

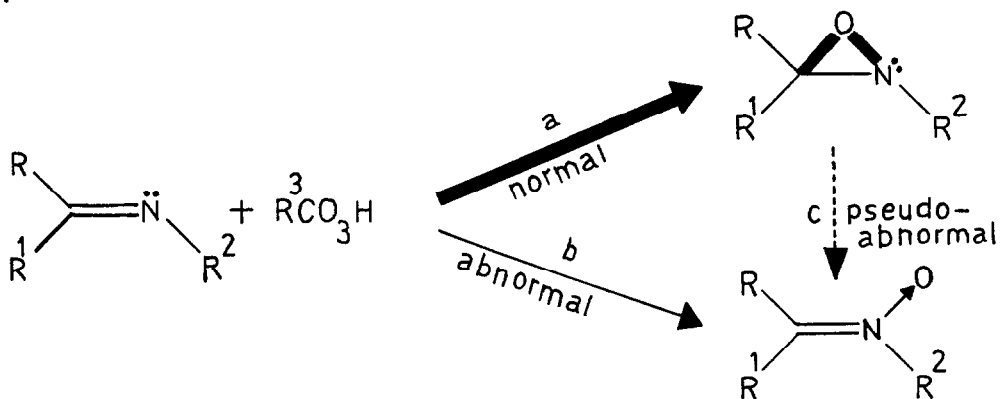
NORMAL, ABNORMAL AND PSEUDO-ABNORMAL REACTION PATHWAYS  
FOR THE IMINE-PEROXYACID REACTION

Derek R. Boyd\*, Peter B. Coulter, and Narain D. Sharma

Department of Chemistry, Queen's University of Belfast, Belfast BT9 5AG  
W. Brian Jennings\* and Valerie E. Wilson  
Department of Chemistry, University of Birmingham, Birmingham B15 2TT

**Summary:** Steric and mesomeric effects have a marked influence upon the formation of oxaziridine (normal pathway) or nitron (abnormal pathway) products from the imine-peroxyacid reaction; n.m.r. studies of the thermal isomerization of oxaziridines to nitrones provide evidence of a pseudo-abnormal oxidation pathway.

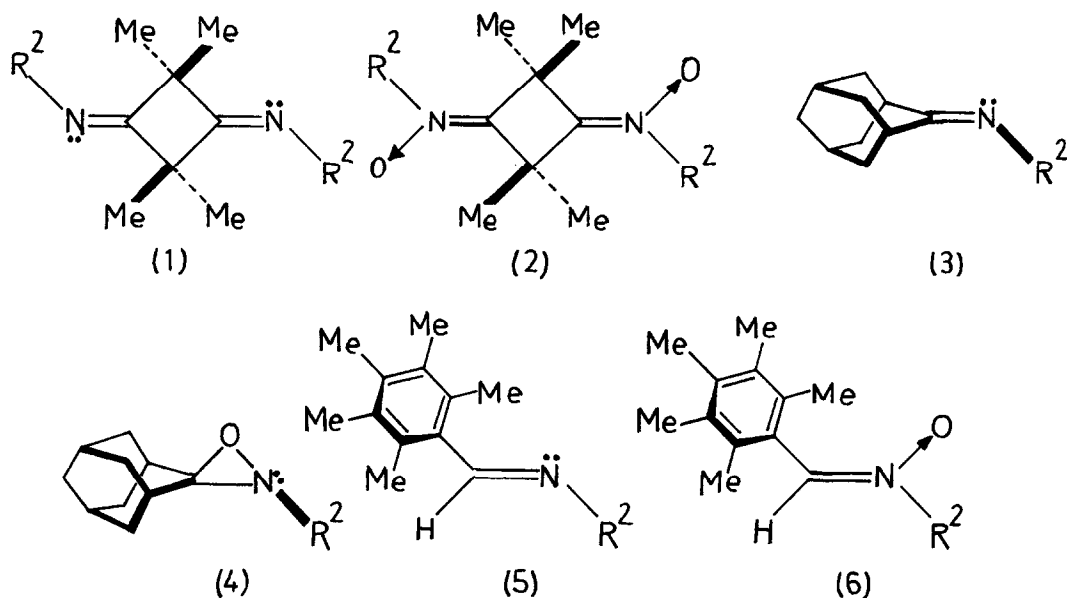
The imine-peroxyacid reaction generally provides a good synthetic route to oxaziridines.<sup>1-5</sup> In view of the very wide range of N-alkyl oxaziridines which has been formed by this method, this reaction pathway (a) may be classified as 'normal'.



Nitrones are usually produced in a relatively small proportion of imine-peroxyacid reactions<sup>4,6,7</sup> and nitron formation (pathway b) may thus be considered as an 'abnormal' reaction. The currently favoured mechanism for the synthesis of oxaziridines from the imine-peroxyacid reaction involves a two-step sequence, *i.e.* nucleophilic attack of the peroxyacid at the imino carbon atom (orthogonal to the imino plane) followed by intramolecular nucleophilic displacement.<sup>4</sup> By contrast, nitron products result from a concerted nucleophilic attack of the imino nitrogen atom on the peroxyacid (in the imino plane).<sup>4</sup> The possibility of nitron being formed *via* the corresponding oxaziridine isomer under the normal reaction or work-up conditions of the imine-peroxyacid reactions (pathway c) has not previously been investigated.

