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MNDO PROPERTIES OF HETEROATOM AND PHENYL SUBSTITUTED NITRENIUM IONS

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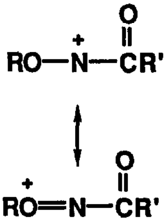
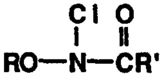
Abstract - MNDO calculations indicate that -NH_2,-PH_2,-SH,-OH and phenyl substituted nitrenium ions and N-formyl nitrenium ions have singlet ground states of comparable stability and ease of formation . *Ab initio* calculations at 6-31G** level yield similar results to MNDO for NH_2^+, and its -NH_2,-PH_2,-SH, and -OH substituted derivatives.

Recently we reported on the intramolecular cyclisations of N-alkoxy-N-acyl nitrenium ions (1) generated by silver induced heterolysis of the corresponding N-chloro-N-alkoxyamides (2).[1,2] These N-chloro species as opposed to N-chloroamides (3) are nitrenium ion precursors since the resultant divalent positive nitrogen is resonance stabilised by the neighbouring lone pair on oxygen.

Recent MNDO calculations support this stabilisation and predict an extremely high π- bond order for the N-O bond (p_{NO}=0.90). [2] In addition the N-alkoxyamidyl radical has a high energy SOMO indicating its low oxidation potential.[3] The mechanistic implications of such a high π-bond order in the transition states leading to intramolecular cyclisation onto aromatics is the subject of a future communication.[4]


$RO-\overset{+}{N}-\overset{\overset{O}{\|}}{C}R' \longleftrightarrow R\overset{+}{O}=N-\overset{\overset{O}{\|}}{C}R'$

(1)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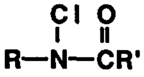
(2)


$R-\overset{\overset{Cl}{|}}{N}-\overset{\overset{O}{\|}}{C}R'$

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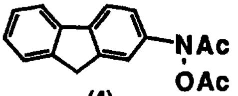

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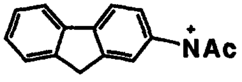

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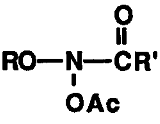
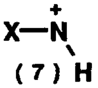

$RO-\underset{\underset{OAc}{|}}{N}-\overset{\overset{O}{\|}}{C}R'$

(6)



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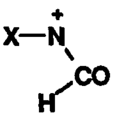


(8)

(a) X=H
(b) $X=NH_2$
(c) $X=PH_2$
(d) X=SH
(e) X=OH
(f) X=Ph
(g) X=OMe

Nitrenium ions are currently of biological interest since they are purported to be the ultimate carcinogens derived from metabolism of aromatic amines.[5,6,7] For example the metabolite N-acetoxy-2-acetylaminofluorene (4) is thought to undergo N-O heterolysis to acetate and N-acetyl-N-(2-fluorenyl)-nitrenium ion (5) which acts as an electrophile towards DNA.[7] The driving force for this is clearly the resonance stabilisation of the arylnitrenium ion [8] as well as the good leaving capacity of the acetoxy group. Although MNDO calculations of arylnitrenium ion properties have been investigated [8] it now seems appropriate that the stabilisation of nitrenium ions by heteroatoms such as O, N, S and P be compared to that imparted by an aryl substituent. Work in these laboratories has recently shown that the new class of compounds, N-acetoxy-N-alkoxyamides (6) are **mutagenic without metabolic activation and thus N-derivatives of hydroxamic esters must be handled with caution.**[9] In this contribution we therefore report on such calculations and on the MNDO properties and ease of formation of such nitrenium ions. In addition a limited comparison has been drawn between the MNDO derived quantities and those from *ab initio* theory at 6-31G** level. (See discussion section)

MNDO COMPUTATIONAL PROCEDURE

MNDO level calculations [10] were performed on a Gould NP1, using AMPAC.[11] Although originally parametrized for neutral molecules, MNDO has displayed the capability of reproducing molecular properties of closed and open-shell cations with accuracy.[12] Geometry optimizations were carried out under control of the BFGS minimization technique [13], a modification [14] made to the original DFP minimization method [15] normally employed in AMPAC· This modification is widely purported to decrease the computation time as well as the residual gradient at exit [16].

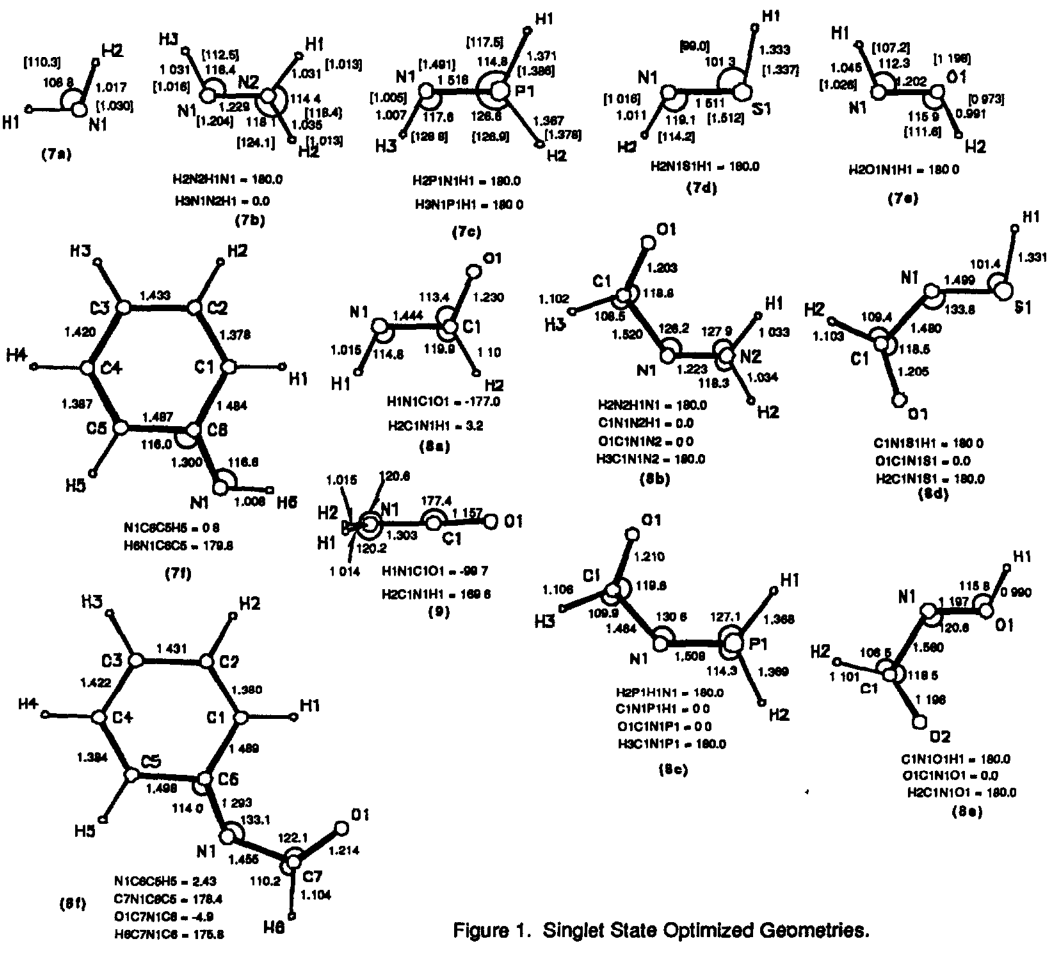


Figure 1. Singlet State Optimized Geometries.

