Preparation of Several New Phosphonic and Phosphinic Acids

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Received December 4, 1957

A previous paper[1] reported that bis(*p*-nitrophenyl)phosphinic acid possesses considerable activity *in vitro* against *Treponema pallidum*, the causative agent of syphilis. This finding has prompted us to investigate the activity of a large number of phosphonic and phosphinic acids which were available in this laboratory. The results of this investigation are being published elsewhere.[2] Among the compounds tested are four which have not been described in the literature. The present note describes the preparation and chemical properties of these compounds.

(*o*-Carboxyphenyl)phenylphosphinic acid and *o*-phenoxyphenylphosphonic acid were originally prepared as possible intermediates for the synthesis of heterocyclic phosphinic acids. 5-Chloro-2-methoxyphenylphosphonic acid was synthesized during the course of some studies on the demethylation of methoxyphenylphosphonic acids. (*o*-Nitrophenyl)phenylphosphinic acid was prepared in low yield from *o*-nitrobenzenediazonium fluoborate and phenyldichlorophosphine after a number of unsuccessful attempts to prepare *o*-nitrophenylphosphonic acid by the diazo reaction.[3]

EXPERIMENTAL

o-Phenoxyphenylphosphonic acid. An intimate mixture of 10.0 g. of *o*-bromophenylphosphonic acid, 20 ml. of redistilled phenol, 10.0 g. of anhydrous potassium carbonate, and 0.2 g. of copper powder was heated under reflux for a period of 16 hr. The reaction mixture was then diluted with about 35 ml. of water, and the excess phenol removed by steam distillation. The residual liquid from the steam distillation was treated with Darco and filtered.[4] The filtrate was evaporated on the steam bath to about 70 ml. and then acidified to Congo red with concentrated hydrochloric acid. The mixture was cooled and the precipitate removed by filtration. Recrystallization from a mixture of one volume of alcohol to 5 volumes of 6*N* hydrochloric acid yielded 6.6 g. (63%) of pure *o*-phenoxyphenylphosphonic acid as long white needles, m.p. 200–202°.

Anal. Calcd. for $C_{12}H_{11}O_4P$: P, 12.38; neut. equiv. (for one ionizable hydrogen per molecule), 250.2. Found: P, 12.39; neut. equiv. (to *p*H 4.3) 254.3.

When the neutral equivalent was determined with thymolphthalein in the usual manner, a sharp end-point was not obtained. This fact suggests that the second dissociation constant of *o*-phenoxyphenylphosphonic acid is abnormally low.[5]

5-Chloro-2-methoxyphenylphosphonic acid. 5-Chloro-2-methoxyaniline (Eastman P 4202) was converted to the corresponding diazonium fluoborate by the method designated by Roe as II A.[6] The diazonium salt, after being dried in a vacuum desiccator, was suspended in dry ethyl acetate and treated with phosphorus trichloride and cuprous bromide in the usual manner.[3a] After steam-distillation of the reaction mixture, the residual liquid was filtered. A small amount of the diarylphosphinic acid remained on the filter but could not be readily purified. The filtrate was evaporated on the steam bath to incipient crystallization, cooled, and filtered. The resulting crude phosphonic acid was dissolved in an excess of 7% sodium hydroxide solution and treated with Darco. The charcoal was removed by filtration and the filtrate acidified to Congo red with concentrated hydrochloric acid. The precipitate obtained was recrystallized from a mixture of one volume of alcohol to 2 volumes of 3*N* hydrochloric acid. The yield was 27%; m.p. 222.5–225°.

Anal. Calcd. for $C_7H_8ClO_4P$: Cl, 15.93; P, 13.92; neut. equiv., 111.3. Found: Cl, 16.01; P, 13.67; neut. equiv., 113.3.

(o-Nitrophenyl)phenylphosphinic acid. This compound was prepared from *o*-nitrobenzenediazonium fluoborate and phenyldichlorophosphine by the general method described previously.[3b] After the reaction mixture was steam-distilled, the residual liquid in the distilling flask was transferred to a beaker and cooled. The crude phosphinic acid was removed by filtration and dissolved in 10% sodium carbonate solution. The alkaline solution was treated with Darco, filtered, and the acid precipitated by the addition of concentrated hydrochloric acid. Further purification was effected by dissolving the phosphinic acid in 95% ethanol (70 ml. per 0.2 mole of diazonium salt used) and adding 15 volumes of ether. The gummy material which separated on cooling was removed by filtration and discarded. The filtrate was evaporated on the steam bath to incipient crystallization and then cooled in a deep-freeze at −25°. The yield of yellow crystals thus obtained was 5%, m.p. 229–232°.

Anal. Calcd. for $C_{12}H_{10}NO_4P$: N, 5.32; P, 11.77; neut. equiv., 263.2. Found: N, 5.27; P, 11.68; neut. equiv., 265.6.

(o-Carboxyphenyl)phenylphosphinic acid was prepared from *o*-carbomethoxybenzenediazonium fluoborate and phenyldichlorophosphine by the general method described previously[3b] and was recrystallized from aqueous acetone. Obviously, the ester was cleaved to the free carboxy group during the course of the reaction. The yield was 55%; m.p. 161–164°.

Anal. Calcd. for $C_{13}H_{11}O_4P$: P, 11.82; neut. equiv., 131.1. Found: P, 11.76; neut. equiv., 131.9.

Acknowledgment. The authors wish to thank Miss Betty Jean Pegram for performing the analyses necessary for this research and Mr. Edward L. Petit for invaluable technical assistance.

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(4) Bromide ion analyses on aliquots of the filtrate showed that all the bromine had been split from the ring.

(5) *Cf.* Jaffé, Freedman, and Doak, *J. Am. Chem. Soc.*, **76**, 1548 (1954).

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