Carcinogen Chemistry. 2.[1] Carbon-13 Nuclear Magnetic Resonance Spectroscopic Study of the Ambident Carbocationic Nature of Iminium Ions and Its Relevance to the Aminoalkylating Ability of Related Chemical Carcinogens

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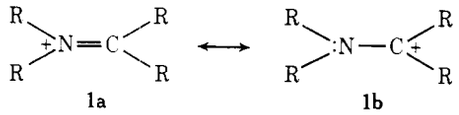
^1H and ^{13}C NMR spectroscopic investigation of aliphatic and aromatic iminium ions was carried out for their structural study and to determine the extent of the contribution of their carbenium ion character based on a comparison of the iminium ions with isoelectronic model compounds. CNDO/2 calculations of simple aliphatic iminium ions were also performed and related to the ^1H and ^{13}C NMR chemical shifts. *N*- and *C*-methyl substituents were found to polarize the charge density of the π bond, resulting in shielding and deshielding effects, respectively.

In our preceding paper we reported the in vitro formation of *N*-methylmethyleniminium in the acid cleavage reaction of *N,N*-dimethylnitrosamine and raised the possible role of iminium ions as aminoalkylating agents responsible for the carcinogenic alkylating ability of nitrosamines.[1] The ^1H NMR spectroscopic study of some protonated imines has been also reported in our previous studies.[2] The results indicated that protonated imines are predominantly iminium ions **1a** with limited contribution from the aminocarbenium ion structures, **1b**. Since ^{13}C NMR spectroscopy has proved to be most useful in studying the structure of carbocationic systems, it was expected to give a better indication of the relative importance of the contribution of **1a** to **1b**.



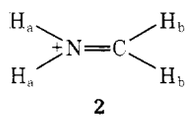
1a **1b**

We have consequently carried out a ^{13}C NMR spectroscopic study of a series of aliphatic and aromatic iminium ions, prepared by known procedures.[3-5] Since it was considered that nucleophilic anions, such as chloride and iodide, would exchange with the iminium centers, the less nucleophilic tetrafluoroborate salts were prepared and used in our study. CNDO/2 calculations of the simple aliphatic iminium ions were also performed, and the results were correlated with the ^1H and ^{13}C NMR data.

Results

The NMR spectroscopic data of alkyliminium ions are summarized in Table I and those of aryliminium in Table II. For a comparison the ^{13}C NMR data of the parent arylimines are listed in Table III.

Methyleniminium Ion. The ^1H NMR spectrum of **2** at 60 MHz shows a complex pattern. A simpler first-order ^1H NMR spectrum is observed at 100 MHz in SO_2 solution at −60 °C. The triplet of doublets of doublets at δ_{1H} (Me_4Si) 10.67 is assigned to the H_a protons on the basis of their J_{N-H} coupling. The J_{N-H} coupling constant of 67.0 Hz is consistent with a sp^2 hybridized nitrogen.[6] The H_b absorption appears as a doublet of doublets at δ_{1H} (Me_4Si) 8.54 with trans and cis coupling constants of 18 and 14 Hz, respectively. The proton-decoupled ^{13}C NMR spectrum of **2** consists of a triplet at δ_{13C} (Me_4Si) 176.1 with J_{N-C} coupling of 0.4 Hz.



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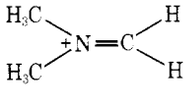
***N,N*-Dimethylmethyleniminium Ion.** The ^1H NMR spectrum of ion **3** in SO_2 at −60 °C shows a broad pentet at δ_{1H} (Me_4Si) 3.63 for the methyl groups and a slightly broadened peak at δ_{1H} (Me_4Si) 7.70 for the methylene protons. The multiplicities can be attributed to the trans and cis coupling of the *N*-methyl groups' protons to the methylene protons. The proton-decoupled ^{13}C NMR spectrum of **3** consists of two triplets at δ_{13C} (Me_4Si) 49.1 and 167.9 with C–N coupling constants of 0.2 and 0.5 Hz, respectively. These two signals correspond to the *N*-methyl and the methylene carbon absorptions, respectively.



