

## **SUPPORTING INFORMATION**

***Title:***

**Reactivity of Aminophosphonic Acids. Oxidative  
Dephosphonylation of 1-Aminoalkylphosphonic Acids by Aqueous  
Halogens**

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**Table 1.1.** Abbreviations for 1-aminoalkylphosphonic acids

$\begin{array}{c} \text{R}^1 \\   \\ \text{H}_2\text{N}-\text{C}-\text{P}(\text{OH})_2 \\   \\ \text{R}^2 \end{array}$											
R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>		
H	H	H	Me	H	Et	H	iPr	H	n-Pr	H	n-Bu
Gly <sup>P</sup>		Ala <sup>P</sup>		Ile <sup>P</sup>		Val <sup>P</sup>		Nva <sup>P</sup>		Nle <sup>P</sup>	
R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>		
H	Ph	H	Bn	H	[CH <sub>2</sub> ] <sub>n</sub> - P(O)(OH) <sub>2</sub>	Me	Me			-(CH <sub>2</sub> ) <sub>5</sub> -	
Pgl <sup>P</sup>		Phe <sup>P</sup>		Asp <sup>P,P</sup> (n=1); Glu <sup>P,P</sup> (n=2)		Mal <sup>P</sup>				ACHA	

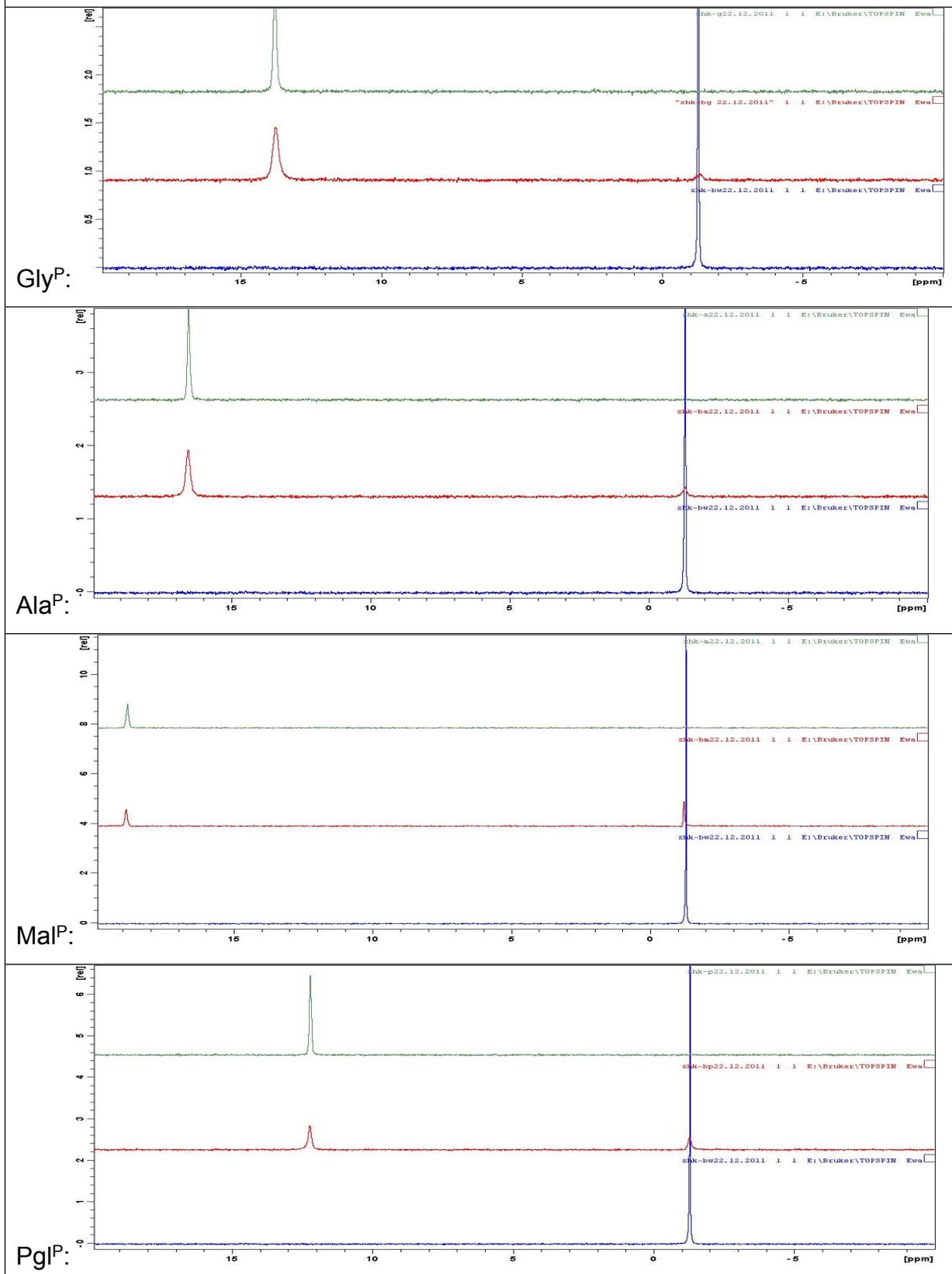
**Table 1.2.** Abbreviations for 1-(N-acylamino)alkylphosphonic acids

