[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CALCO CHEMICAL DIVISION, AMERICAN CYANAMID COMPANY]

The Phosphonation of Aromatic Compounds with Phosphoric Anhydride[1]

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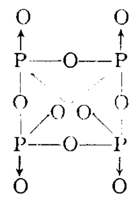
Benzene, chlorobenzene, *o*-xylene and naphthalene are phosphonated by hexagonal phosphoric anhydride in a temperature range of about 275–325°. A primary reaction product is formed by addition of one molecule of the aromatic compound to one molecule of P_4O_{10} with opening of a covalent P–O bond. In the cases of chlorobenzene, *o*-xylene and naphthalene there are also formed secondary reaction products which are phosphonic anhydrides of the type $(ArPO_2)_x$. The primary reaction products are insoluble in the aromatic compound while the secondary ones are soluble. Both the primary and the secondary products give the phosphonic acid when hydrolyzed and the phosphonic dichloride when chlorinated with phosphorus pentachloride.

While the sulfonation and nitration of aromatic compounds belong to the most widely used and best investigated organic reactions, a corresponding phosphonation of the aromatic nucleus by the aid of phosphoric acid or one of its anhydrides has never been accomplished so far.[2] Using specific conditions we have succeeded in phosphonating aromatic compounds with hexagonal phosphoric anhydride.

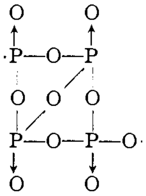
According to Hill, Faust and Hendricks,[3] phosphoric anhydride exists in three crystalline modifications. The commercial "phosphorus pentoxide" consists predominantly of a metastable crystal form belonging to the rhombohedral division of the hexagonal system. There is another metastable orthorhombic form and a stable tetragonal form. The conversion of the hexagonal metastable form into the other two forms is immeasurably slow at room temperature. At 180° the conversion into the orthorhombic form takes about 60 days, but it takes only about 60 minutes at 378°. By interpolation one may conclude that the conversion of the hexagonal form into the orthorhombic form would progress at a reasonable rate in a temperature range between 250 and 325°. It is also within this temperature range that the vapor pressure of hexagonal phosphoric anhydride becomes noticeable, being, *e.g.*, at 216.2° only 0.5 cm., but at 253° 2.2 cm., at 278.4° 5.5 cm., at 300.9° 12.3 cm., and at 324.8° 27.2 cm.[4]

The structure of hexagonal phosphoric anhydride, P_4O_{10}, has been determined by electron diffraction studies[5] as

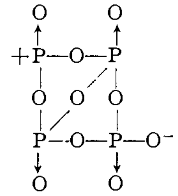


I

On the other hand, the orthorhombic and tetragonal forms represent macromolecules as has been shown by de Decker[6] and by MacGillavry, de Decker and Nijland.[7] It is therefore clear that the conversion of the hexagonal form into the orthorhombic form must start with the breaking of one of the covalent P–O bonds, which might result either in a biradical II or, more probably, in a hybrid ion III.



II



III

Either one should react with aromatic compounds and the reaction of the latter should result in an electrophilic substitution corresponding to that caused by the nitronium ion $+NO_2$.

We have investigated the reaction of pure commercial phosphoric anhydride with some aromatic compounds[8] at various temperatures and have found that at temperatures below 250° the substitution reactions take place only to a minor extent, but that generally in a temperature range of 250 to 325° these reactions do take place and organophosphorus compounds are formed.

The optimum conditions for the reaction of benzene with phosphoric anhydride are a temperature of about 275° and a reaction time of about 24 hours, the reaction being carried out in an autoclave with shaking or stirring. The contents of the cooled autoclave consist of a dark, brittle pitch and unchanged benzene. The weight of the pitch corresponds approximately to the sum of the phosphoric anhydride used plus one molecular equivalent of benzene for each molecular equivalent of P_4O_{10}. Its solution in ice-water does not contain the hydrolysis product of phosphoric anhydride, *i.e.*, tetrametaphosphoric acid, nor does it contain orthophosphoric acid. However, when the aqueous solution is boiled for a short time, complete hydrolysis takes place and afterwards the solution does contain orthophosphoric acid.

It is very probable that this primary reaction product, which is the main constituent of the above mentioned pitch, has the formula V

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(1) Presented at the 124th National ACS Meeting in Chicago, September 7, 1953.

(2) According to F. Jostes and J. Cronjé, *Ber.*, **71B**, 2335 (1938), the brick-red products obtained by H. Giran, *Compt. rend.*, **126**, 592 (1898), and **129**, 964 (1899), from commercial benzene and phosphoric anhydride are due to the former's thiophene content.

(3) W. L. Hill, G. T. Faust and S. B. Hendricks, THIS JOURNAL, **65**, 794 (1943).

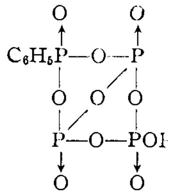
(4) J. C. Southard and R. A. Nelson, *ibid.*, **59**, 911 (1937).

(5) G. C. Hampson and A. J. Stosick, *ibid.*, **60**, 1814 (1938). X-Ray diffraction pattern and crystal structure, *cf.* H. C. J. de Decker and C. H. MacGillavry, *Rec. trav. chim.*, **60**, 153 (1941).

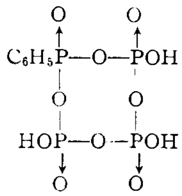
(6) H. C. J. de Decker, *ibid.*, **60**, 413 (1941).

(7) C. H. MacGillavry, H. C. J. de Decker and L. M. Nijland, *Nature*, **164**, 448 (1949).

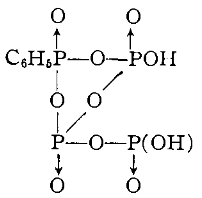
(8) The aromatic compounds must be free of substituents (such as OH, NH_2, COOH, etc.) which *per se* would react with P_4O_{10}.



V



VI



VII

When it is dissolved in water another P–O bridge is opened up and according to titration results, the main product of this cold hydrolysis corresponds to the formula VI to which there may be admixed a small amount of a hydrolysis product of the formula VII. Formula VI is related to that of tetrametaphosphoric acid (OH in place of C_6H_5) which is formed on dissolving phosphoric anhydride in cold water.[9] On the other hand, it is known that diethyl ether and phosphoric anhydride give an ester of isotetrametaphosphoric acid (related to VII, OH in place of C_6H_5).[10] Naturally, further hydrolysis of either VI or VII will result in the formation of phenylphosphonic acid and pyro- and orthophosphoric acids.

