# *Influence of Substituent Groups on Nuclear Reactivity in the Formation of Substituted Biphenyls by Reaction of Aromatic Diazo and Related Compounds with Aromatic Liquids. V. Phenylation of Nitrobenzene and Anisole*

By Takashi INUKAI, Katsumi KOBAYASHI and Osamu SIMAMURA

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A semi-quantitative determination of the partial rate factors for nitrobenzene in the homolytic phenylation by phenyl radicals produced by decomposition of *N*-nitrosoacetanilide and of diazobenzene hydroxide was reported in Part I(1) of this series. Subsequent quantitative experiments(2) on various substiuted benzenes using column chromatography, spectrophotometry, etc., showed that the reactivity towards the phenylation differs rather slightly from compound to compound. Consequently for the comparison of the values of partial rate factors obtained from competitive phenylation to be significant it became necessary to improve the precision of the product analysis. We accordingly have adopted the radioisotope dilution analysis as reliable means accurate enough for the desired determination, and we now report the partial rate factors for phenylation of nitrobenzene and of anisole obtained by this method.

*N*-Nitrosoacet(anilide-$^{14}$C) was allowed to decompose in a large excess of a mixture of known amounts of benzene and nitrobenzene at 20°C. The reaction mixture was analyzed for biphenyl and the three isomeric nitrobiphenyls by the isotope dilution method. The results are presented in Table I. The results of a similar experiment in a mixture of benzene and anisole at 20°C are shown in Table II. The partial rate factors, the relative rates compared with the rate for benzene and the isomer distributions derived from the data shown in these tables are listed in Table III.

The high precision of the present analytical method is evident from the agreement of two independent determinations of the yield of biphenyl in any of the three experiments, as will be seen from the last columns of Tables I and II. Such an excellent agreement, however, was not observed in the partial rate factors for nitrobenzene calculated from the data of Exps. 1 and 2. This is deemed not due to defects in the analytical method, but apparently due to incontrollable minor fluctuations in experimental conditions, which we do not intend to study further for the present.

Recently Hey, Orman and Williams(3) redetermined the relative rate of the homolytic

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

2) O. Simamura, T. Inukai and M. Kurata, ibid., 25, 76 (1952); O. Simamura and T. Migita, ibid., 27, 228 (1954); and unpublished results.

3) D. H. Hey, S. Orman and G. H. Williams, *J. Chem. Soc.*, **1961**, 565.

TABLE I. ISOTOPE DILUTION ANALYSIS OF THE PRODUCTS FROM DECOMPOSITION OF *N*-NITROSOACET(ANILIDE-$^{14}$C) IN A MIXTURE OF BENZENE AND NITROBENZENE AT 20.0°C

Experiment 1: *N*-Nitrosoacetanilide (14.45±0.08 mc./mol.), 5.607 mmol.;
Benzene, 666.7 mmol.; Nitrobenzene, 666.7 mmol.

| Portion of the reaction mixture (133.697 g.) | Carrier added | | Specific activity of recovered material mc./mol. | Yield[a] mmol. |
|---|---|---|---|---|
| | Compound | mmol. | | |
| A (42.578 g.) | Biphenyl | 6.472 | 0.286±0.002 | 0.410 |
| | *o*-Nitrobiphenyl | 8.540 | 0.629±0.006 | 1.230 |
| | *p*-Nitrobiphenyl | 5.484 | 0.492±0.005 | 0.606 |
| B (45.335 g.) | Biphenyl | 3.221 | 0.607±0.006 | 0.415 |
| | *m*-Nitrobiphenyl | 2.496 | 0.300±0.003 | 0.156 |

Experiment 2: *N*-Nitrosoacetanilide (14.18±0.07 mc./mol.), 1.844 mmol.;
Benzene, 248.8 mmol.; Nitrobenzene, 275.7 mmol.

| Portion of the reaction mixture (53.384 g.) | Carrier added | | Specific activity of recovered material mc./mol. | Yield[a] mmol. |
|---|---|---|---|---|
| | Compound | mmol. | | |
| A (27.062 g.) | Biphenyl | 3.242 | 0.228±0.002 | 0.105 |
| | *o*-Nitrobiphenyl | 6.803 | 0.390±0.004 | 0.380 |
| | *p*-Nitrobiphenyl | 4.285 | 0.293±0.002 | 0.180 |
| B (26.280 g.) | Biphenyl | 3.197 | 0.226±0.002 | 0.105 |
| | *m*-Nitrobiphenyl | 2.535 | 0.124±0.002 | 0.0452 |

a) The amount of each compound in the total reaction mixture.

