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MAGNETIC CIRCULAR DICHROISM OF CYCLIC π-ELECTRON SYSTEMS—19†[1]

HETEROCYCLIC ANALOGS OF THE INDENIDE ANION

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Abstract—The physical origin of magnetic circular dichroism of cyclic π-electron systems derived from a (4N + 2)-electron [n]annulene perimeter is briefly summarized and the use of the perimeter model for a back-of-the-envelope PMO prediction of absolute MCD signs of species derived from a charged perimeter is demonstrated on the case of the indenide anion and its various heterocycles which contain a heteroatom in position 1, such as indole. The spectra of analogs containing several heteroatoms, e.g. purine, are discussed, and the potential offered by MCD spectroscopy for the investigation of tautomerism and determination of protonation sites in heterocycles of this type is noted and exemplified on N-methylpurines.

Magnetic circular dichroism of cyclic π-electron systems derived from a (4N + 2)-electron [n]annulene perimeter can be understood in simple terms.[2-4] If $N \neq 0$ (Fig. 1), the ground state of an unperturbed parent perimeter has two degenerate highest occupied molecular orbitals (HOMOs). Since they are degenerate, they can be chosen in the complex form. This is less familiar than the usual real form, but is useful to us at the moment, since it permits a description of net electron circulation, which the real form does not. In one of these complex orbitals, ψ_{-N}, two electrons circulate clockwise; in the other, ψ_N, two electrons circulate counterclockwise. Four low-energy excitations promote an electron from ψ_N or ψ_{-N} into one of the two lowest unoccupied molecular orbitals (LUMOs) which are available unless the perimeter has 2(N + 1) atoms. In one of these complex orbitals, ψ_{-N-1}, the electron circulates clockwise; in the other, ψ_{N+1}, it circulates counterclockwise.

The two transitions in which the sense of electron circulation is preserved during the excitation have large absorption intensity: in $\psi_N \to \psi_{N+1}$ left-handed circular polarized light (CPL) is absorbed, in $\psi_{-N} \to \psi_{-N-1}$ right-handed CPL is required. The two transitions occur at the same energy, which is relatively high (185 nm in benzene), and the excited states form two components of a degenerate state which has been labelled B by Platt.[5] Unlike the ground state, they can have a non-vanishing magnetic moment. Before the excitation, the moment due to the circulation of an electron in ψ_N was exactly cancelled by that due to the circulation of an electron in ψ_{-N}, but once the excited electron is in ψ_{N+1}, its average rate of circulation may have increased or decreased compared to ψ_N, so that the compensation no longer is exact. Since the charge of an electron is negative, the magnetic moment of a counterclockwise circulating electron in ψ_N or ψ_{N+1} is directed away from the viewer, i.e. is negative, and that of a clockwise circulating electron in ψ_{-N} or ψ_{-N-1} is positive. For the most common combinations of n and N values, the loop current is slightly higher in the LUMOs than in the HOMOs, so that the magnetic moment of the state reached upon absorption of left-handed CPL, $\psi_N \to \psi_{N+1}$, is usually weakly negative (we shall refer to it as μ^-; a list of calculated values is given in Ref. 2), while the moment of the state produced by right-handed CPL, $\psi_{-N} \to \psi_{-N-1}$, then is weakly positive (magnetic moment $-\mu^-$). In a magnetic field directed perpendicular to the molecular plane and towards the viewer, Zeeman interaction will split the two levels similarly as in the well-known case of nuclear magnetic moments (NMR), and the state with a positive magnetic moment, $\psi_{-N} \to \psi_{-N-1}$, will be somewhat lower in energy. In measurements of magnetic circular dichroism, $\epsilon_L - \epsilon_R$ is determined as a function of photon energy. As the spectrum is swept in the direction of increasing energy, $\psi_{-N} \to \psi_{-N-1}$ will be reached before $\psi_N \to \psi_{N+1}$ if magnetic field is present. Thus, ϵ_R will reach a maximum before ϵ_L does and the MCD curve will first dip to negative values and then swing to positive values of $\epsilon_L - \epsilon_R$. The resulting S-shaped feature is a spectral signature of a degenerate excited state whose left-handed polarized component has a negative magnetic moment and is referred to as a positive A term. In those rare instances in which μ^- is positive,[2] the B transition of the annulene will have a negative A term, in which the MCD curve first becomes positive and then negative as photon energy increases.

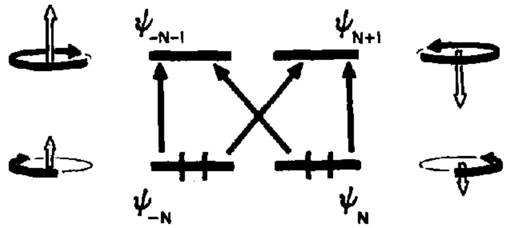

Fig. 1. HOMO and LUMO of a (4N + 2)-electron [n]annulene. The sense and amount of electron circulation and the resulting orbital magnetic moment are shown schematically for each orbital.

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†Dedicated to Professor Michael J. S. Dewar on the occasion of his 60th birthday.

There are two other HOMO→LUMO transitions, $\psi_{-N} \rightarrow \psi_{N+1}$ and $\psi_N \rightarrow \psi_{-N-1}$, in which the excitation reverses the sense of circulation of the promoted electron. These have zero intensity unless symmetry-perturbing vibrations are considered. They are referred to as the L states by Platt[5] and occur at lower energies than the B states. If the perimeter is charged ($n \neq 4N+2$), they form two degenerate components of a single excited L state (320 nm in $C_9H_9^-$). If it is uncharged ($n = 4N+2$), they combine into a lower (L_b) and upper (L_a) state (270 nm and 205 nm in benzene, respectively). The magnetic moment of $\psi_{-N} \rightarrow \psi_{N+1}$ is large and negative (μ^+), that of $\psi_N \rightarrow \psi_{-N-1}$ is large and positive ($-\mu^+$). This is obvious when one considers that in $\psi_{-N} \rightarrow \psi_{N+1}$ the promoted electron no longer compensates the negative magnetic moment due to an electron in ψ_N, as it did when it was still in ψ_{-N}, but actually adds another large negative moment since it now is in ψ_{N+1} and is running counterclockwise. Calculated values of μ^+ are tabulated in Ref. 2. They are typically an order of magnitude larger than the μ^-'s. The large magnetic moment of the L state however is not simply reflected in the MCD spectrum since the purely electronic transition is strictly forbidden ($\epsilon_L - \epsilon_R = 0$ since $\epsilon_L = \epsilon_R = 0$). To explain the observed weak effects, symmetry-breaking vibrations need to be invoked. In the case of an uncharged perimeter, moreover, the configuration with a large negative magnetic moment μ^+ ($\psi_{-N} \rightarrow \psi_{N+1}$) and that with a large positive magnetic moment $-\mu^+$ ($\psi_N \rightarrow \psi_{-N-1}$) mix in a one-to-one ratio in the absence of a magnetic field, so that their contributions to the magnetic moments of the resultant L_b and L_a states exactly cancel.

