AD-A212 713 1H AND 13C NUCLEAR MAGNETIC RESONANCE OF DIHYDROIMIDAZO-PYRIDINE AND IMID..(U) CHEMICAL RESEARCH DEVELOPMENT AND ENGINEERING CENTER ABERDEEN.. 1/1

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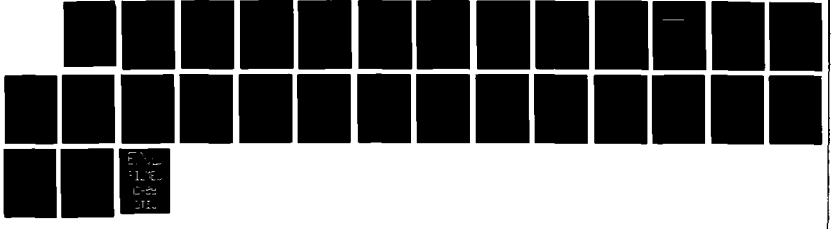

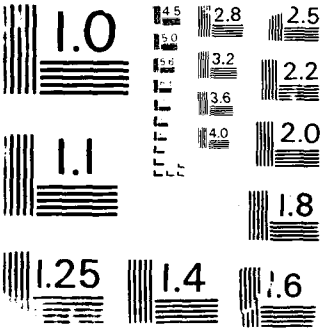
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^{1}H AND ^{13}C NUCLEAR MAGNETIC RESONANCE OF DIHYDROIMIDAZO-PYRIDINE AND IMIDAZO-[1,2-a]-PYRIDINE DERIVATIVES

Shekhar Munavalli, Ph.D.
MUNITIONS DIRECTORATE

Fu-Lian Hsu, Ph.D.
August J. Muller, Ph.D.
Everett O. Lewis, Ph.D.
William T. Beaudry, Ph.D.
Linda L. Szafraniec
RESEARCH DIRECTORATE

July 1989

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1a REPORT SECURITY CLASSIFICATION UNCLASSIFIED	1b RESTRICTIVE MARKINGS
2a SECURITY CLASSIFICATION AUTHORITY	3 DISTRIBUTION / AVAILABILITY OF REPORT Approved for public release; distribution is unlimited.
2b DECLASSIFICATION / DOWNGRADING SCHEDULE	
4 PERFORMING ORGANIZATION REPORT NUMBER(S) CRDEC-TR-059	5 MONITORING ORGANIZATION REPORT NUMBER(S)
6a NAME OF PERFORMING ORGANIZATION CRDEC 6b OFFICE SYMBOL (If applicable) SMCCR-MUC	7a NAME OF MONITORING ORGANIZATION
6c ADDRESS (City, State, and ZIP Code) Aberdeen Proving Ground, MD 21010-5423	7b ADDRESS (City, State, and ZIP Code)
8a NAME OF FUNDING / SPONSORING ORGANIZATION CRDEC 8b OFFICE SYMBOL (If applicable) SMCCR-MUC	9 PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER
8c ADDRESS (City, State, and ZIP Code) Aberdeen Proving Ground, MD 21010-5423	10 SOURCE OF FUNDING NUMBERS PROGRAM ELEMENT NO: PROJECT NO: 1-32-85-000 TASK NO: A-372 WORK UNIT ACCESSION NO:

11 TITLE (Include Security Classification)
^{1}H and ^{13}C Nuclear Magnetic Resonance of Dihydroimidazo-Pyridine and Imidazo-[1,2-a]-Pyridine Derivatives

12 PERSONAL AUTHOR(S)
(see reverse)

13a TYPE OF REPORT	13b TIME COVERED	14 DATE OF REPORT (Year, Month, Day)	15 PAGE COUNT
Technical	FROM 86 Sep TO 88 Jun	1989 July	26

16 SUPPLEMENTARY NOTATION

17 COSATI CODES		
FIELD	GROUP	SUB-GROUP
20	05	

18 SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
^{1}H NMR; Dihydroimidazo-pyridines; ^{13}C NMR; 2D NMR; Imidazo-pyridines; Chemical shifts; Quaternization effects

19 ABSTRACT (Continue on reverse if necessary and identify by block number)

Replacement of the aromatic hydrogens of the pyridinium moiety of the dihydroimidazo-pyridine and imidazo(1,2-a)-pyridine derivatives with electron-donating and electron-withdrawing substituents causes displacement of the chemical shifts of aromatic protons. Quaternization of the nitrogen atoms causes molecular perturbations and affects the ^{1}H and ^{13}C nuclear magnetic resonance chemical shifts. The sign of the C_{α} and $C_{\beta a}$ displacements can be used to detect the site of quaternization.

20 DISTRIBUTION / AVAILABILITY OF ABSTRACT	21 ABSTRACT SECURITY CLASSIFICATION
☒ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT ☐ DTIC USERS	UNCLASSIFIED
22a NAME OF RESPONSIBLE INDIVIDUAL SANDRA J. JOHNSON	22b TELEPHONE (Include Area Code) (301) 671-2914 22c OFFICE SYMBOL SMCCR-SPS-T

DD Form 1473, JUN 86 — Previous editions are obsolete

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[illegible], Ph.D., Hsu, Fu-Lian, Ph.D., Muller, August J., Ph.D., [illegible], Barrett G., Ph.D., Beaudry, William T., Ph.D., Szafraniec, Linda L.

