

PHENYLATION OF N,N-DIALKYLANILINE-N-OXIDES

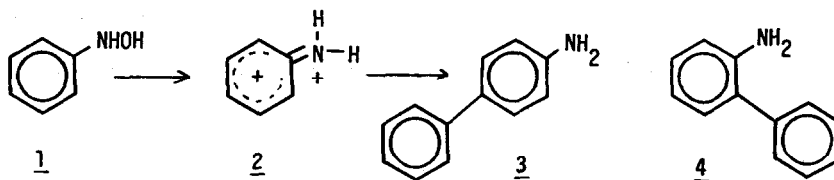
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(Received in Japan 27 October 1976; received in UK for publication 23 November 1976)

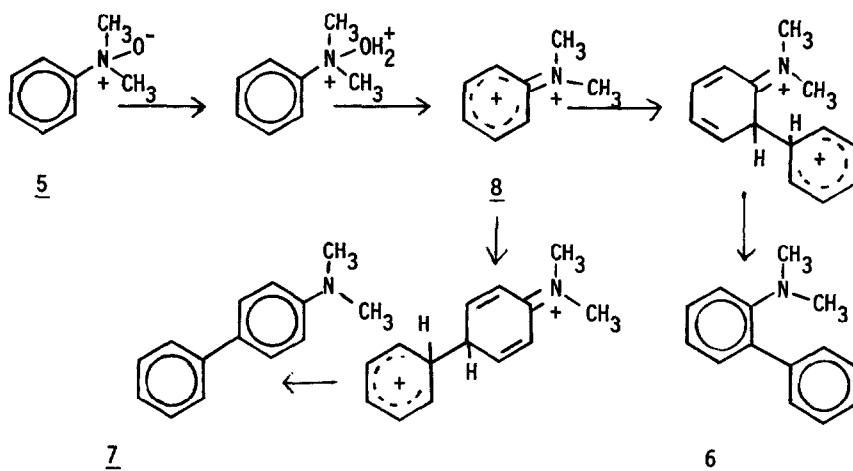
In the acid-catalyzed reaction of arylhydroxylamines with benzene, which yields 2- and 4-aminobiphenyls,^{1,2,3} we proposed a mechanism which involves protonated anilenium ions(2).³ However, we could not convincingly eliminate other possible mechanisms. If the dication (2) is



involved in the reaction, N,N-dialkylaniline-N-oxide which might give an N,N-dialkyl dication should react with benzene giving N,N-dialkylaminobiphenyls in a similar fashion to the case of arylhydroxylamines. The present short communication may give evidence for the dication mechanism, or a related transition state, and illustrate a synthetic application of the reaction.

A mixture of N,N-dimethylaniline N-oxide (5), benzene (60 equiv) and trifluoromethanesulfonic acid (TFSA, 10 equiv) was stirred for 24 hr at room temperatures. The products isolated were 2-(N,N-dimethylamino)biphenyl (6, 4-6%) and 4-(N,N-dimethylamino)biphenyl (7, 64-76%). In the presence of trifluoroacetic acid (TFA) instead of TFSA at the refluxing temperature, the sole product was N,N-dimethylaniline, probably formed from the homolytic cleavage of N⁺-OH. A possible phenylation process is given in Scheme 1. The di-protonation on the oxygen atom followed by elimination of water gives a doubly charged ion, N,N-dimethylimmonium-benzenium ion (8), which then reacts with benzene. The same ionic species has been suggested in the

