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Synthesis of 2-Phosphono Alkyl 1,2-Benzisoselenazol-3(2H)-ones

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SYNTHESIS OF 2-PHOSPHONO ALKYL 1,2-BENZISOSELENAZOL-3(2H)-ONES

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A series of 2-phosphonoalkyl 1,2-benzisoselenazol-3(2H)-ones were designed and synthesized via reaction 2-chloroselenobenzoyl chloride with 1-hydrazinobenzyl phosphonate. The structures of all new compounds were confirmed by spectroscopic methods and microanalyses.

Keywords: 1-Hydrazinobenzyl phosphonate; cyclization; ebselen

INTRODUCTION

In recent years, biologically active organoselenium compounds have been attracting considerable interest due to their unique and diverse potential of pharmacological importance, such as antitumor, ¹ antiviral, ² and antiinflammatory.³ The discovery of the essential role played by seleno-organic compound ebselen (2-phenyl-1,2-benzisoselenazol-3(2H)-one) in the activity of the enzyme glutathione peroxidase (GSH-Px) against biological damage caused in vivo by reactive hydroperoxides, increased a striking interest in developing organoselenium compounds for therapy. In our previous articles, a number of amino acid ester derivatives of benzisoselenazolone were synthesized and these compounds exhibited excellent pharmacological effects.⁵ Here we report the synthesis of some 2-phosphonoalkyl 1,2-benzisoselenazol-3(2H)-ones 5. The easily accessible 1-hydroxyalkylphosphonates reacted with mesyl chloride to give 1-mesyloxyalkylphosphonates 1, which were allowed to react with hydrazine hydrate to produce 1hydrazinoalkylphosphonates 2 in satisfactory yields. Compounds 5 were obtained by compounds 2 reacting with 2-chloroselenobenzoyl

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chloride **4**. The preliminary anticancer tests in vitro were carried out by the conventional method.

RESULTS AND DISCUSSION

Synthesis of 2-Phosphonoalkyl-1,2-benzisoselenazol-3(2H)-ones

The title compounds **5** were synthesized by a multistep route outlined in Scheme 1.

SCHEME 1

Preparation of the 1-hydrazinoalkylphosphonates **2** was readily accomplished in three-step sequence (40–50% overall yield) starting from aldehyde and diethyl phosphite.⁶ First, 1-hydroxyalkylphosphonates can be synthesized by the solid-catalyzed condensation of diethyl phosphite and aldehyde. Then, 1-hydroxyalkylphosphonates reacted with mesyl chloride to give 1-mesyloxyalkylphosphonates **1**. With the mesyloxy substituent as a good leaving group, compounds **1** could be converted to other types of phosphonates. With hydrazine hydrate as the nucleophile, 1-hydrazinoalkylphosphonates **2** can be synthesized in good yield. Santaniello et al.⁷ have reported that the reducing power of sodium borohydride in polyethylene glycols is enhanced

and able to reduce carbonyl compounds. Similarly, under the PEG-KBH₄ reaction system, 1 mmol of selenium was efficiently reduced to Se–Se²⁻ anion by only 0.018 mmol of KBH₄, catalyzed by PEG-600 in aqueous NaOH. Thus, Se–Se²⁻ anion was allowed to react with 2-carboxybenzenediazonium chloride, and the reaction mixture was then acidified to give 2,2′-diselenobis(benzoic acid) 3 in a yield of 90%. 3 was treated with excess thionyl chloride to provide the intermediate 2-(chloroseleno)benzoyl chloride 4 in a yield of 80%. The reaction of 4 with each 1-hydrazinoalkylphosphonate was carried out under the ether-water-NaHCO₃ reaction system in the presence of phase transfer catalyst Bu₄NBr to give products 5 in a yield of 45–78%.