$\begin{array}{c} \text{O} \qquad \qquad \text{O} \\    \qquad \qquad    \\ \text{R}^2-\text{C}-\text{N}-\text{C}-\text{P}(\text{OH})_2 \\   \qquad   \\ \text{H} \qquad \text{R}^1 \end{array}$							
R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>	R <sup>1</sup>	R <sup>2</sup>
H	Me	Me	Me	Me	Ph	Ph	Me
Ac-Gly <sup>P</sup>		Ac-Ala <sup>P</sup>		Bz-Ala <sup>P</sup>		Ac-Pgl <sup>P</sup>	

**Table 1.3.** Abbreviations for phosphonic acids used

$\begin{array}{c} \text{O} \\    \\ \text{R}-\text{P}(\text{OH})_2 \end{array}$	
MPA: R=Me	PPA: R=Ph

<sup>31</sup>P NMR spectra illustrating results listed in Table 1.



Aq. layer: water, buffer (acidified prior to <sup>31</sup>P NMR analysis) and 5M HCl aq. solution

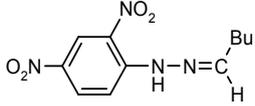
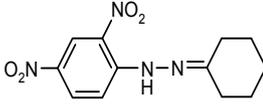
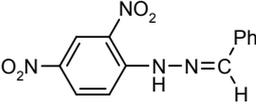
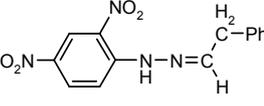
**Table 3.1** GC-MS analysis of organic products of the dephosphonylation of AA<sup>P</sup> (DB-1 column)

$\text{H}_2\text{N}-\overset{\text{R}^1}{\underset{\text{R}}{\text{C}}}-\overset{\text{O}}{\parallel}{\text{P}}(\text{OH})_2$		Chosen volatile organic products of AA <sup>P</sup> dephosphonylation (relative contents [%] in organic phase) <sup>a</sup>				
		Aldol <sup>b,c</sup>		Others identified <sup>d,e</sup>		
AA <sup>P</sup>	R	R <sup>1</sup>	Structure	[m/z] & RC(%)	Structure	m/z & [RC(%)]
Nle <sup>P</sup>	Bu	H	$\begin{array}{c} \text{Bu} \\ \parallel \\ \text{Pr}-\text{C}(\text{O})\text{H} \end{array}$	[154] <sup>b</sup> ; (6.6)		
Pgl <sup>P</sup>	Ph	H				
Phe <sup>P</sup>	Bn	H	$\begin{array}{c} \text{Ph} \\ \parallel \\ \text{Ph}-\text{C}(\text{O})\text{H} \end{array}$	[212] <sup>c</sup> ; (5.6)	$\text{Ph}-\underset{\text{H}_2}{\text{C}}-\text{Br}$	[171] <sup>d</sup> (26.)
ACHPA <sup>P</sup>	(CH <sub>2</sub> ) <sub>5</sub>					[256] <sup>e</sup> (12.)

<sup>a</sup>Determined on the basis of relative surface area of appropriate chromatogram peaks. <sup>b,c</sup>Dehydrated aldols: <sup>b</sup>[154] and <sup>c</sup>[212] (presumably trans). <sup>d,e</sup>Other identified compounds: <sup>d</sup>BnBr [171] and <sup>e</sup>Cyclohexanone×Br<sub>2</sub> [256] (presumably 2,6-dibromo isomer).

