

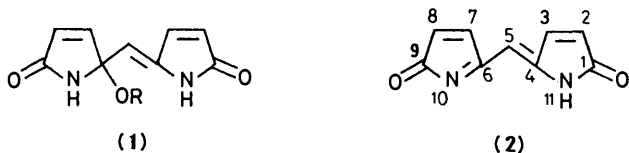
Propentdyopents and Related Compounds. Part 3.† Some Semiempirical Calculations on Propentdyopent Systems

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MINDO/3 (and in some cases MNDO) calculations on substituted Z-propentdyopents, their anions and cations, and some propentdyopent adducts are reported. Using the frontier orbital model, predictions of reactivity are made for the various systems, and are related to known experimental results.

In Part 1¹ the ramified background of the propentdyopent problem was reviewed, and evidence was presented for formulating the skeleton of the alkanol-propentdyopent adducts as (1). Such substances formally arise by attack of an alkanol on the parent propentdyopent system (2) either as such, or as the metal complex (e.g. Zn^{II}), the deprotonated species, or the protonated species derived from (2).



Experimental work in this field is difficult, and has not always led to clearcut results. If it were possible to predict the relative reactivities of the β , *meso*, and valley positions of (2) this would be a useful step forward. We present here the first MO calculations on this system, and use them to rationalise existing experimental observations.

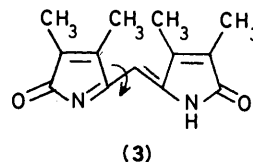
Since *ab initio* procedures require a considerable amount of computing for such complex structures we have turned to the semiempirical methods (MINDO/3 and MNDO) devised by Dewar.^{2,3} With molecules of the complexity of substituted (1) and (2) it needs to be recognised that we may be approaching the boundary beyond which the application of such methods will not be useful. The simple test of usefulness lies in the relation of prediction to experimental result. Using a standard package devised for the University of London CRAY-IS computer by Dr. H. S. Rzepa we have applied MINDO/3 (and in some cases MNDO) semiempirical methods without configuration interaction. Complete optimisation of geometry has been allowed, except that (i) for methyl groups the bond lengths and bond angles to the three hydrogens have been assumed to be identical and (ii) the dihedral angle between the rings has been fixed for each conformation studied. Reactivity parameters have been calculated using the Fukui frontier orbital treatment in its simplest version.^{4,5} The relative reactivities are assumed to be determined by the magnitude of the squares of the atomic orbital coefficients in the highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) at the atomic position in question, such that reactivity parameter = $2\sum_i c_i^2 = 2(c_s^2 + c_{px}^2 + c_{py}^2 + c_{pz}^2)$ where c is the coefficient for the i th valence atomic orbital in the HOMO or the LUMO. For cases of degeneracy or near-degeneracy the next-to-frontier orbital (NHOMO, NLUMO) is also taken into consideration. A relatively large electron density in the HOMO/NHOMO at a given atom is taken to indicate that an electrophile is more readily added to that site, while

a large atomic orbital coefficient in the LUMO/NLUMO at a given atom similarly indicates enhanced reactivity towards nucleophiles. Reactivity towards neutral radicals is estimated simply by averaging the appropriate reactivity indices of the HOMO and LUMO.

For present purposes, the numbering scheme shown in (2) will be employed. Dihedral angles refer to the interplanar angle arising from rotation about the *meso*-single bond [see (3)].

Results and Discussion

In the following sections the reactivities, and, in some cases, the energetics emerging from the calculations are discussed for Z-tetramethylpropentdyopent (3) and its derivatives. The effect of a powerful electron-donating group, and an electron-withdrawing group, at an *exo*- β -position is also examined.



