THE RELATIVE SIGN OF THE PROTON–PROTON COUPLINGS IN DIAZINE *N*-OXIDES

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Although the n.m.r. spectrum of pyridine was originally analysed[1-3] on the basis of a positive value for the coupling across the nitrogen ($J_{2,6}$ $+0\cdot40$ Hz), a recent analysis[4] of the spectrum obtained with simultaneous double-irradiation of the ^{14}N nucleus has established that the coupling is negative ($J_{2,6}$ $-0\cdot13$ Hz). Negative values for $J_{2,6}$ have also been derived[5] for 3-acetylpyridine ($-0\cdot21$ Hz) and other β-monosubstituted pyridines.

During the course of examination of some pyridine *N*-oxides and diazine mono-*N*-oxides, we have observed that whereas the coupling across the nitrogen is negative ($J_{2,4}$ $-0\cdot31$ Hz) in pyrimidine *N*-oxide (I), the coupling is positive ($J_{3,5}$ $+0\cdot38$ Hz) in pyrazine *N*-oxide (II). The common assumption that the magnitude *and sign* of the proton–proton couplings in aromatic compounds may be used in the analysis of related molecules therefore does not apply to the *meta* coupling across a nitrogen atom.
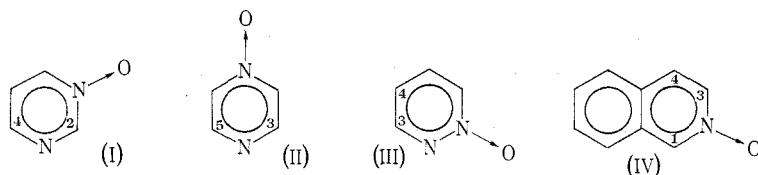
The diazine mono-oxides were prepared according to the literature methods[6,7] and examined as degassed deuterochloroform solutions on a Varian HA60IL spectrometer modified for ^1H–$\{^{14}N\}$ spin-decoupling.[8] The strength of the decoupling field was sufficiently high ($H_2 \simeq 2\cdot5$ G, $\gamma(^{14}N)$ $H_2/2\pi \simeq 800$ Hz) that both ^{14}N

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1 Schneider, W. G., Bernstein, H. J., and Pople, J. A., *Can. J. Chem.*, 1957, **35**, 1487.
2 Schneider, W. G., Bernstein, H. J., and Pople, J. A., *Ann. N.Y. Acad. Sci.*, 1958, **70**, 806.
3 Pople, J. A., Schneider, W. G., and Bernstein, H. J., "High-resolution Nuclear Magnetic Resonance." p. 266. (McGraw–Hill: New York 1959.)
4 Castellano, S., Sun, C., and Kostelnik, R., *J. chem. Phys.*, 1967, **46**, 327.
5 Kowalewski, V. J., Kowalewski, D. G. de, and Ferrá, E. C., *J. molec. Spectrosc.*, 1966, **20**, 203.
6 Koelsch, C. F., and Gumprecht, W. H., *J. org. Chem.*, 1958, **23**, 1603.
7 Itai, T., and Natsume, S., *Chem. pharm. Bull.*, Tokyo, 1963, **11**, 83.
8 Long, G. J., and Moritz, A. G., *Molec. Phys.*, 1968, **15**, 439.

nuclei were simultaneously spin-decoupled from the protons despite the difference in the ^{14}N chemical shifts. Spectra were analysed using modified LAOCOON2 binary computer programmes and the results are shown in Tables 1 and 2 (cf.[9],[10]).

TABLE 1

CHEMICAL SHIFTS (Hz, internal TMS) IN DEUTEROCHLOROFORM

The chemical shifts assigned to compounds (III) and (I) are consistent with those reported in refs. 9 and 10 respectively

Compound	H 2	H 3	H 4	H 5	H 6
Pyridazine N-oxide (III)		509·3	430·1	466·8	493·2
Pyrimidine N-oxide (I)	538·5		492·2	437·5	503·0
Pyrazine N-oxide (II)	506·4	486·6		486·6	506·4

