Accepted Manuscript

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PII: S0040-4020(15)00139-8

DOI: 10.1016/j.tet.2015.02.005

Reference: TET 26393

To appear in: *Tetrahedron*

Received Date: 17 December 2014

Revised Date: 19 January 2015

Accepted Date: 2 February 2015

Please cite this article as: Hua G, Du J, Cordes DB, Slawin AMZ, Woollins JD, Efficient Synthesis of Novel Chalcogen-Containing Derivatives of DNA Nucleobases, *Tetrahedron* (2015), doi: 10.1016/j.tet.2015.02.005.

Graphical Abstract

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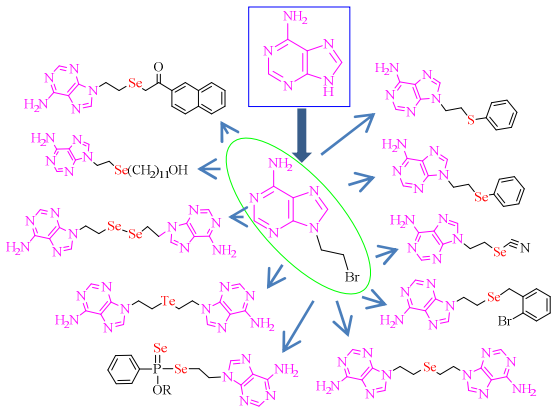

A number of novel DNA nucleobase derivatives containing chalcogens (S, Se and Te) have been synthesized in satisfactory yields.

Tetrahedron
journal homepage: www.elsevier.com

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ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
DNA nucleobases
9-(2-Bromoethyl)adenine
Adenine derivatives
Chalcogens
Woollins' reagent

ABSTRACT

The formation of a library of chalcogen-containing DNA nucleobase derivatives is presented. Reacting easily accessible 9-(2-bromoethyl)adenine with chalcogen-containing nucleophilic reagents led to a series of novel heteroatom derivatives incorporating S, Se and Te atoms prepared in satisfactory yields. Two representative X-ray structures are reported.