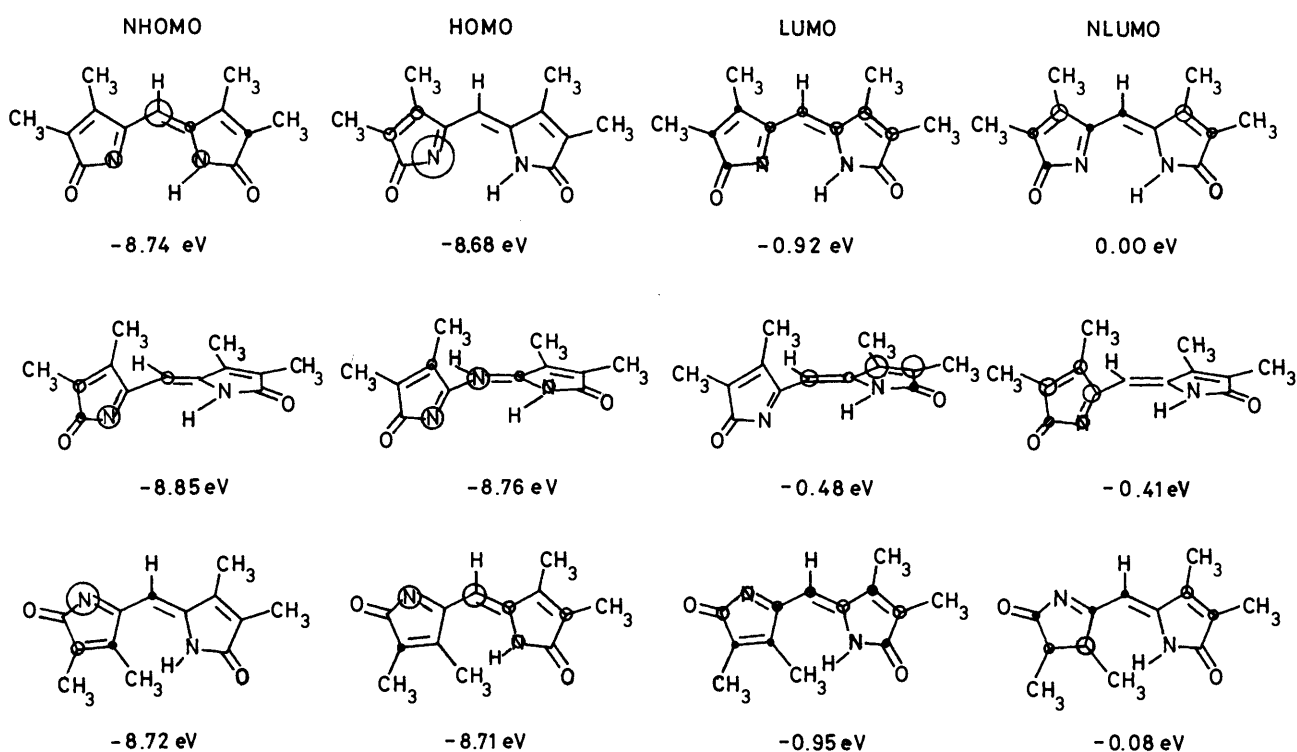
The results of MINDO/3 calculations presented in Table 1 show that the *syn* conformers are more stable than are the *anti* conformers. Optimisation leads to the prediction that the synclinal (56°) conformer [(3) dihedral angle at arrow] will be the most stable. However, the MINDO/3 method is known to underestimate hydrogen bonding.⁶ Since intramolecular hydrogen bonding is expected to contribute significantly to the stabilisation of the synperiplanar conformer, this prediction is not to be accepted at its face value. In any case, the difference in energy between the synperiplanar and synclinal conformers (2.4 kJ mol⁻¹) is small, and, overall, it needs to be recognised that the differences between calculated and experimental standard heats of formation are sometimes much larger than this value (e.g. 20.5 kJ mol⁻¹ for pyrrole⁷). We conclude that, as far as conformational energetics are concerned, these calculations are not helpful in the present example.

Electrophilic Attack.—Table 1 shows that for (3) the HOMO and NHOMO are almost degenerate, especially at small dihedral angles ($E_{\text{HOMO}} - E_{\text{NHOMO}}$ 0°, 0.05; 90°, 0.09; 180°, 0.01 eV). The reactivity parameters⁵ of the NHOMO, HOMO, LUMO, and NLUMO orbitals are shown in a schematic way for the synperiplanar, perpendicular, and antiperiplanar conformers in Figure 1. It is found that the electron density distribution of the HOMO of the synperiplanar conformer is the same as that of the NHOMO of the antiperiplanar conformer. This accounts for the abrupt change observed between 150° and 180° in Figure 2a, where reactivity

† Part 2, R. Bonnett, D. Hamzesh, and M. A. Vallés, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1383.

