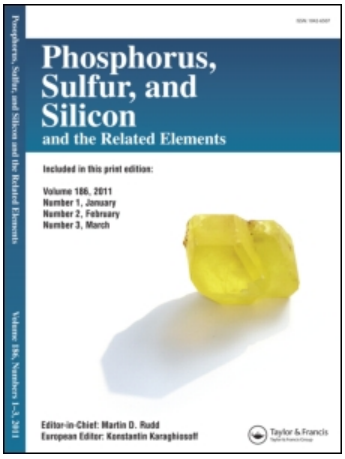



**Phosphorus, Sulfur, and Silicon and the Related Elements**
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

# Synthesis and Characterization of New Symmetrical Bisphosphonates

Janaína Marques Rodrigues[a]; João Batista Neves DaCosta[a]
[a] Departamento de Química, ICE, Universidade Federal Rural do Rio de Janeiro, Rio de Janeiro, Brazil

Online publication date: 27 October 2010

**To cite this Article** Rodrigues, Janaína Marques and DaCosta, João Batista Neves(2002) 'Synthesis and Characterization of New Symmetrical Bisphosphonates', Phosphorus, Sulfur, and Silicon and the Related Elements, 177: 1, 137 — 149
**To link to this Article: DOI:** 10.1080/10426500210231
**URL:** http://dx.doi.org/10.1080/10426500210231

*Phosphorus, Sulfur and Silicon*, 2002, 177:137–149

1042-6507/02 $12.00 + .00

# SYNTHESIS AND CHARACTERIZATION OF NEW SYMMETRICAL BISPHOSPHONATES

*Janaína Marques Rodrigues and João Batista Neves DaCosta**
*Departamento de Química, ICE, Universidade Federal Rural do Rio de Janeiro, km 47 da Antiga Rio-São Paulo, Seropédica 23851-970, Rio de Janeiro, Brazil*

(Received May 11 2001.)

*In order to search for new chelating agents, widely employed methodologies in the chemistry of organophosphorus compounds such as the Michaelis-Arbuzov and Michaelis-Becker reactions were used to synthesize new bisphosphonates in high yields. The importance of the synthesis of these compounds resides in their potential capability of complexing different metals, all the more so because bisphosphonates have been widely employed in the diagnosis and therapy of several bone diseases, such as osteoporosis and hypercalcemia, as extracting agents for alkaline, alkaline earth, and transition metals, and also as reaction catalysts. All bisphosphonates synthesized were characterized by IR, $^{1}$H-NMR, $^{13}$C-NMR, $^{31}$P-NMR, and mass spectroscopy.*

*Keywords:* Bisphosphonates; diamines; organophosphorus compounds

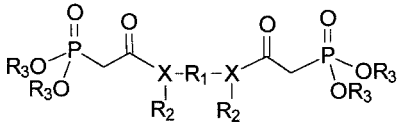


## INTRODUCTION

The chemistry of organophosphorus compounds started to be investigated around the end of the nineteenth century by Michaelis and Arbuzov.[1–3] One of the most valuable contributions coming from this study is the Michaelis-Arbuzov reaction, which involves formation of a C—P bond. This reaction is widely used for the preparation of phosphonates from trialkyl phosphites and alkyl halides.[4–6]

The Michaelis-Arbuzov reaction does not work well for the preparation of $\beta$-ketophosphonates from $\alpha$-haloaldehydes and ketones. In this case, the Perkow reaction takes place affording the dialkyl vinyl phosphate, where the P—O bond is formed instead of the P—C bond.[7]

Address correspondence to João Batista Neves DaCosta, Departamento de Química, ICE, Universidad Federal Rural do Rio de Janeiro, km 47 da Antiga Rio-São Paulo, Seropédica 23851-970, Rio de Janeiro, Brazil. E-mail: dacosta@ufrrj.br



1) X = N, $R_1 = (CH_2)_2$, $R_2$ = H, $R_3$ = Et;
2) X = N, $R_1 = (CH_2)_3$, $R_2$ = H, $R_3$ = Et;
3) X = N, $R_1 = (CH_2)_4$, $R_2$ = H, $R_3$ = Et;
4) X = N, $R_1 = (CH_2)_2$, $R_2 = CH_2$, $R_3$ = Et;
5) X = N, $R_1 = (CH_2)_2$, $R_2$ = H, $R_3$ = Bu;
6) X = O, $R_1$ = -$CH_2CH_2$-, $R_3$ = Et;
7) X = O, $R_1$ = -$CH_2CH_2$-O-$CH_2CH_2$-, $R_3$ = Et.

