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A TRIFLUOROMETHANESULFONIC ACID-CATALYZED REACTION OF ARYLHYDRAZINES WITH BENZENE

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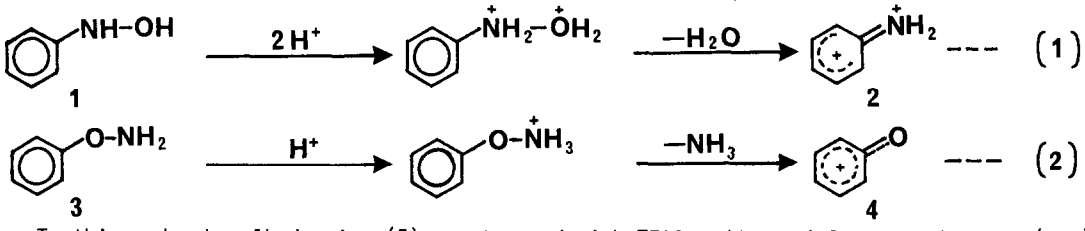
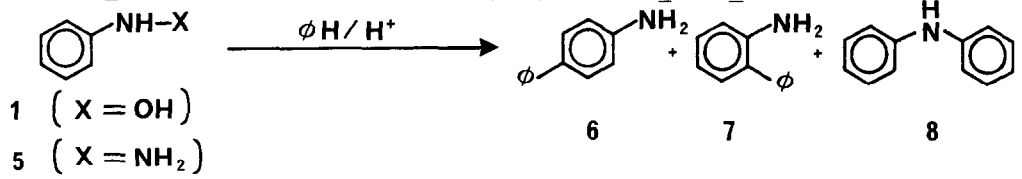
Abstract: Arylhydrazines reacted with benzene in the presence of trifluoromethanesulfonic acid (TFSA) to give aminobiphenyls. This is a general method for the synthesis of aminobiphenyls.

N-Phenylhydroxylamine (1) gives an iminium-benzenium dication (2) after N,O-diprotonation by trifluoromethanesulfonic acid (TFSA) followed by elimination of a water molecule (eq 1),[1] and O-phenylhydroxylamine (3) gives a phenoxenium ion (4) by N-protonation and elimination of an ammonia molecule (eq 2).[2] It seems very likely that phenylhydrazine having an N-N bond instead of the N-O bond of hydroxylamine would give 2 by a similar process, because diprotonations of hydrazine, hydrazobenzene and azobenzene have been reported.[1,3,4]



(1) --- (2)

To this end, phenylhydrazine (5) was treated with TFSA and/or trifluoroacetic acid (TFA) in benzene.[5] The reaction conditions and results are summarized in the Table. The results of TFA- and TFSA-catalyzed reaction of N-phenylhydroxylamine (1) with benzene were reported previously,[1,6] and are also shown in the Table (runs 1-3). The TFSA-catalyzed reaction of 1 with benzene gave diphenylamine (8) as a main product (run 1), and increasing the acidity of the catalyst by adding a small amount of TFSA (a stronger acid than TFA) to TFA decreased the yield of 8 and increased the yields of biphenylamines (6 and 7) (run 2). When TFSA was sub-



1 (X = OH)
5 (X = NH2)

6 7 8

Table Acid-Catalyzed Reactions of N-Phenylhydroxylamine (1) and Phenylhydrazine (5) with Benzene

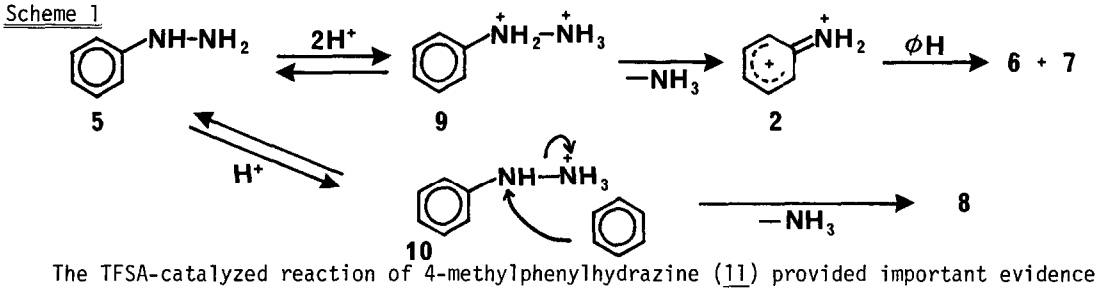
Run	Reaction Conditions						Products (%)[b]		
	Compound	benzene	TFSA	TFA	temp	time	6	7	8
1	1	9.0[a]	0[a]	10.0[a]	RT	12 h	9	8	56
2	1	22.5	2.3	25.0	5°C	30 m	46	25	14
3	1	60.0	20.0	0	5°C	30 m	48	23	1
4	5	60.0	0	30.0	80°C	24 h	0	0	0[c]
5	5	60.0	20.0	10.0	80°C	5 h	5	2	2[c]
6	5	60.0	30.0	0	80°C	6 h	42	22	20
7	5	60.0	30.0	0	40°C	24 h	39	22	17

a; Moles per mole of 1 or 5. b; Based on VPC. c; Unreacted 5 was recovered.

