The Tscherniac–Einhorn Reaction. II. Kinetics and Mechanism

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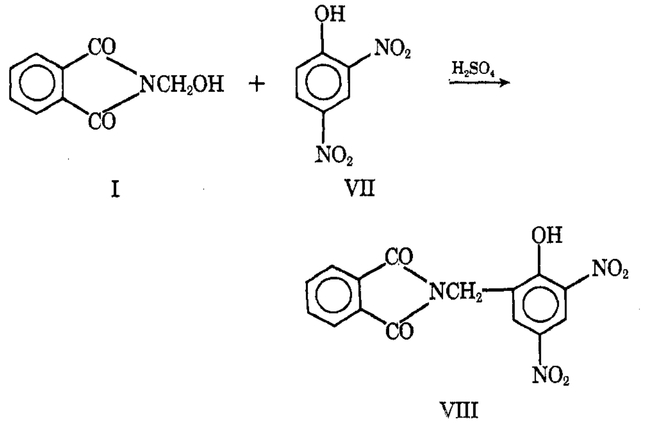
The rate of the reaction of N-hydroxymethylphthalimide (I) with 2,4-dinitrophenol (VII) in 85–100% sulfuric acid is second order with respect to I and zero order in VII. Logarithms of the second-order rate constants are proportional to $0.8H_R$. These observations, along with those of part I, support a mechanism in which the rate-limiting step is the dissociation of the protonated ether IV to the ion VI ($Y^- = HSO_4^-$). Independent evidence for the intermediacy of this ion is derived from preparative experiments involving the action of silver salts on N-chloromethylphthalimide (IX). Further preparative studies indicate, however, that other species derived from I, but less electrophilic than the dissociated ion VI, readily attack aromatic compounds more nucleophilic than 2,4-dinitrophenol. These observations are best rationalized by the intermediacy of associated ionic species less reactive than the "free" imonium ion VI.

The first part[1] of this work showed that solutions of N-hydroxymethylphthalimide (I) in strong sulfuric acid (>75%) contain several species that can act as electrophilic intermediates (or precursors thereof) in the aromatic substitution process known as the Tscherniac–Einhorn reaction. This second part is concerned with a rate study utilizing this reagent and, with some preparative studies, designed to relate the conclusions derived from the kinetic work to some of the broader aspects of aromatic amidoalkylations.[2] As a substrate for the kinetic work, 2,4-dinitrophenol (VII) was the best choice for several reasons. Preliminary investigation revealed that it neither protonates nor sulfonates in 100% sulfuric acid. With I in strong sulfuric acid it gives good yields (>85%) of a single product VIII



even at room temperature, and, being relatively resistant to aromatic substitution, it would be expected to make high demands on the reactivities of whatever electrophilic intermediates might be involved in the process.

TABLE I

RATE CONSTANTS OF THE REACTION OF N-HYDROXYMETHYLPHTHALIMIDE (I) WITH 2,4-DINITROPHENOL (VII) IN SULFURIC ACID AT 35°

Run no.[a]	$[I]_0$, M[b]	$[VII]_0$, M[b]	H_2SO_4 (cor), %	k_2, 10^4 M^{-1} sec^{-1}
1	0.50	0.50	95.85	2.59 ± 0.17
2	0.50	0.50	95.85	2.80 ± 0.13
3	0.50	0.25	95.85	2.09 ± 0.15[c]
4	0.50	0.25	95.85	3.55 ± 0.10[c]
5	0.25	0.25	93.85	0.342 ± 0.052
6	0.80	0.25	93.85	0.467 ± 0.045[c]

[a] In runs 5 and 6, H^C served as the monitor peak. In all others $0.5H^{E'}$ was used. In runs 3 and 4, $0.125(H^D + H^{D'})$ was used in the reference integral instead of $0.25(H^D + H^{D'})$ in order to correct for the twofold difference in concentration between I and VII. In run 6, $0.0781(H^D + H^{D'})$ was the correction factor. [b] Initial concentration. [c] Slope of the plot of $1/[I]$ *vs.* time where $[I]$ is given by $[I]_0 - ([VII]_0 - C)$ where C is obtained by eq 1 (runs 3 and 4) or 2 (run 6) with $C_0 = [VII]_0$ or $0.25\ M$.

Kinetic Results.—Six rate runs at 35° were carried out using an nmr method to follow the progress of the reaction. Results are summarized in Table I. The rate data for the first two runs employing equimolar concentrations of I and VII fitted the requirements of the second-order rate law. However, halving the concentration of VII in two otherwise identical experiments (runs 3 and 4) did not affect significantly the magnitude of the second-order constant *for the rate of disappearance of I.* In two final runs (5 and 6) a more than threefold variation in the concentration of I had little effect on the same second-order rate constant. It is apparent that these results are consistent with a reaction rate which is zero order in 2,4-dinitrophenol and second order in N-hydroxymethylphthalimide (I). A study of the variation of the rate with sulfuric acid concentration further confirmed the validity of this rate law.

