

PATENT SPECIFICATION

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(54) IMPROVEMENTS IN OR RELATING TO PHOSPHONIC ACID ANHYDRIDES

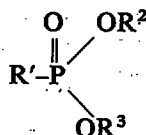
(71) We, GAF CORPORATION, a corporation organized and existing under the laws of the State of Delaware, United States of America, having its main office at 140 West 51st Street, City, County and State of New York, United States of America, do hereby declare the invention for which we pray that a patent may be granted to us, and the method by which it is to be performed, to be particularly described in and by the following statement:—

This invention relates to new and useful *bis* haloalkyl phosphonic acid anhydrides particularly to *bis* 2-haloalkyl phosphonic acid anhydrides, and especially to *bis* beta-chloroethylphosphonic acid anhydride.

The preparation of phosphonic acids is known in the art and in general the phosphonic acids are produced by the hydrolysis of a corresponding ester in the presence of a mineral acid. These processes, however, are not generally suitable for commercial production of such acids, and in particular to the production of beta-chloroethylphosphonic acid. Thus, for example, Kosolopoff *Organophosphorous Reactions* (Page 139) John Wiley and Sons (1950), discloses producing beta-chloroethylphosphonic acid by the hydrolysis of *bis* (2-chloroethyl) beta-chloroethylphosphonate. This process, however, requires a large excess of acid which must be neutralized and in addition produces toxic ethylene chlorohydrin as a by-product which is not completely removed even after evaporation of water, an evaporation which raises the cost of the process. Moreover, the hydrolysis reaction proceeds very slowly, requiring as much as three days to effect completion thereof.

In the co-pending application 15882/68 (Serial No. 1187002) there is described an improved method for the production of aliphatic phosphonic acids in which the aliphatic group is an alkyl or beta-haloalkyl group containing up to six carbon atoms

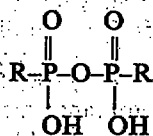
by contacting an ester of the aliphatic phosphonic acid which is stable at a temperature of above about 140°C, e.g. one represented by the following general formula:



wherein R¹, R² and R³ are selected from alkyl and β-haloalkyl groups containing up to 6 carbon atoms, with anhydrous hydrogen bromide or hydrogen chloride, at a temperature above about 140°C and below the decomposition temperature of the ester.

We have now discovered that the product of the said reaction contains, in addition to the expected aliphatic phosphonic acid, a substantial amount of new and useful *bis* aliphatic phosphonic anhydrides, which may be recovered therefrom in high purity. These novel *bis* aliphatic phosphonic acid anhydrides may be hydrolyzed to the aliphatic phosphonic acid, and for many applications the mixture of aliphatic phosphonic acid and *bis* aliphatic phosphonic acid anhydride may be used as produced.

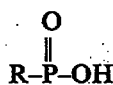
According to one aspect of this invention we provide a *bis* aliphatic phosphonic acid anhydride represented by the general formula:



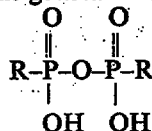
wherein each R represents a haloalkyl group of 2 to 6 carbon atoms inclusive.

According to another aspect of this invention we provide a composition comprising a mixture of:

1. an aliphatic phosphonic acid of the general formula:



2. A *bis* aliphatic phosphonic acid anhydride of the general formula:



5 wherein each R represents a haloalkyl group of 2 to 6 carbon atoms inclusive the ratio of the acid to anhydride being in a ratio range of 1 : 9 to 9 : 1 by weight.

10 The present invention will be described with particular reference to *bis*-(*beta*-chloroethyl phosphonic acid) anhydride and mixtures thereof with *beta*-chloroethyl phosphonic acid, since this anhydride is of particular interest as exerting hormonal effect in plants. The compound *bis*-(*beta*-chloroethyl phosphonic acid) anhydride alternatively named *bis*-(*beta*-chloroethane-phosphonic acid) anhydride (C-EPAA) or Pyro (*beta*-chloroethylphosphonic acid) has hitherto been unknown. The new compound behaves in similar fashion to chloroethane phosphonic acid on plants. We are not certain of the mechanism of the anhydride's action in plants, although presumably it acts as does chloroethane phosphonic acid, by releasing ethylene itself or through promotion of ethylene-formation by enzymatic action.