PREFACE

The work described in this report was authorized under Project No. 1-32-85-000-A-372. This work was started in September 1986 and completed in June 1988.

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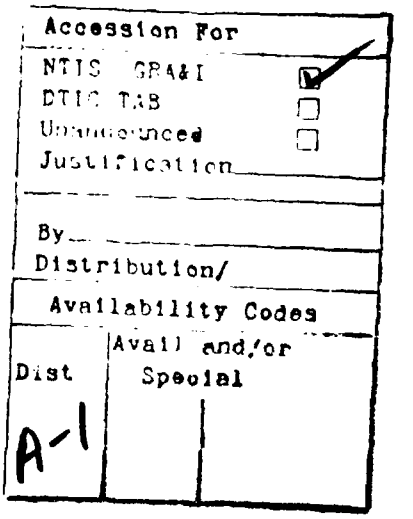

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^1H AND ^{13}C NUCLEAR MAGNETIC RESONANCE OF DIHYDROIMIDAZO-PYRIDINE AND IMIDAZO-[1,2-a]-PYRIDINE DERIVATIVES

1. INTRODUCTION

Because of the structural similarity between the purines and the imidazo-[1,2-a] pyridines, the latter have attracted considerable interest. Several attempts have been made to study this 10 π-electron aromatic system and correlate electron densities with their reactivity, ultraviolet (UV) absorption, and other parameters.[1-5] The ^1H NMR and ^{13}C NMR chemical shifts have been correlated with the total π-electron densities of the ring positions.[1, 3-7] However, difficulties were encountered in calculating electron densities due to the effect of σ electron polarization.[3] Cross-ring effects, para spin-spin coupling, peri-anisotropic effects, and shielding effects associated with atomic dipoles contributed to the chemical shifts of the protons of the azines.[4] The NMR and UV studies led to the conclusion that the imidazo-pyridine molecule is a 10 π-electron aromatic system with considerable delocalization of electrons and the ability to sustain ring currents.

In the study of the aromatic properties and the interplay of ring currents, the ^{13}C NMR has proved to be a versatile tool.[7-9] A linear correlation was reported between ^{13}C chemical shifts and the net electronic charges.[4,9] The NMR spectra of the imidazo-pyridinium salts are considerably different from their free bases.[1] Quaternization affects the chemical shifts of carbons adjacent to the quaternized nitrogen atom. The electron charge buildup on the carbon atom moves its resonance upfield, and the shielding pattern is significantly altered by the quaternization.[7,10] Due to a variety of effects, both N_1 and N_4 are capable of inducing positive and negative net charges.[3]

Imidazo-[1,2-a]-pyridines are no exception to the direct steric effects observed in aromatic heterocyclics.[11,12] The peri-interactions between N_1-R and C_8-R on one hand and C_3-R and C_5-R on the other have been reported.[1,13] The shielding effect for the para position of the substituent has been seen in the ^1H and ^{13}C NMR.[1,15] The substituent induced ortho-effect has been reported to affect ^1H chemical shifts.[17] The presence of a substituent on the pyridine ring of the imidazo-pyridines has no effect on the reactivity of the imidazole moiety and vice versa.[18]

In connection with the synthesis of the dihydroimidazo-[1,2-a]-pyridines,[19] ^1H and ^{13}C NMR spectra were studied. The NMR spectra of the dihydroimidazo-pyridinium salts are strikingly different from those of the free bases and those of the completely aromatic imidazo-pyridinium derivatives. The pyridine protons appear between 6.7 and 9.0 ppm. Most noticeable differences are seen in the spectra of the pyridinium moiety. The substitution of the pyridine hydrogen with a methyl group causes an upfield displacement of the chemical shift of the ortho-protons. A similar observation was reported in the case of imidazo-[1,2-a]-pyridines.[17,20] Clearly seen in the ^{13}C NMR spectra of the dihydroimidazo-pyridinium derivatives is the displacement of the C_7 signal to higher frequency due to the positive charge on N_4. The chemical shifts of C_5 and C_7 are interchanged in all but one; in that, the C_7 signal is displaced to higher frequency, whereas the C_5 signal has shifted to lower frequency. This was further confirmed by 2D-NMR (see the figure). A similar argument may be advanced in the