Using a uv spectrophotometric method to follow the rate of disappearance of VII, a number of reactions were carried out under pseudo-zero-order conditions (*i.e.*, I in large excess) in sulfuric acid solutions ranging from 84 to 100+% (corrected) and over a greater than tenfold range in concentration of I. The observed pseudo-zero-order rate constants were divided by the square of the concentration of I to obtain the corresponding second-order constants (k_2). Results of 22 runs are summarized in Figure 1 which shows a plot of log k_2 *vs.* H_R.[3] The line represents the result of a simple linear regression analysis of the data. Its slope is 0.78 ± 0.04 with a 95% confidence limit of ±0.08 (a similar plot of log k_2 *vs.* H_0[4] gave a slope of 1.39 ± 0.06 with a 95% confidence limit of ±0.13). Of chief interest, however, is the fact that the points (A in Figure 1) corresponding to the first four runs of Table I actually straddle this line, and the two points (B in Figure 1) for the slower runs (5 and 6 in Table I) deviate from it by barely significant amounts.

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[1] H. E. Zaugg, A. M. Kotre, and J. E. Fraser, *J. Org. Chem.*, **34**, 11 (1969).

[2] H. E. Zaugg and W. B. Martin, *Org. Reactions*, **14**, 52 (1965).

[3] H_R values were obtained from an expanded plot of % H_2SO_4 *vs.* H_R using the values at 30° listed by E. M. Arnett and R. D. Bushick, *J. Amer. Chem. Soc.*, **86**, 1564 (1964).

[4] The H_0''' values listed by E. M. Arnett and G. W. Mach, *ibid.*, **86**, 2671 (1964), were used.

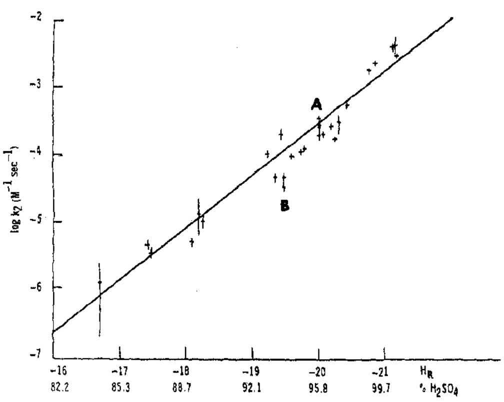
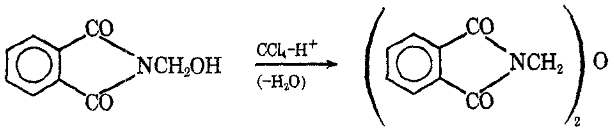


Figure 1.—Plot of log k_2 vs. H_R for the reaction of N-hydroxymethylphthalimide with 2,4-dinitrophenol in sulfuric acid.

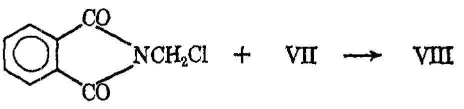
Preparative Results.—Several attempts were made to prepare the substitution product VIII from I and VII under milder acid-catalyzed conditions, but they all failed. In the presence of *p*-toluenesulfonic acid in boiling carbon tetrachloride, a mixture of I and VII gave a 93% yield of bis(phthalimidomethyl) ether (V). (In the absence of VII a 97% yield of V was obtained.)



I V

In contrast, 2-naphthol, under the same conditions, gave a 72% yield of the corresponding 1-phthalimidomethyl derivative, and, when benzene was used as the azeotropic solvent instead of carbon tetrachloride, a 96% yield of N-benzylphthalimide was obtained. Further attempts to effect substitution of 2,4-dinitrophenol (VII) by I in mixtures of trifluoroacetic acid and its anhydride and in anhydride–fluoroboric acid mixtures also failed.

The reaction of N-chloromethylphthalimide (IX) with 2,4-dinitrophenol also was studied. Of many conditions tried, the only ones leading to the product

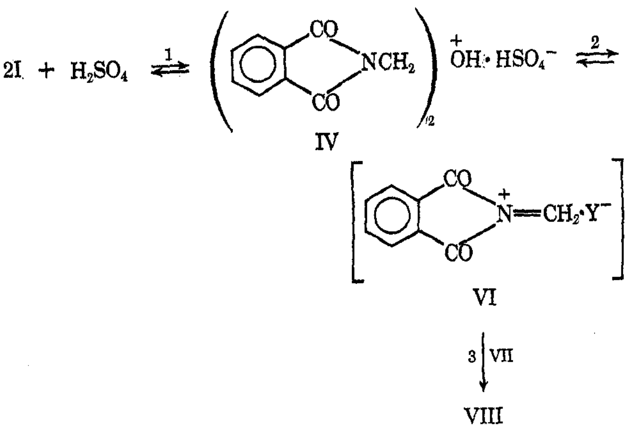


IX

VIII involved treatment of a mixture of the reactants with the silver salt of a very strong acid (*e.g.*, $AgSbF_6$ or $AgBF_4$). The best yield of VIII (72%) was obtained using silver hexafluoroantimonate in sulfur dioxide solution at −30°. The use of Lewis acid catalysts (*e.g.*, $AlCl_3$, $ZnCl_2$, $SnCl_4$, and $SbCl_5$) under a variety of conditions was totally ineffective in this reaction.