30 The properties of *pyro* (chloroethyl-phosphonic acid) and chloroethyl phosphonic acid differ in a manner similar to those of *orthophosphoric acid* and *pyrophosphoric acid* insofar as the two systems can be compared. The *pyro* acid has a higher melting point, is a stronger acid and is hydrolyzed in aqueous solution.

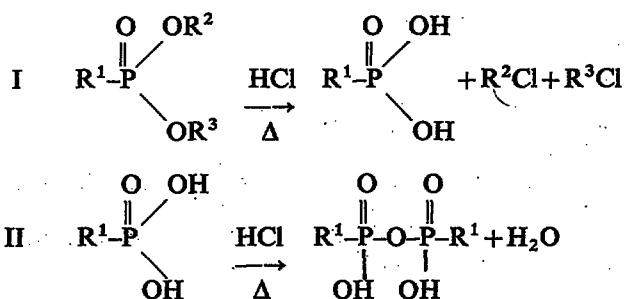
35 The hydrolysis of *pyrochloroethyl phosphonic acid* requires conditions similar to those necessary for the hydrolysis of *pyrophosphoric acid*. In dilute aqueous solution at room temperature the rate of hydrolysis is very slow. The *pyro* acid can be titrated in aqueous solution without the occurrence of detectable hydrolysis. In dilute aqueous solution (0.1% or less) complete hydrolysis requires 4 hours at steam bath temperature. Hydrolysis occurs more rapidly as the concentration is increased because of the increased hydronium ion concentration. Fine crystals of *pyro* (chloroethylphosphonic

acid) exposed to the atmosphere absorb water and rapidly hydrolyze to chloroethyl phosphonic acid. Neutralized solutions of the *pyro* acid are quite stable.

55 Although both *beta*-chloroethyl phosphonic acid and *pyro* (*beta*-chloroethyl-phosphonic acid) contain two acid functions, the potentiometric titration curves of the two compounds differ greatly. Two inflections between pH 4 and 5.8 and between pH 8.6 and 10 occur in the titration of an aqueous solution of *beta*-chloroethyl phosphonic acid with dilute sodium hydroxide. The titration curve of *pyro* (chloroethylphosphonic acid) obtained in the same manner shows only one inflection between pH 4.5 and 9.5. The two acid functions on the *pyro* acid cannot be differentiated and the base consumed at the endpoint of the titration is equivalent to the total acid present. The ionization constant calculated from the titration curve for the *pyro* acid is 7.6×10^{-3} . The calculated constants for *beta*-chloroethyl phosphonic acid are 3.2×10^{-3} and 8.0×10^{-8} .

75 Another important chemical difference between the two compounds lies in their action with warm excess base. The evolution of ethylene at 70°C in excess aqueous base from pure chloroethane phosphonic acid is quantitative, while, under the same conditions, CEPAA releases no ethylene. The new compound is much less soluble in anhydrous ether than is chloroethane phosphonic acid. Highly purified CEPAA, washed with anhydrous ether several times, melts at 96.5-98.5°C. It is a white hygroscopic solid.

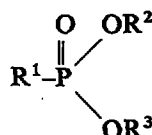
90 While the novel *bis* aliphatic phosphonic acid anhydrides (or *pyroaliphatic phosphonic acid*) of the present invention may be produced by the use of straight dehydration techniques on the corresponding aliphatic phosphonic acid, we prefer to employ the process disclosed in the above-mentioned co-pending application 15882/68 (Serial No. 1187002) viz. the passage of anhydrous HCl (or HBr) gas through a *bis*-aliphatic ester of the corresponding aliphatic phosphonic acid. Although there are several methods possible for the formation of the anhydride, the most reasonable one appears to be the cleavage of the *bis* ester of the aliphatic phosphonic acid with hot anhydrous HCl to the aliphatic phosphonic acid and the dehydration of the acid to the anhydride in the presence of the hot HCl gas, as represented by the following equations



wherein R^1 , R^2 and R^3 are as defined below. We do not, however, wish to be held to any theory of operation.

Without HCl at elevated temperatures, a very impure anhydride occurs. In the case of *bis* (2-chloroethyl) *beta*-chloroethyl phosphonate, the impurities introduced are due to dehydrohalogenation of chloroethane phosphonic acid or CEPAA itself to yield unsaturated compounds. The use of HCl obviously represses the dehydrohalogenation reaction in the direction of the desired CEPAA.