The aqueous solution obtained by complete hydrolysis contains for one molecule of phenylphosphonic acid approximately three molecules of orthophosphoric acid. When this solution is concentrated to a small volume, the phenylphosphonic acid crystallizes out.

An alternate procedure of working up consists in the conversion of the primary reaction product V into the chlorides of phosphoric and phenylphosphonic acids. This conversion is easily accomplished by treating the pitchy intermediate with phosphorus pentachloride dissolved in phosphorus oxychloride

$$C_6H_5P_4O_{10}H + 6PCl_5 \longrightarrow C_6H_5POCl_2 + 9POCl_3 + HCl$$

Subsequent distillation gives phosphorus oxychloride and the phenylphosphonic dichloride. By this process most of the phosphorus can be recovered in the form of usable products.

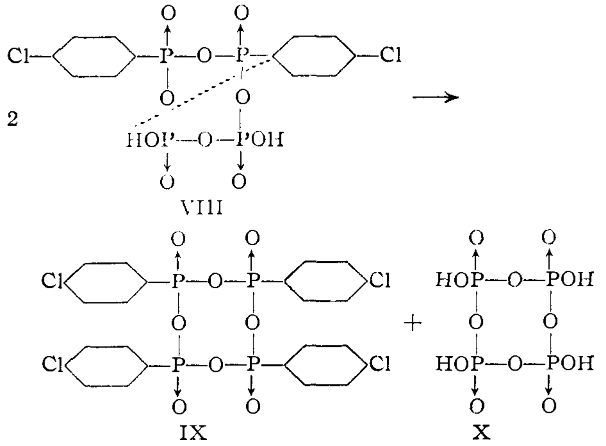
We have studied the variables of the phosphonation of benzene with hexagonal phosphoric anhydride.[11] The practical temperature limits of this reaction are very narrow and we found the same to be true in the phosphonation of the other aromatic compounds we have investigated. The use of a considerable excess of benzene is important.

The reaction of benzene with hexagonal phosphoric anhydride is not typical of the reactions of other aromatic compounds. As a matter of fact, the other aromatic compounds which we have investigated so far, such as, *e.g.*, chlorobenzene, *o*-xylene and naphthalene, behave differently from benzene though the temperature range in which they do react is approximately the same. With these other aromatic compounds the phosphonation reaction gives two different organophosphorus compounds: the primary reaction products correspond in their structure very probably to the primary reaction product of benzene (formula V), are insoluble in the liquid or fused aromatic compound, and are found in the "pitch." There are, however, secondary reaction products formed which are dissolved in the aromatic liquid.

The nature of the secondary product obtained in the phosphonation of chlorobenzene has been investigated and there is little doubt that it is a polymeric anhydride of the phosphonic acid corresponding to the formula $(ClC_6H_4PO_2)_x$. When the chlorobenzene solution was evaporated, a sirupy residue was left, the analysis of which showed approximately the ratio 1 Cl:1 P. The great solubility of the secondary reaction product in aromatic solvents such as chlorobenzene indicates that it is free of $>P\begin{smallmatrix}\rightarrow O\\ -OH\end{smallmatrix}$ groups.

Such anhydrides (Aryl $PO_2)_x$ have been prepared and investigated a long time ago by A. Michaelis and his school.[12] However, in the half century that has passed since Michaelis' work, these compounds have never again been prepared, to the best of our knowledge. Michaelis called them "phosphino" compounds and gave them a monomolecular formula in analogy to aromatic nitro compounds with which they have, however, nothing in common. There is no doubt that such anhydrides would have a polymeric, very probably a tetrameric, formula. So far we have been unable to prepare any such anhydride in a well-defined state because they are exceedingly susceptible to hydrolysis. Their solutions in inert organic solvents such as benzene or chlorobenzene are hydrolyzed by the slightest traces of moisture, which hydrolysis results in the separation of either the corresponding phosphonic acid or a bimolecular anhydride of it.

How then are these polymeric anhydrides formed? We believe that chlorobenzene (and *o*-xylene and naphthalene) have a tendency to open a second P–O bridge in the molecule of the primary reaction product, thus producing an intermediate compound of the formula VIII which breaks down into the tetrameric anhydride (formula IX) and tetrametaphosphoric acid (X). The metaphos-



VIII

IX

X

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(9) Yu. V. Khodakov, *Doklady Akad. Nauk S.S.S.R.*, **43**, 212 (1944); O. F. Hill, "The Structures and Properties of the Polyphosphates," thesis, University of Illinois, 1948; N. I. Rodionova and Yu. V. Khodakov, *Zhur. Obshchei Khim.*, (*J. Gen. Chem.*), **20**, 1347 (1950); R. N. Bell, L. F. Audrieth and O. F. Hill, *Ind. Eng. Chem.*, **44**, 568 (1952).

(10) R. Rätz and E. Thilo, *Ann.*, **572**, 173 (1951).

(11) *Cf.* experimental part.

(12) A. Michaelis and F. Rothe, *Ber.*, **25**, 1747 (1892); F. Guichard, *ibid.*, **32**, 1580 (1899); A. Michaelis and A. Flemming, *ibid.*, **34**, 1294 (1901); A. Michaelis, *Ann.*, **293**, 193 (1896); **294**, 1 (1897); **315**, 43 (1901).

phoric acid, being insoluble in the organic solvent, stays in this case with the pitch, as can be shown by the latter's reactions.

These polymeric anhydrides hydrolyze to give the phosphonic acid and react also with phosphorus pentachloride, giving the phosphonic dichloride and phosphorus oxychloride. For practical purposes it is, of course, not necessary to work up the insoluble and soluble reaction products separately; the combined products may be hydrolyzed or chlorinated.

When the reaction products of chlorobenzene are hydrolyzed, a mixture of chlorophenylphosphonic acids results. The main constituent is the known para acid which can be obtained in pure state by recrystallization. The other constituent is very probably the ortho acid, but we have made no efforts so far to isolate it; however, an *o*-toluidine salt of this isomer has been prepared and its infrared absorption spectrum gave some indication that it is the salt of the ortho isomer.