The Structures of the Products

The structure of all compounds prepared were confirmed by ¹H NMR, ³¹P NMR, IR, MS spectroscopy, and elemental analysis. In the ¹H NMR spectra of 5, the chemical shift of H atom in CH(R = aryl) is in the range of $\delta 6.13-6.31$. Owing to the deshielding effect of the α -benzene ring, these chemical shifts are much bigger than those of CH(R=alkyl), which are in the range of $\delta 3.35-4.06$. Moreover, the H atom in CH(R=aryl) appears as double doublet due the coupling effects of the P atom and H in NH (${}^{2}J_{PCH} = 21.0 - 23.0 \text{ Hz}, {}^{3}J_{HNCH} = 11.0 -$ 12.6 Hz) while that when R=alkyl exhibits complicated peaks due to the phosphorus atom coupling, C-H coupling and N-H coupling. The IR spectra of compounds 5 show normal stretching absorption bands, indicating the existence of groups C=O(1644-1658 cm⁻¹), P=O(1248- 1257 cm^{-1}), and N-H(3337-3354 cm⁻¹). The EI-MS spectra of **5** record the existence of molecular ion peaks, indicating that the heterocycle skeletons are of some stability, the major MS peaks, particularly m/e 199, 156, 137 are common to all compounds, other ion peaks were consistent with their structures and can be clearly assigned. Because there are two major isotope of selenium (approximatively 2:1), the ion which contain two isotopes of selenium abundance ratio is about 2:1.

EXPERIMENTAL

Elemental analyses were performed with CHN PE983 elementary analyzer. NMR spectra were taken on Varian XL200 spectrometer, TMS was used as an internal standard for ¹H NMR, and 85% H₃PO₄ was used as an external standard for ³¹P NMR. Mass spectra were recorded on a Hewlett-Packard 5988A instrument. IR spectra were recorded on a NICOLET AVATAR360. Melting points were determined with a model X4 apparatus and are uncorrected.