Fully optimized geometries, unless otherwise stated, were verified as minima by calculation of the Hessian matrix and by ascertaining that all eigenvalues were positive.

Singlet (S_0) and Triplet (T_1) state properties were calculated without configuration interaction [8] although doublet states were calculated using a minimum CI set (2x2). Singlet states were calculated at Restricted Hartree Fock (RHF), while Triplet states were calculated using Unrestricted Hartree Fock (UHF) and Dewar's Half Electron (HE) formalisms. [17] Where comparisons were made between S_0 and T_1 states, calculated properties used for T_1 states were those arising from the HE method since then both S_0 and T_1 states were at RHF level of theory. [18] Similarly, structures of all triplet state species were those obtained at HE formalism.

All energies are given in kcal mol^{-1}, bond lengths in Angstrom units and angles in degrees. Stuctures were drawn using PLUTO, the molecular model drawing subroutines contained in PLOT79 and implemented on a DEC 2060.

RESULTS and DISCUSSION

The two sets of model nitrenium ions which have been studied are the mono-substituted series (7, a-g) and their formyl derivatives (8, a-g). The geometries of all the singlet nitrenium ions with the exception of (8a)(*vide infra*) were fully optimised to planar structures.Their optimised geometries in the singlet, doublet and triplet states are depicted in Figures 1, 2 and 3 respectively, while relevant molecular orbital characteristics are given in Table1.

Table 1. MNDO derived properties of nitrenium ions (7) and (8)

	Singlet So^{1}					Doublet^{2}		Triplet T_1		
System [X]	ΔH_f kcal/ mol	$\Delta\Delta H_f{}^{3}$ kcal/ mol	π bond order^{5}	LUMO coef. (abs) $N2p_z$	$X2p_z$	E_{SOMO} eV	ΔH_f kcal/ mol	$\Delta H_f{}^{UHF}$ kcal/ mol	$\Delta H_f{}^{RHF}$ kcal/ mol	$\Delta\Delta H_f$ S_0-$T_1{}^{4}$
(7a)[H]	313.47			1.00		-5.77	37.34	288.91	292.16	21.31
(7b)[N]	231.82	-81.65	0.972	0.785	0.619	-4.16	37.95	260.98	263.72	-32.36
(7c)[P]	247.54	-65.93	0.995	0.741	0.672	-5.81	34.28	254.39	260.90	-13.61
(7d)[S]	252.09	-61.38	0.990	0.755	0.655	-4.88	37.33	264.64	270.65	-18.56
(7e)[O]	224.33	-89.14	0.911	0.840	0.542	-4.72	- 3.05	242.71	246.13	-21.80
(7f)[Ph]	241.80^{6}	-71.67	0.914	0.446	0.087^{7}	-4.94	58.88	255.78	267.24	-25.31
(7g)[OMe]	243.14	-70.33	0.909	0.827	0.546					
(8a)[H]	275.67^{8}	-37.81		0.878^{8}		-6.45	6.11^{9}	246.95	255.92	19.75
(8b)[N]	200.37	-113.10	0.964	0.700	0.604	-5.02	2.02^{9}	228.42	239.60	-38.82
(8c)[P]	215.14	-98.31	0.973	0.659	0.678	-6.31	0.24^{9}	220.71	243.52	-28.38
(8d)[S]	218.32	-95.15	0.970	0.689	0.661	-5.73	2.91	225.60	233.37	-15.05
(8e)[O]	191.87	-121.60	0.903	0.788	0.533	-5.66	-35.10	201.22	203.49	-12.03
(8f)[Ph]	215.95^{6}	-97.52	0.895	0.423	0.14^{7}	-5.30	26.44^{9}	220.14	238.26	-22.31
(8g)[OMe]	183.50	-129.97	0.903	0.542						

1. Most stable planar conformer. 2. Limited CI included. 3. Difference between ΔH_f(7, 8 b-f) and ΔH_f(7a). 4. Difference between S_0 and $T_1{}^{RHF}$ states, -ve indicates S_0 ground state. 5. In $2p_z$. 6. Fully optimized ring. 7. See figure 10 for ring coefficients. 8. Acyl proton constrained to 1.10Å from Carbon; 90°twist about N-CO bond; LUMO mainly $N2p_y$. 9. Twisted about N-CO bond.

Geometries were universally entered in Z Matrix form with the N^+, X and a proton bonded to X as the reference plane. Entry in this fashion enabled the extraction of all relevant molecular orbital information. [19] Force constant calculations for the S_0 states found that (7, a-f) were minima (eigenvalues all positive), while (8, a-f) were found to be saddle points (one negative eigenvalue). Subsequent calculations with a redefined geometry in which the N^+-C=O system was in the reference plane resulted in structures which were twisted about the XN^+-CO bond and were of very slightly lower energy than those depicted in figure 1. Calculation of the Hessian showed that these twisted structures, while differing only slightly in energy from planar structures (table 1) were the true minima for the S_0 states. The ΔH_f values, together with the N^+-X bond lengths and twist around the XN^+-CO bond are given in table 2. Comparison of the ΔH_f values and the N^+-X bond length given there and the corresponding values in table 1 and figure 1 indicates that the use of information from the planar structure is justified and all discussion pertains to the planar singlet structures as tabulated in table 1 and depicted in figure 1.[19]

The *trans* conformers of **(7d)** and **(7e)** were computed to be more stable than their *cis* conformers while the conformers of **(8, b-f)** in which the X substituent is *cis* to the carbonyl oxygen are lower in energy than the *trans* conformers (table 3, figure4). Two other conformers were identified for systems **8**, X= S **(8d,14)** and O **(8e,15)** in which the X proton was placed *cis* with respect to the N^+-C bond. In each case geometry optimization yielded structures of substantially higher energy than those displayed in figure 1.

The results for **(7f)** and **(8f)** were derived without the assumption that the aromatic ring is planar although the properties so calculated differed only marginally from those of planar geometries.

