

## Autoxidation Reactions of Imines to form Oxaziridines and Amides

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The formation of oxaziridines and the isomeric amides in equal amounts by the spontaneous autoxidation of several liquid imines *via* peroxyimide acid intermediates is reported.

Imine derivatives of aldehydes and ketones are widely used as simple intermediates both in chemical and enzyme-catalysed syntheses. While the susceptibility of imines to hydrolysis is well documented, to date there appear to be very few reports on the autoxidation reactions of imines. The passage of dioxygen through an aldehyde [in the presence of a  $\text{Co}(\text{OAc})_2$  catalyst] followed by addition of an amine has been reported to yield oxaziridines by an autoxidation process assumed to be occurring *via* a peroxyacid intermediate.<sup>1</sup>

A limited range of *para*-substituted imines (**1**) has previously been synthesised in these and other laboratories without any reports of their autoxidation.<sup>2-6</sup> The present study resulted from the recent synthesis of ten *para*-substituted imines (**1**) which were required for n.m.r. studies.<sup>7</sup> While the majority of these imines (**1**) were solids (m.p. > 25 °C), imines (**1a-c**) were found to be liquids at ambient temperature and all gave correct microanalytical and spectral (n.m.r. and i.r.) characteristics immediately after synthesis and distillation. Within a period of 1-2 days the distillate from (**1a**) solidified and was found to have been converted into three compounds, one of which was totally insoluble in dichloromethane. Imines (**1b**) and (**1c**) both appeared to yield a similar mixture of three components but these were formed at slower rates. Thus imine (**1b**) required a 2-3 week period for complete decomposition and solidification, while imine (**1c**) remained a liquid during this interval and contained only a very minor proportion of the three decomposition products. Although the spontaneous decomposition of imine (**1c**) was extremely slow it was found to occur much more rapidly (30% decomposition within 3 h, 100% decomposition within 2 days) when the neat liquid was stirred in air at ambient temperature in the presence of a trace of benzoyl peroxide.

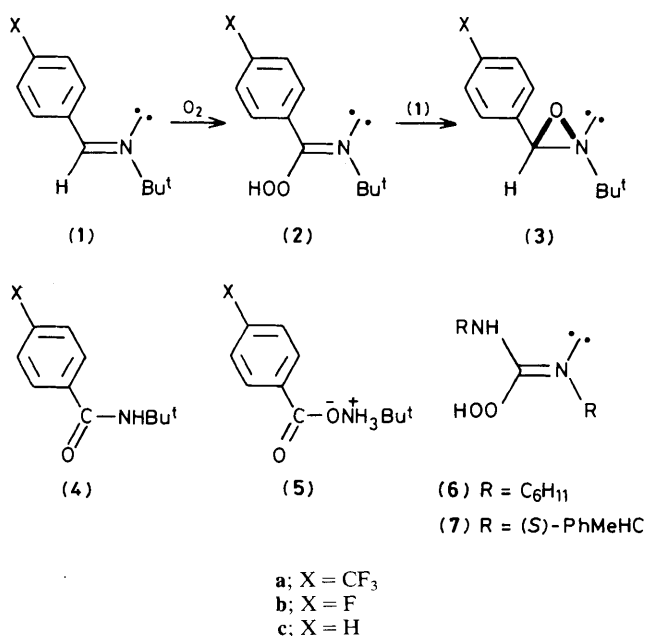
The dichloromethane soluble products obtained from spontaneous decomposition of the imines (**1a-c**) were identified as the corresponding oxaziridines (**3a-c**) and amides (**4a-c**), by several methods including separation and comparison of physical properties, t.l.c. behaviour, and comparison of n.m.r. spectra with authentic samples. In a typical experiment, the imine (**1c**) (2.94 g) was stirred at ambient temperature (2 days) in the presence of benzoyl peroxide (0.004 g) and the resulting dichloromethane-soluble portion contained the oxaziridine (**3c**) (0.98 g) and the amide (**4c**) (1.0 g). The insoluble fraction (0.95 g) was identified as *t*-butylammonium benzoate (**5c**). While the relative proportions of oxaziridines (**3a-c**) and amides (**4a-c**) remained equal in all experiments, the proportion of *t*-butylammonium benzoate products (**5a-c**) obtained was variable.

These observations appear to be in accord with a spontaneous free radical autoxidation mechanism. The initial step in the autoxidation of the imines (**1a-c**) appears to be the formation of unstable and highly reactive neutral peroxyimide acids (**2a-c**) which react with the imines (**1a-c**) to yield the oxaziridines (**3a-c**) and amides (**4a-c**) in equal proportions. Evidence consistent with an autoxidation mechanism includes (a) an increased rate of reaction in the presence of a free radical initiator; (b) the observation of total decomposition in the neat liquid state only; and (c) the faster rate of autoxidation observed for imines derived from readily autoxidizable aldehydes [*e.g.* (**1a**)].

The present spontaneous synthesis of oxaziridines from imines by *in situ* formation of a peroxyimide acid appears to be without precedent. One previous report has indicated that several *C*-alkyl oxaziridines can be formed by the oxidation of imines with peroxyimide acid formed by the reaction of alkaline hydrogen peroxide with benzonitrile.<sup>8</sup>

As a simple extension of the present study, the oxaziridine (**3c**) has also been synthesised in racemic form (68% yield) by oxidation of the imine (**1c**) with the peroxyimide acid (**6**) (generated by treatment of dicyclohexylcarbodiimide with hydrogen peroxide),<sup>9</sup> or in optically active form (51% yield, 3% enantiomeric excess) using the chiral peroxyimide acid (**7**) [formed by reaction of (*S,S*)-*N,N'*-bis( $\alpha$ -phenylethyl)carbodiimide<sup>10</sup> with hydrogen peroxide]. These results confirm that aryl oxaziridines [*e.g.* (**1c**)] can readily be formed by oxidation using peroxyimide acids generated *in situ*. Further studies with the peroxyimide acid (**6**) also indicate that this reagent, although neutral, behaves towards imines in a very similar manner to *meta*-chloroperoxybenzoic acid (MCPBA). Thus, oxidations of aldimines derived from *p*-nitrobenzaldehyde and primary amines ( $\text{RNH}_2$ ; R = Me, Et, Pr<sup>i</sup>, or Bu<sup>t</sup>) with the peroxyimide acid (**6**) gave similar yields and proportions of *cis*- and *trans*-oxaziridine isomers to those found with MCPBA.<sup>11</sup>

The origin of the *t*-butylammonium benzoate products (**5a-c**) formed spontaneously from imines (**1a-c**) has not been unambiguously established. Compounds (**5a-c**) were formed immediately upon mixing the benzoic acids with *t*-butylamine. A mechanism involving partial hydrolysis of imines (**1a-c**) in air, followed by autoxidation of the aldehyde



products, and reaction with the t-butylamine product cannot presently be excluded.

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