TABLE I Experimental Data of Compound 5

| No. R State Mp (°C) Yield ^a (%) Molecular formula C H 5a H Yellowish syrup 45.4 C ₁₂ H ₁₇ N ₂ O ₄ PSe 39.69 4.7 5b Me Yellowish syrup 50.7 C ₁₃ H ₁₉ N ₂ O ₄ PSe 39.69 4.7 5c Ph 134-135 73.6 C ₁₃ H ₂₃ N ₂ O ₄ PSe 41.40 5.0 5d 4-MePh 122-123 75.5 C ₁₉ H ₂₃ N ₂ O ₄ PSe 49.22 4.8 5d 4-MePh 114-115 68.2 C ₁₉ H ₂₃ N ₂ O ₄ PSe 46.31 4.9 5f 4-MeOPh 114-115 68.2 C ₁₉ H ₂₃ N ₂ O ₄ PSe 48.63 4.9 5g 3-CIPh 106-107 72.3 C ₁₈ H ₂₀ CIN ₂ O ₄ PSe 45.64 4.2 5g 3-4-OCH ₂ OPh 148-149 78.0 C ₁₉ H ₂₁ N ₂ O ₆ PSe 47.7 4.3 5g 3-4-OCH ₂ OPh 148-149 78.0 C ₁₉ H ₂₁ N ₂ O ₆ PSe 47.7 4.4 5i 3-4-OCH ₂ OPh 3-3-94 <th< th=""><th></th><th>- raperimentari</th><th>rational Para of Compound of</th><th></th><th></th><th></th><th></th><th></th></th<> | | - raperimentari | rational Para of Compound of | | | | | |
|---|------------|-----------------------|------------------------------|---------------|--|---------|------------------|--------|
| R State Mp ($^{\circ}$ C) Yield a (%) Molecular formula C H Yellowish syrup 45.4 $C_{12}H_{17}N_{2}O_{4}$ PSe 39.69 Me Yellowish syrup 50.7 $C_{13}H_{19}N_{2}O_{4}$ PSe 41.40 Ph $134-135$ 73.6 $C_{18}H_{21}N_{2}O_{4}$ PSe 49.22 4-MePh $122-123$ 75.5 $C_{19}H_{23}N_{2}O_{4}$ PSe 49.11 4-MeOPh $114-115$ 68.2 $C_{19}H_{23}N_{2}O_{4}$ PSe 48.57 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_{2}O_{4}$ PSe 48.57 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_{2}O_{4}$ PSe 45.64 3,4-OCH ₂ OPh $148-149$ 78.0 $C_{19}H_{21}N_{2}O_{6}$ PSe 47.22 2-Furyl $93-94$ 64.8 $C_{16}H_{19}N_{2}O_{6}$ PSe 44.77 46.52 $C_{19}H_{21}N_{2}O_{6}$ PSe 44.77 46.52 $C_{19}H_{21}N_{2}O_{6}$ PSe 47.22 46.53 66.20 66.20 66.20 66.20 66.20 < | | | | | | Fo | Found/Calcd. (%) | (6 |
| $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | No. | R | State Mp (°C) | $Yield^a$ (%) | Molecular formula | C | Н | Z |
| Me Yellowish syrup 50.7 $C_{13}H_{19}N_2O_4$ PSe 41.40 Ph $134-135$ 73.6 $C_{18}H_{21}N_2O_4$ PSe 41.40 $4-Me$ Ph $122-123$ 75.5 $C_{19}H_{23}N_2O_4$ PSe 49.11 $4-Me$ OPh $114-115$ 68.2 $C_{19}H_{23}N_2O_4$ PSe 50.35 $4-C$ IPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4$ PSe 48.57 $4-C$ IPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4$ PSe 48.57 $3-C$ IPh $106-107$ 72.3 $C_{18}H_{20}CIN_2O_4$ PSe 45.64 $3+O$ CH $_2$ OPh $148-149$ 78.0 $C_{19}H_{21}N_2O_6$ PSe 47.39 $3+O$ CH $_2$ OPh $148-149$ 78.0 $C_{19}H_{21}N_2O_6$ PSe 47.38 $2-F$ uryl $93-94$ 64.8 $C_{16}H_{19}N_2O_6$ PSe 44.77 429.2 44.77 42.62 44.77 | 5a | Н | Yellowish syrup | 45.4 | $\mathrm{C_{12}H_{17}N_2O_4PSe}$ | 39.69 | 4.72 | 7.71 |
| Me Yellowish syrup 50.7 $C_{13}H_{19}N_{2}O_{4}$ PSe 41.40 Ph $134-135$ 73.6 $C_{18}H_{21}N_{2}O_{4}$ PSe 49.22 $4-Me$ Ph $122-123$ 75.5 $C_{19}H_{23}N_{2}O_{4}$ PSe 50.35 $4-Me$ OPh $114-115$ 68.2 $C_{19}H_{23}N_{2}O_{5}$ PSe 48.63 $4-C$ IPh $128-129$ 74.6 $C_{18}H_{20}CIN_{2}O_{4}$ PSe 48.57 $4-C$ IPh $106-107$ 72.3 $C_{18}H_{20}CIN_{2}O_{4}$ PSe 45.64 $3+O$ CH ₂ OPh $148-149$ 78.0 $C_{19}H_{21}N_{2}O_{6}$ PSe 47.39 $3+O$ CH ₂ OPh $148-149$ 78.0 $C_{19}H_{21}N_{2}O_{6}$ PSe 47.38 $2-F$ uryl $93-94$ 64.8 $C_{16}H_{19}N_{2}O_{5}$ PSe 44.77 $42.9.2$ 44.77 42.62 44.77 | | | | | 363.2 | (39.75) | (4.81) | (7.65) |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 2 p | Me | Yellowish syrup | 50.7 | $\mathrm{C_{13}H_{19}N_2O_4PSe}$ | 41.40 | 5.08 | 7.43 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | | | | | 377.2 | (41.68) | (5.13) | (7.52) |
