chloride was taken. In the case of reactions conducted in benzene, the 5-ml. aliquot was added with stirring to the appropriate quantity of catalyst in 5 ml. of benzene. After the required time, the reaction mixture was hydrolyzed by adding to ice. The fluorenone was extracted with ether. The ethereal solution was extracted with water, dilute aqueous sodium carbonate solution, dilute ammonia solution, and finally with water. After drying with anhydrous magnesium sulfate, the ether was evaporated to leave a residue of fluorenone. The fluorenone was recrystallized from hexane (0.5 ml. of solvent/0.1 g. of fluorenone) and sublimed. In most instances the resulting product had the proper melting point 83–84°; the few samples which had low melting points were purified by chromatography on silica gel.

In the case of reactions conducted in solvents other than benzene, the 5-ml. aliquot was evaporated *in vacuo* to remove benzene. The residual acid chloride was dissolved in 5 ml. of nitrobenzene or *ca.* 20 ml. of liquid sulfur dioxide and allowed to react with the catalyst in 5 ml. of nitrobenzene or *ca.* 20 ml. of sulfur dioxide.

The products from reactions conducted in nitrobenzene were separated from the nitrobenzene after the usual hydrolysis by chromatography on silica gel.

The yields of fluorenone were good in all instances: an average of about 80% of theory was obtained from evaporation of the ether solutions.

The quantities of catalyst used for each 5-ml. aliquot of acid chloride solution (0.0025 mole of acid chloride) were: 0.67 g. (0.005 mole) of aluminum chloride, 1.30 g. (0.005 mole) of stannic chloride, 0.68 g. (0.005 mole) of zinc chloride.

The first aluminum chloride-catalyzed cyclization in sulfur dioxide was conducted by adding the catalyst to the acid chloride in the solvent. Since the time required to dissolve the catalyst was greater than the reaction time this experiment is classed as heterogeneous. In the second experiment, the aluminum chloride was dissolved in sulfur dioxide and the acid chloride dissolved in sulfur dioxide was added: this experiment is classed as homogeneous.

Table II

Catalyst, chloride	Solvent	Time	Temp., °C.	Atom % D
Zinc	Benzene[a]	5 hr.	29	7.21 ± 0.09, 7.18 ± 0.04
Zinc	Benzene[a]	24 hr.	35	7.26 ± .05, 7.21 ± .05
Stannic	Benzene[b]	30 min.	36	6.59 ± .04, 6.57 ± .05
Stannic	Benzene[b]	60 min.	29	6.51 ± .05, 6.61 ± .04
Stannic	Benzene[b]	90 min.	36	6.60 ± .05, 6.61 ± .04
Stannic	Nitrobenzene[b]	20 min.	26	7.34 ± .05, 7.37 ± .05
Stannic	Sulfur dioxide[b]	20 min.	−10	8.45 ± .05, 8.38 ± .05
Aluminum	Benzene[a]	5 min.	5	9.22 ± .06, 9.17 ± .05
Aluminum	Benzene[a]	10 min.	5	9.23 ± .05, 9.19 ± .05
Aluminum	Benzene[a]	15 min.	5	9.13 ± .04, 9.11 ± .05
Aluminum	Nitrobenzene[b]	10 min.	5	7.41 ± .05, 7.42 ± .05
Aluminum	Sulfur dioxide[a]	15 min.	−10	10.14 ± .06, 10.20 ± .06
Aluminum	Sulfur dioxide[b]	15 min.	−10	9.15 ± .10

[a] Heterogeneous system. [b] Homogeneous system.

The data for the several experiments are summarized in Table II.

New Brunswick, N. J.

[Contribution from the Noyes Chemical Laboratory, Universal of Illinois]

Formation of Cyclohexadienones by Direct Alkylation of Phenols with Saturated Alkyl Derivatives[1]

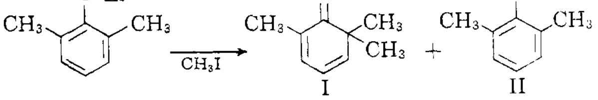
By David Y. Curtin and Robert R. Fraser[2]