Table 1. MINDO/3 calculations: standard enthalpy of formation, dipole moment, and energy of the frontier and next-to-frontier molecular orbitals for the conformers arising from rotation about the *meso*-single bond in *Z*-tetramethylpropentdyopent (3)

Dihedral angle (°)	ΔH_f° kJ mol ⁻¹	μ/D	E_{NHOMO} / eV	E_{HOMO} / eV	E_{LUMO} / eV	E_{NLUMO} / eV
0	-217.4	7.5	-8.74	-8.68	-0.92	-0.00
10	-217.5	7.5	-8.74	-8.69	-0.92	-0.01
20	-218.0	7.4	-8.75	-8.69	-0.89	-0.04
30	-218.7	7.3	-8.77	-8.70	-0.85	-0.07
56	-219.8	6.9	-8.82	-8.73	-0.70	-0.20
60	-219.8	6.8	-8.83	-8.73	-0.67	-0.22
90	-217.8	5.9	-8.85	-8.76	-0.48	-0.42
120	-210.5	4.8	-8.84	-8.77	-0.66	-0.28
150	-194.7	3.5	-8.78	-8.76	-0.85	-0.14
180	-179.6	2.3	-8.72	-8.71	-0.95	-0.08

**Figure 1.** Schematic representation of the MINDO/3 reactivity parameters of the NHOMO, HOMO, LUMO, and NLUMO for the synperiplanar, perpendicular, and antiperiplanar conformers of *Z*-tetramethylpropentdyopent (3)

parameters for the electrophilic attack at the various positions based on the HOMO only are plotted against dihedral angle. Figure 2b shows the situation when HOMO and NHOMO contribute equally to the reactivity parameter. No matter what is the relative participation of HOMO and NHOMO, the azomethine nitrogen (N-10) emerges as the most reactive position. In the planar conformations two electronic effects, the electron-withdrawing effect of the azomethine nitrogen, and the electron-donor effect of the enamidic nitrogen, reinforce one another. In the perpendicular conformation, the removal of conjugation produces a decrease in the reactivity of the azomethine nitrogen and an increase in that of the *meso*-carbon (C-5). In this conformation the molecule is expected to have the reactivity of the individual 5-methylene-3-pyrrolin-2-one and 2*H*-pyrrol-2-one moieties. But MINDO/3 calculations show that the HOMOs of these fragments have approximately the same energy (3,4-dimethyl-5-methylene-3-pyrrolin-2-one

E_{HOMO} MINDO/3 -8.81, MNDO -9.21 eV; 3,4,5-trimethyl-2*H*-pyrrol-2-one E_{HOMO} MINDO/3 -8.78, MNDO -10.36 eV).⁸ This explains why the HOMO and NHOMO of the conformer with a dihedral angle of 90° are almost degenerate and have relatively high atomic coefficients in both moieties of the structure.

Nucleophilic Attack.—Reactivity parameters for nucleophilic attack are plotted against dihedral angle in Figure 3. It is seen that for orbital-controlled reactions⁹ (likely with soft donors such as RSH, R⁻, or CN⁻) attack by the nucleophile at positions 2, 3, 4, and 5 or 6 needs to be considered. For small dihedral angles in which through-conjugation is important, position 2 is predicted to be more reactive than position 3, and 4 more reactive than 5. This indicates that the electron-withdrawing effect of the azomethine group (C-6-N-10) is higher than that of the lactam carbonyl. For the synperiplanar

