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OXIDATION OF PSEUDOBASES DERIVED FROM HETEROCYCLIC IMINIUM SALTS BY MOLECULAR OXYGEN

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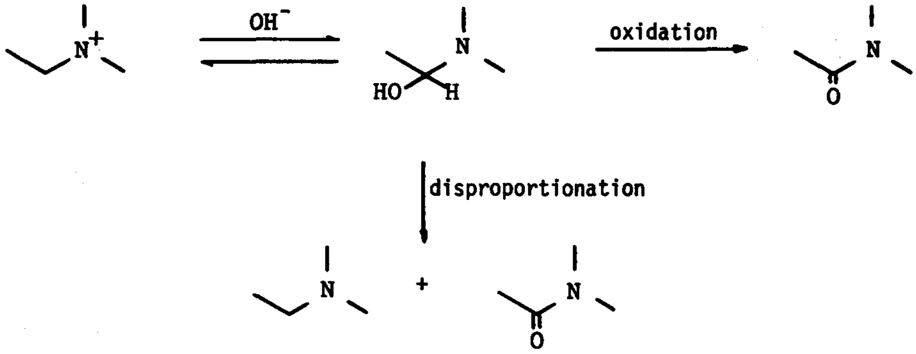
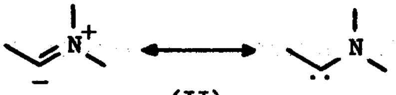
The synthetic utilities of potassium ferricyanide oxidation of pseudobases (e.g. I) derived from the corresponding heterocyclic iminium salt is already well established. Perhaps the best known reaction of this type is the preparation of naturally occurring isoquinolone derivatives from isoquinolinium salts[1]. It has also been observed that the pseudobase undergoes a disproportionation reaction giving the amide and amine[2] (see Scheme), and, more recently, a report has described a detailed quantitative study of the rates and equilibria of pseudobase formation[3]. We now wish to report our findings that have led to a simple, yet high yield synthesis of heterocyclic amides from the corresponding iminium salts.



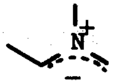
Scheme

When a solution of iminium salt in tert-butanol was treated with solid potassium hydroxide at room temperature followed by oxygen gas[4], the corresponding amide was isolated (see Chart). The choice of solvent in this oxidation reaction seems to be critical since a lower yield was observed with water while undesirable side reactions became significant when methanol or ethanol was used. Upon varying the substituent R (e.g. benzyl) in the starting iminium salts, good yields were consistently observed.

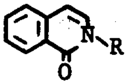
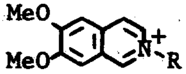
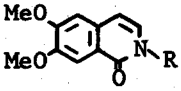
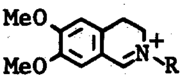
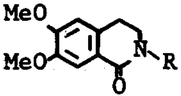
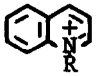
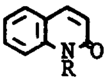
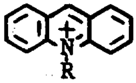
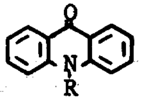
The mechanism of the reaction can be interpreted as a direct oxidation of the intermediate pseudobase by molecular oxygen. Although aware that the reaction might involve the addition of molecular oxygen to the carbene structure (II)[5] or dipolar structure (III)[6] we regard these pathways less attractive.



(II)



(III)

Reactant	Product	% Yield[7]
		R = Me
		82
		73
		64
		83
		81

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2) R.F.Smith and E.D.Otremba, J. Org. Chem., 27, 879 (1962)

3) J.W.Bunting and D.J.Norris, J. Amer. Chem. Soc., 99, 1189 (1977)

4) A typical procedure: To a stirred solution of N-methylisoquinolinium iodide (1 mmol) in tert-butanol (20 ml) was added solid potassium hydroxide (3 mmol) and oxygen was bubbled through until oxidation was complete (5 hr., monitored by TLC.). Solvent was removed, water was added, and the almost pure (NMR.,TLC.) N-methylisoquinolone was obtained by chloroform extraction and further purified by crystallisation.

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7) All yields reported refer to the purified products after crystallization.