**Table 3.2** Identification of carbonyl products of the bromine induced dephosphonylation of Nleu<sup>P</sup>, Pgly<sup>P</sup>, ACHPA<sup>P</sup> and Phe<sup>P</sup>

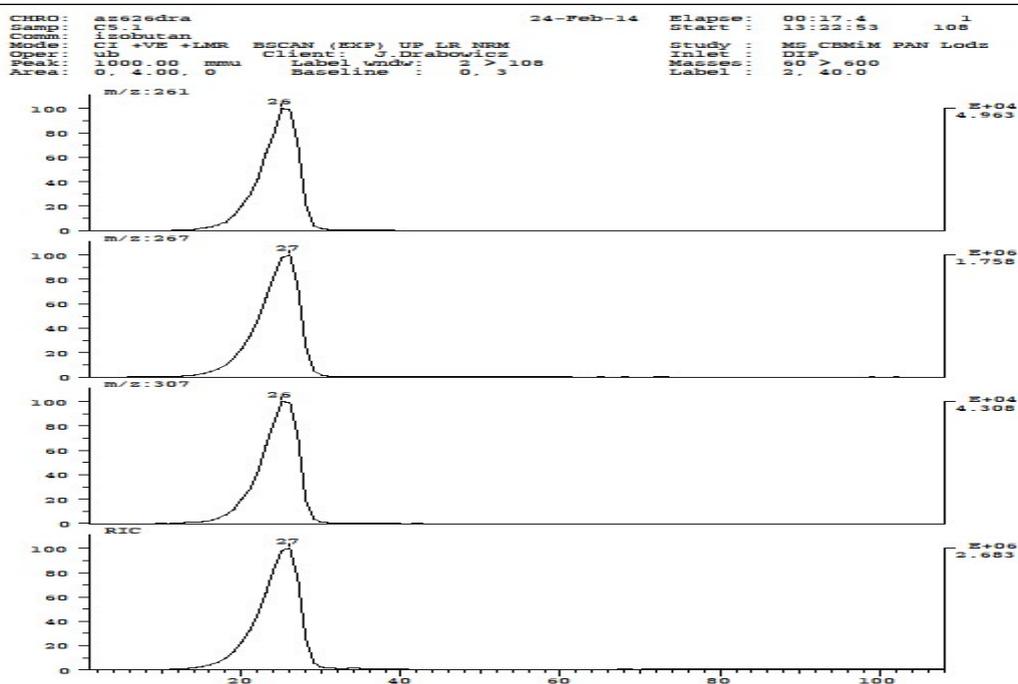
[Supporting material for **Table 3**. GC-MS analysis of organic products of the dephosphonylation of AA<sup>P</sup> (DB-1 column)]

Molecular Masses of hydrazones [M] and Molecular Ions [M+1] determined by MS-Cl							
							
M	M+1	M	M+1	M	M+1	M <sup>b</sup>	M+1 <sup>b</sup>
266	267	278	279	286	287	300/402	301&403
Fig. 3.2.1. (S. C5)		Fig. 3.2.2. (S. CH)		Fig. 3.2.3. (S. Ph)		Fig. 3.2.4. (S. Bn)	

