Influence of Substituent Groups on Nuclear Reactivity in Formation of Substituted Biphenyls through Reactions of Aromatic Diazo and Cognate Compounds with Aromatic Liquids. III. The Substitution of Nitrobenzene by the p-Anisyl Radical

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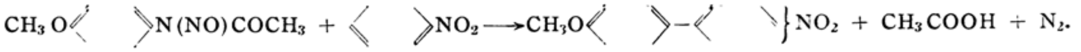
In a previous paper[1] in this series, it has been shown that the ortho, para and even meta positions of nitrobenzene are activated by the nitro group over the benzene nucleus itself towards the substitutive attack by the phenyl radical produced by the decomposition of N-nitrosoacetanilide or of benzenediazo hydroxide, the order of the reactivities of the three isomeric positions being para$>$ortho$>$meta. Augood, Hey and Williams[2] have later reported on the phenylation of nitrobenzene by the decomposition of benzoyl peroxide, the trend of the influence of the nitro group being similar to that found in the above investigation. It seemed of interest to examine how a substituent placed in the phenyl radical alters the nature of the influence of the substituent in an aromatic compound to be attacked by the radical. The present paper deals with the results of experiments on the substitution of nitrobenzene by the *p*-anisyl radical formed by the decomposition of N-nitroso-*p*-acetanisidide, which yields isomeric nitro-4-methoxybiphenyls as follows:



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[1] O. Simamura, T. Inukai and M. Kanazashi, This Bulletin, **23**, 205 (1950).

[2] D. R. Augood, D. H. Hey and G. H. Williams, *J. Chem. Soc.*, **1952**, 2094.

N-Nitroso-*p*-acetanisidide (7.6 g., 0.04 mol.) was decomposed at room temperature in 246 g. (2 mol.) of nitrobenzene giving 0.82 g. of 4-methoxy-4′-nitrobiphenyl, m. p. 110°, and 1.29 g. of 4-methoxy-2′-nitrobiphenyl, m. p. 60° (for the identification of these compounds see the experimental part). When 15 g. (0.077 mol.) of N-nitroso-*p*-acetanisidide was decomposed in a mixture of 288 g. (2.34 mol.) of nitrobenzene and 360 g. (4.62 mol.) of benzene and the reaction mixture worked up as described in the experimental part, 4-methoxybiphenyl, 4-methoxy-4′-nitrobiphenyl and 4-methoxy-2′-nitrobiphenyl were obtained in yields of 2.56 g., 2.38 g. and 3.85 g., respectively, that is, in a millimolar ratio of 13.9 : 10.4 : 16.8. The ratio of the two isomeric methoxynitrobiphenyls formed in the competitive reaction in a mixture of nitrobenzene and benzene was thus found to be in good agreement with that in the reaction in nitrobenzene alone. Any trace of 4-methoxy-3′-nitrobiphenyl could not be detected in the product from this reaction.

On the basis of the molar ratio in which the products were formed and of the amount of the reactants competing for the radical the relative reactivities[1] of the ortho, meta and para nuclear positions of nitrobenzene towards the *p*-anisyl radical are calculated to be 7.24, 0, and 8.95, respectively the reactivity of one nuclear position of benzene itself towards the same radical being taken as unity. These values are compared with the corresponding ones for the reactivity towards the phenyl radical (see Table I); it is noted that the trend is alike in both cases, as far as the ortho and para positions are concerned. The meta position of nitrobenzene is, however, completely unreactive towards the attack by the *p*-anisyl radical whereas it is a little more reactive towards the attack by the phenyl radical than benzene itself. It is generally known that the methoxyl group exerts a polar effect on the para carbon atom, which tends to increase electron density at that atom. On the other hand the polar effect of the nitro group is to decrease electron density at the positions ortho and para to the nitro group below that in the benzene nucleus. Accordingly, it might be expected from a simple electrostatic consideration that the substitution by the *p*-anisyl radical will take place preferentially at the ortho and para positions of nitrobenzene. Further, with an electron-releasing methoxyl group in 4 and an electron-attracting nitro group in 2′ or 4′ position, the biphenyls produced will be more stabilized than otherwise, since such a relative orientation of both groups makes possible their mesomeric conjugation with each other; a resulting gain in extra resonance energy will contribute in lowering the energy of activation for the formation of these isomers. All these considerations point to the preponderant formation of 2- and 4-nitro-4′-methoxybiphenyls. However, as is evident from the comparison of the reactivity values towards the *p*-anisyl with those towards the phenyl radical, the effect due to the co-operation between the *p*-methoxyl group in the attacking radical and the nitro group in the molecule being attacked appears to be very small, if any. In view of both this apparent ineffectiveness of the *p*-methoxyl group in influencing the course of the reaction and the considerable reactivity of the meta position of nitrobenzene towards the phenyl radical, the *p*-anisyl radical is excepted to attack also the meta position of nitrobenzene to an appreciable extent. The reason why 4-methoxy-3′-nitrobiphenyl should actually have not been formed is not clear.