| 4-MePh $122-123$ 75.5 $C_{19}H_{23}N_2O_4PSe$ 50.35 4-MeOPh $114-115$ 68.2 $C_{19}H_{23}N_2O_5PSe$ 48.63 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4PSe$ 48.57 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3,4-OCH ₂ OPh $148-149$ 78.0 $C_{19}H_{21}N_2O_6PSe$ 47.22 2-Furyl $93-94$ 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 | 5 c | Ph | 134 - 135 | 73.6 | $\mathrm{C_{18}H_{21}N_2O_4PSe}$ | 49.22 | 4.82 | 6.38 |
| 4-MePh $122-123$ 75.5 $C_{19}H_{23}N_2O_4PSe$ 50.35 4-MeOPh $114-115$ 68.2 $C_{19}H_{23}N_2O_5PSe$ 48.63 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4PSe$ 45.54 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3-CIPh $166-107$ 72.3 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3-4-OCH ₂ OPh $148-149$ 78.0 78.0 78.0 78.0 47.22 2-Furyl $93-94$ 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 429.2 445.62 445.62 445.62 | | | | | 439.2 | (49.11) | (4.87) | (6.23) |
| 4-MeOPh $114-115$ 68.2 $C_{19}H_{23}N_2O_5PSe$ 48.63 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4PSe$ 48.57 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3,4-OCH ₂ OPh $148-149$ 78.0 $C_{19}H_{21}N_2O_6PSe$ 47.22 2-Furyl $93-94$ 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 429.2 445.62 | 2 q | 4-MePh | 122 - 123 | 75.5 | $\mathrm{C_{19}H_{23}N_2O_4PSe}$ | 50.35 | 5.11 | 6.18 |
| 4-MeOPh $114-115$ 68.2 $C_{19}H_{23}N_2O_5PSe$ 48.63 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3,4-OCH ₂ OPh $148-149$ 78.0 $C_{19}H_{21}N_2O_6PSe$ 47.22 2-Furyl $93-94$ 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 429.2 445.62 445.62 445.62 | | | | | 453.3 | (50.17) | (5.19) | (60.9) |
| 469.3 469.3 48.57 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_{2}O_{4}PSe$ 45.64 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_{2}O_{4}PSe$ 45.64 $3.4-OCH_{2}OPh$ $148-149$ 78.0 $C_{19}H_{21}N_{2}O_{6}PSe$ 47.22 $2-Furyl$ $93-94$ 64.8 $C_{16}H_{19}N_{2}O_{5}PSe$ 44.77 429.2 445.62 | 5e | 4-MeOPh | 114 - 115 | 68.2 | $\mathrm{C_{19}H_{23}N_2O_5PSe}$ | 48.63 | 4.94 | 5.97 |
| 4-CIPh $128-129$ 74.6 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 3-CIPh $106-107$ 72.3 $C_{18}H_{20}CIN_2O_4PSe$ 45.64 $3.4-OCH_2OPh$ $148-149$ 78.0 $C_{19}H_{21}N_2O_6PSe$ 47.22 $2-Furyl$ $93-94$ 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 429.2 429.2 445.62 | | | | | 469.3 | (48.57) | (4.92) | (5.88) |
| 3-ClPh 106–107 72.3 $C_{18}H_{20}ClN_2O_4PSe$ 45.64 473.7 (45.82) 3.4 -OCH ₂ OPh 148–149 78.0 $C_{19}H_{21}N_2O_6PSe$ 47.22 473.7 (45.49) 2 -Furyl 93–94 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 429.2 (45.62) | 2 t | 4-CIPh | 128 - 129 | 74.6 | $\mathrm{C}_{18}\mathrm{H}_{20}\mathrm{ClN}_2\mathrm{O}_4\mathrm{PSe}$ | 45.64 | 4.26 | 5.91 |
| 3-ClPh $106-107$ 72.3 $C_{18}H_{20}ClN_2O_4PSe$ 45.64 473.7 473.7 473.7 45.49) $3,4-OCH_2OPh$ $148-149$ 78.0 $C_{19}H_{21}N_2O_6PSe$ 47.22 473.3 47.22 483.3 47.32 47.32 483.3 47.38) 2 -Furyl $93-94$ 64.8 $C_{16}H_{19}N_2O_5PSe$ 44.77 429.2 445.62) | | | | | 473.7 | (45.82) | (4.33) | (5.97) |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 5g | 3-CIPh | 106 - 107 | 72.3 | $\mathrm{C_{18}H_{20}CIN_{2}O_{4}PSe}$ | 45.64 | 4.26 | 5.91 |
| $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | | | | | 473.7 | (45.49) | (4.31) | (5.96) |
| 2-Furyl 93–94 64.8 $C_{16}H_{19}N_{2}O_{5}PSe$ 44.77 $+29.2$ (45.62) | 2h | $3,4\text{-}OCH_2OPh$ | 148–149 | 78.0 | $\mathrm{C_{19}H_{21}N_2O_6PSe}$ | 47.22 | 4.38 | 5.80 |
| 2-Furyl 93–94 64.8 $C_{16}H_{19}N_2O_5$ PSe 44.77 429.2 (45.62) | | | | | 483.3 | (47.38) | (4.29) | (5.74) |
| (45.62) | 5i | 2-Furyl | 93–94 | 64.8 | $\mathrm{C_{16}H_{19}N_2O_5PSe}$ | 44.77 | 4.46 | 6.53 |
| | | | | | 429.2 | (45.62) | (4.43) | (6.47) |
| | | | , | | | | | |