The geometry optimisation of **(8a)** resulted in a migration of the acyl hydrogen to nitrogen with formation of the carbenium ion **(9)** (figure 1). Ford and Scribner reported a similar rearrangement for

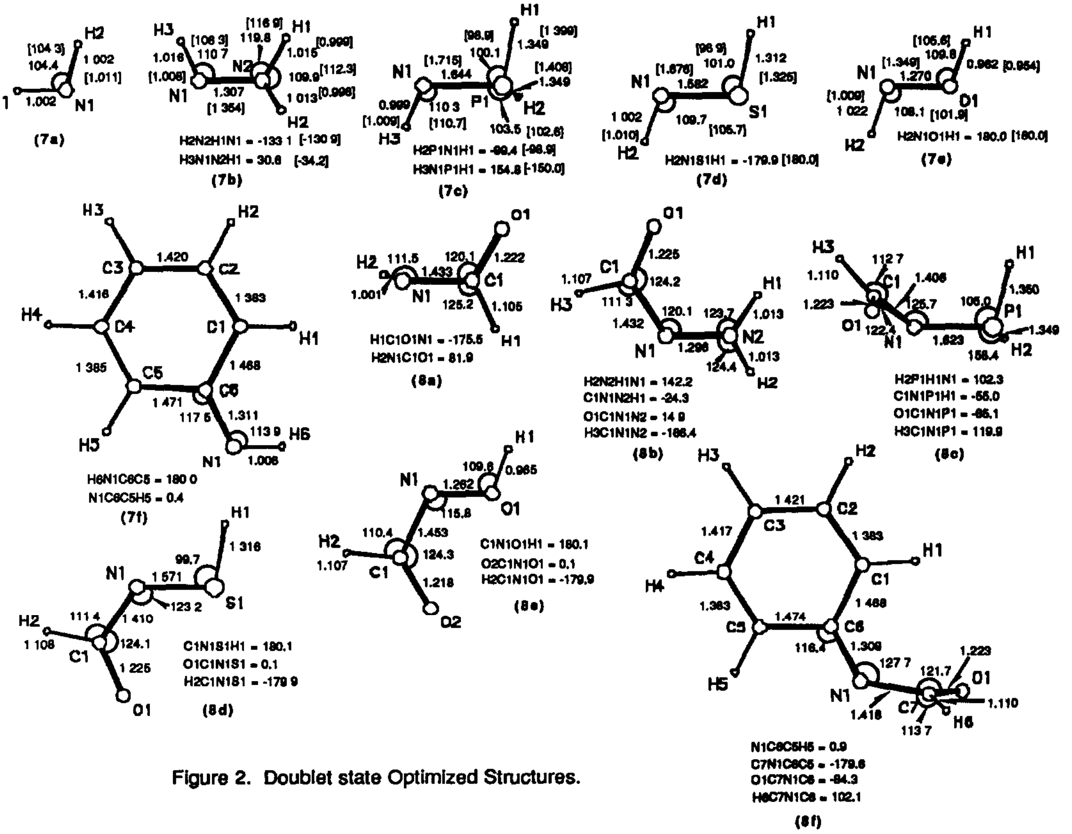


Figure 2. Doublet state Optimized Structures.

N-methyl-N-acetylnitrenium ion . ^{8} This migration is a reflection of the extreme instability of an N-formyl nitrenium ion in the absence of a heteroatom or phenyl substituent. The properties given for **(8a)** were therefore derived by restraining the acyl hydrogen to a bonding distance of 1.10Å from the acyl carbon but with optimisation of the other parameters. This resulted in a twisted structure (figure 1) in which the vacant orbital on nitrogen is $N2p_y$ and overlap is facilitated between the nitrogen lone pair and the carbonyl.

Lower energy triplet states were derived using UHF (table 1), while RHF with HE formalism gave consistently higher ΔH_f for all triplets. ^{20} NH_2^+ **(7a)** is computed to have a triplet ground state at this level as does the N-formyl nitrenium ion **(8a)** if acyl hydrogen migration is prohibited. All the other nitrenium ions are reliably predicted to have lower energy singlet states since the T_1-S_0 energy difference is outside the expected error in the MNDO method. ^{10} In both series of calculations the adjacent heteroatom imparts mesomeric stabilisation which is more effective in the singlet than in the triplet electronic states. With the exception of the N-phenyl nitrenium ions, all the T_1 state geometries show twisting about the N-X bond (figure 3) thereby reducing lone pair interaction with the unshaired electrons on nitrogen. The singlet states on the other hand, optimise to planarity thereby maximising overlap between the X lone pair and the vacant orbital on nitrogen (figure 1). In addition, PH_2 and NH_2 are pyramidal in the T_1 states of **(7b,c)** and **(8b,c)** (figure 3) whereas they are planar in the S_0 states (figure 1). The greatest singlet state stabilisation is derived from an adjacent amino substituent.