In constructing the actual molecule of interest from the parent (4N+2)-electron [n]annulene perimeter by introduction of cross-links, bridges, substituents, heteroatoms etc., symmetry is usually lowered and three or all four transitions become electronically allowed. We shall label them L_1, L_2, B_1 and B_2 in the order of increasing energy. In the case of an uncharged perimeter, it is often possible to distinguish the L_b and L_a parentage of the two L states; either can be lower in energy. A mathematical analysis[3] of the mixing of the four configurations and its effect on transition intensities and MCD behavior shows that the sense-preserving character, and thus the intensity, is now distributed over all four transitions, but most of it still remains in the B transitions. Similarly, the small magnetic moment μ^- of the sense-preserving excitations is now shared by all four transitions but remains largely in the B bands, while the large magnetic moment μ^+ of the sense-reversing excitations is also shared but resides predominantly in the L transitions. In the absence of magnetic field, the intensity-providing configurations $\psi_N \rightarrow \psi_{N+1}$ and $\psi_{-N} \rightarrow \psi_{-N-1}$ are strictly degenerate and therefore both enter always with the same weight into any final state. As a result, $\epsilon_L = \epsilon_R$ at all wavelengths. In the presence of a magnetic field, however, their energies are split by the Zeeman effect and this balance is destroyed. Then, for some of the four transitions, $\epsilon_L > \epsilon_R$, while for others, $\epsilon_L < \epsilon_R$. In the MCD spectrum $\epsilon_L - \epsilon_R$ is plotted, so that positive and negative peaks appear at the appropriate wavelengths, respectively. The areas under these peaks are expressed quantitatively as the so called B terms, positive if $\epsilon_L < \epsilon_R$, negative if $\epsilon_L > \epsilon_R$.

A detailed analysis[3] shows that the B term of each of the four transitions is composed of two contributions, one proportional to μ^-, the other to μ^+. The contribution due to μ^- is small, particularly for the L bands, and is largely independent of the molecular structure: for the L transitions, the B term is weakly positive or zero, depending on details of the structure, for the lower of the B transitions it is more strongly positive, for the upper B transition it is more strongly negative. The contribution due to μ^+ is potentially large, but enters with a weight which depends on the degree to which the splitting of the HOMOs of the original [n]annulene perimeter differs from the splitting of its LUMOs. These splittings, ΔHOMO and ΔLUMO, are induced by the perturbation which converts the perimeter into the actual molecule in question. Qualitatively, such splittings can be viewed as hindering the circulation of particles along the perimeter: the larger the splitting, the larger the hindrance, and the smaller the magnetic moment which results from the circular motion. Clearly, ΔHOMO reflects the hindrance to the circulation of the positive hole which the promoted electron leaves behind in HOMO, and ΔLUMO reflects the hindrance to the circulation of the excited negative electron in LUMO. If ΔHOMO = ΔLUMO, the contribution proportional to μ^+ vanishes; if ΔHOMO > ΔLUMO, electron circulation dominates, and the μ^+ contributions to the B terms of the four transitons are +, −, +, − in the order of increasing energy L_1, L_2, B_1, B_2. If ΔHOMO < ΔLUMO, hole circulation dominates, and the μ^+ contributions to the B terms are just the opposite: −, +, −, + for L_1, L_2, B_1, B_2. The hindrance of electron circulation in the magnetic field by the non-vanishing values of ΔHOMO and ΔLUMO is related to the fact that the real and not the complex description of the four orbitals is now appropriate. This will be used in the rest of the paper.

In view of the above, MCD can be used to obtain information about the relative energies of four key molecular orbitals and in this respect is complementary to photoelectron spectroscopy (PES), which provides a measure of ΔHOMO alone, and electron transmission spectroscopy (ETS), which, in favorable cases, provides a measure of ΔLUMO alone. It is important to keep in mind that the orbital energy differences derived from any one of these methods are only meaningful within a model. The numerous simplifying assumptions which go into the MCD derivations within the perimeter model have been discussed in Refs 2 and 3 and the model appears to perform best for the lowest energy two or three transitions. The assignment of orbital energies from PES and ETS spectra is also based on a well known model assumption (Koopmans' theorem). In spite of their limitations, the MO models involved have already proven extremely useful.

In addition to its value in providing an improved insight into electronic structure, MCD spectroscopy of aromatic molecules may be of some interest as a complementary means of structure determination since the relative size of ΔHOMO and ΔLUMO, which can usually be readily derived from qualitative notions of orbital interactions, is quite sensitive to molecular structure, e.g. in positional isomers. In this respect, MCD is far more powerful than ordinary UV-visible spectroscopy, with which it shares the advantage of requiring only minute amounts of material.

For structural work, soft chromophores (ΔHOMO = ΔLUMO) are particularly intriguing since already weak structural perturbations are capable of converting them into either positive-hard (ΔHOMO > ΔLUMO) or negative-hard (ΔHOMO < ΔLUMO) chromophores, depending on factors such as the nature and position of substitution. Soft chromophores derived from an uncharged perimeter can be double-soft, odd-soft, even-soft, or zero-soft, and their predicted response to substituent effects depends in a regular and easily predictable fashion on which of these categories they are in.[4] Soft chromophores derived from a charged perimeter can be either double-soft (ΔHOMO = ΔLUMO = 0, high-symmetry, e.g. tropylium) or single-soft (ΔHOMO = ΔLUMO $\neq 0$). The response to substitution is less regular in this latter case and usually needs to be considered on a case-by-case basis.

