Acknowledgment. We wish to thank Professor Burgess for his helpful discussion during the inception of this work and for graciously providing us with detailed experimental results of a portion of his own research.

Registry No.—**2,** 59414-23-2; **3a,** 68225-95-6; **3b,** 68225-96-7; **4,** 68225-97-8; **5,** 68225-98-9; **6,** 68225-99-0; **7,** 68226-00-6; **8,** 68226-01-7; *N*-ethylsulfamoyl chloride, 16548-07-5; *N*-isopropylsulfamoyl chloride, 26118-67-2; *N*-methylsulfamoyl chloride, 10438-96-7; *N*-ethylsulfonylamine, 38336-91-3; *N*-isopropylsulfonylamine, 68226-02-8; *N*-methylsulfonylamine, 68226-03-9.

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(8) Since *N*-sulfonylamines are extremely moisture sensitive, this effectively quenches the reaction. It is therefore unlikely that either **5** or **6** arise from reaction of the *N*-sulfonylamine with a partially hydrolyzed form of diene **4**.

Carbon-13 Nuclear Magnetic Resonance Spectra of Substituted Pyridine *N*-Oxides[1]

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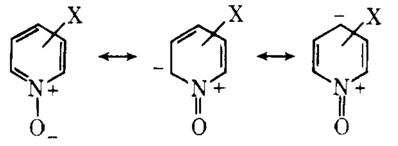
Pyridine *N*-oxides are an interesting class of organic compounds since the *N*-oxide functionality can activate the ring toward both electrophilic and nucleophilic attack.[2] We have studied the carbon-13 NMR spectra of substituted pyridine *N*-oxides in order to probe the ground state electron distribution in this molecular framework. In particular, we wished to assess the relative contributions of the substituent and the *N*-oxide functionality in determining this electron distribution.

Results and Discussion

The carbon-13 chemical shifts for the pyridine *N*-oxides are given in Table I. In order to gain more insight into the effects of the *N*-oxide functionality, the carbon-13 chemical shifts of the substituted pyridine *N*-oxides were compared to those of the corresponding substituted pyridines.[3] Table I also contains the carbon-13 chemical shift difference, Δ, between the pyridine *N*-oxides and pyridines.

In general, the pyridine *N*-oxides show a large shielding effect (~10 ppm) at C-2, C-4, and C-6 relative to that observed in the corresponding pyridines. Surprisingly, the magnitude of the shielding effect is about the same at C-2, C-4, and C-6 for most cases, and is not greatly influenced by the nature or position of the substituent. Minor exceptions to this trend appear in Table I as reductions in the magnitude of the shielding effect. The only conspicuous exception to the trend is the 4-nitro substituted compound **7** in which there is an opposite deshielding effect at C-4. The shieldings observed at positions 2, 4, and 6 may be explained if resonance forms **16** and **17** make a substantial contribution to the pyridine *N*-oxide hybrid. These forms place significant electron density at the 2, 4, and 6 positions. Although other factors are known to be important, increasing electron density at carbon is associated with a shielding effect.[4] These observations apparently indicate that the oxygen of the *N*-oxide functionality is a strong electron donor to C-2, C-4, and C-6 in the molecular ground state and plays a dominant role in determining the electronic distribution at the ring carbon atoms. In some cases, the substituent may interact to perturb this effect. For example, in compound **7**, the strong electron-withdrawing res-



16 **17**

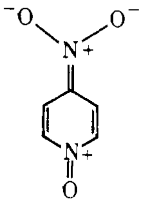


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Table I. Carbon-13 Chemical Shifts for Substituted Pyridine *N*-Oxides[a]

