TRANSITION STATE GEOMETRY IN THE THERMAL GENERATION OF ARYL- AND ACYLNITRENIUM IONS[†]

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Abstract - Molecular mechanics and semiempirical AM1 calculations indicate that N-acyl- and N-alkylarylnitrenium ions generated by heterolysis of appropriate precursors are π-cations formed by the leaving group following a trajectory which moves it progressively out of the plane of the aromatic nucleus so that the transition state has appreciable π-cation character.

There seems to be general agreement that arylnitrenium ions, species thought to be involved in the action of carcinogenic aromatic amines and amides,[1] are π-cations in which the positive charge is appreciably delocalized over the aryl ring ortho- and para-carbons.[2] What is not so obvious is the geometry of the transition state leading to the arylnitrenium ions formed by thermal heterolysis of appropriate N-X bonds.

Haberfield and DeRosa[3] reported that while N-acetoxy-N-acetylaniline (1) solvolyzed readily, N-acetoxy-N-tert-butylaniline (2) was stable under the same conditions. They proposed that the lowest energy conformation of 1 was as shown below (with the lone pair of electrons in the plane of the benzene ring, conjugated with the carbonyl group but not the benzene ring) and that this permitted easy ionization to give π-nitrenium ion 3, in which the charge would be delocalized into the aromatic ring. Since such a delocalization should be partially present in the transition state this would facilitate the solvolysis. On the other hand, the N-tert-butyl derivative (2) was proposed to have the lowest energy conformation as


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shown, in which the lone pair would conjugate with the ring. According to this hypothesis, ionization from this conformation would lead to a high energy σ-cation (4) in which the orbital developing the charge would not be conjugated with the aromatic ring.[3,4]
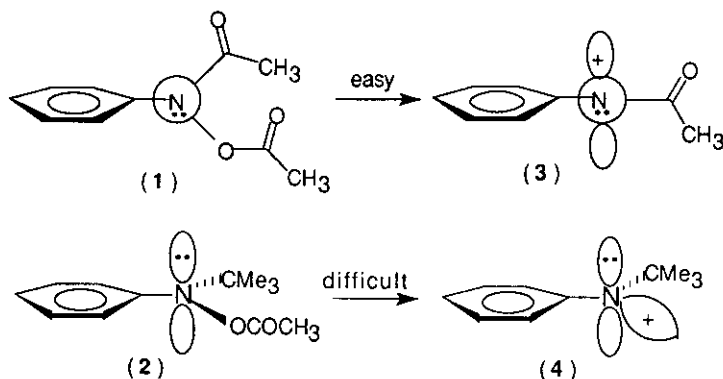
Data in the literature speak against such an interpretation. In N-tosyloxyoxindole (5) the benzene ring, N-atom, and carbonyl group have to be almost coplanar (cf. proposed geometry of 1), but solvolysis at room temperature in alcohols gives the 5-alkyloxyoxindole, presumably via the π-delocalized nitrenium ion[5] (see also the cyclization of the N-acylnitrenium leading to acetamidodihydrophenanthrenes[6]). Similar solvolysis of N-tert-butyl-N-chloroaniline gave o- and p-chloro-N-tert-butylaniline, reportedly via a delocalized π-nitrenium ion[7] (cf. 4). N-tert-Butylphenylhydroxylamines in TFSA/TFA C-arylate aromatic substrates via the delocalized cation,[8] and N-(2,6-dimethylphenyl)hydroxylamine undergoes the Bamberger rearrangement with mild acid via a free arylnitrenium ion.[9] Finally, one might argue that if the tert-butyl group in 2 were almost in the plane of the ring, then the much less bulky acetyl group in 1 should also be, with the added advantage that the nitrogen n-electrons would then be delocalized over both the carbonyl and the phenyl group.