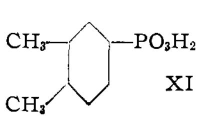
We have spent considerable time in investigating the phosphonation of naphthalene with hexagonal phosphoric anhydride. This reaction works less smoothly than the aforementioned ones because the naphthalene undergoes condensation reactions which result in the formation of phosphonated and non-phosphonated undesirable by-products. Friedel and Crafts[13] observed that aluminum chloride catalyzes disproportionation and condensation reactions of naphthalene, and among the products they isolated 2,2′-binaphthyl. Phosphoric anhydride catalyzes some reactions in a similar manner as aluminum chloride does, but does so only at a higher temperature.[14] It is therefore not surprising that at the high temperature of our reaction it catalyzed the formation of condensation products of naphthalene. We have isolated small amounts of 2,2′-binaphthyl. Because of these side reactions the phosphonation of naphthalene has to be carried out within a rather narrow temperature range between about 275 to 300°.

The naphthylphosphonic acid obtained is the 2-isomer, as was to be expected, since the sulfonation at high temperature produces also mainly the beta compound. Since the 1- and 2-naphthylphosphonic acids[15] have similar melting points, we have proved the identity of our acid with the 2-isomer by synthesizing both isomers through the 1- and 2-mercury compounds of naphthalene.

From the mother liquor of the 2-naphthylphosphonic acid we have isolated a small amount of a naphthylenediphosphonic acid in which the position of the second phosphonic group is in doubt (probably 6 or 7).

Since commercial naphthalene contains appreciable amounts of thionaphthene, we have also phosphonated thionaphthene-free naphthalene.[16] However, the amount of by-product formed was only slightly decreased, otherwise the result was the same. This experiment was done because we observed that naphthalene containing thionaphthene gives a deep red coloration when heated with phosphoric anhydride; naphthalene free from thionaphthene does not. The same observations were made with benzene that did or did not contain thiophene.[2]

The phosphonation of *o*-xylene follows the pattern of the phosphonation of naphthalene: considerable amounts of water-insoluble, tarry condensation products are formed (which is not the case with benzene or chlorobenzene). The hydrolysis product is probably the phosphonic acid XI



XI

and there is only very little, if any, of an isomer formed.

Acknowledgment.—We are indebted to Messrs. W. Seaman and E. M. Allen for the potentiometric titrations of the primary reaction product of benzene with phosphoric anhydride; to Mr. C. E. Maresh for microscopic investigations; to Messrs. O. E. Sundberg and S. G. Redshaw and their associates for the analyses; to Miss E. A. Frolich for some infrared absorption work.

Experimental

General Remarks.—The reactions described in this paper had to be carried out above the boiling points of the aromatic compounds to be phosphonated. Our first exploratory experiments were done in sealed glass tubes which were placed in a shaker autoclave filled with mineral oil; this procedure was unsatisfactory because of poor heat transfer and poor agitation. Before using ordinary autoclaves we determined that our reaction mixtures do not corrode the usual metallic materials of construction at the high temperatures used.[17] We have used nickel and stainless steel shaker autoclaves manufactured by the American Instrument Company and autoclaves with an anchor type stirrer for larger scale experiments.

The phosphoric anhydride used in our laboratory experiments was a pure commercial grade (Phosphorus Pentoxide powder "Baker Analyzed" Reagent).

Preparation of Phenylphosphonic Acid from Benzene and Phosphoric Anhydride.—Since the experiments were done close to the critical temperature of benzene, the great volume increase had to be taken into consideration. The density of benzene at 20° is 0.879 while at its critical temperature of 288.5° it is only 0.3045, *i.e.*, the benzene increases its volume about 3 times when heated to the temperature of reaction. The critical pressure of benzene is 704 lb. per square inch.

The autoclave was first charged with the benzene and then the phosphoric anhydride was introduced. The autoclave was heated with agitation to the reaction temperature and kept there for the time indicated.

When the reaction was carried out under proper conditions, the contents, after cooling, consisted of a hard, black, brittle pitch adhering to the sides of the autoclave and an

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[13] C. Friedel and J. M. Crafts, *Compt rend.*, **100**, 692 (1885); since that time several other authors have studied the reaction of naphthalene with aluminum chloride, among them, *e.g.*, A. Homer, *J. Chem. Soc.*, 1103 (1907); R. Scholl, C. Seer and R. Weitzenböck, *Ber.*, **43**, 2202 (1910).

[14] H. Lecher, *ibid.*, **46**, 2664 (1913); R. Truffault, *Bull. soc. chim. France*, [5] **1**, 391 (1934); **3**, 442 (1936); E. Desparmet, *ibid.*, [5] **3**, 2047 (1936); B. W. Malishev, THIS JOURNAL, **57**, 883 (1935); *Ind. Eng. Chem.*, **28**, 190 (1936); *Oel u. Kohle ver. Erdoel u. Teer*, **14**, 479 (1938).

[15] W. Kelbe, *Ber.*, **9**, 1051 (1876), 1, m.p. 190°; J. Lindner and M. Strecker, *Monatsh.*, **53**, 274 (1929), 2, m.p. 193–194°.

[16] H. Adkins, THIS JOURNAL, **63**, 741 (1941).

[17] Wire coils of the related metal were placed into mixtures of naphthalene (large excess) and phosphoric anhydride which were heated with agitation at 275° for 24 hours. The following corrosion rates were found: silver 0.007″, monel 0.006″, stainless steel #316 0.003″, 0.004″, nickel 0.003″, 0.004″, aluminum 0.001″, and molybdenum 0.001″ per year. Mild steel wire was exposed to a possibly more corrosive reaction mixture $2C_{10}H_8:1P_4O_{10}$ and a corrosion rate of 0.009″ per year was determined.

almost colorless liquid of unreacted benzene, which could be easily poured or siphoned off. The pitch was removed by the aid of hot water which hydrolyzed the primary reaction product to phenylphosphonic and orthophosphoric acids. The aqueous solution was concentrated to a small volume whereupon the phenylphosphonic acid crystallized out.