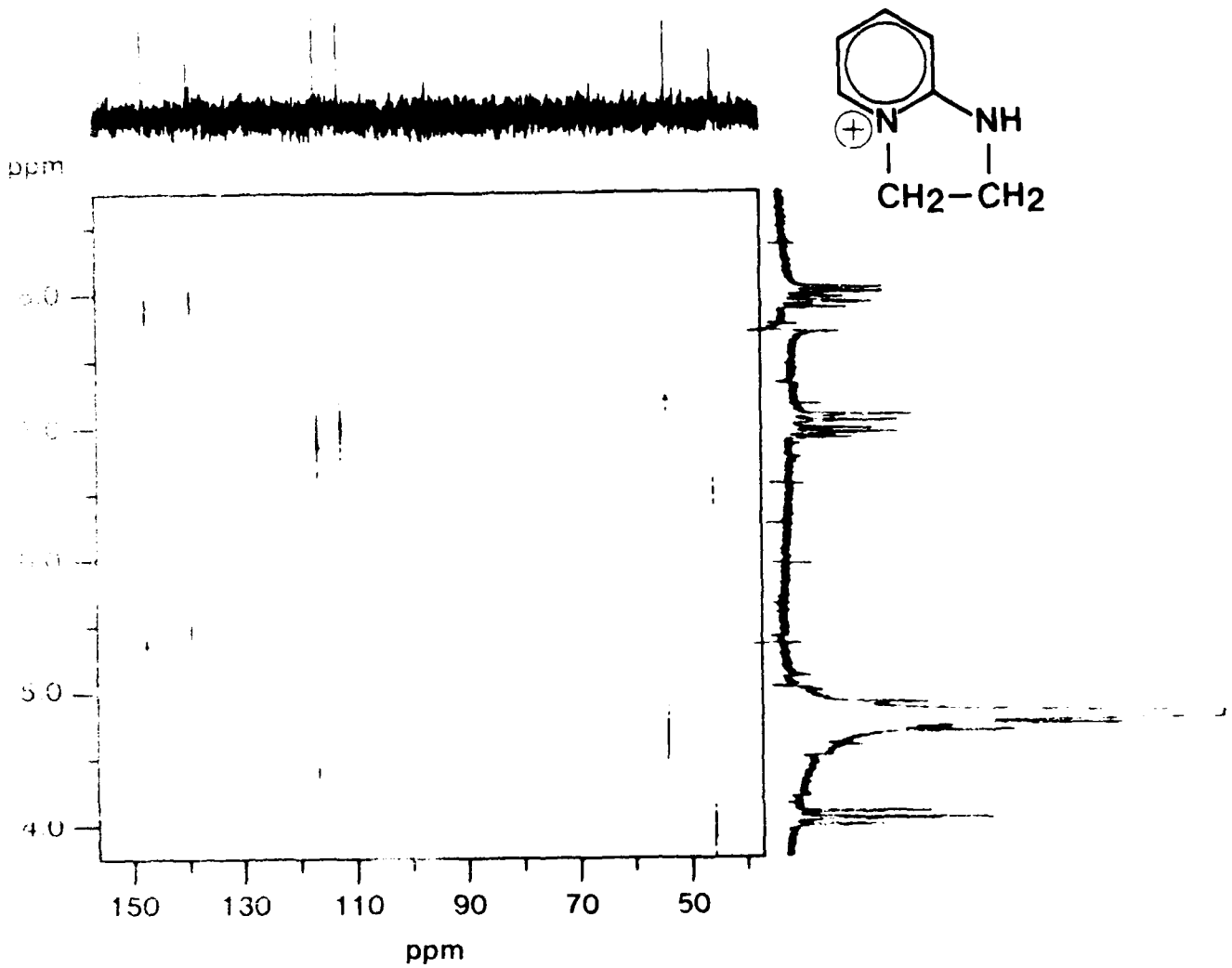


Figure. 2D-NMR

case of the 1-benzyl-2-alkyl-2-hydroxy-2,3-dihydroimidazo-[1,2-a]-pyridinium salt.[14] The one exception being 1b. This may be due to the peri-interactions.[1,10,13]

2. EXPERIMENTAL PROCEDURES

2.1 Compounds.

The synthesis of the dihydroimidazo-[1,2-a]-pyridinium salts was accomplished in a straightforward manner by condensing the respective aminopyridines with 1,2-dibromoethane. The compounds obtained were purified and characterized by elemental and spectrometric analysis.[19] For a review on the synthesis of imidazo-[1,2-a]-pyridines, see Blewitt.[3] Attempted O-demethylation of pyrilamine with trimethylsilyl iodide to obtain tripelennamine, a metabolite of the antihistamine drug, gave a 79% yield of the N-benzyl dihydroimidazo-[1,2-a]-pyridinium salt.[21]

2.2 Measurements.

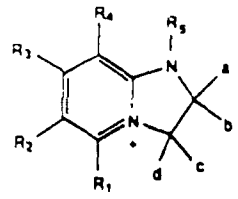
The ^{1}H NMR chemical shift data were obtained on a Varian E-390 NMR spectrometer for 0.2 M solutions of the appropriate compound (the salts in D_2O and the free bases in $CDCl_3$) at the probe temperature (34 °C). The chemical shift values were determined relative to the internal standard sodium 3-trimethylsilyl propionate (TSP) or tetramethylsilane (TMS) as appropriate. All signals were downfield from the reference, and the values reported to the nearest 0.05 ppm were obtained by direct measurement using a 10-ppm sweep width. The ^{13}C data were obtained on a Varian XL-200 or VXR-400S spectrometer using the same parameters as above. The ^{1}H and ^{13}C values are relative to the respective unsubstituted parent compound for each group of compounds. The sign of the upfield displacement of the respective signal in comparison with the parent compound is considered negative, and the downfield displacement is indicated by a positive sign.

3. RESULTS AND DISCUSSION

The nitrogen atoms of the imidazo-pyridine molecule can exert a variety of effects on electron distribution. In principle, they can induce both positive and negative charges on the carbon atom of the imidazo-pyridines and, therefore, present an interesting situation to study the substituents' effects arising from quaternization of the nitrogens, the cross-ring currents, the effect of the presence and absence of the double bond in the imidazole ring, and the influence of the pyridine moiety on the reactivity of the imidazole ring. This report discusses the effects of the substituents and quaternization on the ^{1}H and ^{13}C NMR chemical shifts of the title compounds. The influence of the double bond of the imidazole ring on the ^{13}C chemical shifts of the pyridine moiety is also discussed.