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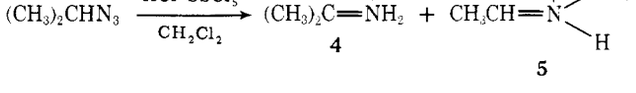
It has been previously found that methyl azide with $HCl–SbCl_5$ gives methyleniminium hexachloroantimonate.[2]

$$CH_3N_3 + HCl–SbCl_5 \rightarrow CH_2{=}N^+H_2SbCl_6^- + N_2$$

In continuation of our studies, ethyl and isopropyl azide were used in attempted preparation of the corresponding iminium salts, but the acid rearrangement of these alkyl azides resulted in mixtures of different iminium salts, due to competitive methyl and hydrogen migrations. The rearrangement products and their relative amounts (determined by peak integration of the iminium ions) are listed in Table IV.

The reaction of isopropyl azide with $HCl–SbCl_5$ in methylene chloride is typical of the acid-catalyzed rearrangement reactions studied. By ^1H NMR spectroscopy of the resulting products, we were able to identify the 2-propylideniminium (**4**) and the *N*-methylethylideniminium (**5**) ions. When the ^{13}C NMR spectrum of this solution was obtained, the high-intensity peaks corresponding to the major product, 2-propylideniminium ion, were easily identified relative to the six lower intensity peaks of the minor products. These latter signals were assigned to the cis and trans isomers of the *N*-methylethylideniminium ions.



4 **5**

The *N*-methyl group of the *N*-methylmethyleniminium ion absorbs at δ_{13C} 42.2. This absorption was used as a model for the trans isomer of the *N*-methylethylideniminium ion **6**. There are two *N*-methyl absorptions, one at δ_{13C} (Me_4Si) 40.4 and the other at δ_{13C} (Me_4Si) 33.9. These are assigned to the

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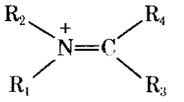
Table I. ^1H and ^{13}C NMR Spectroscopic Data[a] of Aliphatic Iminium Salts



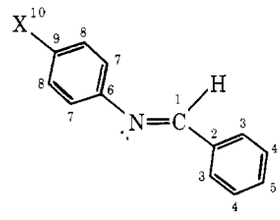
Compd	Registry no.	R_1	R_2	R_3	R_4	^1H NMR (Me_4Si)[b] R_1	R_2	R_3	R_4	$J_{1,2}$	$J_{1,4}$	$J_{1,3}$	J_{NH}	^{13}C NMR (Me_4Si) R_1	R_2	R_3	R_4	$\dot{N}$=C
3	811-63-2	CH_3	CH_3	H	H[c]		3.63 brp		7.70 brm					49.1	49.1			167.9
5	64611-34-3	CH_3	H	H	CH_3[e]	4.00	dt 11.00 brt	8.19 qdd	8.45 tq	5.5	13.0	7.8	66.0	42.2				170.8
2	64611-39-8	H	H	H	H[d]		10.67 tdd		8.54 tdd				67.0					176.1
7	64611-41-2	CH_3	H	CH_3	H[d]	3.80	d	8.5	2.8					33.9		16.9		183.6
6	64611-42-3	CH_3	H	H	CH_3[d]	3.80	d	8.5	2.8					40.4			21.2	183.8
9	56995-77-8	H	H	H	CH_3[d]		9.90 brt	8.80 brm	2.77 brm				69.0				22.3	189.5
10	64611-43-4	CH_3	CH_3	CH_3	CH_3[c]		3.50 sp		2.37 sp		1.0			44.5	44.5	24.5	24.5	189.5
11	64611-35-4	CH_3	H	CH_3	CH_3[e]	3.63	d 9.60 m	2.80 s	2.70 s	6.0				34.2		20.0	27.1	195.5
12	56995-78-9	H	H	CH_3	CH_3[d]		9.40 brt		2.53 brs				64.0			25.3	25.3	201.6

[a] All chemical shifts from external Me_4Si are obtained on a Varian A-56-60 spectrometer for ^1H NMR and an XL-100 spectrometer for ^{13}C NMR. [b] ^1H NMR spectra from the HA-100. [c] In SO_2 solution at −60 °C with BF_4^- as the anion. [d] In SO_2 solution at −60 °C with $SbCl_6^-$ as the anion. [e] In magic acid solution.

