Proton Magnetic Resonance of the Methyl Derivatives of 2-Fluoropyridine. Sigma and Pi Electron Contributions to Spin–Spin Coupling Constants

J. B. ROWBOTHAM, R. WASYLISHEN AND T. SCHAEFER

Department of Chemistry, University of Manitoba, Winnipeg, Manitoba

Received January 26, 1971

The p.m.r. spectra of the methyl derivatives of 2-fluoropyridine are analyzed. The signs and magnitudes of the long-range spin-spin coupling constants between the methyl protons and the ring protons and between the methyl protons and fluorine are consistent with a model in which the nitrogen atom polarizes the signa electron system but leaves the pi electron contribution to the coupling constants relatively unchanged. There are dramatic changes in the ring proton – fluorine couplings while the couplings involving the methyl protons vary little from those in the corresponding toluene derivatives. Thus the coupling over six bonds between fluorine and methyl protons is 1.25 ± 0.03 Hz in 2-fluoro-5-methyl pyridine compared to 1.15 ± 0.02 Hz in *p*-fluorotoluene.

On a analysé les spectres r.m.n. des fluoro-2 pyridines méthylées. Les signes et les valeurs des constantes de couplage à longue distance entre les protons des groupes méthyles et d'une part ceux du noyau et d'autre part les atomes de fluor sont en accord avec un modèle dans lequel on fait l'hypothèse que l'azote polarise le système électronique sigma tout en laissant la contribution des électrons pi aux constantes de couplage relativement intacte. On note des changements dramatiques dans les couplages entre les protons du cycle et le fluor; toutefois les couplages impliquant les protons des groupes méthyles ne varient pratiquement pas par rapport à ce qui est observé dans les toluènes correspondants. Par exemple le couplage reparti sur six liaisons entre le fluor et les protons du groupe méthyle est de $1.25 \pm$ 0.03 Hz dans la fluoro-2 méthyl-5 pyridine alors qu'une valeur de 1.15 ± 0.02 Hz est observée dans le *p*-fluorotoluène.

Canadian Journal of Chemistry, 49, 1799 (1971)

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UNIV LEEDS on 05/18/15 For personal use only.

Introduction

The full analysis of the p.m.r. spectrum of 2-fluoro-3-methylpyridine (1) has been described (1). The signs and magnitudes of the long-range spin-spin coupling constants, $J_{o,m,p}^{H,CH_3}$ and J_o^{F,CH_3} , between methyl protons and J_o^{H,CH_3} between methyl protons and the ring protons or fluorine in 1 are consistent with the assumption (2, 3) that the nitrogen atom primarily polarizes the nearby σ bonds in the molecule, leaving the π electron contribution to the coupling constants relatively unaffected. Because it is a coupling over four bonds only, J_o^{F,CH_3} may contain a sizeable σ electron contribution (4), *i.e.*, $J_o^{F,CH_3} = 1.4_5$ Hz in 1 but is nearer 2 Hz in o-fluorotoluene (5) and its derivatives (6). In this paper the spectral parameters of the isomers of 1, viz., 2, 3, and 4, are reported and discussed in spirit of the σ - π model. A knowledge of the contents of ref. 1 is assumed throughout.

Experimental

(1) Preparation of 2, 3, and 4

These compounds were prepared from the amines by the Schiemann reaction (7, 8) via the diazonium fluoroborates. Colorless 2, 2.6 g, was collected under



vacuum between 30–32 °C. Compound 3, 22.6 g, was collected as a pale yellow liquid, b.p. 153 °C; lit. 155–156 °C at 752 mm (7). Compound 4, 0.6 g, was obtained on distillation from the CCl₄ extract and probably contained some CCl₄. All compounds gave p.m.r. spectra consistent with their structure and with no detectable proton-containing impurities in the spectral region of interest.