1. Introduction

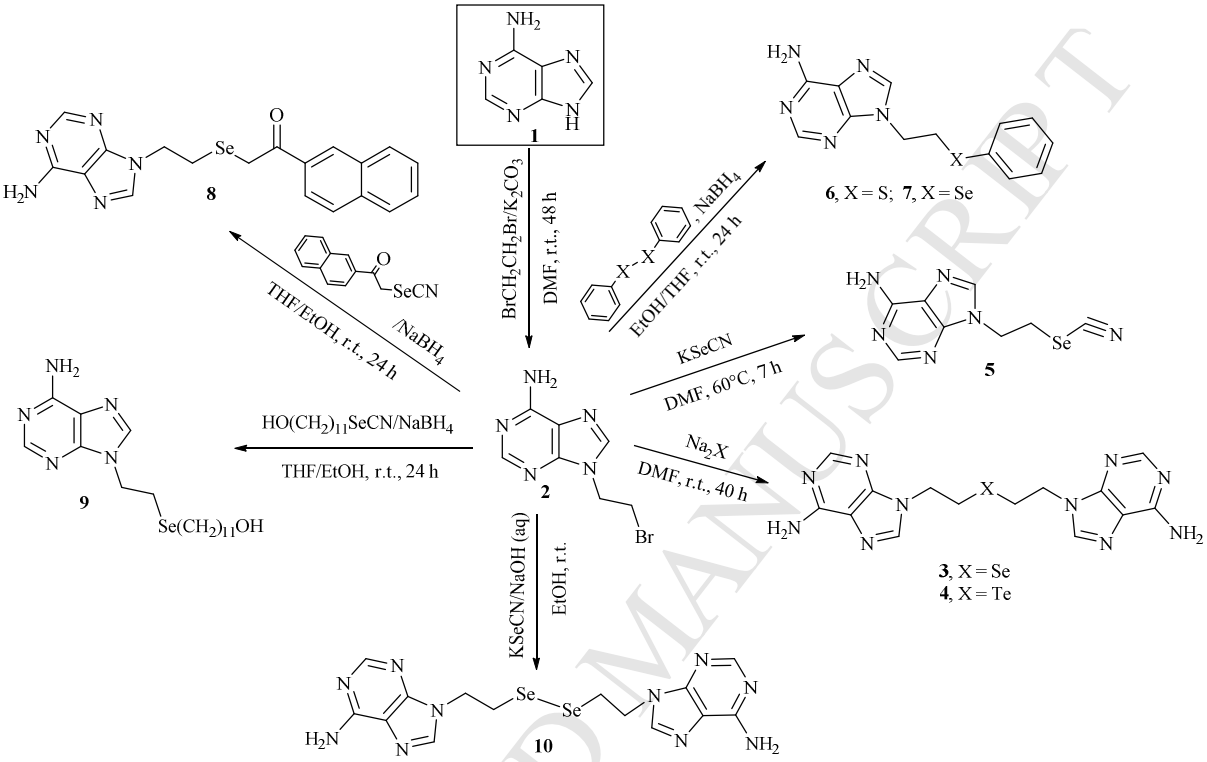
Selenium, an essential micronutrient for humans and animals,[1–6] is a trace element nutrient that functions as selenocysteine for the reduction of antioxidant enzymes such as glutathione peroxidases,[7,8] thioredoxin reductase,[9] and thyroid hormone deiodinases.[10] The entire selenoprotein gene population, 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.[12] 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 the adenine moiety provides a 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)-N_6-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 mM).[21] Furthermore, initial structure activity relationship (SAR) studies around 9-substituted adenine derivatives allowed to identify 9-(2-fluorobenzyl)-*N*6-methyl-2-trifluoromethyladenine as a potent PDE-4 inhibitor (IC50-0.042 mM), with a high selectivity *vs* PDE-3.[21] Moreover, 9-(2-fluorobenzyl)-*N*6-methyl-2-trifluoromethyladenine also elicited anti-inflammatory properties,[22] 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)-*N*6-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 K_2CO_3 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'-(selenobis(ethane-2,1-diyl))bis(9*H*-purin-6-amine) (**3**) and 9,9'-(tellurobis(ethane-2,1-diyl))bis(9*H*-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 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

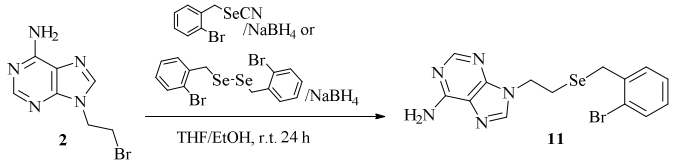
diphenyldisulfide or diphenyldiselenide with a excess of $NaBH_4$ in dry THF/EtOH at room temperature, followed by addition of 9-(2-bromoethyl)adenine followed by stirring at room temperature for 24 h gave rise to 9-(2-(phenylthio)ethyl)adenine (**6**) and (9-(2-(phenylselanyl)ethyl)adenine (**7**) 95% and 80% yields respectively. It is noteworthy that the sulfur starting material proved to be more reactive than its selenium analogue.

In addition, the reaction of 9-(2-bromoethyl)adenine with an equivalent of 1-(naphthalen-2-yl)-2-selenocyanatoethanone, which was obtained from a modified literature method,[25] and $NaBH_4$ in dry THF/EtOH gave 2-((2-(6-amino-9*H*-purin-9-yl)ethyl)selanyl)-1-(naphthalen-2-yl)ethanone (**8**) in 99% yield. Similarly, 11-((2-(6-Amino-9*H*-purin-9-yl)ethyl)selanyl)undecan-1-ol (**9**) was formed from 11-selenocyanatoundecan-1-ol with 9-(2-bromoethyl) adenine under the identical reaction conditions in 99% yield. Both reactions are very straightforward. Furthermore, the reaction of 9-(2-bromoethyl)adenine with one equivalent of potassium selenocyanate in ethanol, followed by hydrolysis with an aqueous solution of NaOH produced 2-(6-amino-9*H*-purin-9-yl)ethyl diselane (**10**) from in 87% yield.