Table II. Carbon-13 NMR Data for the Protonated Aromatic Imines

Compd	Registry no.	X	Rxn mixture	1	2	3	4	5	6	7	8	9	10	J_{C_1-H}, Hz
13	19696-25-4	H	HSO_3F/SO_2ClF	165.6 d	126.0 s		130.0 d	140.2 d	135.4 s	120.6 d	132.8 d	132.2 d		
			BF_4^-/SO_2	165.6 d	126.0 s	130.4 d	130.0 d	139.6 d	136.0 s	121.3 d	133.2 d	129.6 d		
14	64611-44-5	CH_3	Magic acid/SO_2	163.9 d	125.9 s	131.7 d	130.9 d	140.0 d	133.0 s	120.7 d	132.7 d	143.7 s	20.5 q	178.9
			BF_4^-/SO_2	163.9 d	126.2 s	131.4 d	130.6 d	139.2 d	133.5 s	121.0 d	133.2 d	142.9 s	20.6 q	
15	64611-45-6	OCH_3	Cl^-/SO_2	161.9 d	126.0 s	132.4 d	130.7 d	138.9 d	128.8 s	122.5 d	115.7 d	160.9 s	55.1 q	
			Magic acid/SO_2	168.5 d	125.5 s	133.8 d	131.1 d	141.5 d	136.5 s	124.1 d	121.1 d	152.4 s	74.1 q	181.4
16	17321-91-4	Cl	Magic acid/SO_2	165.9 d	125.8 s	131.0 d	131.0 d	140.7 d	134.1 s	122.3 d	133.8 d	137.5 s		
17	64611-46-7	NO_2	HSO_3F/SO_2ClF	171.2 d	125.6 s	131.7 d	131.7 d	144.3 d	142.3 s	124.0 d	131.7	147.3 s		180.5
18	19696-24-3	H	HSO_3F/SO_2ClF	172.7 d	125.7 s	131.7 d	130.6 d	139.2 d	39.5 q					179.1
19	64611-47-8	OCH_3	Magic acid/SO_2	171.2 d	126.9 s	134.9 d	119.2 d	156.6 s	40.5 q	72.7 q				180.0
			BF_4^-/SO_2	169.8 d	118.7 s	134.8 d	115.9 d	167.0 s	39.2 d	55.8 q				

Table III. Carbon-13 NMR Spectroscopic Data of Some Imines



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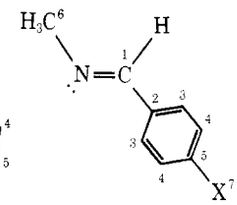

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Compd	Registry no.	X[a,b]	1	2	3	4	5	6	7	8	9	10
20	1613-90-7	CH_3O	159.3 d	137.6 s	129.8 d	129.7 d	132.1 d	146.0 s	115.5 d	123.3 d	159.4 s	56.5 q
21	1613-92-9	CH_3	159.9 d	137.4 s	129.5 d	129.5 d	131.9 d	150.3 s	121.8 d	130.7 d	136.5 s,	21.8 q
8	1750-36-3	H	161.4 d	137.4 s	130.2 d	129.8 d	132.4 d	153.2 s	122.0 d	129.8 d	127.0 d	
22	1613-89-4	Cl	161.4 d	137.0 s	130.2 d	129.9 d	132.6 d	151.4 s	123.3 d	129.8 d	132.6 s	
23	785-81-9	NO_2	163.8 d	136.5 s	130.4 d	130.1 d	133.5 s	159.0 s	122.4 d	126.1 d	146.5 s	
24	25521-74-8	H	162.2 d	137.3 s	129.0 d	128.6 d	130.8 d	48.2 q				
25	60682-83-9	MeO	161.7 d	130.1 s	130.1 d	114.4 d	162.1 s	48.1 q	55.3 q			

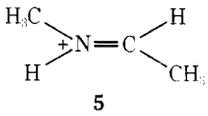
[a] All shifts are reported from Me_4Si. [b] In $CDCl_3$ as solvent.