In a series of experimental papers which accompanied the theoretical analysis (Ref. 6 and papers which follow it), it has been demonstrated that the above described simple model works well on cyclic π-electron molecules derived from an uncharged (4N + 2)-electron perimeter. In the present paper, we describe its application to a set of species derived from the charged 10-electron [9]annulenide perimeter. We shall focus on a single-soft chromophore, the indenide anion, and on its heterocyclic analogs, which represent the parent structures for a very large number of important natural heterocycles.

RESULTS AND DISCUSSION

The indenide anion (**1**). The cross-linking perturbation which produces **1** from the [9]annulenide anion splits the originally degenerate HOMO and the originally degenerate LUMO by approximately equal amounts, ΔHOMO = ΔLUMO $\neq 0$. A simple Hückel estimate yields ΔHOMO = 0.43β, ΔLUMO = 0.39β. The origin of this approximate equality is readily understood when the PMO theory[7] is applied to the real form of the perimeter orbitals in order to describe the cross-linking (see below). Similar reasoning indicates that other bicyclic hydrocarbon ions derived from (4N + 2)-electron annulenide and annulenylium ions by a single cross-link, such as benzotropylium, will also be single-soft MCD chromophores.

The L and B bands have already been identified[8] in the spectrum of **1** and lie at about 335 nm (L_1), 280 nm (L_2), 245 nm (B_1), and 215 nm (B_2). According to the perimeter model, the L_2 band should have vanishing intensity if ΔHOMO and ΔLUMO are exactly equal; it must therefore also have a vanishing B term. The MCD sign of this one transition should then be the most sensitive to perturbations, hence the term "single-soft" chromophore. Pariser–Parr–Pople calculations, both previous[8,9] and present, also predict a very small oscillator strength for L_2 and it has been suggested[8] that much of the observed intensity is due to vibronic borrowing.

The reported[10] MCD spectrum of **1** shows weak positive B terms for both L bands and a stronger positive B term for the B band. It thus is in perfect agreement with the expectations based on the perimeter model for a single-soft chromophore if it is assumed that most of the weak positive B term of the L_2 transition is largely due to vibronic interactions similarly as its intensity in absorption, or more likely, that both are derived from a slight inequality ΔHOMO < ΔLUMO in **1**, which the PPP calculations fail to reproduce (perhaps as a result of their neglect of next-nearest-neighbor interactions). Such a small inequality would cause magnetic L_1–L_2 mixing to add a small negative μ^+ contribution to the B term of transition L_1, and a small positive one to that of transition L_2. Superimposed on the dominant μ^- contributions, this would provide exactly the pattern observed. The μ^- contribution to the B term of L_1 originates in weak magnetic mixing with B_1, those of the B terms of B_1 and B_2 originate in their mutual mixing.

Heterocyclic analogs of the indenide anion (*X*-**1**). In the first approximation, the effects of the introduction of a heteroatom are described by changing the electronegativity of the center ν where the replacement occurs. The change in the energy of the i-th orbital can then be approximated by the PMO theory as $c_{i\nu}^2 \cdot \Delta\alpha_\nu$ where $\Delta\alpha_\nu$ is the change in the Coulomb integral of center ν. The needed values of $c_{i\nu}^2$ obtained from Hückel tables are given in Table 1 and permit an immediate prediction of the relative values of ΔHOMO and ΔLUMO in the derived heterocycles. For the compounds obtained by replacement of $-CH^-$– by $-N^-$–, –NH–, –NR–, –O–, –S–, –Se–, and similar heteroatoms which hold an electron pair more tightly than $-CH^-$– does, the energy $\Delta\alpha$ is negative, so that ΔHOMO < ΔLUMO in 1-X-1 and 4-X-1 (X in an I-dominant[4] position) and ΔHOMO > ΔLUMO in 2-X-1, 3a-X-1, and 5-X-1 (X in an I-subdominant[4] position). The resulting μ^+ contributions will dominate the signs of the B terms of the L transitions (Chart 1; note that a positive B term corresponds to a negative MCD peak). They will also contribute to the B terms of the higher energy B transitions but may not overwhelm the already present μ^- contributions.

In a better approximation, it will also be necessary to consider the effect of the heteroatom on bond lengths and resonance integrals, but this refinement is not essential for qualitative understanding and prediction of MCD signs which is our aim here.

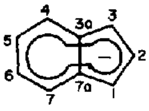

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Table 1 illustrates the general rule that the variety of possible substituent response is larger in single-soft chromophores derived from a charged perimeter, such as **1**, than in the odd-soft and even-soft chromophores, which are derived from an uncharged perimeter. In a single-soft chromophore, all four principal combinations, DD, DS, SD, and SS, are possible, while alternant pairing generally limits the choices to DD or SS in an odd-soft chromophore (D and S for short) and to DS or SD in an even-soft chromophore, even if it holds only approximately[4].

