

CCA-533

541.124:547.853.3

Original Scientific Paper

## Theoretical Study of Methylene Proton Coupling in Some Pyrimidine Radicals

J. N. Herak

*Institute »Ruđer Bošković«, Zagreb, Croatia, Yugoslavia*

Received December 6, 1968

The methylene proton couplings with the unpaired electron have been calculated for a number of pyrimidine radicals. The molecular orbital calculations were performed in the Hückel and McLachlan approximations. The methylene group has been treated both, directly as a member of the conjugated ring («hyperconjugation») and as a perturbation of the parent molecule. Both procedures give satisfactory agreement with the experimental results, better in the Hückel than McLachlan approximation. Complete disagreement has been found only for the 5-acetyl uracil radical. It is possible that in this case the measurements and the calculations do not refer to the same molecular structure.

### INTRODUCTION

Recently, much attention has been paid to the coupling of the unpaired electron, delocalized in the conjugated part of a molecule, with the attached methyl or methylene protons<sup>1-9</sup>. This coupling has been treated in both, molecular orbital and valence bond theories. In most of the papers the methylene proton coupling is explained with «hyperconjugation», although this term is often differently understood<sup>6,8,9</sup>. The calculations have been performed predominantly for hypothetical models like  $-\text{CH}(\text{CH}_2)$  or  $-\text{C}'(\text{CH}_2)\text{C}''-$ . In many cases, particularly in the molecules containing heteroatoms, the situation is much more complicated, since no reliable molecular orbitals can be obtained. Recently, Herak and Gordy measured hyperfine couplings of the methylene protons in a number of pyrimidine derivatives with electron spin resonance<sup>10-13</sup>. However, they did not calculate the  $\text{CH}_2$  proton couplings. In the present study such calculations have been performed and the calculated values are correlated with those experimentally observed.

### METHODS

The molecular orbital theory in the Hückel approximation<sup>14</sup> (HMO) and the McLachlan self consistent field approximation<sup>15</sup> (SCFMO) was used. Two different approaches for taking into account methylene protons were utilized. In the first one, the unpaired electron and, consequently, the wave function of the ground state of the total molecule extends into the substituent — methylene protons. The unpaired electron reaches these protons through the mechanism of «hyperconjugation». «Hyperconjugation» is treated in the simplest way by representing the two methylene hydrogen atoms by two group orbitals. The antisymmetric one

$$\Psi = N (\Phi_1 - \Phi_2) \quad (1)$$

is of the same symmetry as the  $\pi$  orbitals, and thus can be conjugated with them.  $\Phi_1$  and  $\Phi_2$  refer to s-atomic orbitals of the hydrogen atoms 1 and 2, respectively.  $N$  is the normalization constant. Hence, the methylene group is treated as a pseudo-atomic orbital in the linear combination of atomic orbitals (LCAO). Once the distribution of the unpaired electron is known, the coupling of the methylene protons can be evaluated. Levy<sup>7</sup> proposed a simple expression for the coupling:

$$A = 32.7 C_H^2 + 1.98 C_C^2 + 16.1 C_C C_H + (0.6 C_H + 0.15 C_C) (C_{C'} + C_{C''}) - 0.31 (C_{C'}^2 + C_{C''}^2) \text{ mT} \quad (2)$$

(Here mT stands for millitesla.)

This expression has been derived assuming the tetrahedral angles,  $109^\circ 28'$ , between the ligands of the  $-C'(CH_2)C''-$  fragment. 1.09 Å and 1.54 Å were chosen for the C—H and C'—C bonds, respectively.  $C_H$ ,  $C_C$ ,  $C_{C'}$  and  $C_{C''}$  are the coefficients of the methylene protons pseudo-atomic orbital, aliphatic carbon and two neighbouring aromatic carbon atomic orbitals, respectively, in the unfilled molecular orbital. The last term in the above expression is the spin polarization contribution.