The esters which may be cleaved and dehydrated in our preferred process of producing the novel *bis* aliphatic phosphonic acids of this invention are represented by the following general formula:



wherein R^2 and R^3 are either an alkyl group or a haloalkyl group, preferably a 2-haloalkyl group, not containing more than six carbon atoms wherein the halo group is either fluoro, chloro, bromo or iodo; and R^1 is a C_2 - C_6 haloalkyl group.

The hereinabove mentioned esters having identical R^1 , R^2 and R^3 groups may be produced, for example, by the isomerization of the corresponding phosphite. Thus, a *tris* (2-chloroethyl) phosphite, such as *tris* (2-chloroethyl) phosphite may be heated in the absence of a diluent to effect isomerization thereof to *bis* (2-chloroethyl) *beta*-chloroethylphosphonate, as taught by Kabachnik, "Bull. acid sci. U.R.S.S. classe sci. chim." 1946, 403 [C.A. 42 7242 (1948)] also reported in Organic Reactions Vol. VI, Pages 287-8, all hereby incorporated by reference. This reaction, however, is violently exothermic (almost explosive) and very dangerous on a large scale. Consequently, it is preferred to effect the isomerization in the presence of an inert organic diluent, such as *o*-dichlorobenzene, cumene or xylene, at an elevated temperature, for example about 160°C. The organic diluent moderates the isomerization sufficiently to enable large scale production of the phosphonate ester.

The isomerization reaction in the presence of a diluent is further described in German Patent Specification 964,046 of March 16, 1957 and by Geffer C.A. 53 1120a) Zhur. Obschchei Khim 28 1908 (1958), both hereby incorporated by reference.

As representative examples of esters which may be cleaved in accordance with the process of the invention, there may be mentioned: *bis* (2-chloroethyl) *beta*-chloroethylphosphonate and *bis* (2-chloropropyl) *beta*-2-chloropropylphosphonate. It is to be understood, however, that the hereinabove mentioned esters are only illustrative of the esters which may be cleaved in accordance with the process of the invention and the scope of the invention is not to be limited thereby.

The invention will be further described with reference to the following examples.

Example I

1938 grams of crude *bis* (2-chloroethyl) *beta*-chloroethylphosphonate, prepared by the rearrangement of *tris* (2-chloroethyl) phosphite in *o*-dichlorobenzene, were introduced into a 3 litre 3 neck flask, equipped with stirrer, glass inlet tube and a "Y" tube, containing a thermometer which extended below the liquid surface. The other arm of the "Y" tube was attached to a down dropping bulb condenser attached to a one litre one neck distillation flask, containing a side arm which was connected to a cascade water scrubbing tower for a removal of excess hydrogen chloride. The crude ester was heated, with stirring, to a temperature of 171°C., at which temperature hydrogen chloride from a pressure cylinder was introduced beneath the surface of the liquid, resulting in vigorous evolution of 1,2-dichloroethane. The addition of hydrogen chloride was continued for 6.5 hours while maintaining a temperature of 175°C. The evolution of 1,2-dichloroethane was very rapid during the first four hours. After the addition of hydrogen chloride was terminated, nitrogen was bubbled through the reaction mixture at a temperature of 170°C to remove hydrogen chloride therefrom. The resulting product weighed 1039 grams and had a melting point of 35-55°C.

This product, on analysis, was found to consist of about 30% (by weight) of *bis* (chloroethane phosphonic acid) anhydride, and 70% (by weight) of *beta*-chloroethane phosphonic acid. The anhydride is separated from the acid by stirring 1 part of the mixture in 20 parts cold anhydrous ethyl ether. The anhydride is essentially insoluble and is recovered by filtration. Several washings of the filter cake with anhydrous ether raises its m.p. to 96.5-98.5°C.

Example II

50 g. *beta*-chloroethane phosphonic acid are stirred with 10.4 g. thionyl chloride at 90°C. After 1 hour the copious evolution of SO₂ and HCl ceases. The residual gas is removed under vacuum. The clear viscous syrup contains 40% (by weight) *bis* (*beta*-chloroethane phosphonic acid) anhydride on analysis. The remainder of the product is unchanged *beta*-chloroethane phosphonic acid.

The anhydride was separated from the acid in the same manner as Example I, by stirring 1 part of the mixture with 20 parts cold anhydrous ethyl ether. The insoluble anhydride, which precipitated, was recovered by filtration and dried.