By this method of working up it is impossible to recover all the phenylphosphonic acid because of its great solubility and also because of the necessity to wash the recovered product with ice-water to remove adhering orthophosphoric acid. Therefore, the yield figures given below are only of relative significance and do not represent the optimum obtainable yields.

The phenylphosphonic acid was identified by mixed m.p. (158–161°) with a product obtained from Victor Chemical Works. It was also identified by microscopic and crystallographic investigation: habit, diamond shaped plates from water or alcohol; refractive indices, n_α 1.530 ± 0.003, n_β 1.605 ± 0.003; optic axial angle, 74°; extinction, symmetrical; optical character, positive; optical orientation, plates = Bx_0.

In a typical experiment using a ratio of 20 C_6H_6:1 P_4O_{10}, a temperature of 275° and a time cycle of 24 hours the isolated yield was 75.5% of the one calculated for one phenylphosphoric acid from one P_4O_{10}. Under the same conditions, a reaction time of only 10 hours gave only 47.1% yield.

No phenylphosphonic acid could be isolated from experiments carried out at 200 and 225° for 24 hours; at 250° under the same conditions the isolated yield was only 37.2%. At 325° under the same conditions 67% could be isolated, but in an experiment carried out at 350° no phenylphosphonic acid could be isolated.

For obtaining a good yield of the phosphonic acid it is important to use a large excess of benzene. If the ratio was 5C_6H_6 to 1P_4O_{10} only 38% yield could be isolated. In one experiment in which only a small excess of benzene was used (200 cc. (2.2 moles) of benzene and 312 g. (1.1 moles) of P_4O_{10}, nickel shaking autoclave, 275°, 24 hours) some tarry water-insoluble material was formed; the aqueous dark extract gave on concentration a precipitate which after washing with ice-water gave only 22.2 g. (calcd. 174 g.) phenylphosphonic acid. It is very probable that also polyphosphonation occurs when only a very small excess of hydrocarbon is used and that one contaminant of the crude product is a phenylenediphosphonic acid which, however, could not be isolated.

Preparation and Properties of the Primary Reaction Product of Benzene with Phosphoric Anhydride.—Four hundred cc. (4.4 moles) of dry benzene and 62.4 g. (0.22 mole) of phosphoric anhydride were placed in a 3.2-liter silver insert which was fitted into an autoclave provided with an anchor type stirrer. The materials were heated at 275° for 24 hours. After cooling the silver insert was taken out. The "pitch" was broken into pieces and crushed further in a mortar under benzene. The benzene was decanted and the remaining benzene was removed in a vacuum desiccator. In spite of the evident mechanical difficulties, this product was obtained in a yield of 76.7 g. while the calculated yield for a compound of 1P_4O_{10} with 1C_6H_6 would be 79.65 g.

The black pitch is very soluble in ice-water and in methanol. A 10% solution in ice-water was used for the following qualitative experiments. While a solution of orthophosphoric or tetrametaphosphoric acid (prepared from phosphoric anhydride and ice-water) was precipitated by thallous formate and ammonia, the freshly prepared solution of our pitch was not, even when it was boiled for a very short time and cooled. However, when the solution was boiled for several minutes and clarified from a trace of undissolved material and cooled, it gave with ammonia and thallous formate a copious precipitate of thallous phosphate. When the ice-cold aqueous solution was cautiously neutralized with caustic and boiled for several minutes and cooled, thallous formate and ammonia gave some precipitation but not as much as in the experiment where the acid solution had been boiled. It should be noted that an aqueous solution of phenylphosphonic acid is not precipitated by thallous formate and ammonia.

Potentiometric Titrations of the Primary Reaction Product C_6H_6–P_4O_{10} and its Hydrolysis Products.—Several large lumps of the pitch-like primary reaction product were rapidly broken up into smaller lumps in a mortar under an inverted funnel through which a stream of dry nitrogen was passed. The weighed portion was dissolved in carbon dioxide-free water to give an about 0.5% solution which was titrated with carbonate-free sodium hydroxide. A stream of nitrogen was passed through the solution during the dissolving and the titration periods to prevent absorption of carbon dioxide. After the titration of the non-hydrolyzed product was finished, an amount of hydrochloric acid equivalent to the amount of sodium hydroxide used was added and the solution was boiled for a half-hour in order to promote hydrolysis and retitrated after cooling.

In the first experiment the titration was carried out as soon as feasible after dissolution. In the second experiment the alkali was added even before the sample had been completely dissolved, but complete solution had been effected before reaching the first break.

Two breaks were observed—the first one at a *p*H of about 5 and the second one at a *p*H of about 9.5.

In the first experiment one mole of the primary reaction product V consumed 2.88 moles of NaOH to the first break plus 0.60 additional mole to the second break before hydrolysis; after hydrolysis the consumption was 3.24 moles to the first break and an additional 3.09 moles to the second break. In the second experiment 1 mole of the primary reaction product consumed 2.79 moles of NaOH to the first break and an additional 0.47 mole to the second break before hydrolysis; after hydrolysis the consumption was 3.35 moles to the first break and an additional 3.08 moles to the second break. A complete hydrolysis to 1 molecule of phenylphosphonic acid and 3 molecules of orthophosphoric acid would require 4 moles of NaOH each for the first and second breaks. The figures obtained show that the hydrolysis was not complete probably due to the relative stability of pyrophosphoric acid.[18] It will be noted also that a compound of formula VI would consume 3 moles of NaOH to the first break and there would not be any second break. On the other hand, a compound of formula VII would consume 2 molecules of caustic to the first break plus 1 molecule to the second break.

Conversion of the Primary Reaction Product C_6H_6–P_4O_{10} into Phenylphosphonic Dichloride.—Twenty-six grams of the primary reaction product, prepared as described above, and 89.6 g. of phosphorus pentachloride were slurried in 100 cc. of phosphorus oxychloride. The temperature of the reaction mixture was raised gradually to the boil and heating was continued for 5 hours with stirring. Then sulfur dioxide was bubbled into the reaction mixture to destroy any excess phosphorus pentachloride. The thionyl chloride and phosphorus oxychloride were removed under reduced pressure; the phosphonic dichloride distilled at 135–136°(23 mm.), yield 13.1 g. (calcd. 14 g.). The chloride was identified by hydrolyzing it to phenylphosphonic acid. This experiment shows that phenylphosphonic dichloride is obtainable in excellent yield.