TABLE I

RELATIVE REACTIVITIES OF THE ISOMERIC NUCLEAR POSITIONS OF NITROBENZENE.

Source of radical	Relative reactivity			Reference
	o	*m*	*p*	
N-Nitroso-*p*-anisidide	7.24	0	8.95	Present work
Diazotized aniline	6.6	2.8	11	(1)
N-Nitrosoacetanilide	15–5.4	5.8	9.8–30	(1)
Dibenzoyl peroxide	7.0	1.2	7.9	(2)

Experimental

Materials N-Nitroso-*p*-acetanisidide was prepared according to Haworth and Hey[3] by the action of nitrous fumes on *p*-acetanisidide in a mixture of acetic acid and acetic anhydride cooled with ice. The resulting dark green solution was poured into a mixture of ice and water with vigorous stirring, and the pale yellow precipitate of N-nitroso-*p*-acetanisidide was collected, washed

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[3] J. W. Haworth and D. H. Hey, *J. Chem. Soc.*, **1940**, 361.

well with water and dried on a porous plate. Nitrobenzene was purified by distilling commercial nitrobenzene in steam, fractionating through a Vigreux column under reduced pressure, and finally crystallizing the distillate and discarding the liquid portion. Benzene was purified by shaking with concentrated sulfuric acid and then by fractionating through a Vigreux column.

Decomposition of N-Nitroso-*p*-acetanisidide in Nitrobenzene N-Nitrosoacetanisidide (7. 6 g., 0. 04 mol.) was added to 246 g. (2 mol.) of nitrobenzene at room temperature. The solution turned red in ten minutes and the evolution of nitrogen began, which continued for about one hour. After standing two days, the reaction mixture which had become dark brown was distilled under diminished pressure to remove nitrobenzene. Steam-distillation of the residue (10 g.) at 145° gave 3. 2 g. of a distillate, which solidified on standing. This was separated into 0. 82 g. of 4-methoxy-4′-nitrobiphneyl, yellow needles, m. p. 110° (from alcohol) (Found: N, 6. 18; mol. wt., 231 (Rast). Calculated for $C_{13}H_{11}NO_3$: N, 6. 11%; mol. wt., 229. 2), and 1. 29 g. of 4-methoxy-2′-nitrobiphenyl, yellow prisms, m. p. 60° (from alcohol) (Found: N, 6. 31; mol. wt., 235 (Rast). Calc. for $C_{13}H_{11}NO_3$: N, 6. 11 %; mol. wt., 229. 2). The separation was carried out by growing large crystals of the isomers, which could easily be distinguished from each other, from an alcoholic solution and sorting them out. Repeated operations of this procedure gave finally an inseparable mixture, a further separation of which was effected by a chromatography on alumina with a method of fractional elution according to Reichstein and Shoppee.[4]

Identification of Methoxynitrobiphenyls One of the above methoxynitrobiphneyls, m. p. 110°, was identified as 4-methoxy-4′-nitrobiphenyl by oxidizing 0. 08 g. of it with 0. 4 g. of chromic anhydride in acetic acid on a hot water bath to *p*-nitrobenzoic acid.