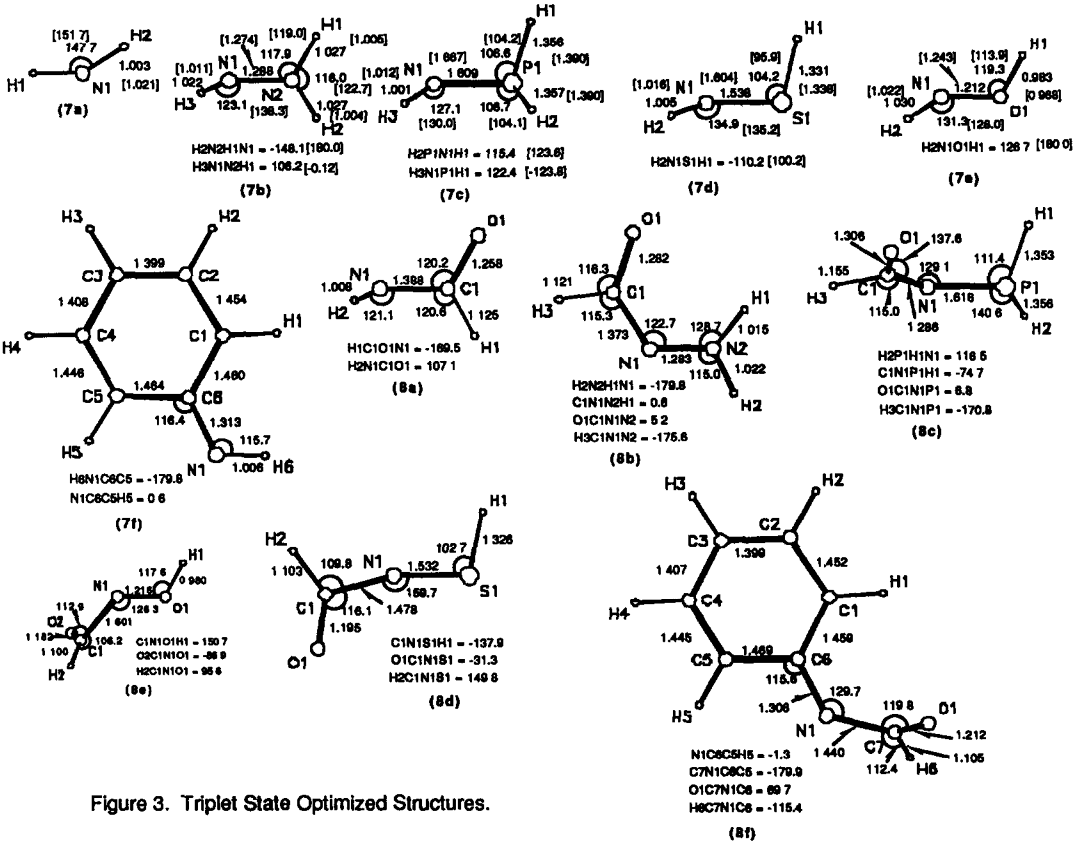


Figure 3. Triplet State Optimized Structures.

Table 2. Properties of true minima of (8, b-f)

System [X]		ΔH_f kcal mol^{-1}	N$^+$-Xbond length Å	twist about XN$^+$-CO deg.
(8b)	[N]	200.20	1.223	33.1
(8c)	[P]	215.11	1.507	11.0
(8d)	[S]	217.31	1.494	63.4
(8e)	[O]	191.12	1.197	66.3
(8f)	[Ph]	213.49	1.293	71.1

Table 3. *cis* - *trans* conformer energies.

System^1 [X]		ΔH_f *cis*^{2} kcal mol^{-1}		ΔH_f *trans* ^{2} kcal mol^{-1}		$\Delta(\Delta H_f)^3$ kcal mol^{-1}
(7)	[S]	253.77	(10)	252.09	(7d)	1.68
(7)	[O]	229.43	(11)	224.33	(7e)	5.10
(8)	[N]	200.37	(8b)	205.38	(12)	5.01
(8)	[P]	215.14	(8c)	221.23	(13)	6.09
(8)	[S]	218.32	(8d)	222.94	(14)	4.62
(8)	[O]	191.87	(8e)	194.61	(15)	2.74
(8)	[Ph]	215.95	(8f)	220.01	(16)	4.06

1. For series (7), *cis* and *trans* is defined as X-H bond relative to N$^+$-H bond while for series (8), *cis* and *trans* is defined as N$^+$-X bond relative to C=O bond. 2. See figure 1 for (7d,e),(8b-f).and figure 4 for (10)-(16). 3. Absolute conformer energy difference.

The relative ordering in the monosubstituted series is also very nearly mirrored in the disubstituted series indicating that the acyl function has little effect upon the ΔH_f other than to decrease it uniformly by about 30 kcal mole^{-1}.

The π-bond orders between the electron deficient nitrogen and the heteroatom are all in the range of those for nearly pure double bonds with that between N$^+$ and an N, P or S substituent being the greatest in accord with their lower electronegativities. The X-N$^+$ bond lengths (figure 1) accord well with experimental bond lengths for pure π bonds involving these atoms in neutral molecules. [21] Clearly the stabilisation imparted by all the substituents is due to mesomeric interaction in which electron density is donated to the deficient nitrogen through the π system resulting in the aforementioned planarity of the optimised structures. at nitrogen. On the basis of π bond orders (table 1) however an alkoxy (hydroxy) and phenyl substituent have marginally less but none-the-less a similar capacity to stabilise N$^+$ by mesomerism.

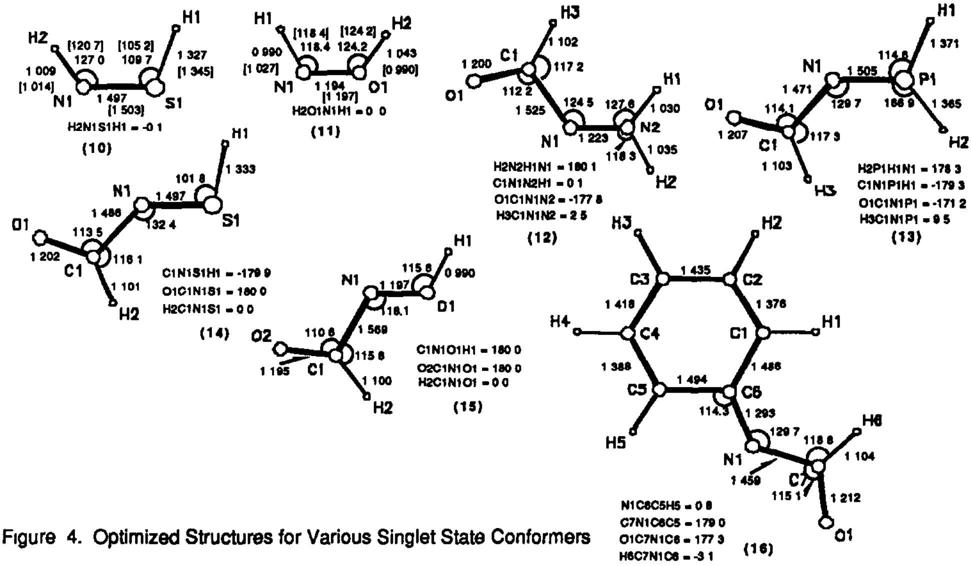


Figure 4. Optimized Structures for Various Singlet State Conformers

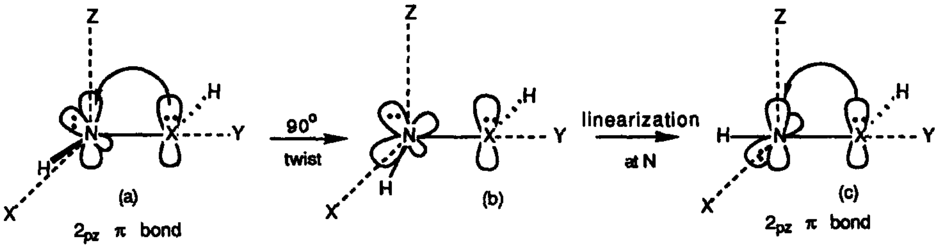


Figure 5. Linearity at Nitrogen at a HN$^+$XH Twist Angle of 90°.