The other approach is to calculate first only the conjugated part of the molecule and then treat the  $CH_2$  fragment as the perturbation. By this procedure one gets certain spin density on the conjugated carbon atoms  $C'$  and  $C''$  in the unperturbed parent molecule. The coupling constant is then calculated with the use of the McConnell type relation:

$$A = Q(q_{C'} + q_{C''}) \quad (3)$$

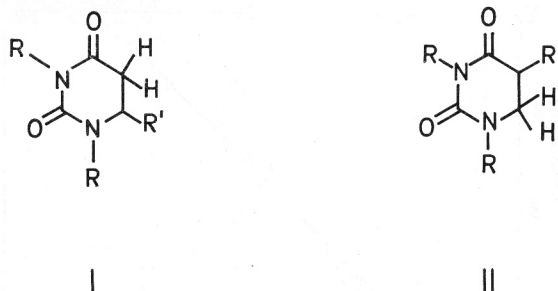
where  $Q$  is a constant of about 4 mT. Alternatively, from the known spin densities at  $C'$  and  $C''$  one calculates the spin density on one of the methylene protons and, subsequently, its coupling constant according to the relation

$$A_H = Q_H q_H \quad (4)$$

In this study, both of these approaches have been used. In the HMO calculations the parameters of Coulson and Crawford<sup>16</sup> were adopted for the methylene or methyl group. Parameters for heteroatoms are those from Pullman and Pullman<sup>17</sup>. The same Hückel orbitals were utilized as the initial orbitals in the McLachlan iteration procedure. Only one iteration step was performed, because further iterations were expected to bring slight corrections only<sup>15</sup>. The adjustable parameter,  $\lambda = 1$  was chosen. These calculations were restricted to the computation of the spin densities only.

#### RESULTS AND DISCUSSION

Several pyrimidine radicals of the general forms I or II have been studied. R is a hydrogen atom except for 1,3-dimethyl uracil, where  $R = CH_3$ . R' is a substituent group. We have studied uracil, thymine (5-methyl uracil), 6-methyl uracil, 5-amino uracil, 5-acetyl uracil, 5-Cl uracil and 1,3-dimethyl uracil. Hydrogen addition radicals of the forms I or II have been previously experimentally studied<sup>10-13</sup>. We reproduce in Table I the observed methylene coupling constants. In uracil and 1,3-dimethyl uracil both forms, I and II, are possible. It has been proved earlier<sup>10</sup>, that in uracil form I is present. For 1,3-dimethyl



uracil no experimental evidence is available. However, electronic indices indicate the preference of form I. (Localization energy is lower for H addition on  $C_{(5)}$  (2.22  $\beta$ ) than on  $C_{(6)}$  (2.50  $\beta$ ). Free valence index is higher at  $C_{(5)}$  (0.527) than at  $C_{(6)}$  (0.386).)

TABLE I  
Observed Methylene Proton Coupling Constants

Parent compound	Radical form	T <sup>o</sup> K	Coupling, mT	Ref.
Uracil	I	300	$A_1 = A_2 = 3.3$	10
Thymine	II	300	$A_1 = A_2 = 3.8$	10
		77	$A_1 = 4.2, A_2 = 3.4$	
6-Methyl uracil	I	300	$A_1 = 3.95, A_2 = 2.05$	12
		77	$A_1 = 6.5, A_2 = 0$	
5-Amino uracil	II	77	$A_1 = A_2 = 2.4$	12
5-Acetyl uracil	II	300	$A_1 = A_2 = 1.1$	12
5-Cl uracil	II	300	$A_1 = 3.8, A_2 = 3.4$	11
1,3-Dimethyl uracil	I	300	$A_1 = 4.6, A_2 = 1.8$	13

Fig. 1 shows the correlation between the experimental coupling constants and the calculated ones. If two different coupling constants,  $A_1$  and  $A_2$ , are observed, the mean value is used in this consideration. The coefficients  $C_i$  are calculated in the HMO. Similar values are obtained if only the first term of eq. (2) is taken into consideration. Such relation was also earlier proposed by Nordio *et al.*<sup>18</sup>. All points are expected to lie on a straight line going through the origin. It can be seen that the correlation between the calculated coupling constants using the HMO method and the experimental ones is quite good, except for the 5-acetyl uracil radical. The calculated values in the SCFMO, if only the first term in eq. (2) is used (not presented) are in much worse agreement with the observed values. Particularly bad results, besides for 5-acetyl uracil, are obtained for thymine and 5-Cl uracil. The complete equation (2) could not be easily applied, because the signs of the coefficients  $C_i$  remain-

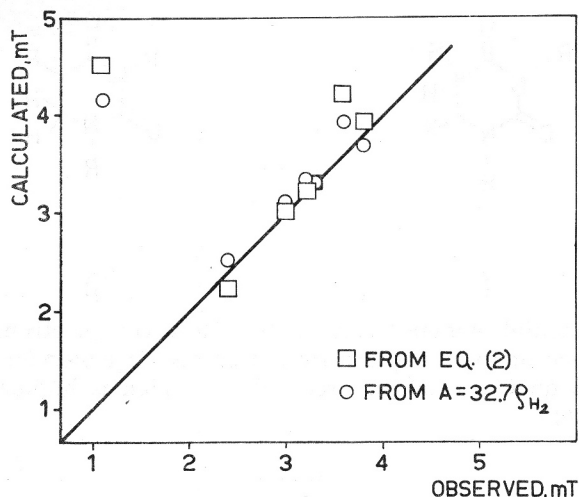


Fig. 1. Correlation between the observed and calculated methylene proton couplings in the Hückel approximation.

ned unknown due to the chosen calculation procedure. However, using only the dominating first term in eq. (2), which is easily computed, is expected to be a good enough approximation, as it is the case for the HMO calculations.

