A number of novel DNA nucleobase derivatives containing chalcogens (S, Se and Te) has been synthesized in satisfactory yields.
Efficient Synthesis of Novel Chalcogen-Containing Derivatives of DNA Nucleobases

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1. Introduction

Selenium, an essential micronutrient for humans and animals,1–6 is a trace element nutrient that functions as selenocysteine for the reduction of antioxidant enzymes such as glutathione peroxidases,7,8 thioredoxin reductase,9 and thyroid hormone deiodinases.10 The entire selenoprotein gene population, designated the selenoproteome, has been identified in humans and rodents,11 and numerous selenoprotein genes have functions in development and health.12 Selenoproteins are also involved in different human genetic disorders.13 The antioxidant activity of selenium plays a protective role in 50 human diseases, including prostate, lung, and intestine/colon cancer, immunodeficiency, and heart diseases.13–16 It is well known that adenine moiety provides the hydrogen bond with a variety of biological molecules and contributes to the diverse biological functions such as molecular recognition in DNA replication and protein biosynthesis.17 Adenine derivatives substituted in position 9 have potent cyclic nucleotide phosphodiesterase (PDE) inhibition properties with high selectivity toward PDE-4.18 For instance, the 9-(2-fluorobenzyl)-N6-methyladenine has been found to be used as a potent anticonvulsant,19 anxiolytic and sedative properties,20 and was a relatively potent PDE-4 inhibitor (IC50=2.0 μM).21 Furthermore, initial structure activity relationship (SAR) studies around 9-substituted adenine derivatives allowed us to identify 9-(2-fluorobenzyl)-N6-methyl-2 trifluoromethyladenine, as a potent PDE-4 inhibitor (IC50=0.042 μM), with a high selectivity vs PDE-3.21 Moreover, 9-(2-fluorobenzyl)-N6-methyl-2-trifluoromethyladenine elicited also anti-inflammatory properties,21 and marked dose-dependent inhibition of arachidonate release from human mononuclear cells stimulated with N-formyl-Met-Leu-Phe, a suitable model to investigate the in vitro anti-inflammatory activity of PDE-4 inhibitors.23 In addition, 9-(2-fluorobenzyl)-N6-methyl-2-trifluoromethyladenine and several 9-substituted adenine derivatives elicited a concentration-dependent inhibition of the TNFa release from mononuclear cells stimulated with lipopolysaccharide (LPS).23 To our knowledge, chalcogen-containing derivatives substituted in position 9 have not been reported. In this paper, we report the synthesis of a series of chalcogen-containing adenine derivatives substituted in position 9 and two related X-ray single crystal structures.

2. Results and Discussion

9-(2-Bromoethyl)adenine (2) was obtained from unprotected adenine (1) according to the literature method.24 Starting from unprotected adenine (1), selective alkylation with dibromoethane in the presence of dry K2CO3 in DMF gave the derivative 2 in 45% isolated yield. 2 was applied to the synthesis of many kinds of chalcogen-containing molecules as a starting material as shown in Scheme 1. Reaction of 2 with 0.5 equiv of sodium selenide or sodium telluride in DMF at room temperature for 40 h gave the corresponding 9,9′-(tellurobis(ethane-2,1-diyl))bis(9H-purin-6-amine) (3) and 9,9′-(tellurobis(ethane-2,1-diyl))bis(9H-purin-6-amine) (4) in respective 95% and 68% yields. The reactions can be accelerated by warming up the reaction solutions; however, brown selenium or dark tellurium being found in the resulting suspension resulted in reduced yields. Furthermore, lower yields were obtained when the reactions were carried out in ethanol/THF (50/50, v/v), DMF seemed to perform much better. The use of an excess of 9-(2-bromoethyl)adenine also improves yields and conversions. Treating a suspension of potassium selenocyanate with 9-(2-bromoethyl)adenine in dry acetone at 60°C led to the formation of 9-(2-selenocyanatoethyl)adenine (5) in 93% yield. Reacting
The synthesis of 9-(2-((2-bromobenzyl)selanyl)ethyl)adenine (11) can be achieved from 9-(2-bromoethyl)adenine by two routes as shown in Scheme 2. Stirring a suspension of 1,2-bis(2-bromobenzyl)diselane (which was prepared following a modified literature method) with NaBH₄ and 9-(2-bromoethyl)adenine in a dry mixed medium of THF/EtOH (1 : 1) at room temperature for 20 h led to the formation of 9-((2-(2-bromobenzyl))selanyl)ethyl)adenine (11) in 86% yield. Alternately, mingleting 1-bromo-2-(selenocyanato)methylbenzene with NaBH₄ and 9-(2-bromoethyl)adenine in dry THF/EtOH (1 : 1) at room temperature for 20 h gave the same product in 61% yield. It is noteworthy that 1,2-bis(2-bromobenzyl)diselane proved to be more efficient starting material than 1-bromo-2-(selenocyanato)methylbenzene for the synthesis of the targeted product with high yield. Both reactions resulted in the expected products without noticeable byproduct.