A satisfactory correlation between the calculated and the predicted chemical shifts for all protons in the imidazo-[1,2-a]-pyridines has been reported.[22] Because the general characteristics of the NMR spectra of these types of compounds are straightforward, the assignment of the chemical shifts does not pose any special problem. Replacement of the pyridine hydrogen with a methyl group causes an increase in the shielding of the proton on the carbon ortho to the carbon carrying the substituent in the imidazo-[1,2-a]-pyridine series.[1,17] Table 1 shows that a similar effect prevails in the dihydroimidazo-pyridinium salts. A para effect is also displayed by the substituent. In other words, both ortho and para effects due to substitution are observed. The presence of the electron withdrawing substituents (NO_2 group in 1g; N_6 and N_8 in 1m and 1n) causes deshielding. As a consequence, the ortho protons are

Table 1. Dihydroimidazo-pyridinium Salts

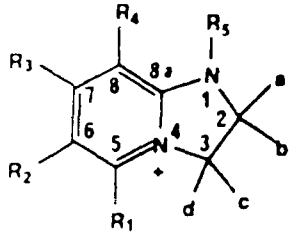


[^{1}H-NMR Chemical Shift Differences (ΔH) of Dihydroimidazo-[1,2-a]-pyridinium and -6-azapyridinium and -8-azapyridinium salts.)]

Compound	H_5	ΔH_5	H_6	ΔH_6	H_7	ΔH_7	H_8	ΔH_8	Ref
1a	8.00	-	6.92	-	7.91	-	7.03	-	20
1b	CH_3	-	6.74	-0.18	7.77	-0.14	6.84	-0.19	20
1c	7.80	-0.20	CH_3	-	6.96	-0.81	7.80	+0.77	20
1d	7.82	-0.18	6.79	-0.13	CH_3	-	6.84	-0.19	20
1e	7.88	-0.12	6.88	-0.11	7.74	-0.17	CH_3	-	20
1f	8.25	+0.25	Br	-	7.88	-0.03	6.98	-0.05	20
1g	9.25	+1.25	NO_2	-	8.61	+0.70	7.13	+0.10	20
1h	8.60	+0.60	6.90	±	7.46	±	8.14	+1.11	14
1i	8.48	+0.43	7.05	±	8.00	±	8.22	+1.19	14
1j	8.50	+0.50	6.75	±	7.57	±	7.75-8.23	+ve	14
1k	8.61	+0.61	6.83	±	7.30	±	7.95-8.40	+ve	14
1l	7.97	-0.03	6.80	-0.12	7.95	+0.04	7.14	+0.09	21
1m	8.7	+0.70	N	-	8.21	+0.30	6.92	-0.11	20
1n	8.74	+0.74	7.03	+0.11	8.51	+0.60	N	-	20

[±means ΔH could not be accurately determined due to the complexity of the signals of these protons]

Table 1. Dihydroimidazo-pyridinium Salts (continued)



1a: R_1, R_2, R_3, R_4, R_5, a, b, c, d – H

b: R_1 – CH_3; R_2, R_3, R_4, R_5, a, b, c, d – H

c: R_2 – CH_3; R_1, R_3, R_4, R_5, a, b, c, d – H

d: R_3 – CH_3; R_1, R_2, R_4, R_5, a, b, c, d – H

e: R_4 – CH_3; R_1, R_2, R_3, R_5, a, b, c, d – H

f: R_2 – Br; R_1, R_3, R_4, R_5, a, b, c, d – H

g: R_2 – NO_2; R_5 – CH_3; R_1, R_3, R_4, a, b, c, d – H

h: R_5 – CH_3; a – CH_3; b – OH; c – CH_3; R_1, R_2, R_3, R_4, d – H

i: R_5 – CH_3; a – C_6H_5; b – OH, R_1, R_2, R_3, R_4, c, d – H

j: R_5 – $CH_2C_6H_5$; a – CH_3; b – OH, R_1, R_2, R_3, R_4, c, d – H

k: R_5 – $CH_2C_6H_5$; a – C_6H_5; b – OH, R_1, R_2, R_3, R_4, c, d – H

l: R_5 – $-CH_2C_6H_4$-OH(p); R_1, R_2, R_3, R_4, a, b, c, d – H

m: dihydroimidazo [1,2-a]-6-azapyridine

n: dihydroimidazo [1,2-a]-8-azapyridine

shifted downfield. An increased shielding effect due to the electron-donating groups such as -CH_3, -OC_2H_5, and -$N(C_2H_5)_2$ on ortho and para protons is also observed in the free bases (Table 2 compounds 3-12). This leads to increased electron density of C_6 and C_8, and this finding is in general agreement with their chemical reactivity vis-a-vis $^+NO_2$.[18] The reversal of the ortho-effect of compounds 13 and 14 may be due to the peri-interaction.

Contrary to the claim that the substituents on the pyridine ring had very little effect on the properties of the imidazole moiety and vice versa,[18] the substituents on the imidazole ring do cause significant changes in the ^1H and ^{13}C chemical shifts of the pyridine moiety of the molecule (Tables 1 and 2). The size (bulk) of the alkyl substituent had no significant effect on the chemical shifts of the ortho protons (compounds 3, 7, and 9).