**FIGURE 1** Novel synthesized bisphosphonates.

However, when $\alpha$-haloamides are employed, the corresponding phosphonates are obtained in good yields.[8]

Another common method for preparing organophosphorus compounds is the Michaelis-Becker reaction,[4] which involves the synthesis of dialkylphosphonates through the alkylation of a salt obtained by the reaction between a dialkylphosphite with a strong base. When an $\alpha$-haloaldehyde or ketone is used, the Michaelis-Becker reaction affords a 1,2-epoxyalkylphosphonate.[9,10] However, when an $\alpha$-haloamide is employed, the desired $\beta$-ketophosphonate is also obtained.

In this work, seven new bisphosphonates (Figure 1) were prepared through the Michaelis-Arbuzov reaction (**1** to **4**), the Michaelis-Becker reaction (**5**), and through transesterification of triethyl phosphonoacetate (**6** and **7**).

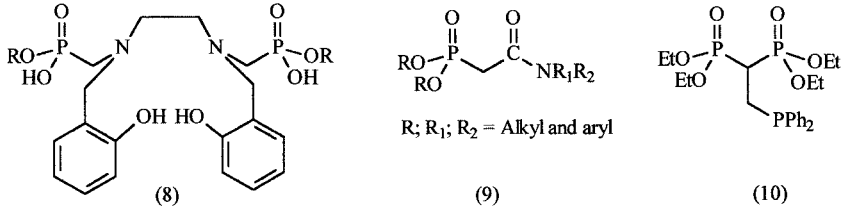
The importance in the synthesis of these compounds resides in their potential capability of complexing different metals.[11]

Analogous compounds, as shown in Figure 2, have had their metal complexing ability investigated and have been widely used in the diagnosis and treatment of several diseases (**8**),[12–16] as extracting agents for alkaline, alkaline earth and transition metals (**9**)[14,15,17,18] and also as reaction catalysts (**10**).[19]



## RESULTS

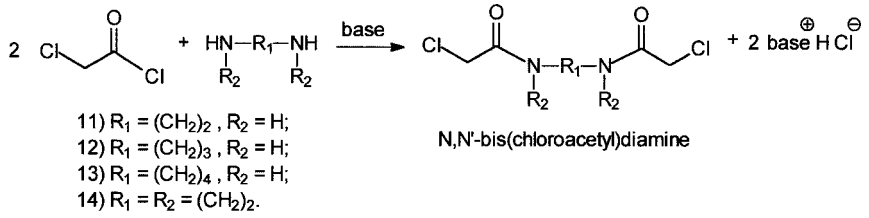
The bisphosphonates where X=N were synthesized in two steps. The first one involved the preparation of N,N′-bis(chloroacetyl)diamines,[20] where the yields varied from 50 to 70% according to Scheme 1.



(8) (9) (10)

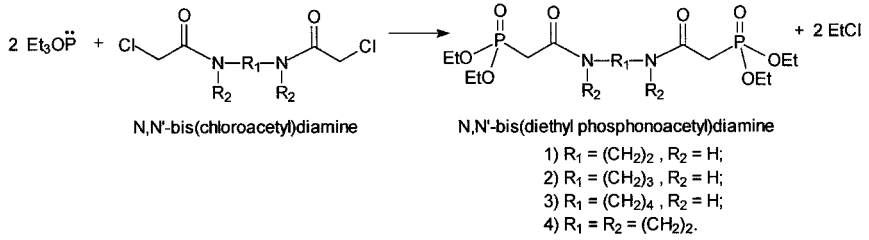
R; $R_1$; $R_2$ = Alkyl and aryl

**FIGURE 2** Analogous compounds with high complexing ability.




**SCHEME 1** Synthesis of N,N′-bis(chloroacetyl)diamine.

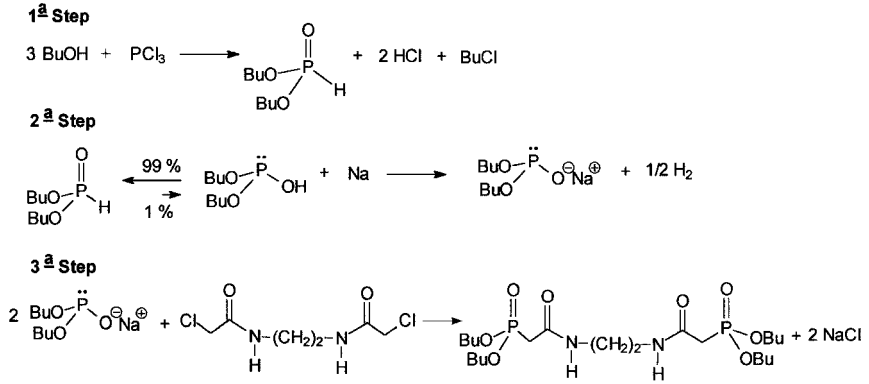
The second step is the Michaelis-Arbuzov reaction,[4,21] where 1 mol of each N,N′-bis(chloroacetyl)diamine reacts with 2 mol of triethyl phosphite according to Scheme 2.