This approach fails to explain non-equivalent methylene proton couplings, which are observed in many of the radicals studied. Namely, the pseudo-atomic orbital (1) implies equal couplings of both protons whatever is the orientation of the orbital with respect to the carbon  $\pi$  orbitals. It means that the methylene protons do couple with the unpaired electron not only because they are in an antisymmetric group orbital. The fact that eq. (2) describes satisfactorily the coupling, is due to the fact, that the parameters like those of Coulson and Crawford have been empirically found to offer satisfactory results in the molecular orbital calculations.

Heller and McConnell<sup>19</sup> postulated that the coupling of the methylene protons depend upon the angle  $\Theta$ , between the planes defined by  $C'CH$  and  $C'C$  with the  $\pi$  orbital in  $C'$  as

$$A_{\Theta} = A_0 \rho \cos^2 \Theta \quad (5)$$

$\rho$  is the spin density on the conjugated carbon atom  $C'$ . Morokuma and Fukui<sup>5</sup> carried out a detailed valence bond calculation for the methylene proton coupling in dependence on the dihedral angle  $\Theta$ . They have found that equation (5) can safely be used with  $A_0 = 5.8$  mT for the rotating conformation. For the rocking conformation, however, much stronger dependence of the proton coupling upon  $\Theta$  is predicted.

Fig. 2 shows the spin densities on the conjugated carbon atom  $C'$ , calculated in both, HMO and SCFMO, plotted vs. the mean observed methylene proton couplings. (The density on the other neighbouring conjugated carbon atom,  $C''$ , is found to be negligible in all studied radicals.) The best fit of equations (3) or (5) (assuming  $\Theta = 30^\circ$  for both protons) determines the constants  $Q$  viz.  $A_0$ . From the HMO calculations the values  $Q = 4.6$ ,  $A_0 = 6.1$  mT

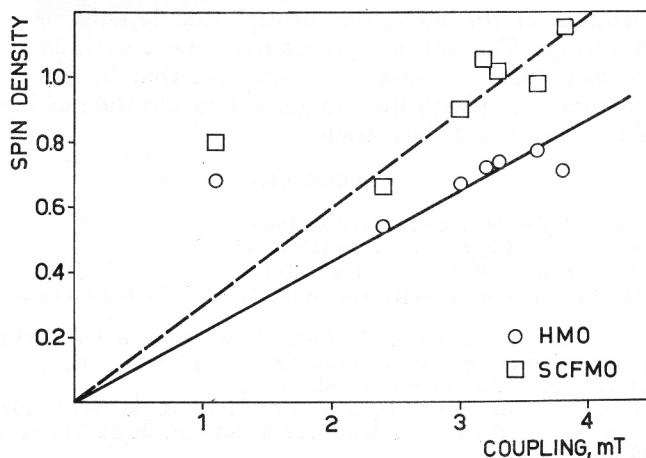


Fig. 2. Calculated spin densities on the neighbouring conjugated carbon atoms plotted against the observed methylene proton couplings. The straight lines represent the best fit of the eq. (3) to the points calculated in the HMO (solid line) and SCFMO, first iteration only (dashed line).

are obtained. The SCFMO calculations lead to  $Q = 3.4$ ,  $A_0 = 4.5$  mT. The calculated spin density for the 5-acetyl uracil radical is discarded in the best fit calculations, because it is systematically much larger than the observed, *i.e.* 1.1mT. It is possible that the molecular structure of the actual compound is different from the structure assumed in these calculations.

The HMO calculations are again in better agreement with the experimental results than the values calculated according to the McLachlan approximation. In some cases the SCFMO gives the spin densities larger than 1, although experimentally, from the  $\alpha$ -proton or methyl-proton couplings, they are found to be about 0.7. This is not surprising, since the heteroatom parameters used in these calculations, are the best empirical values for the Hückel approximation. Different values should be taken to fit best the McLachlan approximation. In addition, the results depend greatly upon the adjustable parameter  $\lambda$ . We have used  $\lambda = 1$ , as originally recommended<sup>15</sup>, though a smaller value would fit better.