(2) Proton Resonance Measurements

Solutions of 2, 3, and 4 (20 mol %) in CS₂ containing trace amounts of trifluoroacetic acid (TFA) and internal tetramethylsilane (TMS) as locking material, were degassed. As described for 1 (1) the amount of TFA was sufficient to cause rapid relaxation of ¹⁴N, leading to sharp peaks for proton 6, but insufficient to cause changes in the spectral parameters. However, addition of even

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UNIV LEEDS on 05/18/15 For personal use only.

Proton chemical shifts^{*} and counting constants[†] in methol derivatives of 2-fluoronvridines TABLE 1.

1800

| | 11 | 2§ | 34 | 44 | 4 ,¶ |
|-----------------------------|-----------------------------|----------------------|----------------------------|-------------------|---------------|
| V3 | | 395.72 | 403.86 | 394.97 | 395.054 |
| ° 7 | 458.58 | I | 452.78 | 453.45 | 453 502 |
| 7 | 426.12 | 413.27 | I | 415.16 | 415.247 |
| V. | 479.82 | 475.9 | 475.72 | I | I |
| V _{CH3} | 132.72 | 139.55 | 136.72 | 143.70 | 143.763 |
| Л.н.н | [7.50(4.5): 5.01(5.6)] | 5.07 | 8.34 | [8.17(3.4): 7.30] | [8.132:7.352] |
| <u>7</u> "н,н | 1.98 | 1.36 | 2.55 | 0.73 | 0.737 |
| <i>J</i> .н,н | I | 0.67 | 0.70 | I | |
| <u>7</u> "н, г | [9, 93(2, 4); -1, 02(2, 6)] | -0.7 | [7, 62; -0.7] | 8.32 | 8.296 |
| J,"H,F | 1.83 | 2.13 | | 2.48 | 2.499 |
| J' ^{H,F} | | -2.18 | -2.81 | -3.12 | -3.084 |
| J H,CH3 | -0.85 | [-0.81(3, 4); -0.66] | [-0.68(4, 5); -0.80(5, 6)] | -0.58 | -0.566 |
| J_H,CH ₃ | 0.40 | 0.29 | 0.38 | 0.27 | 0.269 |
| <i>J</i> "н,сн _з | -0.7 | l | ł | -0.64 | -0.643 |
| J'F,CH3 | 1.45 | ļ | I | ļ | ļ |
| J_F.CH ₃ | : | -0.24 | I | -0.61 | -0.604 |
| $J_p^{"F,CH_3}$ | | | 1.25 | 1 | |

the first proper crucily from ref. 1. the first solution, from ref. 1. gin CS2 solution at 20 mol %. [[Independent calibration and analysis using LAME. See text.] These solutions contained frace amounts of TFA, see Experimental.

very small amounts of TFA to the solution of 2 in CS₂ caused a separation into two layers. The final spectra of 2 were, therefore, taken on solutions containing no TFA, leading to relative large uncertainties in the peak positions of H-6. Addition of as much as 8 mol% of TFA to a more dilute solution of 3 caused significant changes in $J_o^{H,F}$ and $J_m^{H,F}$. An 18 mol% solution of 3 in benzene- d_6 yielded coupling parameters insignificantly different from those in CS₂ solution. In particular, the long-range coupling constants all lay within 0.02 Hz of their values in CS₂ solution.

The proton spectra were recorded at a sweep width of 50 Hz at sweep speeds of 2500 or 5000 s on a DA60I spectrometer. Calibrations were done by reading sweep and manual oscillator frequencies at 5 Hz intervals or less. Double and triple resonance experiments were carried out to find the relative signs of the coupling constants, as described for 1 (1).

Results and Discussion

(1) Spectral Analyses

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UNIV LEEDS on 05/18/15 For personal use only.

The analytical techniques followed those for 1(1), except that the computer program LAOCN 3(9) was used to optimize the parameters. Therefore, the spectra obtained in the single (ABCX₃R) and in the multiple resonance experiments are not reproduced here. Their quality is not inferior to those displayed for 1(1). Note, however, that the necessary absence of TFA in the sample of 2 led to broad peaks for H-6 resulting in larger errors in some of the parameters involving this proton.

