

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

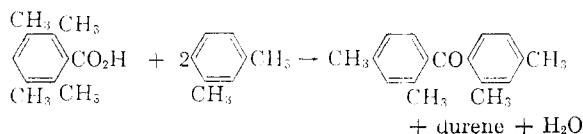
A Synthesis of Symmetrical Diaryl Ketones by a Transcarbonylation Reaction<sup>1</sup>BY REYNOLD C. FUSON, GERALD R. BAKKER<sup>2</sup> AND BRUNO VITTIMBERGA

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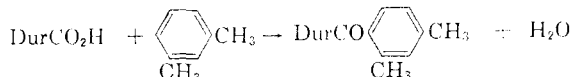
A method has been developed for the synthesis of symmetrical diaryl ketones by transfer of the carbonyl group of duroic acid. It consists in heating duroic acid, in the presence of polyphosphoric acid, with the aromatic compound to which the transfer is to be made. In this way ketones have been prepared from anisole, phenyl ether, *m*-xylene and toluene.

The formation of 2-azafluorenone by the action of polyphosphoric acid on hindered 3-aryl-4-phenylpyridines was assumed to proceed by hydrolytic cleavage of the hindered ketone followed by intramolecular acylation.<sup>3</sup> Extension of this cleavage-acylation sequence to the synthesis of linear ketones seemed feasible and promised a route to symmetrical, diaryl ketones. A method has been developed, in fact, by which the carbonyl group of duroic acid is transferred so as to produce such symmetrical ketones.

When a mixture of duroic acid and *m*-xylene, for example, is heated for an extended period with polyphosphoric acid, 2,2',4,4'-tetramethylbenzophenone is formed along with durene.

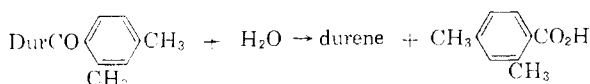


The first step in this transformation was presumed to be the formation of duryl 2,4-dimethylphenyl ketone. When the reaction mixture was



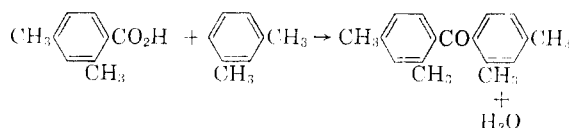
heated at 78° for a number of hours, the chief product (62% yield) proved to be this ketone.

The second phase of the transcarbonylation, the cleavage of duryl 2,4-dimethylphenyl ketone, was brought about, in a separate experiment, by heating the ketone with polyphosphoric acid for 2.5 hr. at 140°; the 2,4-dimethylbenzoic acid was isolated in a yield of 12%. It was accompanied by



durene and the symmetrical ketone 2,2',4,4'-tetramethylbenzophenone. Cleavage of the duryl ketone on either side of the carbonyl group was to be expected in the light of cleavages effected by the action of orthophosphoric acid on other *o*-substituted benzophenones.<sup>4</sup>

The final step, the acylation of *m*-xylene by 2,4-dimethylbenzoic acid, was shown to occur when a mixture of the reactants was heated with polyphosphoric acid at 150° for 4 hr.; under these conditions the yield of ketone was 67%.



The conversion of toluene to di-*p*-tolyl ketone was effected also, but the yield of product was only 4%. Duryl *p*-tolyl ketone was isolated from the reaction mixture in similarly low yields. Experiments with benzene and chlorobenzene gave no indication that even the first step, duroylation, had occurred.

Acylation with duroic acid was accomplished also with anisole, *m*-dimethoxybenzene, phenyl ether and naphthalene. The complete reaction from aromatic compound to symmetrical ketone could be observed with anisole and phenyl ether. In the case of anisole the duryl ketone derived could be made to undergo cleavage and, in the presence of excess anisole, yielded di-*p*-anisyl ketone.