The oxidation of another isomer, m. p. 60°, gave no isolable product. A synthetic method was therefore followed. Aqueous sodium hydroxide was added dropwise to a stirred mixture of 100 cc. of anisole and diazotized *o*-nitroaniline (5 g.) in dilute sulfuric acid and the mixture stirred for a further one hour. The anisole layer was separated, the anisole removed under diminished pressure, the residue distilled with superheated steam, giving 0. 8 g. of reddish brown distillate, which on distillation in vacuo gave a fraction, b. p. 110° at 5 mm. Hg. When this was dissolved in hot alcohol and the solution let stand, 0. 1 g. of yellow crystals was deposited, which on recrystallization from alcohol gave the same compound m. p. 60-61°, as the above methoxynitrobiphenyl, the mixed melting point showing no depression. Of the theoretically possible isomers of methoxy-2-nitrobiphenyls to be produced by this synthesis only 4′-methoxy compound can also be a product from the decomposion of N-nitroso-*p*-acetanisidide in nitrobenzene. Thus, they were identified as 4′-methoxy-2-nitrobiphenyl.

Decomposition of N-Nitroso-*p*-acetanisidide in a Mixture of Benzene and Nitrobenzene N-Nitrosoacetanisidide (1. 5 g., 0. 077 mol.) was added to a mixture of 360 g. (4. 62 mol.) of benzene and 288 g (2. 34 mol.) of nitrobenzene. The reaction took place as described for the run in nitrobenzene alone. Benzene and nitrobenzene were removed from the reaction mixture under diminished pressure yielding 32 g. of residue, which gave 4. 2 g. of solid (A) and further 10. 2 g. of partly solidified distillate (B) on steam-distillation at 120 to 200°. Fraction A gave 4-methoxybiphenyl, m. p. 88°, on recrystallization from alcohol. The solid substance in B was identified with 4-methoxy-4′-nitrobiphenyl. The separation of the two isomers was carried out as before first by sorting out crystals and then by chromatography of the residues from mother liquors of all recrystallizations. Thus the crystalline product isolated were in all 2. 56 g. of 4-methoxybiphenyl, 2. 38 g. of 4-methoxy-4′-nitrobiphenyl and 3. 85 g. of 4-methoxy-2′-nitrobiphenyl. Further, the chromatography yielded 0. 70 g. of a brown oil, which could not be crystallized. As it was suspected that the missing isomer, 4-methxy-3′-nitrobiphenyl, might be present in this oil, it was treated with potassium permanganate in pyridine, but no acidic substance was isolated. The action of 0. 18 g. of anhydrous aluminium chloride on 0. 3 g. of this oil in 100 cc. of nitrobenzene below 120° followed by decomposition with water produced no crystalline compounds. The oily product was dissolved in alkali, heated with 0. 3 g. of potassium permanganate, the mixture acidified and extracted with ether. The ethereal solution was shaken with aqueous sodium carbonate, and the aqueous layer gave traces of benzoic and *o*-nitrobenzoic acids on acidification. *m*-Nitrobenzoic acid could not be detected.

Summary

The decomposition of N-nitroso-*p*-acetanisidide in nitrobenzene at room temperature yielded 4-methoxy-4′-nitrobiphenyl and 4-methoxy-2′-nitrobiphenyl in a ratio of 1: 1. 6. From the result of a similar experiment in a mixture of nitrobenzene and benzene, which compete for the *p*-anisyl radical produced

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[4] T. Reichstein and C. W. Shoppee, *Discussions Faraday Soc.*, No. 7, 305 (1949).

from N-nitroso-*p*-acetanisidide, the relative reactivities of the ortho, meta and para positions of nitrobenzene towards the *p*-anisyl radical are found to be 7.24, 0, and 8.95, respectively, the reactivity of one nuclear position of benzene towards the same radical being taken as unity.

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