QUATERNIZATION

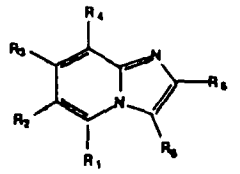
In principle, quaternization is possible at both sites, N_1 and N_4. The N_4 quaternized compounds such as 2,3-dihydroimidazo-[1,2-a]- and imidazo-[1,2-a]-pyridinium compounds can be synthesized from suitably substituted precursors. Protonation decreases the N-C bond, spin-pairing, and paramagnetic contribution and enhances cross-ring perturbations and anomalous upfield shifts of ^{13}C signal of the α-carbons upon protonation of the adjacent nitrogen.[23] Tables 3 and 4 describe the effect of protonation of the bridgehead nitrogen, which produces resonance and inductive effects in the pyridine ring. In the case of dihydro derivatives, the H_5 is displaced upfield in all cases, whereas it exerts mixed effects [illegible]

In general, the pyridinium protons of the imidazo-[1,2-a]-pyridinium salts are strongly deshielded by the quaternization of the pyridine nitrogen (see Table 4). This effect is more pronounced than in the case of the dihydroanalogs. The presence of the double bond in the imidazole ring also contributes to the chemical shift displacement of H_5, H_6, H_9, and H_8. Quaternization of the free bases generally leads to N_1 quaternized products.[2,24] As a consequence, the signal due to H_5 is displaced downfield (Table 4, structures 44-46). This diamagnetic effect is directly attributable to the resonance structures (Table 4, structures 48-49).[24] Table 5 shows the effect produced by the presence of a positively charged nitrogen (N_4) on the ^{13}C chemical shifts of the dihydroderivatives. Except in the case of 1b, the signal due to C_5 is displaced upfield in all compounds examined. The C_{8a} appears to suffer a similar fate.

The quaternization of N_4 produces an upfield displacement of the $^{13}C_{8a}$ signal (-2.7, Table 6), whereas the quaternization of N_4 causes a downfield displacement of $^{13}C_{8a}$ (+3.1). The Δ values of C_5, C_6, C_7, and C_8 reflect cross-ring substituent effects, C_5 corresponding the smallest perturbation. Comparison of the ^{13}C NMR chemical shifts of the quaternium carbons of 36 and 37 indicates that the substituent on N_1 does not make a significant contribution to their chemical shifts. The removal of the double bond between C_2 and C_3 of the N_1 quaternized compound (44) causes definite changes in the ^{13}C chemical shifts (see 44 and 47); more particularly, the Δc values of C_5, C_7, and C_8 and the signal due to C_{8a} is displaced downfield. Nonetheless, the quaternization does produce significant alteration in electronic effects.

Table 7 gives the chemical shift differences (Δc) due to the quaternization of the bases. Although the quaternization occurs at N_1, the overall contribution of the resonance

Table 2. Pyridinium Protons



[(^{1}H-NMR Chemical Shift Differences (ΔH) of Pyridinium Protons of the Imidazo-[1,2-a]-pyridines.)]

Compound	H_5	ΔH_5	H_6	ΔH_6	H_7	ΔH_7	H_8	ΔH_8	Ref
2	8.16	-	6.78	-	7.15	-	7.70	-	1,26
3	CH_3	-	6.78	0.0	7.23	+0.08	7.60	-0.10	1,25
4	7.90	-0.26	CH_3	-	6.99	-0.16	7.60	-0.10	1,2,17
5	7.96	-0.20	6.45	-0.33	CH_3	-	7.36	-0.34	1,2,20
6	8.04	-0.12	6.68	-0.10	6.98	-0.12	CH_3	-	1,2
7	C_2H_5	-	6.62	-0.16	7.19	+0.04	7.61	-0.09	13
8	OC_2H_5	-	5.91	-0.87	7.10	-0.05	7.85	+0.15	18
9	$CH(CH_3)_2$	-	6.62	-0.16	7.19	+0.04	7.61	-0.09	13
10	$N(C_2H_5)_2$	-	6.35	-0.43	7.18	+0.03	7.44	-0.16	25
11	7.83	-0.33	6.38	-0.10	$N(C_2H_5)_2$	-	6.51	-1.19	25
12	7.70	-0.46	6.66	-0.12	6.28	-0.67	$N(C_2H_5)_2$	-	25
13	NHAc	-	7.09	+0.31	7.28	+0.13	7.47	-0.23	25
14	9.22	+1.06	NHAc	-	7.15	0.0	7.55	-0.15	25
15	8.24	+0.08	6.84	+0.06	7.97	+0.82	NHAc	-	25
16	Br	-	6.89	+0.11	6.86	-0.29	7.48	-0.22	26
17	8.32	+0.16	Br	-	7.20	+0.05	7.59	-0.11	25
18	8.19	+0.03	6.95	+0.17	7.25	+0.10	7.67	-0.03	25
19	7.89	-0.27	6.79	+0.01	7.12	-0.03	7.64	-0.06	25,26
20	CH_3	-	6.48	-0.30	7.01	-0.14	7.43	-0.27	26

Table 2. Pyridinium Protons (continued)

