MOLECULAR ORBITAL STUDY OF THE REACTIVITY OF ACTIVE ALKYL GROUPS OF PYRIDINE AND PYRIMIDINE DERIVATIVES

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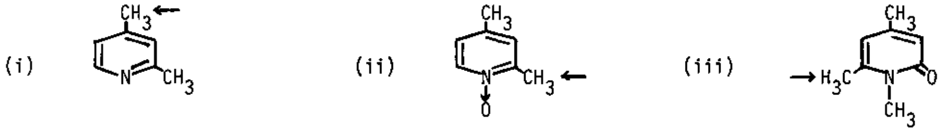
The relative reactivity of active methyl groups in a single molecule of pyridines and pyrimidines was systematically investigated. In the case of the reaction starting from the deprotonation step, the following results were obtained. (i) The reactivity of the methyl group on the γ-position is always larger than that of the methyl group on the α-position of pyridine, quinoline, pyrimidine and quinazoline. (ii) For the case of the corresponding N-oxides, the circumstances are just the reverse of the situation described above, i.e. α-position > γ-position. (iii) In the case of the cyclic amides, the methyl group , which is located on the end of the conjugated system from the carbonyl group, is more active than the others.



(Methyl groups indicated by arrows are more active than the others.)

These conclusions i, ii and iii were derived from the results of the nitrosation, the acylation, the styrylation and the deuterium exchange reaction on 2,4-dimethyl-N-heteroaromatics, without exceptions.

In order to rationalize the above conclusions, we analyzed the nitrosation and the deuterium exchange reaction by the application of the molecular orbital (MO) theory. The present MO study was carried out to interpret the deprotonation step of these reactions. The calculation of the charge transfer ability (CTA) values by the CNDO/2 was applied to the reactivity of alkylheteroaromatics with the amide or hydroxide ion. The CTA calculations relating to the N-oxides were performed to the conformation in which the sodium ion combined to the oxygen atom of the N-oxide group. The experimental results can be well interpreted in terms of the CTA values in the deprotonation step of these reactions. These results suggest that the CT process plays an important role in such intermolecular hydrogen bonding-type activated complexes.