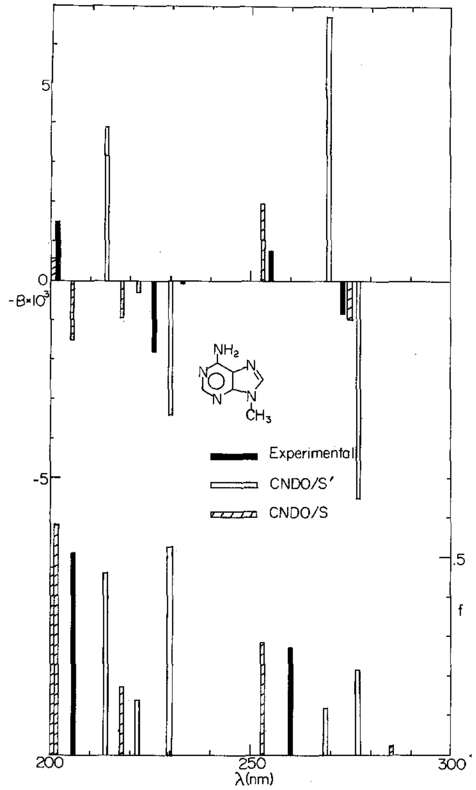

Fig. 4. The calculated (□, CNDO/S′, ▨, CNDO/S) and experimental (■) MCD and absorption spectra of 9-methyladenine

6. Conclusions

Our attempts to revise the existing CNDO/S procedure have led to a definite improvement in the reliability of calculations of MCD spectra. However, the CNDO/S′ calculations apply only to $\pi \rightarrow \pi^*$ excitations and even then do not reproduce the intensities in an accurate way. The most notable problem occurs in both 7- and 9-methyladenine where Band III is calculated to have too high an intensity. Hug and Tinoco [17], in a recent CNDO calculation of nucleic acid base spectra with yet another set of parameters, identify this band in 9 (H) adenine with the second $\pi \rightarrow \pi^*$ band of the triene fragment C2=N3–C4=C5–N7=C8. In a C_{2h} triene, this transition is electric dipole forbidden and Hug and Tinoco thereby explain the weakness of Band III. However, their calculation does not reproduce the splitting pattern in adenine very well (Bands IV and V are calculated to be approximately 4kK too high in energy) and they use different β's for σ and π overlaps much as Del Bene and Jaffé have done. It is therefore our tentative conclusion that no truly satisfactory spectral parameterization of the CNDO method now exists.

Experimentally, the MCD spectra of 7- and 9-methyladenine differ by a constant wavelength shift of about 5 nm and in the intensity of each MCD band. The spectra are reasonably detailed, allowing the identification of five $\pi \rightarrow \pi^*$ states in the 190–280 nm spectral region. Comparison of the spectra confirms that 9(H)adenine is the most stable tautomer.

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Prof. Dr. C. Djerassi
Department of Chemistry
Stanford University
Stanford, California 94305, USA