Table IV. Products of the Acid Rearrangement of the Alkyl Azides with HCl–$SbCl_5$ in Methylene Chloride Solution

RN_3	% yield (rel)	Product ions[a]
R = CH_3–	100.0	Methyleniminium (**2**)
R = Et–	86.6	Acetaldiminium (**9**)
	13.4	*N*-Methylethyleniminium (**5**)
R = *i*-Pr–	68.5	2-Propylideniminium (**11**)
	31.5	*cis*- and *trans*-*N*-methyliminium (**7** and **6**)

[a] As hexachloroantimonate salts.

trans and cis isomers, respectively. Two *C*-methyl absorptions at δ_{13C} (Me_4Si) 21.2 and 16.9 are assigned to the trans and cis isomers, respectively, on the basis that the *cis*-*N*-methyl and -*C*-methyl of **7** are more shielded due to a γ-substituent effect.[7] The *C*-methyl shift of **7** is approximately 5.5 ppm more



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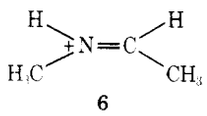

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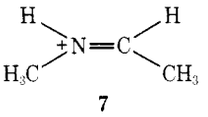

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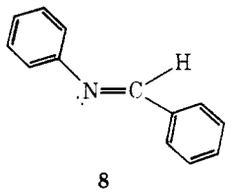
shielded from the *C*-methyl of the ethylideniminium ion used as a model. The iminium carbons were found at δ_{13C} (Me_4Si) 183.8 and 183.6, but no assignment to the cis and trans isomers can be made for these shifts, presently.

The ^{13}C NMR chemical shift assignments of the *N*-phenyl- and *C*-phenylimines were based on NMR measurements, including proton-decoupled, off-resonance, and fully decoupled experiments and their comparison with model compounds. Since the assignments of the carbons of the phenyl group for the *N*-methylbenzaldiminium ion **18** are unambiguous, they were used as models for identifying the ^{13}C NMR absorptions of the *C*-phenyl group of *N*-phenylbenzaldimine (**8**). The *N*-phenyl carbons were assigned by an off-resonance experiment, by peak intensities, and by comparison with ^{13}C NMR spectrum of aniline. The para-substituted *N*-phenyl carbons of **8** were assigned on the basis of simple additivity relationships using the ^{13}C shifts of monosubstituted benzenes (Table III).[8]

The ^{13}C NMR chemical shifts of the protonated aromatic imines **13–19** were assinged in a similar manner. The addivity relationships used to determine the ^{13}C chemical shifts of the *N*-phenyl group of of the protonated imines **13–17** do not fit as closely in this case as found for the parent imines themselves. Specifically, the "magic acid" solutions of N-protonated *p*-methoxy-, *p*-chloro-, and *p*-nitrophenylbenzaldimines **15–17** deviate the most. This could be due to a second protonation on the N-donor function. However, the iminium carbons in the aryl-substituted ions show characteristic chemical shifts in the range of δ_{13C} (Me_4Si) 163.–171.0 (Table II).



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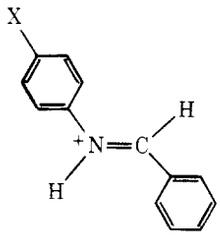
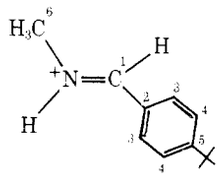


13, X = H
14, X = CH_3
15, X = OCH_3
16, X = Cl
17, X = NO_2

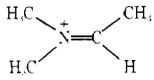


18, X = H
19, X = OCH_3

Charge densities were estimated from CNDO/2 calculations. The geometries of the molecules used were based on standard bond lengths and angles.[9] The 2p (π) and total charge densities for the aliphatic iminium ions are summarized in Table V.

In our previous ^1H NMR study of iminium ions, it was concluded that the iminium resonance forms **1a** are predominant over the aminocarbenium forms **1b**.[1] The basis for this conclusion was the observation that protonated 2-propylidenemethylamine showed two different *C*-methyl groups which by far were not as deshielded as those in a typical carbenium ion, such as the *tert*-butyl cation.[10] From the 17-Hz trans J_{HC-NH} coupling constant of the *N*-methylbenzaldiminium ion, it was concluded that geometry has more effect than charge on the ^1H chemical shifts of iminium ions. This evidence suggests a predominance of resonance structures **1a** over **1b**. However, the carbon shift of the iminium carbon should give a more direct indication of the importance of forms **1a** and **1b** rather than the adjacent proton shift.