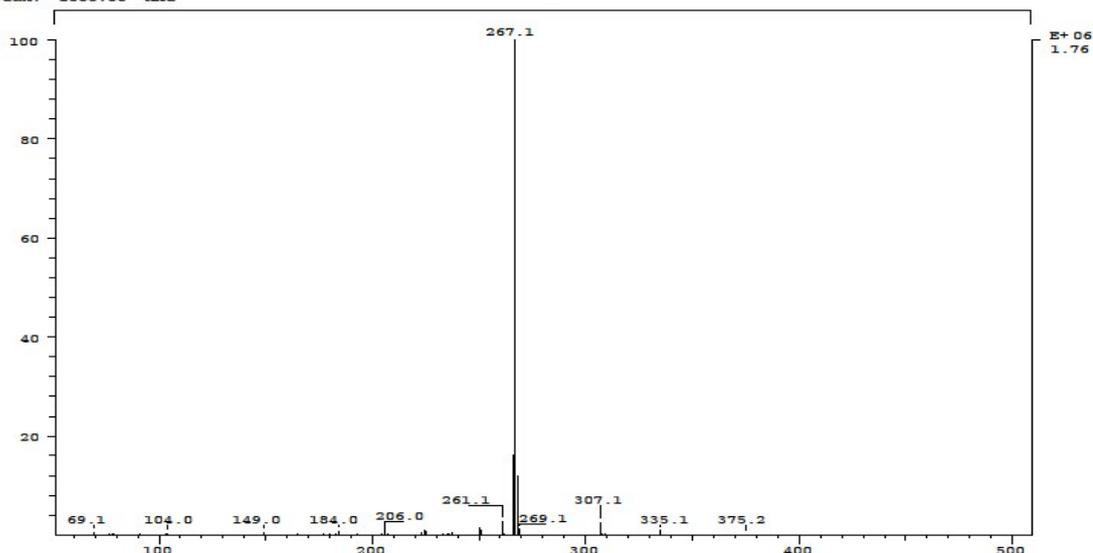
<sup>b</sup> Molecular masses {[M] and/or [M+1]} of dinitrophenylhydrazones of phenylacetaldehyde and corresponding aldol (Scheme 3.2.1).

**Fig. 3.2.1** MS CI spectra of 2,4-dinitrophenylhydrazones isolated (Table 3.2.)

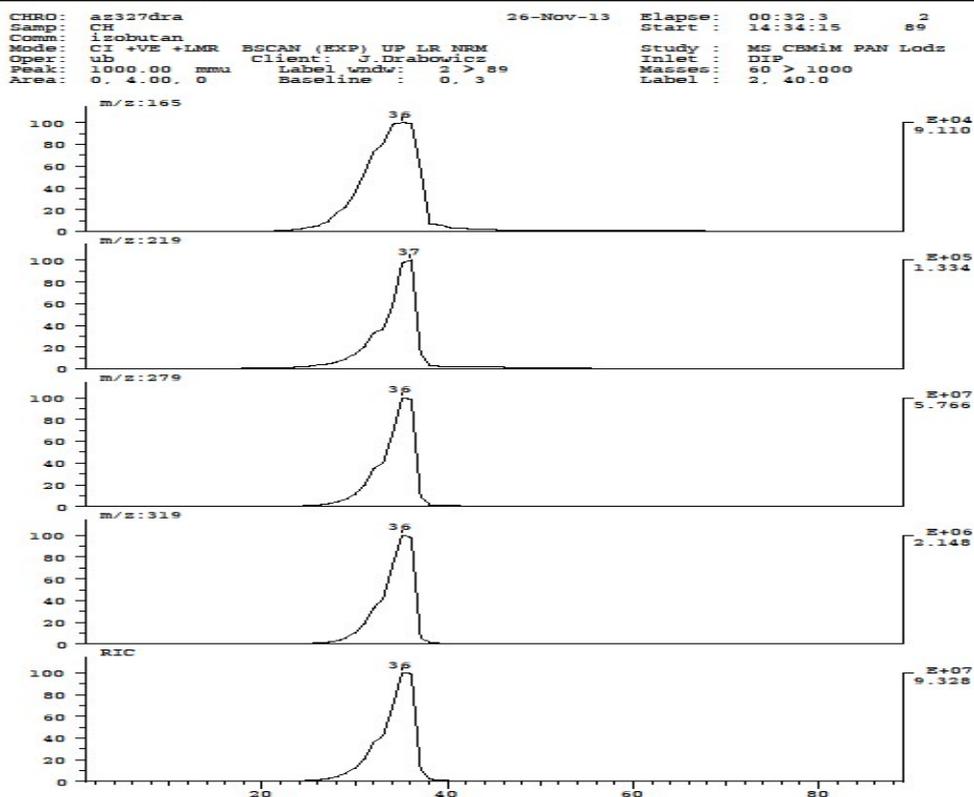
**Fig. 3.2.1.1** MS-Cl mass spectrum of 2,4-dinitrophenylhydrazone of pentanal [C<sub>11</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>; M=266] (samp. C5.1)



```
SPEC: az626dra          24-Feb-14  Elapse:  04:43.5      27
Samp: C5.1              Start:    13:22:53     108
Comm: isobutan
Mode: CI +VE +LMR      BSCAN (EXP) UP LR NRM      Study:  MS CRMIM PAN Lodz
Oper: ub               Client:  J.Drabowicz      Inlet:  DIP
Base: 267.1            Inten:  1757592      Masses: 60 > 600
Norm: 267.1            RIC:    2682795      #peaks: 211
Peak: 1000.00 nmu
```