The dihedral angles,  $\Theta_1$  and  $\Theta_2$ , of the non-equivalent methylene protons in 6-methyl uracil cannot be evaluated using equation (5). Namely, from the coupling of 6.5 mT and the spin density of 0.7 at C', as deduced from the methyl protons coupling,  $A_0 \approx 9.3$  mT is obtained, which is much too large. If the rocking conformation of the  $-\text{C}'(\text{CH}_2)\text{C}''-$  is assumed, hence a change of hybridization of the  $\text{CH}_2$  fragment, the coupling of 6.5 mT can be explained. Using the calculations of Morokuma and Fukui<sup>3</sup>,  $\Theta_1 \approx 20^\circ$  and  $\Theta_2 \approx 60^\circ$  are found to fit best the observed couplings of 6.5 and 0 mT, respectively. Similar considerations for 1,3-dimethyl uracil lead to  $\Theta_1 \approx 25^\circ$ ,  $\Theta_2 \approx 45^\circ$ .

#### CONCLUSION

The present study demonstrates that molecular orbital calculation, even in the simple approximation, can be useful in predicting the methylene proton couplings. Better approximations need not necessarily give better results for this particular problem. The methylene protons may be either represented

with group orbitals in the molecular orbital calculations, or treated in the valence bond theory. The former procedure, however, fails to explain the non-equivalent couplings. Unusual couplings, like that in the 6-methyl uracil radical, are explained well with the change of hybridization of the C—H bonds, namely, with the rocking conformation.

## REFERENCES

1. R. Bersohn, *J. Chem. Phys.* **24** (1956) 1066.
2. D. B. Chesnut, *J. Chem. Phys.* **29** (1958) 43.
3. A. D. McLachlan, *Mol. Phys.* **1** (1958) 233.
4. J. R. Bolton, A. Carrington, and A. D. McLachlan, *Mol. Phys.* **5** (1962) 31.
5. K. Morokuma and K. Fukui, *Bull. Chem. Soc. Japan* **36** (1963) 534.
6. J. P. Colpa and E. de Boer, *Mol. Phys.* **7** (1963—4) 333.
7. D. H. Levy, *Mol. Phys.* **10** (1966) 233.
8. D. Lazdins and M. Karplus, *J. Chem. Phys.* **44** (1967) 1600.
9. J. P. Colpa, E. de Boer, D. Lazdins, and M. Karplus, *J. Chem. Phys.* **47** (1967) 3098.
10. J. N. Herak and W. Gordy, *Proc. Nat. Acad. Sci.* **54** (1965) 1287.
11. J. N. Herak and W. Gordy, *Proc. Nat. Acad. Sci.* **56** (1966) 1354.
12. J. N. Herak and W. Gordy, *J. Am. Chem. Soc.* **89** (1967) 3818.
13. J. N. Herak and W. Gordy, unpublished results.
14. E. Hückel, *Z. Physik* **70** (1931) 204.
15. A. D. McLachlan, *Mol. Phys.* **3** (1960) 233.
16. C. A. Coulson and V. A. Crawford, *J. Chem. Soc.* **1953**, p. 2052.
17. B. Pullman and A. Pullman, *Quantum Biochemistry*, Interscience Publ., New York 1963.
18. P. Nordio, M. V. Pavan, and G. Giacometti, *Theoret. Chim. Acta* **1** (1963) 302.
19. C. Heller and H. M. McConnell, *J. Chem. Phys.* **32** (1960) 1535.

## IZVOD

**Teorijsko ispitivanje interakcije metilenskih protona s nesparenim elektronom u nekim pirimidinskim radikalima**

J. N. Herak

Izračunata je interakcija metilenskih protona s nesparenim elektronima u nizu pirimidinskih radikala. Računanje je vršeno u Hückelovoj i McLachlanovoj aproksimaciji teorije molekularnih orbitala. Metilenska grupa je tretirana na dva načina: direktno kao član konjugiranog sistema (»hiperkonjugacija«) i kao smetnja konjugiranom sistemu. Oba pristupa daju zadovoljavajuće slaganje s eksperimentom, bolje u Hückelovoj nego McLachlanovoj aproksimaciji. Kompletno neslaganje dobiveno je jedino za radikal 5-acetil uracila. Vjerojatno je da se eksperimentalna mjerenja i račun na odnose na istu molekularnu strukturu.

INSTITUT »RUDER BOŠKOVIĆ«  
ZAGREB

Primljeno 6. prosinca 1968.