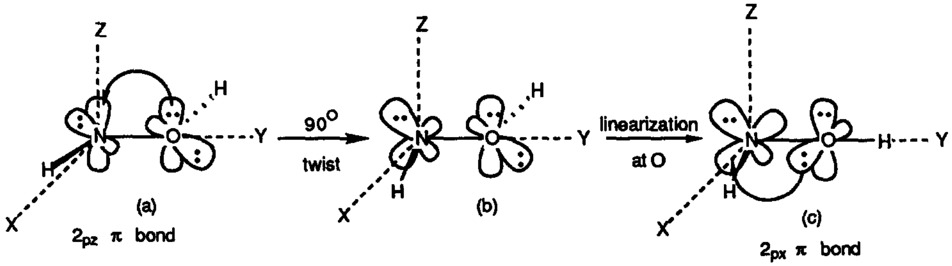


Figure 6. Linearity at Oxygen at a HN$^+$OH Twist Angle of 90°.

A measure of the extent of such overlap is normally the barrier to rotation about the partial π-bond. However computation of such barriers afforded unexpected results in all cases. Rotation about the N-X bond did not generated smooth profiles from which rotational barriers could be measured with accuracy . In the cases of **(7b-d, 7f)** and **(8b-d, 8f)** the angle about N$^+$ approached 180° at twist angles near 90 degrees, resulting in degeneracy of the nitrogen 2p$_z$ and 2p$_y$ orbitals thereby facilitating π overlap between the vacant 2p$_z$ orbital on nitrogen and a lone pair on the heteroatom (figure 5). In the case of oxygen substituted nitrenium ions **(7e** and **8e)**, linearity occurred at oxygen with concomitant degeneracy of the oxygen lone pairs. Once again π overlap was re-established but between 2p$_x$ orbitals (figure 6).

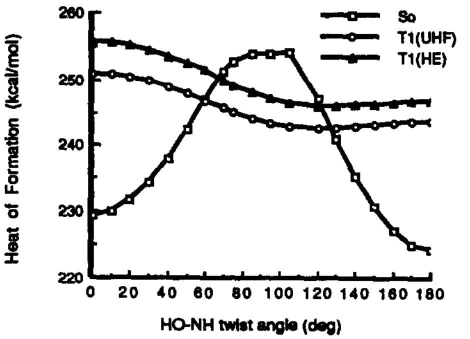
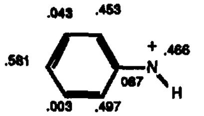
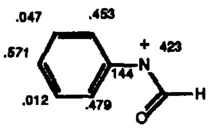


Figure 7. ΔH$_f$ of **(7e)** at various HO-N$^+$H twist angles for S$_0$ and T$_1$ states.



(7f)



(8f)

Figure 8. LUMO coefficients for arylnitrenium ions **(7f,8f)**.

In either case with the exception of **(7e)** and **(8e)** the true profiles could not be completed due to loss of definition of the dihedral angles. [22] Such linearisation at either N^+ or oxygen at high twist angles is however energy demanding and it was found from single point calculations at twist angles of 90° that in some of the cases where the ΔH_f for the singlet state could be computed,[22] the triplet state was lower in energy (table 4). For instance , crossover from singlet to triplet ground state is predicted to occur between twist angles of 120 and 70 degrees for **(7e)** (figure 7) . Further it is seen that the effect of calculation at UHF level is to uniformly reduce the energy of the T_1 state. A reflection of the rotational barriers might therefore be the difference in energy between the planar singlet nitrenium ion (table 1) and the energy of the more stable state at a twist angle of 90°. Such barriers are appreciable for the nitrenium ions **(7b-f)**, and **(8e)** (table 4).

Table 4. ΔH_f of S_0 and T_1 states at twist angle of 90 degrees

System	[X]	S_0			T_1			
		ΔH_f kcal mol^{-1}	pi bond order 2_{pz}	angle at N^+ deg.	HF ΔH_f kcal mol^{-1}	UHF ΔH_f kcal mol^{-1}	$\Delta(\Delta H_f)^1$ kcal mol^{-1}	Rot. bar. kcal mol^{-1}
(7b)	[N]	266.74	0.979	179.96	264.93	261.62	1.81	33.11
(7c)	[P]	266.48	0.985	175.10	263.17	255.87	3.31	15.63
(7d)	[S]	264.83	0.996	180.00	270.53	264.96	-5.70	12.74
(7e)	[O]	254.05	0.919^2	176.51^3	247.69	243.85	6.36	23.36
(7f)	[Ph]	266.39	0.933	179.87	264.06	254.17	2.33	22.26
(8b)	[N]	217.04	$-^4$	179.30	231.04	223.28	-	-
(8c)	[P]	221.54	0 951	172.69	228.15	218.79	-6.61	6.4
(8d)	[S]	219.89	$-^4$	179.23	233.55	226.29	-	-
(8e)	[O]	223.83	0.903^2	169.68^3	206.48	198.91	17.35	14.61
(8f)	[Ph]	222.98	$-^4$	179.10	233.98	275.65	-	-

1. Indicates stability of S_0 state over T_1 state at 90° twist angle, +ve value indicates lower T_1 state. 2. In $2p_x$ orbital. 3. Linear at O. 4. Calculation abandoned due to linearity; data is from last cycle successfully completed before abandonment.

Minimum energy structures and data for the doublet states indicated that the configuration of all radicals was π rather than σ. [3] The spin density was mainly on nitrogen ($N2p_z$) and one electron oxidation of the radical would therefore lead to nitrenium ion formation.

The energies of the singly occupied molecular orbitals (SOMO's) are, through Koopman's Theorem[23], a reflection of the oxidation potential of the corresponding free radicals. Heterolysis of an N-Cl bond can be visualised as a two-step process involving first homolysis to radicals followed by ionisation. Although the former process, being highly endothermic would be facilitated by stabilisation of the resultant aminyl or amidyl radical by the substituent heteroatom, radical stabilisation by an adjacent lone pair is known to be weaker than that for a cation. Whereas the lone pair of electrons next to a cationic centre occupy the resultant low energy π bonding orbital, in the case of radicals this stabilisation is partially offset by semi-occupation of the π^* orbital. [24] (this interaction is responsible for planarity in doublet geometries **(7,8d-f)** however N-X bonds are longer throughout the series relative to the singlet states (figure 2)). Thus radical ionisation potentials can be regarded as a measure of the ease of nitrenium ion formation. Analysis of the SOMO energies of radicals from **(8a)** and **(8e)** (table 1) indicates that N-alkoxy-N-acyl nitrenium ions should form more easily than N-acyl nitrenium ions and we have previously found that whereas N-chloro-N-alkoxyamides react with silver ions to produce nitrenium ions, N-chloro-N-alkylamides are unreactive under the same conditions [2]

The SOMO'S in the N-acyl series are uniformly lower in energy (table1). However N-hydroxyformamidyl radical of **(8e)** and the N-phenylformamidyl radical of **(8f)** would ionise with similar facility and accords with the fact that precursors to these nitrenium ions such as **(4)** and **(6)** may have common biological pathways to mutagenesis.[5,6,7,9] Clearly, it is illuminating that other heteroatom substituted amidyl radicals have even higher energy SOMO's than either **(8e)** or **(8f)**. The higher SOMO energies in the aminyl series **(7, b-f)** likewise indicate that facile nitrenium ion formation might be possible and while this may be of biological importance, such nitrenium ions may also react intramolecularly (e.g. by 1,2 alkyl rearrangement).[25,26] However acyl substitution in series **(8, a-f)** precludes such processes.