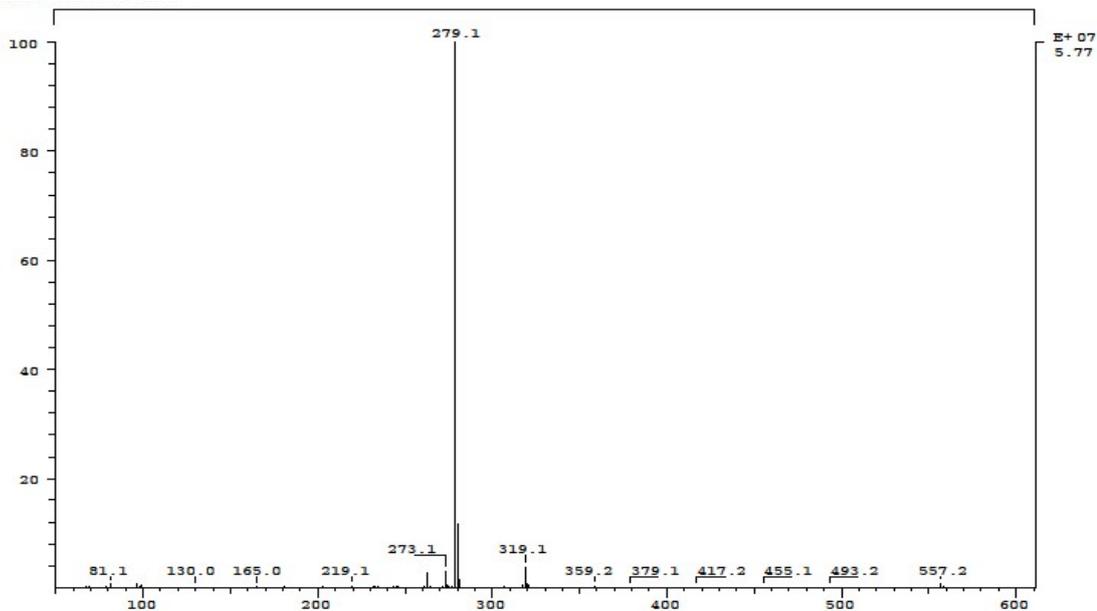


**Fig. 3.2.1.2** MS-CI mass spectrum of 2,4-dinitrophenylhydrazone of cyclohexanone [C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>; M=278] (samp. CH)