stituted for TFA in the reaction of 1, only biphenylamines were formed (run 3). In contrast to the reaction of 1, acid-catalyzed reactions of 5 were very slow. Using only TFA as the catalyst, no reaction occurred even after heating at 80°C for 24 hr (run 4). When TFSA was used in the reaction, heating and a long reaction time were required (80°C, 6 hr or 40°C, 24 hr), and a mixture of aminobiphenyls (∿60%) and diphenylamine (∿20%) was obtained (runs 6 and 7).

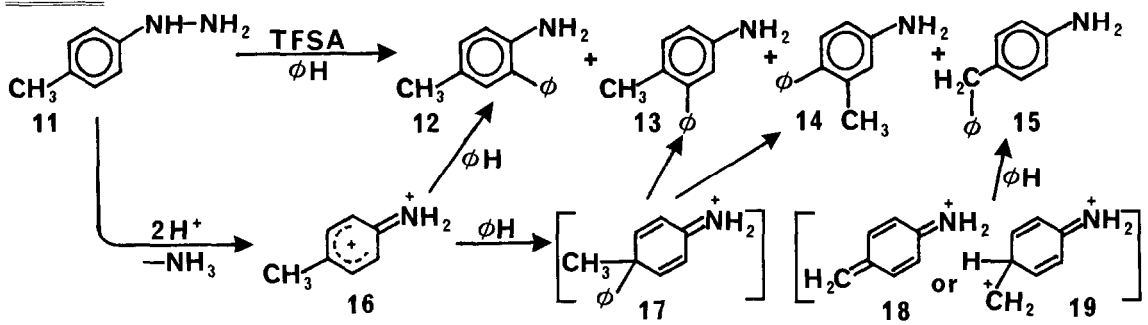
In the case of the reaction of 1 with benzene, the formation of 6 and 7 can be explained by an electrophilic attack of 2 on benzene, and the formation of 8 can be explained by an S_N2-like nucleophilic attack of the benzene molecule on the nitrogen atom of the O-protonated N-phenylhydroxylamine. Ortho/para ratios of biphenylamines formed in the reactions of 1 and 5 were about the same (∿0.5), so that the same intermediate, i.e., 2, was also deduced to be in the TFSA-catalyzed reaction of 5. Therefore a similar mechanism for the reaction of 5, where an ammonia molecule is eliminated instead of a water molecule, might be justified (Scheme 1). The ammonia molecule is a poorer leaving group than the water molecule, so that the formation of 2 from 9 was slow and the nucleophilic attack of benzene on the nitrogen atom of the mono-protonated phenylhydrazine (10) competed with the formation of 2.

Scheme 1



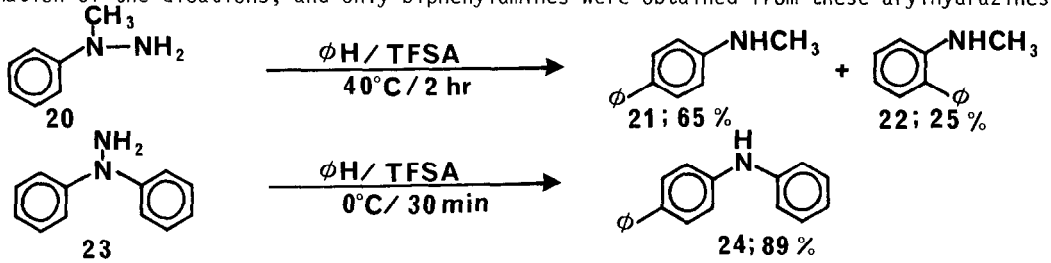
The TFSA-catalyzed reaction of 4-methylphenylhydrazine (11) provided important evidence concerning the mechanism of the reaction of phenylhydrazines. 11 reacted with benzene in the presence of TFSA (30 eqt) faster than 5 (at 5°C for 30 min), and gave 12 (36%), 13 (26%), 14 (trace) and 15 (9%) (Scheme 2). Although 13 may formally be regarded as being produced by