TABLE II. ISOTOPE DILUTION ANALYSIS OF THE PRODUCTS FROM DECOMPOSITION OF *N*-NITROSOACET(ANILIDE-$^{14}$C) IN A MIXTURE OF BENZENE AND ANISOLE AT 20.0°C

*N*-Nitrosoacetanilide (14.18±0.07 mc./mol.), 3.883 mmol.;
Benzene, 231.4 mmol.; Anisole, 741.8 mmol.

| Portion of the reaction mixture (98.296 g.) | Carrier added | | Specific activity of recovered material mc./mol. | Yield[a] mmol. |
|---|---|---|---|---|
| | Compound | mmol. | | |
| A (49.030 g.) | Biphenyl | 3.204 | 0.514±0.004 | 0.249 |
| | *o*-Methoxybiphenyl | 7.089 | 0.892±0.008 | 0.954 |
| | *p*-Methoxybiphenyl | 4.013 | 0.299±0.003 | 0.173 |
| B (48.904 g.) | Biphenyl | 3.879 | 0.445±0.004 | 0.253 |
| | *m*-Methoxybiphenyl | 6.123 | 0.281±0.002[b] | 0.249 |

a) The amount of each compound in the total reaction mixture.
b) The radiochemical assay was made on *m*-hydroxybiphenyl.

phenylation of nitrobenzene by phenyl radicals produced by decomposition of benzoyl peroxide and revised the former value[4], which was considered as a maximum value since it was based on results which may be subject to an error due to loss of rather volatile biphenyl during the course of the analysis. Obviously the isotope dilution analysis adopted in the present work is not liable to such errors due to fractionation of components to be determined. The revised value of 2.94 for the relative rate leads to new values for the partial rate factor of 5.5, 0.86 and 4.9 for the *o*-, *m*- and *p*-position, respectively, of nitrobenzene, whereas the present authors' corresponding values are 9.38, 1.16 and 9.05, respectively, for the phenylation by phenyl radicals produced by the decomposition of *N*-nitrosoacetanilide. The discrepancy between these two sets of values could be accounted for partly on the ground that, although both reactions are of the homolytic nature, the detailed mechanism may not necessarily be the same. But a more important cause is probably the difference in reaction temperature; the decomposition of *N*-nitrosoacetanilide was carried out at 20°C, whereas that of benzoyl peroxide at 80°C, and elevation of the reaction temperature would tend to change the partial rate factors towards unity, it being assumed that both reactions proceed

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[4] D. R. Augood, D. H. Hey and G. H. Williams, ibid., 1952, 2094.

TABLE III. PARTIAL RATE FACTORS, RELATIVE RATES AND ISOMER DISTRIBUTION IN PHENYLATION OF NITROBENZENE AND ANISOLE

| Compound PhX | | Partial rate factors | | | Relative rates | Isomer distribution of $C_6H_5C_6H_4X$, % | | |
|---|---|---|---|---|---|---|---|---|
| | | *o* | *m* | *p* | | *o* | *m* | *p* |
| $PhNO_2$ | Exp. 1 | 8.95 | 1.14 | 8.82 | 4.83 | 61.8 | 7.8 | 30.4 |
| | Exp. 2 | 9.80 | 1.17 | 9.28 | 5.20 | 62.8 | 7.4 | 29.8 |
| | Mean | 9.38 | 1.16 | 9.05 | 5.02 | 62.3 | 7.6 | 30.1 |
| PhOMe | | 3.56 | 0.93 | 1.29 | 1.71 | 69.3 | 18.1 | 12.6 |

by the same mechanism and that the frequency factor in the Arrhenius equation remains constant. Thus it is readily shown that partial rate factors $f(T_1)$ and $f(T_2)$, at two temperatures, $T_1$ and $T_2$, are related with each other by the following equation:

$$T_1 \log f(T_1) = T_2 \log f(T_2)$$

Substitution of the value for the partial rate factor of the *o*-position obtained by the *N*-nitrosoacetanilide reaction and of the corresponding value by the benzoyl peroxide reaction for $f(T_1)$ and $f(T_2)$ in this equation, respectively, gives 1.31 as the value for $T_2/T_1$, which should actually be $353/293=1.20$. A similar substitution of the values for the *p*-position gives 1.39. The approximate agreement of these values with the actual value seems to indicate the validity of this explanation for the observed difference in the partial rate factors, although the values for the meta position give no reasonable value for $T_2/T_1$. Huisgen and Grashey[5] quoted a value of 2.0 for the relative rate of phenylation of anisole by means of *N*-nitrosoacetanilide at 25°C. This value is fairly close to our value of 1.71. As there are no previous data for the partial rate factors for anisole available for comparison, we have calculated, similarly to Williams's calculation[6], the partial rate factors by using the free valence values, 0.422, 0.395 and 0.406 for the *o*-, *m*- and *p*-position of phenol, respectively, derived from Sandorfy's bond order values[7]. In adopting these values as the free valence values of anisole we have neglected the polar effect of the methyl group, which tends to lower the electronegativity of the oxygen atom. The predicted values for the partial rate factors at 20°C are 4.06, 0.84 and 1.60 for the *o*-, *m*- and *p*-position, which compare favourably with the present experimental values of 3.56, 0.93 and 1.29.