The seemingly random distribution of dominant-subdominant position labels derived from the Hückel orbital coefficients listed in Table 1 actually follows in a straightforward manner from the nodal properties of the MOs of the parent [9]annulenide anion $C_9H_9^-$ and can be derived without any computations whatever. This is demonstrated in Fig. 2 which presents the real representation of the MO coefficients of $C_9H_9^-$ in the usual graphical manner. In either of these real orbitals, the electron is equally likely to circulate in either sense, and they would have been unsuitable for our initial qualitative description of the MCD effect. However, they are ideal as a starting point for PMO derivations needed here. The HOMO pair, being the third π level from the bottom, has two nodes perpendicular to the molecular plane in each orbital. These lie at right angles to each other as shown. The LUMO pair is the fourth π level and therefore has three such nodes in each orbital, intersecting at 60° angles. In Fig. 2, the nodal pattern for

Table 1. Squares of HMO coefficients in the indenide anion and expected effects of electronegative heteroatoms on ΔHOMO − ΔLUMO

Orbital	Position 1 = 3	2	3a = 7a	4 = 7	5 = 6
c^2_{-2}	0.067	0.000	0.113	0.026	0.295
c^2_{-1} (LUMO)	0.024	0.118	0.042	0.294	0.081
Δ	0.043	−0.118	0.071	−0.268	0.214
c_1^2 (HOMO)	0.295	0.000	0.026	0.113	0.067
c_2^2	0.042	0.317	0.171	0.009	0.119
Δ	0.253	−0.317	−0.145	0.104	−0.052
Δ(ΔHOMO-ΔLUMO)/(−Δα)	−0.210	0.199	0.216	−0.372	0.266
Position type[a]	ND	dS	sS	Dd	Ss
Type of response to I effect[b]	D	S	S	D	S

[a]Nomenclature of Ref. 4. The first letter refers to the anticipated response of ΔLUMO (dominant, D, if $c^2_{-1} > c^2_{-2}$ and subdominant, S, if $c^2_{-1} < c^2_{-2}$), the second letter to the anticipated response of ΔHOMO (D if $c_1^2 > c_2^2$ and S if $c_1^2 < c_2^2$). A lower case letter indicates a weak D or S character and thus weaker response to inductive and mesomeric effects. Approximate equality of c^2_{-1} and c^2_{-2} or c_1^2 and c_2^2 characterizes neutral (N) positions.

[b]ΔLUMO and ΔHOMO are equally sensitive to inductive effects such as heteroatom replacement, so that an S- or D-type response of a position to an inductive effect is given by the sign of its Δ(ΔHOMO-ΔLUMO)/(−Δα) value.

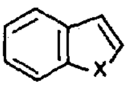
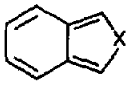
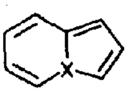
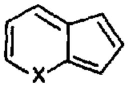
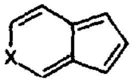
		Predicted μ′-contributions to B terms L_1	L_2
	1-X-1	−	+
	3a-X-1	+	−
	2-X-1	+	−
	4-X-1	−	+
	5-X-1	+	−

Chart 1.

each of the four orbitals is drawn superimposed on the molecular framework which has the shape of a regular nonagon. The size of the MO coefficient on each atom is determined by the sinusoidal nature of the wave function along the perimeter: the closer an atom lies to a nodal point on the perimeter, the smaller the MO coefficient of its orbital. Thus, the relative sizes shown can actually be drawn without calculation.

The introduction of a cross-link which converts the $C_9H_9^-$ anion into the indenide anion **1** is indicated by double-headed arrows in Fig. 2. Its expected first-order effect on the four orbital energies follows from the signs and magnitudes of the orbital coefficients shown and is indicated by vertical arrows. The cross-linking splits the degenerate pairs, and arranges the four orbitals in a definite order, keeping ΔHOMO equal to ΔLUMO to first order. If one now assumes that the orbital coefficients themselves do not change at all as a result of the cross-linking, i.e. that first-order perturbation theory is exact, and compares their sizes within the bonding MO pair and within the antibonding MO pair, one derives the D and S labels for the individual positions in **1** given in Fig. 2. In reality, of course, an inspection of the Hückel orbitals of **1** shows that the first-order approximation is not quite correct. However, the nodal properties of the four orbitals of $C_9H_9^-$ are still preserved perfectly in **1**, as are their relative magnitudes. As a result, the D,S labels derived from the symmetry-determined orbitals of $C_9H_9^-$ agree perfectly with those derived from the Hückel orbitals of **1** given in Table 1. Only the ΔLUMO character of position 1 = 3, expected to be dominant from the argument based on the orbitals of $C_9H_9^-$, turns out to be neutral when the actual Hückel MO's are used.

We believe that the value of this exercise in PMO theory goes beyond demonstrating that MCD signs of a series of biologically important heterocycles such as tryptophan are ultimately determined by the ways in which a square and a hexagon project on a nonagon: the heteroatom and substituent effects in a large number of other single-soft chromophores can be analyzed in the same back-of-the-envelope fashion.

Indole and isolectronic heterocycles (**1**-*X*-**1**). We have selected indole and its isoelectronic analogs with X = N⁻, NMe, S, and O for an experimental verification of the above predictions. The u.v. spectra of these heterocycles have been investigated repeatedly[11] and show a sequence of L_1, L_2, B_1, and B_2 transitions located at somewhat higher frequencies than those of the parent **1**, which