 a Yield determined by isolation based on 4.

TABLE II NMR, IR, and MS Spectral Data of Compound 5

| No. | $^{1} H \ NMR \ (200 \ MHz, CDCl_{3}, TMS) \ or$ $^{31} PNMR \ (200 \ MHz, CDCl_{3}, 85\% \ H_{3} PO_{4})$ $^{\delta} \ (ppm), \ J \ (Hz)$ | ${ m IR}(m v,cm^{-1},KBr)$ | MS (M/e, %) |
|------------|---|-----------------------------|--|
| อืล | 11.67 (d, 1H, NH), 7.27–7.43 (m, 4H, C_6H_4), 3.35 (dd, 2H, CH $^2J_{DCH} = 21.4$, $^3J_{DNCH} = 12.4$), 3.87–4.03 (m, 4H, 2CH $^\circ$). | 3342 (NH) 1656 (s. C=O) | 440 (M ⁺ , 9.3), 199 (100), 166 (25.4), 156 (27.8). |
| | 1.26 (t, 6H, 2CH ₃ , $^{3}_{3}$ $^{3}_{HCCH} = 7.2$ Hz). 31 P: 21.36 (s) | 1252 (s, P=0) | 137 (34.6) |
| 5 b | 11.53 (d, 1H, NH), 7.19–7.36 (m, 4H, C_6H_4), 3.83–4.06 (m, 4H, 2CH ₂), 3.30 (m, 1H, CH), 1.76 (dd, 3H, CH ₂ , $\frac{3.1}{3.1}$ mcon = 7.2 | 3337 (NH) 1658 (s. C=O) | $478 \text{ (M}^+, 6.5), 199 (100), \\ 180 (23.0), 156 (24.6)$ |
| | $^{3}_{ m PPCCH} = 16.8$, 1.18 (t, 6H, 2CH ₃ , $^{3}_{ m JHCCH} = 7.0$) | 1255 (s, P=0) | 137 (46.3) |
| 5 c | 11.67 (d, 1H, NH), 7.23–7.67 (m, 9H, $C_6H_4 + C_6H_5$) 6.13 (dd, 1H, CH, $\frac{21}{2}$ | 3345 (NH) | $440 (\mathrm{M}^+, 5.8), 242 (27.1),$ |
| | $^{-9}$ PCH = 21.0, $^{-9}$ HNCH = 9.0), 3.34-4.05 (m, 4H, 2CH ₂), 1.20 (t, 6H, 2CH ₃ , 3 J _{HCCH} = 7.2). 31 P: 22.45(s) | 1255 (s, P=0) | 137 (28.3) |
| 2 q | 11.72 (d, 1H, NH), $7.24-7.78$ (m, 8H, $2C_6H_4$) 6.26 (dd, 1H, CH, | 3347 (NH) | $454 (M^+, 6.7), 256 (21.3),$ |
| | $^2J_{PCH} = 23.0, ^3J_{HNCH} = 11.0), 3.86-4.10 $ (m, 4H, 2CH ₂), | 1653 (s, C=0) | 199 (100), 156 (32.4), |
| | 2.23 (s, 3H, ArCH ₃ , 1.12 (t, 6H, 2CH ₃ , ³ J _{HCCH} = 7.2) | 1257 (s, P=0) | 137 (16.5) |
| 5e | 11.46 (d, 1H, NH), 7.28–7.63 (m, 8H, $2C_6H_4$) 6.16 (dd, 1H, CH, | 3343 (NH) | 470 (M ⁺ , 8.3), 272 (3.24), |
| | $^2J_{PCH} = 23.0, ^3J_{HNCH} = 12.0), 3.96-4.13 \text{ (m, 4H, 2CH}_2),$ | 1644 (s, C=0) | 199 (100), 156 (16.4), |
| | 3.77 (s, 3H, ArOCH ₃ , 1.23 (t, 6H, 2CH ₃ , ${}^{3}J_{HCCH} = 7.0$) | 1250 (s, P=0) | 137 (20.6) |
| 2 t | 11.60 (d, 1H, NH), 7.21-7.43 (m, 8H, 2C ₆ H ₄) 6.23 (dd, 1H, CH, | 3337 (NH) | $474 \text{ (M}^+, 4.7), 276 (16.5),$ |
| | $^{2}J_{PCH} = 21.0, ^{3}J_{HNCH} = 11.4), 3.88-4.03 \text{ (m, 4H, 2CH}_{2}),$ | 1652 (s, C=0) | 199 (100), 156 (24.5), |