Scheme 2. Synthesis of 9-((2-(2-bromobenzyl)selanyl)ethyl)-9H-purin-6-amine 11

Breaking the four-membered ring in Woollins’ reagent with two molar equivalents of sodium alkanoates formed the sodium O-alkyl phenylphosphonodiselenoates 12 – 14 in high yields, the latter were stirred with an equivalent of potassium selenocyanate in dry THF overnight at room temperature to generate Se-((2-(6-amino-9H-purin-9-yl)ethyl)selenyl) O-alkyl phenylphosphonodiselenoates 15 – 17 in 69% – 87% yields, respectively, as shown in Scheme 3. To reduce the probability of any diselenide byproduct formation, these reactions were performed in an inert atmosphere. It is noteworthy that neither coupling of two O-alkyl phenylphosphonodiselenolate molecules nor decomposed selenium were detected.

Compounds 3 – 11, 15 – 17 were spectrally characterized by multi-nuclear NMR and IR spectroscopy and accurate mass measurement. All of new compounds showed the anticipated molecular ion peaks [M+H]⁺ or [M+Na]⁺ and were confirmed by satisfactory accurate mass measurements. Two stereoisomers were observed by multinuclear NMR in compound 9. The ⁷⁷Se NMR chemical shifts in compounds 3, 5, 7 – 11 fall within the range from 121.6 to 297.9 ppm, the highest ⁷⁷Se NMR chemical shift value is one of two isomers in compound 9 with long alkyl chain alcohol group, whilst the lowest ⁷⁷Se NMR chemical shift value is the compound 3 with a symmetric conformation in Se atom centre. Surprisingly, one of two isomers in compound 9 has very low ⁷⁷Se NMR chemical shift (140.0 ppm). Another sample having high ⁷⁷Se NMR chemical shift value (282.8 ppm) is compound 10, which also adopts a symmetric conformation around the Se-Se bridge. With the similar conformation as compound 3, the ¹²⁵Te NMR chemical shift value in compound 4 is 199.3 ppm. The ³¹P NMR spectra of 15 – 17 show sharp singlets in the range of 79.3 – 83.6 ppm, flanked by two pairs of selenium satellites with ³¹P-⁷⁷Se coupling constants in

Tetrahedron
the ranges of 434 – 439 Hz and 825 – 831 Hz, indicating the presence of both P-Se single bond and P-Se double bond in these three compounds. This was further supported by the $^{77}$Se NMR spectra which showed two pairs of doublets in the range of 307.8 – 338.6 ppm and -105.9 – -92.1 ppm with matching $^{31}$P-$^{77}$Se coupling constants in compounds 15 – 17. The $^1$H NMR spectra of 15 – 17 showed two strong singlets ranging from 7.94 – 8.38 ppm, accompanied by singlet peaks in the range of 7.15 – 7.53 ppm for the adenine NH$_2$ groups, indicating the presence of adenine ring in the molecules. The presence of the adenine rings can further confirmed by their special five carbon chemical shift values in the $^{13}$C NMR spectra.

The P(1) – Se(1) – P(1) 2.118(5), Se(2) 114.9(2), Se(1) – P(1) 2.253(6), Se(2) – C(8) 1.428(11); P(1) – C(9) 1.938(8), P(1) – Se(1) 1.420(3); P(1) – Se(1) – C(9) 100.1(5), Se(1) – C(11) 97.9(4), Se(1) – P(1) – Se(2) 114.9(2), Se(1) – P(1) – C(1) 107.5(8), Se(2) – P(1) – C(1) 114.6(8), P(1) – O(1) – C(7) 124.5(16), Se(1) – C(9) – C(1) 114.5(8); (b) shows the hydrogen bonding of intermolecule within 16.