Table V. Calculated Charge Densities at Nitrogen and Carbon in Iminium Ions

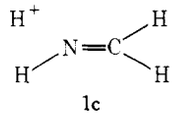
Compd	Registry no.	$2p_z$ (π)[a]		Total charge	
		N	C	N	C
2	28963-72-6	−0.4581	0.4581	−0.050	0.297
9	52900-33-1	−0.5708	0.4657	−0.109	0.332
12	62399-23-9	−0.6440	0.4634	−0.150	0.349
5	54533-35-6	−0.3672	0.3591	0.032	0.236
7	64611-36-5	−0.4902	0.3957	−0.034	0.287
6	64611-37-6	−0.4902	0.3974	−0.036	0.287
11	19696-23-2	−0.5740	0.4130	−0.082	0.316
3	28149-27-1	−0.2850	0.2690	0.098	0.180
	52594-29-3	−0.4137	0.3293	0.031	0.243
10	44364-22-9	−0.5062	0.3611	−0.020	0.282

[a] Charge represented in electrons.

Discussion

In the present work, a study of the carbenium ion character of the methyleniminium ion was carried out in relation to substituent on nitrogen and carbon. The ^{13}C NMR chemical shifts were compared with respect to inductive and polarization effects of the double bond by changing methyl substituents. This method was used in a study of trigonal carbons with methyl substituents by Olah and Forsyth.[11]

It was instructive to compare the ^{1}H and ^{13}C NMR data with the charge density calculations of the parent methyleniminium ion **2** by CNDO/2. The total charge density calculations show a charge on nitrogen of −0.05 and on carbon of 0.297. The hydrogens bonded to nitrogen are significantly positive relative to the hydrogens of the methylene and one can infer the importance of a nonbonded proton and the methylenimine structure **1c**.[12] However, the methylene moiety



1c

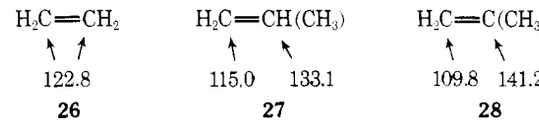
is still more positively charged than that of the ammonium group.

The ^{1}H NMR chemical shifts of the hydrogens of ammonium and the methylene group, respectively, found at δ 10.67 and 8.54,[13,14] are deshielded from those of the isoelectronic ethylene of δ 5.3. The deshieldings demonstrate the positive character of the methyleniminium ion, in accord with the CNDO/2 calculations, which also indicate more positive character of the ammonium hydrogens relative to methylene hydrogens. The ^{13}C NMR chemical shift of the methyleniminium ion of $\delta_{^{13}C}$ 176.1 is deshielded from that of the isoelectronic ethylene of $\delta_{^{13}C}$ 122.0 and shows a more positively charged methylene carbon for the methyleniminium ion than that of ethylene.[15]

The ^{1}H and ^{13}C NMR data correlate qualitatively well with the CNDO/2 calculations of the methyleniminium ion. In the simple resonance argument, they represent the importance of **1b** and **1c** over **1a.** The deshielding of 54.1 ppm from the ethylene to methleniminium carbon shows a strong contribution of the aminocarbenium form. However, the comparison of the ^{13}C NMR shifts of protonated formaldehyde or a carbenium ion indicates a much lesser contribution of carbenium character for the methyleniminium ion.

In the simple methyleniminium ion studied, CNDO/2 charge density calculations for the 2p (π) orbitals of nitrogen and carbon showed a strongly polarized double bond, with electron donation to the nitrogen. However, in the σ framework the inductive effect is in the opposite direction. With *N*-methyl substitution, there is a decrease in the polarization of the π bond, with carbon becoming more negative and nitrogen positive. This increase in electron density at carbon with *N*-methyl substitution coincides with the shielding of the iminium carbon.

The shieldings of the β carbon are not unusual. Although the magnitude of the shieldings are different for the ^{13}C chemical shifts for the methylene groups of the isoelectronic alkenes (**26–28**) and iminium ions, the direction of the

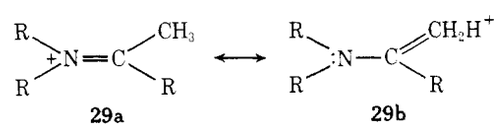


26 **27** **28**

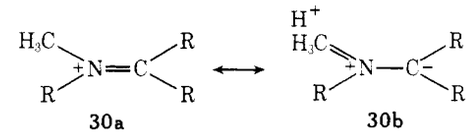
chemical shift differences indicates that π polarization is the predominant effect.