Scheme 1. Synthesis of a series of new selenium-containing derivatives **2** - **10** of adenine

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 literature method[26]) with $NaBH_4$ 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, mixing 1-bromo-2-(selenocyanatomethyl)benzene with $NaBH_4$ 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 a more efficient starting material than 1-bromo-2-(selenocyanatomethyl)benzene for the synthesis of the targeted product with high yield. Both reactions resulted in the expected products without noticeable byproduct.

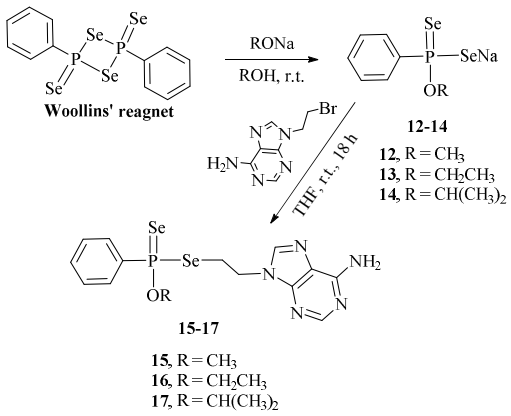


Scheme 2. Synthesis of 9-(2-((2-bromobenzyl)selanyl)ethyl)-*9H*-purin-6-amine **11**

Breaking the four-membered ring in Woollins' reagent with two molar equivalents of sodium alkanolates formed the sodium *O*-alkyl phenylphosphonodiselenoates **12** – **14** in high yields,[27] the latter were stirred with an equivalent of 9-(2-bromoethyl)adenine in dry THF overnight at room temperature to generate *Se*-(2-(6-amino-9*H*-purin-9-yl)ethyl) *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 phenylphosphonodiselenoate molecules nor decomposed selenium were detected.

Compounds **3** – **11**, **15** – **17** were 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** (see Experimental Section). The ^{77}Se NMR chemical shifts in compounds **3**, **5**, **7** – **11** fall within the range from 121.6 to 297.9 ppm, the highest ^{77}Se NMR chemical shift value is one of two isomers in compound **9** with a long alkyl chain alcohol group, whilst the lowest ^{77}Se NMR chemical shift value is the compound **3** with a symmetric conformation at the Se atom centre. Surprisingly, one of two isomers in compound **9** has very low ^{77}Se NMR chemical shift (140.0 ppm). Another sample having a high ^{77}Se NMR chemical shift value (282.8 ppm) is compound **10**, in which also adopts a symmetric conformation around the Se-Se bridge. With the similar conformation as compound **3**, the ^{125}Te NMR chemical shift value in compound **4** is 199.3 ppm. The ^{31}P 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 ^{31}P-^{77}Se

coupling constants in the ranges of 434 – 439 Hz and 825 – 831 Hz, indicating the presence of both a 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, indicated the presence of adenine ring in the molecules. The presence of the adenine rings can be further confirmed by their special five carbon chemical shift values in the ^{13}C NMR spectra.



Scheme 3. Synthesis of Se-(2-(6-amino-*9H*-purin-9-yl)ethyl) *O*-alkyl phenylphosphonodiselenoates **15 - 17**