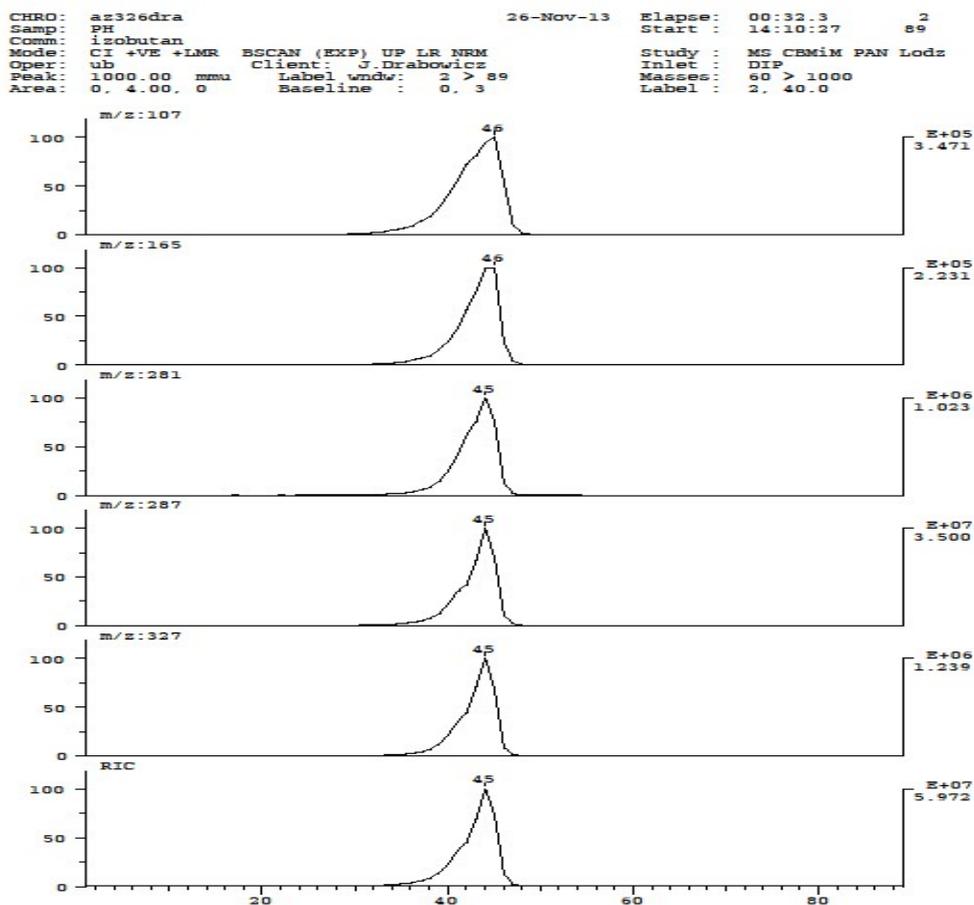


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SPEC: az327dra          26-Nov-13  Elapse: 07:35.2    36
Samp: CH                Start : 14:34:15    89
Comm: izobutan
Mode: CI +VE +LMR      BSCAN (EXP) UP LR NRM      Study : MS CBMIM PAN Lodz
Oper: ub               Client: J.Drabowicz        Inlet : DIP
Base: 279.1            Inten : 57655808           Masses : 60 > 1000
Norm: 279.1            RIC : 93275926             #peaks: 457
Peak: 1000.00 mmu
    