**SCHEME 2** Synthesis of N,N′-bis(diethyl phosphonoacetyl)diamine.

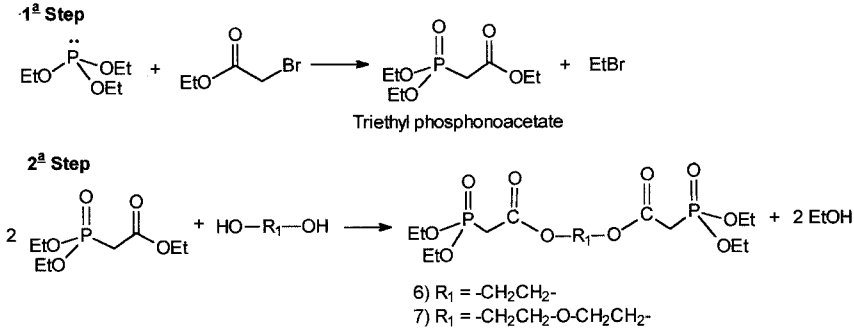
The N,N′-bis(dibutyl phosphonoacetyl)ethylenediamine (**5**) was synthesized via the Michaelis-Becker reaction[4,22] in three steps according to Scheme 3.

Ethyleneglycol-bis(diethyl phosphonoacetyl) (**6**) and diethyleneglycol-bis(diethyl phosphonoacetyl) (**7**) were synthesized in two steps. The second step involves a transesterification[23,24] between the triethyl




**SCHEME 3** Synthesis of **5**.

phosphonoacetate and ethyleneglycol or diethyleneglycol as described in Scheme 4.




**SCHEME 4** Synthesis of **6** and **7**.



## STRUCTURAL DETERMINATION OF THE BISPHOSPHONATES

IR spectra of these compounds show absorption bands at 1240–1276 $cm^{-1}$, relative to P=O stretching and also at 1023–1030 $cm^{-1}$ which refer to P—O asymmetric stretching[25–27] (Table I).

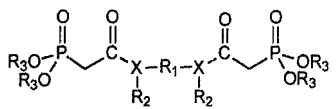
The main indication that the Michaelis-Arbuzov reaction took place can be seen in the $^{1}H$ NMR spectrum, where the formation of a P—$CH_2$ bond is represented by a doublet at 2.8–3.0 ppm with J=22 Hz[28,29] (Table II). The formation of the P—C bond can also be evidenced in the $^{13}C$ NMR spectrum with a doublet at 34 ppm with a coupling constant in the range of 127–134 ppm[30] (Table III).

Other important signals in the spectra of the amide bisphosphonates are at 16 and 62.0 ppm, which are relative to the ethoxy groups of the ester. The coupling of these carbon atoms with the phosphorus atom (J = 6 Hz)[31] can also be seen. Compound 4 shows two signals belonging to the piperazine ring, C$\alpha$ at 41.5 ppm and C$\beta$ at 46.3 ppm,[32] which is due to the diamagnetic anisotropy effect. Thus, as is shown in Figure 3, the C$\beta$, which is on the same side as the carbonyl, is deshielded relative to C$\alpha$.

The conformational analysis of this compound, through the use of PM3 Hamiltonian from the MOPAC package, shows that the most stable conformation is a chair in which the substituents of the nitrogen atom are equatorial, as can be seen in Figure 4.

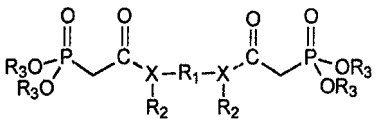
All bisphosphonates synthesized are symmetrical and their $^{31}P$ NMR spectra show only one peak at 20–25 ppm, suggesting that the two phosphorus atoms are in identical environments. The $^{1}H$ coupled