Compound	H_5	ΔH_5	H_6	ΔH_6	H_7	ΔH_7	H_8	ΔH_8	Ref.
21	OC_2H_5	-	-	-	8.30	+1.15	6.13	-1.57	18
22	CH_3	-	7.35	+0.57	7.85	+0.70	7.85	+0.15	25
23	Br	-	6.89	+0.09	6.86	-0.29	7.48	-0.22	26
24	NH_2	-	5.8	-0.98	6.93	-	6.93	-	26
25	9.0	+0.84	7.40	+0.62	8.40	+1.25	NHAc	-	25
26	Br	-	6.89	+0.11	6.86	-0.29	7.48	-0.22	26
27	7.90	-0.26	CH_3	-	7.00	-0.15	7.51	-0.19	18
28	8.05	-0.09	6.70	-0.08	6.98	-0.17	CH_3	-	18
29	8.21	+0.05	Cl	-	7.15	0.0	7.60	-0.10	18
30	NO_2	-	-	-	6.48	-0.67	8.60	+0.90	18
31	9.45	+1.27	7.53	+0.75	7.83	+0.68	8.05	+0.35	25

Table 3. Dihydroimidazo-[1,2-a]-Pyridines and Pyridinium Salts

[(^{1}H-Chemical Shift Differences (ΔH) of Dihydroimidazo[1,2-a]-pyridines and-Pyridinium salts.)]

Compounds* ++	ΔH_5	ΔH_6	ΔH_7	ΔH_8
1a and 2	-0.16	+0.14	+0.76	-0.65
1b and 3	-	-0.04	+0.54	+0.76
1c and 4	-0.10	-	-0.03	+0.20
1d and 5	-0.10	+0.33	-	-0.31
1e and 6	-0.16	+0.20	+0 24	-

* Values are taken from Tables 1 and 2.

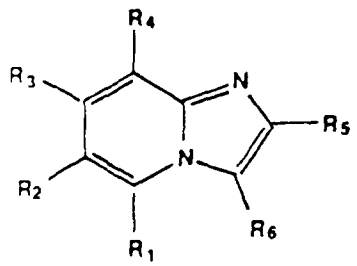
++ Downfield displacement +ve, upfield displacement -ve with respect to the free base.

Table 4. Pyridinium Protons

(^{1}H-NMR Chemical Shift Differencs (ΔH) of Pyridinium Protons of the Imidazo[1,2-a]pyridinium salts.)

Compound	^+N	H_5	ΔH_5	H_6	ΔH_6	H_7	ΔH_7	H_8	ΔH_8	Ref
2	-	8.20	-	6.80	-	7.21	-	7.56	-	26
38	$^+N_4$	8.62	+0.42	CH_3	-	7.87	+0.66	7.87	+0.31	2
39	$^+N_4$	8.58	+0.38	7.33	+0.53	CH_3	-	7.68	+0.12	2
40	$^+N_4$	8.73	+0.53	7.53	+0.73	7.40	+0.69	CH_3	-	2
41	$^+N_4$	8.56	+0.36	CH_3	-	7.93	+0.72	7.93	+0.37	2
42	$^+N_4$	8.62	+0.42	7.40	+0.60	CH_3	-	7.84	+0.28	2
43	$^+N_4$	8.67	+0.47	7.46	+0.66	7.83	+0.62	CH_3	-	2
44	$^+N_1$	9.70	+1.5	-	-	-	-	-	-	14
45	$^+N_1$	9.14	+0.94	-	-	-	-	-	-	14
46	$^+N_1$	8.89	+0.79	-	-	-	-	-	-	14

Table 4. Pyridinium Protons (continued)



2 R_1, R_2, R_3, R_4, R_5, R_6 - H

3 R_1-CH_3; R_2, R_3, R_4, R_5, R_6 - H

4 R_2-CH_3; R_1, R_3, R_4, R_5, R_6 - H

5 R_3-CH_3; R_1, R_2, R_4, R_5, R_6 - H

6 R_4-CH_3; R_1, R_2, R_3, R_5, R_6 - H

7 R_1-C_2H_5; R_2, R_3, R_4, R_5, R_6 - H

8 R_1-OC_2H_5; R_2, R_3, R_4, R_5, R_6 - H

9 R_1-$CH(CH_3)_2$; R_2, R_3, R_4, R_5, R_6 - H

10 R_1-$N(C_2H_5)_2$; R_2, R_3, R_4, R_5, R_6 - H

11 R_3-$N(C_2H_5)_2$; R_1, R_2, R_4, R_5, R_6 - H

12 R_4-$N(C_2H_5)_2$; R_1, R_2, R_3, R_5, R_6 - H

13 R_1-NHAc; R_2, R_3, R_4, R_5, R_6 - H

14 R_2-NHAc; R_1, R_3, R_4, R_5, R_6 - H

15 R_4-NHAc; R_1, R_2, R_3, R_5, R_6 - H

16 R_1-Br; R_2, R_3, R_4, R_5, R_6 - H

17 R_2-Br; R_1, R_3, R_4, R_5, R_6 - H

18 R_6-Br; R_1, R_2, R_3, R_4, R_5 - H

19 R_6-CH_3; R_1, R_2, R_3, R_4, R_5 - H

20 R_1-CH_3; R_6-Br, R_2, R_3, R_4, R_5 - H

21 R_1-OCH_5; R_6-NO_2; R_2, R_3, R_4, R_5 - H

22 R_1-CH_3; R_6-NO_2; R_2, R_3, R_4, R_5 - H

23 R_1-Br; R_6-CH_3; R_2, R_3, R_4, R_5 - H

24 R_1-NH_2; R_6-CH_3; R_2, R_3, R_4, R_5 - H

25 R_4-NHAc; R_6-NO_2; R_2, R_3, R_4, R_5, - H

26 R_1-Br; R_5-CH_3; R_2, R_3, R_4, R_6 - H

Table 4. Pyridinium Protons (continued)