Figure 1. (a) Single crystal X-ray structure of 1-(naphthalen-2-yl)-2-selenocyanatobenzothiazole 17. Selected bond lengths (Å) and angles (°) (esd in parentheses): Se(1)-P(1) 2.246(2), Se(2)-P(1) 2.081(2), Se(1)-C(9) 1.938(8), P(1)-C(11) 1.774(8), P(1)-O(1) 1.609(8), O(1)-C(8) 1.428(11); P(1)-Se(1)-C(1) 98.7(2), Se(1)-P(1)-O(1) 103.6(3), Se(2)-P(1)-O(1) 116.8(3), O(1)-P(1)-C(11) 97.9(4), Se(1)-P(1)-Se(2) 114.14(9), Se(1)-P(1)-C(11) 107.3(3), Se(2)-P(1)-C(11) 115.4(3), P(1)-O(1)-C(8) 124.7(6), Se(1)-C(1)-C(2) 114.1(5); (d) shows the hydrogen bonding of intermolecule within 17.

In conclusion, a series of new chalcogen-containing derivatives of DNA nucleobases having the adenine functionality were successfully prepared and characterized. Reaction of 9-(2-bromoethyl) adenine with sodium selenide, sodium telluride, potassium selenocyanate, diphenyl disulfide/NaBH$_4$, diphenyl diselenide/NaBH$_4$, 1-(naphthalen-2-yl)-2-selenocyanatobenzothiazole and 11-selenocyanatoundecan-1-ol with 9-(2-bromoethyl) adenine resulted in the corresponding chalcogen-containing heteroatom compounds in good to excellent yields. Furthermore, treating 9-(2-bromoethyl) adenine with three Woolins’ reagent derivatives of alcohols led to the expected formation of three phosphorus-selenium heteroatom compounds in excellent yields. The new chalcogen-containing DNA nucleobases derivatives might provide a valuable addition to the library of selenium-containing heteroatom compounds known.