Discussion

Mechanism of the Reaction of N-Hydroxymethylphthalimide (I) with 2,4-Dinitrophenol (VII).—The results of the work described in this and the preceding[1] paper are consistent with the mechanism given above in which the second step is rate limiting.



Of the several equilibrium species found[1] to be present in sulfuric acid solutions of I, the protonated ether IV is the only one with a second-order concentration dependence with respect to I. The subsequent slow ionization of IV to VI ($Y^- = HSO_4^-$) followed by rapid reaction of VI with VII further accounts for the observed zero-order rate dependence with respect to VII. That the protonated ether IV is not itself sufficiently electrophilic to react with VII is demonstrated by the failure of the acid-catalyzed reaction of the ether V and VII *in nonpolar media.* That prior ionization to the more electrophilic VI ($Y^- = HSO_4^-$) *is* necessary is indicated by the fair correlation of the rate with H_R[5] and by the observed requirements for the reaction of VII with N-chloromethylphthalimide (IX). Only when IX is treated with a silver salt containing a very stable anion is any product formation from VII observed. It is in the presence of precisely these counterions (*i.e.*, $Y^- = SbF_6^-$ or BF_4^-) that a reactive cation like VI would be most stable.[7] The failure of the chloride IX to react under Friedel–Crafts conditions further suggests that the action of Lewis acids on IX does not produce dissociated ions (*i.e.*, VI, $Y^- = AlCl_4^-$ or $SbCl_6^-$, etc.) to a kinetically significant extent.[9]

In sulfuric acid, too, species other than IV that are known[1] to be present (*i.e.*, II and III) clearly do not ionize to VI ($Y^- = HSO_4^-$) at significant rates. As already noted,[1] IV contains one more basic center than either II or III, albeit a weak one. It is tempting to suggest that protonation at this center with simultaneous or subsequent scission of the unstable dication to VI and II accounts for the successful ionization *via* IV.

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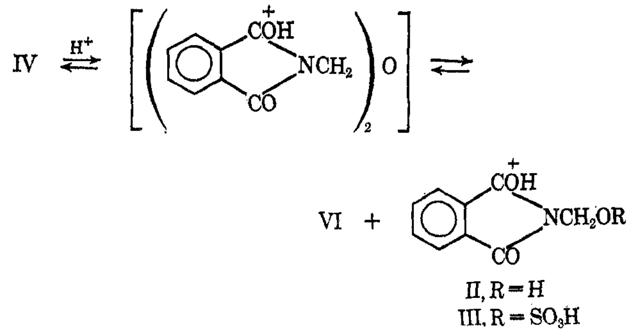
[5] Since amides (and presumably imides) are known not to be Hammett bases,[6] it would be surprising indeed if an ionization such as IV → VI would follow exactly the corresponding ionizations of the structurally unrelated arylcarbinols upon which the H_R acidity function is empirically based.

[6] A. R. Katritzky, A. J. Waring, and K. Yates, *Tetrahedron,* **19**, 465 (1963); A. R. Katritzky, J. B. Stevens, and K. Yates, *Can. J. Chem.*, **42**, 1957 (1964).

[7] Direct nmr observations of VI ($Y^- = SbF_6^-$) in 1,2-dichloroethane solution was suggested by the presence of an unstable peak in a region (916 Hz vs. TMS) consistent with that expected[8] for the highly deshielded protons of the methylene group.

[8] G. A. Olah and C. U. Pittman, Jr., *Advan. Phys. Org. Chem.*, IV, 305 (1966).

[9] Compare M. Baaz and V. Gutmann in "Friedel–Crafts and Related Reactions," Vol. 1, G. A. Olah, Ed., Interscience Publishers, New York, N. Y., 1963, pp 373–377.



Other Mechanisms of Amidoalkylation.—Successful substitution of benzene and 2-naphthol by I or V under conditions that preclude the formation of the dissociated "carbonium–imonium" ion VI indicates that other mechanisms are operative in these cases. Either these aromatic substrates, unlike VII, are sufficiently nucleophilic to effect SN2 displacements on species such as II, III, or IV, or, as seems more likely, intermediates less reactive than the dissociated ion VI are formed from these equilibrium species in a rate-limiting step (*i.e.*, an SN1 process). The more nucleophilic aromatic compounds (benzene and 2-naphthol) are then able to react with these intermediates in a final fast step, but the relatively inert 2,4-dinitrophenol (VII) is not. Presumably, these moderately reactive intermediates are nothing more than tightly solvated analogs of VI in which the leaving group (H_2O from II and H_2SO_4 from III) remains associated with the cation to form what amounts to an associated (intimate or solvent separated) ion pair. Ample evidence for the discrete existence of these species comes indirectly from solvolysis studies[10] and from direct observation.[11] The Tscherniac reagent apparently furnishes an interesting system in which one intermediate (*i.e.*, IV) is able to give dissociated ions while others (*i.e.*, II and III) are not.