27 R_2-CH_3; R_5 - $CO_2C_2H_5$; R_1, R_3, R_4, R_6 - H

28 R_4-CH_3; R_5-$CO_2C_2H_5$; R_1, R_2, R_3, R_6 - H

29 R_2-Cl; R_5-$CO_2C_2H_5$; R_1, R_3, R_4, R_6 - H

30 R_1-NO_2; R_5-$CO_2C_2H_5$; R_2, R_3, R_4, R_6 - H

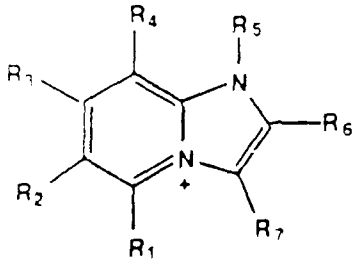
31 R_6-NO_2; R_1, R_2, R_3, R_4, R_5 - H

32 R_5-$CO_2C_2H_5$; R_1, R_2, R_3, R_4, R_6 - H

33 R_2-NO_2; R_5-$CO_2C_2H_5$; R_1, R_3, R_4, R_6 - H

34 R_4-NO_2; R_5-$CO_2C_2H_5$; R_1, R_2, R_3, R_6 - H

35 R_2-Cl; R_1, R_3, R_4, R_5, R_6 - H



(36-43)

36: R_1, R_2, R_3, R_4, R_5, R_6, R_7 - H

37: R_5-CH_3; R_1, R_2, R_3, R_4, R_6, R_7 - H

38: R_2-CH_3; R_1, R_3, R_4, R_5, R_6, R_7 - H

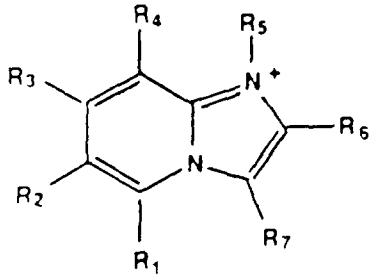
39: R_3-CH_3; R_1, R_2, R_4, R_5, R_6, R_7 - H

40: R_4-CH_3; R_1, R_2, R_3, R_5, R_6, R_7 - H

41: R_2, R_5 - CH_3; R_1, R_3, R_4, R_6, R_7 - H

42: R_3, R_5 - CH_3; R_1, R_2, R_4, R_6, R_7 - H

43: R_4, R_5 - CH_3; R_1, R_2, R_3, R_6, R_7 - H



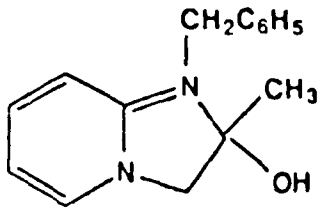
(44-46)

44: R_5 - $CH_2C_6H_5$; R_6 - CH_3; R_1, R_2, R_3, R_4, R_7 - H

45: R_5 - $CH_2C_6H_5$; R_6 - C_6H_5; R_1, R_2, R_3, R_4, R_7 - H

46: R_5 - $CH_2C_6H_5$; R_6, R_7 - CH_3; R_1, R_2, R_3, R_4 - H

Table 4. Pyridinium Protons (continued)



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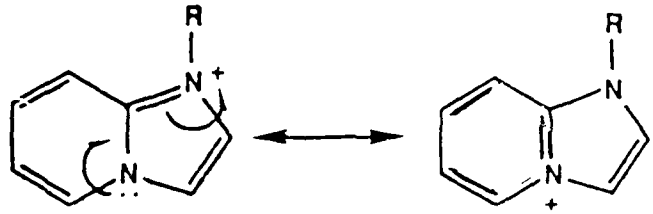

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Table 5. Pyridinium Carbons

[^{13}C-NMR: Chemical Shift Differences (Δc) of the Pyridinium Carbons of the Dihydroimidazo-[1,2-a]pyridinium Derivatives.]

Compound	C_5	ΔC_5	C_6	ΔC_6	C_7	ΔC_7	C_8	ΔC_8	C_{8a}	ΔC_{8a}	Ref
1a	139.20	-	116.50	-	147.30	-	112.20	-	158.90	-	20
1b	150.80	+11.60	116.30	-0.20	147.30	0.0	108.80	-3.40	159.20	+0.30	20
1c	135.70	-3.50	127.30	+10.80	137.00	-10.30	118.80	+6.60	149.30	-9.60	20
1d	138.70	-1.20	118.60	+2.10	161.00	+13.70	111.10	-1.10	158.60	-0.30	20
1e	136.20	-3.00	116.60	+0.10	145.60	-1.70	123.00	+10.80	158.90	0.0	20
1f	137.50	-1.70	114.90	-1.60	145.60	-1.70	108.20	-4.00	153.40	-5.50	20
11	144.60	+5.40	112.70	-3 80	138.00	-9.30	107.70	-4.50	157.20	-1.70	21

Table 6. Pyridinium Carbons of Imidazo-[1,2-a]-Pyridines

[^{13}C-NMR: Effect of the Substituents on Chemical Shift Difference (ΔC) of Pyridinium Carbons of Imidazo-[1,2,-a]-Pyridines.]