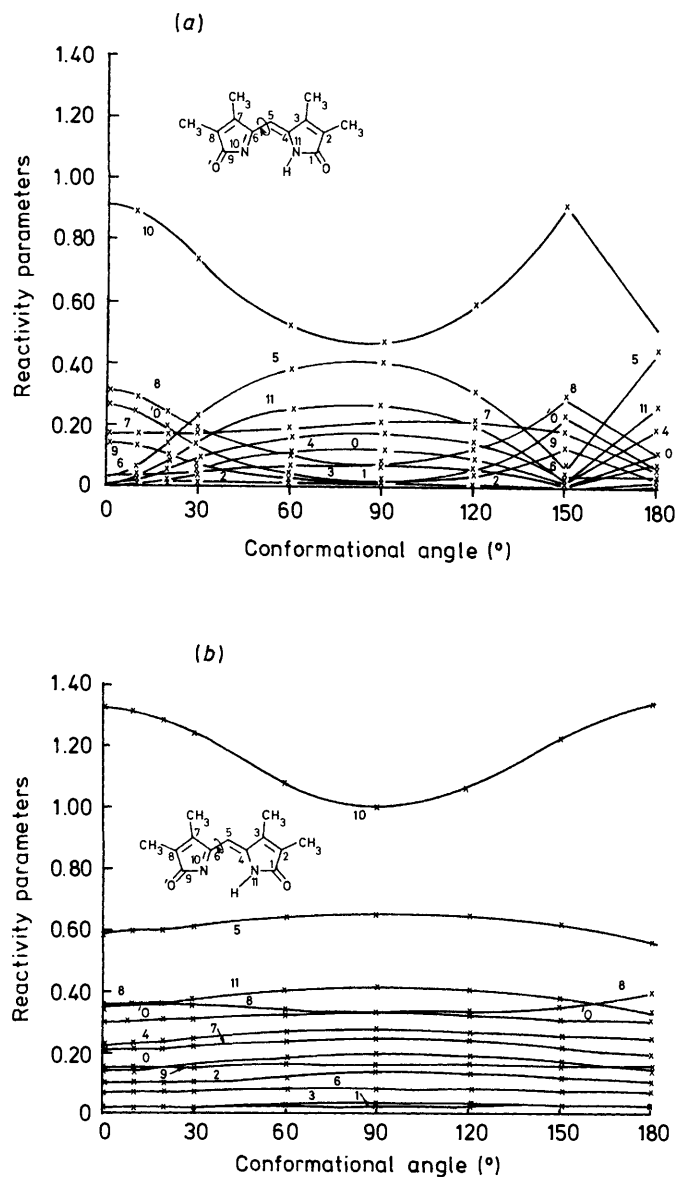


Figure 2 a. Reactivity towards electrophiles (HOMO only) of the conformers arising from rotation about the *meso*-single bond in *Z*-tetramethylpropentdyopent (3), calculated by MINDO/3. b. Reactivity towards electrophiles (HOMO + NHOMO) of the conformers arising from rotation about the *meso*-single bond in *Z*-tetramethylpropentdyopent (3), calculated by MINDO/3

conformation (in the range θ 0–25°), which is expected to be the most stable, the choice is between positions 2 and 4. With increase of dihedral angle and decreasing through-conjugation, the reactivities of positions 3 and 5 increase, while that of 4 decreases. Table 1 shows that at 90° the LUMO and NLUMO are almost degenerate ($E_{\text{LUMO}} - E_{\text{NLUMO}}$ 0.07 eV), and Figure 1 indicates that these two orbitals are individually localised on the two parts of the structure.

For charge-controlled reactions,⁹ which are expected for hard donors such as water and alkanols, the atomic charge distributions presented in Figure 4 show that for the synperiplanar conformation attack at the carbon (C-6) of the azomethine double bond is likely to occur. The atomic charge distribution is only slightly dependent on the dihedral angle, and this does not cause changes in the reactivity order.