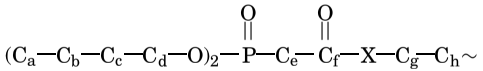
**TABLE I** IR Absorptions Data and Yields of Bisphophonates



| | | | | | | IR ($cm^{-1}$) | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| No. | $R_1$ | $R_2$ | $R_3$ | X | Yield (%) | $\nu$(NH) | $\nu$(C═O) | $\nu$(P═O) | $\nu$(P—O) | $\nu$(C—O) |
| 1 | —$CH_2CH_2$— | H | Et | N | 60 | 3275.1 | 1672.8 | 1246.5 | 1023.7 | 983.2 |
| 2 | —$CH_2CH_2CH_2$— | H | Et | N | 80 | 3290.6 | 1660.6 | 1242.0 | 1027.3 | 972.5 |
| 3 | —$CH_2CH_2CH_2CH_2$— | H | Et | N | 94 | 3346.7 | 1648.3 | 1240.4 | 1030.8 | 962.5 |
| 4 | —$CH_2CH_2$— | —$CH_2$— | Et | N | 95 | — | 1637.1 | 1253.7 | 1027.3 | 965.9 |
| 5 | —$CH_2CH_2$— | H | Bu | N | 25 | 3283.1 | 1664.1 | 1228.1 | 1025.9 | 989.5 |
| 6 | —$CH_2CH_2$— | — | Et | O | 80 | — | 1737.2 | 1270.5 | 1027.2 | 971.1 |
| 7 | —$CH_2CH_2OCH_2CH_2$— | — | Et | O | 80 | — | 1735.3 | 1276.3 | 1028.2 | 975.5 |

**TABLE II** $^1$H NMR Data of Bisphosphonates

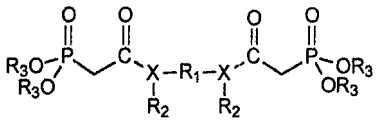


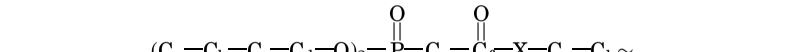


| No. | $R_1$ | $R_2$ | $R_3$ | X | X*H* | $H_a$ | $H_b$ | $H_c$ | $H_d$ | $H_e$ | $H_g$ | $H_h$ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | $^1$H NMR $\delta$(ppm) J(Hz) | | | | | | |
| 1 | —$CH_2CH_2$— | H | Et | N | 7.8(s)[a] | — | — | 1.35(t) J = 7.04 | 4.17(q/d) J = 7.16 | 2.8(d) J = 21.2 | 3.37(m) | — |
| 2 | —$CH_2CH_2CH_2$— | H | Et | N | 8.2(s) | — | — | 1.37(t) J = 7.16 | 4.15(q/d) J = 7.14 | 3.0(d) J = 21.9 | 3.38(m) | 1.78(m) |
| 3 | —$CH_2CH_2CH_2CH_2$— | H | Et | N | 7.9(s) | — | — | 1.21(t) J = 6.91 | 4.02(q/d) J = 6.90 | 2.8(d) J = 21.6 | 3.04(m) | 1.39(m) |
| 4 | —$CH_2CH_2$— | —$CH_2$— | Et | N | — | — | — | 1.35(t) J = 7.08 | 4.18(q/d) J = 7.08 | 3.1(d) J = 23.2 | 3.67(m) | — |
| 5 | —$CH_2CH_2$— | H | Bu | N | 7.7(s) | 0.89(t) J = 7.21 | 1.36(m) J = 6.88 | 1.63(m) J = 6.64 | 4.04(t/d) J = 6.64 | 2.83(d) J = 21.2 | 3.32(m) | — |
| 6 | —$CH_2CH_2$— | — | Et | O | — | — | — | 1.32(t) J = 6.98 | 4.19(q/d) J = 6.98 | 2.97(d) J = 21.4 | 3.72(s) | — |
| 7 | —$CH_2CH_2OCH_2CH_2$— | — | Et | O | — | — | — | 1.35(t) J = 7.06 | 4.20(q/d) J = 7.08 | 3.01(d) J = 21.4 | 4.30(m) | 3.72(m) |

[a]Multiplicity pattern: s-singlet; d-doublet; t-triplet; m-multiplet; t/d-triplet of doublet; q/d-doublet quartet.