The primary reaction product can be converted into the phosphonic dichloride also by the aid of thionyl chloride. However, the reaction is very sluggish and the yield is less satisfactory.

Phosphonation of Chlorobenzene, Investigation of the Insoluble Reaction Products.—No reaction occurred at 275°. However, reaction did occur in a temperature range of approximately 300–310°.

In several experiments 338 g. (3.0 moles) of chlorobenzene and 42.7 g. (0.15 mole) of P_4O_{10} were heated with agitation at 310° for 24 hours. After the charge was cooled to room temperature, the chlorobenzene solution amounting to 280 cc. was poured off. There remained in the autoclave a pitch which was somewhat difficult to chip out and weighed approximately 32 g.

(1) **Undissolved Matter.**—In one of the experiments this pitch was boiled with a large excess of water, the solution obtained was treated with Darco, clarified and concentrated to a volume of 200–225 cc. Upon cooling, a first crop (5.0 g.) crystallized out which softened at 160° and melted at 179–182° and was mainly *p*-chlorophenylphosphonic acid; after recrystallization from water the melting point rose to 183–186–187°; the literature gives a melting point of this phosphonic acid at 188°.[19] The acid was also identified by its infrared spectrum recently reported by Daasch and Smith.[20]

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(18) E. Bamann and E. Nowotny, *Ber.*, **81**, 442 (1948); R. N. Bell, *Ind. Eng. Chem.*, **39**, 136 (1947).

(19) H. Bauer, This Journal, **63**, 2137 (1941).

(20) L. W. Daasch and D. C. Smith, *Anal. Chem.*, **23**, 853 (1951).

The acid was converted into two salts. A solution in aqueous sodium hydroxide was precipitated with dilute hydrochloric acid and the product obtained was identified as the hemisodium salt.

Anal. Calcd. for $C_{12}H_{11}Cl_2NaO_6P_2$: Cl, 17.43. Found: Cl, 17.6.

The aqueous solution of the acid was also converted into an *o*-toluidine salt which after recrystallization from alcohol melted at 196–209° with decomposition and development of a purple color.

Anal. Calcd. for $C_{13}H_{15}ClNO_3P$: Cl, 11.83; N, 4.68. Found: Cl, 11.6; N, 4.47.

The mother liquor from that first crop of a chlorophenylphosphonic acid was concentrated stepwise and the last crop was converted into an *o*-toluidine salt which was crystallized from water and from alcohol and gave a small amount of a product melting at 218–220° after softening at 190° (dec., purple color).

Anal. Calcd. for $C_{13}H_{15}ClNO_3P$: Cl, 11.83; N, 4.68. Found: Cl, 11.7; N, 4.47.

Its infrared absorption curve indicated that it is probably the salt of the *o*-chlorophenylphosphonic acid.

The insoluble matter obtained in a duplicate experiment was converted into the phosphonic dichloride as described above for the phenyl derivative. The chlorophenylphosphonic dichloride distilled at 132–133° (10–11 mm.); 8.67 g. When this experiment was performed we did not know the nature of the chlorobenzene-soluble product and did not know that the insoluble material contained metaphosphoric acid. For this reason the amount of phosphorus pentachloride used was probably insufficient. The phosphonic dichloride was hydrolyzed by boiling with 25 cc. of water. The crude phosphonic acid thus obtained showed a melting point of 168–170° (softening 161°) and after recrystallization 183.5–186.5° (softening 177°).

The insoluble matter obtained in these phosphonation reactions of chlorobenzene is easily soluble in ice-water. This solution gives a heavy precipitate when treated with thallous formate and ammonia. On the other hand, the insoluble matter obtained in the phosphonation of benzene gives a precipitate with thallous salt only after it has been hydrolyzed by boiling.

(2) **Soluble Reaction Product.**—The chlorobenzene solution poured off from the insoluble matter showed an orange-red color. When it was exposed to a humid atmosphere it became cloudy and separated large amounts of a phosphorus-containing precipitate. When a sample was boiled with water and the ammonium molybdate reagent, a yellow precipitate was formed.

About one half of the chlorobenzene solution was evaporated, leaving behind 19.5 g. of a sirup (still containing some chlorobenzene). This sirup was diluted with 50 cc. of phosphorus oxychloride and then a considerable excess, namely, 65 g. of phosphorus pentachloride was added. This mixture was refluxed overnight and then treated with sulfur dioxide to destroy the excess phosphorus pentachloride, b.p. of the chlorophenylphosphonic dichloride, 118–120° (3 mm.); yield 9.55 g. The acid chloride was hydrolyzed by boiling with 25 cc. of water. The crude acid showed a very unsharp melting point, 145–154° (softening 100°), but after recrystallization 181–184° (softening 177°). This experiment shows that the chlorobenzene-soluble product is a parent substance of the chlorophenylphosphonic acids.

One-half of the chlorobenzene solution obtained from another experiment was hydrolyzed by refluxing with a little water for 4 hours and separated crude chlorophenylphosphonic acids (8.46 g.).

Anal. Calcd. for $C_6H_6ClO_3P$: C, 37.4; H, 3.14; Cl, 18.42; P, 16.12; for 91.7% $C_6H_6ClO_3P$ + 8.3% HO_3P: C, 34.30; H, 2.88,[21] Cl, 16.90; P, 18.00. Found: C, 34.2, 34.4; H, 3.03, 3.04; Cl, 16.8, 16.6; P, 17.93, 17.93.

These figures show that this crude chlorophenylphosphonic acid was contaminated by metaphosphoric acid which could also be found in qualitative tests.

The other half of the chlorobenzene solution was evaporated first under ordinary pressure, eventually under reduced pressure, leaving behind a dark, viscous liquid which at room temperature solidified to a brittle pitch (12.2 g.).

Anal. Calcd. for tetrameric 4-chlorophenyl-oxophosphine oxide $(C_6H_4ClO_2P)_4$: C, 41.25; H, 2.31; Cl, 20.31; P, 17.78. Found: C, 40.6, 40.9; H, 2.58, 2.62; Cl, 19.3; P, 17.2, 17.5.