The reactivity parameters indicate that, for the planar and

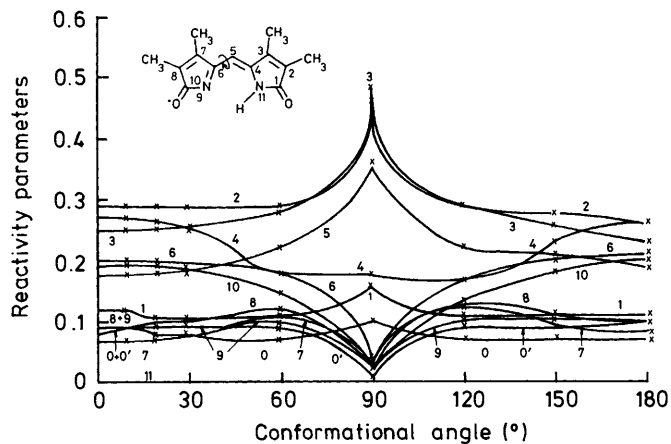


Figure 3 Reactivity towards nucleophiles of the conformers arising from rotation about the *meso*-single bond in *Z*-tetramethylpropentdyopent (3), calculated by MINDO/3

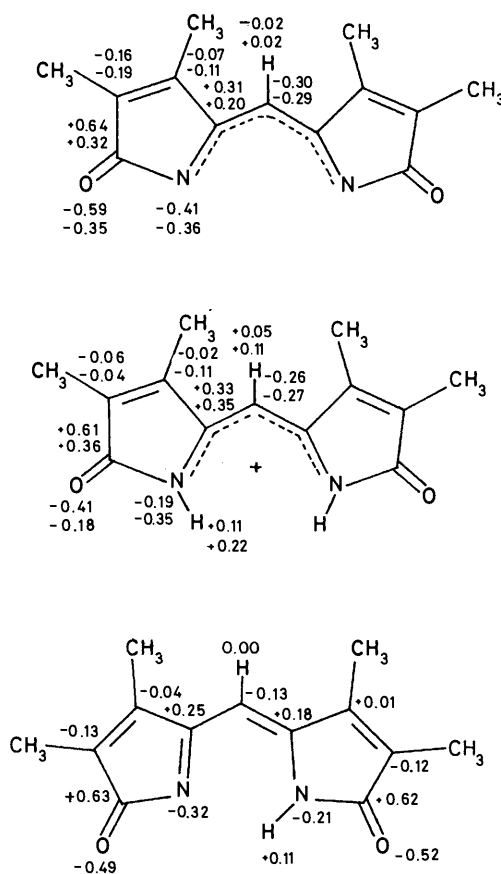
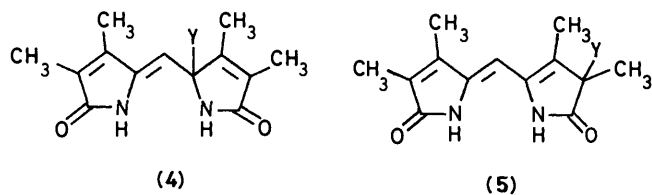


Figure 4 Net atomic charge distribution for the synperiplanar conformation of the anion (6) and cation (7) of *Z*-tetramethylpropentdyopent (MINDO/3 values above MNDO values) and of the parent substance (3) (MINDO/3 values only)

near-planar conformations the reaction with a soft nucleophile and a protic reagent (YH) can occur by 1,4-addition across the C-4–N-10 system, or by 1,6-addition across the C-2–N-10 system to give (4) and (5), respectively.

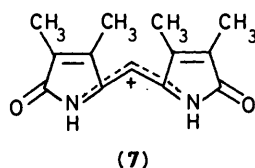
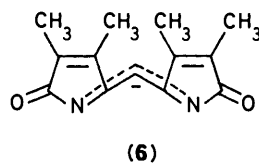
Of these two systems (4) is regarded as the more stable since it contains two conjugated systems:¹⁰ since the acid-catalysed reaction is likely to involve a rapid equilibration of N-10



protonated (3) with (4) and (5), the thermodynamically more stable adduct (4) is expected to result. In the case of a hard nucleophile (such as water) a 1,2-addition to the azomethine bond would be expected, also leading to (4).

For hypothetical conformations with a dihedral angle between 60 and 120°, a mixture of 1,2-addition to the azomethine double bond and nucleophilic or even electrophilic substitution at C-5 is predicted for soft reagents (Figure 1).

