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# Preparation, Crystal and Molecular Structure, and Evaluation of Plant Growth Regulating Activity of Guanidinoalkanephosphinates and Phosphonates

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## ABSTRACT

*A series of previously unknown α-guanidinoalkanephosphonous, α- and β-guanidinoalkanephosphonic acids has been prepared in order to study their structures and biological activity. Aminoalkanephosphonous and phosphonic acids have been converted into their guanidino derivatives by means of S-methylisothiourea hydroiodide or cyanamide amidination. The crystal and molecular structures of three guanidino acids have been determined by single-crystal X-ray diffraction. The plant growth regulating activity of all synthesized guanidinoalkanephosphinates and phosphonates has been evaluated on Lepidium sativum.* © *1995 John Wiley & Sons, Inc.*

## *INTRODUCTION*

Aminoalkanephosphonates, commonly defined as phosphorus analogues of amino acids, may act as their antimetabolites and thus influence various biological processes. This results in activity of these compounds ranging from antibacterials to pesticides. Such a wide biological activity stimulates interest in this class of compounds and their derivatives. Guanidinoalkanephosphonates, containing the modified amino group, can be considered as such compounds. The literature data on their synthesis and properties are, however, scarce. The very first report concerns the phosphorus analogues of creatine prepared and tested as substrates for creatine kinase by Rowley et al. [1]. In the seventies, guanidinoalkanephosphonic acids attracted some interest as potential neuroactive compounds [2–4]. Recently, a range of α- and ω-aminoalkanephosphonic acids and their guanidino derivatives has been prepared by Cameron et al. and shown to exert interesting fungicidal activity [5–8].

Continuing our efforts to synthesize and study the properties of this class of compounds [9–12], we report here the preparation of a series of new α-guanidinoalkanephosphonous acids and determination of their crystal and molecular structure.

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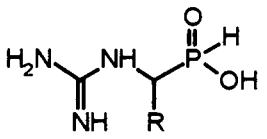
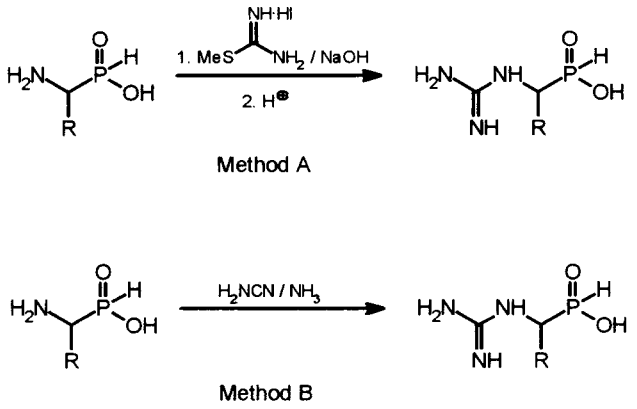
**TABLE 1** Physical Properties and Analytical and Spectroscopic Data of α-Guanidinoalkanephosphonous Acids



| R | Formula | Yield (%) (Method) | Mp (°C) | Found (Calcd.), (%) N | Found (Calcd.), (%) P | $^1$H NMR, δ | IR, cm$^{-1}$ |
|---|---|---|---|---|---|---|---|
| $CH_3$ | $C_3H_{10}N_3O_2P$ | 56 (A) | 256–257 | 27.71 (27.81) | 21.24 (20.50) | 1.08 (dd, 3H, $CH_3$, $J$ = 7 Hz, 18 Hz)<br>3.42–3.90 (m, 1H, CH)<br>5.87–6.33 (m, 4H, NH)<br>6.74 (d, 1H, PH, $J$ = 571 Hz) | 3500–2700, 2300, 1700–1600, 1165, 1130, 1055, 1030, 950 |
| $C_2H_5$ | $C_4H_{12}N_3O_2P$ | 20 (B) | 267–269 | 25.14 (25.45) | 19.02 (18.76) | 1.03 (t, 3H, $CH_3$, $J$ = 7 Hz)<br>1.24–1.52 (m, 2H, $CH_2$)<br>3.33–3.82 (m, 1H, CH)<br>5.83–6.26 (m, 4H, NH)<br>6.52 (d, 1H, PH, $J$ = 567 Hz) | 3600–2700, 2300, 1720–1600, 1170, 1075, 1050 |
| $n$-$C_3H_7$ | $C_5H_{14}N_3O_2P$ | 18 (A) | 249–251 | 22.98 (23.45) | 17.61 (17.29) | 1.10 (t, 3H, $CH_3$, $J$ = 7 Hz)<br>1.29–1.68 (m, 4H, $2CH_2$)<br>3.94–4.35 (m, 1H, CH)<br>6.12–6.52 (m, 4H, NH)<br>7.29 (d, 1H, PH, $J$ = 568 Hz) | 3600–2600, 2300, 1700–1600, 1180, 1050 |
| $n$-$C_4H_9$ | $C_6H_{16}N_3O_2P$ | 28 (A) | 247–248 | 21.62 (21.75) | 16.18 (16.03) | 0.98 (t, 3H, $CH_3$, $J$ = 7 Hz)<br>1.18–1.62 (m, 6H, $3CH_2$)<br>3.80–4.23 (m, 1H, CH)<br>5.95–6.37 (m, 4H, NH)<br>6.66 (d, 1H, PH, $J$ = 567 Hz) | 3600–2500, 2300, 1700–1580, 1185, 1070 |
| $n$-$C_5H_{11}$ | $C_7H_{18}N_3O_2P$ | 31 (A) | 266–268 | 20.31 (20.28) | 15.05 (14.95) | 0.93 (t, 3H, $CH_3$, $J$ = 7 Hz)<br>1.16–1.67 (m, 8H, $4CH_2$)<br>3.72–4.15 (m, 1H, CH)<br>6.04–6.50 (m, 4H, NH)<br>7.02 (d, 1H, PH, $J$ = 567 Hz) | 3600–2600, 2290 1700–1580, 1180, 1070 |
| Ph | $C_8H_{12}N_3O_2P$ $H_2O$ | 15 (A) 37 (B) | 274–276 | 18.32 (18.18) | 13.77 (13.38) | 5.02 (dd, 1H, CH, $J$ = 8 Hz, 17 Hz)<br>6.02–6.38 (m, 4H, NH)<br>7.43 (s, 5H, PhH)<br>7.18 (d, 1H, PH, $J$ = 598 Hz) | 3500–2700, 2290, 1680–1550, 1540, 1440, 1400, 1330, 1180, 1040, 960 |