Likewise, N-chloromethylphthalimide (IX) readily undergoes Lewis acid catalyzed reactions with more reactive aromatic substrates such as benzene.[2,12] Apparently the contact ion pairs or ion-pair aggregates presumably present in these systems[9] do not satisfy the electrophilic demands of 2,4-dinitrophenol for "free" ions.

Experimental Section

Nmr spectra were obtained with a Varian Model A-60 spectrometer. A Bausch and Lomb Spectronic 600 (with Sargent Model SRL recorder) was used for the uv-visible absorption spectra. Melting points are uncorrected.

Behavior of 2,4-Dinitrophenol (VII) in Sulfuric Acid.—The ultraviolet spectrum of 2,4-dinitrophenol, mp 111–112° [$\text{uv}_{\max}$ (98% H_2SO_4), 270 (ϵ 13,500) and 320 mμ (ϵ 11,000)], does not change significantly in the range of sulfuric acid concentrations from 85 to 99%. In particular there is no appearance of absorption in the visible region (400–440 mμ) at higher acid concentrations as is characteristic of the protonation of *p*-nitrophenol.[13] Therefore, it can be concluded that 2,4-dinitrophenol is like 2,4-dinitrotoluene which is appreciably protonated only in fuming sulfuric acid.[14] To determine whether any sulfonation of VII occurs in strong sulfuric acid, a solution (0.0593 g of VII in 25 ml of 97.35% acid) was kept at 50° for several days. At appropriate times, 4-ml aliquots were withdrawn, quenched in ice–water (~50 ml), and extracted with ether (four 20-ml portions). The combined ether extracts were partitioned with 10% aqueous sodium bicarbonate solution (four 20-ml portions), and the combined extracts were diluted (equally in all cases) to a volume suitable for uv examination. The following absorbances at 360 mμ were observed at the times indicated: 0.5 hr, 0.750; 70.5 hr, 0.712; 71.0 hr, 0.750; 72.0 hr, 0.748. It is evident that as much VII is recoverable after 70 hr as at 0.5 hr. If sulfonation had occurred, it would not have been extractable by ether from the original aqueous solution.

Preparation of N-(2-Hydroxy-3,5-dinitrobenzyl)phthalimide (VIII).—A mixture of 2.22 g (0.0125 mol) of N-hydroxymethylphthalimide (I) and 2.30 g (0.0125 mol) of 2,4-dinitrophenol (VII) was treated with 25 ml of 97.35% sulfuric acid. Solution was effected by occasional swirling, and the clear yellow mixture was allowed to stand at room temperature for 4 days. The solution was poured and washed into ice–water; the product was collected at the filter, resuspended in water, collected again, and washed to neutrality with more water. The dried product, mp 195–205°, weighed 3.31 g (85% yield). Recrystallization gave 2.72 g (70%) of pure VIII: mp 212–214° [identity and purity checked by ir and elemental analysis (lit.[15] mp 210–211°)].

Determination of the Rate Law in the Reaction of N-Hydroxymethylphthalimide (I) with 2,4-Dinitrophenol (VII).—Preliminary nmr measurements of the reactants and product separately dissolved in strong sulfuric acid (>95%) provided the following assignments where the numbers refer to individual peak positions in hertz relative to TMS in capillary, and where H^{A}, H^{B}, and H^{C} are the 3, 5, and 6 protons of 2,4-dinitrophenol (VII); H^{D} and H^{E} are the aromatic and methylene protons, respectively, of N-hydroxymethylphthalimide (I); and the primed symbols represent the corresponding protons in the product VIII: H^{A}, 560, 563; H^{B}, 519, 522, 529, 532; H^{C}, 453, 463; H^{D}, 514, 515; H^{E}, 386; $H^{A'}$, 560, 563; $H^{B'}$, 535, 538; $H^{D'}$, 492; $H^{E'}$, 324. It is apparent that either the rate of disappearance of H^{C} or the rate of appearance of $H^{E'}$ would serve to monitor the reaction using other peaks or combinations of them as internal references. In practice it was found that both could be used but that $H^{E'}$, involving two protons, was a more sensitive indicator. The following procedure was employed after it was first established that a 5% solution of I in 100% sulfuric acid gave an nmr spectrum that was stable indefinitely (>24 hr) at room temperature as evidenced by the constancy of the integration ratio of H^{E} to H^{D}.

