

Synthesis of the New Type of Water-Soluble Ligand N,N-Bis-(diphenylphosphinomethyl)-2-aminoethylphosphonic Acid ($(\text{Ph}_2\text{PCH}_2)_2\text{NCH}_2\text{CH}_2\text{PO}_3\text{H}_2$) and Its Sodium Salt

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Abstract: The novel water-soluble ligand, N,N-bis(diphenylphosphinomethyl)-2-aminoethylphosphonic acid, $(\text{Ph}_2\text{PCH}_2)_2\text{NCH}_2\text{CH}_2\text{PO}_3\text{H}_2$, had been synthesized in quantitative yield by reaction of 2-aminoethylphosphonic acid with bis(hydroxymethyl)-diphenylphosphonium chloride in water. Its mono- and disodium salts, which can be used as water-soluble ligands for transition metal complex catalysts, were also easily prepared under mild conditions.

Keywords: N,N-Bis(diphenylphosphinomethyl)-2-aminoethylphosphonic acid; Synthesis

Introduction

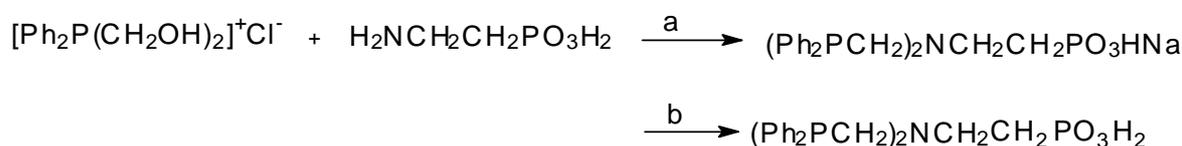
The potential advantages of homogeneous over heterogeneous catalysis are well recognized, but the problem of separating products from catalysts continues to be a major obstacle for the development of the technique. To date, one of the promising methods involves performing the reaction in a biphasic system (water/organic phase) using water-soluble catalysts. The growing interest in aqueous organometallic chemistry and the application of water-soluble phosphine ligand-transition metal complex in homogeneous catalysis has prompted the search for new type of water-soluble

tertiary phosphines. The importance of these water-soluble phosphines and their transition metal complexes is highlighted by the use of a sulfonated triphenylphosphine as a ligand for rhodium in the design of a water-soluble homogeneous catalyst for the hydroformylation reaction [1-3]. Due to their high solubility and similar electronic properties, a large number of alternative ligands containing a variety of functional groups have been prepared, e.g. $-\text{CO}_2\text{Na}$ [4], $-\text{OH}$ [5, 6], $-\text{PMe}_3^+$ [7], $-\text{NMe}_3^+$ [8], $-\text{PO}_3\text{Na}_2$ [9] and polyethers [10], which all render the phosphines water-soluble. In light of the strong chelating ability of N and P atoms, our own interest in the synthesis of new hydrophilic phosphonic acid functionalized phosphine ligands and their corresponding salts arose from several different perspectives. First, the anionic phosphonate group has been previously used to render phosphines water-soluble [9], but, to the best of our knowledge, the synthetic methods involved are complicated and give low yields. Also, the introduction of diphenylphosphine moiety into a phosphonic acid by P-C-N bond formation has not been reported. In our previous work, we reported a new and simple route for preparing 2-aminoethylphosphonic acid and its N-substituted compounds [11], whereby the diphenylphosphinomethyl group was introduced into an amine via a Mannich-type condensation reaction under mild conditions (60-80°C) and no special reagents were necessary to obtain high yields. Finally, the transition metal salts of the phosphonic acids, especially tetravalent metals such as Zr (IV), Ti (IV), Ce (IV) and Th (IV) could form a kind of layered organometallic inorganic polymer no matter whether they are crystalline, semicrystalline, noncrystalline or amorphous, which are useful as absorbents, ion exchangers, chelating agents, catalysts and catalyst supports [12].

Results and Discussion.

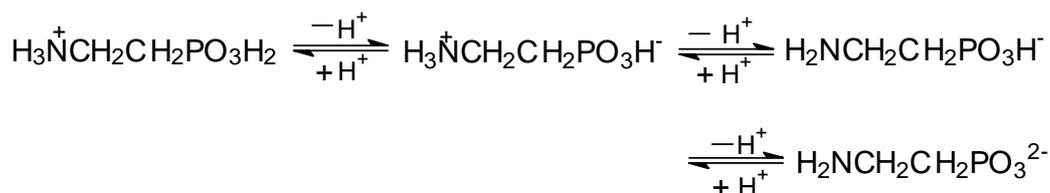
In this paper the new diphenylphosphinomethylamine derivative, N,N-bis(diphenylphosphinomethyl)-2-aminoethylphosphonic acid, was prepared in quantitative yield by reaction of 2-aminoethyl-phosphonic acid with bis(hydroxymethyl)diphenylphosphonium chloride in water (Scheme 1). This reaction proceeded readily at room temp. via a Mannich-type condensation reaction [13].