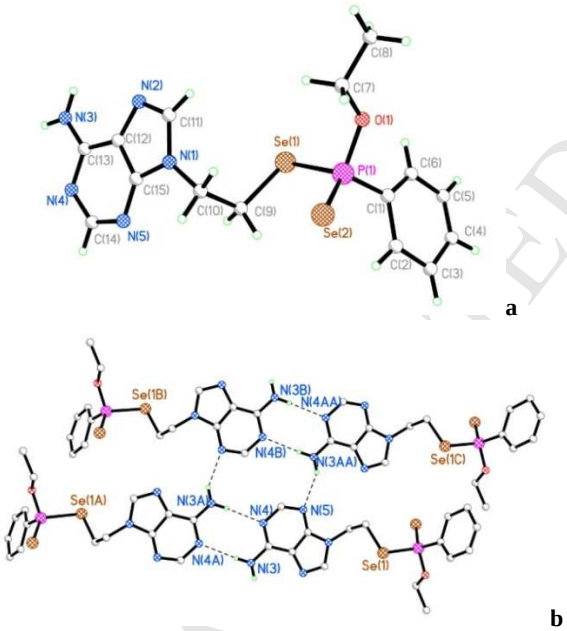


Figure 1. (a) Single crystal X-ray structure of 1-(n aphthalen-2-yl)-2-selenocyanatoethanone **16.** Selected bond lengths (Å) and angles (˚) (esds in parentheses): Se(1)-P(1) 2.253(6), Se(2)-P(1) 2.118(5), Se(1)-C(9) 1.936(14), P(1)-C(1) 1.640(2), P(1)-O(1) 1.612(13), O(1)-C(7) 1.420(3); P(1)-Se(1)-C(9) 100.1(5), Se(1)-P(1)-O(1) 103.5(6), Se(2)-P(1)-O(1) 113.2(6), O(1)-P(1)-C(1) 101.8(9), 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 intermomelecule within **16**.

Single crystals of **16** (colorless) and **17** (colorless) obtained from diffusion of hexane into dichloromethane solutions of the compounds in air at room temperature were investigated by X-ray diffraction method and the structures of two compounds were determined.[28] The structures of **16** (Figure 1a) and **17** (Figure 2a) are in the triclinic space group *P-1* though **17** contains two independent molecules. The structural conformations have the phenyl ring and the adenine ring inclined to one another at 75.85° for **16** and 55.45° for **17**. The P(1)-Se(1)-Se(2) mean planes are nearly perpendicular to the Se(1)-C-C mean planes (88.26° for **16** and 86.35° for **17**). The P(1)-Se(1) and P(1)-Se(2) distances [2.253(6) and 2.118(5) Å for **16**, 2.246(2) and 2.081(2) Å for **17**] are typical P-Se single bond and P=Se double bond characters, comparable to that in the similar structures.[29]