A 0.50 *M* solution of N-hydroxymethylphthalimide (I) in slightly fuming sulfuric acid (0.05% SO_3) was prepared [0.4429 g of I in 5 ml (8.5514 g) of acid]. The nmr spectrum (single peak at 386 Hz for H^{E}) showed that no appreciable amount of the solute was in the form of II. Therefore, on the assumption that 71% of the substrate was in the form of the sulfate ester III and 29% as the protonated ether IV, calculations[1] gave 95.85% as the corrected acid concentration. A weighed quantity (2.8949 g) of this solution was placed in a thermostat at 35 ± 0.05°. A requisite amount (0.1481 g to give a concentration of 0.50 *M*)[16] of 2,4-dinitrophenol (VII) was added, and, as soon as it was dissolved, a sample was transferred to a tightly stoppered nmr tube. The nmr spectrum was integrated three times in the region 300–600 Hz. The tube was then replaced in the thermostat and removed at suitable intervals only long enough to carry out the spectral scans. The nine integrations corresponding to $H^{A} + H^{A'}$ (560–563 Hz), $H^{B} + H^{B'}$ (519–538 Hz), and 0.25 $(H^{D} + H^{D'})$ (492–515 Hz) were averaged to give a reference integral called A. The three integrations corresponding either to $0.5H^{E'}$ (324 Hz) or to H^{C} (453–463 Hz) were averaged to provide the variable function. When $H^{E'}$ was used, as in this instance, the concentration, *C*, of reactants was calculated by

$$C = \frac{C_0(A - 0.5H^{E'})}{A} \qquad (1)$$

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[10] A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 167–170.

[11] T. E. Hogen-Esch and J. Smid, *J. Amer. Chem. Soc.*, **88**, 307, 318 (1966).

[12] The phenolysis of N-bromomethylphthalimide is even autocatalytic; *cf.* H. E. Zaugg and A. D. Schaefer, *J. Org. Chem.*, **28**, 2925 (1963).

[13] V. Gold and D. P. N. Satchell, *J. Chem. Soc.*, 3609 (1955).

[14] J. C. D. Brand, W. C. Horning, and M. B. Thornley, *ibid.*, 1374 (1952).

[15] M. Yamaguchi [*Nippon Kagaku Zasshi*, **73**, 393 (1952)] reported a 95% yield of VIII using 5% oleum at 100° for 1 hr.

[16] In calculating the molarity of VII, it was assumed that 5 ml of the 0.50 *M* solution of I weighed 8.9943 g (grams of H_2SO_4 + grams of I) and that addition of VII does not increase the volume appreciably so that, in this instance, (0.1481/184.1)(1.7989/2.8949)(1000) = 0.50 *M*.

where C_0 is the initial concentration. When H^C was used, C was obtained by

$$C = \frac{C_0H^C}{A} \tag{2}$$

Experimental data from this run (using $H^{E'}$) are summarized as follows (time in hours, A, $0.5H^{E'}$, $1/C$): 0.17, 17.4, 1.6, 2.20; 0.67, 17.8, 5.0, 2.78; 1.17, 17.2, 6.4, 3.19; 1.67, 19.2, 9.4, 3.92; 2.17, 18.7, 9.1, 3.90; 2.67, 17.9, 10.2, 4.65; 3.17, 16.5, 10.0, 5.08.

Graphical analysis of the data showed that the best linear correlation between time and concentration was obtained in a plot of $1/C$ *vs.* time, characteristic of a second-order reaction.[17] The data were therefore submitted to linear regression analysis to obtain the best value for the slope (*i.e.*, k_2). Results (with standard errors) are summarized in Table I along with those of three other determinations (runs 2–4) also conducted in 95.85% sulfuric acid. In runs 3 and 4 where equimolar amounts of reactants were not used, the rate constants were obtained from the slope of a plot of $1/[\mathrm{I}]$ *vs.* time where $[\mathrm{I}] = [\mathrm{I}]_0 - ([\mathrm{VII}]_0 - C)$ and where C was obtained from eq 1 with $C_0 = [\mathrm{VII}]_0$ or 0.25 M. This gave second-order constants for the rate of disappearance of I.

Comparison of runs 3 and 4 on the one hand with 1 and 2 on the other shows that the rate is not significantly changed by halving the concentration of VII. This indicates that the reaction is zero order in 2,4-dinitrophenol and second order in the N-hydroxymethylphthalimide. As a further check on this type of second-order behavior, half-times ($t_{1/2}$) of these four runs were determined graphically (plot of [I] *vs.* t) and compared with corresponding half-times calculated from the statistical rate constants using the appropriate second-order relationship, $t_{1/2} = 1/k_2C_0$,[18] where C_0 was obtained from the statistical intercept at $t = 0$. Results [run no., graphical $t_{1/2}$, statistical $t_{1/2}$ ($\times 10^{-4}$ sec)] were as follows: 1, 0.90, 0.82 ± 0.05; 2, 0.72, 0.85 ± 0.03; 3, 1.08, 0.89 ± 0.07; 4, 0.58, 0.65 ± 0.02. It will be noted that the statistical half-time of run 3 is not significantly different from those of runs 1 and 2, and that of run 4 is just outside the limit of standard error with respect to the other three.

