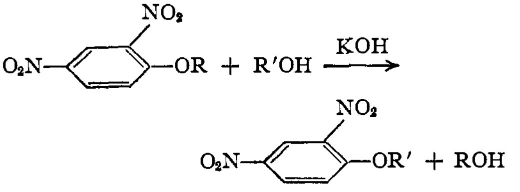
[CONTRIBUTION FROM THE DEPARTMENT OF INDUSTRIAL CHEMISTRY, THE FACULTY OF ENGINEERING, KYOTO UNIVERSITY]

Nucleophilic Substitution in Aromatic Ethers. I. Ethers in which Nucleophilic Substitution is Possible

BY YOSHIRO OGATA[1] AND MASAYA OKANO

Just like *p*-nitrochlorobenzene, *p*-nitroanisole is converted to *p*-nitrophenetole when boiled in ethyl alcohol in the presence of caustic alkali.[2] The substitution may be called an ether interchange. In an attempt to extend this reaction, we studied the interchange of *p*-nitroanisole with polyhydric alcohols and alcohols of the C_3–C_4 range. It was found that little or no reaction occurred. When an alkoxyl group was activated by the introduction of nitro groups into the 2 and 4 positions of anisole, however, substitution occurred readily



(1)

In this paper a number of such substitution reactions are described.

The reaction was found to be reversible when the group R was alkyl but irreversible when R was aryl (Equation 1). In the same way, 2,4-dinitroanisole or 2,4-dinitrodiphenyl ether reacted with aniline, forming 2,4-dinitrodiphenylamine.[3] Benzyl methyl ether, benzhydryl methyl ether, anisole or anisoles substituted with electronegative groups other than nitro (*e.g.*, CH_3CO) were incapable of interchange.

Experimental

Ether Interchange.—The experiments summarized in Table I were carried out according to a standardized procedure which may be illustrated by the preparation of 2,4-dinitrophenyl isobutyl ether. In 30 cc. of isobutyl alcohol was dissolved 0.2 g. of potassium hydroxide by boiling. To this solution was added 3 g. of 2,4-dinitroanisole (m. p. 88°) and the mixture was boiled under a reflux condenser for ten hours. After removing the alcohols by distillation and evaporation, the residue was cooled and washed with water. The crude 2,4-dinitrophenyl isobutyl ether (m. p. 27-29°) weighed 2.8 g. (77%). It was recrystallized from ethanol to which a drop of concentrated hydrochloric acid was added. The product separated in the form of laminae, m. p. 34-35°, and recrystallization involved about a 10% loss of material.

Anal. Calcd. for $C_{10}H_{12}O_5N_2$: C, 50.00; H, 5.04; N, 11.66. Found: C, 49.58; H, 4.93; N, 10.9.

The same product (m. p. 33-35°) was isolated from the reaction of 2,4-dinitrochlorobenzene with sodium isobutoxide. A mixed melting point determination of this material with the product obtained from the ether interchange reaction showed no depression.[4]

Under approximately the same conditions anisole, *p*-acetylanisole, *p*-chloroanisole, 2,4,6-tribromoanisole and potassium *p*-methoxybenzenesulfonate did not react with ethanol. Similarly *p*-nitroanisole did not undergo interchange with isopropyl alcohol, isobutanol, allyl alcohol, ethylene glycol, or phenol. In boiling aniline solution, however, 2,4-dinitrodiphenyl ether and 2,4-dinitrophenyl *β*-naphthyl ether gave good yields (80 and 97%, respectively), of 2,4-dinitrodiphenylamine, m. p. 156-157°. 2,4-Dinitroanisole also reacted, but a large amount of amorphous material was formed. The yield of 2,4-dinitrodiphenylamine was less than 20%.

In the run in which glycerol was employed, the general procedure was modified to the extent that the reaction mixture was heated with stirring at 160-180° in an oil-bath.