The CNDO/2 calculations for *C*-methyl substitution show an increase in electron density at the 2p (π) orbital on nitrogen. However, the π-electron density on the iminium carbon shows no change. The decrease of the σ-electron density on the iminium carbon is much too small to account for the deshieldings in the ^{13}C NMR spectra. Since hyperconjugative electron donation of the *C*-methyl group should be important to the iminium center in this electron-deficient cation,[16] the polarization of the iminium double bond will increase as reflected in the 2p (π) electron density on nitrogen. Thus, on *C*-methyl substitution the iminium carbon receives electron density from the methyl group and donates to the nitrogen through the π system. In the CNDO/2 calculations for the iminium carbon, this balances out to almost no change in the 2p (π) charge density.

The results can be rationalized using simple resonance arguments. Since a *C*-methyl group can stabilize the iminium ion **29a** by hyperconjugation (**29b**), a polarization of the iminium double bond through the π system will increase the importance of structure **1b** to **1a.** However, on *N*-methyl substitution hyperconjugative stabilization is much less likely (**30b**) and inductive stabilization (**30a**) delocalizes electron



29a **29b**

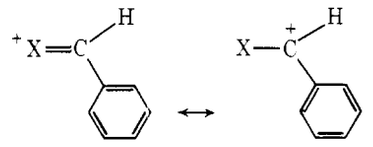


30a **30b**

density into nitrogen. This causes a reverse polarization of the iminium bond, increasing the importance of **1a** and **1b.**

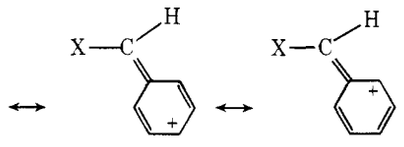
It has been generally recognized that delocalization of charge to a phenyl ring is related to the amount of charge

Scheme I



31a, X = CH_3
32a, X = Cl
33a, X = OH
18a, X = $NHCH_3$
34a, X = CH_2

18b, 31-34b



18c, 31-34c 18d, 31-34d

compd	registry no.	carbon-13 shifts C$^+$	ortho	para
31	25414-93-1	230.7	155.1	161.6
32	56683-65-9	210.7	153.5	163.2
33	3441-73-4	204.7	146.1	148.9
18	63933-59-5	172.7	131.7	139.2
34	34504-74-0	135.8	126.7	128.2[a]

[a] See ref 23.

density on the carbenium center. From ^{13}C NMR chemical shift data and CNDO/2 calculations, it has been shown that the carbenium center and the ortho and para carbons of the phenyl substituent are of particular importance. Thus, the effects of *C*-phenyl and *N*-phenyl substitution on imines were investigated by ^{13}C NMR spectroscopy. A comparison of the ^{13}C NMR chemical shifts of the isoelectronic phenylcarbenium ions with substituents such as CH_3, Cl, OH, and CH_2^- (**31–34**) with the protonated imines should give an indication of the importance of the aminocarbenium structure **1a.**

From CNDO/2 calculations for **31–33**[17] the electron density of the cations was correlated with the ^{13}C chemical shifts. Since the delocalization patterns are similar to those obtained from resonance structures, the latter will be used for simplicity. The ^{13}C NMR chemical shift of the carbenium center and the ortho and para carbons for **31–34** and **18** are listed in Scheme I. A comparison of these ^{13}C shifts will demonstrate the means of stabilization in the *C*-phenyl-substituted iminium ions. Since the phenyl group is common among **31–34** and **18,** the resonance delocalization of the phenyl ring will be relative to the stabilization provided by the other groups. With a strongly stabilizing group, delocalization into the phenyl ring will become less important and vice versa. For example, in the case of the phenylmethylcarbenium ion **31,** there is no interaction with a nonbonded pair of electrons from the methyl group. Consequently, in ion **31,** the charge is delocalized primarily into the phenyl ring by resonance stabilization as shown by the deshielding of the ^{13}C NMR shift of the carbenium center and those of the ortho and para carbons of the phenyl ring. However, stabilization by a nonbonded pair of electrons as in styrene (**34**) results in very little delocalization of electron density into the phenyl ring.