3. Experimental section

3.1 General
3.2. Synthesis of 9,9'-Diselenobi(3,5-diyl)adenine (4).

A suspension of diphenyl diselenide (0.156 g, 0.5 mmol) and NaBH₄ (0.041 g, 1.1 mmol) in 30 mL of dry THF and 5 mL of dry EtOH was stirred at room temperature until a pale yellow solution was formed, then 9-(2-bromoethyl)adenine (0.241 g, 1.0 mmol) was added. The mixture was stirred at room temperature for 24 h. Upon evaporating to remove solvent the residue was purified by gel column (1 : 4 methanol/dichloromethane as eluent) to give 0.256 g as a white solid in 95% yield. M.p. 150 - 152°C. Selected IR (KB, cm⁻¹): 1683(vs), 1607(vs), 1574(s), 1477(s), 1418(s), 1331(m), 1302(s), 1239(m), 1071(m), 1020(m), 881(m), 795(m), 747(s), 692(s). 1H NMR (DMF-d₆, δ): 8.27 (s, 1H, adenine-H), 8.42 (s, 1H, adenine-H), 7.48 (d, J(δ,δ) = 8.0 Hz, 1H, Ar-H), 7.41 (d, J(δ,δ) = 8.0 Hz, 1H, Ar-H), 7.35 (s, 1H, NH), 7.26-7.21 (m, 2H, Ar-H), 4.71 (t, J(δ,δ) = 6.9 Hz, 2H, NCH₂), 4.05 (t, J(δ,δ) = 6.9 Hz, 2H, SCH₂), 3.59 (s, 2H, SCHR₂). 13C NMR (DMF-d₆, δ): 151.8 (adenine-C), 151.6 (adenine-C), 119.6 (adenine-C), 103.4 (N=C), 44.2 (NCH₂), 29.3 (SeCH₂) ppm. 7Se NMR (DMF-d₆, δ), 197.1 ppm. Mass spectrum [C¹⁺, m/z]: 269 [M⁺H]⁺. Accurate mass measurement [C¹⁺, m/z]: 269.0046 [M⁺H]⁺, calculated mass for C₁₁H₁₂N₅SeH: 269.0048.
A suspension of potassium selenocyanate (1.50 g, 10.3 mmol) in 30 mL of dry acetone was heated to 60 °C, and 2-bromo-1-(naphthalen-2-yl)ethanone (2.125 g, 8.57 mmol) in 10 mL of acetone was slowly added dropwise. The resulting mixture was stirred at 60 °C for another 5 h. Upon cooling to room temperature the mixture was hydrolyzed (10 mL water) and extracted ether (2 x 30 mL). The ether layers were combined and dried over MgSO₄ overnight. The solvent was evaporated in vacuo and the residue was purified by silica gel column chromatography (1 : 4 methanol/dichloromethane as eluent) to give 0.405 g as a white cream solid in 98% yield. Mp. 118 - 119 °C. Two diastereoisomers were found in ca. 2 : 1 intensity ratio. Selected IR (KBr, cm⁻¹): 1674(m), 1642(m), 1501(s), 1470(s), 1419(m), 1305(s), 1253(m), 1059(s), 793(m), 716(m). ¹H NMR (DMF-d₅, δ): 8.24 (s, 1H, adenine-H), 7.32 (s, 1H, adenine-H), 7.26 (s, 1H, adenine-H), 6.81 (s, 2H, NH₂), 6.80 (s, 2H, NH₂), 4.92 (t, J(H,H) = 6.1 Hz, 2H, NCH₃), 4.50 (t, J(H,H) = 6.1 Hz, 2H, NCH₃), 4.39 (t, J(H,H) = 6.1 Hz, 2H, SeCH₃), 4.04 (t, J(H,H) = 6.1 Hz, 2H, SeCH₃), 3.49 (t, J(H,H) = 6.1 Hz, OCH₃), 3.11 (t, J(H,H) = 6.1 Hz, 2H, SeCH₃), 2.95 (t, J(H,H) = 6.1 Hz, OCH₃), 2.75 (s, 1H, OH₂, OCH₃), 2.58 (t, J(H,H) = 6.1 Hz, 2H, SeCH₃), 1.76-1.30 (m, 18Hx2, CH₂ ppm). ¹³C NMR (DMF-d₅, δ), 162.2 (adenine-C), 161.8 (adenine-C), 156.7 (adenine-C), 156.6 (adenine-C), 152.9 (adenine-C), 152.8 (adenine-C), 141.2 (adenine-C), 141.1 (adenine-C), 119.1 (adenine-C), 119.0 (adenine-C), 61.6 (OCH₃), 45.2 (SeCH₃), 44.1 (SeCH₃), 33.2 (CH₃), 31.3 (CH₃), 30.9 (CH₃), 29.9 (CH₃), 29.7 (CH₃), 29.6 (CH₃), 29.4 (CH₃), 28.9 (CH₃), 28.5 (CH₃) ppm. ¹⁹F NMR (CDCl₃, δ): 196.3 ppm. Mass spectrum [C¹⁺, m/z]: 414 [M⁺H⁺]⁺. Accurate mass measurement [C¹⁺, m/z]: 414.1759 [M⁺H⁺]⁺, calculated mass for C₁₉H₁₃NO₅SeF: 414.1767.