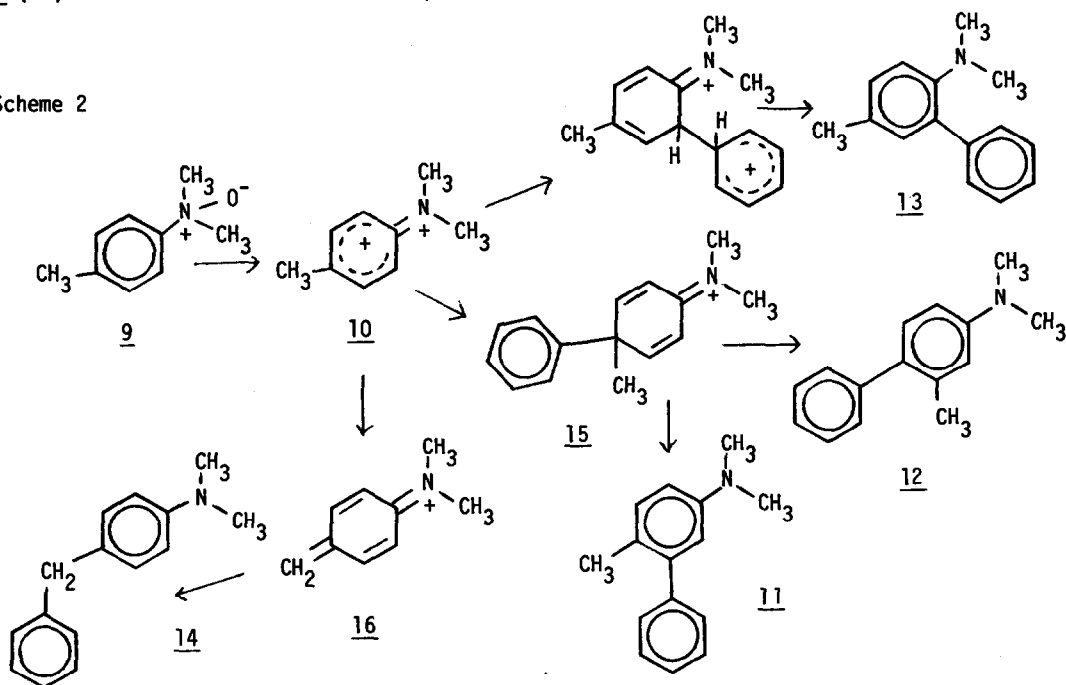
Scheme 1



electrochemical oxidation of N,N-dimethylaniline.⁵

A very similar reaction to that of 4-tolylhydroxylamine,³ was observed in the acid-catalyzed reaction of N,N-dimethyl-p-toluidine-N-oxide (9) with benzene. The major product was 5-(N,N-dimethylamino)-2-methylbiphenyl (11, 46%). Isomeric products, 12 (2%), 13 (8%), and 14 (4%) were also obtained. The composition of products closely relates to that of the

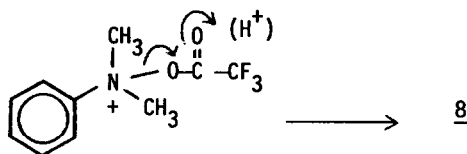
Scheme 2



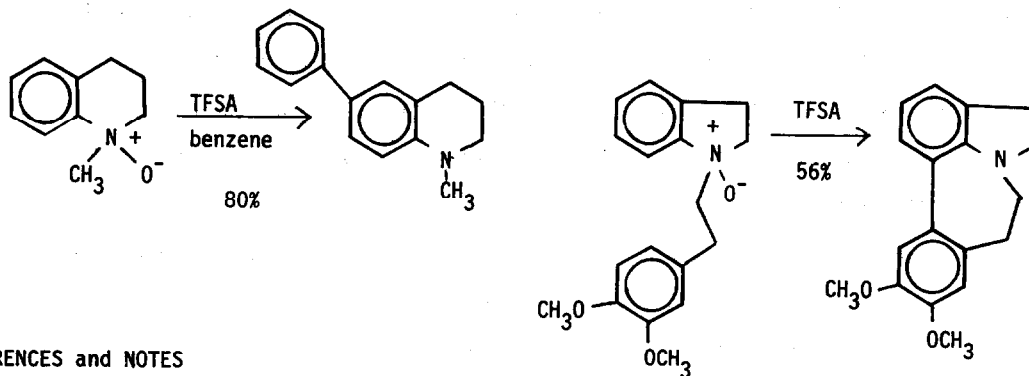
reaction products in the case of 4-tolylhydroxylamine. This strongly suggests that the same kind of intermediate participates in both reactions. The Scheme 2 shows a possible pathway to the products. The major products, 11 and 12 are formed by the rearrangement from an intermediate cyclohexadienimmonium ion (15). The compound 14 is formed by the reaction of benzene with the triene (16).⁶

Thus, we can eliminate possibilities which involve a nitrene, a nitrenium ion, and a benzenium ion⁷ (Scholl type reaction) with certainty. The possibility of a concerted nucleophilic attack by benzene on the developing positive charge simultaneous with the departure of water has been considered. However, such an SN_2 like mechanism may not account for the following results: (i) the attack of benzene on the ipso (tertiary) carbon in the reactions of 9 and of p-substituted phenylhydroxylamines,³ and (ii) the high m/p ratio in the reaction of 1 with toluene which suggests a very reactive species is involved.³ We believe that the above and additional evidences⁸ provide for an SN_1 -like formation of an intermediate, or N-O bond cleavage has to have proceeded to a large extent to account for the phenylation.

In addition to the acid-catalyzed reaction, trifluoroacetic anhydride catalyzes the reaction of N,N-dimethylaniline-N-oxide with benzene. The yield of 4-dimethylaminobiphenyl (7) is low (1-2%) in the presence or absence of sodium bicarbonate since the reaction competes with acetoxy migration to the ortho position.¹² In the presence of TFA (2-4 equiv) in addition to trifluoroacetic anhydride, however, the yield increased to 7%. Acetic anhydride did not work. This result showed that the heterolytic cleavage of the N-O bond can be caused by conversion to such good leaving groups as $OCOCF_3$ or protonated $OCOCF_3$.

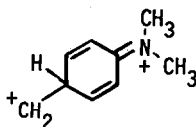


Besides the mechanistic interest, the present reaction has a potential application to synthetic problems. N-Methyl-6-phenyl-1,2,3,4-tetrahydroquinoline and apoerysopine dimethyl ether¹³ were prepared by the phenylation reaction.



REFERENCES and NOTES

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6. A rearranged primary carbonium ion,



may be an alternative active species in such a very strong acidic medium.

16 can be derived directly from the protonated N-oxide also.

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8. The following facts and observations must be considered also: (a) in the strong acid-catalyzed phenylation of nitrosobenzene,⁹ the initial active species is diprotonated nitrosobenzene, (b) phenylhydrazine gave 2- and 4-aminobiphenyls, and the ratio of 2-/4- is close to that in the reaction of phenylhydroxylamine, suggesting the same intermediate participates in both reactions, (c) direct observations of protonated nitrenium ions¹⁰ and other related species.^{5,11}
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