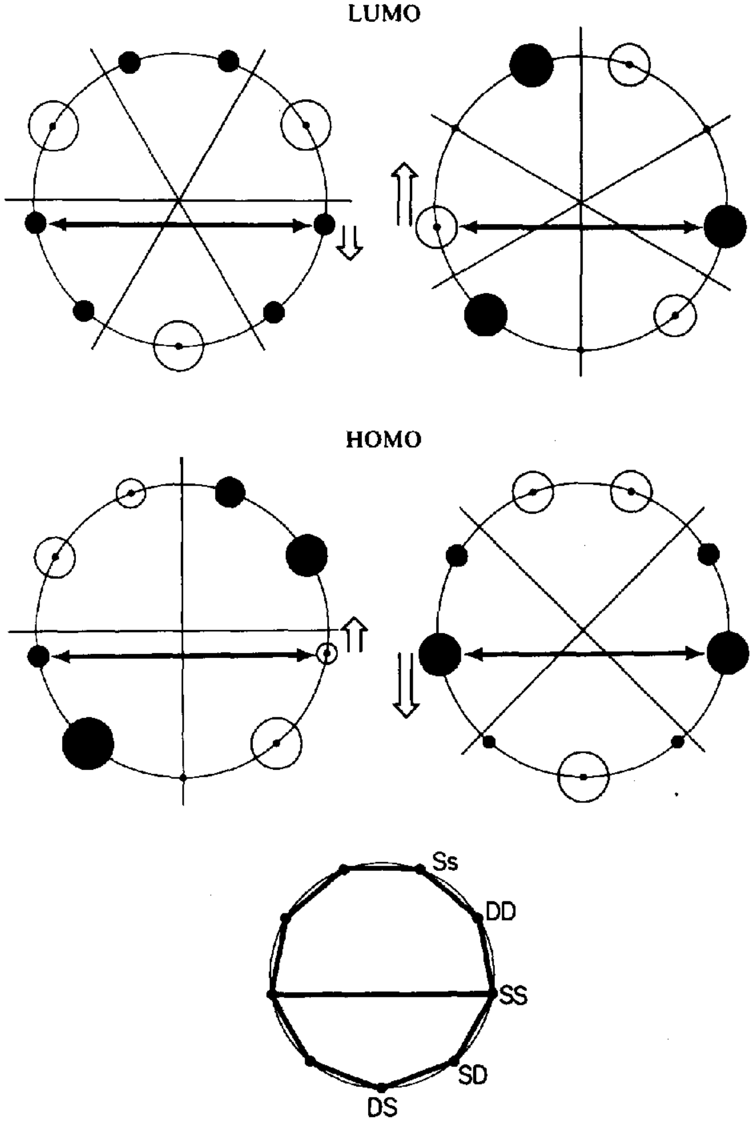


Fig. 2. MO Coefficients of the [9]annulenide anion (top) and predicted response of the MCD of the indenide anion 1 to substituent and heteroatom effects (bottom).

makes the observation of B_2 difficult. It is customary to refer to the L_1 transition as L_b and to L_2 as L_a, although strictly speaking the a and b labels of Platt's perimeter model should be reserved for π-electron systems derived from uncharged [4N+2]annulene perimeters. In indole and its derivatives (but not its anion) the L_1 and L_2 bands overlap severely and considerable attention has been paid to determining their independent existence and relative intensity by polarized spectroscopy[12] (the two transitions are polarized in mutually perpendicular directions, as required by the perimeter model) and by investigations of substituent effects.[13] The two transitions are cleanly separated in MCD spectra which have been reported for indole and its derivatives such as tryptophan and various alkaloids.[14-16] The characteristic and strong MCD band of the L_1 transition of tryptophane permits quantitative and selective determination of tryptophane residues in proteins by MCD.[14]

The MCD spectra of 1-N$^-$-1, 1-NCH$_3$-1, 1-O-1, and 1-S-1 are shown in Figs 3–6. The bands assigned as L_1, L_2, and B_1 are labeled 1, 2, and 3, respectively. The sequence of signs in all of the spectra is the same and agrees with that previously known for indole[14-16] (1-NH-1): the B term of L_1 is negative, those of L_2 and B_1 are positive. We conclude that the MCD signs of the L bands are dominated by the μ^+ contributions due primarily to their mutual magnetic mixing and agree with expectations for ΔHOMO < ΔLUMO, while the μ^+ contributions to the B term of the B_1 transition is not large enough to overcome the μ^- contribution inherent to the parent anion 1. The negative B term of L_1 is smaller in absolute value than the positive B term of L_2, presumably because it also contains a positive μ^- contribution present already in 1.

Satisfied that we now understand qualitatively the origin of the observed MCD signs, we have also attempted a more quantitative interpretation, using a semiempirical calculation of the Pariser–Parr–Pople type. In these calculations, only nearest-neighbor interactions are usually considered and this is quite compatible with the other assumptions introduced.[17] While this approximation is quite adequate for the calculation of most

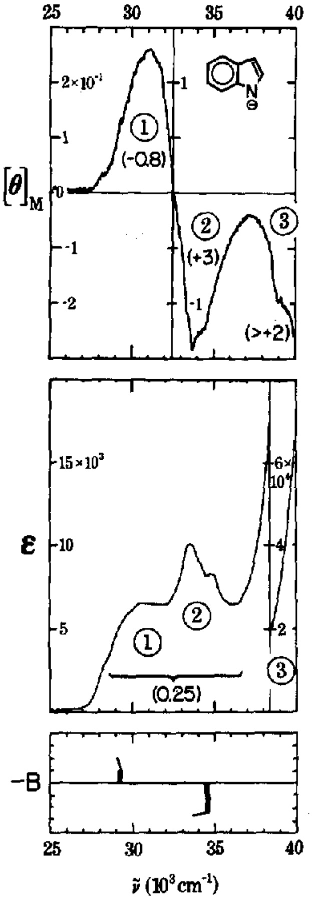


Fig. 3. Indole Nitranion. Top, MCD (B terms given in units of $10^{-3}\beta_e D^2/cm^{-1}$); center, absorption spectrum (oscillator strengths given); bottom, PPP calculation. Calculated $-B$ values are indicated by the length of the bars (short, below 1; medium, 1–5; long, greater than 5; in units of $10^{-3}\beta_e D^2/cm^{-1}$); calculated oscillator strengths are given by the three grades of thickness (narrow, less than 0.1; medium 0.1–0.5; thick, greater than 0.5); and calculated polarizations with respect to the formula shown are given by directions of the flags at the end of the bars.

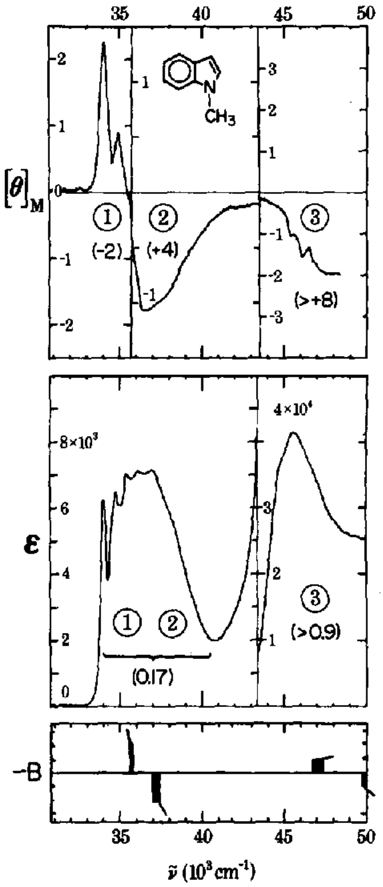


Fig. 4. N-methylindole. See caption to Fig. 2.