To a suspension of 9-(2-bromoethyl)adenine (0.723 g, 3.00 mmol) in 50 mL of dry ethanol was added potassium selenocyanate (0.541 g, 3.75 mmol) at 20 °C. The mixture was stirred at that temperature for 4 h. Then, an aqueous solution of NaOH (0.24 g, 6.0 mmol in 10 mL of water) was added to the mixture and stirring was continued for another 2 h. After extraction with dichloromethane (30 mL x 3) and washing with water (20 mL x 3), the organic layer was dried over MgSO₄. The organic residue was further purified by silica gel chromatography (1 : 5 ethyl acetate / dichloromethane as eluent) to give 0.420 g as a off-white solid in 87% isolated yield. Mp. 159 - 161 °C. Selected IR (KBr, cm⁻¹): 1688(s), 1648(s), 1603(s), 1570(m), 1513(m), 1477(m), 1419(m), 1302(m), 1294(s), 1209(m), 1209(s), 950(m), 887(s), 873(m), 712(s), 641(s), 592(m), 344(m). ¹H NMR (DMF-d₅, δ): 8.57 (s, 2H, adenine-H), 8.30 (s, 2H, adenine-H), 7.54 (s, 4H, adenine-NH₂), 6.22 (t, J(H,H) = 6.9 Hz, 4H, NCH₃), 5.18 (t, J(H,H) = 6.9 Hz, 2H, SeCH₃), 3.67 (s, 4H, SeCH₃) ppm. ¹³C NMR (DMF-d₅, δ), 162.7 (adenine-C), 156.8 (adenine-C), 153.6 (adenine-C), 139.0 (adenine-C), 119.9 (adenine-C), 45.3 (N-C), 31.4 (SeCH₃) ppm. ¹⁹F NMR (DMF-d₅, δ), 282.8 ppm. Mass spectrum [C¹⁺, m/z]: 485 [M⁺H⁺]⁺. Accurate mass measurement [C¹⁺, m/z]: 484.9979 [M⁺H⁺]⁺, calculated mass for C₁₉H₁₃NO₅SeF: 484.9965.

3.2.9. 9-(2-(2-Bromobenzyl)selenyl)ethyl)adenine (11).

Method 1: 1,2-Bis(2-bromobenzyl)diselane was prepared by a modified literature method. A suspension of 1,2-bis(2-bromobenzyl)diselane (0.250 g, 0.5 mmol) and NaBH₄ (0.041 g, 1.1 mmol) in 30 mL of dry THF and 5 mL of dry EtOH was stirred at room temperature until a pale yellow solution was formed, then 9-(2-bromoethyl)adenine (0.241 g, 1.0 mmol) was added. The mixture was stirred at room temperature for 20 h. Upon evaporating to remove solvent the residue was purified by silica gel column chromatography (1 : 4 methanol/dichloromethane as eluent) to give 0.405 g as a white cream solid in 98% yield. Mp. 118 - 119 °C. Two diastereoisomers were found in ca. 2 : 1 intensity ratio. Selected IR (KBr, cm⁻¹): 1674(m), 1642(m), 1501(s), 1470(s), 1419(m), 1305(s), 1253(m), 1059(s), 793(m), 716(m). ¹H NMR (DMF-d₅, δ): 8.24 (s, 1H, adenine-H), 8.32 (s, 1H, adenine-H), 7.32 (s, 1H, adenine-H), 7.26 (s, 1H, adenine-H), 6.81 (s, 2H, NH₂), 6.80 (s, 2H, NH₂), 4.92 (t, J(H,H) = 6.1 Hz, 2H, NCH₃), 4.50 (t, J(H,H) = 6.1 Hz, 2H, NCH₃), 4.39 (t, J(H,H) = 6.1 Hz, 2H, SeCH₃), 4.04 (t, J(H,H) = 6.1 Hz, 2H, SeCH₃), 3.67 (s, 4H, SeCH₃) ppm. ¹³C NMR (DMF-d₅, δ), 162.7 (adenine-C), 156.8 (adenine-C), 153.6 (adenine-C), 139.0 (adenine-C), 119.9 (adenine-C), 45.3 (N-C), 31.4 (SeCH₃) ppm. ¹⁹F NMR (DMF-d₅, δ), 282.8 ppm. Mass spectrum [C¹⁺, m/z]: 485 [M⁺H⁺]⁺. Accurate mass measurement [C¹⁺, m/z]: 484.9979 [M⁺H⁺]⁺, calculated mass for C₁₉H₁₃NO₅SeF: 484.9965.
bromomethyl)adenine (0.241 g, 1.0 mmol) was added. The mixture was stirred at room temperature for 20 h. Upon evaporating to remove solvent the residue was purified by silica gel column (1 : 4 methanol/dichloromethane as eluent) to give 0.354 g as an yellowish white solid in 86% yield. Method 2: A mixture of 1-bromo-2-(selencycloanatomethyl)benzene (0.275 g, 1.0 mmol) and NaBH₄ (0.041 g, 1.1 mmol) in 30 mL of dry THF and 5 mL of dry EtOH was stirred at room temperature until a pale yellow solution was formed, then 9-(2-bromoethyl)adenine (0.241 g, 1.0 mmol) was added. The mixture was allowed to stir at room temperature for 20 h. Upon evaporating to remove solvent the residue was purified by silica gel column (1:4 methanol/dichloromethane as eluent) to give 0.250 g as an yellowish white solid in 61% yield. M.p. 118 - 119°C. Selected IR (KBr, cm⁻¹): 1609(s), 1599(vs), 1477(s), 1416(s), 1325(m), 1306(s), 1230(m), 1069(m), 1021(m), 797(m), 759(m), 657(m). ¹H NMR (DMF-d₅, δ), 8.26 (s, 1H, adenine-H), 8.23 (s, 1H, adenine-H), 7.65-7.33 (m, 4H, Ar-H), 7.54 (t, J(H,H) = 6.9 Hz, 2H, CH₂), 4.05 (t, J(H,H) = 6.9 Hz, 2H, CH₂), 3.59 (s, 2H, CH₂) ppm. ³¹C NMR (DMF-d₅, δ), 162.3 (adenine-C), 161.8 (adenine-C), 156.6 (adenine-C), 152.8 (adenine-C), 141.3 (Ar-C), 139.4 (Ar-C), 133.2 (Ar-C), 131.2 (Ar-C), 129.0 (Ar-C), 124.0 (Ar-C), 119.5 (adenine-C), 45.2 (NCH₃), 31.3 (SeCH₂), 26.9 (SeCH₂) ppm. ⁷⁷Se NMR (DMF-d₅, δ), 225.4 ppm. Mass spectrum [CI⁺, m/z]: 409 [M+H]⁺. Accurate mass measurement [CI⁺, m/z]: 408.9705 [M+NH₄]⁺, calculated mass for C₁₀H₁₂N₄O₂SeH: 408.9708.