**SCHEME 1**

In order to evaluate plant growth regulating properties, we also synthesized the previously unknown phosphonic acid analogues of guanidinoaspartic and glutamic acids.

## *RESULTS AND DISCUSSION*

### *Synthesis*

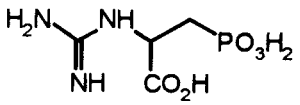
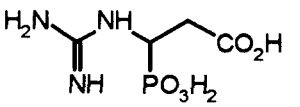
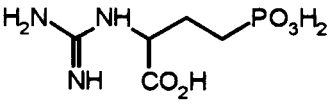
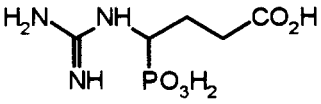
The starting aminoalkanephosphonous and phosphonic acids were prepared according to the known procedures described in the literature (see the Experimental section). Their guanidino derivatives were synthesized by means of *S*-methylisothiourea hydroiodide or cyanamide amidination of the amino group [1] (Scheme 1).

Spectroscopic and physical data of all new compounds are given in Tables 1 and 2.

Structures of three guanidino acids were determined by X-ray crystallography, namely, guanidinophenylmethanephosphonous, α-guanidinoethanephosphonous, and α-guanidinoethanephosphonic acids.* The crystals of guanidinophenylmethanephosphonous acid hydrate are triclinic,

*Full crystallographic data were deposited at the Cambridge Crystallographic Data Centre, Cambridge, United Kingdom.

**TABLE 2** Physical Properties and Analytical and Spectroscopic Data of Phosphonic Analogues of Guanidinoaspartic and -glutamic Acids

| Guanidino Acid | Formula | Yield (%) (Method) | Mp (°C) (Dec.) | Found (Calcd.), (%) N | Found (Calcd.), (%) P | $^1H$ NMR, δ | IR, $cm^{-1}$ |
|---|---|---|---|---|---|---|---|
|  | $C_4H_{10}N_3O_5P$ | 60 (A) | 310–311 | 20.15 (19.90) | 14.78 (14.67) | 2.27–2.72 (m, 2H, $CH_2$) 4.39–4.83 (m, 1H, CH) 6.11–7.60 (m, 4H, NH) | 3400–2400, 1740, 1720–1600, 1210, 1110, 1090, 1030, 920 |
|  | $C_4H_{10}N_3O_5P$ | 54 (A) | 307–308 | 19.76 (19.90) | 15.02 (14.67) | 2.78–3.15 (m, 2H, $CH_2$) 3.92–4.23 (m, 1H, CH) 6.76–7.04 (m, 4H, NH) | 3500–2500, 1720, 1700–1600, 1280, 1240, 1150, 1070, 920 |
|  | $C_5H_{12}N_3O_5P$ | 60 (A) | 257–259 | 18.21 (18.66) | 14.17 (13.76) | 1.73–2.50 (m, 4H, $2CH_2$) 4.00–4.42 (m, 1H, CH) 7.06–7.38 (m, 4H, NH) | 3500–2500, 1730, 1700–1500, 1230, 1180, 1100, 1040, 920 |
|  | $C_5H_{12}N_3O_5P$ | 41 (A) | 265–267 | 18.66 (18.66) | 13.79 (13.76) | 2.08–2.82 (m, 4H, $2CH_2$) 4.15–4.63 (m, 1H, CH) 7.18–7.57 (m, 4H, NH) | 3500–2500, 1720, 1700–1520, 1260, 1170, 1100, 1070, 920 |