These two systems (**31** and **34**) represent the extremes in stabilization. In **31,** where there is no stabilization by a nonbonded pair of electrons, maximum electron delocalization into the ring results in the deshielding of the ^{13}C chemical shifts of the ortho and para carbons. Thus, structures **31b–d** are important compared to **31a.** However, in **34,** where the nonbonded pair fully contributes, the resonance structure **34a** is the most important one.

In the *C*-phenyl-substituted iminium ion, there is a balance between stabilization by resonance and a nonbonded pair of electrons. Although the ^{13}C NMR chemical shift data demonstrate the importance of **18a,** the deshieldings of the carbenium center and the ortho and para carbons of the phenyl ring do show the ambident carbenium ion nature of the iminium ion. This is also supported by ^{13}C NMR data of the parent imine **24.** It should be noted again that charge delocalization is relative to the charge density on the carbenium center.

Conclusions

It is apparent from the present ^{13}C NMR spectroscopic study and related CNDO/2 calculations that the iminium structures **1a** predominate over the aminocarbenium ion forms **1b,** when comparing iminium ions to carbenium ions and protonated ketones. This is due to the ability of the nonbonded electron pair of the nitrogen atoms to stabilize the adjacent positive charge. The various C substituents slightly change the importance of **1a** relative to **1b,** but **1a** still remains the most important. The aminocarbenium forms are, however, significant and cannot be neglected as indicated by the deshielding of iminium carbon as compared to the parent imine. The present study thus clearly establishes the ambident carbocationic nature of iminium ions. Iminium ions therefore should be able to act as electrophilic aminoalkylating agents through involvement of their aminocarbenium ion character. As nitrosamines were shown to readily form in vitro iminium ions under acid-catalyzed conditions and, therefore, probably also under in vivo conditions, we are extending our studies to the alkylation of suitable nucleophiles, including nucleic acid bases. with iminium ions and nitrosamines, respectively.

Experimental Section

Aliphatic iminium salts were prepared by reported methods.[3-5] Methyleniminium hexachloroantimonate was prepared from methyl azide,[18] hydrochloric acid, and antimony pentachloride in methylene chloride.[3] Ethylideniminium and 2-propylideniminium hexachloroantimonate were prepared from ethyl azide[19] and isopropyl azide, respectively, using the above method. A small amount of the *N*-methylmethyleniminium ion (14%) was found in the ethyl azide rearrangement product. Similarly, *cis*- and *trans*-*N*-methylethylideniminium hexachloroantimonates (31.5%) were identified in the 2-propylideniminium salt.

***N*-Methylmethyleniminium Ion.** This ion was prepared by heating *N*-nitrosodimethylamine (~200 mg) in fluorosulfonic acid (2 mL) for 2 days at 130 °C. The ion was identified by both its ^1H and ^{13}C NMR spectra.

***N*-Methyl-2-propylideniminium Ion.** This ion was prepared by dissolving the imine[2] (~200 mg) in SO_2 (1 mL) cooled in a dry ice–acetone bath. This solution was added with good stirring to a solution of "magic acid" (1 mL) and SO_2 (1 mL) and cooled in a dry ice bath.

***N,N*-Dimethylmethyleniminium Tetrafluoroborate.** *N,N*-Dimethylmethyleniminium iodide was previously prepared[4] from the thermoylsis of iodomethyltrimethylammonium iodide. Since it is thought that the iodide is a too reactive nucelophile, we exchanged iodide for tetrafluoroborate by dissolving the iodide salt in sulfur dioxide and adding an excess of silver tetrafluoroborate. The solution was filtered through a glass wool filter and analyzed by ^1H NMR and ^{13}C NMR.

***N,N*-Dimethyl-2-propylideniminium tetrafluoroborate** was prepared using dimethylammonium tetrafluoroborate and acetone by Leornard's method.[5]

All aromatic imines have been previously prepared from the corresponding amines and aldehydes.[20,21] The iminium salts of these imines were prepared by passing anhydrous hydrochloric acid into an etheral solution of the imine. This method was found to be generally useful. Salts such as the hydrochloride of 2-propylidene-*N*-isopropylimine were isolated as crystalline salts.

