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(12) The reaction of the bissulfide **6** with 1 equiv of LDA and lithium thiophenoxide, respectively, under identical reaction conditions as described for effecting monosulfenylation, afforded only unreacted **6**.
(13) See footnote *b*, Table I.

Carbon-13 Nuclear Magnetic Resonance Study of Pyridine *N*-Oxide

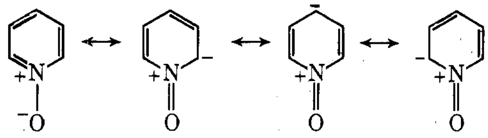
F. A. L. Anet* and Issa Yavari

Contribution No. 3647 from the Department of Chemistry, University of California, Los Angeles, California 90024

Received May 25, 1976

Carbon-13 chemical shifts and one-bond carbon–hydrogen coupling constants of pyridine *N*-oxide and of model compounds in a variety of neutral and acidic solvents are reported and discussed. Large shieldings (relative to pyridine) and solvent effects are observed for the α- and γ-carbon chemical shifts in pyridine *N*-oxide. The observed variations in $^1J_{CH}$'s indicate that there are appreciable contributions, other than the Fermi contact contribution, to the coupling constants. The α-carbon resonances are appreciably broadened (except in pyridine itself) as a result of ^{14}N–^{13}C coupling.

Pyridine *N*-oxide (I) is interesting in that its N–O moiety can act both as an electron donor and electron acceptor.[1] The difference (2.0 D) in dipole moments of I (4.2 D) and of pyridine (2.2 D) is smaller than that (4.8 D) between trimethylamine *N*-oxide (5.4 D) and trimethylamine (0.6 D), reflecting the contributions of resonance structures Ia, Ib, and Ic.[2]



I Ia Ib Ic

In view of the structural relationship of I to furoxans, whose ^{13}C NMR features have been recently reported,[3] we have undertaken a study of I and related model compounds. Previous investigations of the ^{1}H[4] and ^{14}N[5] NMR spectra of I exist, but the only ^{13}C NMR data on this compound concerns lanthanide-induced chemical shifts.[6] The ^{13}C NMR spectra of 3-hydroxypyridine *N*-oxide and some of its derivatives as anions in water have been measured;[7] however, the compounds and the conditions are rather special.

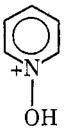
The ^{13}C chemical shifts of I, pyridine, and *N*-methylpyridinium iodide (II) in various solvents were measured and are listed in Table I. The solvents chosen were carbon tetrachloride, a nonpolar aprotic solvent; dimethyl sulfoxide, a polar aprotic solvent; chloroform a weakly interacting "aprotic" solvent; 95% ethanol, a neutral protic solvent; hexafluoro-2-propanol (HFP), a weakly acidic protic solvent ($pK_a = 9.3$);[8] trifluoroacetic acid (TFA), a strongly acidic protic solvent ($H_0 = -3$);[9] and finally, 98% H_2SO_4, a very strongly acidic protic solvent ($H_0 = -12$).[9] Chemical shifts were measured with respect to internal tetramethylsilane, with the exception of solutions in TFA and sulfuric acid, where an external reference had to be used. Although no correction was made for differences in magnetic susceptibilities, the error introduced thereby is expected to be less than 1 ppm.[10]

Since I has a pK_a in water of 1.9,[11] it is expected to be extensively protonated in trifluoroacetic acid, and essentially completely protonated in 98% sulfuric acid. Hydrogen bonding of I should take place in ethanol and in HFP, and to a smaller extent in chloroform.[12]

An examination of Table I shows that the γ-carbon resonance of I in carbon tetrachloride occurs at an unusually high field as compared to the same signal in pyridine or pyridinium salts. Since the chemical shift of a ^{13}C atom is known to depend in part on the excess electronic charge[13] at that atom, the high-field shift of the γ carbon implies a high electron density at this position, in agreement with a significant contribution of Ib to the resonance hybrid of I. The α-carbon signal in I occurs at about 11 ppm to higher field of the corresponding carbon resonance in pyridine in contrast to the α carbons of saturated tertiary amine *N*-oxides, which are deshielded by about 15 ppm compared to the same carbons in the parent amines.[14]