| | $1.25 (t, 6H, 2CH_3, {}^3J_{HCCH} = 7.2)$ | 1249 (s, P=0) | 137 (28.6) |
| 5g | 11.54 (d, 1H, NH), $7.34-7.56$ (m, 8H, $2C_6H_4$) 6.31 (dd, 1H, | 3338 (NH) | $474 \text{ (M}^+, 5.4), 276 (14.3),$ |
| | CH, $^2J_{PCH} = 21.0$, $^3J_{HNCH} = 12.6$), $3.84-4.07$ (m, 4H , 2CH_2), | 1648 (s, C=0) | 199 (100), 156 (23.4), |
| | $1.23 (t, 6H, 2CH_3, {}^3J_{HCCH} = 7.0)$ | 1252 (s, P=0) | 137 (26.7) |
| $_{ m 2h}$ | 11.48 (d, 1H, NH), $7.28-7.58$ (m, 7H, $C_6H_4+C_6H_3$), 6.25 (dd, 1H, CH, | 3346 (NH) | 484 (M ⁺ , 8.5), 286 (25.6), |
| | $^2\mathrm{J}_{\mathrm{PCH}} = 21.6,~^3\mathrm{J}_{\mathrm{HNCH}} = 11.6),~4.56~\mathrm{(s,~2H,~OCH}_2\mathrm{O)},$ | 1656 (s, C=0) | 199 (100), 156 (27.5), |
| | $3.89-4.07 \text{ (m, 4H, 2CH}_2), 1.19 \text{ (t, 6H, 2CH}_3, {}^3J_{HCCH} = 7.0)$ | 1256 (s, P=0) | 137 (32.4) |
| 5i | 11.62 (d, 1H, NH), 6.15–8.09 (m, 7H, $C_6H_4 + C_6H_3$), | 3354 (NH) | 430 (M ⁺ , 14.6), 232 (34.7) |
| | $6.25 (dd, 1H, CH, {}^2J_{PCH} = 21.4, {}^3J_{HNCH} = 11.0),$ | 1652 (s, C=0) | 199 (100), 156 (36.4), |
| | 4.56 (s, 2H, OCH ₂ O), 3.86–4.23 (m, 4H, 2CH ₂), | 1248 (s, P–O) | 137 (28.3) |
| | $1.15 (t, 6H, 2CH_3, ^{\circ} J_{HCCH} = 7.0). ^{\circ 1} P! 21.3$ | | |

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2-Chloroseleno benzoyl chloride $\mathbf{4}^8$ and 1-hydrazinobenzyl phosphonate $\mathbf{2}^6$ have been prepared following literature methods.

2-Phosphonoalkyl 1,2-Benzisoselenazol-3(2H)-ones 5

To a stirred mixture of α -hydrazinobenzyl phosphonate (5 mmol), potassium bicarbonate (16 mmol) and tetrabutylammonium bromide (catalytic amount) in $H_2O(10 \text{ mL})$ -ether(25 mL) system cooled with an ice bath was added a solution of 2-chloroseleno benzoyl chloride **2** (5 mmol) in 20 mL of ether over 30 min. Then the mixture was stirred for an additional 7 h at room temperature. The organic product was extracted with ether, and the layers were separated. Combined organic extracts were dried (Na₂SO₄), and the solvent was removed under reduced pressure. The residue was purified by column chromatography on silica gel, eluting with ethyl acetate/petroleum ether.

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