The final parameters in CS_2 solution are given in Table 1. As many as 177 peaks per compound were assigned in iterating to these numbers. The r.m.s. errors in the fits varied between 0.009 and 0.033 (for 2). The probable errors in the parameters ranged from 0.002 to 0.009 Hz and the worst assignment was 0.095 Hz (for some of the broad peaks in 2). Calcomp plots of the spectra using the parameters in Table 1 agreed very well with the experimental spectra, in particular with the methyl proton resonances in a manner demonstrated for *p*-fluorotoluene (10*a*).

In a separate experiment on 4, a recalibration of the spectrum at 0.01 Hz/s and its analysis using the program LAME (10*a*) gave the results listed in the last column of Table 1. In this analysis the r.m.s. error was 0.0088, the maximum standard deviation in the parameters was 0.005 Hz (otherwise between 0.001 and 0.003 Hz), and in the correlation matrix of dimension 14, there were two elements with a magnitude above 0.2 and none with a magnitude greater than 0.3. Over 250 transitions were assigned and the biggest deviation between observed and calculated transitions was 0.033 Hz (normally below 0.02 Hz).

(2) The Methyl Proton – Ring Proton Coupling Constants

To within experimental error, J_p^{H,CH_3} in 1 and 4 is the same as in toluene (11). By the methyl group replacement technique (12, 13), Macdonald and Reynolds (4) have shown that J_p^{H,CH_3} in toluene derivatives arises from a π electron mechanism. Consequently the nitrogen atom does not significantly alter the π electron contribution to this coupling constant or to J_p^{HF} in 1 and 4.

In ref. 1 evidence is adduced that the $J_o^{\rm H,CH_3}$ value of -0.85 Hz in 1 is consistent with a contribution from the resonance structure 5. This



structure increases the mobile bond order between C-3 and -4 and between C-5 and -6 relative to that between C-4 and -5. Because the negative π electron contribution to $J_o^{\rm H,CH_3}$ is expected to increase as the bond order of the intervening C····C bond increases (14), structure 5 implies a larger magnitude of $J_o^{\rm H_3,CH_3}$ in 2 and of $J_o^{\rm H_4,CH_3}$ in 3 than of $J_o^{\rm H_5,CH_3}$ in 2 and of $J_o^{\rm H_4,CH_3}$ in 3. Indeed, the former are larger in magnitude than the latter by up to 0.2 Hz (see Table 1). However, $J_o^{\rm H_5,CH_3} = -0.58$ Hz in 4, rather

However, $J_o^{H_5,CH_3} = -0.58$ Hz in 4, rather smaller than predicted by structure 5. There are two possible reasons. The first invokes structure 6,



supported by ¹⁴N quadrupole resonance studies (15), which decreases the mobile bond order¹ between C-5 and -6. The second possible reason lies in an indicated negative σ electron contribution (4) to J_o^{H,CH_3} , suggesting a decrease in the

¹A referee points out that the larger and unequal values of J_o^{H,CH_3} in 2 can be taken as evidence against a resonance form for 2 analogous to 6. He points out that in this connection the methyl derivatives of 3- and 4-fluoropyridine should be examined. We have synthesized a number of these compounds and are studying their proton resonance spectra.

magnitude of this contribution in 4 and caused by polarization of the σ core by the nitrogen atom. Qualitatively, it is simply that the electronegative nitrogen atom reduces the σ electron density near the bonded C-6 atom thereby reducing the σ contribution to $J_o^{\rm H,CH_3}$ in 4.

Because there is very likely a positive σ contribution to J_m^{H,CH_3} (perhaps as large as 0.2 Hz (1, 4)), the second reason above implies a decrease in this contribution to J_m^{H,CH_3} in both 4 and 2 because C-6 is involved in the coupling path. In fact, J_m^{H,CH_3} is 0.1 Hz smaller in 4 and 2 than in 1 and 3. In the latter two compounds J_m^{H,CH_3} has the same magnitude as in toluene (11). Other workers (2) have noted that polarization of the σ core in pyridine does not appreciably extend beyond the ortho carbon atoms.