TABLE I

ETHER INTERCHANGE OF SOME 2,4-DINITROPHENYL ALKYL OR ARYL ETHERS

R in Eq. 1	R' in Eq. 1	Reaction time, hr.	Yield, %	Product, m. p., °C.
CH_3	*n*-C_3H_7	10	73	28–30[a]
CH_3	iso-C_3H_7	10	73	51–53[a]
CH_3	*n*-C_4H_9	10	70	Oil[a]
CH_3	iso-C_4H_9	10	77	34–35[b]
CH_3	$CH_2{=}CHCH_2$	10	0	
CH_3	C_6H_5	10	0	
CH_3	$C_6H_5CH_2$	10	0	
CH_3	*n*-$C_{15}H_{31}CH_2$	2	0	
CH_3	—CH_2CH_2—	2	69	109–110[c]
CH_3	—CH_2CHCH_2—	6	26	84–85
CH_2CH_2OH	CH_3 $\vert$	10	70	88–89
CH_2CH_2OH	iso-C_3H_7	10	64	51–53
C_6H_5	CH_3	10	82	87–89
C_6H_5	C_2H_5	10	73	84–86
C_6H_5	iso-C_3H_7	20	71	51–52
C_6H_5	—CH_2CH_2—	6	51	108–110[c]
C_6H_4Cl-*p*	CH_3	2	71	88–89
C_6H_4Cl-*p*	—CH_2CH_2—	2	66	109–110[c]
$C_6H_4NO_2$-*p*	CH_3	2	77	88–89
$C_6H_4NO_2$-*p*	—CH_2CH_2—	2	72	109–110[c]
$C_6H_4CH_3$-*p*	CH_3	10	82	88–89
$C_6H_4CH_3$-*o*	CH_3	10	76	88–89
$C_6H_4CH_3$-*m*	CH_3	10	84	88–89
$C_6H_4OCH_3$-*p*	CH_3	10	78	87–89
$C_{10}H_7$-*α*	CH_3	10	86	88–89
$C_{10}H_7$-*β*	CH_3	10	87	88–89

[a] Blanksma and van der Weyden, *Rec. trav. chim.*, **39**, 629 (1940). [b] New compound; see the Experimental part. [c] The melting point of this compound agrees with that of the monoglycol ether $(NO_2)_2C_6H_3OCH_2CH_2OH$, recently found by Blanksma and Fohr, *Rec. trav. chim.*, **65**, 706, 711 (1946); *cf. C. A.* **41**, 5484 (1947).

---

[1] Present address: Kyoto University, Yoshida, Kyoto, Japan.

[2] Oliverio, *C. A.*, **33**, 9302 (1939).

[3] For the reaction of 2,4-dinitroanisole with ammonia, see Salkowski, *Ber.*, **5**, 872 (1872).

[4] The tarry matter inevitable to the reaction of 2,4-dinitrochlorobenzene with sodium alkoxides is never produced in the ether interchange. It should therefore prove to be a better general method for the preparation of higher 2,4-dinitrophenyl ethers.

Summary

The methoxyl group of 2,4-dinitroanisole is convertible to another alkoxyl group, by boiling dinitroanisole in the presence of caustic alkali with polyhydric alcohols or alcohols of the C_2–C_4 range. Aniline leads to 2,4-dinitrodiphenylamine.

Similar reactions are possible with some other 2,4-dinitrophenyl alkyl or aryl ethers.

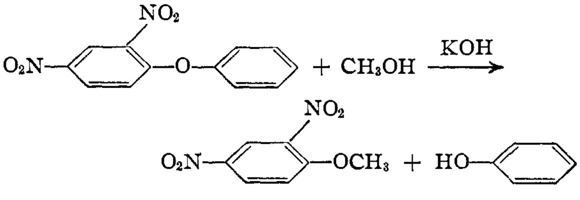
KYOTO, JAPAN RECEIVED FEBRUARY 28, 1949

[CONTRIBUTION FROM THE DEPARTMENT OF INDUSTRIAL CHEMISTRY, THE FACULTY OF ENGINEERING, KYOTO UNIVERSITY]

Nucleophilic Substitution in Aromatic Ethers. II. Kinetics of the Methanolysis of 2,4-Dinitrodiphenyl Ethers

BY YOSHIRO OGATA AND MASAYA OKANO

In the preceding paper[1] it was shown that 2,4-dinitroanisole is formed irreversibly, when a solution of 2,4-dinitrodiphenyl ether is boiled in alkaline methanol



In the present paper, the rate of reaction and the effect of structure on the rate were studied. The rate was determined by taking out aliquots of the reaction mixture after suitable time intervals, and estimating the phenol produced iodometrically.