Transacylation, as a separate reaction, has been realized in two cases. In the presence of polyphosphoric acid, duryl *p*-anisyl ketone reacts with anisole to give di-*p*-anisyl ketone. Di-*p*-phenoxyphenyl ketone has been made in a similar way from phenyl ether and duryl *p*-phenoxyphenyl ketone.

The cleavage of hindered ketones with phosphoric acid has been known since 1885, when Louise used orthophosphoric acid to effect hydrolytic scission of mesityl phenyl ketone.<sup>5</sup> Other examples of this reaction also may be cited.<sup>6,7</sup>

The first use of polyphosphoric acid for this purpose appears to have been made by Nowlin in 1950.<sup>8</sup> The suggestion has been made that phosphoric acid catalysis of the cleavage of hindered ketones may be very similar to the influence of strong sulfuric acid in the same reaction.<sup>9</sup> A considerable amount of work<sup>10</sup> has been done in the elucidation of the mechanism of the sulfuric acid-catalyzed cleavage of hindered ketones and similar reactions.<sup>11</sup>

Acylation catalyzed by polyphosphoric acid, a well-known reaction, has been reviewed by Popp and McEwen.<sup>12</sup>

(5) E. Louise, *Ann. chim. phys.*, [6] **6**, 174 (1885).

(6) A. Klages and C. Stamm, *Ber.*, **37**, 924 (1904).

(7) R. E. Lutz, E. C. Johnson and J. L. Wood, *THIS JOURNAL*, **60**, 716 (1938).

(8) G. Nowlin, *ibid.*, **72**, 5754 (1950).

(9) H. H. Wasserman, "Steric Effects in Organic Chemistry," edited by M. S. Newman, John Wiley and Sons, Inc., New York, N. Y., p. 361.

(10) See W. M. Schubert and H. Burkett, *THIS JOURNAL*, **78**, 61 (1956).

(11) For an investigation of the action of aluminum chloride on acetomesitylene and similar compounds, see G. Baddeley and A. G. Pendleton, *J. Chem. Soc.*, 807 (1952).

(12) F. D. Popp and W. E. McEwen, *Chem. Revs.*, **58**, 321 (1958).

(1) This work was supported in part by a grant from the Office of Ordnance Research, U. S. Army (Contract No. DA-11-022-ORD-874).

(2) Ethyl Corporation Fellow, 1957-1958.

(3) R. C. Fuson and J. J. Miller, *THIS JOURNAL*, **79**, 3477 (1957).

(4) A. Klages and G. Lickroth, *Ber.*, **32**, 1549 (1899).

The authors are indebted to the Victor Chemical Co. for a generous supply of polyphosphoric acid.

### Experimental<sup>13</sup>

**Acylation with Duroic Acid.**—These experiments involved 2.0 g. ( $1.1 \times 10^{-2}$  mole) of duroic acid, 35 ml. of commercial polyphosphoric acid and from 0.16 to 0.32 mole of the compound to be acylated. The reaction mixture was heated slowly, with continuous stirring, to a temperature varying from 75 to 90° and held there for a number of hours. While still hot the mixture was poured into de-ionized water, and the product was isolated by extraction with ether.

The acylation of *m*-xylene was accomplished by heating the reaction mixture to 78° over a 30-min. period and keeping it at that temperature for 4.5 hr. The duryl 2,4-dimethylphenyl ketone was crystallized from ethanol and then sublimed, m.p. 113–114°, yield 1.8 g. (60%). The infrared spectrum has bands which can be ascribed to aromatic and aliphatic hydrogen (3010 and 2918  $\text{cm}^{-1}$ ), a hindered diaryl ketone (1663  $\text{cm}^{-1}$ ) and two adjacent aromatic hydrogen atoms (815  $\text{cm}^{-1}$ ).

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{22}\text{O}$ : C, 85.67; H, 8.33. Found: C, 85.82; H, 8.30.

In addition to the ketone, 0.1 g. of duroic acid was isolated.

