Influence of Substituent Groups on Nuclear Reactivity in Formations of Substituted Biphenyls through Reactions of Aromatic Diazo and Cognate Compounds with Aromatic Liquids. I. The Nitro Group[1]

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Diazo hydroxides and *n*-nitrosoacetylarylamines decompose in an aromatic liquid to yield biphenyls according to the following formulae:

$$ArN_2OH \quad + Ar'H \longrightarrow ArAr' + N_2 + H_2O,$$

$$ArN(NO)Ac + Ar'H \longrightarrow ArAr' + N_2 + AcOH.$$

The preparative aspects of these reactions have recently been fully reviewed by Bachmann and Hoffman.(2) As regards the mechanism of the formation of biaryls there has been amassed a considerable number of evidences to warrant the conclusion that the reaction takes place through a mechanism involving free aryl radicals which, having been produced by decomposition of diazo hydroxides or nitrosoacetylarylamines, react with aromatic compounds giving corresponding biphenyls. In support of the free radical mechanism is, among others, the observation that para and ortho substituted biphenyls are invariably formed in these reactions irrespective of the nature of the substituent groups, a fact which is unaccountable on the basis of the usual polar influences of substituents accepted as operative in the substitution by kationoid or anionoid reagents. Furthermore, it is striking that nitro group was found to exert its influence by activating the benzene nucleus to which it is attached in the substitution reaction by phenyl radical as was shown by the fact that nitrobiphenyls were obtained in a yield greater than methylbiphenyls in a competitive reaction in a mixture of nitrobenzene and toluene.(3)

With a view to further elucidating the nature of influences of substituent groups in the substitution by the aryl radical a series of analytical investigations of these reactions has been undertaken in this laboratory, and the results obtained from the investigations on the influence of the nitro group are described in the present report. By determining the ratio in which biphenyl and three isomeric nitrobiphenyls were formed by the reactions of diazobenzene hydroxide and nitrosoacetanilide respectively in a mixture of benzene and nitrobenzene the reactivities of the various nuclear positions of nitrobenzene relative to that of benzene could approximately be estimated.

Results and Discussion

Careful fractionation of a reaction mixture from nitrosoacetanilide and nitrobenzene at 20° yielded a mixture of isomeric nitrobiphenyls in yields varying from 30 to 37% based on the nitrosoacetanilide utilized. From this mixture readily crystallizable *p*-nitrobiphenyl was separated as much as possible and weighed after recrystallization. As the isolation of the other isomerides turned out difficult, recourse was made to the estimation of *m*-nitrobiphenyl by titration with titanous chloride and subsequently with a bromide-bromate mixture according to the method, developed by Francis and Hill,(4) with a slight modification. Thus, it was found that *m*-nitrobiphenyl constituted as much as 23% of the original mixture, and the *p*-nitrobiphenyl which was isolated as a pure specimen amounted to 17%. The remaining 60% were regarded as composed of the whole of the ortho isomeride formed and of that part of para isomeride which could not be isolated.

When nitrosoacetanilide was decomposed in a mixture of nitrobenzene and benzene (in a molar ratio of 1:30:60), biphenyl and nitrobiphenyls were obtained in yields of 4.6 and 19.7%, respectively, on the basis of the nitrosoacetanilide used. It was found by the same

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(2) W. E. Bachmann and R. A. Hoffman, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, 1944, p. 224.

(3) W. S. M. Grieve and D. H. Hey, *J. Chem. Soc.*, **1934**, 1797.