In an attempt to determine the kinetic order with respect to I more directly, two rates were measured in which the concentration of I was intended to be the only variable. Using calculations and assumptions previously described, a stock solution 0.25 M in I and 93.85% (cor) in sulfuric acid was prepared [0.2214 g of I in 9.0245 g (5 ml) of 95.83% acid]. Sufficient 2,4-dinitrophenol (0.2301 g) was added to this to give a 0.25 M solution, and the reaction rate was measured (Table I, run 5). In another run, 0.2833 g of I was dissolved in 3.6453 g (2 ml) of 100.13% (0.13% SO_3) sulfuric acid to give an 0.80 M solution of I in 93.85% (cor) acid. To this solution 0.0920 g of VII was added to give a solution 0.25 M in 2,4-dinitrophenol. The rate of this reaction was then measured (Table I, run 6). It will be noted that, considering the experimental uncertainties in arriving at "identical" sulfuric acid concentrations, the *second-order* rate constants for the two runs are in fair agreement despite the more than threefold variation in initial concentration of the N-hydroxymethylphthalimide.

Variation of the Rate with Sulfuric Acid Concentration.—The following procedure for one kinetic run serves to illustrate the method used. A weighed sample (2.2688 g) of N-hydroxymethylphthalimide (I) was dissolved in about 20 ml of 98.95% sulfuric acid in a tared 25-ml volumetric flask. The solution was placed in a thermostat at 35 ± 0.05°. After sufficient time was allowed for temperature equilibration, a weighed sample (0.0529 g) of 2,4-dinitrophenol was added, the solution was quickly made up to volume with preheated (35°) 98.95% acid, and the whole was weighed to determine the exact amount (42.6985 g) of acid used. This was taken as zero time. The resulting solution was 0.5127 M in I and 0.011 M in VII. At appropriate time intervals, 5-ml aliquots of the reaction mixture were pipetted into 50 ml of ice–water. Insoluble material (I, V, and VIII) was removed by filtration and washed with three 5-ml portions of water. The combined washings and filtrate were extracted with four 20-ml portions of ether, and the combined ether extracts were shaken with four 20-ml portions of 10% aqueous sodium bicarbonate solution or until both layers were colorless. The combined aqueous extracts were brought to 100 ml in a volumetric flask and 10 ml of this solution was diluted to 100 ml to give a concentration (10^{-4}–10^{-5} M) of the sodium salt of VII suitable for uv assay in a 1-cm cell. The absorbances at $\mathrm{uv}_{\max}$ 360 mμ, at the times (in seconds) indicated, were as follows: 240, 0.685; 1800, 0.647; 3600, 0.565; 5400, 0.511; and 7200, 0.482. A simpler linear regression analysis of a plot of the negative absorbance *vs.* time gave a slope of $3.167 \pm 0.277 \times 10^{-5}$ M sec^{-1}, equal to the pseudo-zero-order rate constant, k_0.[18] Dividing this constant by the square of the concentration of I (*i.e.*, 0.2629 M^2) gave the second-order rate constant, $k_2 = 1.20 \pm 0.11 \times 10^{-4}$ M^{-1} sec^{-1}. During the run, a small sample of the solution was transferred to an nmr tube, and the spectrum was scanned in the 350–400-Hz region to give, in this case, $[\mathrm{III}]/[\mathrm{II}] = 0.91$. The solution was then returned to the main reaction vessel. (In many runs, only four aliquots were removed, and the residual solution was used for the nmr scan.) Using the known weights of I and sulfuric acid, the measured ratio of [III] to [II], the known original concentration of the acid, and the method previously described,[1] the corrected concentration of acid was calculated as 94.84%. Results of 22 runs, in which the concentration of 2,4-dinitrophenol (VII) varied from 0.0110 to 0.0137 M, are summarized as follows (molarity of I, corrected per cent of H_2SO_4, $k_2 \times 10^4$ M^{-1} sec^{-1}): 0.5046, 84.39, 0.0131 ± 0.0106; 0.5270, 86.76, 0.0476 ± 0.0013; 0.5104, 86.92, 0.0359 ± 0.0063; 0.5678, 88.92, 0.0552 ± 0.0079; 0.4860, 89.27, 0.136 ± 0.066; 0.5246, 89.49, 0.110 ± 0.024; 0.9352, 92.95, 1.05 ± 0.06; 0.5009, 93.36, 0.474 ± 0.039; 0.8585, 93.74, 2.10 ± 0.02; 0.5860, 94.30, 1.02 ± 0.07; 0.5127, 94.84, 1.20 ± 0.11; 0.4999, 95.04, 1.33 ± 0.10; 0.5588, 96.03, 2.14 ± 0.14; 0.5045, 96.51, 2.69 ± 0.22; 0.2362, 96.74, 1.75 ± 0.24; 0.2457, 96.96, 3.04 ± 0.75, 0.5048, 97.93, 5.69 ± 0.54; 0.4092, 98.76, 17.8 ± 1.9; 0.3634, 99.15, 23.6 ± 1.2; 0.0614, 100.26, 42.4 ± 6.2; 0.0590, 100.28, 43.5 ± 14.5; 0.3574, 100.44, 29.8 ± 3.1. It will be noted that concentrations of I varied over more than a ten-fold range (0.06–0.9 M). With the exception of the two runs in the 0.06 M region, all rates thus were measured using molar ratios greater than 17:1 for the pseudoorder conditions.