The acylation of anisole occurred in 80% yield when the reaction mixture was heated to 80° over a period of 1 hr. and held there for 4 hr. The duryl *p*-anisyl ketone crystallized from methylcyclohexane in transparent rods melting at 144–145° (reported<sup>14</sup> m.p. 143.4–144.5°).

*m*-Dimethoxybenzene underwent duroylation smoothly when heated for 5 hr. at 60°. The duryl 2,4-dimethoxyphenyl ketone separated from methanol as colorless rods, m.p. 125–128°, yield 76%. The infrared spectrum has bands attributable to aromatic and aliphatic hydrogen (3090 and 2962  $\text{cm}^{-1}$ ), a split peak for a diaryl carbonyl group (1668 and 1653  $\text{cm}^{-1}$ ), a sharp peak for a duryl group (866  $\text{cm}^{-1}$ ) and a band for two adjacent aromatic hydrogen atoms (836  $\text{cm}^{-1}$ ). Recrystallization of the colorless rods, once from ethanol and twice from methanol, produced transparent, rectangular crystals melting at 128.2–128.8°.

*Anal.* Calcd. for  $\text{C}_{19}\text{H}_{22}\text{O}_3$ : C, 76.48; H, 7.43. Found: C, 76.77; H, 7.73.

An acidic by-product melting at 169–171°, gave a positive test<sup>15</sup> for phosphorus. This compound was not identified.

Duroylation of phenyl ether was carried out at 75°, within a 10-hr. period. The duryl *p*-phenoxyphenyl ketone crystallized from ethanol as nearly colorless plates, m.p. 143.5–146°, yield 52%. Another recrystallization of the ketone from ethanol gave colorless crystals melting at 145–146.5° (reported<sup>16</sup> value 146–147.5°). A mixed melting point determination with an authentic sample showed no lowering.

The condensation with naphthalene was attempted at 90°, the time of heating being 4 hr. The duryl  $\alpha$ -naphthyl ketone crystallized from ethanol as colorless platelets, m.p. 169–170° (yield 17%).

This ketone was made also by the Friedel-Crafts method from durene ( $4.5 \times 10^{-2}$  mole) and  $\alpha$ -naphthoyl chloride ( $4.5 \times 10^{-2}$  mole). The condensation, carried out in carbon disulfide and in the presence of aluminum chloride ( $4.5 \times 10^{-2}$  mole), gave 9.3 g. (79%) of the product, m.p. 167–169.5°. The analytical sample was prepared by recrystallization from ligroin from which it separated as needles melting at 170–171°. The infrared spectrum has bands attributable to a hindered carbonyl group (1660  $\text{cm}^{-1}$ ), a duryl group (868  $\text{cm}^{-1}$ ) and a vicinal trisubstitution (801  $\text{cm}^{-1}$ ).

*Anal.* Calcd. for  $\text{C}_{21}\text{H}_{20}\text{O}$ : C, 87.46; H, 6.99. Found: C, 87.41; H, 6.81.

**Acylation of *m*-Xylene with 2,4-Dimethylbenzoic Acid.**—A mixture of 1.7 g. of 2,4-dimethylbenzoic acid, 30 ml. of *m*-xylene and 35 ml. of polyphosphoric acid was heated to 150° over a period of 1 hr. Nitrogen was passed slowly over the mixture while the temperature was maintained at 150° for 4 hr. At about 80° the mixture assumed a green color, which darkened slowly until at the end of the reaction time it was a greenish-brown. Hydrolysis was accomplished with 100 ml. of de-ionized water. The 2,2',4,4'-tetramethylbenzophenone was obtained in a 67% yield.

**Di-*p*-tolyl Ketone.**—Acylation of toluene with *p*-toluic acid in the presence of polyphosphoric acid gave the symmetrical ketone, m.p. 93–94°, yield 53%.

**Transcarbonylation.**—The combined acylation-cleavage-acylation procedure involved heating at 80–85° for 5 hr. followed by a similar period of heating at 150°. During the second period of heating the reaction vessel was kept open, and nitrogen was passed over the reaction mixture to aid in the removal of durene.