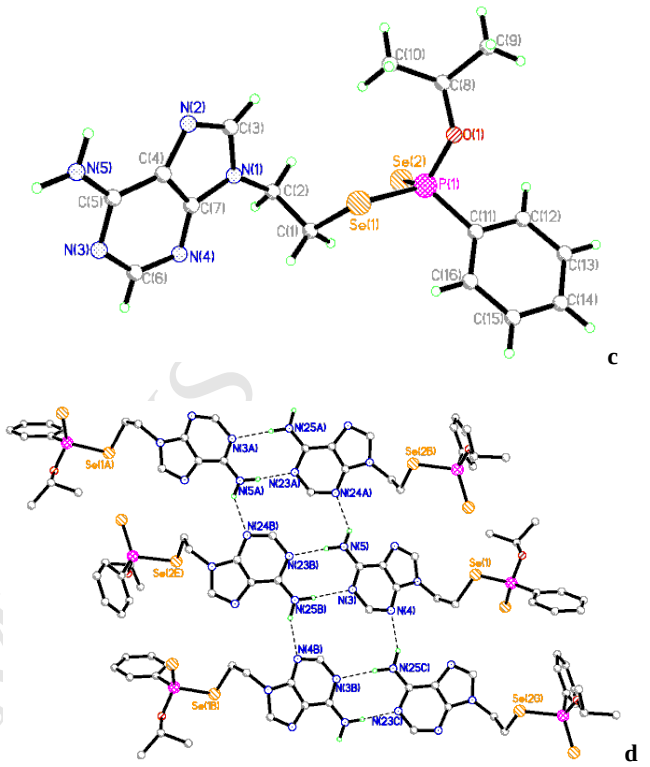


Figure 2. (c) Single crystal X-ray structure of 1-(n aphthalen-2-yl)-2-selenocyanatoethanone **17.** Selected bond lengths (Å) and angles (˚) (esds in parentheses): Se(1)-P(1) 2.246(2), Se(2)-P(1) 2.081(2), Se(1)-C(9) 1.938(8), P(1)-C(11) 1.774(8), P(1)-O(1) 1.609(8), O(1)-C(8) 1.428(11); P(1)-Se(1)-C(1) 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 intermomelecule 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, diphenyldisulfide/ $NaBH_4$, diphenyldiselenide/ $NaBH_4$, 1-(naphthalen-2-yl)-2-selenocyanateethanone 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 Woollins' 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

Unless otherwise stated, all reactions were carried out under an oxygen free nitrogen atmosphere using pre-dried solvents and standard Schlenk techniques, subsequent chromatographic and work up procedures were performed in air. ^{1}H (270 MHz), ^{13}C (67.9 MHz), ^{31}P-{^{1}H} (109 MHz) and ^{77}Se-{^{1}H} (51.4 MHz referenced to external Me_2Se) NMR spectra were recorded at 25 °C (unless stated otherwise) on a JEOL GSX 270. IR spectra were recorded as KBr pellets in the range of 4000-250 cm^{-1} on a Perkin-Elmer 2000 FTIR/Raman spectrometer. Mass spectrometry was performed by the EPSRC National Mass Spectrometry Service Centre, Swansea and the University of St Andrews Mass Spectrometry Service. X-ray crystal structures were determined for compounds **16** and **17** at -148(1) °C on a Rigaku ACTOR-SM, Saturn 724 CCD area detector [the St Andrews Automated Robotic Diffractometer (STANDARD)][31] with SHINE optic using Mo Ka radiation (k = 0.71073 A). The data were corrected for Lorentz, polarisation and absorption. The data was collected and processed using CrystalClear (Rigaku).[32] The structures were solved by direct methods[33] and expanded using Fourier techniques.[34] Hydrogen atoms were refined using the riding model. All calculations were performed using the CrystalStructure[35] and SHELXL 97.[36] These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk. CCDC 985908-985919

3.2. Synthesis

3.2.1. Synthesis of 9,9'-(Selenobis(ethane-2,1-diyl))bisadenine (3).

A mixture of sodium selenide (0.127 g, 1.0 mmol) and 9-(2-bromoethyl)adenine (0.482 g, 2.0 mmol) in dry DMF (10 mL) was stirred at room temperature for 40 h. Upon filtering to remove the solid the filtrate was diluted with water and extracted with dichloromethane (3x50 mL). The combined organic layer was dried over Na_2SO_4. After evaporative removal of solvent the crude product was purified by column chromatography (silica gel) with 15% MeOH in dichloromethane as eluent to give 0.385 g of the titled compound **3** as a peach yellow solid in 95% yield. M.p. 193-195°C. Selected IR (KBr, cm^{-1}): 1680(s), 1655(s), 1602(s), 1574(m), 1485(s), 1417(s), 1328(s), 1308(s), 1252(m), 1224(m), 1074(m), 796(m), 650(s). ^{1}H NMR (DMF-d_7, δ), 8.23 (s, 2H, adenine-H), 8.22 (s, 2H, adenine-H), 7.35 (s, 4H, NH_2), 4.53 (t, *J*(H,H) = 6.9 Hz, 4H, CH_2), 3.18 (t, *J*(H,H) = 6.9 Hz, 4H, CH_2) ppm. ^{13}C NMR (DMF-d_7, δ), 156.6 (adenine-C), 152.9 (adenine-C), 150.1 (adenine-C), 141.1 (adenine-C), 119.5 (adenine-C), 43.7 (CH_2), 22.5 (CH_2) ppm. ^{77}Se NMR (DMF-d_7, δ), 121.6 ppm. Mass spectrum [CI$^+$, m/z]: 405 [M+H]$^+$. Accurate mass measurement [CI$^+$, m/z]: 405.0799 [M+H]$^+$, calculated mass for $C_{14}H_{17}N_{10}Se$: 405.0797.

