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CONCENTRATION-DEPENDENT ORIENTATIONS IN FREE-RADICAL PHENYLATIONS OF HETEROAROMATIC COMPOUNDS

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Abramovitch and Saha (1) recently demonstrated that free-radical arylations of pyridine are effected in excellent yields using aqueous solutions of arenediazonium salts. It would be expected that benzenediazonium tetrafluoroborate (I) would act similarly, generating free phenyl radicals by homolysis of the species B^{+}-N:N-Ph (B = heterocyclic base), which should form readily by electrophilic addition of benzenediazonium ion to a ring nitrogen of a strongly basic heteroaromatic compound.

We find this expectation to be correct for the phenylations of pyridine and 1-methylimidazole (pK_as of cations: 5.17 and 7.33) provided that low concentrations of the benzenediazonium salt are used: under these conditions, the proportions of the isomeric phenylation products are closely similar to those obtained using other phenyl-radical

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sources (2, 3). However, as shown in Table 1, *the isomer proportions change appreciably when the concentration of diazonium salt is increased*.

TABLE 1

Phenylations of Pyridine and of 1-Methylimidazole by Benzenediazonium Tetrafluoroborate (I)[#]

Molar ratio (I): pyridine	Reaction temp.	Isomeric phenylpyridines (%) 2-	3- + 4-
1:250	40°	53	47
" "	70	54	46
1:10	40	86	14
" "	70	86	14
1:6	70	93	7

Molar ratio (I): 1-methylimidazole		Isomeric phenyl-1-methylimidazoles (%) 2-	4- + 5-
1:250	70	61	39
1:29	40	80	20
1:4	70	80	20
1:3	70	81	19

[#] Isomer proportions and product yields (which exceeded 50% in all instances) were established using gas-liquid chromatography.

Although these results indicate a reaction path other than simple free-radical phenylation of the neutral heteroaromatic substrates, the observed orientations surely cannot result from electrophilic phenylations.

The generation of phenyl radicals in the experiments using high concentrations of (I) was confirmed by a series of competition reactions between the heteroaromatic substrates and nitrobenzene, using a molar ratio of (I) to total substrates of 1:6.20. The resulting mixtures of nitrobiphenyls showed isomer ratios characteristic of phenyl-radical substitution of nitrobenzene (4). However, the isomer distributions of the phenylated heteroaromatics remained abnormal, and the total rates of phenylation (deduced from the competitive experiments with nitrobenzene assuming that nitrobenzene is three times as reactive as benzene (5), or from direct competitive experiments with benzene) were significantly higher than those observed for "normal" free-radical phenylations (where the total rate of phenylation of pyridine is 1.14 (1) and that of 1-methylimidazole is 1.2 (2) (rate of phenylation of benzene = 1)). The results are summarized in Table 2.

TABLE 2

Competitive Phenylations[†]

Competing substrate	Nitrobiphenyls (%) 2-	3-	4-	Phenylpyridines (%) 2-	3- + 4-	Total rate
$PhNO_2$	65.5	8.5	26	87	13	1.60
PhH				82	18	2.44
				Phenyl-1-methylimidazoles (%) 2-	4- + 5-	
$PhNO_2$	72	6	22	78.5	21.5	2.60
PhH				74	26	2.38

[†] The competing substrates were used in equimolar amounts. Isomer proportions and product yields were determined using gas-liquid chromatography. Reactions were carried out at 70°.

The abnormal isomer distributions and enhanced apparent reactivities are ascribed to the occurrence of phenyl-radical attack on the 1-phenylazopyridinium and

3-phenylazo-1-methylimidazolium ions, which we regard as analogs of pyridinium and methylimidazolium ions. We propose that these species are so much more reactive towards phenyl radicals than the uncomplexed heterocycles that they can dominate the orientation of substitution at high concentrations of (I).

Our proposal is based upon R. D. Brown's calculations of localization energies for radical substitution in the pyridinium and imidazolium ions (6,7), which predict high reactivity at the 2-positions in these species (use of the localization energy to predict partial rate factors for attack at the 2-positions (cf. Brown (8)) suggests values of ca. 100).

We plan to investigate the reactions of the conjugate acids of heteroaromatic compounds with phenyl radicals, in order to test these predictions further.

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