We have carried out MMX force field calculations[10a] to try and predict what the lowest energy conformations of 1 and 2 would be. MMX could not be used to compute the geometry of O-acetyl-N-tert-butylhydroxylamine,[11] and ALCHEMY II[10b] was used instead. The global minimum energy structures so derived are shown in Figure 1. It is clear from Figure 1a that the nitrogen atom in 1' remains sp^2 as expected and the computed dihedral angle between N-C(=O) and phenyl is 14°. This is in
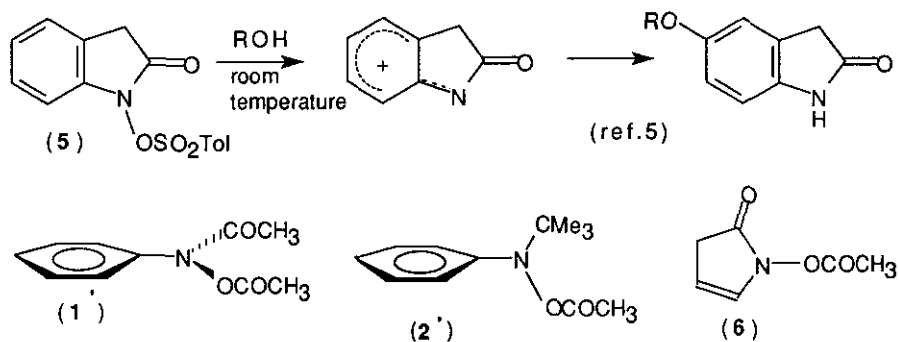
excellent agreement with the torsion angle of 15.3° observed for crystalline N-acetylphenylhydroxylamine,[12] and clearly contradicts proposed[3] geometry 1. For the N-tert-butyl compound (Figure 1b) the torsional angle between N-O(-C) and phenyl is 37°, while that between N-C(Me$_3$) and phenyl is 84.5° i.e. the O-N-C(Me$_3$) angle is 121° and the tert-butyl group is almost orthogonal to the benzene ring, as might have been expected on the basis of steric hindrance between the tert-butyl and the ortho-hydrogens. If an sp^2 nitrogen is introduced for 2 in the starting conformation and the geometry is minimized in ALCHEMY the final geometry retains the sp^2 nitrogen but the N-C(Me$_3$)/Ph dihedral angle is 21.8°. The actual geometry is probably somewhere in between the two.
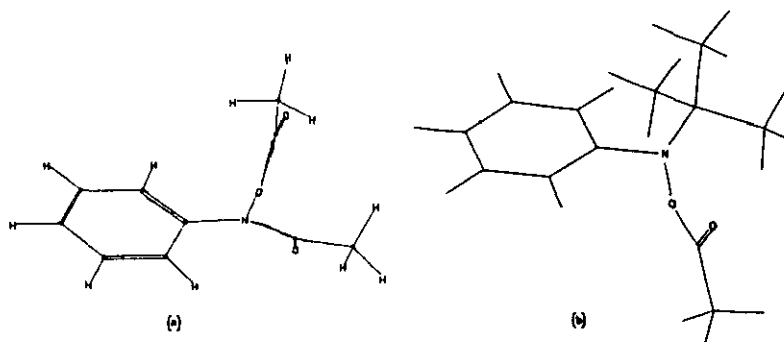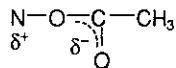

Figure 1:   (a) MMX-computed geometry of 1
             (b) ALCHEMY II-computed geometry of 2

MNDO calculations on N-formyl-N-phenylnitrenium confirm that the positive charge is delocalized over the aromatic nucleus.[13] One can visualize two possibilities for producing the p-cation from 5 (and from almost coplanar 1), say: (i) 'least motion' heterolytic cleavage of the N-O bond leading to a σ-cation, followed by a fast π- to σ-electron demotion, or (ii) heterolytic N-O cleavage concommitent with an out of

the plane trajectory of the leaving group, so that a rehybridization of the N is occurring en route to the transition state and a π-cation is formed directly.

To test these two possibilities we have carried out AM1[14] SCF-MO calculations[15] on a model compound, namely N-acetoxy-2-pyrrolidin-5-one (6) and an O-protonated derivative (7). Figure 2(a) shows the computed geometry of the parent (6). The $C_{(1)}$-$C_{(2)}$-$N_{(3)}$-$O_{(11)}$ dihedral angle is 138.5°.[16] The angle becomes more acute in the protonated species (Figure 2(b)): 133.3°. As the N-O bond stretches the angle is 101° in the transition state (Figure 2(c)), and the breaking bond is almost orthogonal to the plane of the ring. Clearly, hypothesis (ii) above obtains, and the heterolysis follows a trajectory in which the leaving group moves out of the plane, leading directly to the conjugated π-nitrenium ion. This must also be happening with (1'), but with (2'), going to a similar T. S. leading to the formation of a π-cation would result in severe interactions between the tert-butyl group and the ortho-hydrogens, hence the difficulty encountered[3] in its formation. That the N-O bond in 6 is out of the plane of the ring suggests that it has some dipolar character $\begin{matrix} N-O\overset{..}{=}C-CH_3 \\ \delta^+ \quad \delta^- \overset{||}{\underset{O}{}} \end{matrix}$ and this is confirmed by the fact that in the O-protonate species the angle becomes more acute (since the nitrenium ion itself is a π-cation).
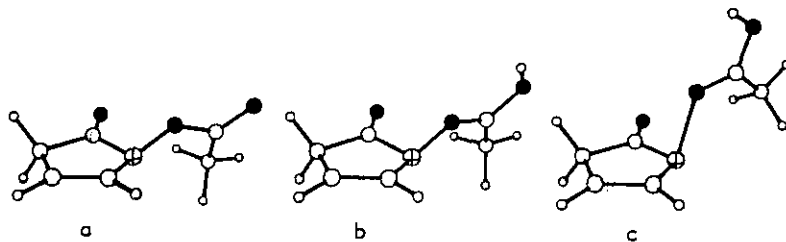