Radical Attack.—The frontier orbital treatment allows an estimate of a reactivity parameter for radical attack by taking the average of the electrophilic and nucleophilic parameters. When this is done for the HOMO and LUMO orbitals only, the atoms which emerge as the most reactive are N-10 and C-5. At small dihedral angles a mixture of 1,4-addition (N-10—C-4) and 1,2-addition (N-10—C-6) may again be predicted. A 1,4-addition across the N-10—C-8 system is also possible, but the product will not be favoured thermodynamically. An increase in the dihedral angle towards 90° is predicted to increase 1,2-addition to the *meso* double bond (C-5—C-4).



The MINDO/3 study of the syn- and anti-periplanar conformations of the anion (6) shows that the *anti* conformation ($\Delta H_f^0 - 278.8 \text{ kJ mol}^{-1}$) must be less stable than the *syn* conformation ($\Delta H_f^0 - 311.6 \text{ kJ mol}^{-1}$; energy minimum). Reactivity parameters and atomic charge distribution, while very similar for the two systems, show for the antiperiplanar conformation a small loss of symmetry. In the synperiplanar conformer the highest reactivity parameter for electrophilic attack is at the *meso*-carbon (0.79). This value is almost double that for the nitrogens (0.47). The reactivity parameters for the remaining positions are negligible. The MNDO calculation on the same conformer agrees with these values (*meso*-C, 0.90; N, 0.41, $\Delta H_f^0 - 228.5 \text{ kJ mol}^{-1}$). The HOMO energy is also found to be similar by the two methods (MINDO/3, -3.98 ; MNDO, -4.04 eV). MNDO shows a much less exaggerated atomic charge separation³ especially at the carbonyl double bond (Figure 4). Nitrogens have a high negative charge density, and must be regarded as the point of attack by a hard electrophile.

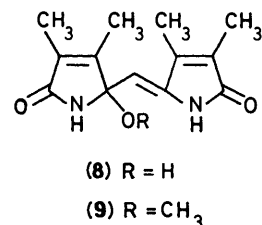
MINDO/3 and MNDO calculations on the synperiplanar conformation of the protonated species (7) (ΔH_f^0 MINDO/3, $+295.2$; MNDO, $+544.8 \text{ kJ mol}^{-1}$) show that the valley positions (C-4, C-6) are the most reactive (MINDO/3, 0.45;

Table 2. MINDO/3 calculations: standard enthalpy of formation, dipole moment, and energy of the frontier orbitals for two different conformations of the water and methanol adducts of Z-tetramethylpropentdyopent

Compound	$\Delta H_f^0 / \text{kJ mol}^{-1}$	μ / D	$E_{\text{HOMO}} / \text{eV}$	$E_{\text{LUMO}} / \text{eV}$
(8a)	-557.0	3.5	-8.70	-0.42
(9a)	-506.0	3.5	-8.73	-0.45
(8b)	-548.6	5.9	-8.81	-0.47
(9b)	-499.3	6.0	-8.83	-0.53

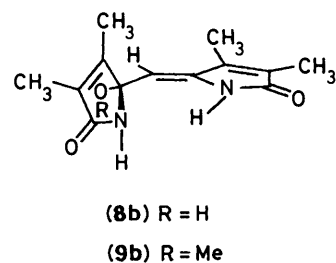
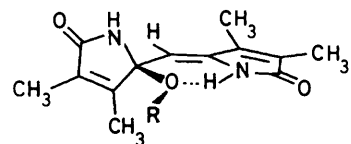
MNDO, 0.53) towards nucleophiles, followed by the carbons α to carbonyl (C-2, C-8) (both methods give a reactivity parameter of 0.17). The calculated LUMO energy is -5.31 (by MINDO/3) and -6.34 eV (by MNDO). With respect to atomic charge distribution, differences are observed between the two methods (and MINDO/3 seems to be the more reasonable, compare the charges on nitrogen and oxygen in Figure 4). In spite of numerical differences, both methods indicate that in terms of atomic charge, the valley positions of (7) must be highly reactive.

Water and Methanol Adducts of Z-Tetramethylpropentdyopent (8) and (9).—Two different conformations of the water (8) and methanol (9) adducts of Z-tetramethylpropentdyopent



have been studied by MINDO/3. One set of conformations (8a), (9a) has an intramolecular hydrogen bond; the other set (8b), (9b) does not.