When applied to *m*-xylene, this procedure gave 2,2',4,4'-tetramethylbenzophenone in a 27% yield. The product was taken up in ether as usual. Evaporation of the ether solution left an oil, which distilled under a pressure of 1.0 mm. as a clear, slightly yellow liquid,  $n_D^{20}$  1.5790. The 2,4-dinitrophenylhydrazone of the ketone melted at 198–199° after recrystallization from an ethanol-ethyl acetate mixture (reported<sup>17</sup> m.p. 198°). The infrared spectrum of the ketone has bands at 3020, 2922, 1657, 875 and 819  $\text{cm}^{-1}$ , which can be attributed, respectively, to aromatic hydrogen, aliphatic hydrogen, a diaryl ketone group, an isolated aromatic hydrogen atom and two adjacent aromatic hydrogen atoms.

More satisfactory results were obtained with anisole, perhaps because the second period of heating was extended to 7 hr. The di-*p*-anisyl ketone separated from ethanol as white needles, m.p. 142.5–144.5° (reported<sup>18</sup> m.p. 143–144°), yield 54%. A mixed melting point determination with an authentic specimen showed no lowering.

The procedure with phenyl ether involved prolonged heating, initially at 85° (11 hr.) and subsequently at 170° (13 hr.). The di-*p*-phenoxyphenyl ketone was recrystallized successively from ligroin and methanol, m.p. 145–146° (reported<sup>19</sup> value 147°), yield 24%.

Experiments with toluene were disappointing. The product was a mixture of duryl *p*-tolyl ketone and di-*p*-tolyl ketone. By painstaking manipulation of the crude product the symmetrical ketone was obtained in a yield of 4%. This ketone, purified by chromatography and by recrystallization from cyclohexane, formed long, colorless needles, m.p. 92.5–94° (reported values 95°<sup>20</sup> and 98°<sup>21</sup>).

The oxime melted at 163.5–164° (reported<sup>22</sup> value 163°). The duryl *p*-tolyl ketone, likewise obtained in small amount, melted at 142–145° (reported<sup>14</sup> value 144–145°).

**Cleavage of Duryl 2,4-Dimethylphenyl Ketone.**—A mixture of 1 g. of the ketone with 35 ml. of polyphosphoric acid was heated at a temperature of 140° for 2.5 hr. The reaction vessel was swept with nitrogen continuously to drive out the durene. The 2,4-dimethylbenzoic acid, isolated by usual procedures, crystallized from an ethanol-water mixture as long white needles melting at 121–123° (reported<sup>23</sup> m.p. 124.5–125°). The yield of the crude acid was 12%. Its infrared spectrum was superimposable on that of an authentic specimen and a mixed melting point determination with the two samples showed no depression. 2,2',4,4'-Tetramethylbenzophenone was isolated in a yield of 49% from the neutral fraction obtained from the reaction mixture.

**Transacylation.**—The conversion of duryl *p*-anisyl ketone to di-*p*-anisyl ketone was realized by heating a mixture of 1.0 g. of the ketone with 30 ml. of anisole and 20 ml. of polyphosphoric acid at a temperature of 150°. Durene was allowed to escape during the 8-hr. period of heating. The yield of the symmetrical ketone was 45%.

(13) All melting points are corrected. The infrared spectra were recorded by Mr. Paul E. McMahon and Miss Mary DeMott. The microanalyses were performed by Mr. Josef Nemeth, Miss Claire Higham and Mrs. Frederick Ju.

(14) R. C. Fuson, B. C. McKusick and J. Mills, *J. Org. Chem.*, **11**, 60 (1946).

(15) F. Feigl, "Spot Tests II, Organic Applications," Elsevier Press, New York, N. Y., 1954, p. 77.

(16) R. C. Fuson and W. S. Friedlander, *THIS JOURNAL*, **76**, 4989 (1954).