(4) A. W. Francis and A. J. Hill, *J. Am. Chem. Soc.*, **46**, 2498 (1924).

procedure as above that the nitrobiphenyl mixture consisted of 22% of the meta and of at least 19% of the para isomerides, the remaining 59% being made up of the ortho and para isomerides. The isomeric ratio from this competitive reaction agrees well with those obtained in the experiments with nitrobenzene as a sole component of the solvent. Taking the average of these figures and assuming the isomeric ratio to be $o:m:p = 58:23:19$, we estimate the relative reaction rate constants, which may be called reactivities, of the ortho, meta and para positions of the nitrobenzene nucleus to be 15, 5.8 and 9.8, respectively, relative to the rate constant at one position of the unsubstituted benzene nucleus taken as unity. Since the attack on the aromatic compound by the substituting entity, in whatever form it may react, is unimolecular with respect to the aromatic compound, the principle underlying our estimation is similar to that set forth by Ingold and Smith(5) and therefore it need not be described here. In the above calculation the ortho-para ratio was assumed to be 58:19 on the basis of the amount of the p-nitrobiphenyl isolated as a pure specimen, and the actual ortho-para ratio must therefore be smaller. In one experiment, o-nitrobiphenyl amounting to 21% of the total yield of nitrobiphenyls was isolated from the mixture of nitrobiphenyls from which para isomeride had already been separated. If this figure, in place of 58%, is taken to express the amount of the ortho isomeride actually formed, and consequently 56, in place of 19%, that of the para isomeride, the reactivities of the ortho and para positions will be altered to 5.4 and 30, respectively. The true reactivity lies, therefore, between 5.4 and 15 for the ortho, and between 9.8 and 30 for the para positions.

From the reaction of diazotized aniline in the presence of aqueous sodium hydroxide with nitrobenzene at 10° there was obtained a mixture of nitrobiphenyls in a yield of 15% based on the aniline used. The percentages of the isomerides formed were estimated to be 46 for the ortho, 18 for the meta and 36% for the para compounds, and the value for the para isomeride being based on the amount isolated as a pure specimen, the figures for the ortho and para nitrobiphenyls are subject to the same uncertainty as in the case described above.

When diazotized aniline was decomposed in a mixture of nitrobenzene and benzene (in a molar ratio of 1:30:60), biphenyl and a mixture of nitrobiphenyls were obtained in yields, based on the aniline used, of 5.2 and 12.7%, respectively. m-Nitrobiphenyl as titrated amounted to 20.3% of the total nitrobiphenyls and the para isomeride actually isolated to 34.4%. Assuming that the isomerides are formed in the ratio $o:m:p = 46:19:35$, the reactivities of the various positions of the nitrobenzene nucleus are estimated to be 6.6, 2.8 and 11 for the ortho, meta and para positions, respectively, relative to one position of the unsubstituted benzene nucleus.

Although ortho-para substitutions were observed in most cases of the formation of biaryls by the reaction under discussion, it was reported by some workers that the reaction between diazobenzene hydroxide and ethyl benzoate gave all of the possible isomeric ethyl biphenylcarboxylates,(6) and that in the decompositions of 4-nitrosoacetaminobiphenyl in both chloro- and bromo-benzene the substitution by the biphenyl group took place at the meta as well as at the ortho and para positions in the halogenobenzene nucleus.(7) The present results afford another example of the formation of the meta isomeride in a condiderable quantity along with the ortho and para isomerides. In view of these facts together with those that will be later reported from this laboratory it seems that the concomitant formation of all three isomerides in these reactions is the general rule. It is significant too that even the meta position of nitrobenzene was found to be more reactive than the benzene nucleus itself towards the substituting agent formed by the decomposition of nitrosoacetanilide and diazobenzene hydroxide.

Experimental

Materials.—n-Nitrosoacetanilide was prepared according to O. Fischer(8) by introducing into a solution of acetanilide in glacial acetic acid nitrous fumes generated by reducing concentrated nitric acid with potato starch and by adding the dark green solution thus obtained to a large quantity of water. The precipitated nitrosoacetanilide was separated from the aqueous layer, washed several times with water and dried on a porous plate. Samples prepared in this way melted at 50-51° with decomposition. Benzene and nitrobenzene were purified by repeated fractionations through a Vigreux

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(5) C. K. Ingold and M. S. Smith, *J. Chem. Soc.*, **1938**, 905.

(6) D. H. Hey, *J. Chem. Soc.*, **1934**, 1967.