(3) The Methyl Proton – Fluorine Coupling

In 3, $J_p^{F,CH_3} = 1.25$ Hz, only 0.10 Hz larger than in *p*-fluorotoluene (10*a*). Since it is unlikely that other than a π mechanism is important for this coupling in the latter, the present result strongly suggests that the heteroatom does not appreciably affect the π contribution to J_p^{F,CH_3} in 3. A similar, less strong, conclusion was reached for J_o^{F,CH_3} in 1 (1).

In 4-amino-5-bromo-3-fluorotoluene $J_m^{\rm F,CH_3} = -0.4_3$ Hz (6), little different in magnitude from the value originally estimated for this coupling in *m*-fluorotoluene (5). The values of $J_m^{\rm F,CH_3}$ in **2** and **4** suggest that, again, the presence of the heteroatom has little effect on the π contribution to this coupling. By the methyl group replacement criterion, the effect of the nitrogen atom on $J_m^{\rm F,H_6}$ occurs predominantly through the σ electron system. For, $J_m^{\rm H,F} = 5.6$ Hz in fluorobenzene (16) but is -1 Hz in **1**; yet $J_m^{\rm F,CH_3}$ remains constant to within 0.2 or 0.3 Hz even when a nitrogen atom replaces the carbon atom in the "coupling path".

(4) The Ring Proton and Ring Proton – Fluorine Couplings

The magnitudes of all these couplings are consistent with an alternating electronegativity effect of the substituents (2, 17) as discussed for 1 (1) and for *p*-fluorotoluene (10*a*); an effect acting primarily through the σ electron system, as suggested originally by Castellano and Kostelnik (2), and now also supported by the couplings with methyl protons reported here.

The additivity of substituent effects on coupling constants between protons in benzene derivatives (1, 18, 19) can be extended to the present pyridine derivatives. Using the coupling constants reported for pyridine dissolved in CCl₄ (20), for benzene (18, 21), fluorobenzene (16), and toluene (11), the predicted and observed values for 1, 2, and 3 agree to at least 0.2 Hz for $J_o^{H,H}$ and $J_m^{H,H}$ and to better than 0.1 Hz for $J_n^{H,H}$. In other words, the substituent effects of CH₃ and F on benzene are substantially the same as in pyridine in this regard. The deviations of the predicted from the calculated values are generally in the direction expected if the substituent effects of F (22) and CH_3 are somewhat less than in the monosubstituted benzenes themselves, i.e., as if a saturation effect were occurring; as already noted for trisubstituted benzenes (23). These deviations become as large as 0.4 Hz for $J_{o}^{H,H}$ in 4 where both substituents are attempting to polarize the σ core at C-2 and -6 when it is already markedly polarized by the heteroatom, in agreement with the idea of a saturation effect.

In 3, partial protonation of the nitrogen atom by addition of TFA (see Experimental) causes an algebraic increase of 1 Hz in $J_o^{H,F}$, an increase of 0.2 Hz in $J_m^{H_6,F}$, and a decrease of 0.2 Hz in $J_m^{H_4,F}$ of the values in Table 1. These changes are in order if the proton acts as an electronegative substituent polarizing the σ system (2). On this basis the long-range couplings involving methyl protons, particularly J_p^{F,CH_3} , should remain unchanged, as observed experimentally.

Conclusions

A model in which σ and π electron contributions to ring proton and ring proton – fluorine spinspin coupling constants are distinguished can be extended to pyridine derivatives. In this model the nitrogen atom polarizes the σ electron system but does not strongly alter the π electron contribution to the coupling constants. The most dramatic effects are observed for $J_{o,m,p}^{H,F}$. Thus in fluorobenzene $J_o^{H,F} = 8.9$, $J_m^{H,F} = 5.6$, $J_p^{H,F} =$ 0.2 Hz (16). In 2-fluoropyridine $J_o^{H,F} = -2.8$, $J_m^{H,6,F} = -1.0$, and $J_p^{H,F} = 2$ Hz (24). Yet $J_{o,m,p}^{F,CH_3}$ in 1, 2, 3, and 4 are almost the same as in the fluorotoluenes and are a measure of the π electron contributions to the corresponding ring proton and ring proton – fluorine couplings.

