Nucleophilic Character of Acyl Radicals: a New Selective Type of Aromatic Acylation

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WE have qualitatively[1] and quantitatively[2] shown in reactions with conjugated olefins and heteroaromatic bases, the nucleophilic character of the alkyl and α-hydroxyalkyl radicals generated in redox processes: t-hydroperoxides–Fe^{2+}, acylperoxides–Cu^{+}†, aliphatic substrates–Fenton reagent, oxaziranes–Fe^{2+}, alkanoic acids–Pb^{4+}.

The polar character of the carbon free-radicals is shown by the relative magnitudes of the redox potentials, E_{-e} and E_{+e}, for the two equilibria:[3]

$$R\cdot \rightleftharpoons R^{+} + e \qquad E_{-e}$$
$$R\cdot + e \rightleftharpoons R^{-} \qquad E_{+e}$$

Hence acyl radicals should be more nucleophilic owing to the stability of the ions $R{\cdot}CO^{+}$ relative to RCO^{-}, particularly in solvents such as water.

This is confirmed by a new type of aromatic free-radical acylation. The acyl radicals are generated from aldehydes with t-butyl hydroperoxide or hydrogen peroxide and ferrous sulphate:

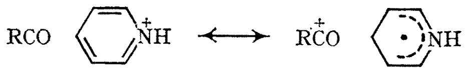
$$R^{1}O{\cdot}OH + Fe^{2+} \rightarrow R^{1}O\cdot + FeOH^{2+}$$
$$R^{1}O\cdot + RCHO \rightarrow R^{1}OH + R^{2}\text{-}\dot{C}O$$

The reaction is of synthetic interest with heteroaromatic bases, because of its high selectivity and the simplicity of the experimental conditions.

To a stirred and cooled (5—10°) solution of quinoline (0·016 mole), acetaldehyde (0·1 mole), and sulphuric acid (0·016 mole) in water (5 ml.), a solution of $FeSO_4,7H_2O$ (0·1 mole) in water (70 ml.) and t-butyl hydroperoxide (0·1 mole) were simultaneously added; the precipitated 2,4-diacetylquinoline (0·01 mole), m.p. 69° was filtered off. The aqueous solution was basified and a mixture of quinoline, 2- and 4-acetylquinoline and traces of 2- and 4-methylquinoline were obtained (g.l.c.). Benzothiazole, acetaldehyde, and sulphuric acid under the same condtiions give 2-acetylbenzothiazole, m.p. 112°. Similar results are obtained with pyridine, acridine, isoquinoline, pyrazine, pyrimidine, quinoxaline sulphates, acetaldehyde, benzaldehyde, and higher aldehydes. With isobutyraldehyde, isopropylation of the heteroaromatic bases also takes place *via* partial decarbonylation of the acyl radical:

$$Me_2CH\text{–}\dot{C}O \rightarrow Me_2\dot{C}H + CO$$

The nucleophilic driving force for this radical acylation is clearly indicated by the orientation and reactivity (aromatics such as *NN*-dimethylaniline or *NN*-dimethyl-2-phenethylamine sulphates do not react under the same experimental conditions); it suggests a remarkable contribution of polar forms in the transition state:



This new type of free-radical acylation is therefore exactly opposite to the traditional electrophilic aromatic acylation, with regard to reactivity and orientation.

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[2] F. Minisci, M. Cecere, R. Galli, and R. Bernardi, *Tetrahedron*, in the press.

[3] D. S. MacKinnon and W. A. Waters, *J. Chem. Soc.*, 1953, 323.