(7) H. France, I. M. Heilbron and D. H. Hey *J. Chem. Soc.*, **1938**, 1364.

(8) O. Fischer, *Ber.*, **9**, 463 (1876).

column.

Determination of *m*-Nitrobiphenyl.— The amount of *m*-nitrobiphenyl in a mixture of isomeric nitrobiphenyls was determined by titration with a standard titanous chloride solution and subsequently with a bromide-bromate mixture. The procedure adopted was essentially that of Francis and Hill.(4) However, ethyl alcohol proposed by them as a solvent proved inadequate because it consumed bromine. After several experiments, it was found that glacial acetic acid which was refluxed with 2% of chromium trioxide and then twice distilled was a satisfactory solvent for the determination of nitrobiphenyls. The reduction was carried out in an atmosphere of carbon dioxide with boiling for fifteen minutes, and the bromination at 5 to 10°. Separate experiments with pure specimens of nitrobiphenyls showed that the number of bromine atoms taken up could be determined within the accuracy of 2%.

Decomposition of Nitrosoacetanilide.— When nitrosoacetanilide (0.5 g.) was dissolved in 27 cc. of nitrobenzene at 20°, decomposition took place evolving nitrogen without a perceptible rise in temperature. A set of twenty reaction mixtures similar to the above was prepared and allowed to react simultaneoulsly. After a few days, when the reaction had been completed, the reaction mixtures were combined and the nitrobenzene was removed under reduced pressure through a Vigreux column 30 cm. in length. The residue was subjected to further fractionation under reduced pressure, and 4.18 g. of a reddish-brown viscous oil passed over at 150 to 185° at 15 mm. of mercury. The oil deposited crystals of *p*-nitrobiphenyl, which on recrystallization from petroleum ether melted at 113° (yield 0.560 g.). The mother liquor of recrystallization and the remaining oil were combined and filtered through a column of activated alumina in order to remove a coloring matter. A further crop of *p*-nitrobiphenyl (47 mg.) was obtained by extracting the alumina with alcohol. The remainder was recovered as an oily mixture (3.05 g.), which was analyzed for the nitro group by titration with a standard titanous chloride and was found to contain only nitrobiphenyls. Subsequent titration with a bromide-bromate mixture showed that the mixture contained 28% of *m*-nitrobiphenyl.

In one experiment a fraction, which distilled after a substantial part of nitrobenzene had been removed, was reduced with tin and hydrochloric acid to remove nitrobenzene. Any traces of biphenyl which might have resulted from the dimerization of phenyl radicals were not detected.

The competitive reaction was accomplished by dissolving one gramme of nitrosoacetanilide in a mixture of 18.7 cc. of nitrobenzene and 32.7 cc. of benzene at 20°. Nine of such reaction mixtures were combined and worked up similarly to the experiment described above. That part of biphenyl which passed over with the vapor of nitrobenzene was recovered by converting the latter into aniline by treatment with tin and hydrochloric acid.

Decomposition of Diazobenzene Hydroxide.— To a stirred mixture of 430 cc. of nitrobenzene and diazotized aniline prepared from 13 g. of aniline, 33 cc. of concentrated hydrochloric acid (d. 1.17), 10.5 g. of sodium nitrite and 26 cc. of water there was added dropwise a solution of 14.4 g. of sodium hydroxide in 75 cc. of water in the course of thirty minutes, the temperature being kept at 8-10°, and stirring was continued for further five hours. The product separated from the aqueous layer was worked up as before. In the competitive reaction a mixture of 215 cc. of nitrobenzene and 373 cc. of benzene was used for the diazotized aniline from 6.5 g. of aniline. Products from two of such reactions were combined and worked up.

Summary

The reactions of both *n*-nitrosoacetanilide and diazobenzene hydroxide with nitrobenzene give all three isomeric nitrobiphenyls, whereas the formation of only the ortho and para isomerides has been reported in the literature.(3) All the nuclear positions of nitrobenzene are more reactive than that of benzene towards the substituting phenyl radical.

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