Example III

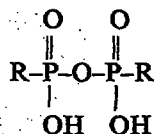
Using the procedure described in Example I, 1,000 g. of *bis* (2-chloropropyl) *beta*-chloropropyl phosphonate were cleaved with anhydrous hydrogen chloride to produce 525 g. of a mixture of *beta*-chloropropyl phosphonic acid and *bis* (*beta*-chloropropyl phosphonic acid) anhydride. 1,2-dichloropropane was recovered as a by-product.

The *bis* (*beta*-chloroethane phosphonic acid) anhydride of the present invention is particularly valuable for use as a plant growth regulator by application to plants, either alone or in admixture with the *beta*-chloroethyl phosphonic acid, in essentially any proportions, i.e. in relative proportions by weight of the anhydride to acid of from 1:99 to 99:1, although as a practical matter, it is preferred to employ such mixtures in the ratio of 1:9 to 9:1 by weight.

The effect of the *bis* (*beta*-chloroethane phosphonic acid) anhydride on living plants and its manner of use thereon, is essentially the same as that of the *beta*-chloroethane phosphonic acid.

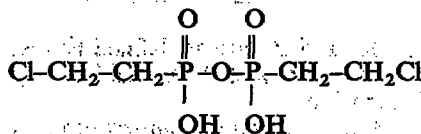
WHAT WE CLAIM IS:—

1. A *bis* aliphatic phosphonic acid anhydride represented by the general formula:

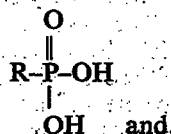


wherein each R represents a haloalkyl group of 2 to 6 carbon atoms inclusive.

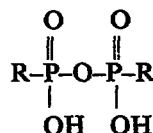
2. *Bis* (2-chloroethane phosphonic acid) anhydride of the formula:



3. A composition comprising a mixture of:
1. an aliphatic phosphonic acid of the general formula:



2. a *bis* aliphatic phosphonic acid anhydride of the general formula:



wherein each R represents a haloalkyl group of 2 to 6 carbon atoms inclusive, the ratio of the acid to the anhydride being in a ratio range of 1:9 to 9:1 by weight.

4. The composition of matter defined in Claim 3, wherein the aliphatic phosphonic acid is 2-chloroethane phosphonic acid and the *bis* aliphatic phosphonic acid anhydride is *bis* (2-chloroethane phosphonic acid) anhydride.

5. A *bis* aliphatic phosphonic acid anhydride according to Claim 1 or Claim 2 substantially as herein described and exemplified.

6. The composition defined in Claim 3 substantially as herein described and exemplified.

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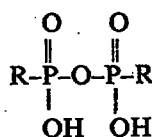
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The *bis* (*beta*-chloroethanephosphonic acid) anhydride of the present invention is particularly valuable for use as a plant growth regulator by application to plants, either alone or in admixture with the *beta*-chloroethylphosphonic acid, in essentially any proportions, i.e. in relative proportions by weight of the anhydride to acid of from 1:99 to 99:1, although as a practical matter, it is preferred to employ such mixtures in the ratio of 1:9 to 9:1 by weight.

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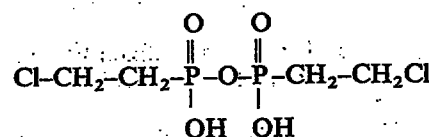
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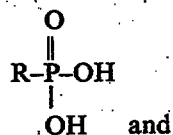


wherein each R represents a haloalkyl group of 2 to 6 carbon atoms inclusive.

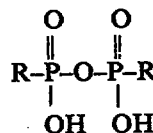
2. *Bis* (2-chloroethanephosphonic acid) anhydride of the formula:



3. A composition comprising a mixture of:
1. an aliphatic phosphonic acid of the general formula:



2. a *bis* aliphatic phosphonic acid anhydride of the general formula:



wherein each R represents a haloalkyl group of 2 to 6 carbon atoms inclusive, the ratio of the acid to the anhydride being in a ratio range of 1:9 to 9:1 by weight.

4. The composition of matter defined in Claim 3, wherein the aliphatic phosphonic acid is 2-chloroethanephosphonic acid and the *bis* aliphatic phosphonic acid anhydride is *bis* (2-chloroethanephosphonic acid) anhydride.

5. A *bis* aliphatic phosphonic acid anhydride according to Claim 1 or Claim 2 substantially as herein described and exemplified.

6. The composition defined in Claim 3 substantially as herein described and exemplified.

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