Received June 23, 1958

Factors affecting the position of methylation of salts of 2,6-dimethylphenol in non-polar medium have been investigated. It has been found that, in toluene, methyl iodide alkylates sodium 2,6-dimethylphenoxide with a ratio of attack on oxygen relative to attack in the *ortho* positions some 30 times as great as the corresponding ratio with benzyl chloride. It is estimated also that benzyl iodide undergoes alkylation several hundred times faster than methyl iodide. The aluminum and bromomagnesium salts of this phenol react too slowly to be useful. The alkylations of lithium phenoxide and *o*-cresoxide have also been found to lead to mixtures of carbon- and oxygen-alkylated products. Comparison of the ratios in methyl iodide medium indicates that the phenol salt undergoes attack in each *o*-position at about the same rate as attack on oxygen while the *o*-cresol salt undergoes attack at the unsubstituted *o*-position and at the oxygen at about the same rate, but attack at the methyl-substituted position about one-third as fast. It is concluded in agreement with the work of Zagorevsky[11,12,14] that a halide which reacts by a more nearly limiting mechanism gives more carbon alkylation under the conditions employed. However, methyl *p*-bromobenzenesulfonate with sodium 2,6-dimethylphenoxide gives only oxygen alkylation.

The demonstration by Claisen, Kremers, Roth and Tietze[3] that sodium salts of phenols undergo alkylation in an *o*-position when treated with allyl and benzyl halides recently has been extended[4] to 2- or 2,6-substituted phenol salts which yield alkylcyclohexadienones on alkylation in suitable non-polar solvents.

It was implied by Claisen and has since been generally accepted[5] that carbon-alkylation was peculiar to benzylic and allylic halides when monocyclic monohydroxylic phenol salts were being alkylated. It has been reported recently[6] in preliminary communication,[6] however, that the lithium salt of 2,6-dimethylphenol reacts with methyl iodide at 150° without solvent, forming 2,6,6-



---

[1] Supported in part by the Office of Ordnance Research, U. S. Army. Abstracted from the Ph.D. Thesis submitted to the University of Illinois, by Robert R. Fraser, June, 1958. This work was partially described in a preliminary communication [D. Y. Curtin and R. R. Fraser, *Chemistry & Industry*, 1358 (1957)].

[2] Texas Company Fellow, 1957–1958.

[3] L. Claisen, F. Kremers, F. Roth and E. Tietze, *Ann.*, **442**, 210 (1925).

[4] (a) See D. Y. Curtin, Robert J. Crawford and M. Wilhelm, This Journal, **80**, 1391 (1958); (b) D. Y. Curtin and M. Wilhelm, *J. Org. Chem.*, **23**, 9 (1958).

[5] See, for example, L. F. Fieser, "Organic Chemistry," edited by H. Gilman, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 190; R. H. Thompson, *Quart. Revs.*, 29 (1956).

[6] (a) D. Y. Curtin and R. R. Fraser, *Chemistry & Industry*, 1358 (1957); (b) T. L. Brown, D. Y. Curtin and R. R. Fraser, This Journal, **80**, 4339 (1958).

trimethyl-2,4-cyclohexadienone (I) which can conveniently be isolated as the dimer in 16% yield. The dienone I is accompanied by some 40% of 2,6-dimethylanisole (II). The present paper is concerned with a more complete discussion of the factors affecting the ratio of dienone to methyl ether in this case and also with the alkylation of certain related phenol salts.

It is of interest to compare the ratio of oxygen to carbon attack in the alkylation of sodium 2,6-dimethylphenoxide with methyl iodide with the ratio obtained with benzyl chloride under the same conditions. In toluene suspension at 110° sodium 2,6-dimethylphenoxide, prepared from the reaction of the phenol with sodium methoxide and removal of the methanol by partial distillation of the solution, reacted with methyl iodide to give 40% of the ether II and 2% of the dienone I, or a ratio of oxygen to carbon attack of about 20. Under the same conditions, benzyl chloride, as shown by a spectroscopic examination of the neutral products gave some 12% of dienone I and 7% of ether II, or a ratio of 0.6.[7] Previously, under somewhat different conditions of time and temperature a ratio of 0.23 was obtained.[4a] In this case, the sodium salt was prepared by reaction of 2,6-dimethylphenol with sodium metal. Traces of methanol which might affect the ratio (and which may have been present when the salt was prepared from sodium methoxide) cannot have been present. Even with a liberal allowance for the discrepancy between the two ratios it seems clear that the alkylation with benzyl chloride gives an oxygen/carbon ratio considerably smaller (and probably about one-thirteenth as large as the alkylation with methyl iodide). A more proper comparison would have employed benzyl iodide instead of benzyl chloride. However, previous experiments[4a] have suggested that the effect on the product ratio of changing the halogen from chloride to iodide should be small. The conclusion is suggested, then, that carbon alkylation in non-polar media is favored by halides which tend to react by a mechanism at the S_N1 or **lim** end[8] of the mechanistic spectrum.[9]

