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IDENTIFICATION OF ISOMERIC DIHYDRO-AZINES BY BENZENE INDUCED SHIFTS IN NMR SPECTRA. VI[1]

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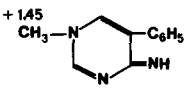
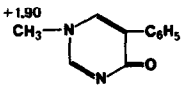
It is well known that alkylation of 4-amino- or 4-hydroxy -pyrimidines may give two isomeric 1,4- or 1,6-dihydro-N-alkyl derivatives, which can be identified by chemical or spectroscopic methods[2]. Of special interest is the determination with nmr spectroscopy based either on the chemical shifts[3] or on the coupling constants of pyrimidine protons[4,5]. However, we have found that the solvent shifts induced by benzene on nmr spectra can successfully be used for structure determination of isomeric dihydro-forms of N-alkyl azines.

The first compound studied was the methylation product[6] of 4-amino-5-phenyl-pyrimidine, which was identified, by chemical means, as 1,4-dihydro-1-methyl-4-imino-5-phenyl-pyrimidine (I). The nmr spectrum of I in benzene showed for the $N-CH_3$ protons an unusually large diamagnetic shift $\Delta^{CDCl_3}_{C_6H_6}$ equal to 1.45 p.p.m.



I



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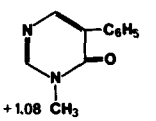


III

Solvent shifts measurements made on the pair of 1,4-dihydro- and 1,6-dihydro-pyrimidone (II,III) showed that there is a dramatic difference on the shifts of methyl protons in II and III, Δ_{N-CH_3} being +1.90 and 1.08 p.p.m. respectively.

Examination of some other isomeric pairs analogous to II-III showed that the diamagnetic shift induced by benzene on N-alkyl protons is much higher in 1,4-dihydro-derivatives than it is in 1,6-, the corresponding shifts Δ_{N-CH3} being 1.17-1.90 and 0.45-1.08 p.p.m. This method can easily and conclusively be used for structure

determination of various isomeric dihydro-azines.

The solvent shifts induced by benzene relative to $CDCl_3$ ($\Delta=\delta_{CDCl_3}-\delta_{C_6H_6}$ p.p.m.) of the compounds studied are reported in Table 1.

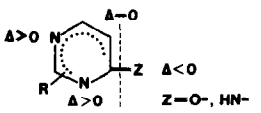
TABLE 1

Induced shifts by benzene relative to $CDCl_3$ ($\Delta=\delta_{CDCl_3}-\delta_{C_6H_6}$ p.p.m.) on various dihydro-azines.

Compound	$\Delta_{N\text{-alkyl protons}}$ a*	b*	Compound	$\Delta_{N\text{-alkyl protons}}$ a*	b*
I	1.45		1,4-Dihydro-1-methyl-pyridone-4	1.32	
II	1.90				
III		1.08	1,2-Dihydro-1-methyl-pyridone-2		0.58
1,4-Dihydro-1-methyl-4-imino-pyridine	1.17		1,2-Dihydro-1-methyl-2-imino-pyrimidine		0.62
1,2-Dihydro-1-methyl-2-imino-pyridine		0.45	1,4-Dihydro-1-ethyl-4-imino-pyridine	0.75 CH_2 0.58 CH_3	
			1,2-Dihydro-1-ethyl-pyridone-2		0.33 CH_2 0.27 CH_3

*a, b Dihydro-azines analogous to II and III.

The observed difference in solvent shifts in various dihydro-forms (II-III) could be explained on the basis of the carbonyl plane rule[7,8]. In this case the 1,4-dihydro-form should be expected to exhibit a larger shift than the 1,6-isomer (IV). Furthermore, in the latter case a steric effect might be operated in the "collision-complex" causing a smaller shift in alkyl protons.



IV

It should be also noticed that the shifts induced by benzene are larger in oxo-derivatives than they are in imino-.

The nmr spectra were obtained with a Varian A-60A spectrometer at ~40°, with TMS as an internal standard. The measurements were made in 2% solutions (w/v) in $CDCl_3$ and C_6H_6. The solvent shifts Δ are given in p.p.m. The compounds studied were prepared by known procedures; their physical constants were in agreement with those of the literature.

REFERENCES

1. Part V, to appear in Org. Magn. Res.
2. For an extensive survey of the subject see: D.J.Brown, "The Chemistry of Heterocyclic Compounds. The Pyrimidines, Supplement I", Interscience, N. York, 1970.
3. A.R.Katritzky and A.J.Waring, J. Chem. Soc., 3046 (1963); 1523 (1964).
4. L.Bauer, G.E.Wright, B.A.Mikrut and C.L.Bell, J.Heterocyclic Chem., 4, 447 (1965).
5. Y.Inoue, N.Furutachi and K. Nakanishi, J. Org. Chem., 31, 175 (1966).
6. T.Soulis, Ph.D.Thesis, University of Thessaloniki, 1970.
7. D.H.Williams and N.S.Bhacca, Tetrahedron, 21, 2021 (1965).
8. J.H.Bowie, D.W.Cameron, P.Schutz, D.H.Williams and N.S.Bhacca, ibid., 22, 1771(1966).