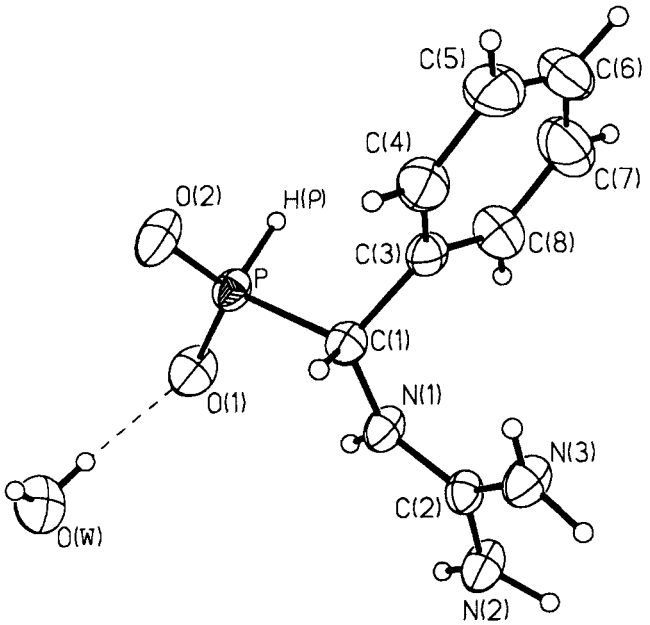



**FIGURE 1** Perspective view of guanidinophenylmethanephosphonous acid hydrate

of the space group $P1$, $a$ = 6.666(1) Å, $b$ = 8.219(2) Å, $c$ = 11.019(2) Å, $\alpha$ = 89.40(3)°, $\beta$ = 76.86(3)°, $\gamma$ = 70.57(3)°, and $Z$ = 2. The crystals of α-guanidinoethanephosphonous acid are orthorhombic, of

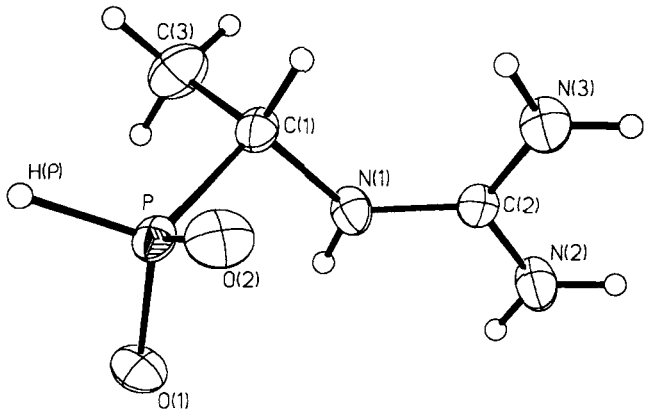



**FIGURE 2** Perspective view of α-guanidinoethanephosphonous acid

the space group $Pca2_1$, $a$ = 21.401(4) Å, $b$ = 9.216(2) Å, $c$ = 7.321(1) Å, and $Z$ = 8. The crystals of α-guanidinoethanephosphonic acid are monoclinic, of the space group $P2_1/c$, $a$ = 6.917(1) Å, $b$ = 16.291(3) Å, $c$ = 6.643(1) Å, $\beta$ = 114.80(3)°, and $Z$ = 4. The structures, solved by the direct method, have been refined to a final $R$ = 0.033, $R$ = 0.065, and $R$ = 0.026, respectively. There are two crystallographically independent molecules (A and B) of α-guanidinoethanephosphonous acid in the asymmetric unit. This effect was not observed for the phosphonic acid analogue.

**TABLE 3** Guanidino Acids—Crystallographic Data and Details of Refinements

| | *Guanidinophenylmethanephosphonous Acid Hydrate* | *α-Guanidinoethanephosphonous Acid* | *α-Guanidinoethanephosphonic Acid* |
|---|---|---|---|
| Chemical formula | $C_8H_{14}N_3O_3P$ | $C_3H_{10}N_3O_2P$ | $C_3H_{10}N_3O_3P$ |
| Molecular weight | 231.19 | 151.11 | 167.11 |
| Cell constants | | | |
| *a* (Å) | 6.666 (1) | 21.401 (4) | 6.917 (1) |
| *b* (Å) | 8.219 (2) | 9.216 (2) | 16.291 (3) |
| *c* (Å) | 11.019 (2) | 7.321 (1) | 6.643 (1) |
| $\alpha$ (°) | 89.40 (3) | — | — |
| $\beta$ (°) | 76.86 (3) | — | 114.80 (3) |
| $\gamma$ (°) | 70.57 (3) | — | — |
| *V* (Å$^3$) | 553.0 (2) | 1443.9 (5) | 679.5 (4) |
| Space group | $P_1$ | $Pca2_1$ | $P2_1/c$ |
| *Z* | 2 | 8 | 4 |
| *F* (000) | 244 | 640 | 352 |
| *T* (K) | 293 | 293 | 293 |
| $D_m$ (mg/m$^3$) ($C_6H_6/CHCl_3$) | 1.39 | 1.39 | — |
| $D_o$ (mg/m$^3$) | 1.388(1) | 1.390(1) | 1.633(1) |
| Radiation | Mo $K_\alpha$ ($\lambda$ = 0.71069 Å) | Mo $K_\alpha$ | Mo $K_\alpha$ |
| $\mu$ (cm$^{-1}$) | 2.41 | 3.18 | 3.57 |
| Reflection determining the lattice | 25 | 25 | 25 |
| $\theta$ range (°) | $20 < \theta < 26$ | $18 < \theta < 23$ | $20 < \theta < 83$ |
| $\theta$ maximum (°) | 54 | 55 | 55 |
| Number of standard reflections | 3 (100) | 3 (100) | 3 (100) |
| Variation in standard reflections (%) | 3 | 4 | 3 |
| Number of reflexions | | | |
| Collected | 2456 | 1675 | 1570 |
| Observed ($I > 2\sigma(I)$) | 2083 | 1217 | 1335 |
| Number of variables | 192 | 163 | 131 |
| *R* | 0.033 | 0.065 | 0.026 |
| *Rw* | 0.089 | 0.184 | 0.074 |
| *S* | 1.073 | 1.071 | 1.090 |
| $\Delta/\sigma$ (for non-H atoms) | 0.01 | 0.02 | 0.01 |
| $\Delta/\sigma$ (for H atoms) | 0.04 | — | 0.04 |
| $\Delta\rho$ ($e$/Å$^3$) | −0.28; 0.19 | −0.34; 0.37 | −0.22; 0.41 |