A similar conclusion was reached by Nesmeyanov and Kabachnik[11] in discussing results of Zagorevsky[11] which recently have been published[12] in detail. For example, Zagorevsky found that the alkylation of sodium phenoxide in dioxane solution gave a ratio of oxygen/carbon attack of 0.8 when the halide was trityl chloride, but that the ratio was 50 with tri-(*p*-nitrophenyl)-methyl chloride. A similar difference was found in the alkylation of sodium β-naphthoxide in acetone solution where the ratio was 2 with *p*-methoxybenzyl bromide and >7 with *p*-nitrobenzyl bromide.[12]

A further point of interest in the comparison of the reactions of methyl iodide and benzyl chloride with sodium 2,6-dimethylphenoxide is the implication concerning the relative reactivities of the two halides. Whereas the methyl iodide reaction was about 40% complete in 24 hours the reaction with benzyl chloride was at least 15% complete in 1 hour. In general alkyl iodides appear[13] to react faster than chlorides by factors of 100–1000. It seems likely then that the benzyl iodide reaction would be several hundred times faster than that of methyl iodide under the same conditions.

It was hoped that salts of other metals might lead to increased carbon alkylation. Aluminum 2,6-dimethylphenoxide, prepared from aluminum isopropoxide and the phenol, failed to react appreciably with methyl iodide in 22 hours at 110° in toluene solution, however. Zagorevsky[14] has recently reported the effect of change of the cation on the position of alkylation of β-naphthol salts. In dioxane solution under conditions in which the alkali metal salts gave ratios of attack on the oxygen atom to attack on the 1-position of the ring of 0.9 (lithium salt) to 1.4 (potassium salt) the bromomagnesium salt gave only carbon alkylation. However, even when reaction with methyl iodide was allowed to proceed at 150° for 24 hours, little alkylation of 2,6-dimethylphenoxymagnesium bromide on oxygen and no alkylation on carbon was detected.

Attempts to obtain dramatic acceleration of the alkylation and to increase the amount of carbon attack by adding Lewis acids such as stannic chloride and aluminum chloride failed. For example, the lithium salt of 2,6-dimethylphenol failed to react detectably with methyl iodide in the presence of 10 mole % of anhydrous aluminum chloride in 24 hours at 30° and only 3% of dienone and 11% of the methyl ether were formed in the presence of 10 mole % of anhydrous stannic chloride after 24 hours at 130°. The use of a slight (5%) excess of 2,6-dimethylphenol as a catalyst[15] appeared to be beneficial. An attempt to increase the proportion of carbon alkylation by shifting the mechanism farther in the **lim** or S_N1 direction by employing methyl brosylate as the alkylating agent instead of methyl iodide also failed. Thus, sodium 2,6-dimethylphenoxide reacted with methyl brosylate in toluene medium at 110° to give 80% of the theoretical amount of the methyl ether after 20 hours and no dienone was detected by examination of the ultraviolet spectrum of the neutral fraction.

The reactions of lithium phenoxide and lithium *o*-methylphenoxide with excess methyl iodide as solvent have also been examined. The product mixture was rather more complex than had been found by Claisen, Kremers, Roth and Tietze[3] in their study of the reaction of sodium phenoxide

---

(7) Another reaction carried out by Mr. Richard Tuites, identical with the reaction described in this paper except that the mixture was heated under reflux for 1 hour and allowed to stand at room temperature for 3 hours longer, gave 23% of dienone and 12% of ether or a ratio of 0.5 in agreement with the result described here.

(8) See A. Streitwieser, Jr., *Chem. Revs.*, **56**, 571 (1956).

(9) It is to be noted that this is the converse of the generalization arrived at by Kornblum, Smiley, Blackwood and Iffland[10] from a consideration of the effect of polarity of the solvent. Recently Kornblum and Lurie [Abstracts, 133rd Meeting, American Chemical Society, San Francisco, Cal., April, 1958, p. 14-N] have advanced evidence that the metal salts of phenol and 3-alkylphenols had to be present as a solid phase in order that carbonalkylation occur. In the present work the importance of heterogeneity has not been investigated.

(10) N. Kornblum, R. A. Smiley, R. K. Blackwood and C. Iffland, THIS JOURNAL, **77**, 6269 (1955).

(11) A. N. Nesmeyanov and M. I. Kabachnik, *J. Gen. Chem.* (*U.S.S.R.*), **25**, 41 (1955).