```

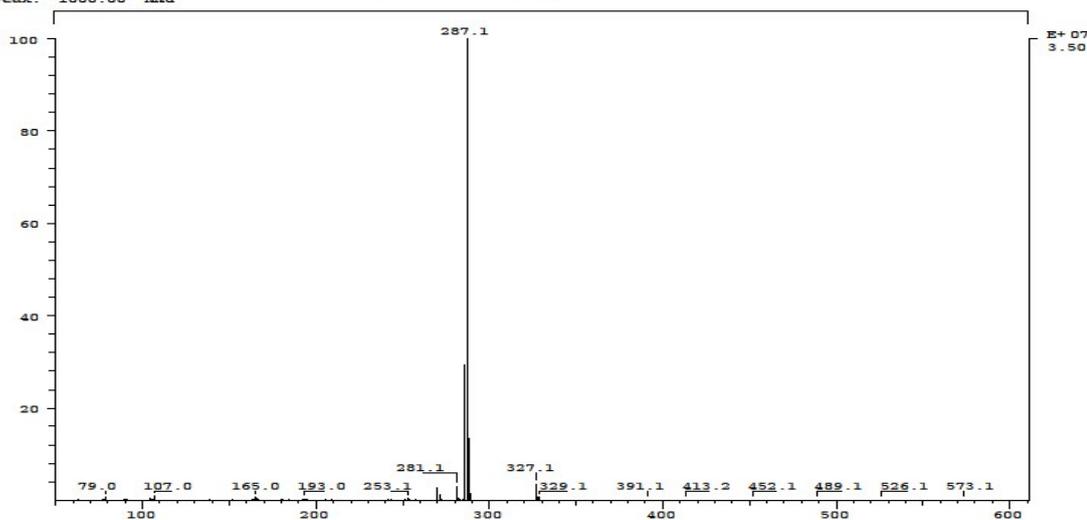


**Fig. 3.2.1.3 MS-CI mass spectrum of 2,4-dinitrophenylhydrazone of benzaldehyde [C<sub>12</sub>H<sub>14</sub>N<sub>4</sub>O<sub>4</sub>; M=278] (samp. PH)**



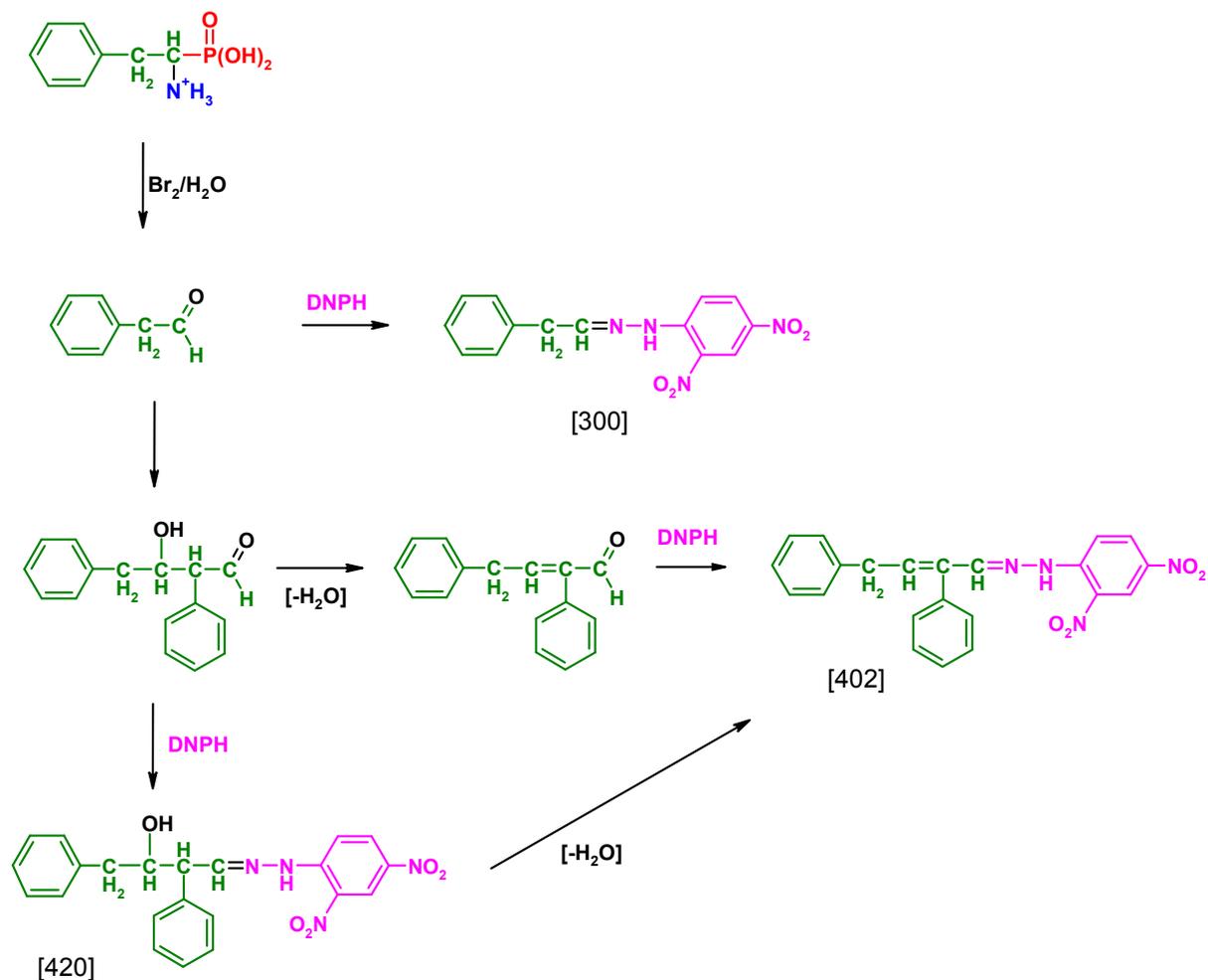
```

SPEC: az326dra          26-Nov-13  Elapse: 09:27.2    45
Samp: PH                Start : 14:10:27    89
Comm: isobutan
Mode: CI +VE +LMR  BSCAN (EXP) UP LR NRM      Study : MS CBMIM PAN Lodz
Oper: ub              Client: J.Drabcowicz     Inlet : DIP
Base: 287.1           Inten : 35004672        Masses: 60 > 1000
Norm: 287.1           RIC : 59716944          #peaks: 417
Peak: 1000.00 mmu
    