**TABLE 4** Guanidinophenylmethanephosphonous Acid Hydrate—Selected Bond Lengths (Å) with Estimated Standard Deviations in Parentheses

| | | | |
|---|---|---|---|
| P–O(1) | 1.492(1) | P–H(P) | 1.32(2) |
| P–O(2) | 1.487(1) | N(1)–H(N1) | 0.82(2) |
| P–C(1) | 1.852(2) | N(2)–H(1N2) | 0.93(3) |
| N(1)–C(1) | 1.458(2) | N(2)–H(2N2) | 0.98(2) |
| N(1)–C(2) | 1.336(2) | N(3)–H(1N3) | 0.93(2) |
| N(2)–C(2) | 1.332(2) | N(3)–H(2N3) | 0.90(2) |
| N(3)–C(2) | 1.316(2) | | |

The details of the crystal data collection and the refinements are given in Table 3. The solution methods are also described in the Experimental section. Perspective views of all the solved structures of the guanidino acids are shown in Figures 1–3. Selected geometric parameters, bond lengths and angles, are given in Tables 4–7.

The molecules of the guanidino acids exist as zwitterions with the guanidino group protonated and the phosphonous or phosphonic group containing a four-coordinate, negatively charged phosphorus atom. The nitrogen atoms of the flat guanidino groups are in resonance with each other as indicated by the C(2)–N bond lengths. Similar resonance is observed for the O(1) and O(2) atoms of the phosphonous or phosphonic group. The H(P) atoms of phosphonous acids are bound directly to the phosphorus atoms.

The conformations of the title compounds are determined by the torsion angles as given in Tables 8 and 9. The phosphonate group in all solved structures of α-guanidinoethanephosphonates has different orientations, regarding the N(1) and C(3) atoms. The presence of two symmetry independent molecules A and B of α-guanidinoethanephosphonous acid with different orientations of the phosphonous group may suggest a relatively low barrier of the rotation around the P–C(1) bond in the studied compound.

The crystal structures are stabilized by the intermolecular hydrogen bonds involving the guani-

**TABLE 5** α-Guanidinoethanephosphonous and -phosphonic acid—Selected Bond Lengths (Å) with Estimated Standard Deviations in Parentheses

| *α-Guanidinoethanephosphonous Acid* | | | *α-Guanidinoethanephosphonic Acid* | | | |
|---|---|---|---|---|---|---|
| | *Molecule A* | *Molecule B* | | | | |
| P–O(1) | 1.479(7) | 1.485(7) | P–O(1) | 1.486(1) | O(3)–H(O3) | 0.80(2) |
| P–O(2) | 1.502(7) | 1.489(8) | P–O(2) | 1.508(1) | N(1)–H(N1) | 0.82(2) |
| P–C(1) | 1.852(12) | 1.822(10) | P–O(3) | 1.585(1) | N(2)–H(1N2) | 0.81(2) |
| N(1)–C(1) | 1.439(10) | 1.467(13) | P–C(1) | 1.826(2) | N(2)–H(2N2) | 0.90(2) |
| N(1)–C(2) | 1.347(11) | 1.308(14) | N(1)–C(1) | 1.456(2) | N(3)–H(1N3) | 0.89(2) |
| N(2)–C(2) | 1.311(11) | 1.346(12) | N(1)–C(2) | 1.323(2) | N(3)–H(2N3) | 0.85(2) |
| N(3)–C(2) | 1.297(11) | 1.305(12) | N(2)–C(2) | 1.323(2) | | |
| P–H(P) | 1.35(2) | 1.34(3) | N(3)–C(2) | 1.333(2) | | |

A, B = two symmetry independent molecules of α-guanidinoethanephosphonous acid.

dino groups and the oxygen atoms of the phosphonate groups, and also the water molecule in the case of guanidinophenylmethanephosphonous acid. Interatomic distances and bond angles of the hydrogen bonds are given in Table 10.

### *Plant Growth Regulating Activity of Guanidinoalkanephosphinates and Phosphonates*

Structures, yields, and melting points of all the guanidino acids screened for their potential plant growth regulating activity are given in Table 11.