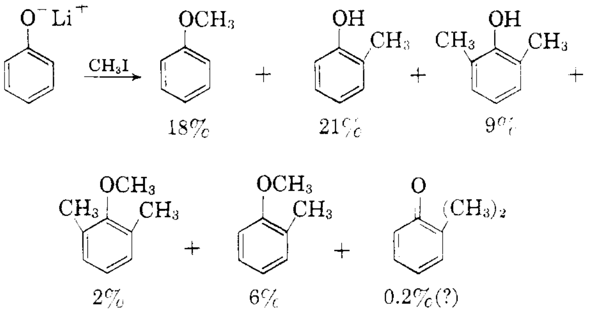
(12) V. A. Zagorevsky, *ibid.*, **27**, 488 (1958).

(13) See ref. 7, p. 602, Table 16.

(14) V. A. Zagorevsky, *J. Gen. Chem.* (*U.S.S.R.*), **27**, 3055 (1957).

(15) P. D. Bartlett and H. J. Dauben, Jr., THIS JOURNAL, **62**, 1339 (1940).

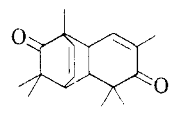
with allyl and benzyl halides. Thus lithium phenoxide gave at least six different products as shown. These were characterized by separation of the acid



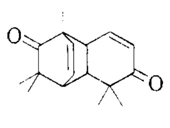
and neutral fractions and subjecting each of them to vapor chromatography. The retention times of the components were compared with those of the components of known mixtures. An ultraviolet spectrum indicated that there was a trace of a dienone, presumably 6,6-dimethyl-2,4-cyclohexadienone.

The alkylation of lithium *o*-cresoxide also gave, under the same conditions, methyl *o*-cresyl ether together with methylated phenols similar to those obtained from the lithium salt of phenol.

The alkylation mixture obtained from *o*-cresol was allowed to stand in order to convert the dienones present to dimeric products and the mixture of dimers then was separated by distillation of the other more volatile products under vacuum. Chromatography led to the separation of small amounts of the dimer of 2,6,6-trimethyl-2,4-cyclohexadienone which has been shown[6b] to be *endo*-1,4,6,6,9,9-hexamethyl-$\Delta^{3,11}$-tricyclo[2.2.2.-4^{2,7}]dodecene-5,10-dione (III). A second substance (IV) with an infrared spectrum similar to that of III was also separated. This compound had the correct analysis for an adduct formed from one molecule of the dimethyl dienone I and one molecule of 2,6,6-trimethyl-2,4-cyclohexadienone. The ultraviolet spectrum of IV in cyclohexane showed absorption at 233 mμ (ε 7650), whereas the dimer III showed absorption at 240 mμ (ε 9000). This suggests that the two structures differ by a methyl group attached to the α,β-unsaturated carbonyl function.[16] If the relative orientations of the components are assumed to be similar in the two adducts III and IV (an assumption which can be made only with some reluctance), the structure of IV is that shown below. None of the corresponding dimer of I was isolated.

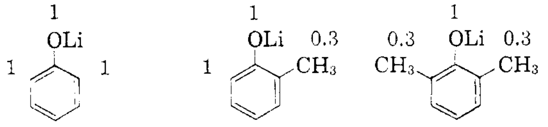


III



IV

Recently Alder, Flock and Lessenich[17] have reported the synthesis of 6,6-dimethyl-2,4-cyclohexadienone by epoxidation of dimethylfulvene and pyrolysis of the epoxide dimer. The complications introduced in the direct alkylation of lithium *o*-cresoxide clearly make their method a better one for the synthesis of this dienone. Reasonable assumptions concerning the origin of the polyalkylated products lead to the conclusion that the ratios of attack on oxygen and in the two *o*-positions for reaction of methyl iodide with the lithium salts of phenols in excess methyl iodide as the medium are as summarized below (reactivity at the oxygen atom taken as 1 in each case). Again,



as was observed in the benzylation of sodium methylphenoxides,[4b] reaction at an *o*-position already occupied by a methyl substituent is somewhat slower than at an *o*-position occupied by a hydrogen atom in the same ring.

Experimental[18]

Alkylation of Sodium 2,6-Dimethylphenoxide with Benzyl Chloride.—The sodium salt of 2,6-dimethylphenol was prepared in a nitrogen atmosphere by heating under reflux a solution of 2.4 g. (0.02 mole) of 2,6-dimethylphenol in 30 ml. of freshly distilled toluene containing 1.06 g. (0.02 mole) of commercial sodium methoxide. After distillation of 10 ml. of the solvent (to remove methanol and water), 2.5 g. (0.02 mole) of benzyl chloride was added and the mixture heated under reflux for 1 hr. After the reaction mixture had cooled, an equal volume of water was added and the mixture extracted with two 20-ml. portions of Claisen alkali.[19] The aqueous extracts were extracted with 12 ml. of toluene, and the combined toluene extracts dried over sodium sulfate. A comparison of the absorption in the infrared spectrum of the filtered toluene solution with the corresponding absorption in the corresponding spectrum of benzyl 2,6-dimethylphenyl ether[4a] led to an estimate of 7% of this ether, while the ultraviolet spectrum in ethanol showed absorption at 311 mμ (employing ε 5000) corresponding to a 12% yield of 2,6-dimethyl-6-benzyl-2,4-cyclohexadienone.[4a]