Some unexpected cases of abnormal imine oxidation have recently been found in these laboratories. Oxidation of bis-imines (1, R<sup>2</sup> = Pr<sup>i</sup> or Bu<sup>t</sup>) derived

from 2,2,4,4-tetramethylcyclobutanedione with *m*-chloroperoxybenzoic acid (MCPBA) in chloroform or dichloromethane afforded the bis-nitron (2) exclusively. This is a totally abnormal reaction (pathway b) as the bis-oxaziridine isomer (prepared by photolysis of 2)<sup>8</sup> survived under the reaction conditions. It contrasts with the observed totally normal oxidation of many trialkyl ketimines including imines (3, R<sup>2</sup> = Pr<sup>i</sup> or Bu<sup>t</sup>) derived from adamantanone where oxaziridines (4) are formed exclusively.<sup>9</sup>



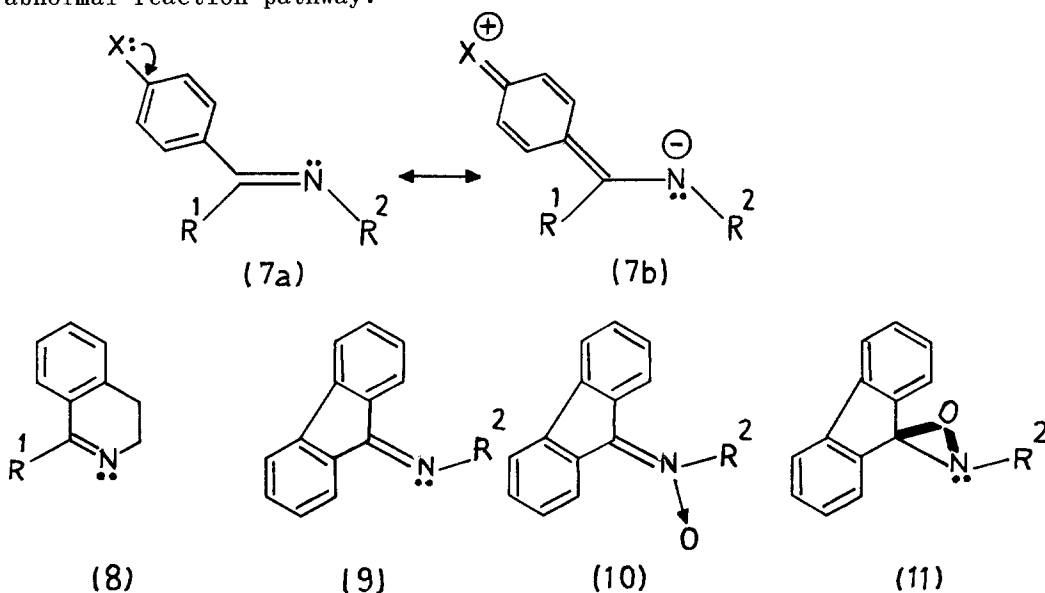
The abnormal behaviour of (1) can be rationalized in terms of the steric effects of the ring methyl groups which hinder the approach of the peroxyacid to the imino carbon in a plane perpendicular to the C=N bond. Steric effects probably also account for the observed abnormal oxidation (ambient temperature, CH<sub>2</sub>Cl<sub>2</sub>) of polymethylated benzaldimines, e.g. (5, R<sup>2</sup> = Me, Bu<sup>t</sup>) to the corresponding nitrones (6, R<sup>2</sup> = Me, 100%; R = Bu<sup>t</sup>, 80%). These ortho-disubstituted imines will adopt a preferred non-coplanar conformation with the aryl ring almost orthogonal to the imino plane, hence the ortho methyl groups will hinder the approach of the peroxyacid to the imino carbon atom (favouring nitron formation).

Ortho-unsubstituted benzaldimines exist in a preferred conformation which is nearly coplanar and upon peroxyacid oxidation yield oxaziridines as the preponderant or exclusive product. An appreciable degree of nitron formation (abnormal, pathway b) is observed where the benzaldimine bears an electron donating para-substituent (Table).

Table. Nitron-oxaziridine distribution from MCPBA oxidation (0°C, CDCl<sub>3</sub>) of imines (7) and (9) by n.m.r. analysis

Ar	R <sup>1</sup>	R <sup>2</sup>	Nitron (%)	Oxaziridine (%)
4-NO <sub>2</sub> .C <sub>6</sub> H <sub>4</sub> .	H	Bu <sup>t</sup>	0	100
4-Cl.C <sub>6</sub> H <sub>4</sub> .	H	Bu <sup>t</sup>	0	100
C <sub>6</sub> H <sub>5</sub> .	H	Bu <sup>t</sup>	0	100
4-Me.C <sub>6</sub> H <sub>4</sub> .	H	Bu <sup>t</sup>	9	91
4-MeO.C <sub>6</sub> H <sub>4</sub> .	H	Bu <sup>t</sup>	25	75
4-Me <sub>2</sub> N.C <sub>6</sub> H <sub>4</sub> .	H	Bu <sup>t</sup>	78	22
- Fluorenyl	-	Me	47	53
- Fluorenyl	-	Et	35	65
- Fluorenyl	-	Pr <sup>i</sup>	30	70
- Fluorenyl	-	Bu <sup>t</sup>	100	0