Interestingly the SOMO energy of N-hydroxy formamidyl radical of **(8e)** is similar to that for a simple aminyl of **(7a)** . Amines bearing a leaving group (e.g N-chloro, N-sulphonyloxy) at nitrogen are also known to be nitrenium ion sources,[26,27] however the chemistry of these species is complicated by purported triplet state and radical reactivity. [26] This may be as a consequence of the triplet ground state or a preference for homolysis to free radicals under solvolytic conditions. ΔH_{react} for heterolysis of N-X bonds is predicted to be much more endothermic in the absence of stabilising substituents (*vide infra).*

The heats of formation for the N-chloro precursors **(17,a-f)** and **(18, a-f)** are given in table 5, and their optimized structures appear in figure 9. N-Cl bond breaking in **(18e)** by progressive elongation resulted in homolysis to a chlorine atom and an amidyl radical. In order to evaluate the ease of heterolysis, a hydrogen cation was placed at the MNDO optimised H-Cl bond distance for hydrogen chloride (1.3479Å) from chlorine in the optimized geometry of the N-chloro-precursors **(17, a-f)** and **(18, a-f)**.

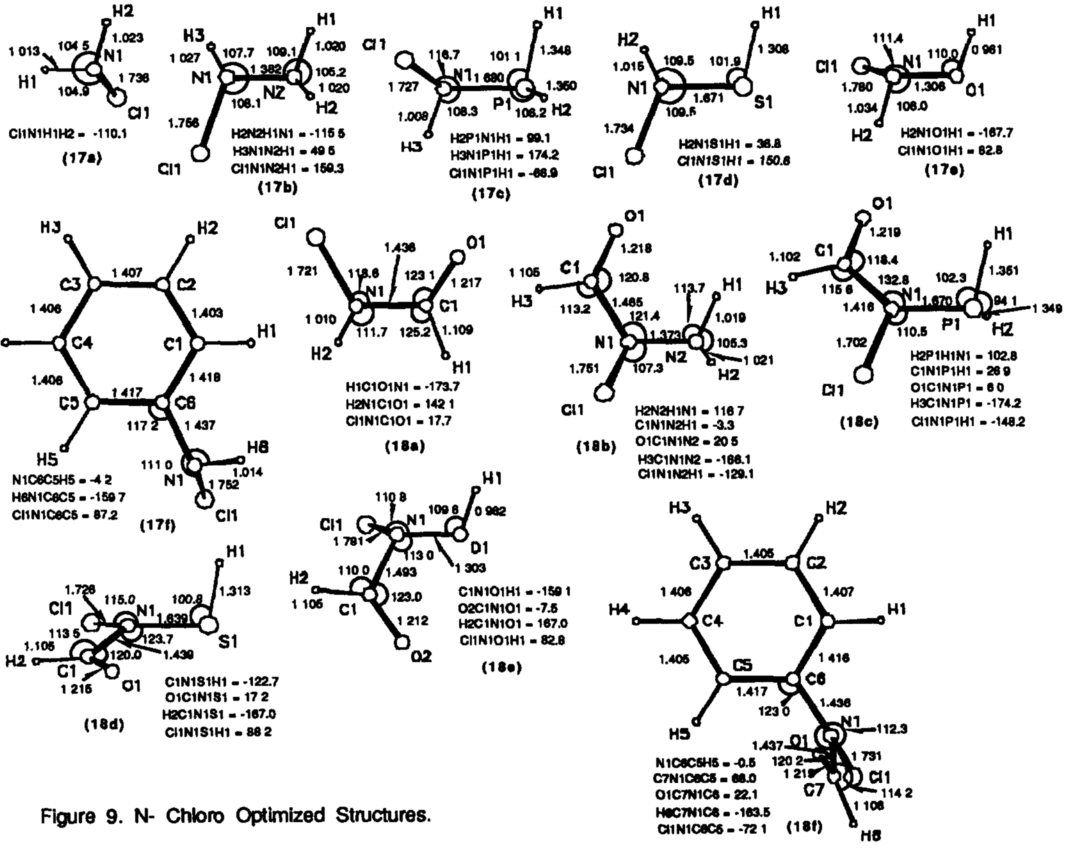


Figure 9. N- Chloro Optimized Structures.

Full geometry optimisation, resulted in the formation of nitrenium ions (**7, b-f** and **8, b-f**) and a remote hydrogen chloride molecule in a highly endothermic reaction. An illustrative example is that for N-chloro-N-hydroxyformamide (**18e**), which gave the nitrenium ion (**8e**), with a N+-O bond length of 1.197Å (cf. figure 1) and a hydrogen chloride molecule situated 3.675Å from the N+ center (table 5). Similar results were found for both series of N-chloro precursors (**17** and **18,b-f**). In the case of (**17a**) and (**18a**) geometry optimization resulted instead in a high energy adduct with a slight lengthening of the N-Cl bond (1.933 and 1.780Å respectively). This is again indicative that N-Cl heterolysis is facilitated by an adjacent heteroatom.

The Heat of reaction (ΔH_{react}) for the heterolysis of the N-Cl bond in the above fashion can be calculated through

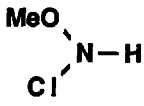
$$\Delta H_{react} = \Delta H_f(N^+\text{-}X) + \Delta H_f(HCl) - \Delta H_f(Cl\text{-}N^+\text{-}X) - \Delta H_f(H^+)$$

A hydrogen ion ($\Delta H_f = 0$) and hydrogen chloride molecule are common to all these reactions and so can be ignored in a comparison of ΔH_{react}. Data for N-Cl heterolysis (table5) shows that in all cases the reaction would be facilitated by heteroatom substitution relative to the parent N-chloroamine (**17a**) and N-chloroamide (**18a**) . The formation of the N-phenylnitrenium ions (**7f**) and (**8f**) by heterolysis were likewise much more favourable.