Experimental

Materials.—Methanol (b. p. 64.5–65°) was purified by repeated rectifications from calcium oxide and silver nitrate. The 2,4-dinitrodiphenyl ethers were prepared by the condensation of 2,4-dinitrochlorobenzene with the corresponding sodium phenolates. They were recrystallized (twice) slowly from acetone or, with the α- or β-naphthyl derivatives, from a mixture of acetone and methanol. Among them, the 4′-chlorophenyl, 4′-nitrophenyl, α-naphthyl and β-naphthyl ethers were prepared in methanol (many hours boiling was necessary in the case of the nitro or naphthyl derivatives). The melting points agreed with those in the literature[2] as follows. 2,4-Dinitrodiphenyl ether, 70–71°; 2′-methyl, 89–90°; 3′-methyl, 72–73.5°; 4′-methyl, 91–92.5°; 4′-chloro, 122–123.5°; 4′-nitro, 115–116°; α-naphthyl 127–128°; β-naphthyl, 93–94.5°.

Apparatus and Procedure.—About 0.0025 mole of one of the ethers was weighed out and dissolved in 200 cc. of methanol. The solution was poured into a four-necked flask and placed in a thermostat (20 ± 0.1°) until temperature equilibrium was established. The flask was fitted with a stirrer[3] in its central neck, and in the other three were placed a thermometer, a tube suitable for withdrawing samples, and a tube into which air could be blown for pushing out the sample. The proper amount of potassium hydroxide was then dissolved in boiling methanol and its concentration was determined by titration with 0.05 *N* oxalic acid. An accurately measured amount of this solution (50 cc.) was taken out and kept in the thermostat until temperature equilibrium was reached and was then poured into the flask with gentle agitation (250–300 r. p. m.). This time was taken as the beginning of the reaction. A 25-cc. sample was taken out at regular intervals and run into a glass-stoppered flask containing 3 cc. of concentrated hydrochloric acid and 50 cc. of water. Twenty cc. of 0.1 *N* bromine water (a solution prepared from potassium bromate and bromide), were then added, the flask was stoppered tightly, and it was allowed to stand for fifteen seconds or thirty minutes before analysis.[4] The mixture was then treated with 5 cc. of 20% potassium iodide solution, and the freed iodine was titrated with 0.05 *N* sodium thiosulfate. The difference between the needed volume of thiosulfate solution and the blank test corresponded to the amount of phenol formed.

Results and Calculations

The bimolecular rate constants shown in Tables I and II were calculated by means of the following equation

$$k = \frac{2.303}{60t(b-a)} \log \frac{a(b-x)}{b(a-x)} \text{ (l./moles} \times \text{sec.)}$$

Here, a is the initial concentration of ether (moles/l.), b that of alkali (moles/l.), x the concentration of phenol after t minutes (mole/l.).[5] In Table I is shown the effect of changes in concentration on the second order rate constant of the methanolysis of 2,4-dinitrodiphenyl ether. It is evident that the rate of formation of phenol is proportional to the product of the concentration of the original ether and methylate ion.

In Table II are shown the rate constants for a number of runs in which various changes were made in the 2,4-dinitrodiphenyl ether molecule. It will be observed that the substitution of an electron attracting group (*e. g.*, NO_2) in the 4′ posi-

---

[1] Ogata and Okano, THIS JOURNAL, **71**, 3211 (1949).

[2] (a) Raiford and Colbert, *ibid.*, **48**, 2652 (1926); (b) Bost and Nicholson, *ibid.*, **57**, 2368 (1935).

[3] Agitation was necessary, for the methanol solution tended to become heterogeneous when it was allowed to stand for a long time.

[4] From the results obtained with pure materials under these conditions, it was found that standing for thirty minutes is too long for *o*-, *m*-, *p*-cresol, and α- or β-naphthol. Even when the potassium iodide solution was added after fifteen seconds, the estimations of *o*- and *p*-cresol showed that the values were about 103 and 104% of the theoretical values. These estimations were, therefore, carried out rapidly and corrected by dividing the results by 1.04 and 1.03, respectively. See Day and Taggert, *Ind. Eng. Chem.*, **20**, 545 (1928).

[5] It should be noted that phenol and *m*-cresol consume 3 moles of bromine per mole. *p*-Substituted phenols and β-naphthol consume 2 moles, but α-naphthol reacts with 1 mole. Moreover, with *o*- and *p*-cresol, x should be divided by 1.03 and 1.04, respectively; see ref. 4.