**TABLE III** $^{13}C$ and $^{31}P$ NMR Data of Bisphosphonates





| No. | $R_1$ | $R_2$ | $R_3$ | X | $C_a$ | $C_b$ | $C_c$ | $C_d$ | Ce | $C_f$ | Cg | $C_h$ | NMR-$^{31}$P $\delta$(ppm) P=O |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | $^{13}$C NMR $\delta$(ppm) J(Hz) | | | | | | |
| 1 | $-CH_2CH_2-$ | H | Et | N | — | — | 16.4(d) J = 6.1 | 62.8(d) J = 6.1 | 35.6(d) J = 128.9 | 165.3(d) J = 6.1 | 38.7 | — | 24.3 |
| 2 | $-CH_2CH_2CH_2-$ | H | Et | N | — | — | 16.5(d) J = 6.3 | 63.0(d) J = 7.1 | 35.5(d) J = 127.5 | 164.6(d) J = 5.4 | 39.5 | 27.8 | 25.1 |
| 3 | $-CH_2CH_2CH_2CH_2-$ | H | Et | N | — | — | 16.34(d) J = 6.07 | 62.7(d) J = 6.1 | 35.2(d) J = 128.9 | 164.3(d) J = 4.6 | 39.1 | 25.7 | 24.2 |
| 4 | $-CH_2CH_2-$ | $-CH_2-$ | Et | N | — | — | 16.0(d) J = 6.0 | 62.4(d) J = 6.0 | 33.0(d) J = 130.8 | 163.0(d) J = 6.1 | $C_\alpha$ = 41.5(d) J = 16.7 / C$\beta$ = 46.3(d) J = 18.2 | — | 21.1 |
| 5 | $-CH_2CH_2-$ | H | Bu | N | 13.4 | 18.5 | 32.2(d) J = 6.0 | 66.3(d) J = 6.3 | 35.2(d) J = 129.3 | 165.1(d) J = 4.6 | 38.5 | — | 24.1 |
| 6 | $-CH_2CH_2-$ | — | Et | O | — | — | 16.2(d) J = 6.1 | 62.7(d) J = 6.2 | 34.1(d) J = 133.6 | 165.7(d) J = 6.10 | 63.7 | — | 20.3 |
| 7 | $-CH_2CH_2OCH_2CH_2-$ | — | Et | O | — | — | 16.2(d) J = 6.1 | 62.7(d) J = 6.1 | 34.1 J = 133.4 | 165.6(d) J = 6.10 | 68.7 | 64.4 | 20.3 |

[a]Multiplicity pattern: d-doublet.

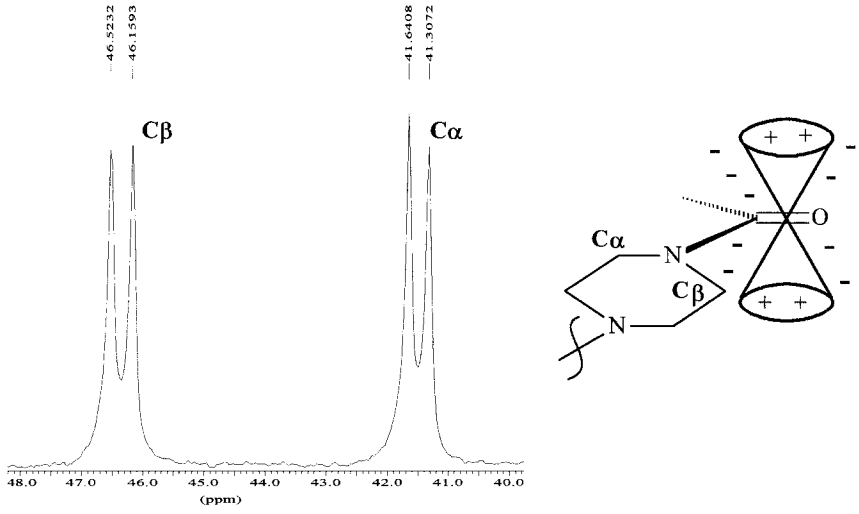



**FIGURE 2** Anisotropic effect in compound **4**.



phosphorus spectra show a quintuple triplet, which is due to the coupling of P with the methylene next to it ($H_2C$—P=O) and also with the methylenes of the alkoxide portion (PO—$CH_2CH_n$, n = 2, 3).

The mass spectra of the bisphosphonates did not show the molecular ion, which may be due to the high energy of the electron beam. However, the fragmentation pattern is in accordance with the structures.

## EXPERIMENTAL

All solvents used for reactions and in the purification procedures were previously distilled or purified according to usual methods described in the literature.[33] Melting points were determined with a Buchi 510 and are uncorrected.

**FIGURE 3** Tridimensional structures of compound **4**.

Infrared spectra were run on a Perkin-Elmer 1600 FT apparatus, using NaCl cells for liquid samples and KBr pellets for solid samples. Gas chromatography was carried out with a Finnigan model 9001 and a Varian 3000.