The results are presented in Table 2. Conformers (8a), (9a) with the intramolecular hydrogen bonding are calculated to be 6.7 – 8.4 kJ mol^{-1} the more stable, but, as before, we expect this to be an underestimate.⁶



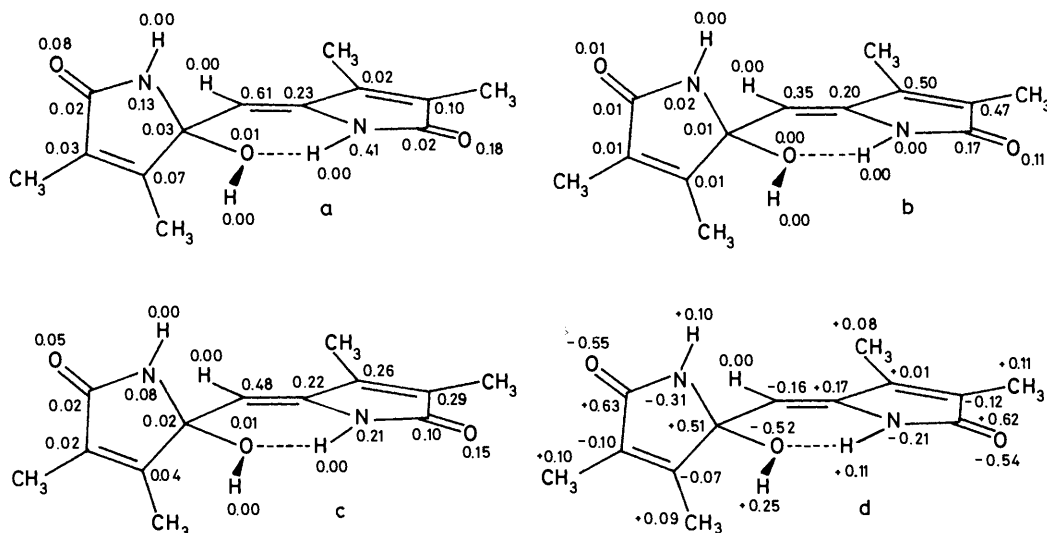
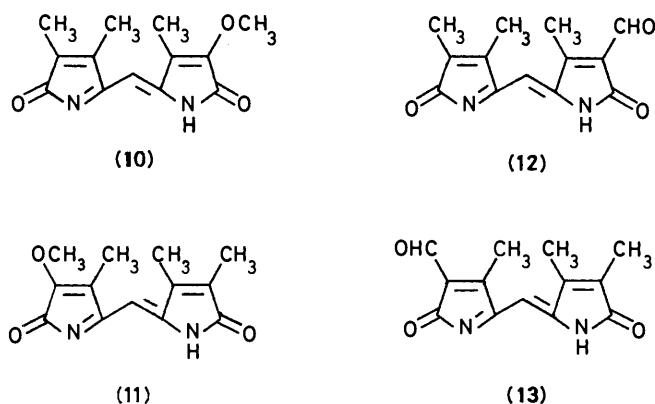


Figure 5. Reactivity parameters towards electrophiles (a), nucleophiles (b), and radicals (c), and net atomic charge distribution (d) for the water adduct of *Z*-tetramethylpropentdyopent (**8a**)

The reactivity parameters are the same and do not depend on the conformation. The conjugation between the rings is interrupted by an sp^3 -hybridised carbon atom, and each ring should therefore have its own reactivity. MINDO/3 and MNDO calculations show that the HOMO and LUMO of 3,4-dimethyl-5-methylene-3-pyrrolin-2-one (E_{HOMO} MINDO/3, -8.81 ; MNDO, -9.21 eV, E_{LUMO} MINDO/3, -0.11 ; MNDO, -0.79 eV)⁸ are more reactive than those of 3,4,5-trimethyl-3-pyrrolin-2-one (E_{HOMO} MINDO/3, -9.49 ; MNDO, -10.13 eV, E_{LUMO} MINDO/3, 0.28 ; MNDO, -0.33 eV).⁸ Thus, provided the amino hemiacetal function is not attacked, the propentdyopent adducts are expected to have the reactivity of a 5-methylene-3-pyrrolin-2-one and no degeneracy should appear. Figure 5 shows that the results from the MINDO/3 calculations agree with this prediction. Soft electrophiles and soft nucleophiles are expected to react at the *meso*-carbon. However, the atomic charge distribution shows that the alkoxy or hydroxy oxygen must be the point of attack by a hard electrophile, such as a protic acid. In the water adducts the hydroxylic hydrogen is expected to be the most reactive towards a hard nucleophile (base).