Influence of the guanidino acids on the growth characteristics of *Lepidium sativum* was studied. Data shown in Table 12 are limited only to those compounds that exhibited herbicidal or stimulatory action. Compounds not included in the table were completely inactive toward *L. sativum*.

Most of the studied compounds show weak or moderate herbicidal activity, with complexes

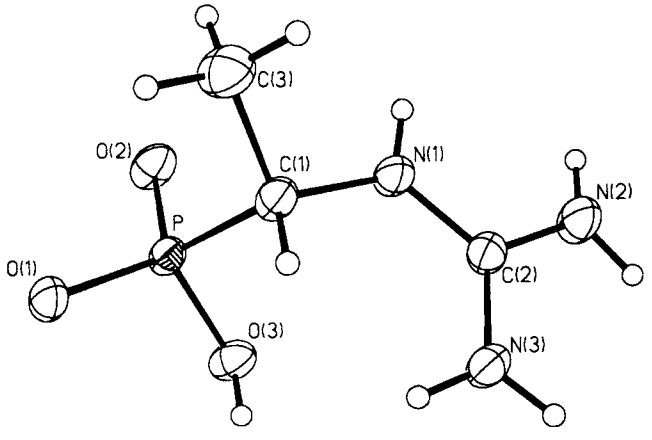



**FIGURE 3** Perspective view of α-guanidinoethanephosphonic acid

**TABLE 6** Guanidinophenylmethanephosphonous Acid Hydrate—Selected Bond Angles (°) with Estimated Standard Deviations in Parentheses

| | | | |
|---|---|---|---|
| O(1)–P–O(2) | 119.2(1) | C(1)–N(1)–H(N1) | 118(1) |
| O(1)–P–C(1) | 108.1(1) | C(2)–N(1)–H(N1) | 117(1) |
| O(2)–P–C(1) | 108.2(1) | C(2)–N(2)–H(1N2) | 120(1) |
| P–C(1)–N(1) | 107.8(1) | C(2)–N(2)–H(2N2) | 119(1) |
| N(1)–C(2)–N(2) | 118.5(1) | C(2)–N(3)–H(1N3) | 120(1) |
| N(1)–C(2)–N(3) | 121.3(1) | C(2)–N(3)–H(2N3) | 120(1) |
| N(2)–C(2)–N(3) | 120.2(1) | H(1N2)–N(2)–H(2N2) | 119(2) |
| O(1)–P–H(P) | 110(1) | H(1N3)–N(3)–H(2N3) | 119(2) |
| O(2)–P–H(P) | 109(1) | | |

$Zn(Ia)_2 \cdot H_2O$ and $Ni(Ib)_2$ being the most active. Additional experiments indicated, however, that this effect was due to the toxic effect of metal ions, not to the action of the complexes. Worthy of notice is the significant herbicidal activity of α-guanidino-γ-phosphonobutyric acid (**IVd**)—an analogue of phosphinotricin. Quite surprisingly, the guanidino derivative of phosphinotricin (**IVe**) appeared to be less active. Plant stimulatory action of α-guanidinopropanephosphonous acid (**IIIb**) at lower concentrations is also interesting.

## *EXPERIMENTAL*

### *Measurements*

Melting points were determined with a Boetius apparatus and were not corrected. $^1H$ NMR spectra were recorded on Tesla 60 or 80 MHz spectrometers. Measurements were made in trifluoracetic acid solutions. Chemical shifts are relative to tetramethylsilane used as internal standard. IR spectra were recorded in KBr pellets with a Perkin-Elmer 377 spectrometer. Microanalyses were made by the Central Analytical Laboratory of the Technical University of Wroclaw.

**TABLE 7** α-Guanidinoethanephosphonous and -phosphonic Acid—Selected Bond Angles (°) with Estimated Standard Deviations in Parentheses

| *α-Guanidinoethanephosphonous Acid* | | | *α-Guanidinoethanephosphonic Acid* | | | |
|---|---|---|---|---|---|---|
| | *Molecule A* | *Molecule B* | | | | |
| O(1)–P–O(2) | 117.5(5) | 115.3(5) | O(1)–P–O(2) | 116.4(1) | P–O(3)–H(O3) | 110(2) |
| O(1)–P–C(1) | 109.0(4) | 109.1(4) | O(1)–P–O(3) | 111.0(1) | C(1)–N(1)–H(N1) | 117(1) |
| O(2)–P–C(1) | 108.0(5) | 109.8(4) | O(2)–P–O(3) | 107.8(1) | C(2)–N(1)–H(N1) | 118(1) |
| P–C(1)–N(1) | 107.3(7) | 110.4(6) | O(1)–P–C(1) | 106.7(1) | C(2)–N(2)–H(1N2) | 120(2) |
| N(1)–C(2)–N(2) | 116.1(8) | 113.6(9) | O(2)–P–C(1) | 109.9(1) | C(2)–N(2)–H(2N2) | 118(1) |
| N(1)–C(2)–N(3) | 125.1(8) | 124.8(10) | O(3)–P–C(1) | 104.4(1) | C(2)–N(3)–H(1N3) | 119(1) |
| N(2)–C(2)–N(3) | 118.8(8) | 121.6(10) | P–C(1)–N(1) | 110.4(1) | C(2)–N(3)–H(2N3) | 118(1) |
| O(1)–P–H(P) | 105.2(3) | 115.3(3) | N(1)–C(2)–N(2) | 119.8(1) | H(1N2)–N(2)–H(2N2) | 120(2) |
| O(2)–P–H(P) | 101.0(3) | 98.9(3) | N(1)–C(2)–N(3) | 121.6(1) | H(1N3)–N(3)–H(2N3) | 120(2) |
| | | | N(2)–C(2)–N(3) | 118.6(1) | | |