Alkylation of Sodium 2,6-Dimethylphenoxide with Methyl Iodide.—To a solution of 2.4 g. (0.02 mole) of 2,6-dimethylphenol in 75 ml. of toluene in a nitrogen atmosphere was added 1.06 g. (0.02 mole) of sodium methoxide and 10 ml. of the solvent distilled to remove small amounts of methanol and water. The mixture was placed in a Pyrex tube together with 36 g. (0.25 mole) of methyl iodide and the tube was sealed and heated at 110° for 24 hr. After cooling in a Dry Ice–acetone mixture the tube was opened, the contents added to 20 ml. of water and then extracted with two 20-ml. portions of Claisen alkali.[19] The organic layer was washed with water and dried over sodium sulfate. Removal of the solvent gave 1.7 g. of liquid which was estimated by the infrared absorption at 1095 cm.$^{-1}$, when compared with that of 2,6-dimethylanisole (both 10% solutions in chloroform in 0.1 mm. cells) to contain 1.1 g. (38% of the theoretical amount) of 2,6-dimethylanisole (II). The yield of dienone I was estimated by the intensity of the absorption at 306 mμ in the ultraviolet to be 1.7%. The calculation was based on an assumption of ε 5000 for pure dienone.

Methylation of Sodium 2,6-Dimethylphenoxide with Methyl *p*-Bromobenzenesulfonate. 2,6-Dimethylanisole (II).—Sodium 2,6-dimethylphenoxide was prepared in a ni-

---

(16) L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 3rd edition, 1949, pp. 184 ff.

(17) Alder, F. H. Flock and H. Lessenich, *Chem. Ber.*, **90**, 1709 (1957).

(18) All melting points are corrected. Microanalyses were performed by Mr. J. Nemeth, Miss C. Higham, Mrs. M. Stingl and Mrs. F. Ju. Infrared spectra were measured by Mr. P. McMahon, Mr. J. Brader, Mr. B. Cloonan and Miss M. DeMott using 0.1-mm. cells with a model 21 Perkin–Elmer spectrophotometer. Ultraviolet spectra were determined by Mr. M. Chao and Mr. J. Chiu in 1-cm. cells with a Cary model 14M spectrophotometer. Photographs of the original spectra are available in the Thesis of R.R.F.,[1] available on microfilm from University Microfilms, Ann Arbor, Mich.

(19) A solution of 350 g. of potassium hydroxide in 250 ml. of water diluted with methanol to a total volume of 1 l.

trogen atmosphere from 2.4 g. (0.02 mole) of the phenol and 1.06 g. (0.02 mole) of sodium methoxide in 75 ml. of freshly distilled toluene followed by distillation of 10 ml. of the solvent to remove methanol. After the addition of 25 g. (0.10 mole) of methyl *p*-bromobenzenesulfonate the mixture was heated under reflux for 20 hr. and the neutral fraction separated as in the preceding experiment and distilled through a Holtzmann column to give 2.5 g. of liquid, b.p. 83–85° (20 mm.), n^{25}D 1.5017. The infrared spectrum of the distillate showed strong absorption at 1095 cm.$^{-1}$ from which the yield of ether II was estimated to be 2.34 g. (80% of the theoretical). The spectrum indicated that a trace of methyl brosylate was still present but showed no sign of the dienone I or its dimer. Redistillation gave 1.45 g. (54%) of ether, b.p. 66–67° (11 mm.), n^{25}D 1.5003. An acid fraction amounting to 0.4 g., probably unreacted dimethylphenol, was not examined further.

The 2,6-dimethylanisole used as authentic sample was similarly prepared from methyl tosylate and after the second distillation as above was purified by chromatography through an alumina column using cyclohexane as an eluent. Distillation of the eluted sample gave a fraction, b.p. 81° (21 mm.), n^{25}D 1.5000 (lit.[20] b.p. 182°, n^{14}D 1.5053). The infrared spectrum of a 10% chloroform solution showed strong absorption at 1095, 1175 and 1268 cm.$^{-1}$.