Scheme 2

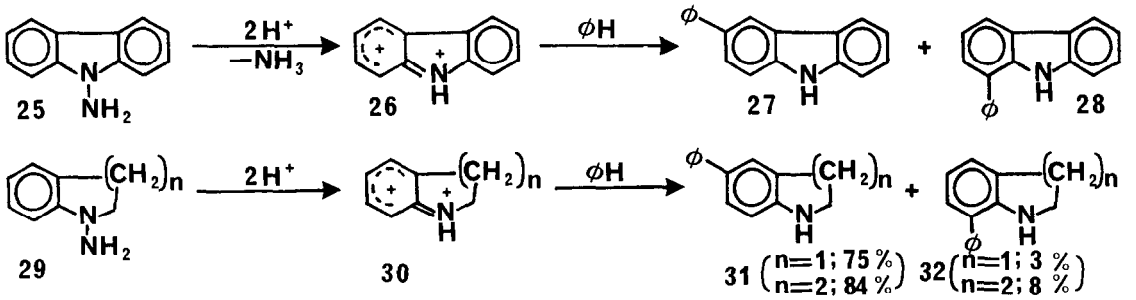


meta substitution, the presence of 14 in the reaction mixture suggests that 13 and 14 are formed by rearrangement of an intermediate (17), the phenyl group being a better migrating group than the methyl group. The formation of 15 is considered to arise from the reaction of 18 or 19 with benzene. A similar mixture of products corresponding to 12, 13, 14 and 15 was also obtained from the TFSA-catalyzed reaction of N-(4-methylphenyl)hydroxylamine and N,N-dimethyl-p-toluidine N-oxide with benzene.[1,7] The result of the reaction of 11 strongly supports the formation of iminium-benzenium dications from phenylhydrazines in TFSA.

α-Methylphenylhydrazine (20) also smoothly reacted with benzene (60 eqt) in the presence of TFSA (30 eqt) and gave methylaminobiphenyls (21 and 22) and no diphenylamines. Using a similar procedure to the above, N-aminodiphenylamine (23) also reacted with benzene to give 4-phenyldiphenylamine (24) in 89% yield. Introducing a methyl or a phenyl group at the α-nitrogen atom or the para position of the benzene ring of 5 seemed to accelerate the rate of formation of the dications, and only biphenylamines were obtained from these arylhydrazines.

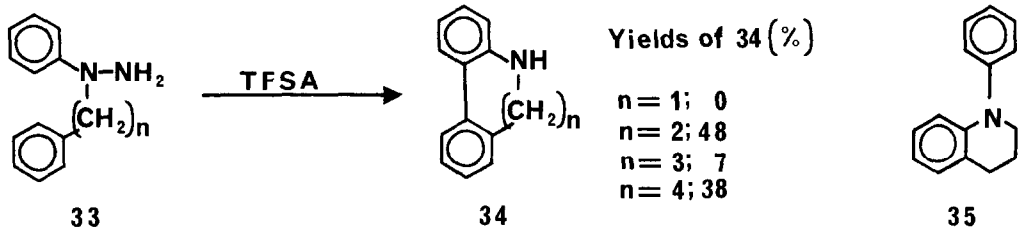


Next we applied this reaction to the phenylation of some heterocyclic compounds. N-Aminocarbazole (25), which was prepared by N-nitrosation of a carbazole followed by reduction with $TiCl_4/Mg$,[8] reacted with benzene (60 eqt) in the presence of TFSA (30 eqt) at 5°C for 1 hr to give phenylcarbazoles (27; 54% and 28; 15%). By a similar procedure, N-aminoindoline (29;



n=1) and N-amino-1,2,3,4-tetrahydroquinoline (29; n=2) were also phenylated. The sites of phenylation of these compounds were fully characterized by ^{1}H-NMR and could be explained in terms of involvement of the iminium-benzenium dications (26 and 30).

Finally we wish to describe an application of this process to intramolecular phenyl-phenyl bond formation of hydrazines (33)[9] to cyclic compounds (34). Although N-amino-N-benzylaniline (33; n=1) did not cyclize under any conditions tested, treatment of N-amino-N-phenethylaniline (33; n=2; 2.6 mmole) in TFSA (25 mL) at 80°C for 30 min gave the desired dibenz[b,d]azepine (34; n=2) in 48% yield. N-Amino-N-phenylpropylaniline (33; n=3) also cyclized to dibenz[b,d]azocine (34; n=3) in a low yield, accompanied by 29% yield of N-phenyl-1,2,3,4-tetrahydroquinoline (35) formed by cyclization at the nitrogen atom of 33. N-Amino-N-phenylbutylaniline (33; n=4) also cyclized to dibenz[b,d]azonine in a yield of 38%.



33 34 35

We have thus demonstrated that phenylhydrazine gives the iminium-benzenium dication, and have described some applications to the synthesis of aminobiphenyls. This procedure has the advantage that arylhydrazines are more redily prepared than N-arylhydroxylamines, so that this is a convenient method for the synthesis of aminobiphenyls as well as the reductive phenylation of nitroarenes.[10]

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References and Notes

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