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FREE-RADICAL PHENYLATIONS OF 1-METHYLDIAZOLES

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There is abundant evidence showing that freeradical phenylations of benzenoid compounds involve phenylcyclohexadiene radicals as intermediates or transition states (1-3). The absence of any great positional selectivity (most partial rate factors for phenylations of substituted benzenes fall between 1 and 5) indicates that the energies of phenylcyclohexadiene radicals are only mildly dependent upon the orientation or nature of a substituent in the cyclohexadiene moiety.

We now report some instances of marked positional selectivity in the phenylations of some five-membered nitrogen heterocycles. Thus, thermal decomposition of benzoyl peroxide at 80° or of N-nitrosoacetanilide at 40° in 20 % solution in 1-methylpyrazole gave 12-20 % yields of mixed 1-methyl-x-phenylpyrazoles, analyzed by gas-liquid chromatography as 94 % 5-, 5 % 3-, and 1 % 4-isomer (4). Despite the low yields, competition experiments using benzene and 1-methylpyrazole in varying molar ratios gave results consistent with competing first-order reactions involving each substrate species (5,6): the reactivity of 1-methylpyrazole towards phenylation at 80° was 0.62 ± 0.10 times that of benzene (7). Similar phenylations of 1-methylimidazole using N-nitrosoacetanilide at 40° or diazoaminobenzene at 140° gave 10-20 % yields of mixed 1-methyl-x-phenylimidazoles, estimated by gas-liquid chromatography as 67 % 2- and 33 % 5-isomer (4).

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The proportion of 4-isomer was less than 2 %, virtually at the limit of estimation. Competition experiments with benzene showed that the reactivity of 1-methylimidazole towards phenylation was 1.2 ± 0.2 times that of benzene.

We wish to point out that these selective phenylations at positions adjacent to the electron-donating heteroatom are to be expected on the basis of simple resonance concepts. Thus, the species I, resulting from attack adjacent to the l-nitrogen atom, is stabilized by conventional odd-electron delocalization (as Ia), while for species II, delocalization necessarily involves a higherenergy charge-separated structure (as IIa). These considerations should hold for all five-membered heteroaromatic compounds, and the radicals formed by nuclear attack of phenyl radicals on such compounds should have energies which are markedly dependent upon the position of attack.



In agreement with expectation, furans (8), pyrroles (9,10), thiophen (11), and thianaphthen (12) are phenylated predominantly at <u>alpha</u>-positions, while the pattern of phenylation of thiazole (13) closely resembles that of 1-methylimidazole. Furthermore, the relative reactivity of <u>ca</u> 2:1 noted for 1-methylimidazole as compared with 1-methylpyrazole is to be expected, since 1-methylimidazole has two possible sites of substitution adjacent to

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the 1-nitrogen atom, and 1-methylpyrazole has one.

Our results provide a check for some molecularorbital calculations made for pyrazole and imidazole (Orgel et al. (14), Hamano and Hameka (15)), since phenylation should occur most readily at the carbon atom of highest free valence. The calculated free valences are (reference; compound: position, free valence): (14); pyrazole: 3-, 0.392, 4-, 0.392, 5-, 0.442; imidazole: 2-, 0.482, 4-, 0.392, 5-, 0.472; (15); pyrazole: 3-, 0.440, 4-, 0.286, 5-, 0.395; imidazole: 2-, 0.528, 4-, 0.373, 5-, 0.546. The differences in the relative and absolute magnitudes of the free valences at the various carbon atoms reflect differences in the choice of Coulomb parameters for the two nitrogen atoms (Hamano and Hameka use parameters such that the 1-nitrogen is more electronegative, and the 2- (or 3-) nitrogen less electronegative, than in the model used by Orgel et al.) The experimental results for the 1-methyldiazoles agree well with the calculations of Orgel et al., although in related work with 1-phenylpyrazole (16), we found predominant 3-phenylation, as predicted by Hamano and Hameka's calculation. Thus, the difference in orientation may reflect the effect of the electron-attracting phenyl group on the electronegativity of the 1-nitrogen atom, rendering Hamano and Hameka's choice of Coulomb parameters more appropriate (the electronegativity of the 1-nitrogen atom in 1-phenylpyrazole is certainly higher than that of the 1-nitrogen of 1-methylpyrazole).

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