BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 47 (9), 2351—2352 (1974)

The Diazo-coupling Reaction of Phenol in Organic Solvents. The Isomer Ratio

Hideo YAMADA, Yōji HASHIDA, Shizen SEKIGUCHI, and Kohji MATSUI
Department of Synthetic Chemistry, Faculty of Engineering, Gunma University, Tenjincho, Kiryu, Gunma 376

(Received March 11, 1974)

Synopsis. The *ortho*:*para*-ratios in the reaction of phenol with benzenediazonium fluoroborate have been investigated in organic solvents. It has been found that the *o*/*p* ratios in protic solvents were smaller than those in aprotic solvents. The results were interpreted in terms of the difference in solvation toward the phenolate ion.

In diazo-coupling reactions, it is known[1)] that the ratio of the isomers depends upon various factors, such as the structures of the diazo and coupling components, the pH values of the media, the reaction temperatures, and the catalysts. In a previous paper,[2)] we reported that the rate of the reaction of 2-naphthol with benzene diazonium salt was markedly affected by the solvent. Thus, in the diazo-coupling reaction of phenol, the isomer ratio can be expected also to be influenced by the solvents, as has been reported for the other aromatic electrophilic substitutions.[3,4)] However, the effect of solvents on the isomer ratios has not been studied systematically in connection with this reaction. This paper will report the *ortho*:*para*-ratios for the diazo-coupling reactions of phenol with benzenediazonium salt in organic media.

Experimental

Materials. Commercial phenol and triethylamine were purified by distillation prior to use. The benzenediazonium fluoroborate was prepared by the usual method and were dried over phosphorus pentoxide.

Solvents. The solvents used were purified by the usual methods.[5)]

Syntheses of Azo-compounds. The *p*-hydroxyazobenzene,[6)] *o*-hydroxyazobenzene,[6)] and 2,4-bis(phenylazo)phenol[7)] were prepared by the usual procedure. Their purities were checked by observing their melting points, by elemental analyses, and by thin-layer chromatography. The optical properties of these azo-compounds are shown in Table 1.

TABLE 1. OPTICAL PROPERTIES OF AZO-COMPOUNDS

Azo-compound	Mp (°C)	$\lambda_{\max}$(nm)	ε[a)]
2-Hydroxyazobenzene	83—83.5	322	19100
4-Hydroxyazobenzene	154—155	346	25300
2,4-Bis(phenylzao)phenol	130—131	335	44700

a) In methanol.

Measurements of the Product Distributions. The product distributions were measured spectrophotometrically by the method described below. To 100 ml of a solution of phenol (0.471 g, 5×10^{-3} M) and triethylamine (1.52 g, 1.5×10^{-2} M) in an appropriate solvent, we added finely-powdered benzenediazonium fluoroborate (0.960 g, 5×10^{-3} M) at 0 °C. The reaction mixture was stirred for a few hours after the diazonium salt had been dissolved, and the reaction mixture was concentrated; then the azo-compounds thus produced were separated by silica gel thin-layer chromatography, using a mixture of *n*-hexane and acetone (20: 1, v/v) as the developing solvent. From the thin-layer chromatogram each azo-compound was extracted and diluted to a definite volume with methanol; its extinction was measured spectrophotometrically.

Results and Discussion

As has been reported[6)] for the coupling reaction in water, phenol gave *o*-, *p*-, and 2,4-di-substituted[8)] products even in the reactions in organic solvents. The product distributions in various solvents are given in Table 2.

TABLE 2. PRODUCT DISTRIBUTIONS FOR THE REACTION OF PHENOL WITH BENZENEDIAZONIUM FLUOROBORATE (0 °C)

No.	Solvent	(Molar comp. of) product (%) *o*-	*p*-	2,4-di-	*o*/*p*×100
1	Water	0.7	99.1	0.2	0.7
2	Methanol	1.2	97.5	1.3	1.2
3	Methanol[a)]	1.4	98.3	0.3	1.4
4	2-Propanol	1.6	98.4	—[b)]	1.7
5	Phenol	3.2	96.8	—[b)]	3.3
6	*t*-Butanol	4.3	89.9	5.8	4.8
7	Acetone	3.2	93.1	3.6	3.5
8	Tetrahydrofuran	3.6	96.3	—[b)]	3.8
9	Acetonitrile	3.8	91.5	4.7	4.2
10	Dimethylsulfoxide[c)]	4.6	90.7	4.7	5.0
11	Nitromethane	4.7	93.1	2.2	5.0
12	Dioxane	5.2	93.2	1.6	5.6
13	Dimethylformamide	6.5	88.7	4.8	7.3
14	Pyridine	6.7	86.7	6.6	7.7

a) Pyridine was used as a base (see Experimental Section). b) The product ratio could not be measured by the method of T.L.C., because of the formation of unknown by-product. c) At 20 °C.

In diazo-coupling reactions, many examples are known[1)] in which the isomer ratio depends upon the base used and upon its concentration. To examine the effect of bases on isomer ratios, the reaction was carried out in methanol in the presence of triethylamine and/or pyridine; however, these bases scarcely affected the *o*/*p* ratio at all (No. 2, 3).