Mesomeric effects evidently favour the abnormal oxidation. In terms of a simple resonance formalism (7), electron donating para-substituents (x) will tend to increase the electron density at nitrogen thereby favouring N-oxidation. This mesomeric effect will also reduce the reactivity of the C=N bond to addition of the peroxyacid in the normal reaction. Previously reported<sup>10</sup> values for the barrier ( $\Delta G^\ddagger$ ) to thermal isomerization of oxaziridines to nitrones (derived from this series of para-substituted imines) indicate that the corresponding nitrones formed by peroxyacid oxidation are probably genuine products of an abnormal reaction pathway.



Conjugation will be optimized if the C-aryl group is confined to the imino plane by cyclization, e.g. imines (8) and (9). It has been reported<sup>4</sup> that MCPBA oxidation of ketimine (8, R<sup>1</sup> = Me) in benzene gave mainly ketonitrone (R<sup>1</sup> = Me, 75%) although this proportion was reduced to 5% when the C-methyl substituent was absent (8, R<sup>1</sup> = H). Ketimines derived from fluorenone (9) also gave a considerable proportion of ketonitrone (10) upon oxidation with MCPBA in CDCl<sub>3</sub> solution (Table). The exclusive formation of nitrone (10) having an N-t-butyl substituent is remarkable and appears to be an exception to the trend of decreasing proportions of nitrone being associated with an increase in N-alkyl substituent size (R<sup>2</sup> = Me, Et and Pr<sup>1</sup>). However, when the MCPBA oxidation of (9, R<sup>2</sup> = Bu<sup>t</sup>) was carried out at a lower temperature (-50°C) in an n.m.r. probe (CFCl<sub>3</sub> as solvent) oxidation occurred predominantly by the normal pathway (ca. 95% oxaziridine). On raising the temperature to 0°C the initially produced oxaziridine (11, R<sup>2</sup> = Bu<sup>t</sup>) rapidly isomerized to the corresponding nitrone (10, R<sup>2</sup> = Bu<sup>t</sup>). Accordingly, the exclusive formation of this nitrone at 0°C in CDCl<sub>3</sub> solvent can be classified as a 'pseudo-abnormal' oxidation proceeding by pathways a and c rather than pathway b.

Oxaziridines (11) having smaller N-alkyl substituents (R<sup>2</sup> = Me, Et, or Pr<sup>1</sup>) isomerize to nitrones (10) only at higher temperatures [ $\Delta G^\ddagger$  27.5, 27.2 and 26.8 kcal mol<sup>-1</sup> respectively in toluene-d<sub>8</sub> at 65°C]. The unusually low isomerization barrier in the t-butyl member of the oxaziridine series (11,  $\Delta G^\ddagger$  21.1 kcal mol<sup>-1</sup> in toluene-d<sub>8</sub> at 65°C) can be ascribed to a relief of steric and angular strain in the transition state linking the oxaziridine (11) and nitrone (10). The results now indicate that, in addition to electronic factors<sup>10</sup>, steric effects can influence the barrier to isomerization of oxaziridines to nitrones.

Acknowledgement. We thank the SERC for postgraduate (V.E.W.) and postdoctoral (N.D.S.) awards and the DENI for a postgraduate award (P.B.C.).

#### References.

1. W.D. Emmons, J.Amer.Chem.Soc., 1957, 79, 5739.
2. R.G. Pews, J.Org.Chem., 1967, 32, 1628.
3. V. Madan and L.B. Clapp, J.Amer.Chem.Soc., 1969, 91, 6078; 1970, 92, 4902.
4. Y. Ogata and Y. Sawaki, J.Amer.Chem.Soc., 1973, 95, 4687, 4692.
5. D.R. Boyd, D.C. Neill, C.G. Watson and W.B. Jennings, J.Chem.Soc.Perkin Trans 2, 1975, 1815.
6. J. Bjørgero, D.R. Boyd, D.C. Neill and W.B. Jennings, J.Chem.Soc.Perkin Trans 1, 1977, 254.
7. D.R. Boyd and D.C. Neill, J.Chem.Soc.Perkin Trans 1, 1977, 1308.
8. A.J. Boyd, D.R. Boyd, J.F. Malone, N.D. Sharma, K. Dev and W.B. Jennings, Tetrahedron Letters, 1984, 25, 2497.
9. J. Bjørgero and D.R. Boyd, J.Chem.Soc.Perkin Trans 2, 1973, 1575.
10. D.R. Boyd, P.B. Coulter, W.J. Hamilton, W.B. Jennings and V.E. Wilson, Tetrahedron Letters, 1984, 25, 2287.

(Received in UK 4 February 1985)