properties, it is not good enough for MCD unless μ^+ contributions completely dominate, since the μ^- contributions to B terms originate primarily from non-nearest-neighbor contributions [in uncharged $(4N+2)$-electron perimeters, exclusively so].[2] We have therefore used the procedure of Ref. 18, which differs from the standard PPP approach in that next-nearest-neighbor interactions have been added in the evaluation of magnetic moments. The results of the calculations shown in Figs. 2–5 are in quite satisfactory agreement with experiment. Some of the discrepancies observed are undoubtedly of experimental nature (it is difficult to evaluate the B terms of strongly overlapping transitions), but the rest must be ascribed to inadequacies in the PPP model or unsuitable parameter choice (the parameters are those of Ref. 6 and no attempt at optimization was made). Perhaps the most fundamental inadequacy in any π-electron model for MCD spectroscopy is the neglect of magnetic mixing between $\pi\pi^*$ states on the one hand and $n\pi^*$, $\sigma\pi^*$, and $\pi\sigma^*$ states on the other. This point has been emphasized in Ref. 16 in a discussion of the MCD spectrum of indole, and by several other authors. The usually adopted remedy is to use an all-valence-electron method of calculation such as CNDO/S. This is reasonable but so far there is no evidence that methods of this type produce reliable results for $\sigma\pi^*$ and $\pi\sigma^*$ states of molecules such as indole. Indeed, they are known to produce quite unsatisfactory results for the $n\pi^*$ transitions of some molecules (for instance, the $n\pi^*$ transitions of pyridones calculated by the CNDO/S method appear at much too low energies).[19] It seems to us that explicit consideration of all valence electrons may well be important for a truly quantitative prediction of the B terms of $\pi\pi^*$ transitions, perhaps by methods other than CNDO/S, but that the primary features of the results are due to $\pi\pi^*$–$\pi\pi^*$ mixings alone. Some possible reasons for this have been offered in Ref. 3.

Analogs of **1** *containing several heteroatoms.* Since the simple perimeter model performs well for the heterocycles of type 1-X-1, it is quite probable that its predictions for other hetero analogs of **1**, shown in Table 1, are reliable. It is now possible to go a step further and enquire about the effect of additional heteroatoms. Aza nitrogens are of particular interest since their introduction leads to a series of parent systems for many natural and man-made derivatives of biological importance, such as benzimidazoles, purines, etc.

In order to predict the μ^+ contributions to the B terms of the unsubstituted parent heterocycles with several heteroatoms, it appears most reasonable to consider the strongest perturbation first, i.e. to start with the neutral heterocycles of the type X-1, and to estimate the effect of additional aza substitution on their ΔHOMO and ΔLUMO values. In the way of example, the squares of the PPP MO coefficients of indole are given in Table 2. In indole itself, ΔHOMO < ΔLUMO, but the difference is

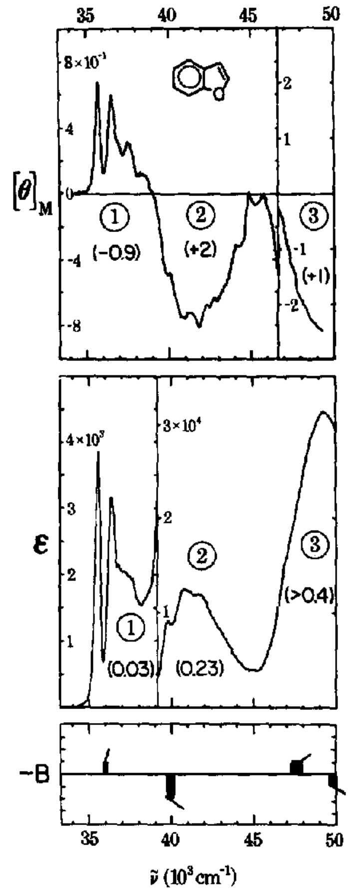


Fig. 5. Benzofuran. See caption to Fig. 2.

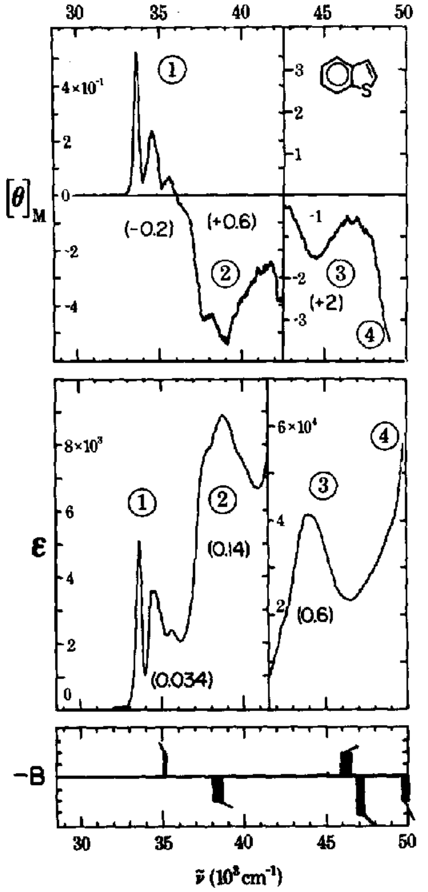


Fig. 6. Benzothiophene. See caption to Fig. 2.

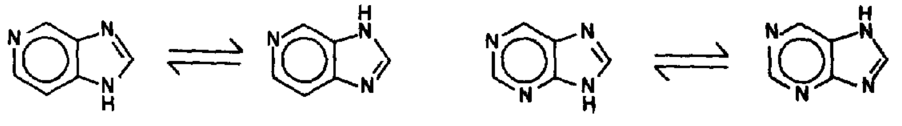
relatively small and could be reversed by a strong perturbation (with the parameters of Ref. 6, ΔHOMO − ΔLUMO = 0.13 eV). The difference will be increased and the negative μ^+ contributions to the B terms of transitions L_1 and B_1 as well as the positive μ^+ contributions to those of transitions L_2 and B_2 will be augmented if the aza nitrogen is introduced into any of the dominant positions 2, 3, 4, or 7. Aza replacement in the neutral position 6 should have little effect. Only in the subdominant 5 position will aza substitution tend to decrease the magnitude or reverse the sign of the ΔHOMO–ΔLUMO difference.