a   b   c

Figure 2: Plots of AM1 calculations for 6 (a), 7(b) and T. S. (c)

REFERENCES AND NOTES

1.   E. Defrancq, N. Pelloux, A. Leterme, M. -F. Lhomme, and J. Lhomme. <u>J. Org. Chem.</u>, **1991**, <u>56</u>, 4817, and refs. cited therein.

2.   Y. Li, R. A. Abramovitch, and K. N. Houk, <u>J. Org. Chem.</u>, **1989**, <u>54</u>, 2911. R. A. Abramovitch, M. Cooper, S. Iyer, R. Jeyeraman, and J. A. R. Rodrigues, <u>J. Org. Chem.</u>, 1982, <u>47</u>, 4819. J. J. Campbell, S. A. Glover, and C. A. Rowbottom, <u>Tetrahedron Lett.</u>, **1990**, <u>31</u>, 5377.

3.   P. Haberfield and M. DeRosa, <u>J. Chem. Soc., Chem. Commun.</u>, **1985**, 1716.

4.   Alternatively,[3] a π-nitrenium ion could be generated from a conformation 90° away along the aromatic-N-axis, but this would require the energy of uncoupling of the N n-electrons from ring conjugation.

5.   P. G. Gassman and G. A. Campbell, <u>J. Chem. Soc., Chem. Commun.</u>, **1971**, 1437. See also reactions of the corresponding 6-membered ring: Y. Hashimoto, T. Ohta, K. Shudo, and T. Okamoto, <u>Tetrahedron Lett.</u>, **1979**, 1611.

6.   R. A. Abramovitch, K. Evertz, G. Huttner, H. H. Gibson, Jr., and H. G. Weems, <u>J. Chem. Soc., Chem. Commun.</u>, **1988**, 325.

7.   P. G. Gassman, G. A. Campbell, and R. C. Frederick, <u>J. Am. Chem. Soc.</u>, **1972**, <u>94</u>, 3884. P. G. Gassman and G. A. Campbell, <u>ibid.</u>, **1971**, <u>93</u>, 2567; **1972**, <u>94</u>, 3891.

8.   T. Okamoto, K. Shudo, and T. Ohta, <u>J. Am. Chem. Soc.</u>, **1975**, <u>97</u>, 7184.

9.   J. C. Fishbein and R. A. McClelland, <u>J. Am. Chem. Soc.</u>, **1987**, <u>109</u>, 2824.

10.   (a) Using PCMODEL from Serena Software, Bloomington, IN. (b) ALCHEMY II, Tripos Associates, St. Louis, MO.

11.   MMX automatically introduces an sp^2 hybridized N as the default atom in anilines, and this led to highly unreasonable geometries. ALCHEMY II allows the intital introduction of an sp^3 N in these cases, which can flatten towards sp^2 if the energy demands it.

12.   R. R. Mocherla, D. K. Powell, C. L. Barnes, and D. van der Helm, <u>Acta Cryst.</u>, **1983**, <u>C39</u>, 868.

13.   S. A. Glover and A. P. Scott, <u>Tetrahedron</u>, **1989**, <u>45</u>, 1763.

14.   M .J. S. Dewar, E. G. Zoebisch, E. F. Healy, and J. J. P. Stewart, <u>J. Am. Chem. Soc.</u>, **1985**, <u>107</u>, 3902.

15.   Using a locally modified version of the MOPAC program: S. Olivella, <u>QCPE Bull.</u>, **1984**, <u>4</u>, 109.

16.   The initial geometry before optimization had a $C_{(1)}$-$C_{(2)}$-$N_{(3)}$-$O_{(11)}$ dihedral angle of 180° i.e. the groups were assumed to be coplanar.