Unsuccessful Attempts to Phthalimidomethylate 2,4-Dinitrophenol (VII) with N-Hydroxymethylphthalimide (I).—A stirred mixture of I (5.3 g, 0.03 mol), VII (6.1 g, 0.033 mol), and *p*-toluenesulfonic acid (2 g, 0.01 mol) in carbon tetrachloride (75 ml) was heated at reflux for 4 hr in an apparatus designed to remove water azeotropically. The solid, that had begun to form after the first hour, was removed from the cooled reaction mixture by filtration. It was slurried in an excess of a saturated sodium bicarbonate solution, collected once more at the filter, washed with water, and dried. The product (4.70 g, mp 206–209°) proved (ir and mixture melting point) to be fairly pure bis(phthalimidomethyl) ether (V, 93% yield). When the 2,4-dinitrophenol was omitted from this procedure, the ether V was produced in 97% yield. This is the method of choice for the preparation of V. Lower yields of V were obtained when the reaction was carried out in chloroform using methanesulfonic acid either with or without anhydrous aluminum chloride as catalyst. Attempts to effect substitution of VII by I in a 9:1 mixture of trifluoroacetic anhydride and trifluoroacetic acid (room temperature, 48 hr) led to the trifluoroacetate of I as the only isolable product. Similarly, using a 10% solution of fluoroboric acid in propionic anhydride gave only the propionate of I in poor yield (36%).

Phthalimidomethylation of Benzene with N-Hydroxymethylphthalimide.—When benzene was substituted for the carbon tetrachloride as solvent in the foregoing procedure and heating under reflux was continued for 16 hr, the dried product obtained after removal of the benzene by distillation, followed by aqueous washing of the residue, weighed 6.8 g, mp 110–114°. It proved (ir and mixture melting point) to be a 96% yield of nearly pure N-benzylphthalimide, lit.[19] mp 113–114°.

Phthalimidomethylation of 2-Naphthol.—2-Naphthol (5 g, 0.035 mol) was substituted for the 2,4-dinitrophenol in the above procedure (in CCl_4). The 6.6 g (72%) of crude product, mp 190–195°, was recrystallized from glacial acetic acid (100 ml) to give 4.94 g (54%) of pure N-(2-hydroxy-1-naphthylmethyl)phthalimide, mp 200–202° dec, identified by ir, nmr, and elemental analyses. Repeated recrystallizations did not change the melt-

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[17] A. A. Frost and R. G. Pearson, "Kinetics and Mechanism," 2nd ed, John Wiley & Sons, Inc., New York, N. Y., 1961, p 13.

[18] R. Livingston, "Investigation of Rates and Mechanisms of Reactions," S. L. Friess, E. S. Lewis, and A. Weissberger, Ed., 2nd ed., Interscience Publishers, New York, N. Y., 1961, pp 114, 115.

[19] Reference 2, p 126.

ing point, lit.[20] mp 215–220°. When ether V (5.05 g, 0.015 mol) was substituted for I in this procedure, a 59% yield of the substituted 2-naphthol was obtained. When benzene was used instead of carbon tetrachloride as solvent in the reaction of I with 2-naphthol, the substitution product was still formed in 45% yield despite the presence of the competitive reaction with benzene.

Phthalimidomethylation of 2,4-Dinitrophenol (VII) with N-Chloromethylphthalimide (IX).—To a stirred solution of N-chloromethylphthalimide[21] (1.95 g, 0.01 mol) and VII (1.84 g, 0.01 mol) in liquid sulfur dioxide (50–60 ml) cooled to −40° in a chloroform–Dry Ice bath, silver hexafluoroantimonate (Ozark-Mahoning Co., Tulsa, Okla.) (3.43 g, 0.01 mol) was added in several portions (5–10 min). After the mixture stirred at −25 to −30° for 3–4 hr, the solvent was allowed to evaporate overnight. The residual mixture of product and silver chloride was suspended in water and collected at the filter. The dried mixture (4.71 g) was boiled with 100 ml of stirred dichloroethane for several minutes and filtered hot to remove insoluble silver chloride (1.29 g, 90%). The clear, amber filtrate was concentrated to one-third of its volume and cooled. The product VIII (2.47 g, 72%) crystallized in nearly pure form, mp 210–214°. A number of variations of solvent and temperature were tried with the following results: SO_2, −10°, 67%; $(CH_2)_2Cl_2$, −15°, 59%; $(CH_2)_2Cl_2$, 0°, 40%; $(CH_2)_2Cl_2$, 25°, 26%; CH_3NO_2, 10°, 46%. Clearly, low temperatures favor the desired reaction, presumably by reducing the incidence of side reactions of the carbonium ion VI with solvent. This explanation received further support from an experiment in which IX in nitromethane was treated with the silver salt and allowed to stand for 16 hr at 25° before the phenol VII was added. Under these conditions no VIII could be isolated. The instability of the intermediate ion VI also was suggested by attempts to determine its nmr spectrum. Treatment of the N-chloromethylphthalimide (IX), dissolved in 1,2-dichloroethane, with silver hexafluoroantimonate at room temperature gave the theoretical amount of silver chloride, and the filtrate showed a weak, moderately broad peak at 916 Hz (*vs.* TMS in solution). However, its area relative to that of the aromatic peak (475 Hz) indicated that less than 20% of the material could be in the form of VI (assigning the 916 peak to the $>N^{+}{=}CH_2$ protons). This downfield peak disappeared immediately on the addition of 2,4-dinitrophenol, and overnight on standing at room temperature. Using silver tetrafluoroborate instead of the antimonate gave a 42% yield of VIII, but with silver trifluoroacetate only the trifluoroacetate of I was formed.