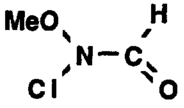
Table 5. Properties of N-chloro precursors of nitrenium ions (7) and (8) and data for heterolytic cleavage reactions.

N-chloro species	[X]	ΔH_f				N+HCl system[1]		
		X-N-Cl kcal mol^{-1}	N+-X[2] kcal mol^{-1}	ΔH_{react}[3] kcal mol^{-1}	Δ[4] kcal mol^{-1}	ΔH_f[5] kcal mol^{-1}	N+-HCl[6] Å	N+-X[7] Å
(**17a**)	[H]	8.27	313.47	305.20				
(**17b**)	[N]	26.64	231.82	205.17	100.02	212.70	4.134	1.229
(**17c**)	[P]	5.35	247.54	242.19	63.01	228.77	3.958	1.516
(**17d**)	[S]	26.25	252.09	225.84	79.36	234.27	3.864	1.497
(**17e**)	[O]	-12.66	224.33	236.99	68.21	209.57	3.798	1.194
(**17f**)	[Ph]	38.24	241.80	203.56	101.64	223.89	4.316	1.300
(**17g**)	[OMe]	14.75	243.14	228.39	76.81			
(**18a**)	[H]	-19.20	275.67[8]	294.87	10.33			
(**18b**)	[N]	1.12	200.22	199.10	106.10	181.51	3.974	1.224
(**18c**)	[P]	-26.65	215.14	241.79	63.41	196.19	4.165	1.508
(**18d**)	[S]	-6.97	218.32	225.29	79.91	198.39	4.034	1.497
(**18e**)	[O]	-38.12	191.87	229.99	75.20	172.59	3.675	1.197
(**18f**)	[Ph]	12.87	215.95	203.18	102.02	195.35	4.011	1.293
(**18g**)	[OMe]	-23.88	183.50	207.38	97.82			

1. Data from H+ + X-N-Cl system (see text). 2. See table 1. 3. ΔH_{react}-ΔH_f(HCl). 4. Difference in ΔH_{react}(17, 18 b-f) and ΔH_{react}(**17a**). 5. ΔH_f =(approx) $\Delta H_f(N^+\text{-}X)$ + ΔH_f(HCl). 6. Distance HCl optimized away from N+ centre. 7. Bond length of N+-X in residual nitrenium ion (*cf.* figure 1). 8. Acyl proton constrained to 1.10Å.



(17g)



(18g)

Finally, analysis of the LUMO coefficients (table 1) indicates that nucleophilic attack on the nitrenium ions would occur preferentially at the nitrenium ion centre in all but the phenyl derivatives which predictably have substantial charge deficiency on the aromatic ring (figure 8) . In these, nucleophilic attack would also be expected to occur at the *ortho* and *para* positions. These reactivity patterns are endorsed by products from solvolysis of N-acetoxy- and N-methanesulphonyloxyacetanilides which yield hydroxamic acids by N attack or the ring substituted products. [6] Ring substitution has also been widely observed in the decomposition of aryl azides.[26,28] In addition studies in these laboratories have shown that solvolysis of N-chloro-N-alkoxyamides in aqueous alcohols yields N,N-dialkoxy amides in good yields.[29] Intramolecular aromatic cyclisation products from silver induced heterolyses also indicate exclusive reaction upon the N^+.[1,2,30]

In this and earlier studies[2] we have assumed that hydroxy formyl nitrenium ion **(8e)** is a suitable model for more general alkoxy formyl nitrenium ions. To validate this assumption and to ascertain the extent to which molecular properties are varied by alkyl substitution at oxygen, calculations were undertaken on a methoxy monosubstituted and a methoxy formyl disubstituted nitrenium ion **(7g and 8g)** as well as their N-chloro precursors **(17g and 18g)**. Methyl protons in all cases were restricted to tetrahedral symmetry. Properties of singlet states of **(7g and 8g)** appear in table 1, while results for **(17g and 18g)** appear in table 5. Comparison with data for **(7e)**,**(8e)**,**(17e)** and **(18e)** indicates that the use of a hydroxy group in place of a simple alkoxy group is justified.

Ab Initio CALCULATIONS

The validity of the MNDO technique in the calculation of molecular properties of charged nitrogen species was supported by *ab initio* calculations on the nitrenium ions **(7, a-e)** and their doublets. Initial studies were made at 6-31G** level using standard exponents contained in CADPAC.[31] Closed shell ions were calculated at spin-restricted Hartree-Fock (RHF), while open shell species were calculated at Unrestricted Hartree-Fock (UHF) levels of theory. SOMO energy levels were obtained at both open shell (OSCF) and UHF levels of theory. Trial cartesian co-ordinates were obtained from the MNDO optimized geometries seen in figure 1.

The HF/6-31G** model gave the optimised geometrical parameters seen in figures 1, 2 and 3 (in brackets) and are in good agreement with the MNDO optimised structures. Table 6 gives the *ab initio* and MNDO vibrational frequencies and zero point energies[32] based upon the optimised geometries. The vibrational frequencies are in reasonable agreement while the *ab initio* Zero Point Energies are uniformly lower in energy by 1 kcal mol^{-1}. Calculation of the second derivatives also verified that the stationary points were minima on the potential energy surface.

Table 6. Calculated vibrational frequencies for Nitrenium ions **(7 a-e)**[1]

System	frequencies (cm^{-1}) MNDO values in ()	ZPE[2]	ZPE(MNDO)[3]
(7a)(S_0)	1512 (1587), 3462 (3387), 3566 (3430)	10.87	11.99
(7a)(T_1)	820, 3342, 3701	10.00	
(7b)[4]	1177 (1090), 1296 (1172), 1373 (1182), 1605 (1520), 1780 (1688), 1974 (2043), 3603 (3301), 3648 (3317), 3744 (3357)	25.71	26.76
(7c)	684 (517), 687 (682), 892 (991), 1001 (998), 1222 (1162), 1374 (1287), 2700 (2455), 2781 (2466), 3804 (3500)	19.28	20.21
(7d)(*cis*)[4]	1016, 1132, 1251, 1269, 2777, 3676	14.16	
(7d)(*trans*)	1080 (954), 1184 (1025), 1210 (1186),1316 (1323), 2838 (2754), 3655 (3452)	14.36	15.31
(7e)(*cis*)[4]	1270, 1491, 1666, 1826, 3512, 3767	17.22	
(7e)(*trans*)	1344 (1173), 1443 (1315), 1732 (1649),1833 (2074), 3542 (3246), 3782 (3510)	17.40	18.66

[1] vibrational frequencies are calculated from the HF/6-31G** equilibrium geometries.[2] vibrational frequencies have been scaled by 0.89 to calculate ZPE (in kcal mol^{-1}). Given freqencies have not been scaled. [3] ZPE calculated at MNDO level by invoking FORCE and PRECISE keywords. [4] MNDO frequencies were not determined.

