

ENHANCED NUCLEOPHILIC REACTIVITY: THE "DISAPPEARING"

LONE-PAIR

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In previous work<sup>1</sup> we have advanced two explanations for the  $\alpha$ -effect.<sup>2</sup>

The first invokes intramolecular base catalysis for amidoximes, for the anions of hydroxamic acids in the imino form, and for hydroxylamine, and the second lone-pair lone-pair repulsion, leading to orbital splitting. In the latter case the H.O.M.O. of the nucleophile interacts strongly with the electrophilic centre thus increasing the reactivity.

The enhanced reactivity due to this cause is conformation dependent and this has recently been demonstrated.<sup>3</sup>

There remain several difficulties in explaining the increased reactivity of these species. In particular, the following questions remain:

(a) why does the lone-pair splitting not lead to an increased affinity for the proton?<sup>4</sup>

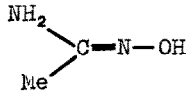
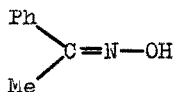
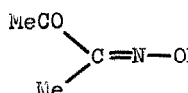
(b) why do some " $\alpha$ -nucleophiles" show enhanced reactivity and others of very similar structure do not?

In a recent note<sup>5</sup> we have explained the  $\alpha$ -effect in terms of charge and orbital interactions,<sup>6</sup> so that combination with the proton is more strongly influenced by charge densities than by orbital splitting. We now deal with the second problem.

In several reactions (Table 1), we find that the anions of basic oximes show the same reactivity as anions of phenols or alcohols of comparable basicity. The introduction of electron attracting groups however produces large enhancements of reactivity in some cases (particu-

larly acylation).

**Table 1.** Relative values of the bimolecular rate constants for an oximate ion and phenoxide anion of the same basicity in reactions with I p-nitrophenyl acetate; II O-p-nitrophenyl diphenylphosphinate in water at 25° and III with benzyl bromide in 5% aqueous acetone at 25°.

	pKa	Relative reactivity		
		I	II	III
	12.9	1.2	-	-
Et <sub>2</sub> C=N-OH	12.6	1.0	0.6	-
Me <sub>2</sub> C=N-OH	12.42	1.0	1.0	1.0
	11.48	2.7	1.0	-
	9.38	100	16.5	4.0
(MeCO) <sub>2</sub> C=N-OH	7.38	933	25.0	-
Brønsted β		0.8	0.38	0.29

Explanations<sup>7</sup> based on intramolecular catalysis are probably not tenable since (smaller) rate increases are observed for reactions of alkyl halides. Moreover catalysis involving cyclic transition states would lead to low  $\Delta S^\ddagger$  values, which is not the case.<sup>8</sup> The explanation must therefore be a general one.

The ionised oxygen atom has two degenerate lone pairs ( $p_x p_y$ ). One ( $p_x$ ) is involved in conjugation to give  $\pi$  orbitals, the other orthogonal  $p_y$  orbital (Fig. 1) interacts with the  $p_y$  lone pair orbital of nitrogen, viz.,

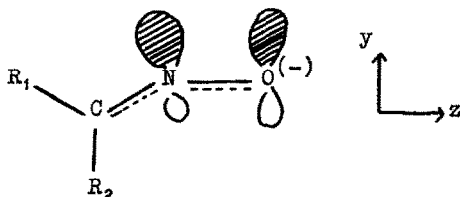
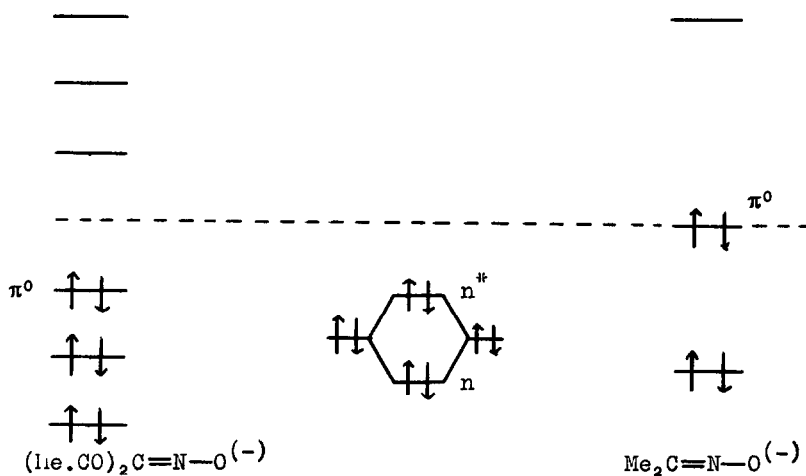


Fig. 1

The main question is which orbital  $\pi_x$  or  $\pi_y$  is at higher energy? Reference to Walsh's rules<sup>9</sup> and to recent photoionisation spectra<sup>10</sup> shows that the lone pair energy is relatively insensitive to substitution, whereas the H.O.M.O. ( $\pi^0$ ) is strongly affected such that electron donating substituents increase its energy.

Orbital splitting of  $p_y$  on oxygen and nitrogen produces a H.O.M.O. ( $n^*$ ) which may lie above or below the H.O.M.O. ( $\pi^0$ ) of the  $\pi_x$  levels (Fig. 2) depending on the structure of oximate ion



Electron attracting substituents (e.g. R.CO) generally reduce the energies of  $\pi$  and  $\pi^*$  levels (as in the case of carbonyl compounds).

For the more basic oximes (e.g. acetoxime) the highest occupied "lone-pair" orbital ( $n^*$ ) may be below the H.O.M.O. of the conjugated  $\pi$  system ( $\pi^0$ ). Under these conditions the oxime behaves as a typical alkoxide ion.

As the  $pK_a$  of the oxime decreases with the incorporation of electron attracting substituents, the highest occupied  $\pi$  orbital ( $\pi^0$ ) is brought below the split lone-pair level ( $n^*$ ). The oximate ion then behaves as an  $\alpha$ -nucleophile. In agreement with this explanation we find that the ions  $(MeCO)_2C: NO^{(-)}$  and  $MeCO(Me)C:N-O^{(-)}$  show weak  $n \rightarrow \pi^*$  bands at 360 and 400  $m\mu$  respectively in addition to strong  $\pi \rightarrow \pi^*$  bands at 275-280  $m\mu$ . No  $n \rightarrow \pi^*$  absorption is found for the acetoximate ion. These spectra

give the relative positions of  $n^*$  and  $\pi^0$  orbitals which change with substitution, so that the  $n^*$  orbital lies below the  $\pi^0$  orbital for the most basic oximes.

A similar situation is found with cyclic diazines. The (lone-pair) IP. of pyridazine which shows enhanced reactivity towards both acylating and alkylating agents<sup>5,11</sup> is found to be ca. 0.5 eV lower than the values normally found for other nitrogen heterocycles (lying close to that of benzene (9.25 eV)) for the removal of  $\pi^0$  electrons.<sup>12</sup>

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