Preparation of Isopropyl Azide.[22] Isopropyl bromide (40.0 g, 0.34 mol) was refluxed overnight in 200 mL of dimethylformamide containing 50 mL of water and sodium azide (25.0 g, 0.39 mol). The product was distilled out of the reaction mixture, dried with sodium sulfate, and upon redistillation gave 21.0 g (90%) of isopropyl azide.

NMR Spectroscopic Studies. All ^1H and ^{13}C NMR spectra were obtained on Varian A-56-60, HA-100, and XL-100 instruments equipped with a variable temperature unit. All chemical shifts are reported from external Me_4Si.

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Registry No.—5·$SbCl_6^-$, 64611-38-7; 11·$SbCl_6^-$, 56995-78-9; **26**, 74-85-1; **27**, 115-07-1; **28**, 115-11-7.

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Oxyfunctionalization of Hydrocarbons. 8.[1] Electrophilic Hydroxylation of Benzene, Alkylbenzenes, and Halobenzenes with Hydrogen Peroxide in Superacids

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The hydroxylation of benzene, alkylbenzenes, and halobenzenes with hydrogen peroxide was carried out in high yields in superacidic media at low temperature. Phenols formed are protonated by the superacid and thus are deactivated against further electrophilic attack or secondary oxidation.

Introduction

Although there have been reports of the direct, one-step hydroxylation of aromatic compounds with peracids in the presence of acid catalysts, monohydroxylated products, i.e., phenols, have generally been obtained in only low yield.[2] While moderate to good yields of phenols, based on the amount of hydrogen peroxide used, were reported for the $AlCl_3$-catalyzed reaction of simple aromatics with hydrogen peroxide, a tenfold excess of the aromatics was used over hydrogen peroxide.[2k] The conversion of the aromatics thus was low, probably due to the fact that introduction of an OH group into the aromatic ring markedly increases its reactivity and thus tends to promote further reactions.[3]

It is well recognized that phenols are completely protonated in superacidic solutions.[4] This raised the possibility that protonation of phenols, once formed in these media, might cause their deactivation to further electrophilic attack. We wish to report the results of the electrophilic hydroxylation of aromatics with hydrogen peroxide in superacidic media, which allow the clean, high-yield preparation of monohydroxylated products.

Results and Discussion

Solutions of aromatics were reacted with 98% hydrogen peroxide in FSO_3H–SO_2ClF and FSO_3H–SbF_5 (1:1)–SO_2ClF solution at −78 °C, respectively. Formed protonated phenols were analyzed by ^1H NMR spectroscopy.[4] Results are summarized in Table I.

Data indicate that protonation of the starting aromatics, which are benzene, ethylbenzene, toluene, *p*-xylene, in increasing order, themselves decrease the yields of hydroxylation in magic acid (FSO_3H–SbF_5 (1:1)–SO_2ClF) solution. In the weaker acid system, FSO_3H–SO_2ClF, the protonation of aromatic hydrocarbons is reversible; thus, no such deactivation is apparent. No hydroxylation of phenol and anisole was observed with hydrogen peroxide in superacids, as was also the case with nitrobenzene and benzonitrile. The formally strongly electron-donating –OH and OCH_3 groups protonate in the reaction medium, preventing further reaction. Yields (based on the aromatics used) are high, because the phenols produced are protonated and thus deactivated toward further electrophilic attack.

A more comprehensive study of the hydroxylation of halo- and alkylbenzenes is summarized in Table II, showing isomer distributions and yields obtained. Data, in this case, were obtained by quenching the solutions and analyzing acidic products by gas–liquid chromatography. All aromatics, including polymethylbenzenes, show predominant ortho–para orientation. Hydroxylation of *m*-xylene, for example, did not yield 3,5-dimethylphenol. It should be noticed, however, that in several cases the position of the methyl group of phenols produced differs from that of the starting hydrocarbons. This is the case for 2,6-dimethylphenol obtained from *o*-xylene, 2,4-dimethylphenol from *p*-xylene, 2,3,6-trimethylphenol from 1,2,3-trimethylbenzene, and 2,4,6-trimethylphenol from 1,2,4-trimethylbenzene. The amount of these products cannot

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