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(18) K. Auwers, *Ann.*, **356**, 124 (1907).

(19) W. Dilthey and F. Harenberg, *J. prakt. Chem.*, **136**, 49 (1933).

(20) H. Limpricht, *Ann.*, **312**, 91 (1900).

(21) H. Stephen, W. F. Short and G. Gladding, *J. Chem. Soc.*, **117**, 510 (1920).

(22) J. Böeseken, *Rec. trav. chim.*, **26**, 285 (1907).

(23) C. S. Marvel, J. H. Saunders and C. G. Overberger, *THIS JOURNAL*, **68**, 1085 (1946).

In a similar way di-*p*-phenoxyphenyl ketone was made from duryl *p*-phenoxyphenyl ketone and phenyl ether. A mixture of 1.0 g. of the duryl ketone, 20 ml. of phenyl ether and 20 ml. of polyphosphoric acid was brought to 150° over

a 1-hr. period and maintained at that temperature for 6 hr. The yield of di-*p*-phenoxyphenyl ketone was 41%.

URBANA, ILL.

[CONTRIBUTION FROM THE POLYMER RESEARCH INSTITUTE, POLYTECHNIC INSTITUTE OF BROOKLYN]

## Reactions of Polymers with Reagents Carrying Two Interacting Groups. II. Bromine Displacement from $\alpha$ -Bromoacetamide and the Bromoacetate Ion by Poly-(methacrylic Acid) and Poly-(vinylpyridine Betaine)<sup>1,2</sup>

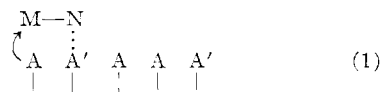
BY HARRY LADENHEIM AND HERBERT MORAWETZ

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The second-order rate constants for bromine displacement from  $\alpha$ -bromoacetamide by carboxylate groups of singly and doubly ionized dicarboxylic acids show a very slight increase of reactivity with increasing basicity of the carboxylate. The carboxylates in partially ionized poly-(methacrylic acid) are 4–10 times as reactive as those in the dicarboxylic acids and their reactivity decreases sharply with rising degree of ionization of the polymer. A similar effect was observed with poly-(vinylpyridine betaine) which displaces bromine from both bromoacetamide and bromoacetate, although the reaction rate of its monofunctional analog 4-methylpyridine betaine is not experimentally observable. All these observations may be accounted for by a concentration of the low molecular weight reagent in the region of the macromolecular coil. The dependence of the reaction rate of poly-(methacrylic acid) with bromoacetamide on the degree of ionization of the polymer suggests that the amide is bound to the carboxyl groups and that the bond is stronger when the carboxyls are un-ionized.

### Introduction

In a previous report<sup>3</sup> we described the result of the first of a series of studies concerned with the reaction rates of polymers with bifunctional reagents. The main purpose of this program is to define conditions leading to cooperative effects as represented below diagrammatically. Here the functional group A carried by the polymer is engaged in a displacement reaction on M, while the



energetic interaction between A' and N serves to accelerate the reaction by stabilizing the transition state. The groups A and A' may be identical or may represent different states of ionization of the groups attached to the polymer chain.<sup>4</sup>

In the present investigation we measured the rates of bromine displacement from  $\alpha$ -bromoacetamide and bromoacetate ion by partially ionized poly-(methacrylic acid) and by isoelectric poly-(4-vinylpyridine betaine), which were compared with the analogous reaction of singly or doubly ionized dicarboxylic acids and 4-methylpyridine betaine.

### Experimental

**Materials.**—Bromoacetic acid and  $\alpha$ -bromoacetamide were obtained as in the previous investigation.<sup>3</sup> Glutaric acid was recrystallized from benzene (m.p. 96.5°, neutralization equivalent weight 66.8). Maleic anhydride recrystallized from chloroform (m.p. 52°, neutralization equivalent weight 49.7) was used to prepare solutions of maleic acid. Fumaric acid (m.p. 282°) had a neutralization equivalent weight 58.7.