Although separate experiments[8] show that the abstraction of a hydrogen atom by aryl radicals produced from *N*-nitrosoacetanilides occurs only to a very limited extent in an aromatic compound which contains no reactive methyl group, in the decomposition of *N*-nitrosoacetanilide in a mixture of anisole and benzene the phenyl radicals generated should readily abstract a hydrogen atom from the methyl group of anisole resulting in the formation of benzene-$^{14}C$. To examine this probability the benzene recovered from the reaction mixture was nitrated with a mixture of fuming nitric acid and concentrated sulphuric acid, and the resulting *m*-dinitrobenzene was recrystallized from ethanol to give a specimen of a constant activity of $0.018\pm0.001$ mc./mol. This value corresponds to the production of $0.30\pm0.02$ mmol. of benzene-$^{14}C$, and shows that 15.4% of the phenyl radicals generated and accounted for as biphenyls and benzene gave benzene by abstracting a hydrogen atom.

## Experimental

All melting points are corrected.

**Materials.**—Thiophene-free benzene was purified by repeated fractional freezing, m. p. 5.7°C. Nitrobenzene, prepared from the above benzene by nitration, was fractionally distilled and further purified by repeated fractional freezing, m. p. 5.7°C. Anisole was prepared by methylation of purified phenol and purified by distillation and fractional freezing, m. p. −37.5°C.

Commercial biphenyl was repeatedly recrystallized from 90% ethanol and sublimed under reduced pressure, m. p. 70°C.

Nitrobiphenyls and 4-methoxybiphenyl were prepared from the corresponding nitroanilines and anisidine by the Gomberg-Bachmann reaction[9] and purified by recrystallization from methanol; the melting points were: 2-$NO_2$, 37; 3-$NO_2$, 61; 4-$NO_2$, 113.5; and 4-MeO, 91°C.

2-Methoxybiphenyl was similarly prepared from *o*-anisidine, recrystallized twice from petroleum ether, and converted into 2-hydroxybiphenyl, m. p. 58.5°C (from petroleum ether), by heating (210~220°C, 16 hr.) with pyridine hydrochloride[10], and

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[5] R. Huisgen and R. Grashey, *Ann.*, **607**, 46 (1957).

[6] G. H. Williams, "Homolytic Aromatic Substitution", Pergamon Press, Oxford (1960), p. 15.

[7] C. Sandorfy, *Bull. soc. chim. France*, **1949**, 615.

[8] T. Inukai, K. Kimura, O. Simamura and T. Suehiro, This Bulletin, **35**, 129 (1962); R. Itô, T. Migita and O. Simamura, to be published.

[9] W. E. Bachmann and R. A. Hoffman, "Organic Reactions", Vol. II, John Wiley and Sons, Inc., New York, (1944), p. 247.

[10] V. Prey, *Ber.*, **74**, 1219 (1941) **75**, 350 (1942).

this compound was methylated with dimethyl sulphate again to afford pure 2-methoxybiphenyl, m. p. 32°C (from methanol).

3-Methoxybiphenyl was prepared from 3-nitrobiphenyl by reduction to 3-aminobiphenyl (b. p. 187~188°C/18 mmHg), diazotization and hydrolysis in diluted sulphuric acid at 65°C to give 3-hydroxybiphenyl, m. p. 76.8°C (from petroleum ether), which was then methylated with dimethyl sulphate to afford pure 3-methoxybiphenyl, b. p. 159°C (12 mmHg), a colourless oil.

*N*-Nitrosoacet(anilide-$^{14}$C) was prepared from benzene-1-$^{14}$C (The Radiochemical Centre, Amersham) by nitration and catalytic reduction to aniline followed by acetylation and finally by nitrosation of the resulting acetanilide. The experimental procedure is described elsewhere[11].