Unsuccessful Attempts to Phthalimidomethylate 2,4-Dinitrophenol (VII) with N-Chloromethylphthalimide (IX).—A stirred mixture of VII (2.21 g, 0.012 mol), IX (2.35 g, 0.012 mol), and stannic chloride (15 ml) was heated at 85° for 5 hr. The stannic chloride was removed by distillation under reduced pressure; the residue was suspended in cold ethanol and collected at the filter. The product (3.85 g, mp 80–100°) was a complex mixture in which none of the desired product VIII could be detected (ir). Similar negative results were obtained using the following conditions: $SnCl_4$, 25°, 16 hr; $SbCl_5$, 25°, 16 hr; $ZnCl_2$-CH_3NO_2, 100°, 5 hr; and $AlCl_3$-CH_3SO_3H-$CHCl_3$, 60°, 18 hr.

Registry No.—I, 118-29-6; VII, 51-28-5; sulfuric acid, 7 664-93-9.

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[20] R. Maki, Y. Ishida, K. Satake, and R. Oda, *Kogyo Kagaku Zasshi*, **57**, 44 (1954); *Chem. Abstr.*, **49**, 10907*d* (1955).

[21] H. Böhme, R. Broese, and F. Eiden, *Chem. Ber.*, **92**, 1258 (1959).

Oxidative Coupling of Toluene through Organometallic Intermediates

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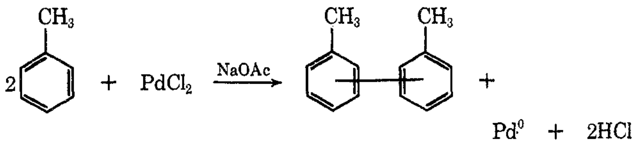
Organomercury compounds have been shown to undergo substitution by palladium salts with subsequent reduction of the palladium(II) to palladium(0) and oxidative coupling of the aromatic rings. The system, toluene–mercuric acetate–palladium acetate, was investigated in detail. A mechanism is proposed based on the isomer distribution of the bitolyls.

van Helden and Verberg[1,2] have shown that palladium chloride in the presence of sodium acetate can oxidatively couple aromatic compounds. Benzene yields biphenyl, while substituted aromatic compounds lead to a mixture of the various possible biaryl isomers.

If toluene is treated with palladium chloride in an acetic acid–sodium acetate medium, a mixture of the six possible isomeric bitolyls is obtained.



The rate of the reaction and the isomer distribution are temperature dependent, the reaction proceeding very slowly at room temperature. Table I shows the isomer distribution at various reaction temperatures. It can be seen that coupling involving an *ortho* position increases with decreasing temperature at the expense of the *meta*- and *para*-derived isomers.

Table I

Temperature Dependence of Bitolyl Isomer Distribution in the $PdCl_2$–NaOAc System

	Amount, mol %						Yield,[a]	
T, °C	*o,o′*	*o,m′*	*o,p′*	*m,m′*	*m,p′*	*p,p′*	%	Time
200[b]	Traces	12.5	12.2	18.8	35.3	21.4	28	2 hr
110	Traces	12.7	13.4	17.2	35.2	21.2	54	3 hr
90	Traces	12.4	17.9	14.5	34.6	20.4	58	6 hr
50	Traces	15.3	27.2	11.6	28.4	17.4	31	4 days
25	Traces	24.5	44.5	5.0	14.9	11.6	16	7 days

[a] Based on $PdCl_2$ charged. [b] Shaker tube run.

The distribution of the bitolyl isomers is not considerably altered by changes in solvent, or by the addition of cocatalysts, buffers, acids, or ligands. One exception was found in that addition of catalytic amounts of perchloric acid resulted in an increase in the rate of the reaction and a shift in the isomer distribution toward *meta*- and *ortho*-derived isomers.

Recently it was shown by Bryant, McKeon, and

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[1] R. van Helden, G. Verberg, and B. Balder, U. S. Patent 3,145,237 (Aug 18, 1964).

[2] R. van Helden and G. Verberg, *Rec. Trav. Chim. Pays-Bas*, **84**, 1263 (1965).