Attempted Methylation of the Bromomagnesium Salt of 2,6-Dimethylphenol.—The bromomagnesium salt of 2,6-dimethylphenol was prepared by the addition of a solution of 5.2 g. (0.044 mole) of 2,6-dimethylphenol in 25 ml. of ether in a nitrogen atmosphere to a slurry of methylmagnesium iodide in 25 ml. of ether prepared by the addition of 7.6 g. (0.054 mole) of methyl iodide in 25 ml. of anhydrous ether to 1.0 g. (0.041 mole) of magnesium turnings. The ether was distilled off and the gray solid remaining was heated in a sealed tube with 56 g. (0.40 mole) of methyl iodide for 5 hr. at 115°. After cooling, the contents of the tube were poured into 50 ml. of water and separated into an acidic and neutral fraction as before. The neutral fraction after removal of ether weighed 0.9 g. and showed no absorption in the carbonyl region. The ultraviolet spectrum of this liquid had no absorption in the 300 mμ region. The acid fraction weighed 3.4 g. This liquid was washed with a 10% solution of sodium thiosulfate and water, dried over magnesium sulfate and distilled. The distillate, b.p. 115–120° (35 mm.), was subjected to vapor phase chromatography using a polyethylene glycol column. The graph obtained had only a single peak with the same retention time as that of pure 2,6-dimethylphenol. It was found that a mixture of 2,6-dimethylphenol and mesitol was separated on this column.

Alkylation at 150° of Lithium 2,6-Dimethylphenoxide in Excess Methyl Iodide.—This reaction was carried out as described previously.[6b] In each case the amount of dienone I was estimated from the ultraviolet absorption at 299 mμ, the dienone dimer from the infrared absorption at 1723 cm.$^{-1}$ and ether II from the infrared absorption at 1095 cm.$^{-1}$ as described.[6b] The results of four different runs gave ether/dienone + dimer ratios of 1.7, 2.0, 2.0 and 2.1.

Methylation of the Lithium Salt of *o*-Cresol at 150°.—The lithium salt of *o*-cresol was prepared by heating 9.1 g. (0.084 mole) of *o*-cresol, b.p. 105–107° (35 mm.), and 0.56 g. (0.080 mole) of lithium metal under reflux in 70 ml. of toluene for 16 hr. The toluene was distilled off and the white solid which remained was heated in a sealed tube at 150° for 24 hr. with 100 g. (0.705 mole) of methyl iodide. The tube was cooled and opened and its contents transferred to a flask from which the excess methyl iodide was distilled. The neutral fraction, separated as before, was distilled through a Holtzmann column giving 2.95 g. of yellow liquid, b.p. 75–120° (20 mm.). The infrared spectrum contained a strong band at 1125 cm.$^{-1}$ from which the presence of 2.05 g. (21%) of *o*-methylanisole was estimated. Assuming the extinction coefficients to be the same as those for the products from 2,6-dimethylphenol, the yield of dienone dimer was estimated to be 0.45 g. (4.6%) from the band at 1715 cm.$^{-1}$. The yield of dienone calculated from the maximum at 299 mμ in the ultraviolet was 0.14 g. (1.5%). After allowing the neutral distillate to stand for 24 hr. the *o*-methylanisole was distilled off under high vacuum at room temperature leaving 0.45 g. of solid dimer. The acid fraction was distilled giving 2.8 g. of a colorless liquid, b.p. 114–117° (45 mm.), which was subjected to vapor phase chromatography over silicone oil at 190°. A comparison of the retention times with those of a known mixture of *o*-cresol (13.5 min.), 2,6-dimethylphenol (16.5 min.) and mesitol (22 min.) indicated that the distillate contained 1.6 g. (16%) of 2,6-dimethylphenol and 0.21 g. (2%) of a trimethylphenol together with 0.98 g. of unreacted *o*-cresol, the proportions being calculated from the areas under the peaks. The distillate from the high vacuum distillation of the neutral fraction was collected in a Dry Ice trap and purified by chromatography over alumina. The eluent was distilled giving 1.2 g. of colorless methyl ether, b.p. 65° (12 mm.), n^{25}D 1.5125, (lit.[20] b.p. 172°, n^{20}D 1.517). The infrared spectrum contained a strong band at 1125 cm.$^{-1}$ and a weak band at 1095 cm.$^{-1}$. From vapor phase chromatography over silicone oil at 185° the presence of di- and trimethylated anisoles in addition to 75% of *o*-methylanisole was shown as evidenced by a comparison of their retention times with those of known *o*-methylanisole and 2,6-dimethylanisole.

