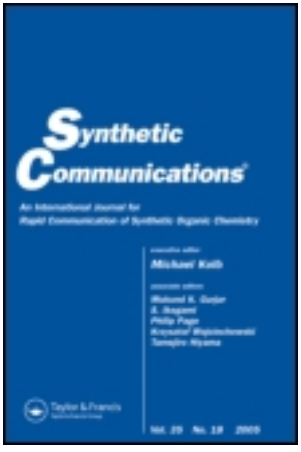

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A New Simple Route To N-Substituted 2-Aminoethylphosphonic Acids

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A NEW SIMPLE ROUTE TO N-SUBSTITUTED 2-AMINOETHYLPHOSPHONIC ACIDS

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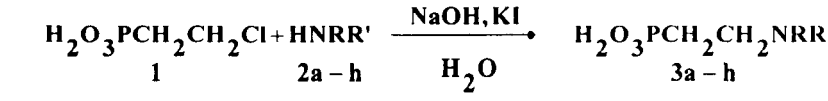
Abstract: 2-Aminoethylphosphonic acid (AEPA) and its N-substituted compounds were prepared by one step reaction using 2-chloroethylphosphonic acid with ammonia and amines (H_2NMe, HNMeMe, HNEtEt, H_2NPr-n, H_2NCH_2ph,$H_2NCH_2CH_2NH_2$ and $H_2N(C{=}NH)NH_2$ in a dilute alkaline solution below 20 ℃ with simple work-up and easy purification. The reaction was accelerated by catalytic amount of potassium iodide. The yield for the reaction products were 35.6 to 48.6% for the KI absence and 78.2 to 88.0% for the KI presence.

2-Aminoethylphosphonic acid $H_2O_3PCH_2CH_2NH_2$ (ciliatine) (AEPA) is the first compound having a C-P bond to be isolated from biological materials[1]. Since

then, it has been found that AEPA is widely distributed in numerous animals, and appears to be an important biochemistry compound which could find wide applications as metablic regulators, potential bactericide, fungicides, algicidal, fireproofing and complexing agents. Its transition metal salts, especially Zr(IV), Ti(IV),U(IV),Th(IV),Ce(IV) et al,could form a kind of layered or amorphous organometallic inorganic polymers, which are useful as absorbents, adsorbents, ion exchangers, chelating agents, catalysts and catalyst supports[2].

A lot of synthetic methods for AEPA and its analogues have been reported [3 - 9], but most of these procedures are involved at least two steps, tiresome work-up and complex purification for the product, and with relatively low overall yields. Only one patent literature [10] described a direct manufacture method by treating H_3PO_3 with ethyleneimine ,but it is not available for preparation of the N-substituted analogues.

In this communication we wish to report a new and simple route to AEPA and its N-substituted compounds by one step reaction using 2-chloroethylphosphonic acid (CEPA) with ammonia or amines with simpler work-up and purification for the products. CEPA is a very common and cheap chemical, which is industrial available and used as a ripener for fruits. Nobody has been used it for synthetic purpose yet, because it is easy to decompose when it was used in the medium of pH above 4. We found that CEPA was able to react with ammonia and amines in a dilute aqueous alkaline solution if the reaction temperature was controlled below about 20 ℃, and the reaction was accelerated by catalytic amount of potassium iodide.



For 2 and 3	a	b	c	d	e	f	g	h
R=	H	H	Me	Et	H	H	H	H
R′=	H	Me	Me	Et	n-Pr	$phCH_2$	$CH_2CH_2NH_2$	$C(=NH)NH_2$

Experimental

All melting points are uncorrected. IR spectra were recorded on a PK 60000 FTIR instrument for KBr tablets. NMR spectra were run on a Varian EM 360L spectrometer in D_2O. Elemental analysis were performed by a PE 2400 instrument. All the reagents were CP or AR, and were used as received from suppliers. CEPA(40% solution) was purchased from Nanjing Electrochemistry Works (Nanjing, China)

General Procedure

0.2mol of CEPA 1 (40% solution),300 g of ice water, o.2 ~ 0.25mol of amine 2a ~ h and o.3g of KI were mixed and stirred at room temperature, followed by addition of 160 ml of 10% cold NaOH solution. The reaction temperature was controlled below 20 ℃ by cold water bathe. The reaction solution was stirred for 120 to 148 hours, every half a day checked the pH value of the solution and about

Table 1 The M.P and yields for the N-substituted AEPA

compd.	R	R′	M.P(℃)	yield% KI absent	yield% KI present
3a	H	H	>305dec.(289-290dec.)[a]	48.6	88.0
3b	H	CH_3	>305[d]$_{dec.}$ (>260)[b]	35.6	78.2
3c	CH_3	CH_3	>305dec.(244)[c]	36.2	79.3
3d	Et	Et	280dec.	35.8	79.2
3e	H	n-C_3H_7	>305dec.	37.5	79.9
3f	H	phCH_2	219-220(>260)[b]	42.8	84.5
3g	H	$CH_2CH_2NH_2$	238-240dec.	47.5	86.5
3h	H	C(=NH)NH_2	>305[d]$_{dec.}$	43.8	85.2

a.b.c.The M.P. in parentheses are cited from [6],[9],[7] respectively.

d. Anhydrous compounds should be obtained by treating the hydrate in vacuum-baking.

10ml of 10% cold NaOH solution was added, in order to maintain the pH value of the solution above 8, until the pH value of the solution no longer changed. The reaction solution was standed for another 24 hours and then evaporated under reduced pressure. After about 3/4 volume of water was removed, hydrochloride acid (8N) was added dropwise to adjust the pH value of the solution below 4. The concentrated solution was standed or kept in refrigerator for 40 hours for

crystalization. Then the white solid of 3a ~ h was filtrated, washed with cold water and dried in vacuo. Recrystallization of 3a ~ h was carried out in water,pure products were obtained.

Results

The reaction results for KI present and absent are summarized in Table 1.

All the products are known and characterized by IR, NMR and elementary analysis .They are all white crystal with high melting points, and can be obtained by directly work-up and purification. For 3b,3d,3h,they are easily form hydrate $H_2O_3PCH_2CH_2NRR' \cdot nH_2O$,in which n is about 6, and the M.P of hydrate for 3b,3d,3h are usually not above 60 ℃. The anhydrous compounds for 3b, 3d,3h are obtained by keeping the hydrate in vacuum baking at 120 ℃ until weight constant.

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Registry No.——3a,2041-14-7;3b,14596-55-5;3c,14596-56-6;3d,69303-27-1; 3e,79782-63-1;3f,72696-92-5;3g,112013-36-2;3h,55215-15-1.

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