3.2.2. Synthesis of 9,9'-(Tellurobis(ethane-2,1-diyl))bisadenine (4).

A suspension of sodium telluride (0.176 g, 1.0 mmol) and 9-(2-bromoethyl)adenine (0.482 g, 2.0 mmol) in dry DMF (10 mL) was stirred at room temperature for 40 h. Upon filtering to remove the solid the filtrate was diluted with water and extracted with dichloromethane (3x50 mL). The combined organic layer was dried over Na_2SO_4. After evaporative removal of solvent the crude product was purified by column chromatography (silica gel) with 15% MeOH in dichloromethane as eluent to give 0.310 g of the titled compound **4** as a mustard yellow solid in 68% yield. M.p. 196-198°C. Selected IR (KBr, cm^{-1}): 1654(s), 1598(s), 1573(m), 1482(s), 1414(s), 1331(s), 1308(s), 1247(s), 1072(m), 1008(m), 796(m), 724(m), 645(s). ^{1}H NMR (DMF-d_7, δ), 8.22 (s, 2H, adenine-H), 8.20 (s, 2H, adenine-H), 7.32 (s, 4H, NH_2), 4.59 (t, *J*(H,H) = 6.9 Hz, 4H, CH_2), 3.21(t, *J*(H,H) = 6.9 Hz, 4H, CH_2) ppm. ^{13}C NMR (DMF-d_7, δ), 156.6 (adenine-C), 152.9 (adenine-C), 150.0 (adenine-C), 140.8 (adenine-C), 119.5 (adenine-C), 45.7(CH_2), 1.9(CH_2) ppm. ^{125}Te NMR (DMF-d_7, δ), 199.3 ppm. Mass spectrum [CI$^+$, m/z]: 455 [M+H]$^+$. Accurate mass measurement [CI$^+$, m/z]: 455.0681 [M+H]$^+$, calculated mass for $C_{14}H_{17}N_{10}Te$: 455.0695.

3.2.3. Synthesis of 9-(2-Selenocyanatoethyl)adenine (5).

A suspension of potassium selenocyanate (0.145 g, 1.0 mmol) in dry acetone (30 mL) was heated to 60°C, and 9-(2-bromoethyl)adenine (0.241 g, 1.0 mmol) in dry acetone (5 mL) was added dropwise. The resulting mixture was stirred at 60 °C for another 7 h. Upon cooling to room temperature the mixture was hydrolysed by adding water (10 mL) and extracted with diethyl ether (2x30 mL). The ethereal layers were combined and dried over $MgSO_4$ overnight. The solvent was evaporated *in vacuo* and the residue was purified by silica gel column (dichloromethane as eluent) to give 0.250 g of the titled compound **5** as a pale purple solid in 93% yield. M.p. 210-212°C. Selected IR (KBr, cm^{-1}): 1675(s), 1645(m), 1607(s), 1573(m), 1478(m), 1420(m), 1331(m), 1306(m), 1235(m), 1072(m), 1016(m), 670(m), 599(m), 540(m), 504(m). ^{1}H NMR (DMF-d_7, δ), 8.25 (s, 1H, adenine-H), 8.22 (s, 1H, adenine-H), 7.33 (s, 2H, NH_2), 4.74 (t, *J*(H,H) = 6.6 Hz, 2H, NCH_2), 3.73 (t, *J*(H,H) = 6.6 Hz, 2H, $SeCH_2$) ppm. ^{13}C NMR (DMF-d_7, δ), 156.6 (adenine-C), 152.8 (adenine-C), 150.2 (adenine-C), 141.1 (adenine-C), 119.5 (adenine-C), 103.4 (C≡N), 44.2 (NCH_2), 29.3 ($SeCH_2$) ppm. ^{77}Se NMR (DMF-d_7, δ), 197.1 ppm. Mass spectrum [CI$^+$, m/z]: 269 [M+H]$^+$. Accurate mass measurement [CI$^+$, m/z]: 269.0046 [M+H]$^+$, calculated mass for $C_8H_8N_6SeH$: 269.0048.