Mass spectra were run on a HP-5890—70 eV, $^{1}H$ (200 MHz) and $^{13}C$ NMR (50.3 MHz) spectra were obtained with a Bruker AC-200 and $^{31}P$ NMR (121 MHz) spectra were obtained with a Varian VXR 300. TMS was used as internal standard for the $^{1}H$ and $^{13}C$ spectra and 85% phosphoric acid for the $^{31}P$ spectra.

Molecular modelling of compound **4** was carried out using a Pentium 200 MHz computer with 32 MB of RAM. The PM3 Hamiltonian from the MOPAC package was employed and the calculations were done considering the final value of the energy when the gradient reached a value lower than 0.1 kcal (rad or A)$^{-1}$.



## Synthesis of N,N′-bis(diethyl phosphonoacetyl)diamines

*General Procedure.* The corresponding N,N′-bis(chloroacetyl)diamine and triethyl phosphite in excess were mixed in a 50 mL round flask fitted with a reflux condenser and the mixture was refluxed at 150°C for 5 h. At the end of this period, a white solid precipitated, which was collected and dried under vacuum for 4 h.

### *Synthesis of N,N′-bis(diethyl phosphonoacetyl)ethylenediamine (1)*

N,N′-bis(chloroacetyl)ethylenediamine (**11**) 0.5 g ($2.39 \times 10^{-3}$ mol) was mixed with 1.6 mL (1.6 g, $9.34 \times 10^{-3}$ mol) of triethyl phosphite. The reaction yielded 0.6 g (60%) of (**1**). White solid, m.p. 105–107°C. IR see Table I. $^{1}H$ NMR ($CDCl_3$) see Table II. $^{13}C$ NMR ($CDCl_3$) see Table III. $^{31}P$ NMR-($H_3PO_4$) decoupled see Table III, coupled $J_{P-CH_2} = 21.08$ Hz, $J_{P-OCH_2} = 6.90$ Hz.

### *Synthesis of N,N′-bis(diethyl phosphonoacetyl)propylenediamine (2)*

N,N′-bis(chloroacetyl)propylenediamine (**12**) 0.5 g ($2.33 \times 10^{-3}$ mol) and 1.2 mL (1.2 g, $7.0 \times 10^{-3}$ mol) of triethyl phosphite afforded a viscous brown oil, which was dissolved in dichloromethane and treated with active charcoal. The filtrate was dried with magnesium sulfate and the solvent was evaporated under vacuum, affording 0.8 g of product (80%) yellow oil. IR see Table I. $^{1}H$ NMR ($CDCl_3$) see Table II. $^{13}C$ NMR ($CDCl_3$) see Table III. $^{31}P$ NMR ($H_3PO_4$) decoupled see Table III, coupled $J_{P-CH_2} = 21.72$ Hz, $J_{P-OCH_2} = 7.96$ Hz.

### *Synthesis of N,N′-bis(diethyl phosphonoacetyl)butylenediamine (3)*

N,N′-bis(chloroacetyl)butylenediamine (**13**) 0.9 g ($3.85 \times 10^{-3}$ mol) and 3.0 mL (2.9 g, $1.75 \times 10^{-3}$) of triethyl phosphite afforded 1.6 g (94%) of product. White solid, m.p. 80–82°C. IR see Table I. $^{1}$H NMR (DMSO) see Table II. $^{13}$C NMR ($CDCl_3$) see Table III. $^{31}$P NMR ($H_3PO_4$) decoupled see Table III, coupled $J_{P-CH_2} = 21.18$ Hz, $J_{P-OCH_2} = 7.98$ Hz.

### *Synthesis of N,N′-bis(diethyl phosphonoacetyl) piperazine (4)*

N,N′-bis(chloroacetyl)piperazine (**14**) 0.5 g ($2.26 \times 10^{-3}$ mol) and 1.5 mL (1.5 g, $8.73 \times 10^{-3}$ mol) of triethyl phosphite reacted for 5 h at 100°C, affording 0.95 g (95%) of product. White solid, m.p. 49–51°C. IR see Table I $^{1}$H NMR ($CDCl_3$) see Table II. $^{13}$C NMR ($CDCl_3$) see Table III. $^{31}$P NMR ($H_3PO_4$) decoupled see Table III, coupled $J_{P-CH_2} = 22.05$ Hz, $J_{P-OCH_2} = 7.25$ Hz.



## Synthesis of Dibutyl Phosphite[34]

In a two neck 125 mL round flask, equipped with an addition funnel and a reflux condenser fitted with a device which prevents contact with humidity, were added 100 mL (81 g, 1.09 mol) of butyl alcohol. Freshly distilled phosphorus trichloride (32 mL, $3.64 \times 10^{-3}$ mol) was added dropwise with stirring at 0°C. After all the phosphorus trichloride had been added, the mixture was heated at 50°C for approximately 1 h. Distillation under reduced pressure (3 mm Hg) afforded 37.0 mL (52%) of product.