**TABLE 8** Guanidinophenylmethanephosphonous and α-Aminoethanephosphonic Acid—Selected Torsion Angles (°) with Estimated Standard Deviations in Parentheses

| *Guanidinophenylmethanephosphonous Acid* | | *α-Aminoethanephosphonic Acid* | |
|---|---|---|---|
| H(P)–P–C(1)–N(1) | −91.5(11) | H(O3)–O(3)–P–C(1) | −96.8(6) |
| H(P)–P–C(1)–C(3) | 32.9(10) | O(1)–P–C(1)–N(1) | 171.1(2) |
| O(1)–P–C(1)–N(1) | 23.6(2) | O(1)–P–C(1)–C(3) | −67.1(2) |
| O(1)–P–C(1)–C(3) | 148.0(2) | O(2)–P–C(1)–N(1) | −61.9(3) |
| O(2)–P–C(1)–N(1) | 153.9(2) | O(2)–P–C(1)–C(3) | 59.9(2) |
| O(2)–P–C(1)–C(3) | −81.7(2) | O(3)–P–C(1)–N(1) | 53.4(2) |
| P–C(1)–N(1)–C(2) | −175.4(2) | O(3)–P–C(1)–C(3) | 175.3(2) |
| P–C(1)–C(3)–C(4) | 86.6(2) | P–C(1)–N(1)–C(2) | −96.5(2) |
| P–C(1)–C(3)–C(8) | −88.9(2) | C(1)–N(1)–C(2)–N(2) | −178.7(3) |
| C(1)–N(1)–C(2)–N(2) | 175.4(2) | C(1)–N(1)–C(2)–N(3) | −0.3(3) |
| C(1)–N(1)–C(2)–N(3) | −4.5(3) | | |

**TABLE 9** α-Aminoethanephosphonous Acid—Selected Torsion Angles (°) with Estimated Standard Deviations in Parentheses

| | *α-Aminoethanephosphonous Acid* | |
|---|---|---|
| *Torsion Angle* | *Molecule A* | *Molecule B* |
| O(1)–P–C(1)–N(1) | −38.8(7) | 170.9(8) |
| O(1)–P–C(1)–C(3) | 84.0(8) | −65.8(8) |
| O(2)–P–C(1)–N(1) | 89.8(8) | −61.9(8) |
| O(2)–P–C(1)–C(3) | −147.3(8) | 61.5(8) |
| P–C(1)–N(1)–C(2) | −109.9(10) | −90.5(10) |
| C(1)–N(1)–C(2)–N(2) | 179.4(12) | 169.8(10) |
| C(1)–N(1)–C(2)–N(3) | −1.3(14) | −9.9(12) |

## *Preparation of the Starting Aminoalkanephosphonous and Phosphonic Acids*

α-Aminoalkanephosphonous acids were synthesized by addition of hypophosphorous acid to diphenylmethylimines or by modifications of this method described by Baylis et al. [13]. The overall yields of α-aminoalkanephosphonous acids ($C_3$–$C_6$) were about 40%. The structures of all the compounds were supported by their IR spectra (characteristic signals of the phosphonous group: $\nu_{P-H}$ = 2360 $cm^{-1}$, $\nu_{P=O}$ = 1180 $cm^{-1}$, $\nu_{P-O}$ = 1030–1040 $cm^{-1}$) and $^1H$ NMR spectra ($J_{P-H}$ = 500–501 Hz), as well as by elemental analyses ($N \pm 0.19\%$, $P \pm 0.33\%$). Aminophenylmethanephosphonous acid was obtained by amidoalkylation of hypophosphorous acid with phenylmethylidene-bisacetamide [14]. Phosphonic acid analogues of aspartic and glutamic acids were synthesized according to the known procedures [15–17]. Their structures were additionally supported by comparison of their spectroscopic data with the literature values.