The γ-carbon chemical shift of I is sensitive to the polarity of the solvent and especially to the presence of a hydrogen-bond donor in the solvent. In HFP, which is the strongest hydrogen-bonding solvent that does not protonate I, the γ carbon is shifted by 9.4 ppm to lower field as compared to its position in carbon tetrachloride, but the α and β carbons are deshielded by only 2.0 and 2.8 ppm, respectively. The small effect of hydrogen bonding on the α carbons may result from a cancellation of a downfield shift due to a reduced electron density and an upfield shift due to a higher excitation energy[15] and/or a change in the bond order to the α-carbon atoms.[16,17]

The ^{13}C chemical shifts of protonated pyridine *N*-oxide (III) in sulfuric acid are similar to those of protonated pyridine (IV) or of pyridine methiodide (II) in the same solvent. In III, the electron donor effect of the N–O moiety is greatly reduced and the ring carbon chemical shifts are expectedly close to those in II and IV.



III

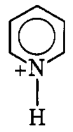


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Table I. ^{13}C Chemical Shifts[a] of Pyridine, Pyridine *N*-Oxide, and *N*-Methylpyridinium Iodide in Various Solvents

Compd (registry no.)	Solvent	α-^{13}C	β-^{13}C	γ-^{13}C	^{13}C-H_3
Pyridine (110-86-1)	CCl_4	149.7	123.2	135.1	
	$CDCl_3$	149.9	123.8	136.0	
	EtOH (95%)	150.1	125.1	137.7	
	HFP	148.9	126.7	140.7	
	TFA[b,c]	141.9	128.5	148.6	
	H_2SO_4 (98%)[b,c]	142.6	129.4	149.7	
Pyridine *N*-oxide (I) (694-59-7)	CCl_4	138.7	125.6	123.2	
	Me_2SO	139.0	126.7	125.2	
	$CDCl_3$	139.4	127.2	125.7	
	EtOH (95%)	140.3	127.9	129.5	
	HFP	140.7	128.4	132.6	
	TFA[b,c]	140.4	129.4	141.1	
	H_2SO_4 (98%)[b,c]	141.1	130.5	145.5	
N-Methylpyridinium iodide (II) (930-73-4)	EtOH (95%)	146.0	128.6	146.0	49.8
	HFP	146.6	129.7	147.0	50.4
	TFA[b]	146.3	129.5	146.6	50.1
	H_2SO_4 (98%)[b]	148.1	132.1	148.8	54.6

[a] In parts per million downfield from internal tetramethylsilane, except where otherwise stated. [b] With respect to external tetramethylsilane in 1:1 mixture with acetone-d_6. [c] The solutes are protonated in these media.

Table II. $^1J_{CH}$ for Pyridine, Pyridine *N*-Oxide, and *N*-Methylpyridinium Iodide (Hz)

Compd	Solvent	α-^{13}C	β-^{13}C	γ-^{13}C
Pyridine	None	179	162	161
	$CDCl_3$	179	163	161
	HFP	180	164	164
	TFA	192	176	172
	H_2SO_4	192	177	172
Pyridine *N*-oxide	$CDCl_3$	188	169	171
	EtOH	190	171	172
	HFP	191	172	173
	TFA	196	178	173
	H_2SO_4	197	178	173
N-Methylpyridinium iodide[a]	TFA	192	176	172

[a] $^1J_{CH}$ for the methyl group is 147 Hz.

The one-bond carbon-hydrogen coupling constants, $^1J_{CH}$, were measured for pyridine, I, and II in various solvents and are shown in Table II. There are discrepancies in the values previously reported in the $^1J_{CH}$'s for pyridine.[18] Our results are in excellent agreement with those reported by Lauterbur,[18c] but differ by 6–9 Hz from those given by other workers.[18a,b]