The residue from the high vacuum distillation of the neutral fraction obtained from two 0.080-molar runs by the methylation at 150° was passed through a column of alumina using hexane as eluent. Fractions of 100 ml. of eluent were collected. The first fractions after removal of solvent gave 0.33 g. of white solid, m.p. 72–92°. The middle fractions gave an oil whose infrared spectrum possessed a band at 3640 cm.$^{-1}$ in addition to bands at 1715 and 1682 cm.$^{-1}$. Sublimation of this oil gave a white solid, m.p. 61–66°, which had a very strong phenolic odor. The middle fractions after recrystallization from hexane and then methanol gave 0.42 g. of IV, 4,6,6,9,9-pentamethyl-$\Delta^{3,11}$-tricyclo-[2.2.2.$4^{-,7}$]dodecene-5,10-dione (or its structural isomer 3,3,5,9,9-pentamethyl-$\Delta^{5,11}$-tricyclo[2.2.2.$4^{2,7}$]dodecene-4,-10-dione), m.p. 113–116°.

Anal. Calcd. for $C_{17}H_{22}O_2$: C, 79.0; H, 8.6. Found: C, 79.1; H, 8.7.

The first eluted fractions, m.p. 72–92°, were subjected to a more scrupulous chromatography over alumina. The first fractions eluted in hexane gave, after removal of solvent, 70 mg. of white dimer III, m.p. 107–110° which showed no m.p. depression when mixed with a sample of III. Fractions 14–18 gave 70 mg. of dimer IV, m.p. 113–116°, which showed a marked depression of m.p. when mixed with a sample of III. The ultraviolet spectrum in cyclohexane showed λ_{max} 233 mμ (ε 7650). The infrared spectrum of this dimer was the same as that of dimer III except for minor variations in the fingerprint regions.

Anal. Calcd. for $C_{17}H_{22}O_2$: C, 79.0; H, 8.6. Found: C, 79.1; H, 8.7.

Repetition of the reaction at a temperature of 170° for 24 hr. and analysis as before indicated that the neutral fraction, 3.59 g., contained 2.5 g. (26%) of *o*-methylanisole, 0.39 g. (4%) of dienone and 0.18 g. (2%) of dimer. The acid fraction, 5.0 g., contained 2.0 g. of unreacted *o*-cresol and 2.66 g. (27%) of 2,6-dimethylphenol. In addition the presence of 0.33 g. (3.4%) of a trimethylphenol was indicated. Four other runs gave similar results.

Alkylation of Phenol.—A solution of 15.8 g. (0.168 mole) of phenol in 100 ml. of toluene was heated under reflux for 16 hr. with 1.12 g. (0.160 mole) of finely cut lithium metal. The toluene was then distilled off and the dry white lithium salt was transferred to a Pyrex tube. Care was taken to remove any unreacted lithium. Methyl iodide (100 g., 0.705 mole) was added and the tube sealed and heated at 150° for 24 hr. Using the same workup as employed for the alkylation of *o*-cresol, a neutral fraction was obtained which upon distillation gave 4.07 g. of liquid, b.p. 85–95° (45 mm.). After purification by chromatography on alumina, the liquid was found from vapor phase chromatography over silicone oil at 180° to contain 2.7 g. (16%) of anisole, 1.0 g. (5%) of *o*-methylanisole and 0.37 g. (2%) of 2,6-dimethylanisole whose peaks were identified by their retention times. The acidic fraction was distilled giving 7.2 g. of liquid, b.p. 118–127° (50 mm.), which contained 2.6 g. of unreacted phenol, 3.04 g. (17%) of *o*-cresol and 1.57 g. (8%) of 2,6-dimethylphenol, calculated from the areas under the peaks in the graph obtained by vapor phase chromatography over silicone oil at 182°. The

---

[20] K. von Auwers and A. Frühling, *Ann.*, **422**, 181 (1921).

peaks were identified by a comparison of their retention times with those of a known mixture of phenols. The amount of dienone present in the neutral fraction was found to be 0.04 g. (0.2%) calculated from its absorption in the ultraviolet.

URBANA, ILL.