As can be seen from Table 2, the solvents do have significant effects on the isomer ratio, even though every value of the *o*/*p* ratio is small: in pyridine and DMF, the yields of the *o*-isomer were greater than that in water by a factor of about ten. The solvents employed can be divided into two groups: the protic (No. 1—6) and aprotic solvents (No. 7—14).

In the protic solvents, the *o*/*p* ratios were small; however, within a series of protic solvents with similar structures, the yield of the *o*-isomer increased with a decrease in the solvent polarity in this order: $H_2O <$ MeOH$<$*i*-PrOH$<$*t*-BuOH.

On the contrary, in the aprotic solvents there was no significant correlation between the *o*/*p* ratio and the solvent polarity. However, as a whole, in the aprotic solvents higher yields of the *ortho*-substituted derivatives were obtained than in the protic solvents.

In the ordinary electrophilic substitutions of monosubstituted benzenes, many factors have been suggested[9] as affecting the *o*/*p* ratio; however, little is known about the effect of solvents on the isomer distribution. Therefore, it was of interest to consider the solvent effect on the isomer ratio in this reaction.

One of the most important factors of the solvent effect in this reaction is considered to be the influence on the reactivities of the reaction components by solvation. According to the selectivity relationship,[10] the difference in yields between *ortho*- and *para*-products is also assumed to increase as the reactivity of the reagent decreases;[11,12] this concept is consistent with the results described above. It was pointed out in a previous work[2] that, in the diazo-coupling reaction of 2-naphthol, the reactive species of the substrate is the naphtholate ion, even in organic solvents, and that the reaction is remarkably enhanced in dipolar aprotic solvents, presumably because of the decrease in the solvation of the naphtholate ion in these solvents.[2] A similar relation between the reactivities of the substrates and the kind of solvent is considered to hold for the reaction of phenol; therefore, the coupling reaction of benzenediazonium salt with phenol is considered to proceed more rapidly in dipolar aprotic solvents than in protic solvents. Therefore, the finding that, in this reaction, relatively high *o*/*p* ratios were obtained in the aprotic solvents is quite reasonable. Furthermore, the tendency for, in protic solvents, the *o*/*p* ratio to increase with a decrease in the solvent polarity may be ascribed to a decrease in solvation in the less polar solvent, which thus increases the reactivity of the phenolate ion. Thus, the increased reactivity of the phenolate ion leads to a decrease in selectivity.

On the other hand, it is also known[10] that the *o*/*p* ratio of the aromatic electrophilic substitution is governed by the steric effect of the substituents of the substrates. The change in the *o*/*p* ratio described above may be also explained by assuming that the steric effect of the $-O^-$ group varies with the solvents, as has been pointed out by several authors.[4,13] For example, the total bulkiness of the $-O^-$ group may be larger in protic solvents than in aprotic solvents, for the $-O^-$ group is considered to be strongly solvated in protic solvents by means of the general hydrogen-bonding. The bound solvent molecules would interfere with the *ortho*-substitution.

Either of the two concepts may explain our results satisfactorily, but it is difficult to conclude at present which of the effects plays the leading role; the isomer ratios are probably affected by the combined action of both the effects.

References

1) H. Zollinger, "Azo and Diazo Chemistry," Interscience Publishers, New York (1961), p. 253.

2) Y. Hashida, H. Ishida, S. Sekiguchi, and K. Matsui, This Bulletin, **47**, 1224 (1974).

3) L. M. Stock and A. Himoe, *Tetrahedron Lett.*, **1960**, 9.

4) A. Campbell and D. J. Shields, *Tetrahedron*, **21**, 211 (1965).

5) J. A. Riddick and W. B. Bunger, "Organic Solvents," Wiley-Interscience, New York, (1970), Chapter 5.

6) E. Bamberger, *Ber.*, **33**, 3188 (1900).

7) E. Bamberger, *ibid.*, **35**, 1606 (1902).

8) 2,4-Disubstituted product has been reported to be produced from the reaction of *p*-substituted product with diazonium salt [Kishimoto, *et al.*, *Kogyo Kagaku Zasshi*, **71**, 1195 (1968)]. Therefore, it may be reasonable that *o*/*p* ratio should be calculated from the *o*/*p*+2,4-disubstituted compound. However, there was no serious difference between *o*/*p* and *o*/*p*+2,4-substituted derivative.

9) R. O. C. Norman and R. Taylor, "Electrophilic Aromatic Substitution in Benzenoid Compounds,"Elsevier Publishing Co., Amsterdam (1965), p. 301.

10) L. M. Stock and H. C. Brown, "Advance in Physical Organic Chemistry," Vol. 1, ed. by V. Gold, Academic Press., London (1963), p. 35.

11) P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworths Scientific Publications, London (1959), p. 83.

12) R. O. C. Norman and G. K. Radda, *J. Chem. Soc.*, **1961**, 3610.

13) W. J. Le Nobel, *J. Amer. Chem. Soc.*, **85**, 1470 (1963).