(1) Taken in part from a thesis submitted by H. Ladenheim in partial fulfillment of the requirements for a Ph.D. degree, June, 1958.

(2) Financial assistance of this study by the Office of Ordnance Research, U. S. Army, and by a grant of the Monsanto Chemical Co. are gratefully acknowledged.

(3) H. Ladenheim, E. M. Loebl and H. Morawetz, *THIS JOURNAL*, **81**, 20 (1959).

(4) A study of M. L. Bender and Y.-L. Chow (*ibid.*, **81**, 3929 (1959)) is concerned with a similar problem involving the reaction of two bifunctional small molecules, *o*-nitrophenyl hydrogen oxalate and 2-aminopyridinium ion.

The preparation of 4-methylpyridine betaine which has not been reported previously was carried out as described for pyridine betaine.<sup>5</sup> The product lost one mole of water of crystallization when heated at atmospheric pressure at 100° and decomposed at 180°. The ultraviolet spectrum had maxima at 232 m $\mu$  ( $\epsilon$  6710) and 257 m $\mu$  ( $\epsilon$  4630).

*Anal.* Calcd. for C<sub>5</sub>H<sub>7</sub>NO<sub>2</sub>·H<sub>2</sub>O: C, 56.79; H, 6.55; N, 8.28. Found: C, 56.64; H, 6.72; N, 8.38.

Poly-(methacrylic acid) was prepared from methacrylic acid diluted with a sixfold volume of methanol and containing 1.6  $\times 10^{-3}$  mole of azo-bis-isobutyronitrile initiator per mole of monomer by heating for 20 hours at 65°. The polymer solution was diluted with water, exhaustively dialyzed and freeze-dried. The drying of the polymer was completed under reduced pressure at 50°. The carboxyl content determined by potentiometric titration was in exact agreement with theory; the light scattering molecular weight was 187,000. The preparation of the poly-(4-vinylpyridine betaine) used in this work has been described in a previous report.<sup>6</sup>

**Kinetic Runs and Interpretation of Data.**—Initial rates at 50° were followed by bromide evolution as described previously, making the appropriate correction for the hydrolysis of the C-Br bond<sup>3</sup> in the interpretation of the data. The results were expressed in terms of a second-order rate constant  $k_2$  (l.-equiv.<sup>-1</sup> min.<sup>-1</sup>). For the reaction of  $\alpha$ -bromoacetamide with poly-(methacrylic acid) (PMA),  $k_2$  was defined by

$$R_T - R_H = k_2(\text{BAC})C_p\alpha' \quad (2)$$

where  $R_T$  is the total observed rate of bromide evolution,  $R_H$  the rate due to hydrolysis, (BAC) the  $\alpha$ -bromoacetamide concentration,  $C_p$  the normality of the PMA and  $\alpha'$  its degree of ionization, which was obtained from the degree of neutralization  $\alpha$  and the hydrogen ion concentration by  $\alpha' = \alpha + (\text{H}^+)/C_p$ . With the dicarboxylic acids kinetic runs were carried out in solutions in which the fraction of neutralized carboxyls was 1/4 or 3/4, so that the reagent served also to buffer the solution. The results of the two runs were interpreted by

$$R_T - R_H = (\text{BAC})[k_2'(\text{HA}^-) + 2k_2''(\text{A}^{2-})] \quad (3)$$

where (HA<sup>-</sup>) and (A<sup>2-</sup>) are the concentrations of the singly and doubly ionized acid, while  $k_2'$  and  $k_2''$  are second-order rate constants characterizing ionized carboxyl groups in these two species.

With bromoacetic acid, second-order rate constants were calculated for reactions of the bromoacetate ion from the difference of the total observed rate of bromide evolution  $R_T$

(5) E. v. Gerichten, *Ber.*, **15**, 1251 (1882).

(6) H. Ladenheim and H. Morawetz, *J. Polymer Sci.*, **26**, 251 (1957).