These analyses taken at their face value would indicate the presence of one phosphorus atom for one chlorophenyl group. However, the apparent accuracy of this ratio is misleading because it had been difficult to free the product completely from chlorobenzene and there is probably some chlorobenzene present, the figures of which are compensated by simultaneous presence of metaphosphoric acid or of the intermediate VIII. Actually a hot aqueous extract contained some phosphoric acid.

2-Naphthylphosphonic Acid, Preparation.—In a typical experiment 2050 g. of naphthalene and 227 g. of phosphoric anhydride (ratio $20C_{10}H_8:1P_4O_{10}$) were charged into a nickel autoclave provided with an anchor type stirrer. The charge was heated to 275° within 5 hours and then kept at this temperature for 25 hours longer. When it had reached 125° the autoclave was opened. It contained a tar coating the stirrer and the sides, and a yellowish melt which was removed by decantation.

A sample of the undissolved pitch proved to be quite soluble in ice-water and a 10% solution easily was obtained; this proves that the 2-naphthylphosphonic acid was not present yet since it shows a solubility of less than 0.2% at 0°. The aqueous solution of the pitch was kept in the refrigerator for approximately one week without apparent change and without precipitation of the phosphonic acid.

The bulk of the pitchy material was repeatedly treated with large amounts of boiling water, which caused hydrolysis with formation of a water-insoluble by-product which was isolated by filtration, using decolorizing and filtering aids. The decanted melt was likewise repeatedly treated with large amounts of boiling water, partly using the aqueous extracts from the pitch; after the final extraction, the napthalene now was free of phosphorus. Some of the aqueous extracts separated on cooling 2-naphthylphosphonic acid which was recovered by filtration. Eventually, the combined aqueous extracts were concentrated to a small volume whereupon on cooling the bulk of the phosphonic acid crystallized out and was isolated. The total yield of 2-naphthylphosphonic acid amounted to about 83 g.

The material that was left behind in the extractions with hot water weighed 111 g. (but contained considerable amounts of filtering and decolorizing aids). It was extracted with a hot aqueous solution of sodium hydroxide and the filtrate was precipitated with dilute hydrochloric acid, giving a recovery of about one-third of the original weight. This was a dark material insoluble in water or mineral acids, soluble in sodium hydroxide and sodium carbonate solutions, and insoluble in organic solvents such as benzene. It contained some sulfur, stemming from the thionaphthene content of the naphthalene used. It did not reduce alkaline permanganate and did not give a color reaction with ferric chloride in alcohol (no naphthol). It was spectroscopically free of iron.

Ten grams of this material was heated in a distilling flask and immersed in a metal bath to a temperature of about 330°. The material swelled considerably like a "Pharaoh's serpent" and eventually filled the whole flask while only very little sublimed off. The residue (9.6 g.) was extracted with hot water, the residue weighing 9.0 g.; the aqueous extract gave a very strong molybdate test for phosphoric acid. The solid residue was extracted with 50 cc. of benzene, decolorized and filtered, and left on evaporation 0.38 g. which after extraction with hexane and recrystallization from alcohol gave crystals melting at 184–185° (softening 181°). This was apparently 2,2'-binaphthyl.[22] In benzene solution it was converted into its picrate which showed a melting point of 185–187° (softening 179°).[23]

In other experiments which were carried out on a rather large scale in an autoclave provided with an anchor type stirrer the ratio of $C_{10}H_8:P_4O_{10}$ was decreased to 5:1, the temperature and the time cycle being the same as in the former experiment. Here it was possible to isolate a naphthylenediphosphonic acid by concentrating the aqueous mother liquors from the last crops of the 2-naphthylphosphonic acid. This diphosphonic acid was recrystallized

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[21] Without the H of HO_3P which would not come off in the combustion.

[22] M.p. 187.8°; F. D. Chattaway, *J. Chem. Soc.*, 653 (1895).

[23] M.p. of the picrate of 2,2'-binaphthyl 184–185°; P. Ferko, *Ber.*, **20**, 660 (1887).

from methanol, giving colorless crystals which sintered at 322° and melted at 338–345° with decomposition and gas evolution; yield exceedingly small. A titration was carried out to the first and second breaks.

Anal. Calcd. for $C_{10}H_{10}O_6P_2$: P, 21.5; neut. equiv., 144 and 72. Found: P, 21.7, 21.0; neut. equiv., 146 and 73.

When the ratio of $C_{10}H_8$:P_4O_{10} is further decreased to 1.1:1, the yield of isolated 2-naphthylphosphonic acid becomes very small.

The formation of organophosphorus compounds that would hydrolyze to give appreciable yields of 2-naphthylphosphonic acid is limited to a very narrow temperature range for the reaction of naphthalene with phosphoric anhydride. At 350° no 2-naphthylphosphonic acid could be isolated, at 325° only a trace. At the lower temperature of 245° most of the naphthalene remained unchanged, even if the reactants were used in a molecular ratio of 1:1.

2-Naphthylphosphonic acid, properties: colorless crystals, m.p. 193–194°; very soluble in alcohol and acetone, somewhat soluble in ether.

Anal. Calcd. for $C_{10}H_9O_3P$: C, 57.7; H, 4.3; P, 14.9; neut. equiv., 104. Found: C, 57.7; H, 4.2; P, 15.2; neut. equiv., 107.5.

Solubility in water, g./100 cc. water		Solubility in phosphoric acids at 25°, g./100 cc. aqueous acids	
Temp., °C.	Soly., g.	Phosphoric acid, %	Soly., g.
0	0.16	5	0.52
25	0.62	10	0.16
52	1.08	25	*ca.* 0.10
75	1.88	50	Negligible
95	2.57		
100	3.44		

When 2-naphthylphosphonic acid is heated in a sealed tube for 24 hours at 275°, it decomposes completely into naphthalene and metaphosphoric acid.

2-Naphthylphosphonic Acid, Salts.—The hemisodium salt is obtained when an alkaline solution of the phosphonic acid is precipitated by addition of hydrochloric acid.

Anal. Calcd. for $C_{20}H_{17}NaO_6P_2$: C, 54.76; H, 3.91; Na, 5.25; P, 14.17; neut. equiv., 146. Found: C, 54.5, 54.8; H, 3.9, 4.05; Na, 5 ± 0.5; P, 14.1, 14.0; neut. equiv., 150.