Compound	C_5	ΔC_5	C_6	ΔC_6	C_7	ΔC_7	C_8	ΔC_8	C_{8a}	ΔC_{8a}	Ref
2*	125.80	-	112.20	-	124.30	-	117.70	-	145.40	-	10
3*	134.40	+8.60	112.20	0.0	124.30	0.0	115.00	-2.7	145.80	+0.4	13
4*	123.50	-2.30	121.90	+9.7	127.60	+3.3	117.00	-0.7	144.60	-0.8	13
5*	125.10	-0.7	115.00	+2.8	135.30	+11.0	116.40	-1.6	146.00	+0.6	13
6*	123.70	-2.1	112.00	+0.8	123.30	-1.2	127.50	+9.9	146.00	+0.6	13
7*	139.90	+14.1	109.30	-2.9	124.6	+0.3	115.20	-2.5	146.10	+0.7	13
8*	148.30	+22.50	88.50	-23.70	125.90	+1.6	108.70	-9.0	145.90	+0.50	18
9*	144.30	+18.5	107.20	-5.0	124.60	+0.3	115.30	-2.4	146.10	+0.70	13
36*	129.29	+3.49	117.12	+4.92	133.59	+9.29	112.06	-5.64	139.18	-6.22	10
37*	129.32	+3.52	117.08	+4.88	133.27	+8.97	118.42	+0.72	139.16	-6.25	10
47*	137.50	+11.70	114.90	+2.70	145.60	+21.30	108.20	-9.5	153.43	+8.03	14
32**	127.60	-	117.80	-	126.50	-	118.00	-	144.60	-	18
28**	125.20	-2.40	118.50	+0.70	124.70	-1.8	127.40	-9.4	145.20	+0.6	18
29**	127.50	-0.10	120.50	+2.7	125.40	-1.10	118.70	+0.7	142.90	-1.70	18
33**	120.20	-7.4	138.50	+20.7	128.80	+2.3	120.50	+2.5	144.50	-0.10	18
34**	139.90	+6.30	119.80	+2.00	125.70	-0.80	137.20	+19.2	137.50	-7.1	18
35**	125.20	-0.60	118.90	+6.7	124.90	-0.60	117.60	-0.40	143.00	-2.40	18

*ΔC values with respect to 2.
**ΔC values with respect to 32.

Table 7. Pyridinium Carbons of Imidazo-[1,2-a]-Pyridines Due to Quaternization

[^{13}C-NMR: Chemical Shift Difference (ΔC) of Pyridinium Carbons of Imidazo-[1,2-a]Pyridines Due to Quaternization of N_1.]*

Compound	ΔC_5	ΔC_6	ΔC_7	ΔC_8	ΔC_{8a}	Ref
4	+4.2	+0.8	+4.2	-0.7	-0.8	18
6	-0.1	+0.5	+2.4	-0.7	-0.9	18
8	+0.4	+2.7	+2.7	-2.2	-2.2	18
28	+0.8	+0.5	+1.4	+0.7	-1.5	18
29	+5.4	+2.0	+1.4	-2.6	-1.9	18
32	+1.9	-2.8	+1.9	-1.9	-1.3	18
35	+2.1	+1.2	+0.6	-1.0	-1.2	18

* With respect to 2.

structure [illegible] Except in the case [illegible] is shifted downfield in all the compounds. Therefore, we can use the [illegible] to detect and decide which of the two nitrogen atoms is quaternized.

Comparison of the ^{13}C [illegible] introduction of a methyl [illegible] displacement of the ^{13}C NMR [illegible]

5. CONCLUSIONS

The origin, magnitude, and mode of transmission of the substituent induced electronic effects of the pyridines and their salts have been the subject of intensive investigations. These effects seem to persist even in the case of the bicyclic systems such as the imidazo pyridines. [illegible] study of ^{1}H and ^{13}C NMR spectra of dihydroimidazo and imidazo pyridines, we conclude that:

- The [illegible]

- [illegible] electron donating groups cause an upfield displacement of the pyridine protons, whereas the electron withdrawing groups induce a downfield displacement. (This is reminiscent of the substituent effects observed in the case of the [illegible] bispyridinium derivatives[27] and substituted pyridinium compounds[24,25]).

- The size (bulk) of the alkyl substituent [illegible] chemical shifts of the pyridine protons.

- The sign of the displacement of the C_5 and the C_{2a} can be used to detect the site of quaternization (see Table 7).

- The ^{13}C signal of the C_7 of dihydroimidazo [illegible] pyridinium salts is shifted to higher frequency, and the C_5 signal is shifted to lower frequency, due to quaternization of the bridgehead nitrogen.

- The presence of a positive [illegible] proton, namely, the H_5 (see Table 6).

- As confirmed by ^{15}N NMR [illegible] chemical [illegible] nitrogen.

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