

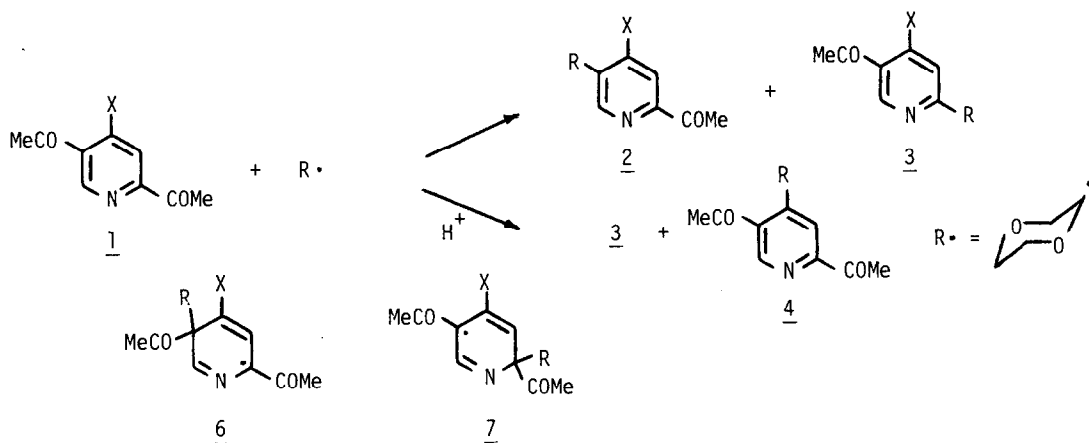
SELECTIVITY OF RADICAL IPSO ATTACK. ALKYLDEACYLATION REACTIONS BY DIOXANYL RADICALS
IN UNPROTONATED ACETYLPIRIDINES

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SUMMARY: Under neutral conditions the reaction of dioxanyl radicals with 2,5-diacetylpyridine gives the ipso substitution products; on the contrary, in the presence of sulphuric acid the substitution occurs at the 2- and 4- positions.

The displacement of an acyl group by a nucleophilic alkyl radical has been observed so far only in the case of protonated nitrogen containing heteroaromatic compounds such as benzothiazole,^{1,2} pyridine,^{1,3} and quinoline.^{1,4} We now report the first examples in which this process occurs with the unprotonated substrates. Thus, from the comparison of the results obtained in the two cases it is now possible to have a better knowledge of the factors controlling the selectivity of these homolytic aromatic substitution reactions.



Dioxanyl radicals⁵ react with 2,5-diacetylpyridine, 1 (X=H), to give a mixture of the ipso substitution products, 2-acetyl-5-dioxanylpyridine, 2 (X=H) (15%) and 2-dioxanyl-5-acetylpyridine, 3 (X=H) (25%); similarly, 2,4,5-triacetylpyridine, 1 (X=COMe) gives 2 (X=COMe) (10%) and 3 (X=COMe) (45%). No ipso substitution products were obtained from 2,4-diacetylpyridine, 5; the only product obtained in this case was 2 (X=COMe) (35%) deriving from the addition of the dioxanyl radical at the unsubstituted 5- position. Different results were obtained from 2,5-diacetylpyridine, 1 (X=H) when the reaction was carried out in the presence of sulphuric acid. Two compounds were obtained in this case; the ipso substitution product 3 (X=H) (30%)

and the 2,5-diacetyl-4-dioxanylpyridine, 4 (25%).

The positional selectivity observed in the presence of sulphuric acid is that expected when polar effects intervene during the addition step;^{1,7} the attack by the nucleophilic radicals occurs at the most positive sites of the molecule, i.e. the α and γ positions which are conjugated with the positive nitrogen atom. The unprotonated pyridines are not sufficiently electron deficient and polar effects cannot operate. In these cases the radical addition occurs selectively at the ring positions which are para to the electron-withdrawing substituents to give the intermediates 6 and 7. These are the most stable intermediates which can be formed from 1 (X=H, COMe) and 5, because the unpaired electron can be delocalized into the substituents; the selectivity of the radical addition is therefore determined by the relative stability of the σ -complex intermediates. The ipso substitution reactions now observed confirm the hypothesis formulated in the case of the reactions of alkyl radicals with nitro aromatic compounds;^{1,8} when polar effects cannot intervene, selective ipso attack can be observed only if it gives an intermediate which has a considerably greater stability than those derived from attack at other ring positions.

An important synthetic consequence of the results described above is that different isomers can be obtained from the same substrate if the radical alkylation is carried out in the presence or in the absence of sulphuric acid. We are presently carrying out experiments with other nitrogen containing heteroaromatic compounds to confirm this observation.

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