compd	X	$\delta_{C^{13}}$ C$_2$	C$_3$	C$_4$	C$_5$	C$_6$	X
1	H	138.2 (−11.3)[b]	125.3 (2.0)	124.8 (−10.7)	125.3 (2.0)	138.2 (−11.3)	
2	4-CH_3	137.2 (−11.8)	125.6 (1.6)	136.2 (−10.1)	125.6 (1.6)	137.2 (−11.8)	Me, 18.8 (−1.5)
3	4-$N(CH_3)_2$	138.6 (−10.7)	107.4 (1.2)	150.5 (−3.3)	107.4 (1.2)	138.6 (−10.7)	Me, 39.6 (1.1)
4	4-OCH_3	139.8 (−10.3)	111.6 (2.5)	158.1 (−6.7)	111.6 (2.5)	139.8 (−10.3)	Me, 55.9 (1.6)
5	4-$COCH_3$	139.2 (−11.3)	124.8 (4.1)	132.0 (−10.2)	124.8 (4.1)	139.2 (−11.3)	Me, 25.9 (−0.2); CO, 193.4 (−3.4)
6	4-Cl	139.9 (−10.5)	126.5 (2.7)	133.7 (−10.0)	126.5 (2.7)	139.9 (−10.5)	
7	4-NO_2	140.1 (−8.1)	120.7 (0.4)	142.0 (2.4)	120.7 (0.4)	140.1 (−8.1)	
8	3-$COCH_3$	139.2 (−10.4)	135.5 (3.5)	125.9[c] (−9.2)	124.4[c] (1.1)	142.2 (−11.0)	Me, 26.5 (0.2); CO, 193.6 (−2.8)
9	3-CN	141.6[c] (−10.5)	112.8 (3.1)	129.4 (−9.5)	126.7 (3.4)	143.0[c] (−9.6)	CN, 113.6 (−2.5)
10	3-Cl	138.6[d] (−10.0)	133.2 (1.3)	125.6[c] (−9.9)	125.8[c] (1.8)	137.6[d] (−9.7)	
11	3-Br	140.4 (−10.3)	120.1 (−0.5)	128.9 (−9.4)	125.8 (1.4)	137.7 (−9.8)	
12	2-CH_3	148.5 (−9.6)	125.0 (2.1)	126.1 (−9.8)	123.1 (2.8)	138.8 (−10.1)	Me, 17.2 (−6.9)
13	2-OCH_3	157.9 (−6.1)	108.1 (−2.6)	130.0 (−8.2)	117.1 (0.7)	139.6 (−7.1)	Me, 56.9 (3.9)
14	2-$COCH_3$	146.5 (−6.8)	126.1[c] (4.9)	126.4 (−10.1)	127.8[c] (1.1)	140.4 (−8.3)	Me, 30.2 (4.9); CO, 194.6 (−5.0)
15	2-Cl	141.1 (−10.1)	125.4 (1.3)	126.7 (−11.7)	123.6 (1.6)	140.0 (−9.5)	

[a] Chemical shifts were converted to the Me_4Si scale using the relationship $\delta_{Me_4Si} = \delta_{CDCl_3} + 76.91$. [b] Numbers in parentheses are the carbon-13 chemical shift differences, Δ, between the substitued pyridine *N*-oxides and the substituted pyridines: $\Delta = \delta_{^{13}C}$(substituted pyridine *N*-oxide) − $\delta_{^{13}C}$(substituted pyridine). A negative value, therefore, indicates greater shielding in the pyridine *N*-oxide. [c,d] Chemical shifts of these carbons may be reversed for the indicated pyridine *N*-oxide.

Table II. Substituent Effects for Substituted Pyridine *N*-Oxides[a] and Pyridines[b]

compd	X	C_2	C_3	C_4	C_5	C_6
2	4-CH_3	−1.0 (−0.5)[c]	0.3 (0.7)	11.4 (10.8)	0.3 (0.7)	−1.0 (−0.5)
3	4-$N(CH_3)_2$	0.4 (−0.2)	−17.9 (−17.1)	25.7 (18.3)	−17.9 (−17.1)	0.4 (−0.2)
4	4-OCH_3	1.6 (0.6)	−13.7 (−14.2)	33.3 (29.3)	−13.7 (−14.2)	1.6 (0.6)
5	4-$COCH_3$	1.0 (1.0)	−0.5 (−2.6)	7.2 (6.7)	−0.5 (−2.6)	1.0 (1.0)
6	4-Cl	1.7 (0.9)	1.2 (0.5)	8.9 (8.2)	1.2 (0.5)	1.7 (0.9)
7	4-NO_2	1.9 (−1.3)	−4.6 (−3.0)	17.2 (4.1)	−4.6 (−3.0)	1.9 (−1.3)
8	3-$COCH_3$	1.0 (0.1)	10.2 (8.7)	1.1 (−0.4)	−0.9 (0)	4.0 (3.7)
9	3-CN	3.4 (2.6)	−12.5 (−13.6)	4.6 (3.4)	1.4 (0)	4.8 (3.1)
10	3-Cl	0.4 (0.1)	7.9 (8.6)	0.8 (0)	0.5 (0.7)	−0.6 (−2.2)
11	3-Br	2.2 (1.2)	−5.2 (−2.7)	4.1 (2.8)	0.5 (1.1)	−0.5 (−2.0)
12	2-CH_3	10.3 (8.6)	−0.3 (−0.4)	1.3 (0.4)	−2.2 (−3.0)	0.6 (−0.6)
13	2-OCH_3	19.7 (14.5)	−17.2 (−12.6)	5.2 (2.7)	−8.2 (−6.9)	1.4 (−2.8)
14	2-$COCH_3$	8.3 (3.8)	0.8 (−2.1)	1.6 (1.0)	2.5 (3.4)	2.2 (−0.8)
15	2-Cl	2.9 (1.7)	0.1 (0.8)	1.9 (2.9)	−1.7 (−1.3)	1.8 (0)