Solubilities of the hemisodium salt in 100 cc. of water: 0.60 g. at 25° and 2.97 g. at 100°. This hemisodium salt may be converted into the free phosphonic acid by boiling its suspension in alcohol with concd. hydrochloric acid, filtering and evaporating.

Likewise, hemiammonium and hemipotassium salts are obtained when the 2-naphthylphosphonic acid is dissolved in aqueous ammonia or potassium hydroxide, respectively, and the solution obtained is precipitated with hydrochloric acid.

Anal. (hemiammonium salt) Calcd. for $C_{20}H_{21}NO_6P_2$: C, 55.39; H, 4.89; N, 3.23. Found: C, 55.2; H, 4.91; N, 3.13, 3.16.

The magnesium, calcium and barium salts are only sparingly soluble in water.

The mono-*o*-toluidine salt is obtained by heating an aqueous solution of the phosphonic acid with *o*-toluidine; the hot solution is filtered and cooled whereupon the salt crystallizes out. It may be recrystallized from water or alcohol; m.p. 198–200°.

Calcd. for $C_{10}H_7{\cdot}PO_3H_2,H_2N{\cdot}C_6H_4{\cdot}CH_3$: neut. equiv., 157.6; nitrite equiv., 315.3. Found: neut. equiv., 151; nitrite equiv., 323.

2-Naphthylphosphonic Acid, Alkali Fusion.—The neutral sodium salt of 2-naphthylphosphonic acid is not hydrolyzed to 2-naphtholate and phosphate in the alkali fusion. Thirteen grams of the hemisodium salt was dissolved with a slight excess (4.0 g.) of sodium hydroxide in water and the solution was evaporated. Fifteen grams of sodium hydroxide and 3 cc. of water were heated in a nickel crucible at 260° and the sodium salt was added in portions while the temperature was gradually raised to 330° and held there 45 minutes longer. The melt was dissolved in 100 cc. of boiling water and 50% sulfuric acid was added at the boil until the reaction was strongly acid. The precipitate formed was filtered at room temperature and consisted of 13 g. of the hemisodium salt of 2-naphthylphosphonic acid; no 2-naphthol could be detected. When the same experiment is performed with the free phosphonic acid, part of it decomposes into naphthalene and metaphosphate; *cf.* above.

Synthesis of the Isomeric Naphthylphosphonic Acids from the Isomeric Dinaphthylmercury Compounds.—Di-2-naphthylmercury was prepared by the procedure described in "Organic Syntheses."[24] Di-1-naphthylmercury was prepared by the same method.

For the preparation of 2-naphthylphosphonic acid[15] a mixture of 0.0165 mole of di-2-naphthylmercury and 0.0863 mole of phosphorus trichloride was heated in a sealed glass tube with agitation at 200° for 69 hours. The phosphorus trichloride layer was decanted from tarry material and the latter was extracted several times with carbon tetrachloride. The phosphorus trichloride layer and the carbon tetrachloride extracts were combined and treated with chlorine whereupon the crystalline tetrachloro-2-naphthylphosphorane crystallized. The latter was hydrolyzed with boiling water. A small amount of gummy material was removed by hot filtration and the solution upon concentration separated the desired 2-naphthylphosphonic acid, which after recrystallization from water showed the m.p. of 191–193°.

For the preparation of 1-naphthylphosphonic acid[15] likewise a mixture of 0.033 mole of di-1-naphthylmercury and 0.175 mole of phosphorus trichloride was heated in a sealed tube with agitation at 200° for 66 hours. The reaction mixture was worked up in the same fashion and yielded the 1-naphthylphosphonic acid, m.p. 182–186°; after oxidation with a little $HgCl_2$ and repeated recrystallization, 197.5–198.5° (Kelbe 190°[15]).

Proof of the Structure of 2-Naphthylphosphonic Acid.—The mixed melting point of samples of 2-naphthylphosphonic acid prepared from di-2-naphthylmercury and by phosphonation of naphthalene with phosphoric anhydride was 191–193° and therefore did not show any depression. On the other hand, the mixed melting points of samples of 1-naphthylphosphonic acid prepared from di-1-naphthylmercury and of 2-naphthylphosphonic acid prepared either from di-2-naphthylmercury or by phosphonation of naphthalene with phosphoric anhydride were 160–175° and 155–167°, respectively, and therefore showed a considerable depression.

That the naphthylphosphonic acid obtained by phosphonation of naphthalene with phosphoric anhydride is the beta compound was also confirmed by a crystallographic investigation of this acid and the two acids obtained from the dinaphthylmercury compounds as described above. The optical character of the alpha acid is positive; optic axial angle, 3–4°; refractive indices, $n\alpha$ 1.66 ± 0.01, $n\beta$ 1.66 ± 0.01. Both beta acids showed positive character; optical axial angles, 77°; refractive indices, $n\beta$ 1.11 ± 0.01, $n\beta$ 1.66 ± 0.01.

2-Naphthylphosphonic Dichloride.—The conversion of either 2-naphthylphosphonic acid or the organophosphorus compounds obtained as intermediates in the phosphonation reaction into the phosphonic dichloride cannot be accomplished by the aid of thionyl chloride, but phosphorus pentachloride must be used as the chlorinating agent. Probably because of simultaneously occurring chlorination of the naphthalene nucleus the yields are not satisfactory.

For the conversion of the phosphonic acid 15 g. was dissolved in 40 cc. of phosphorus oxychloride. This solution was added to an agitated slurry of 30 g. of phosphorus pentachloride in 40 cc. of phosphorus oxychloride. After completion of the addition, the resulting black liquid was heated for one hour at 80° whereupon the phosphorus oxychloride and the 2-naphthylphosphonic dichloride were distilled under reduced pressure; yield 9 g., m.p. 45–47°, b.p. 167–168° (2 mm.).

Anal. Calcd. for $C_{10}H_7Cl_2OP$: C, 48.97; H, 2.88; P, 12.67. Found: C, 49.01, 49.14; H, 2.82; P, 12.7, 12.47.