## Synthesis of N,N′-bis(dibutyl phosphonoacetyl)ethylenediamine (5)

In a three neck 125 mL round flask equipped with a reflux condenser and a septum, were added 30.0 mL of dry toluene, 0.4 g ($1.87 \times 10^{-3}$ mol) of metallic sodium and 3.7 mL (3.6 g, $1.87 \times 10^{-3}$ mol) of dibutyl phosphite. The mixture was stirred and kept at room temperature until all the metal had reacted, which took around 3 h.

N,N′-bis(chloroacetyl)ethylenediamine (2.0 g, $9.39 \times 10^{-3}$ mol) was rapidly added followed by reflux at 110°C for 4 h. The reaction mixture was filtered and the filtrate was evaporated under reduced pressure at 120°C for 4 h affording 1.2 g of a yellowish solid, which was washed with ethyl ether to give (**5**) with a 25% yield. White solid, m.p. 63–65°C. IR see Table I $^{1}$H NMR ($CDCl_3$) see Table II. $^{13}$C NMR ($CDCl_3$) see

Table III. $^{31}P$ NMR ($H_3PO_4$) decoupled see Table III, coupled $J_{P-CH_2} = 21.17$ Hz, $J_{P-OCH_2} = 7.22$ Hz.

## Synthesis of Triethyl Phosphonoacetate

To 4.0 mL (5.0 g, $3.61 \times 10^{-2}$ mol) of ethyl $\alpha$-bromoacetate, in a 50 mL round flask equipped with a reflux condenser, were added 7.4 mL (7.2 g, $4.32 \times 10^{-2}$ mol) of triethyl phosphite. This mixture was stirred at 100°C for 6 h. The reaction mixture was then submitted to reduced pressure at 80°C for 5 h. This treatment afforded 7.0 g (87%) of product, which did not need any further purification. Colorless liquid. IR see Table I $^1H$ NMR ($CDCl_3$) see Table II. $^{13}C$ NMR ($CDCl_3$) see Table III.

## Synthesis of Ethyleneglycol-bis(diethyl phosphonoacetyl) (6)



To 1.0 mL (1.1 g, $4.78 \times 10^{-3}$ mol) of triethyl phosphonoacetate in a 50 mL round flask, connected to a vacuum line, were added 0.1 mL (0.2 g, $2.39 \times 10^{-3}$ mol) of ethylene glycol. The reaction mixture was stirred at 160°C for 7 h under vacuum. This reaction afforded 0.8 g (80%) of (**6**). Colorless oil. IR see Table I $^1H$ NMR ($CDCl_3$) see Table II. $^{13}C$ NMR ($CDCl_3$) see Table III. $^{31}P$ NMR ($H_3PO_4$) decoupled see Table III coupled $J_{P-CH_2} = 21.46$ Hz, $J_{P-OCH_2} = 7.98$ Hz.

## Synthesis of Diethyleneglycol-bis(diethyl phosphonoacetyl) (7)

To 0.9 mL (1.0 g, $4.29 \times 10^{-3}$ mol) of triethyl phosphonoacetate in a 50 mL round flask, connected to a vacuum line, were added 0.2 mL (0.2 g, $2.15 \times 10^{-3}$ mol) of diethyleneglycol. This mixture was heated at 160°C for 7 h, with stirring under vacuum. In this way, 0.8 g (80%) of (**7**) were obtained. Yellowish oil. IR see Table I. $^1H$ NMR ($CDCl_3$) see Table II. $^{13}C$ NMR ($CDCl_3$) see Table III. $^{31}P$ NMR ($H_3PO_4$) decoupled see Table III, coupled $J_{P-CH_2} = 21.71$ Hz, $J_{P-OCH_2} = 8.58$ Hz.

## CONCLUSION

The methodology employing Michaelis-Arbuzov or Michaelis-Becker reactions for the synthesis of bisphosphonates is extremely satisfactory since these compounds are obtained in good yield and in a simple way.

## ACKNOWLEDGMENTS

We thank the Brazilian agencies CAPES and $CNP_q$ for financial support and Prof. Whei Oh Lin for some of the chemicals employed in this work.