Scheme 1



Reagents: (a) $\text{N}(\text{Et})_3$, Na_2CO_3 , $\text{pH}=8.5-9.5$, water as solvent; (b) H^+ .

To our delight, distilled water was found to be optimum solvent as the starting materials were soluble and the product was easy to crystallize. Like glycine, 2-aminoethylphosphonic acid contains two dissociable protons which are involved in the dissociation of the $-\text{PO}_3\text{H}^-$ and $-\text{NH}_3^+$ groups, as indicated by the following processes:



All the 2-aminoethylphosphonic acid species in the equations above can be monitored and quantified by the measurement of the corresponding dissociation constants. It is known that the pK_1 and pK_2 values characteristic of the dissociation of $-\text{PO}_3\text{H}_2$ in 2-aminoethylphosphonic acid are 6.21 and 10.92 respectively [14]. Therefore, $\text{H}_2\text{NCH}_2\text{CH}_2\text{PO}_3\text{H}^-$ (pH 6.21-10.92), $\text{H}_3\text{N}^+\text{CH}_2\text{CH}_2\text{PO}_3\text{H}^-$ (pH \leq 6.21) and $\text{H}_2\text{NCH}_2\text{CH}_2\text{PO}_3^{2-}$ species (pH \geq 10.92) are predominantly formed in the studied range of pH values (3–11) for the systems. For this reason 1.0 equiv. of sodium carbonate was added to maintain the pH of the media in the range of 8.5-9.5 in order to obtain quantitative yields. The introduction of the diphenylphosphinomethyl group into the 2-aminoethylphosphonic acid moiety should not affect the dissociation processes of the product. In other words, N,N-bis(diphenylphosphinomethyl)-2-aminoethylphosphonic acid will have almost as same dissociation processes and dissociation constants as 2-aminoethylphosphonic acid.

Taking into account the different species existing under differing acidity conditions, the corresponding monosodium salt $(\text{Ph}_2\text{PCH}_2)_2\text{N}-\text{CH}_2\text{CH}_2\text{PO}_3\text{HNa}$ was obtained at pH 8.5-9.5 by reaction of 2-aminoethylphosphonic acid with bis-(hydroxymethyl)phosphonium salt in water, and the $(\text{Ph}_2\text{PCH}_2)_2\text{N}^+\text{HCH}_2\text{CH}_2\text{PO}_3\text{H}^-$ species formed at pH 4.0-5.0 and was collected by filtration after acidification at low pH values (<1). The IR data shows that the protonation of tertiary phosphines ($\equiv\text{P}^+-\text{H}$), which hindered the formation of corresponding transition metal complexes, is evidenced by an absorption at 2560 cm^{-1} . Table 1 shows the yields for the $(\text{Ph}_2\text{PCH}_2)_2\text{N}^+\text{HCH}_2\text{CH}_2\text{PO}_3\text{H}^-$ species obtained after the pH of the media shown in step (a) of Scheme 1 was adjusted as indicated.

Table 1. Yields of $(\text{Ph}_2\text{PCH}_2)_2\text{N}^+\text{HCH}_2\text{CH}_2\text{PO}_3\text{H}^-$ species

Reaction conditions	a	b	c	d	e
Yields (%)	62.0	85.6	100	96.8	78.2

Conditions: (a) $\text{N}(\text{Et})_3$ and Na_2CO_3 absent, pH 4-5;

(b) only $\text{N}(\text{Et})_3$ present, pH 7-8;

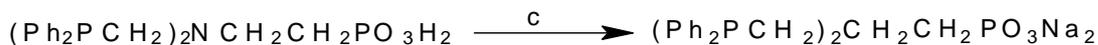
(c) $\text{N}(\text{Et})_3$ and Na_2CO_3 present, pH 8.5-9.5;

(d) $\text{N}(\text{Et})_3$ and Na_2CO_3 present, aqueous ethanol as solvent, pH 8.5-9.5;

(e) NaOH present, pH=10.

The compound disodium N,N-bis(diphenylphosphinomethyl)-2-aminoethylphosphonate, $(\text{Ph}_2\text{PCH}_2)_2\text{NCH}_2\text{CH}_2\text{PO}_3\text{Na}_2$, has been prepared by reaction of N,N-bis(diphenylphosphinomethyl)-2-aminoethylphosphonic acid with sodium hydroxide in methanol as solvent (Scheme 2).