Small pieces of sodium (0.046 g, 2.0 mmol) were stirred in alcohol (30 mL) at room temperature until fully dissolved. To this solution Woolfins' reagent (0.54 g, 1.0 mmol) was added and heated at 60°C for 15 min. The reaction mixture was allowed to cool to room temperature and the resulting yellow solution was filtered through a small Celite pad. The filtrate was dried under vacuum and 30 mL of THF was added. To this solution 9-(2-bromoethyl)adenine (0.2482 g, 2.0 mmol) was added and the mixture was stirred at room temperature overnight. The resultant mixture was filtrated to remove solid and the filtration was dried in vacuo, the residue was purified by silica gel column (5% methanol/95% DCM) to give the corresponding products 15 - 17.

3.2.10.1. Se-(2-(6-Amino-9H-purin-9-yl)-ethyl) O-ethyl phenylphosphonodiselenoate (15).

0.800 g as greyish white solid in 87% yield. M.p. 123-125°C. Selected IR (KBr, cm⁻¹): 3323(s), 3138(s), 1648(s), 1598(s), 1481(m), 1415(m), 1301(m), 1251(m), 1105(m), 1019(m), 744(m), 710(m), 687(m), 549(s), 499(s). ¹H NMR (DMF-d₅, δ), 8.26 (s, 1H, adenine-H), 8.22 (s, 1H, adenine-H), 7.69-7.58 (m, 2H, Ar-H), 7.47-7.37 (m, 3H, Ar-H), 7.32 (s, 2H, NH), 5.14 (d, J(P,H) = 12.0 Hz, 3H, OCH₂), 4.54-4.49 (m, 2H, NCH₃), 3.42-3.29 (m, 2H, SeCH₂) ppm. ³¹C NMR (DMF-d₅, δ), 157.0 (adenine-C), 153.8 (adenine-C), 153.0 (Ar-C), 141.5 (Ar-C), 139.3 (Ar-C), 133.3 (Ar-C), 130.7 (Ar-C), 128.0 (Ar-C), 119.7 (adenine-C), 53.1 (OCH₂), 43.5 (NCH₃), 31.7 (SeCH₂) ppm. ³¹P NMR (DMF-d₅, δ), 83.6 (s, J(P,Se) = 439 Hz, J(P,Se) = 831 Hz) ppm. ⁷⁷Se NMR (DMF-d₅, δ), 307.8 (d, J(P,Se) = 439 Hz, -105.9 (d, J(P,Se) = 830 Hz) ppm. Mass spectrum [APCI⁺, m/z]: 462 [M+H]⁺. Accurate mass measurement [APCI⁺, m/z]: 461.9493 [M+NH₄]⁺, calculated mass for C₁₀H₁₁N₄O₂SeP: 461.9498.

