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A NEW,HIGHLY SELECTIVE,TYPE OF AROMATIC SUBSTITUTION.
HOMOLYTIC AMINATION OF PHENOLIC ETHERS.

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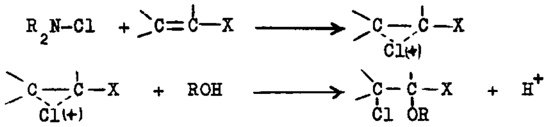
A characteristic feature of the homolytic aromatic substitutions is their poor selectivity,at least in comparison with the heterolytic substitution[1].

We wish to report here a new homolytic aromatic substitution,characterized by high selectivity.We have recently pointed out that,owing to their electrophilic character,the amino-radicals,generated by the redox systems N-chloroamine and ferrous or cuprous salts,

$$R_2N\text{-}Cl + Fe^{++} \longrightarrow R_2N\cdot + FeCl^{++}$$

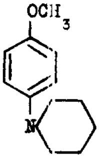
are able to attack olefinic bonds with good yields ,except when these are conjugated with strong electron-withdrawing groups[2].On the other hand, if the nucleophilic character of the olefin is increased by electron-releasing groups (X),the electrophilic chlorination of the olefin prevails



This is,for example,the case of vinyl ethers.

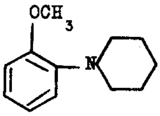
Now we have tested a few aromatic derivatives in which the nucleophilic character of the ring is increased by electron-releasing groups (dimethylaniline and phenolic ethers).While the ionic interaction prevails with dimethylaniline and results in ortho-para chlorination, the direct amination of the aromatic ring takes place in the case of phenolic ethers.

With anisole the reaction was carried out in methanolic solution with ferrous sulphate and furthermore without any solvent with ferrous lactate as a reducing salt.Reaction products were determined quantitatively by gas-liquid chromatography and characterized as picrates. In methanolic solution the yield is 11% based on N-chloroamine (N-chloropiperidine) and the following reaction products are present:



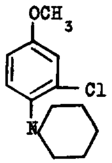
I 90,5%

(picrate m.p.181°)



II 4,5%

(picrate m.p.128°)



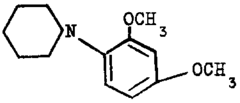
III 5%

(picrate m.p.154°)

No meta isomer was found;N-chloropiperidine is mostly reduced to amine by ferrous salt

With ferrous lactate and anisole without any other solvent the amination yield increases(19,5%),but also the chlorination of the amine produced increases considerably;the ortho-para isomer ratio does not change; I,II and III are present in 37,6% , 4,4% and 58% respectively.

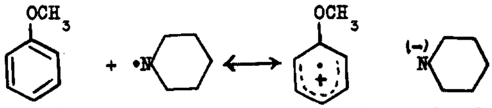
With 1,3-dimethoxybenzene in methanol the yield based on N-chloropiperidine increases (25,5%) and the gas-liquid chromatography shows the presence of only two products.I.R. and elementary analysis of the main product (93%) and its picrate(m.p.174°) and the results obtained with anisole are in accordance with the structure IV



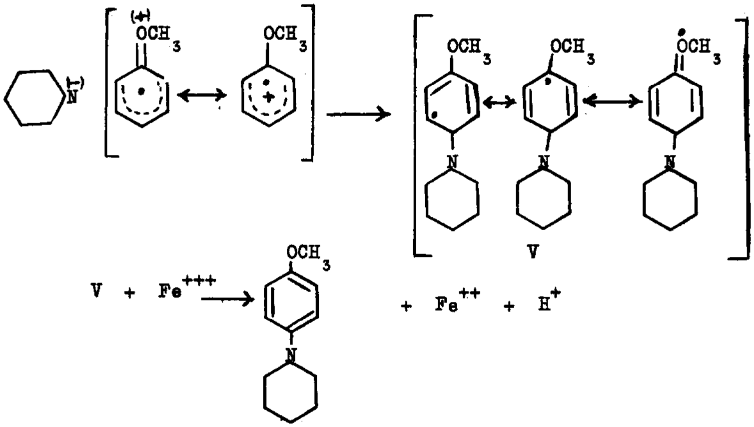
IV

In this case we have observed no chlorination of the amine and the side product (7%),not isolated,is probably 1-piperidino-2,6-dimethoxybenzene.

The activation (unsubstituted benzene or benzene substituted with electron-withdrawing groups do not react) and the orientation show clearly that the polar features are very important in this radical interaction:they can be explained by a charge-transfer phenomenon



with contribution to the transition state of polar forms,stabilized by electron-releasing groups



Such a high para-ortho isomer ratio is unusual and can be attributed to steric factor;actually in homolytic aromatic substitutions the ortho isomer generally predominates[1].Thus,in the hydroxylation of the anisole by hydroxyl radical,generated by Fenton's reagent,or cuprous ion and hydrogen peroxide or ultraviolet irradiation of hydrogen peroxide, the isomer distribution is 84% ortho and 16% para,whereas the meta isomer is absent,owing to the electrophilic nature of the hydroxyl radical[3].

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