Protonation or N-methylation of pyridine leads to an increase of 12–15 Hz in $^1J_{CH}$ for all the carbon nuclei in these molecules. Comparable increases in $^1J_{CH}$'s of some oxazoles and thiazoles upon protonation have been reported[19] and interpreted in terms of a change in the amount of carbon "s" character in the C–H bond. However, the hybridization of the ring carbons in these compounds should not change appreciably upon protonation because the ring geometry should remain constant. More recent treatments have shown that the "effective nuclear charge" on carbon is important in determining the value of J_{CH}.[20] The greater the effective nuclear charge, the greater is J_{CH}. Such an effect would predict an increase in $^1J_{CH}$ for a carbon atom next to a nitrogen atom as a result of protonation, but there should be little change in the $^1J_{CH}$'s of carbons that are remote from the nitrogen. Experimentally, the protonation leads to an increase in the $^1J_{CH}$'s of all the ring carbons in oxazoles, thiazoles,[19] and pyridines, and this is not in agreement with an effective nuclear charge effect. Since the change observed in $^1J_{CH}$'s cannot be explained satisfactorily on the basis of either hybridization or an effective nuclear charge argument, it is possible that there are significant contributions other than the Fermi contact term to the coupling constant.

Theoretical calculations employing finite perturbation method at the INDO level of approximation have been reported for $^1J_{CH}$'s in pyridine.[21] The calculated values of $^1J_{CH}$'s were 20–25 Hz too low, but the general trend of the experimental coupling constants was reproduced, even though only the Fermi contact contribution was considered in the calculations. Recent calculations[22] on directly bonded carbon–carbon coupling constants have shown that the contributions from orbital–dipole and magnetic spin–dipolar terms become more important when the coupled carbons are π bonded. It may well be that such terms are also of significance for $^1J_{CH}$ in pyridine and related compounds and that an understanding of the changes in $^1J_{CH}$ upon protonation of these compounds requires quantum mechanical calculations that take into account these terms as well as the Fermi contact contribution.

The $^1J_{CH}$ for all carbon nuclei in pyridine *N*-oxide are substantially higher than those observed for the corresponding carbons in pyridine. Similar changes have been observed in aromatic heterocycles upon N-oxidation[23] or N-methylation[19] in cases that lead to positively charged nitrogen atoms. Protonation of pyridine *N*-oxide (at oxygen) leads to a 9-Hz increase in $^1J_{CH}$ for both α and β carbons, while the $^1J_{CH}$ for the γ carbon does not change appreciably. The $^1J_{CH}$ for the γ carbon in pyridine *N*-oxide is essentially the same as the $^1J_{CH}$ for the γ carbon in pyridinium ion or pyridinium methiodide, but this is probably a coincidence resulting from cancellation of different effects, as shown by the fact that the $^1J_{CH}$ for the β carbons is lower by about 8 Hz compared to the C–N coupling constants observed for the same nuclei in pyridinium salts.

Line width effects are observed in some of the compounds investigated. The α-carbon resonance is always broader than the β or γ line by about 5–7 Hz except for pyridine in the free base form. In general, the line width (and line shape) of a ^{13}C nucleus which is spin–spin coupled to a ^{14}N nucleus depends on the coupling constant, J_{NC}, and the ^{14}N nuclear quadrupole relaxation rate.[24] For the α carbon of pyridine-^{15}N, Lichter and Roberts[25] found that $^1J_{NC}$ was almost zero,[27] and thus it is not surprising that this carbon gives rise to a sharp line. By contrast, $^1J_{NC}$ for the α carbon in the pyridinium-^{15}N ion has an absolute value of 12 Hz, which corresponds to 8.6 Hz for $|^1J_{NC}|$ in pyridine-^{14}N. All other ^{15}N–^{13}C coupling constants in both pyridine and its salts are comparatively small. It is likely that relatively large ^{14}N–^{13}C coupling constants exist for the α carbons in all pyridine derivatives that do not have lone pairs of electrons on the nitrogen atoms. Thus the α carbons in these compounds can give rise to broad lines if the ^{14}N quadrupole relaxation times lie in an appropriate region, as is probably in our work. The T_1's for ^{14}N depend on the nuclear quadrupole coupling constants and the correlation times for random rotation. Although these latter two quantities are not known for all the pyridine derivatives shown in Table I, they probably do not vary drastically, and thus the observed broadening pattern of the ^{13}C lines is understandable.