3.2.10.1. Se-(2-(6-Amino-9H-purin-9-yl)-ethyl) O-ethyl phenylphosphonodiselenoate (16).

0.740 g as white solid in 78% yield. M.p. 157-159°C. Selected IR (KBr, cm⁻¹): 3333(m)(m), 3147(m), 1649(vs), 1596(vs), 1576(s), 1483(s), 1437(m), 1345(m), 1236(m), 1233(s), 1105(s), 1015(s), 943(s), 796(m), 740(m), 685(m), 645(m), 601(m), 549(s), 493(s). ¹H NMR (DMF-d₅, δ), 8.05 (s, 1H, adenine-H), 7.94 (s, 1H, adenine-H), 7.87-7.76 (m, 2H, Ar-H), 7.50-7.46 (m, 3H, Ar-H), 7.15 (s, 2H, NH₃), 4.35 (dt, J(H,H) = 6.6 Hz, J(P,H) = 1.7 Hz, 2H, NCH₂), 4.14-3.90 (m, 2H, OCH₂), 3.27-3.18 (m, 2H, SeCH₂), 1.22 (t, J(H,H) = 7.0 Hz, 3H, CH₃) ppm. ³¹C NMR (DMF-d₅, δ), 156.9 (adenine-C), 153.2 (adenine-C), 150.4 (adenine-C), 141.2 (adenine-C), 137.5 (Ar-C), 133.2 (Ar-C), 130.6 (Ar-C), 129.2 (Ar-C), 119.8 (adenine-C), 63.0 (OCH₂), 43.4 (NCH₃), 31.7 (SeCH₂), 15.6 (CH₃) ppm. ³¹P NMR (DMF-d₅, δ), 79.3 (s, J(P,Se) = 436 Hz, J(P,Se) = 826 Hz) ppm. ⁷⁷Se NMR (DMF-d₅, δ), 319.7 (d, J(P,Se) = 434 Hz) ppm. Mass spectrum [APCI⁺, m/z]: 476 [M+H]⁺. Accurate mass measurement [APCI⁺, m/z]: 475.9652 [M+NH₄]⁺, calculated mass for C₁₀H₁₁N₄O₂SePNa: 475.9655.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at XXXX.

References and Notes

Crystal structure of 16: colorless chip crystal 0.12 x 0.06 x 0.06 mm, \( \text{C}_1\text{H}_{18}\text{N}_2\text{OPSe}_2 \), \( M = 473.23 \), triclinic, space group P-1, \( a = 6.8207(5) \), \( b = 7.5233(5) \), \( c = 18.5628(13) \), \( \alpha = 81.694(9) \), \( \beta = 87.199(10) \), \( \gamma = 75.331(9) \), \( V = 912.59(12) \), \( Z = 2 \), \( \rho_{\text{calc}} = 0.104 \text{ g cm}^{-3} \), \( \mu = 41.526 \text{ cm}^{-1} \), 6728 reflections collected, 3187 unique \( [R_{\text{int}} = 0.0470] \), \( R_1 = 0.1145 \), \( wR_2 = 0.3620 \). CCDC 1037362. Crystal structure of 17: colorless chip crystal 0.13 x 0.04 mm, \( \text{C}_1\text{H}_{18}\text{N}_2\text{OPSe}_2 \), \( M = 487.26 \), triclinic, space group P-1, \( a = 8.7661(11) \), \( b = 11.9430(14) \), \( c = 18.963(2) \), \( \alpha = 97.052(9) \), \( \beta = 94.508(3) \), \( \gamma = 98.497(3) \), \( V = 1939.2(4) \), \( Z = 4 \), \( \rho_{\text{calc}} = 1.669 \text{ g cm}^{-3} \), \( \mu = 39.111 \text{ cm}^{-1} \), 23876 reflections collected, 7077 unique \( [R_{\text{int}} = 0.0556] \), \( R_1 = 0.0743 \), \( wR_2 = 0.2430 \). CCDC 1037363.


SIR97, 2nd Ed., pp. 1-1770.