[a] Substituent effect = $\delta_{^{13}C}$(substituted pyridine *N*-oxide) − $\delta_{^{13}C}$(pyridine *N*-oxide). [b] Substituent effect = $\delta_{^{13}C}$(substituted pyridine) − $\delta_{^{13}C}$(pyridine). [c] Numbers in parentheses are substituent effects for pyridines. A negative value indicates shielding.

onance effect of the nitro group is capable of delocalizing the electron density contributed to the 4 position. This evidently requires a substantial contribution from resonance form **18** to the hybrid which characterizes **7**. The observed deshielding, and hence lower electron density, at the 4 position of **7** is consistent with the known nucleophilic reactivity at this position.[2]

The effects of the *N*-oxide functionality are much smaller at C-3 and C-5 and are, in general, opposite to those at C-2, C-4, and C-6. Inspection of Table I shows that C-3 and C-5 are generally slightly more deshielded in the pyridine *N*-oxides when compared to the pyridines. This observation is consistent with the lack of resonance interaction of the *N*-oxide functionality with C-3 and C-5, and with the electron-withdrawing inductive effect of the positively charged nitrogen atom. Again, this trend appears to be consistent irrespective of the nature and position of the substituent. The notable exception is the 2-methoxy compound **13** in which C-3 is actually shielded. In this case, the substituent must perturb the *N*-oxide effect causing electron density to be augmented at C-3.

The effects of the substituents in the pyridine *N*-oxides were compared to the corresponding pyridines in order to see if the substituent effect would be the same for both molecular frameworks. The results of this comparison are shown in Table II. The substituent effects at C-4 for compounds **3**, **4**, and **7** and at C-2 for compounds **13** and **14** are significantly larger for the pyridine *N*-oxides than for the corresponding free bases. These substituents are characterized by an electron-withdrawing α effect.[5] The effectiveness of these substituents in removing electron density is enhanced in the pyridine *N*-oxides relative to the pyridines. This enhancement must be due to the ability of these substituents to remove some of the excess electron density which is characteristic of C-4 and C-2 in the pyridine *N*-oxides. The shielding effect at C-3 for *N*-oxide **13** is enhanced relative to that in the corresponding pyridine. Apparently, the ability of the 2-methoxy group to increase electron density at C-3 is greater for the *N*-oxide than for the pyridine.

The similarity of the *N*-oxide and pyridine substituent effects for the remaining carbon atoms indicates that the substituents exert their influence irrespective of the nitrogen atom oxidation state.

In order to further investigate and substantiate the relationship between charge density and substituent effect used above, INDO calculations were performed on pyridine *N*-oxide (**1**) and pyridine. The calculated π-electron densities for **1** were C-4 (1.04), C-3 (0.965), and C-2 (1.11). For pyridine they were C-4 (0.949), C-3 (1.03), and C-2 (0.955). Interestingly the changes in π-electron density upon oxidation reflect the changes in chemical shifts. The π-electron density changes for C-2 and C-4 are similar, as are the chemical shift changes.

Carbon-13 chemical shift trends have provided for a detailed analysis of the ground state charge distribution in substituted pyridine *N*-oxides.

Experimental Section

Natural abundance carbon-13 NMR spectra were obtained using a Varian XL-100-12 NMR spectrometer operating at 25.15 MHz. The spectrometer was equipped with a Nicolet TT-100 pulse apparatus and a NIC-1180 computer. A 90° pulse took 13 μs, and the time between pulses was 20 s. The sweep width was 2400 Hz, and 8K data blocks were used for time domain data collections. Free induction decays were collected using quadrature phase detection. Samples were prepared approximately 10% in $CDCl_3$ as solvent. More polar solvents were avoided because of the reported substantial solvent effects on carbon-13 chemical shifts and carbon–hydrogen coupling constants.[6] The $CDCl_3$ also provided the signal for an internal deuterium field-frequency lock as well as an internal chemical shift standard. Chemical shifts were converted to the Me_4Si scale using the expression $\delta_{Me_4Si} = \delta_{CDCl_3} + 76.91$. Proton coupled spectra were recorded as an aid in signal assignment. An additional assignment aid was realized by the observation that the signal from C-2 was slightly broadened because of ^{14}N–^{13}C coupling and nitrogen quadrupolar interaction.[6] The probe temperature was 36 °C.

The pyridine *N*-oxides used in the study were either commercially available or synthesized by literature routes.

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Registry No.—**1**, 694-59-7; **2**, 1003-67-4; **3**, 1005-31-8; **4**, 1122-96-9; **5**, 2402-96-2; **6**, 1121-76-2; **7**, 1124-33-0; **8**, 14188-94-4; **9**, 14906-64-0; **10**, 1851-22-5; **11**, 2402-97-3; **12**, 931-19-1; **13**, 20773-98-2; **14**, 2457-50-3; **15**, 2402-95-1.

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