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UNIV LEEDS on 05/18/15 For personal use only.

This work was supported by the National Research Council of Canada. We are grateful to Mr. L. Olynyk for the synthesis of 2-fluoro-5-methylpyridine.

- 1. T. SCHAEFER, S. S. DANYLUK, and C. L. BELL. Can. J. Chem. 47 1507 (1969).
- S. CASTELLANO and R. KOSTELNIK. J. Am. Chem. 2. Soc. 90, 141 (1968).
- 3. J. B. MEMORY and J. H. GOLDSTEIN. J. Am. Chem. Soc. 88, 5560 (1966).
- C. J. MACDONALD and W. F. REYNOLDS. Can. J. Chem. 48, 1002 (1970).
- 5. R. E. RICHARDS and T. SCHAEFER. Trans. Faraday Soc. 54, 1447 (1958).
- 6. D. J. BLEARS, S. S. DANYLUK, and T. SCHAEFER. J. Chem. Phys. 47, 5037 (1967).
- 7. J. T. MINOR, G. F. HAWKINS, C. A. VANDERWERF, and A. ROE. J. Am. Chem. Soc. 71, 1125 (1949).
- A. ROE, P. H. CHECK, and G. K. HAWKINS. J. Am. Chem. Soc. 71, 4152 (1949).
- S. CASTELLANO and A. A. BOTHNER-BY. J. Chem. Phys. 41, 3863 (1964).
- 10. (a) R. WASYLISHEN and T. SCHAEFER. Can. J. Chem. 49, 94 (1971). (b) C. W. HAIGH and J. M. WILLIAMS. J. Mol. Spectrosc. 32, 398 (1969).
- 11. M. P. WILLIAMSON, R. J. KOSTELNIK and S. M. CASTELLANO. J. Chem. Phys. 49, 2218 (1968).

Can. J. Chem. Downloaded from www.nrcresearchpress.com by UNIV LEEDS on 05/18/15 For personal use only.

- 12. R. HOFFMAN. Arkiv Kemi, 17, 1 (1961).
- 13. R. HOFFMAN and S. GRONOWITZ. Arkiv Kemi, 16, 471 (1960).
- 14. K. D. BARTLE. D. W. JONES, and R. S. MATTHEWS. Rev. Pure and Appl. Chem. 19, 191 (1969).
- 15. L. GUIBÉ and E. A. C. LUCKEN. Mol. Phys. 14, 79 (1968).
- 16. J. E. LOEMKER, J. M. READ, JR., and J. H. GOLDSTEIN. Mol. Phys. 13, 433 (1967).
- 17. A. D. COHEN and T. SCHAEFER. Mol. Phys. 10, 209 (1965).
- 18. S. CASTELLANO and R. KOSTELNIK. Tetrahedron Lett. 51, 5211 (1967).
- 19. J. M. READ, JR., R. M. CRECELY, R. S. BUTLER, J. E. LOEMKER, and J. H. GOLDSTEIN. Tetrahedron Lett. 10, 1215 (1968).
- 20. S. CASTELLANO, C. SUN, and R. KOSTELNIK J. Chem. Phys. 46, 327 (1967).
- 21. J. M. READ, JR., R. E. MAYO, and J. H. GOLDSTEIN. J. Mol. Spectrosc. 22, 419 (1967).
- 22. J. E. LOEMKER, J. M. READ, JR., and J. H. GOLDSTEIN. J. Phys. Chem. 72, 991 (1968).
- 23. T. SCHAEFER, G. KOTOWYCZ, H. M. HUTTON, and J. W. S. LEE. Can. J. Chem. 46, 2531 (1968). 24. J. C. DECK. Ph.D. Thesis. University of Illinois,
- Urbana, Illinois, 1966.