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA]

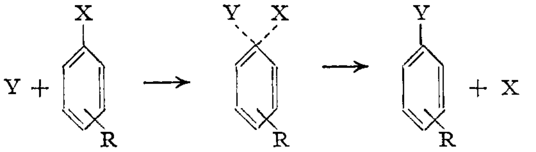
Base Catalysis of the Reaction of N-Methylaniline with 2,4-Dinitrofluorobenzene. Proof of the Intermediate Complex Mechanism for Aromatic Nucleophilic Substitution[1]

BY J. F. BUNNETT[2] AND JOHN J. RANDALL

RECEIVED MARCH 7, 1958

The reaction of N-methylaniline with 2,4-dinitrofluorobenzene is sensitive to base catalysis, whereas reactions with the corresponding chlorine and bromine compounds are not. In ethanol, the catalyzed rate is linearly dependent on potassium acetate concentration. In 60% dioxane–40% water, the catalyzed rate shows less than linear response to hydroxide ion concentration at higher concentrations of the base (Fig. 3). The acetate-catalyzed rate is not depressed by added acetic acid; the reaction is thus *general* base catalyzed. These observations are inconsistent with any form of one-step mechanism for the displacement reaction. They are, however, rationally interpretable in terms of the intermediate complex mechanism shown in Chart I. In combination with other evidence previously published, the present work firmly establishes the intermediate complex mechanism for a large group of aromatic nucleophilic substitution reactions, and makes this mechanism extremely probable for all such reactions.

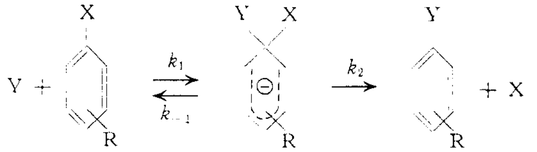
The mechanism of nucleophilic displacement at aromatic carbon has been a subject of active discussion in recent years. Many chemists have advocated a one-step, S_N2-like mechanism which has often been represented as



(1)

Others have favored a two-step mechanism involving a metastable intermediate complex. The latter view was strongly advocated by Bunnett and Zahler[3] and has been further supported in recent papers from this Laboratory.

The intermediate complex mechanism is represented by equation 2.



(2)

intermediate complex

This mechanism predicts second-order kinetics, as commonly observed, and the over-all second-order rate coefficient depends on the rate coefficients of the individual steps

$$k = k_1k_2/(k_{-1} + k_2) \qquad (3)$$

Reactions occurring by this mechanism may be classified according to the relative magnitudes of k_{-1} and k_2: (class A) If $k_2 >> k_{-1}$, that is, if X is expelled from the intermediate complex much faster than Y, equation 3 simplifies to $k = k_1$; the rate is determined by the rate of formation of the intermediate complex. (class B) If $k_{-1} >> k_2$, equation 3 becomes $k = k_1k_2/k_{-1}$; the rate is equal to the equilibrium concentration of the intermediate complex times the rate coefficient (k_2) for its transformation into products. (class C) If k_2 and k_{-1} are of comparable magnitude, equation 3 cannot be simplified; the over-all rate is affected both by the rates of bond-making (k_1) and of bond-breaking (k_2), as well as by k_{-1}.

The case for the intermediate complex mechanism comprises the following principal arguments: 1. The transition state for the one-step, S_N2-like mechanism is difficult to rationalize quantum-mechanically, whereas the transition states and intermediate for the intermediate complex mechanism are easily rationalized.[3] 2. Certain highly activated substrates have been observed to form *stable* complexes similar to the intermediate complex in equation 2; it is reasonable that when less activation is present complexes of this sort are also formed though their stability may not be sufficient to permit isolation.[3] 3. In reactions known to involve breaking of a carbon–halogen bond in the rate-determining step, the carbon–fluorine bond is broken very much slower than other carbon–halogen bonds. Yet in many aromatic nuclophilic substitution reaction series, the order of mobility of the halogens is F >> Cl ~ Br ~ I. It is therefore concluded that in such reaction series the C–X bond is not broken in rate-determining steps. This result is incompatible with the S_N2-like mechanism,[4] but is agreeably explained in terms of the intermediate complex mechanism, class A, in which the rate is determined by the rate of formation of the intermediate.[5] 4. In reactions of piperidine with several 1-substituted-2,4-dinitrobenzenes,[5] six substituents with first atoms representing five elements were displaced at nearly the same rate.[6] Since there

---

[1] Financial assistance from the Office of Ordnance Research, U. S. Army, is gratefully acknowledged. Presented in part at the Southeastern Regional American Chemical Society Meeting, Durham, N. C., November, 1957.

[2] Department of Chemistry, Brown University, Providence, R. I.

[3] J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 297 (1951).

[4] With this exception: the result could be accommodated by an unlikely one-step mechanism in which bond-breaking had made little or no progress at the rate-determining transition state.[5]

[5] J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, THIS JOURNAL, **79**, 385 (1957).

[6] A similar result has been obtained in reactions of sodium thiophenoxide with the same substrates; *cf.* J. F. Bunnett and W. D. Merritt, Jr., *ibid.*, **79**, 5967 (1957).