The conversion of the intermediate products was investigated in the following experiment. The phosphonation of naphthalene was carried out as described above, but only one-fourth of the materials was taken, *i.e.*, 512 g. of naphthalene and 56.8 g. of phosphoric anhydride. The naphthalene phase was evaporated, eventually under reduced pressure. The residue (which had solidified on cooling) was

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[24] "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 432 and 381.

dissolved in 250 cc. of phosphorus oxychloride and then the naphthalene-insoluble pitch resulting from the reaction was added (after it had been broken up into lumps), 250 g. of phosphorus pentachloride was added. The temperature was raised slowly to 110° and kept there for approximately 20 hours. Since it appeared that there was still unreacted material in the flask, another 41.5 g. of phosphorus pentachloride was added and heating was continued for 5 hours longer at 110°. Sulfur dioxide was bubbled through the reaction mixture to destroy any excess of phosphorus pentachloride. Then the phosphorus oxychloride and the phosphonic dichloride were distilled, the latter under reduced pressure. There was obtained 13 g. of 2-naphthylphosphonic dichloride.

Phosphonation of *o*-Xylene.—Two hundred sixty-five grams (2.5 moles) of *o*-xylene and 71.0 g. (0.25 mole) of P_4O_{10} were heated in a stainless steel shaker autoclave at 275° for 24 hours. When the phosphoric anhydride was mixed with the xylene a cherry red color developed which is very probably due to a thioxene content of the *o*-xylene used. After the autoclave had reached room temperature, its content consisted of an orange-brown liquid xylene phase, which was removed by decantation, and a dark brown pitch, which was chipped from the autoclave and weighed approximately 91.5 g. A sample of the pitch when dissolved in water gave a strong test with the ammonium molybdate reagent. In another similar experiment the xylene solution had been evaporated and had left approximately 30.5 g. of a brown sirup (essentially the anhydride of the phosphonic acid). In this experiment, however, both the comminuted pitch and the xylene solution were combined and treated with hot water to promote hydrolysis. The xylene was stripped off. The still residue consisted of an undissolved dark oil and a dark solution which was decanted and clarified. The filtrate (500 cc.) separated on cooling a first crop of 33.8 g. of *o*-xylylphosphonic acid and the mother liquor yielded on further concentration a second crop of 10.6 g. A sample when recrystallized from water and dehydrated by drying showed a melting point of 150–151.5°.

Anal. Calcd. for $C_8H_{11}O_3P$: C, 51.58; H, 5.96. Found: C, 51.4; H, 5.61.

BOUND BROOK, NEW JERSEY

[CONTRIBUTION FROM THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY]

Trifluoromethyl Derivatives of Hydroxybenzoic Acids and Related Compounds[1]

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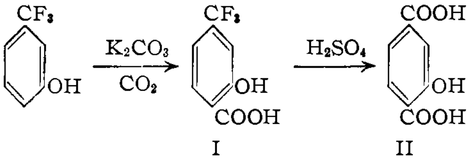
4-Trifluoromethylsalicylic acid (I) has been synthesized in 88% yield by the reaction of *m*-trifluoromethylphenol with potassium carbonate and carbon dioxide, as well as by the Kolbe–Schmidt reaction on both sodium and potassium *m*-trifluoromethylphenolates. Hydrolysis of I with sulfuric acid affords an excellent synthesis of 2-hydroxyterephthalic acid. 3-Trifluoromethyl-5-hydroxybenzoic acid, 2-trifluoromethyl-4-hydroxybenzoic acid, and I, have been synthesized by reaction sequences involving intermediate formation of new trifluoromethyl derivatives of amino acids, nitro acids, and chloro-, nitro-, amino-, hydroxynitriles. Observations on the relative ease of acid hydrolysis of the trifluoromethyl group in certain isomeric compounds are reported. Acetyl-4-trifluoromethylsalicylic acid and methyl 4-trifluoromethylsalicylate, trifluoromethyl derivatives of well known pharmaceuticals, have been prepared.

As part of a search for new chemotherapeutic agents, we wished to synthesize several trifluoromethylhydroxybenzoic acids as intermediates. Since *m*-trifluoromethylphenol was readily accessible, the most direct method for the preparation of trifluoromethylsalicylic acid and possibly 2-trifluoromethyl-4-hydroxybenzoic acid appeared to be the Kolbe–Schmidt reaction. The question remained, however, as to whether the strong electron-withdrawing influence of the trifluoromethyl group might deactivate this phenol sufficiently to seriously curtail its reactivity. It was therefore somewhat surprising to find that 4-trifluoromethylsalicylic acid (I) was formed in 88% yield when *m*-trifluoromethylphenol, anhydrous potassium carbonate and carbon dioxide were allowed to react under pressure by progressively heating the mixture from room temperature to 220°.



I II

I was also obtained from sodium and potassium *m*-trifluoromethylphenolates *via* the Kolbe–Schmidt reaction. The *p*-isomer, 2-trifluoromethyl-4-hydroxybenzoic acid (XII), was not detected in any of these experiments. In addition several attempts to convert the potassium salt of I into the *p*-isomer according to the procedure[2] for transforming salicylic acid into *p*-hydroxybenzoic acid, failed.

The very convenient method using potassium carbonate and the phenol (rather than its salt) has been described[3] for the carbonation of *p*-cresol in which case only one isomeric product was possible. In the present reaction it is obvious that three isomers could have been produced as two ortho and one para positions were unoccupied. The structure of the single isomer actually formed was determined by treatment with concentrated sulfuric acid, which gave 2-hydroxyterephthalic acid (II) in 85% yield (a most convenient synthesis of the latter acid!).

It was next considered interesting to determine which isomer would be formed on treating *m*-cresol, the hydrocarbon analog, with carbon dioxide and potassium carbonate under conditions identical to the above. 4-Methylsalicylic acid was formed in 88% yield, and similarly the *p*-isomer could not be detected.

4-Trifluoromethylsalicylic acid was next prepared by the following sequence of reactions

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(1) Presented at the 124th Meeting of the American Chemical Society, Chicago, Illinois, Sept. 6–11, 1953.

(2) C. A. Buehler and W. E. Cate in "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 341.

(3) D. Cameron, H. Jeskey and O. Baine, *J. Org. Chem.*, **15**, 233 (1950).