Experimental Section

The ^{13}C NMR spectra for CCl_4, $CDCl_3$, TFA, and sulfuric acid solutions were obtained in 8-mm tubes at 30 °C on a 20-MHz Varian CFT-20 spectrometer. Tetramethylsilane was used as an internal reference for CCl_4 and $CDCl_3$ solutions. For TFA and sulfuric acid solutions the reference was tetramethylsilane in the form of a 50% solution in acetone-d_6 placed in a coaxial 5-mm tube. A coaxial tube containing neat acetone-d_6 was employed for lock purposes when CCl_4 was the solvent. Protons were noise decoupled and the spectra are Fourier transform of the sums of 1000–2000 free induction decays obtained under the following conditions: 45° pulse angle, 4K data points, 4000 Hz spectrum width, and a pulse delay of 0.5–1.0 s.

Measurements for ethanol, Me_2SO, and HFP solutions were made in 10-mm tubes at 30 °C on a 63.1-MHz superconducting solenoid spectrometer.[26] Tetramethylsilane was used as an internal reference and the fluorine signals of C_6F_6 or HFP were employed as lock. Protons were noise decoupled and the spectra are Fourier transforms of the sums of 1000–2000 free induction decays obtained under the following conditions: 30° pulse angle, 8K data points, 11 000 Hz spectrum width. All coupling constants and line width measurements were done on this spectrometer with 30° pulse angle, 8K data points, 4000 Hz spectrum width, and an exponential broadening function corresponding to 1–2 Hz.

Acknowledgment. This work was supported by the National Science Foundation.

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(27) **Note Added in Proof.** Recent INDO calculations indicate that the Fermi contact term makes a dominant contribution to $^1J_{NC}$ in I and IV, and that the low value of $^2J_{NC}$ in pyridine is caused by a cancellation effect because of the presence of the lone pair of electrons on nitrogen [J. M. Schulman and T. Venanzi, *J. Am. Chem. Soc.*, **98**, 4701 (1976); see also T. Bundgaard and H. J. Jakobsen, *Tetrahedron Lett.*, 1621 (1976)].

Nuclear Magnetic Resonance Determination of Rotational Barriers in Five-Membered Heterocycles

Michael Davis,* Ram Lakhan, and Bela Ternai

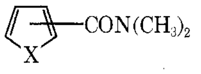
Department of Organic Chemistry, La Trobe University, Bundoora, Victoria, Australia 3083

Received January 14, 1976

Dynamic NMR has been used to obtain the values of the rotational barriers in furan, pyrrole, and thiophene-2- and -3-*N*,*N*-dimethylcarboxamides.

There is continuing interest in the electronic structure of five-membered heterocycles, and recent reports have described the calculation of σ^+ substituent constants from reaction rate[1,2] or quantitative infrared spectroscopic data.[3] An alternative approach is the use of NMR data to determine rotational barriers in suitable *N*,*N*-dimethylamides, since Jackman and his co-workers[4] have shown that a correlation exists between σ^+ values and the magnitude of such barriers in substituted *N*,*N*-dimethylbenzamides. More recently Riddell and Williams[5] have extended Jackman's results to a pyridyl-substituted dimethylamide. In this journal[6] it was recently reported that $\Delta G^{\ddagger}_{298.2}$ for the rotational barrier in *N*,*N*-dimethyl-2-furanamide was 16.8 kcal/mol, a value that seems anomalously high. It implies that furan, relative to benzene ($\Delta G^{\ddagger}$ = 15.8 kcal/mol),[6] is an electron *acceptor* at its 2 position, a result contrary to chemical experience.

We have prepared all six possible amides I (X = NH, O, S), and determined the rates of internal rotation about the N–C(O) bond in these amides at temperature intervals of 5–10 °C, using computer-simulated band-shape analysis of the exchange-broadened NMR signals of the dimethylamino



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protons. The free energy of activation, $\Delta G^{\ddagger}_{298.2}$, was obtained through use of Eyring plots of these rates. These $\Delta G^{\ddagger}$ values, and other NMR parameters, are given in Table I. For 3-thiophenamide the small value of $\Delta\nu$, and the low T_c, precluded meaningful calculation of $\Delta G^{\ddagger}_{298.2}$.

The partial double bond character of the C(O)–N bond in the amide group, and hence the barrier to rotation about that bond, arise from resonance interaction between the lone pair of electrons on the N atom and the electronegative oxygen of the carbonyl group. An electron donor attached to this car-