Effect of an Electron-donating or an Electron-withdrawing Group at the exo- β -Position of the Propentdyopent Nucleus (10)–(13).—Synperiplanar isomers of the propentdyopent nucleus bearing a methoxy group [(10), (11), tautomers] or a



formyl group [(12), (13), tautomers] have been studied by MINDO/3. The stabilities of (10) and (11) are very similar: for the other pair the stability of (13) is slightly greater (4.0 kJ mol⁻¹) than that of (12). Surprisingly, the introduction of these very dissimilar groups does not have a *substantial* effect on the reactivity parameters of the system. The methoxy group increases the reactivity of the HOMO + NHOMO towards electrophiles, while the formyl group decreases it. But N-10 is always the most reactive position.

The effect of the methoxy group on the reactivity towards nucleophiles appears to be different in each tautomer. In (11) the LUMO is scarcely affected, but in (10) the electron density on the π -system linking the rings is increased. Thus in tautomer (10) position 4 is still the most reactive, but its reactivity is diminished. The formyl group increases the reactivity towards nucleophiles. The electron-withdrawing effect of the formyl group is greater than that of the azomethine function, and as a consequence the reactivity of C-3 and C-5 increases in structure (12). However, in tautomer (13) the formyl group and the azomethine function reinforce one another, and position 4 is still expected to be the most reactive. The azomethine carbon atom must always be expected to be the most reactive site for attack by a hard nucleophile.

The results of these calculations can be summarised as follows. As far as the conformational energetics of the system are concerned, the *syn* conformation of (3), (6), and (7) are preferred over the *anti* conformations. The calculation for (3) optimises for a synclinal conformation (56°) but this result is discounted since the method underestimates the stabilisation by intramolecular hydrogen bonding arising in the synperiplanar conformation and overall predictions with respect to energetics are not very useful.

Predictions concerning reactivity are much more useful, and are in agreement with experimental results where these are available. Thus the formation of the methanol propentdyopent adduct from the zinc(II) complex of tetraethylpropentdyopent in acidic methanol can be understood as a proton (hard electrophile) attack at a nitrogen of the anion (model for the zinc complex) to give the *Z*-propentdyopent. In acidic medium the latter is expected to protonate at the azomethine nitrogen and the protonated form will react with a nucleophile at one of the valley positions. The calculations thus support and rationalise the formulation (1) rather than alternatives (*meso*- and β -addition) which have also been considered.^{1,11} The

isolation of deuteriated tetraethyl(methanol)propentdyopent, which does not possess C–D bonds (i.r.) and which still possesses a *meso*-proton (δ 4.75), by treatment of the zinc(II) tetraethylpropentdyopent complex with MeOD–CF₃CO₂D accords with a charge-controlled attack by D⁺ on the zinc complex. Again, the high negative charge on the hydroxy (or alkoxy) oxygen of the water (or methanol) adduct (Figure 5) explains its ready protonation and elimination of water (or methanol) to form the propentdyopent cation, and the formation of the methanol (or water) adduct in high yield when treated with refluxing methanol (or water) in the presence of a trace of acid.^{1,11} In the presence of methanolic sodium methoxide, tetraethyl(water)propentdyopent loses the hydroxylic hydrogen since it has the highest positive charge (Figure 5) and no methanol adduct can be isolated. However when excess of methyl iodide is present the methanol adduct can be isolated in 52% yield due to electrophilic attack on the anionic oxygen.¹²

Acknowledgements

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