## *Preparation of the Guanidino Acids*

*Method A.* The aminoalkanephosphonous acid (0.01 mol) was dissolved in 5 mL of a 4.0 M aqueous solution of sodium hydroxide (0.02 mol) [or in 10 mL (0.04 mol) in the case of the phosphonic acid

**TABLE 10** Guanidinophenylmethanephosphonous and α-Aminoethanephosphonic Acid—Interatomic Distances (Å) and Angles (°) of Hydrogen Bonds with Estimated Standard Deviations in Parentheses

| *D–H...A* | *D–H* | *H...A* | *D...A* | $\alpha_{DHA}$ |
|---|---|---|---|---|
| | | Guanidinophenylmethanephosphonous Acid | | |
| O(W)–H(1W)···O(2)$^{i}$ | 0.89(3) | 1.84(3) | 2.699(2) | 162(3) |
| O(W)–H(2W)···O(1) | 0.82(3) | 1.89(3) | 2.716(2) | 177(3) |
| N(2)–H(1N2)···O(W)$^{ii}$ | 0.93(3) | 1.95(3) | 2.851(2) | 162(2) |
| N(2)–H(2N2)···O(2)$^{iii}$ | 0.98(2) | 1.87(3) | 2.836(2) | 168(2) |
| N(3)–H(1N3)···O(W)$^{iv}$ | 0.93(2) | 2.03(3) | 2.955(2) | 174(2) |
| N(3)–H(2N3)···O(1)$^{v}$ | 0.90(2) | 2.08(3) | 2.768(2) | 132(2) |
| Symmetry code | (i): | $-x$ | $1 - y$ | $1 - z$ |
| | (ii): | $-x$ | $-y$ | $1 - z$ |
| | (iii): | $1 + x$ | $y - 1$ | $z$ |
| | (iv): | $1 - x$ | $y$ | $1 - z$ |
| | (v): | $1 + x$ | $y$ | $z$ |
| | | α-Aminoethanephosphonic Acid | | |
| O(3)–H(O3)···O(1)$^{i}$ | 0.80(2) | 1.85(2) | 2.634(2) | 168(3) |
| N(1)–H(N1)···O(2)$^{ii}$ | 0.82(2) | 2.01(2) | 2.826(2) | 171(2) |
| N(2)–H(2N2)···O(2)$^{iii}$ | 0.90(2) | 2.00(2) | 2.896(2) | 172(2) |
| N(3)–H(1N3)···O(1)$^{ii}$ | 0.89(2) | 2.08(2) | 2.951(2) | 165(2) |
| N(3)–H(2N3)···O(1)$^{i}$ | 0.85(2) | 2.16(2) | 2.950(2) | 156(2) |
| Symmetry code | (i): | $1 - x$ | $1 - y$ | $z$ |
| | (ii): | $x$ | $1.5 - y$ | $z$ |
| | (iii): | $x - 1$ | $y$ | $z - 1$ |

analogues of aspartic and glutamic acids], and *S*-methylisothiourea hydroiodide 4.4 g (0.02 mol) [18] in water (5 mL) was added dropwise (5 hours) with stirring, the temperature being maintained at 45–55°C. Stirring and heating was continued 8–10 hours, and then the mixture was left for crystallization for several days. The resulting crystals of the sodium salts were dissolved in a small amount of water (~5 mL), and the solutions were then acidified with acetic acid and left for crystallization. The products were filtered off, washed with ethanol, and air-dried. In the cases where sodium salts did not precipitate, the mixtures were acidified with concentrated hydrochloric acid to pH 1. In order to obtain free guanidino acids, the products were precipitated from ethanolic solutions of their hydrochlorides with propylene oxide and then recrystallized from water or a water-acetone mixture.

*Method B.* The aminoalkanephosphonous acid (0.01 mol) and cyanamide 0.5 g (0.012 mol) were dissolved in a minimum quantity of water, and a drop of concentrated ammonia was added to catalyze the reaction. The mixture was left for crystallization for several days. The product was filtered off, washed with ethanol, and air-dried. It was recrystallized from water or a water-acetone mixture. Spectroscopic and physical data of compounds obtained are collected in Tables 1 and 2.

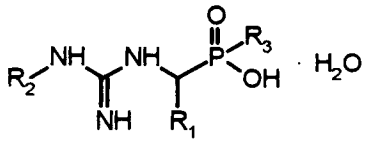
*Structure*

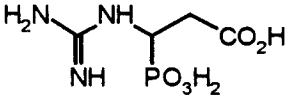
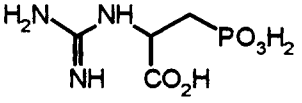
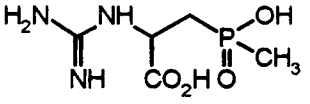
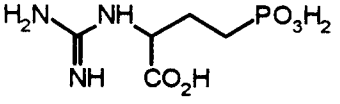
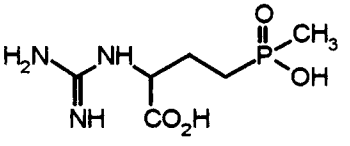
The guanidino acids were recrystallized from water in order to prepare single crystals for the data collection. Colorless, well-defined crystals of guanidinophenylmethanephosphonous and α-guanidinoethanephosphonic acid were obtained. Crystals of α-guanidinoethanephosphonous acid were of poor quality even though various solvents and mixtures were tested.

The densities were measured by flotation in a chloroform/benzene mixture. The space groups and approximate unit-cell dimensions were determined from rotation and the Weissenberg photographs. The diffraction data were determined on a KM4 κ-axis computer-controlled four-circle diffractometer with graphite-monochromated Mo $K_\alpha$ radiation [19]. The diffracted intensities were corrected for Lorentz and polarization effects, but not for absorption or extinction.