Scheme 2



Reagents: (c) NaOH, H₂O/EtOH, N₂

Oxidation of phosphine is the main side reaction. Commonly, the diphenylphosphine oxide content of the reaction mixture be detected by using ³¹P NMR spectra. In our work, the ³¹P NMR signal of the corresponding oxide (Ph₂P(O)CH₂)₂NCH₂CH₂PO₃Na₂ was found at δ37.70. With this in mind, the reactions were therefore carried out under N₂ atmosphere at 5-10°C in aqueous ethanol. Under these conditions the ³¹P NMR spectrum (D₂O) showed that no oxidation of diphenylphosphine to diphenylphosphinylide occurred, even after standing or storage for several months (Table 2).

Table 2 . The oxidation of phosphines and yields obtained for (Ph₂PCH₂)₂NCH₂CH₂PO₃Na₂ under different conditions

Conditions	a	b	c	d
³¹ P NMR (≡P=O)	37.71	37.70	/	/
yields(%)	75.8	92.4	91.2	76.8

Conditions: (a): NaOH / H₂O; (b): MeONa / MeOH; (c): NaOH, H₂O (50% w/v) / EtOH, N₂ protection; (d): NaOH, H₂O / N₂ protection.

Acknowledgements

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Experimental

General

Melting points are uncorrected. ¹H-NMR and ³¹P-NMR spectra were recorded on a Bruker DPX-300 spectrometer. Chemical shifts are given in ppm relative to an internal tetramethylsilane standard. IR spectra were recorded on a PK-6000 FTIR instrument (KBr pellets). Elemental analyses were performed with a PE 2400 instrument. Bis(hydroxymethyl)diphenylphosphonium chloride and 2-aminoethylphosphonic acid were synthesized according to literature procedures [8,10]. All other solvents and reagents were used as received from suppliers.

N,N-bis(diphenylphosphinomethyl)-2-aminoethylphosphonic acid. Bis(hydroxymethyl)diphenylphosphonium chloride (42.4g, 0.15mol) and water (60mL) were placed in a three necked round bottom flask equipped with a mechanical stirrer, an addition funnel and a thermometer and the mixture was then heated to dissolve all solids and afterwards cooled to maintain the temperature in the range of

20°C to 30°C. To this mixture 2-aminoethylphosphonic acid (9.4 g, 0.075mol) and sodium carbonate (8 g, 0.075mol) dissolved in water (30 mL) were added dropwise. Then triethylamine (15.3 g, 0.15mol) was added to maintain the pH in the range of 8.5 to 9.5, and the mixture was heated to 80°C. After 2h, a pale-yellow organic phase was formed. The reaction mixture was cooled and acidified to pH = 4-5 with 3N HCl. The white solid product was allowed to crystallize overnight in refrigerator, then filtered off, washed with ethanol/water and dried in vacuo to give the title compound (34.6g), mp 146-148°C. Anal. % calcd for C₂₈H₃₀NO₃P₃: C, 64.52; H, 5.76; N, 2.69. Found: C, 64.40; H, 5.71, N 2.66. IR (KBr pellet): $\nu(\text{P=O})$ 1192cm⁻¹, $\nu(\text{P-O})$ 1118, 1055, 997 cm⁻¹. ¹H-NMR (CCl₃D): δ 7.93-7.18 (m, 20H, C₆H₅), 5.15 (s, 4H, P-CH₂-N), 3.21-3.17 (t, 2H, N-CH₂-C), 1.52-1.47 (t, 2H, C-CH₂-P), 1.33 (s, 1H, O-H). ³¹P NMR (CCl₃D): δ 14.41 (s, PO), -22.36 (m, PPh₂).

Disodium N,N-bis (diphenylphosphinomethyl)-2-aminoethylphosphonate. N,N-Bis-(diphenylphosphinomethyl)-2-aminoethylphosphonic acid (20.0g, 0.38mol) was dissolved in methanol. Then NaOH (50%, w/v) was added under a N₂ atmosphere. After 30 min, the residue was cooled in a refrigerator, allowed to crystallize overnight, filtered and dried in vacuo at 50°C. Mp >300°C. Anal. % calcd. for C₂₈H₂₈Na₂NO₃P₃: C, 59.94; H, 4.95; N, 2.48. Found: C, 59.91; H, 4.94; N, 2.46. IR (KBr pellet): $\nu(\text{P=O})$ 1265cm⁻¹, $\nu(\text{P-O})$ 1123, 1068, 996 cm⁻¹. ¹H-NMR (D₂O): δ 7.69-7.35 (m, 20H, C₆H₅), 4.69(s, 4H, P-CH₂-N), 4.49-4.44 (t, 2H, N-CH₂-C), 3.50-3.38 (t, 2H, C-CH₂-P). ³¹P NMR (CCl₃D): δ 3.79(s, PO), -10.25 (s, PPh₂). Its transition metal complexes and their catalytic properties are currently under investigation.

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Sample Availability: Samples are available from the authors.

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