3.2.4. Synthesis of 9-(2-(Phenylthio)ethyl)adenine (6).

A suspension of diphenyldisulfide (0.107 g, 0.5 mmol) and $NaBH_4$ (0.041 g, 1.1 mmol) in dry THF (30 mL) and dry EtOH (5 mL) 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 silica gel column (1 : 4 methanol/dichloromethane as eluent) to give 0.256 g of the titled compound **6** as a white solid in 95% yield. M.p. 150-152°C. Selected IR (KBr, 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). ^{1}H NMR (DMF-d_7, δ), 8.27 (s, 1H, adenine-H), 8.24 (s, 1H, adenine-H), 7.48 (d, *J*(H,H) = 8.0 Hz, 1H, Ar-H), 7.41 (d, *J*(H,H) = 8.0 Hz, 1H, Ar-H), 7.35 (s, 2H, NH_2), 7.26-7.21 (m, 3H, Ar-H), 4.71 (t, *J*(H,H) = 6.9 Hz, 2H, NCH_2), 3.59 (s, 2H, SCH_2) ppm. ^{13}C NMR (DMF-d_7, δ), 156.6 (adenine-C), 153.0 (adenine-C), 150.2 (adenine-C), 141.3 (adenine-C), 135.3 (Ar-C), 129.3 (Ar-C), 129.0 (Ar-C), 126.4 (Ar-C), 119.5 (adenine-C), 45.3 (NCH_2), 31.4 ($SeCH_2$) ppm. Mass spectrum [CI$^+$, m/z]: 272 [M+H]$^+$. Accurate mass measurement [CI$^+$, m/z]: 272.0962 [M+H]$^+$, calculated mass for $C_{13}H_{13}N_5SH$: 272.0964.

3.2.5. Synthesis of (9-(2-(Phenylselanyl)ethyl)adenine (7).

A suspension of diphenyldiselenide (0.156 g, 0.5 mmol) and $NaBH_4$ (0.041 g, 1.1 mmol) in dry THF (30 mL) and dry EtOH (5 mL) 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 silica gel column (1 : 4 methanol/dichloromethane as eluent) to give 0.256 g of the titled compound **7** as a white solid in 80% yield. M.p. 149-150°C. Selected IR (KBr, cm^{-1}): 1677(s), 1643(m), 1602(vs), 1575(m), 1478(s), 1417(s), 1329(m), 1305(s), 1252(m), 1229(m), 1071(m), 1-19(m), 741(m), 691(m). ^{1}H NMR (DMF-d_7, δ), 8.26 (s, 1H, adenine-H), 8.24 (s, 1H, adenine-H), 7.63 (d, *J*(H,H) = 8.0 Hz, 1H, Ar-H), 7.55 (d, *J*(H,H) = 8.0 Hz, 1H, Ar-H), 7.36 (s, 2H, NH_2), 7.32-7.17 (m, 3H, Ar-H), 4.70 (t, *J*(H,H) = 6.9 Hz, 2H, NCH_2), 3.98 (s, 2H, $SeCH_2$) ppm. ^{13}C NMR (DMF-d_7, δ), 156.7 (adenine-C), 152.9 (adenine-C), 150.1 (adenine-C), 141.3 (adenine-C), 141.1 (Ar-C), 132.1 (Ar-C), 129.5 (Ar-C), 127.1 (Ar-C), 119.5 (adenine-C),

45.2 (NCH_2), 31.4 ($SeCH_2$) ppm. ^{77}Se NMR (DMF-d_7, δ), 267.7 ppm. Mass spectrum [CI^+, m/z]: 320 $[M+H]^+$. Accurate mass measurement [CI^+, m/z]: 320.0408 $[M+H]^+$, calculated mass for $C_{13}H_{13}N_5SeH$: 320.0409.

