Reversibility of the Homolytic Acylation. Substitution of Acyl Groups in Protonated Heteroaromatic Bases by Nucleophilic Free Radicals

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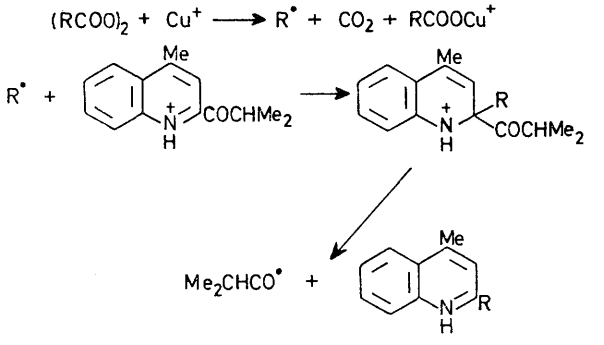
Summary Nucleophilic alkyl and acyl radicals effect homolytic substitution of acyl groups in protonated heteroaromatic compounds; the results indicate the reversibility of the addition of the acyl radicals to heteroaromatic bases.

HOMOLYTIC alkylation and acylation of protonated heteroaromatic bases are of considerable synthetic and theoretical interest owing to the nucleophilic character of the alkyl and acyl radicals.[1] In a recent communication[2] the substitution of the acyl group by alkyl radicals was explained by a complex mechanism which was different from the general mechanism proposed by us.[1] This prompted us to report our results of closely related reactions which, in our opinion, confirm the general mechanism[1] and throw new light on the problem of the reversibility of homolytic aromatic acylation.

The reaction of protonated 2-isobutanoyl-4-methylquinoline (I) with pentanoyl and 2-methylbutanoyl peroxides and CuOAc in acetic acid–water (1 : 1) at 25 °C results in clean substitution and gives 2-butyl-4-methyl-

quinoline and 2-(1-methylpropyl)-4-methylquinoline in quantitative yields based on the converted heteroaromatic base, and in 30 and 35%, respectively, based on the peroxides. The products were identified by g.l.c. (10%

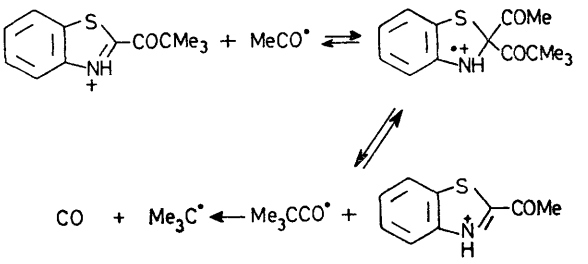


SCHEME 1

UCC-W-982 on ChromosorbW.a.w. DMCS) by comparison with authentic samples.[3] The side-reaction products were butenes formed by oxidation of the alkyl radicals [equation (1)] and a trace of methylpropanoic acid.

$$Me{-}CH_2{-}CH_2{-}CH_2{\cdot} + Cu^{2+} \xrightarrow{k} Me{-}CH_2{-}CH{=}CH_2 + Cu^{+} + H^{+} \quad (1)$$

Since the rate of reaction (1) is known[4] under similar condition ($k = 2{\cdot}7 \times 10^6$ l mol^{-1} s^{-1}) a value of *ca.* 10^5 l mol^{-1} s^{-1} can be evaluated for the attack of the alkyl radical on (I). The mechanism proposed by Tiecco *et al.*[2] for closely related reactions, by Ag^+ catalysed decarboxylation of a carboxylic acid by $(NH_4)_2S_2O_8$, seems highly unlikely because (i) it involves the simultaneous formation of two different radicals (a radical cation from the heterocyclic species and an alkyl radical from the carboxylic acid) by the same radical source, and (ii) it assumes that these radicals survive in solution in order to give cross-coupling with the formation of a highly unstable cation. We suggest for our results and also for those obtained by Tiecco *et al.* the mechanism shown in Scheme 1 which assumes that the addition of acyl radicals to heteroaromatic bases is a reversible process. Confirmation of this assumption was obtained by reaction of the acetyl radical with protonated 2-pivaloylbenzothiazole (II). The reaction of (II) with $Bu^tO{\cdot}OH{-}Fe^{2+}$ and acetaldehyde gave (Scheme 2) 2-acetylbenzothiazole in 35% yield (based on $Bu^tO{\cdot}OH$). The product was identified by comparison with an authentic sample.[3] This is also in agreement with our results[5] that



SCHEME 2

the addition of acyl radicals to olefins is a reversible process. Recently we[6] investigated the absolute rate constant in the addition of acyl radicals to protonated heteroaromatic bases; the conclusions of this communication suggest that the kinetics of these reactions require a more complex treatment including the reversibility of the process.

We thank Professor Minisci for helpful discussions.

(*Received, 2nd August* 1976; *Com.* 892.)

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