## REFERENCES

[1] A. E. Arbuzov, *Phys. Chem. Soc.*, **38,** 687 (1906).
[2] A. E. Michaelis and R. Kaehne, *Ber. Stsch. Chem. Ges.*, **31,** 1048 (1898).
[3] R. G. Harvey and E. R. Desombre, *Topics in Phosphorus Chemistry* (Interscience, 1964), vol. 1, p. 57.
[4] J. I. G. Cadogan, *Organophosphorus Reagents in Organic Synthesis* (Academic Press, London, 1979), 1st ed, pp. 4–6.
[5] A. H. Ford-Moore and B. J. Perry, *Org. Syn. Coll.*, **4,** 955 (1963).
[6] V. Mark, *Mech. Mol. Migr.*, **2,** 319 (1969).
[7] W. Perkow, K. Ullerich, and F. Meyer, *Naturwiss.*, **39** (15), 353 (1952).
[8] B. J. Walker, *Organophosphorus Chemistry*, Specialist Periodical Reports (The Chemical Society, London), vol. 1–10, ch. 5.
[9] G. W. Kenner, *Proc. Chem. Soc.*, 136 (1957).
[10] G. Sturtz, *Bull. Soc. Chim. France*, **9,** 2333–2340 (1964).
[11] T. H. Sidall, *J. Inorg. Nucl. Chem.*, **25,** 883–892 (1963).
[12] H. Fleisch, *Osteoporosis International*, Suppl. **3**(3), S3–S5 (1993).
[13] R. G. G. Russell and M. J. Rogers, *British Journal of Rheumatology*, Suppl. **1**(36), 10–14 (1997).
[14] M. Mathew, B. O. Fowler, G. Golomb, I. S. Alferiev, and N. Eidelman, *Inorg. Chem.*, **37,** 6485–6494 (1998).
[15] J. P. Räsänen, E. Pohjala, H. Nikander, and T. A. Pakkanen, *J. Phys. Chem.* A, **101,** 5196–5204 (1997).
[16] J. Ochocki, A. Erxleben, and B. Lippert, *J. Heterocycl. Chem.*, **34,** 1179–1184 (1997).
[17] S. Kannan, V. Venugopal, *Polyhedron*, **14** (17–18), 2349–2354 (1995).
[18] M. P. Belciug, A. M. Modro, T. A. Modro, and P. L. Wessels, *J. Phys. Org. Chem.*, **8,** 605–609 (1995).
[19] I. L. Gall, P. Laurent, E. Soulier, J. Y. Salaün, and Abbayes., *J. Organomet. Chem.*, **567,** 13–20 (1998).
[20] J. B. N. DaCosta, Master in Science Thesis, Instituto Militar de Engenharia (1987).
[21] W. O. Lin, M. C. Souza, and J. B. N. DaCosta, Química Nova, **18,** 431–434 (1995).
[22] G. Sturtz, Mémoires Présentés a la Société Chimique (Paris, 1964), 5th ed., **384,** 2333–2340.
[23] G. H. Posner and M. Oda, *Tetrahedron Lett.*, **22,** 5003–5006 (1981).
[24] S. S. Rana, J. J. Barlow, and K. L. Matta, *Tetrahedron Lett.*, **22,** 5007–5010 (1981).
[25] L. J. Bellamy, *The Infrared Spectra of Complex Molecules* (Wiley, New York, 1958), 2nd ed.
[26] K. Nakanishi, *Infrared Absorption Spectroscopy* (Holden-Day, San Francisco, 1969), pp. 231.
[27] C. D. Cross, *Introduction to Practical Infrared Spectroscopy* (Butterworth, London, 1964), 2nd ed.
[28] H. David, G. Martin, G. Mavel, and G. Sturtz, *Mémoires Présentés A La Société Chimique* (Sorbonne, Paris, 1962), **272**.

[29] L. C. Thomas, *The Identification of Functional Groups in Organophosphorus Compounds* (Academic Press, London, 1974), 1st ed.
[30] B. M. Rapko, E. N. Duesler, D. Frutos, and R. T. Paine, *Polyhedron,* **14** (17–18), 2361–2369 (1995).
[31] H. O. Kalinowski, S. Berger, and S. Braun, *Carbon-13 NMR Spectroscopy* (Wiley, New York, 1988), 1st ed., p. 234.
[32] D. H. Williams and I. Fleming, *Spectroscopic Methods in Organic Chemistry* (McGraw-Hill Book, London, 1995), 5th ed.
[33] D. D. Perrin, W. L. F. Armarego, and D. R. Perrin, *Purification of Laboratory Chemicals* (Pergamon Press, 1966).
[34] H. Mc Combie, B. C. Saunders, and G. J. Stacey, *J. Am. Chem. Soc.*, **93,** 380–382 (1945).