In summary, as long as the first-order PMO estimate of orbital energies is correct, azaindoles should have at least as strong a negative B term for the L_1 transition and positive B term for the L_2 transition as indole itself, 5-azaindole being the lone exception. Numerical calculations using the PPP method and procedures of either Ref. 6 or Ref. 20 suggest that for the usual parameter values the 5-aza "substituent" prevails over the 1-NH "substituent". Thus, we expect the B terms of the L bands of 5-azaindole to have signs opposite to those of indole itself.

Most of the predictions for the aza derivatives cannot be tested against experiment at present. A brief mention of the MCD spectrum of benzimidazole in Ref. 15b indicates that the signs agree with those of indole as would be expected from the present arguments. This is also true of 7-methylpurine, 9-methylpurine, and 9-methyl-8-azapurine, discussed in more detail below.

Tautomerism. The large difference in the effect of 5-aza and 6-aza substitution has interesting implications for MCD spectra of the tautomeric azabenzimidazoles: of the two tautomers, 3,6-N-1-NH-1 and 3,5-N-1-NH-1, the latter will have a less negative (more positive) B term for the L_1 transition, and a more negative (less positive) B term for the L_2 transition. Calculations by the method of Ref. 20 actually suggest that the effect of the 5-N heteroatom will prevail over both 3-N and 1-NH, so that L_1 will actually have a small positive B term and L_2 a negative one. This numerical result may be a sensitive function of the parameters used, but the relative values for the tautomers are undoubtedly predicted correctly. The MCD spectra of the tautomers of purine, 3,4,6-N-1-NH-1 and 3,5,7-N-1-NH-1 should differ similarly: the latter should have a less negative B term for the L_1 transition and a more negative B term for the L_2 transition. This time, calculations suggest that the effect of 5-N is not sufficient to prevail over 3-N, 7-N and 1-NH, so that the MCD signs of the L transitions in both tautomers will be the same as in indole itself. Literature data on 3,4,6-N-1-NCH_3-1 (7-methylpurine) and 3,5,7-N-1-NCH_3-1 (9-methylpurine) are available[21]. In both, the signs of the B terms of the L bands indeed are as in indole itself, and, as expected from the above, the B term of transition L_1 is less negative and that of transition L_2 less positive in 9-methylpurine than in 7-methylpurine. Not surprisingly, also the signs reported[22] for 9-methyl-8-azapurine agree with those of indole.

All the arguments presented above rely heavily on the use of first-order perturbation theory to estimate relative values of orbital energies. In order to gain confidence



3,5-N-1-NH-1 3,6-N-1-NH-1 3,5,7-N-1-NH-1 3,4,6-N-1-NH-1

Table 2. Squares of PPP MO coefficients in indole and expected effects of aza replacement on ΔHOMO – ΔLUMO

	Position					
Orbital	2	3	4	5	6	7
c_{-2}^2	0.032	0.005	0.068	0.307	0.134	0.013
c_{-1}^2 (LUMO)	0.175	0.068	0.256	0.032	0.141	0.237
Δ	−0.143	−0.063	−0.188	0.275	−0.007	−0.224
c_1^2 (HOMO)	0.132	0.243	0.191	0.044	0.097	0.163
c_2^2	0.138	0.000	0.017	0.242	0.101	0.037
Δ	−0.006	0.243	0.174	−0.198	−0.004	0.126
Δ(ΔHOMO–ΔLUMO)/(−Δα)	−0.137	−0.306	−0.362	0.473	−0.003	−0.350
Position type[a]	dN	ND	DD	SS	NN	Dd
Response to I effect[a]	d	D	D	S	N	D

[a] See footnotes to Table 1.

about the use of such a primitive approach for prediction of trends in MCD spectra, we have performed several dozen calculations of the B terms in the spectra of various azaindoles by the computational π-electron methods of Refs 6 and 20. We find that the two quite diverse methods of calculation both give results in agreement with each other and with the simple deductions based on the ΔHOMO—ΔLUMO difference as evaluated by the first-order PMO method from Table 2. Thus, it appears that the PMO theory is adequate for a qualitative understanding of general trends. Still, for actual use of MCD spectra in structure assignment we would recommend that a numerical PPP calculation of orbital energies be performed, using one of the readily available standard programs. An example of a case where a first-order perturbation approximation is inadequate follows.

