# Mechanism of Direct Side-chain Acylamination and Aminoarylation of 2- and 4-Picoline 1-Oxides

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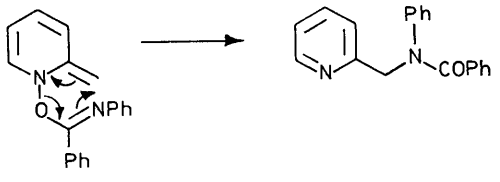
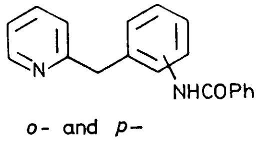
*Summary* The isolation of radical coupling products and the observation of appropriate C.I.N.D.P. signals suggest that most of the title reactions proceed by homolysis of the anhydro-bases (**4**) or (**9**) followed by radical recombinations; a diaza-oxy-Cope rearrangement may still account for the formation of α-acylamination products.

TREATMENT of 2- and 4-picoline 1-oxides (and related compounds) with an *N*-arylbenzimidoyl chloride and a strong base leads to a mixture of side-chain acylaminated and acylaminoarylated products.[1] A diaza-oxy-Cope rearrangement (**1**) was initially suggested[2] as a possible explanation of the formation of (**2**), but the production of aminoarylated products (**3**) from 2-picolines and of similar products from 4-picolines required a reconsideration of the mechanism.

Heterolytic or homolytic cleavages of the anhydro-bases (**4**) and (**9**) and concerted intramolecular processes were considered. Attempts to trap an intermediate picolyl

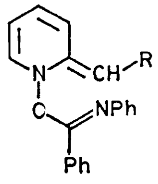


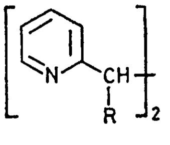
(1) (2)

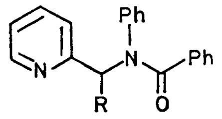


(3)

cation[3] were unsuccessful. Thus, when 2- or 4-picoline 1-oxide was treated with *N*-phenylbenzimidoyl chloride in the presence of triethylamine and *m*-dimethoxybenzene no picolyldimethoxybenzenes were formed.

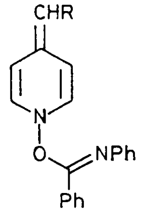

**(4)**

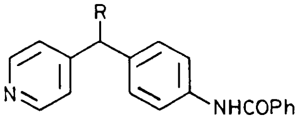

**(5)** R = Ph
**(6)** R = Me

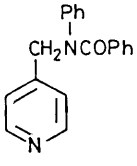

**(7)** R = Ph
**(8)** R = Me

Strong evidence for a radical pathway has now been obtained. Thus, when 2-benzylpyridine 1-oxide was boiled in $(CH_2Cl)_2$ with *N*-phenylbenzimidoyl chloride and triethylamine, αα′-*bis*-(2-pyridyl)bibenzyl (**5**)† (38%) was obtained, in addition to *N*-(2-pyridylphenylmethyl)benzanilide (**7**) (40%) and benzanilide (36%). Analytically pure dimer (**5**) was separated into two components by h.p.l.c., undoubtedly corresponding to the *threo*- and *erythro*-diastereoisomers, but these were not collected and characterised further. Similarly, 2-ethylpyridine 1-oxide gave the dimer (**6**) (11%) and the expected (**8**) (17%). On the other hand, only *p*-(4-pyridylphenylmethyl)benzanilide (**10**) (44%) and benzanilide (27%) were isolated from 4-benzylpyridine 1-oxide, and no dimer or side-chain *N*-substituted product was observed.

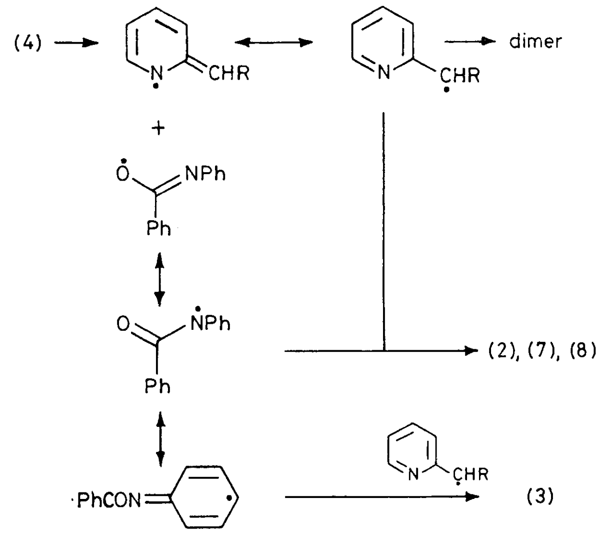
Direct evidence for the formation of radical pairs in these reactions comes from the observation of the appropriate C.I.D.N.P. signals. When the reaction of 2-picoline 1-oxide with *N*-phenylbenzimidoyl chloride in ethylene dichloride was carried out in an n.m.r. tube in the presence of $Et_3N$ at room temperature, and the spectrum was monitored as a function of time, an emission singlet was observed at δ 4·05. Its intensity reached a maximum after *ca.* 95 s and then decayed to an apparent zero at 115 s, following which it grew into an absorption singlet corresponding to that of the α-$CH_2$ in *p*-(**3**). No C.I.D.N.P. signal was detected corresponding to radical coupling leading to α-acylamination (**2**) so that a concerted (diaza-oxy-Cope) process remains a possible pathway to this product.


**(9)**


**(10)** R = Ph
**(11)** R = H


**(12)**

When the reaction of 4-picoline 1-oxide with the imidoyl chloride and base at room temperature was monitored by n.m.r. *two* emission C.I.D.N.P. signals were observed at δ 5·1 and 3·9 with a lifetime of 90 and 120 s, respectively. The corresponding absorption singlets were found to be those of the γ-$CH_2$ in 4-(*N*-benzoyl-*N*-phenyl)picolylamine (**12**) and the γ-$CH_2$ in (**11**), respectively. Similarly, for the reaction of 4-benzylpyridine 1-oxide an emission C.I.D.N.P. singlet at δ 5·5 was observed, corresponding to the γ-methine proton in (**10**). No emission is expected for the formation of the dimer, if any is formed.



Scheme

The results are most conveniently explained in terms of the homolysis of the N–O bond in the anhydro-bases (**4**) and (**9**) followed by radical coupling [with the proviso that (**2**) may rise in a concerted manner], as illustrated for (**4**) in the Scheme. As expected, α-$C_5H_4N\dot{C}HR$ (R = Ph, Me) are longer lived than the corresponding α-picolyl radical (R = H) thus permitting their dimerisation. It would appear as though coupling of γ-$C_5H_4\dot{C}HPh$ and $PhCO\dot{N}Ph$ is faster than dimerisation of the former.

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† All new compounds gave satisfactory microanalytical and spectral data.

[1] R. A. Abramovitch, D. A. Abramovitch, and P. Tomasik, *J. Chem. Soc., Chem. Commun.*, 1979, 956.

[2] R. A. Abramovitch and T. D. Bailey, *J. Heterocycl. Chem.*, 1975, **12**, 1079.

[3] T. Cohen and G. L. Deets, *J. Am. Chem. Soc.*, 1967, **89**, 3939.