The structures were solved by the direct method with the SHELXS-86 program [20] and refined by the full-matrix least-squares method, using the SHELXL structure determination system [21]. All nonhydrogen atoms were refined with anisotropic thermal parameters. A difference Fourier map clearly afforded the positions of the hydrogen atoms, and their positional parameters were incorporated into a subsequent refinement cycle. The positions of the hydrogen atoms of α-guanidino-

**TABLE 11** Guanidino Acids Tested for Plant Growth Regulating Activity



| Compound | $R_1$ | $R_2$ | $R_3$ | n | Yield (%) | Mp (°C) | Ref. |
|---|---|---|---|---|---|---|---|
| **Ia** | H | H | OH | 1.5 | 75 | 321–322 | 9 |
| **Ib** | $CH_3$ | H | OH | — | 42 | 286–287 | 9 |
| **Ic** | *n*-$C_3H_7$ | H | OH | — | 22 | 295–296 | 9 |
| **Id** | *i*-$C_3H_7$ | H | OH | — | 25 | 302–303 | 9 |
| **Ie** | *i*-$C_4H_9$ | H | OH | — | 28 | 310–311 | — |
| **If** | $C_6H_5$ | H | OH | 1 | 24 | 296–299 | 9 |
| **Ig** | *p*-$CH_3OC_6H_4$ | H | OH | — | 19 | 311–312 | — |
| **Ih** | *m*-$O_2NC_6H_4$ | $NH_2$ | OH | — | — | 274–276 | — |
| **Ii** | *m*-$O_2NC_6H_4$ | *n*-$C_3H_7$ | OH | — | 74 | 279–281 | 10 |
| **Ij** | *m*-$O_2NC_6H_4$ | *n*-$C_5H_{11}$ | OH | — | 75 | 267–269 | 10 |
| **IIa** | $C_2H_5$ | H | $C_6H_5$ | — | — | 277–282 | — |
| **IIIa** | $CH_3$ | H | H | — | 56 | 256–257 | — |
| **IIIb** | $C_2H_5$ | H | H | — | 20 | 267–269 | — |
| **IIIc** | $C_6H_5$ | H | H | 1 | 37 | 274–276 | — |
| **IVa** |  | | | | 54 | 307–308 | — |
| **IVb** |  | | | | 60 | 310–311 | — |
| **IVc** |  | | | | 52 | 236–239 | — |
| **IVd** |  | | | | 60 | 257–259 | — |
| **IVe** |  | | | | 44 | oil | — |

ethanephosphonous acid were incorporated with affixes into a subsequent refinement cycle. Refinement to convergence led to $R = 0.033$ for guanidinophenylmethanephosphonous acid, $R = 0.065$ for α-guanidinoethanephosphonous, and $R = 0.026$ for α-guanidinoethanephosphonic acid. Neutral atomic scattering factors were taken from the *International Tables for X-ray Crystallography* [22]. The scattering factors for non-H atoms were corrected for real and imaginary components.

### *Test on Lepidium Sativum*

Groups of 40 seeds of L. sativum were placed in 9 cm Petri dishes filled with cotton wool, which was

**TABLE 12** Plant Physiological Activity of Guanidino Acids Measured as Percentage Change in the Lengths of *Lepidium sativum* Roots and Shoots

| Compound | Root or Shoot | Concentration (mM) 0.05 | 0.15 | 0.5 | 1.5 |
|---|---|---|---|---|---|
| Glyphosate | R | −60 | −68 | −78 | −84 |
| | S | N | N | N | −22 |
| **Ic** | R | +19 | N | N | N |
| | S | N | N | N | N |
| **Ie** | R | N | N | N | −21 |
| | S | N | N | N | N |
| **Ig** | R | N | −25 | −36 | −40 |
| | S | N | N | N | N |
| **Ih** | R | N | N | −26 | −46 |
| | S | N | N | N | N |
| **Ij** | R | N | N | N | +38 |
| | S | N | N | N | +19 |
| **IIIb** | R | +72 | +64 | N | N |
| | S | N | N | N | N |
| **IIIc** | R | N | N | N | N |
| | S | N | N | N | −19 |
| **IVd** | R | N | N | −49 | −70 |
| | S | N | N | −10 | N |
| **IVe** | R | N | N | −14 | −43 |
| | S | N | N | N | −15 |
| $Zn(\mathbf{Ia})_2 \cdot H_2O$ | R | N | N | −33 | −75 |
| | S | N | N | N | −10 |
| $Ni(\mathbf{Ib})_2$ | R | −30 | −60 | −90 | −96 |
| | S | N | N | −35 | −59 |

N = results statistically not significant.

kept damp by occasional spraying with distilled water until germination occurred (2 days). Then 10 mL of distilled water (control) or aqueous solutions of the test compounds at the concentration of 0.05, 0.15, 0.5, and 1.5 mM, respectively, were applied to the roots. Plants were grown for 7 days at 25°C with 9 hour day length under fluorescent tube lights (2500–3000 lux at plant level). The lengths of roots and shoots were then measured.

### *Statistical Treatment*

Dixon's Q test was used to reject the unreasonable results. The means of control and sample were compared by testing the null hypothesis at the 5% significance level [23]. Results statistically not significantly different from control are marked as "N" in Table 12.

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