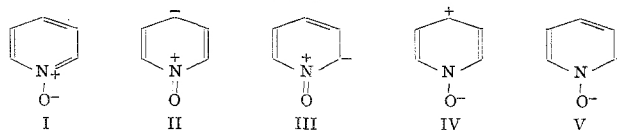


On the Reactivity of Pyridine-N-Oxide

Pyridine-N-oxide occupies an unique position in the quantum mechanical theory of organic reactivity. It undergoes both cationoid and anionoid substitution at the same positions, namely primarily at 4 and to a lesser extent at 2 position. The molecular orbital method of calculating electron density cannot correctly predict the reactivity of this compound, since it cannot predict maximum electrophilic and nucleophilic reactivity for the same position. Accordingly pyridine-N-oxide is an example of a compound violating the non-crossing rule. This peculiarity of N-oxide has been explained by the contribution of the various charge-separated canonical structures to the resonance hybrid in the valence bond approximation and by the fact that the N-oxide function is strongly polarizable in both directions.



Object of the present investigation is to show that molecular orbital can explain this peculiar reactivity of N-oxide. First we make a straightforward MO calculation of the electron densities at various positions of the pyridine-N-oxide. We have used the following values for the MO parameters of the hetero atoms,

$$\text{Coulomb integral } E_O = E_C + 2\beta \quad \text{and}$$

$$E_N = E_C + \beta, \quad E_{C'} = E_C + 0.01\beta \quad (\text{C attached to N})$$

$$\text{Resonance integral } \beta_{C-N} = 0.6\beta_{C-C} \quad \text{and} \quad \beta_{N-C} = 1.2\beta_{C-C}$$

The calculated electron densities are shown in the Fig. 1. It is evident that anionoid attack should be at 4 and 2 positions, as is actually the case. The cationoid attack should, however, take place at 3 position, while in actual practice the positions attacked are 4 and 2. Now the cationoid attack means nitration, sulphonation, etc., which are usually performed in strongly acidic medium. It is logical to expect that in acidic medium the compound exists primarily as IV and V, and there will be a strong tendency for protonation of oxygen. In the structure of the type IV and V with negatively charged oxygen, the electron affinity, hence the coulomb integral of oxygen will be reduced, compared to neutral (or almost neutral) oxygen as used in the first calculation. We may set this approximately equal to $E_C + \beta$ instead of $E_C + 2\beta$ used previously. The recalculated electron densities are shown in the Fig. 2. It is evident that the cationoid attack should

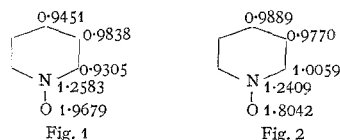


Fig. 1 and 2. Calculated resp. recalculated electron densities. (See text)

now go to 2 and 4 positions, as is observed experimentally. In practice the 4 position is more reactive than the 2 position probably because of steric requirements and the proximity of a positively charged nitrogen atom at 1 position. Similar conclusion was arrived at by JAFFE¹⁾ from the localisation energies of the various positions in pyridine-N-oxide.

Apart from the importance for its own sake the present analysis shows that the reactivity of an organic compound is determined not by the structure, as it is written on paper, alone, but also by the nature of the medium into which the compound finds itself.

Department of Chemistry, University College of Science,
92 Upper Circular Road, Calcutta-9, India

SADHAN BASU and KANAI LAL SAHA

Eingegangen am 31. Oktober 1957

¹⁾ JAFFE: J. Amer. Chem. Soc. 76, 3527 (1954).