Tetrahedron Letters No.39, pp. 3333-3336, 1969. Pergamon Press. Printed in Great Britain.

SHIFTS IN NUCLEAR MAGNETIC RESONANCE SPECTRA OF PYRIMIDINE BASES INDUCED BY AROMATIC HYDROCARBONS

I. Rosenthal

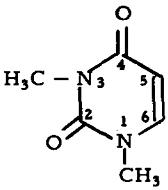
Department of Chemistry, The Weizmann Institute of Science, Rehovoth, Israel

(Received in UK 2 June 1969; accepted for publication 10 July 1969)

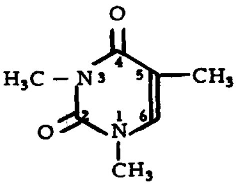
Molecular association between nucleic acids and aromatic hydrocarbons has been reported in the literature (1). Such association is likely to occur at the purine and pyrimidine basic sites in the nucleic acids.

In the present study the nature of the association between the pyrimidine bases and benzene and toluene was investigated using the nuclear magnetic resonance technique. To this end attention was confined to 1, 3-dimethyluracil (DMU) and 1, 3-dimethylthymine (DMT), pyrimidine bases possessing adequate solubility characteristics.

The n. m. r. spectrum of DMU (I) exhibits four absorption signals with relative intensities 1:1:3:3. The pair of singlets appearing at τ =6.64 and τ =6.72 arise from absorption of the two methyl groups and have been assigned as 1-methyl and 3-methyl respectively. The n. m. r. spectrum of DMT (II) shows an additional signal at τ =8.115 due to the 5-methyl group.



I



II

Upon replacing CCl_4 in a solution of DMU or DMT with aromatic solvents both the 1- and 3-methyl resonance signals are shifted to higher field with the 1-methyl singlet having a greater shift than its 3-methyl counterpart. Thus at a given proportion of aromatic solvent to CCl_4 the 1- and 3-methyl singlets overlap; increase of this ratio will shift the 1-methyl singlet to higher field than the 3-methyl. Chemical shift data are given in Table I (2).

Table I. Shifts for Solutions of DMU and DMT in CCl_4 and Aromatic Donor

Sample	Benzene						Toluene					
	m	DMU		DMT			m	DMU		DMT		
		δ_1	δ_3	δ_1	δ_3	δ_5		δ_1	δ_3	δ_1	δ_3	δ_5
1	0.0	119.5	114	116.5	114	29.5	0.0	119.5	114	116.5	114	29.5
2	0.364	111	111	110	112	25.5	0.311	111.5	111.5	110.5	112	26.5
3	0.75	103.5	108	103	109	22	0.629	106	109	105	109.5	23.5
4	1.15	97.5	106.5	97.5	107.5	20	0.966	100	106.5	98	106.5	19.5
5	1.569	90.5	103.5	92.5	105.5	17	1.307	92.5	103	94	104.5	17.5
6	2.00	87.5	102.5	86.5	102.5	13.5	1.686	88	101	88.5	102.5	14
7	2.322	80.5	99.5	81	100	9.5	2.08	84	100	83	100	11
8	2.89	74.5	97	76.5	98.5	7.5	2.47	78	97	80.5	99	9.5
9	3.47	70	95	72	96.5	5	2.93	74.5	96	75.5	97	7
10	4.01	65.5	93	68.5	95	3	3.4	69.5	93	72	94.5	5
11	4.6	60	90.5	65	94	1.5						

It has been shown (4) that n. m. r. data in molecular complex systems can be analyzed by the equation:

$$\frac{1}{(\Delta_{obs})_i} = \frac{1}{Q_m \Delta_{AD}} \times \frac{1}{m_i} + \frac{1}{\Delta_{AD}}$$

where $(\Delta_{obs})_i$ is the observed shift of acceptor protons relative to the shift of acceptor protons in the absence of complexing donor, Δ_{AD} is the corresponding shift of acceptor protons in the pure complex and Q_m is the equilibrium quotient for association of the complex (5). The concentration of the donor is represented by m_i in $\frac{\text{mol}}{\text{kg}}$.

Based on the shifts for 1-methyl $\frac{1}{\Delta_{obs}}$ was plotted against $\frac{1}{m_D}$ to give a straight line, whose slope $\frac{1}{Q_m \Delta_{AD}}$ and intercept $\frac{1}{\Delta_{AD}}$ were determined by a least-squares analysis.

The resulted equilibrium quotients of DMU and DMT complexes with benzene and toluene are given in Table II.

Table II.

	Benzene	Toluene
DMU	0.232	0.316
DMT	0.124	0.151

These results may lead to the conclusion that the aromatic molecule associates with the pyrimidine ring in a vertical stacking arrangement where the 1-methyl group will be either above or below the aromatic ring and will thus be affected by the aromatic ring currents. Furthermore, it may be concluded that both pyrimidines act as acceptors in these complexes, this being shown by the fact that progressively greater methyl subtitution on the benzene ring ceases increase in the equilibrium quotients (6). These results are in agreement with the model that aromatic hydrocarbon molecules acting as election donors will avoid the negative end of a dipole (7, 8) thus preferentially solvating the pyrimidine molecule close to N_1.

The electron acceptor characteristics of pyrimidine bases may lead to a better understanding of the mechanism of photoreduction of these compounds (9).

Acknowledgement. We are grateful to Prof. D. Elad for valuable advice and encouragement.

REFERENCES

1. E. Boyland and B. Green, Brit. J. Cancer, 16, 507 (1962); A. M. Liquori, B. De Lerma, F. Ascoli, C. Botre and M. Frascicatti, J. Mol. Biol., 5, 521 (1962); P. O. P. Ts'o and P. Lu, Proc. Natl. Acad. Sci., U.S., 51, 17 (1964); E. Boyland and B. Green, J. Mol. Biol., 9, 589 (1964).

2. The n.m.r. spectra were recorded on a Varian A60 spectrometer with probe temperature 30 ± 0.5°. The solvent used was CCl_4. The DMU concentration was maintained at 0.0375 M whereas DMT concentration was 0.0325 M. Donor concentration varied from 0.3-4.6 m. Cyclohexane served as external standard. Chemical shifts are expressed in H_z measured downfield from cyclohexane. The values given are the average of the least three measurements, errors within ± 0.2 c./sec. DMU and DMT were prepared according to (3).

3. D. Davidson and O. Baudisch, J. Amer. Chem. Soc., 48, 2379 (1926).

4. M. W. Hanna and A. L. Ashbaugh, J. Phys. Chem., 68, 811 (1964); A. A. Sandoval and M. W. Hanna, J. Phys. Chem., 70, 1203 (1966); R. Mathur, E. D. Becker, R. B. Bradley and N. C. Li, J. Phys. Chem., 67, 2190 (1963).

5. The term equilibrium quotient Q represents the quotient of concentrations of products and reactants. The equilibrium constant K is equal to the product of Q and the appropriate quotient of activity coefficients $\gamma_{AD}/\gamma_A\gamma_D$. Equilibrium quotient is the more accurate term if activity coefficients are not evaluated.

6. Cf. M. W. Hanna and A. Sandoval, Biochim. Biophys. Acta., 155, 433 (1968).

7. J. Ronayne and D. H. Williams, J. Chem. Soc. (B), 540 (1967).

8. For dipole values D. Weinblum, F. P. Ottensmeyer and G. F. Wright, Biochim. Biophys. Acta, 155, 24 (1968).

9. D. Elad and I. Rosenthal, Chem. Commun., 879 (1968).