Protonation. The protonation of an aza nitrogen increases its electronegativity and thus has a simply predictable effect on the magnitude of the ΔHOMO − ΔLUMO difference if the MO coefficients of the four frontier orbitals on the nitrogen are known or can be estimated and if first-order theory is applicable. If several aza nitrogens are present, predicted effects of protonation on each can be compared with the experimental effect of protonation on the B terms of the L bands assuming that their energy separation remains roughly constant. In favorable cases, conclusions regarding the position of protonation can be drawn. We shall illustrate the procedure using the reported[21] MCD spectra of the four isomeric N-methylpurines in neutral and acidic solutions and using MO coefficients obtained from a PPP calculation on various tautomers of purine itself. The reported spectra of all four neutral species showed a negative B term for the L_1 transition and a positive B term for the L_2 transition. Protonation had hardly any effect on their magnitudes in the case of 1-methylpurine and 7-methylpurine, but it increased them greatly in the case of 3-methylpurine and reduced them greatly in the case of 9-methylpurine without affecting the L_1–L_2 energy difference substantially. Chart 2 provides a summary of the Δ(ΔHOMO − ΔLUMO)/(−Δα) values for the positions in which aza nitrogens are located. These were obtained from the MO coefficients using first-order perturbation theory, similarly as in Tables 1 and 2. Since Δα for protonation is negative, a positive value of Δ(ΔHOMO − ΔLUMO)/(−Δα) for a given position of protonation means that the difference ΔHOMO − ΔLUMO becomes more positive or less negative upon protonation, whereas a negative value means that the difference ΔHOMO − ΔLUMO becomes less positive or more negative upon protonation. In the former case, the B term of the L_1 transition will become more positive or less negative, the B term of the L_2 transition will become less positive or more negative. In the latter case, the opposite will be true for both B terms. In the neutral compounds, the first B term is negative and the second one positive. Thus, protonation in a position for which Chart 2 gives a positive value for Δ(ΔHOMO − ΔLUMO)/(−Δα) should decrease the MCD peaks, protonation in a position for which Chart 2 gives a negative value for Δ(ΔHOMO − ΔLUMO)/(−Δα) should increase them, and protonation in a position for which Chart 2 lists a value which is small or zero should have little effect. Comparison of the reported[21] effects of protonation with the values given in Chart 2 provides an agreement for only one position of protonation in each case, italicized in Chart 2, and could be used to assign the positions of protonation. However, the introduction of a positive charge represents a rather severe perturbation and one might well ask whether the first-order PMO approximation is adequate to describe it. We have therefore performed PPP calculations by the method of Ref. 6 and found that in one case, 7-methylpurine, the calculated effects on the magnitude of ΔHOMO − ΔLUMO differ from those expected at the PMO level. In 3-methylpurine, the PPP result is compatible not only with protonation in position 7, suggested by the PMO argument, but equally well also with protonation in position 9 so that an unambiguous assignment cannot be reached. The calculated B terms followed the trends in the ΔHOMO − ΔLUMO values. The PPP results lead us to assign the protonation sites as 9 in 1-methylpurine, 7 or 9 in 3-methylpurine, 3 in 7-methylpurine, and 1 in

9-methylpurine (indicated by arrows in the formulas). In almost all cases, the two pyrole-like nitrogen atoms, -NR-, are on opposite sides of the molecule. For 9-methylpurine, our result agrees with the previously available assignment reached in an nmr study[23]. Thus, it appears that protonation is a strong enough perturbation that the simple PMO description, although probably still of some use for the interpretation of general trends, cannot be used reliably for prediction of the effects on ΔHOMO − ΔLUMO. On the other hand, there is presently no reason to doubt that the ΔHOMO − ΔLUMO values calculated by the PPP method are useful guides for the evaluation of the effects of protonation of ΔHOMO − ΔLUMO. Still, before the MCD method can be considered generally useful for assignment of protonation sites, additional comparisons with independent methods such as nmr will be necessary.

CONCLUSION

We feel that we have achieved both physical understanding and qualitative predictability for the MCD spectra of azaindoles. We see no reason why the same procedures should not be successful with the aza analogs of other heterocycles derived from the indenide anion 1 by the introduction of the NH group, such as isoindole (2-NH-1), indolizine (3a-N-1), and the azulene-like pyrindines (4-NH-1 and 5-NH-1), or, for that matter, by the introduction of other heteroatoms such as -O-, -S-, etc. In summary, then, we believe that the simple perimeter model description of Refs 2–4 provides a prediction and/or rationalization of the MCD signs of the L bands of a vast number of heterocycles derived from 1, utilizing only the simplest of means, and will be useful for structural work, in particular investigations of tautomerism. On the other hand, although general qualitative understanding of the effects of protonation of heterocycles of this type on their MCD spectra can also be obtained from similar back-of-the-envelope PMO arguments, the determination of the protonation sites from MCD spectra requires a numerical calculation.

EXPERIMENTAL

The compounds used in the measurement were commercial samples purified by glc or gradient sublimation. The spectra were measured in spectral grade cyclohexane, except for the indole nitranion (1-N⁻-1), which was prepared for measurement in freshly distilled hexamethylphosphoramide from indole and sodium hydride under N_2. The techniques of measurement and B term evaluation were those of Ref. 6.

The calculations were performed as in Ref. 6 using the higher set of parameter values given there for A_{X^+}, except that the matrix elements of the magnetic dipole moment operator between atomic orbitals on next-nearest neighbors were not set to zero but to −0.15 times the values for nearest neighbors as recommended in Ref. 18 (calculation 2 on p. 425). The geometries consisted of regular polygons except for that of 1-S-1 which was taken from the crystal structure of dibenzothiophene.[24] The results were almost independent of the choice of origin and the signs compared well with the origin-independent results obtained by the program of Seamans and Linderberg.[20]

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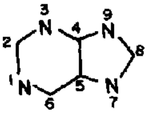
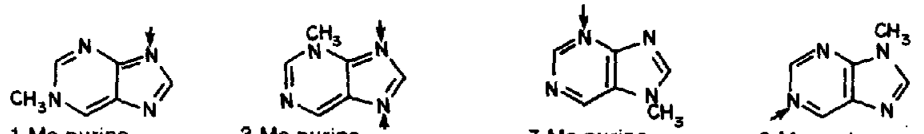


Δ(Δ*HOMO* − Δ*LUMO*)/(−Δα):	Position of protonation[a] 1	3	7	9
1-Me-purine	—	+0.31	−0.41	−***0.04***
3-Me-purine	+0.38	—	−***0.41***	**+0.15**
7-Me-purine	+*0.08*	**−0.33**	—	−0.29
9-Me-purine	+***0.44***	−0.19	−0.25	—

[a] The value for the one position of protonation in each isomer which is compatible with the MCD spectra at the PMO level of approximation is italicized. The value which corresponds to the result of a numerical PPP calculation is in bold face; we propose that this is the actual position of protonation. Some ambiguity exists in the case of 3-methylpurine.



1-Me-purine (1,3,7-N-5-NCH_3-1)
3-Me-purine (1,3,6-N-4-NCH_3-1)
7-Me-purine (3,4,6-N-1-NCH_3-1)
9-Me-purine (3,5,7-N-1-NCH_3-1)

Chart 2. First-order (PMO) approximation protonation sites in N-methylpurines and the ΔHOMO − ΔLUMO difference.

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