```









**Scheme 3.2.1** Identification of phenylacetaldehyde formed during bromine promoted dephosphonylation of Phe<sup>P</sup>, isolated in forms of corresponding 2,4-dinitrophenylhydrazones

## Solutions

**2M acetate buffer solution** (pH=4.79) was obtained by a partial neutralization of acetic acid (150 mmol, 9.0 g) with potassium hydroxide (100 mmol; 5.70 g), and dilution of the so formed mixture with water to a total volume of 50 mL.

**1M solution of bromine in chloroform** was prepared by dissolving 5 mmol Br<sub>2</sub> (5 mmole, 0.8 g, 0.26 mL) in 5 mL of chloroform.

**0.05M standard solution of 2,4-dinitrophenylhydrazine** was prepared, by modification of the Zhdankina procedure [Zhua et al., 2006],<sup>29</sup> by dissolving 1mmol (0.198 g) of 2,4-dinitrophenylhydrazine in a mixture consisting of 17 mL of EtOH, 2.0 mL of H<sub>2</sub>O and 1.0 mL of H<sub>2</sub>SO<sub>4</sub> (98%). This standard solution of DNPH was stable for days and remained clear after dilution with chloroform in a 1:1 ratio (v/v).

## Procedures

### **Potentiometric Measurements:**

The dissociation (protonation) constants of the amino acids were determined by pH-metric titration by means of a computer aided automatic titrator connected to EMU-meter (Politechnika Wroclawska, Poland), fitted with a combined glass microelectrode Crison 5028 [Radomski et al., 1995].<sup>30</sup> The electrode system was calibrated by use of computer program GLEE [Gans & O'Sullivan, 2000].<sup>31</sup> This program provides an estimate of the carbonate ion contamination of the base, the pseudo-Nernstian standard potential and slope of the electrode, ionic product of solvent and concentration of the base. Titrations were carried out in a vessel thermostatted at 20.0±0.2°C, at ionic strength adjusted to 0.1 M with potassium nitrate. Inert atmosphere was ensured by a constant flow of argon. The concentrations of amino acids (in a sample of 4 mL) were approximately 0.05 M. The purities and exact concentrations of these compounds were confirmed simultaneously with the calculation of protonation constants. The titrations (200 measurements with increment of 1µl each) were performed in the presence of excess nitric acid in the pH range of 2-12, with a carbonate ion-free potassium hydroxide

solution of known concentration (ca. 0.4 M). Each titration was repeated at least 4 times. The protonation/dissociation constants were calculated using the HYPERQUAD program [Gans et al., 1996, 2000].<sup>31,32</sup>

**Table 2:** Results of the protonation/dissociation equilibria determination of 1-aminoalkylphosphonic acids(AA<sup>P</sup>)

Entry	AA <sup>P</sup>			Logarithms of protonation constants		
	AA <sup>P</sup>	R <sup>1</sup>	R <sup>2</sup>	LogK <sub>1</sub>	LogK <sub>2</sub>	LogK <sub>3</sub>
1	Gly <sup>P</sup>	H	H	10.04±0.04; 10.45 <sup>[14]</sup>	5.32±0.02; 5.43 <sup>[14]</sup>	<1; <1 <sup>[14]</sup>
2	Ala <sup>P</sup>	H	Me	10.44±0.04; 10.67 <sup>[14]</sup>	5.75±0.02; 5.49 <sup>[14]</sup>	<1; <1 <sup>[14]</sup>
3	Mal <sup>P</sup>	Me	Me	10.59±0.04	5.87±0.03	<1
4	Pgl <sup>P</sup>	H	Ph	9.59±0.05; 9.76 <sup>[14]</sup>	5.72±0.03; 5.72 <sup>[14]</sup>	<1; <1 <sup>[14]</sup>

## References

- (29) C. Zhua, A. Yoshimuraa, Y. Weib, V. N. Nemykina and V.V. Zhdankina, *Tetrahedron Lett.*, 2006, **47**, 6305–6308.
- (30) R. Radomski, M. Radomska, M. Dankowski, K. Szajowska and Z. Wisialski, *Computers Chem.*, 1995, **19**, 303-323.
- (31) P. Gans and B. O'Sullivan, *Talanta*, 2000, **51**, 33-37.
- (32) P. Gans, A. Sabatini and A. Vacca, *Talanta*, 1996, **43**, 1739-1753.