The *ab initio* derived total energies for the singlet, triplet nitrenium ions **(7, a-e)**.and their doublet states are given in table 7. Comparisons may be made between the S_0 and T_1 states of all species, and between the conformers of **(7d)** and **(7e)**.

Singlet-Triplet energy differences (table 7) were calculated utilizing *isogyric* equations [34] and the exact dissociation energy of hydrogen (0.174511*au.* or 109.48 kcal mol^{-1}). [35] The value for NH_2^+ of 0.042318*au.* or 26.55 kcal mol^{-1} correlates well with the MNDO predicted separation of 24.56 kcal mol^{-1} (at UHF level), and a value of 28.64 kcal mol^{-1} which was derived from a much enhanced basis set, together with electron correlation to fourth order, and which can be considered to be synonomous with the experimental S_0-T_1 value. [36,37]

Table 7. *Ab-initio* derived energies for series **(7, a-e)**.

System	energy[1]				
	S_0	Doublet		T_1	S_0-T_1[2]
	RHF *au.*	UHF *au.*	SOMO[3] *eV*	UHF *au.*	kcal mol^{-1}
(7a)	-55.13508	-55.56482	-4.41	-55.21704	26.55
(7b)	-110.31744	-110.58119	-2.51	-110.26255	-59.30
(7c)	-396.57211	-396.86645	-4.37	-396.56306	-32.07
(7d)(*trans*)	-452.75065	-453.07177	-4.04	-452.74544	-25.39
(7d)(*cis*)	-452.74627	[4]			
(7e)(*trans*)	-130.05002	-130.38931	-3.44	-130.04032	-30.95
(7e)(*cis*)	-130.03616	[4]			

[1] 1*au.* = 627.53 kcal mol^{-1}. [2] calculated through the use of *isogyric* equations, and using values of total energy for H_2 and H atom as in reference 35. [3] SOMO energy values are from open shell RHF calculation to provide direct comparison with MNDO values, and converted to *eV* by the factor 1*eV* = 0.036749 *au.*; respective UHF SOMO energy values are -13.49, -9.74, -9.78, -9.78 and -11.53 *eV*. [4] *cis* structures for **(7,d-e)** for Doublet and Triplet states were found to be higher in energy than the *trans* structures and thus are not considered here.

Ab initio Singlet-Triplet separations for the other nitrenium ions in the **(7)** series are in qualitative agreement with MNDO in that only the parent nitrenium ion **(7a)** is predicted to exist in a Triplet ground state. *Ab initio* predicts the S_0- T_1 separation of **(7, b-e)** to be greater than the separation predicted by MNDO in all cases.

Conformer energy differences of **(7d and 7e)** are predicted to be 2.75 kcal mol^{-1} and 8.69 kcal mol^{-1} respectively. The MNDO conformer energy difference were similar at 1.68 kcal mol^{-1} and 5.10 kcal mol^{-1} respectively.

Comparison of the SOMO energy levels for the series shows that the relative ordering for the radicals is well reproduced when compared to the MNDO values (table 1)

Heats of formation at the HF/6-31G** level are not expected to be absolute. However, comparison between Heats of Formation for the above series should be possible at this level. Such calculations involve the use of *isogyric* equations to calculate the atomization energy, ΣD_0 - the energy required to completely dissociate the molecule into it's constituent atoms [36,37] and HF/6-31G** total energies for H,H_2,N,N^+,O,P,S.[35,38] The theoretical Heats of Formation (using the 6-31G** geometry) at zero K and at 298K are given in table 8. Corrections to 298K from 0K were made according to the method of Pople *et al*[36] and assumes that the Heat capacity corrections for the ions are linear with temperature.

Table 8. HF/6-31G** calculated atomisation energies (ΣD_0) and derived Heats of Formation.

System	ΣD_0	ΔH_f^0 [1]	ΔH_f^{298}	$\Delta(\Delta H_f)$[2]
(7a)(S_0)	259.60	291.31	295.18	-
(7a)(T_1)	287.02	263.89	267.92	27.26
(7b)	544.64	170.44	174.46	-120.72
(7c)	485.05	192.50	197.22	-97.96
(7d)(*cis*)	393.37	223.65	226.16	-69.02
(7d)(*trans*)	395.92	221.10	223.64	-71.54
(7e)(*cis*)	406.63	203.27	205.60	-89.58
(7e)(*trans*)	415.14	194.76	197.08	-98.10

1. Experimental atomic Heats of Formation are taken from reference 39. 2. $\Delta H_f - \Delta H_f(7a)(S_0)$

The theoretical Heat of Formation for singlet NH_2^+ as well as that determined by MNDO (313.47 kcal mol^{-1}) are close to the experimentally determined value of 304kcal mol^{-1}.[8] In addition the S_0-T_1 energy separation for NH_2^+ at MNDO UHF level (24.56 kcal mol^{-1}) is in reasonable agreement with the HF/6-31G** value of 27.26kcal mol^{-1}. and the experimentally determined value of 30.2kcal mol^{-1}.[40] While both MNDO and HF/6-31G** both predict substantial stabilisation of a nitrenium ion centre adjacent to O,S,P and N, relative to $NH_2^+$the *ab initio* method reverses the stabilities of N and O substituted nitrenium ions.

CONCLUSIONS

Nitrenium ions derive stabilisation from adjacent heteroatom lone pairs which can overlap with the vacant orbital on nitrogen generating high N=X π character. As a consequence such nitrenium ions have lower energy singlet ground states unlike parent nitrenium ions, NH_2^+ and its N-formyl derivative which have triplet ground states. Loss of such overlap through rotation results, in some of the cases studied, in a lower energy triplet state at twist angles approaching 90°. Heteroatom substitution is calculated to reduce the endothermicity of N-Cl heterolysis by between 70 and 100 kcal mol^{-1} relative to the parent N-chloroamine and N-chloroformamide.

The stabilisation by an oxo substituent is computed to approximate that imparted by a phenyl group. Both substituents favour heterolytic cleavage of the N-chloro nitrenium ion precursors.

The MNDO results for series (7 a-e) are in reasonable agreement with those derived for this series from *ab initio* calculations at the 6-31G** level.

The mutagenic behaviour of aromatic amides activated by leaving groups at nitrogen can be accounted for by either nucleophilic attack by nucleotides at nitrogen or by electrophilic attack of nitrenium ion intermediates on the same.[5,6,7] Our computations indicate that N-alkoxyamides with leaving groups at nitrogen ought to behave similarly. This accords well with our finding that N-acetoxy-N-alkoxybenzamides are mutagenic.[9]

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