**Decomposition of *N*-Nitrosoacet(anilide-$^{14}$C) in a Mixture of Benzene and Nitrobenzene.**—The results are tabulated in Table I. *N*-Nitrosoacet-(anilide-$^{14}$C) with a specific activity of 14.45 mc./mol., (920.42 mg., 5.607 mmol.) was dissolved in a mixture of 52.0 g. of benzene (666.7 mmol.) and 82.0 g. of nitrobenzene (666.7 mmol.) maintained at 20.0°C in a thermostat and allowed to decompose until at last the nitrogen evolved reached a final value of 68% of the theoretical. A portion (A, 42.578 g.) was weighed out from the reaction mixture (133.697 g.), and to this portion were added 0.9975 g. (6.472 mmol.) of biphenyl, 1.7011 g. (8.540 mmol.) of *o*-nitrobiphenyl, and 1.0924 g. (5.484 mmol.) of *p*-nitrobiphenyl. From the resulting solution benzene and nitrobenzene were removed under reduced pressure. The residue was distilled through a Vigreux column 15 cm. in height giving a biphenyl fraction, b. p. 117~120°C (6.5 mmHg), an *o*-nitrobiphenyl fraction, b. p. 140~150°C (5 mmHg), and a *p*-nitrobiphenyl fraction, b. p. 155~160°C (5 mmHg). Biphenyl and *o*-nitrobiphenyl were purified by chromatography on activated alumina in petroleum ether, and *p*-nitrobiphenyl was purified by chromatography on acetivated alumina in 1 : 1 mixture of petroleum ether and benzene. Another portion (B, 45.335 g.) was taken from the original reaction mixture, and to this portion were added 0.4962 g. (3.221 mmol.) of biphenyl and 0.4972 g. (2.496 mmol.) of *m*-nitrobiphenyl. The mixture was worked up as above, that is, by distillation to give a biphenyl and a *m*-nitrobiphenyl fraction and by chromatography of these fractions on activated alumina in petroleum ether. The two specimens of biphenyl from portion A and portion B were finally purified by repeated recrystallizations from 90% ethanol and sublimation under vacuum (1~2 mmHg). Nitrobiphenyls were further purified by recrystallization from methanol. The purification was deemed complete when the specific activity of a specimen remained constant on further recrystallization. A second experiment was carried out in a similar way.

**Decomposition of *N*-Nitrosoacet(anilide-$^{14}$C) in a Mixture of Benzene and Anisole.**—The results are summarized in Table II. *N*-Nitrosoacet(anilide-$^{14}$C) with a specific activity of 14.18 mc./mol., (637.43 mg., 3.883 mmol.), was dissolved in a mixture of 18.08 g. of benzene (231.4 mmol.) and 80.22 g. of anisole (741.8 mmol.) and allowed to decompose at 20.0°C; nitrogen evolved amounted to 82.5% of the theoretical value. Two portions (A, 49.030 g., and B, 48.904 g.) were weighed out from the reaction mixture (98.296 g.). To portion A were added 0.4942 g. (3.204 mmol.) of biphenyl, 1.3061 g. (7.089 mmol.) of 2-methoxybiphenyl, and 0.7393 g. (4.018 mmol.) of 4-methoxybiphenyl, and from the resulting solution benzene and anisole were removed under reduced pressure. The residue was dissolved in a mixture of petroleum ether and benzene (4 : 1), and subjected to chromatography on activated alumina in petroleum ether to afford biphenyl, 2-methoxybiphenyl and 4-methoxybiphenyl by elution with petroleum ether (b. p. 40~60°C). To portion B above were added 0.5982 g. (3.879 mmol.) of biphenyl and 1.1281 g. (6.123 mmol.) of 3-methoxybiphenyl, and from the resulting solution benzene and anisole were removed under reduced pressure. The residue was chromatographed on activated alumina in petroleum ether to give biphenyl and 3-methoxybiphenyl. The specimens of biphenyl from portions A and B were purified by recrystallization and sublimation as in the experiments in a mixture of nitrobenzene and benzene. 2- and 4-Methoxybiphenyl were purified by repeated recrystallizations from methanol. The oily 3-isomeride was converted into 3-hydroxybiphenyl by heating with pyridine hydrochloride, and this was purified by repeated recrystallizations from petroleum ether to a constant activity of 0.281±0.002 mc./mmol.

**Radioactivity Determination.**—Radiocarbon assays were carried out by oxidizing samples according to the method of Van Slyke and Folch[12] and by converting the resulting carbon dioxide into barium carbonate, the activity of which was then counted with an end-window Geiger-Müller counter on an "infinitely thick" layer.

## Summary

*N*-Nitrosoacet(anilide-$^{14}$C) has been decomposed at 20°C in a mixture of benzene with nitrobenzene or with anisole, and the reaction products have been analyzed for biphenyl and isomeric nitrobiphenyls or isomeric methoxybiphenyls by isotope dilution method. From these results the partial rate factors for the phenylation have been calculated to be for nitrobenzene: *o*, 9.38; *m*, 1.16; and *p*, 9.05; and for anisole: *o*, 3.56; m, 0.93; and *p*, 1.29.

*Department of Chemistry*
*Faculty of Science*
*The University of Tokyo*
*Hongo, Tokyo*

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11) H. Koyama, N. Morikawa, T. Migita, R. Itô and G. Tsuchihashi, *Radioisotopes* (*Tokyo*), **9**, 112 (1960).

12) D. D. Van Slyke and J. Folch, *J. Biol. Chem.*, **136**, 509 (1940).