TABLE 2

COUPLING CONSTANTS (Hz) IN DEUTEROCHLOROFORM

Compound	$J_{2,3}$	$J_{2,4}$	$J_{2,5}$	$J_{2,6}$	$J_{3,4}$	$J_{3,5}$	$J_{3,6}$	$J_{4,5}$	$J_{4,6}$	$J_{5,6}$
Pyridazine N-oxide	—	—	—	—	5·39	2·54	0·99	7·67	0·92	6·49
Ref. 9					5·3	2·5	1·0	8·0	1·0	6·5
Pyrimidine N-oxide		−0·31	1·06	2·07	—	—	—	4·71	1·50	6·63
Ref. 10		c. 0	1·0	2·0				4·9	1·6	6·8
Pyrazine N-oxide	4·10	—	0·83	1·75	—	0·38	0·83	—	—	4·10

For pyrimidine N-oxide, the relative signs were determined from simultaneous $^1H-\{^{14}N\}$ and selective $^1H-\{^1H\}$ spin-decoupling experiments:

Sel. decoupling of lines due to proton 4   rel. signs detd. $\pm J_{2,5}\pm J_{4,5}$ $\pm J_{2,6}\pm J_{4,6}$

         5            $\mp J_{2,4}\pm J_{4,5}$ $\pm J_{2,6}\pm J_{5,6}$

In the case of a four-spin system, two relative signs are determined simultaneously by this method.[11] Similar experiments were carried out for pyridazine N-oxide (III) and the results are:

Sel. decoupling of lines due to proton 3   rel. signs detd. $\pm J_{3,4}\pm J_{4,6}$ $\pm J_{3,5}\pm J_{5,6}$

         4            $\pm J_{3,4}\pm J_{3,6}$ $\pm J_{4,5}\pm J_{5,6}$

         5            $\pm J_{3,4}\pm J_{4,5}$ $\pm J_{3,6}\pm J_{5,6}$

The lines due to the high-field protons of pyrazine N-oxide (II) are shown in Figure 1. Analysis of this spectrum according to the method of Gutowsky et al.[12] established that $N = 4·93$, $L = 3·27$, $K = 2·13$, and $M = 1·37$ Hz. As $L < N$, the coupling constants $J_{2,3}$ and $J_{2,5}$ are of the same sign. The K and M parameters are clearly identified, and as $K > M$, $J_{2,6}$ and $J_{3,5}$ are of the same sign. Iterative

[9] Tori, K., Ogata, M., and Kano, H., *Chem. pharm. Bull., Tokyo*, 1963, **11**, 235.
[10] Ogata, M., Watanabe, H., Tori, K., and Kano, H., *Tetrahedron Lett.*, 1964, 19.
[11] Freeman, R., Bhacca, N. S., and Reilly, C. A., *J. chem. Phys.*, 1963, **38**, 293.
[12] Grant, D. M., Hirst, R. C., and Gutowsky, H. S., *J. chem. Phys.*, 1963, **38**, 470.

computer calculations gave values for the line positions which agreed with the observed values with a r.m.s. error of $0 \cdot 02$ Hz. Calculations established that the sign of K relative to N could not be determined unambiguously within the precision
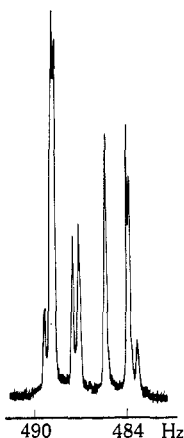

Fig. 1.—Part of the proton spectrum of pyrazine N-oxide in deuterochloroform with simultaneous strong irradiation of the ^{14}N nuclei.

of the measurements, so that the sign of $J_{2,6}$ or $J_{3,5}$ relative to $J_{2,3}$ or $J_{2,5}$ could not be determined. It is probable, however, that $J_{2,6}$ is positive. The magnitude of $J_{2,6}$ in pyrazine N-oxide ($1 \cdot 75$ Hz) is similar to that observed[13] for $J_{1,3}$ ($1 \cdot 73$ Hz) in isoquinoline N-oxide, which is known to be of the same sign as $J_{3,4}$ from selective decoupling experiments.[13] Furthermore, a complete analysis[13] of the ^{14}N spin-decoupled spectrum of pyridine N-oxide has shown that $J_{2,6}$ ($1 \cdot 88$ Hz) is of the same sign as $J_{2,3}$.

[13] Moritz, A. G., and Paul, D. B., unpublished data.