3.2.6. Synthesis of 2-((2-(6-Amino-9H-purin-9-yl)ethyl)selanyl)-1-(naphthalen-2-yl)ethanone (8).

A suspension of potassium selenocyanate (1.50 g, 10.3 mmol) in dry acetone (30 mL) was heated to 60 °C, and 2-bromo-1-(naphthalen-2-yl)ethanone (2.125 g, 8.57 mmol) in acetone (10 mL) was added dropwise. The resulting mixture was stirred at 60 °C for another 5 h. Upon cooling to room temperature the mixture was hydrolysed by adding water (10 mL) and extracted ether (2 x 30 mL). The ethereal layers were combined and dried over $MgSO_4$ overnight. The solvent was evaporated *in vacuo* and the residue was purified by silica gel column (dichloromethane as eluent) to give 2.74 g of 1-(naphthalen-2-yl-)-2-selenocyanatoethanone as a pale yellow solid in 99% yield. M.p. 100-102°C. Selected IR (KBr, cm^{-1}): 2151(m), 1656(s), 1624(m), 1468(m), 1383(m), 1356(m), 1299(m), 1177(s), 1123(m), 996(m), 941(m), 850(m), 821(s), 744(m), 586(m), 474(s). ^{1}H NMR (CD_2Cl_2, δ), 8.43 (s, 1H, Nap-H), 7.96-7.88 (m, 4H, Nap-H), 7.70-7.59 (m, 2H, Nap-H), 5.00 (s, 2H, $SeCH_2$) ppm. ^{13}C NMR (CD_2Cl_2, δ), 193.3 (C=O), 136.2 (Nap-C), 132.3 (Nap-C), 131.3 (Nap-C), 131.2 (Nap-C), 129.8 (Nap-C), 129.6 (Nap-C), 129.1 (Nap-C), 128.0 (Nap-C), 127.4 (Nap-C), 123.4 (Nap-C), 102.0 (C≡N), 39.1 (Se-C) ppm. ^{77}Se NMR (CD_2Cl_2, δ), 155.7 ppm. Mass spectrum [CI^+, m/z]: 293 $[M+NH_4]^+$. Accurate mass measurement [CI^+, m/z]: 293.0191 $[M+NH_4]^+$, calculated mass for $C_{13}H_9NOSeNH_4$: 293.188.

A mixture of 1-(naphthalen-2-yl)-2-selenocyanatoethanone (0.275 g, 1.0 mmol) and $NaBH_4$ (0.041 g, 1.1 mmol) in dry THF (30 mL) and dry EtOH (5 mL) 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 (1 : 4 methanol/dichloromethane as eluent) to give 0.350 g of the titled compound **8** as a pal purple solid in 85% yield. M.p. 178-180°C. Selected IR (KBr, cm^{-1}): 1672(vs), 1600(vs), 1575(s), 1478(m), 1418(m), 1327(m), 1306(s), 1228(m), 1070(m), 1011(m), 662(s), 598(m), 542(m). ^{1}H NMR (DMF-d_7, δ), 8.73 (s, 1H, Nap-H), 8.26 (s, 1H, adenine-H), 8.24 (s, 1H, adenine-H), 8.05-8.03 (m, 4H, Nap-H), 7.70-7.61 (m, 2H, Nap-H), 7.38 (s, 2H, NH_2), 3.58 (s, 2H, $SeCH_2$), 2.92 (t, *J*(H,H) = 6.1 Hz, 2H, NCH_2), 2.75 (t, *J*(H,H) = 6.1 Hz, 2H, $SeCH_2$), ppm. ^{13}C NMR (CD_2Cl_2, δ), 193.2 (C=O), 162.7 (adenine-C), 162.2 (adenine-C), 161.8 (adenine-C), 156.6 (adenine-C), 152.9 (adenine-C), 141.6 (Nap-C), 141.3 (Nap-C), 130.6 (Nap-C), 129.8 (Nap-C), 128.7 (Nap-C), 128.5 (Nap-C), 127.9 (Nap-C), 127.1 (Nap-C), 123.7 (Nap-C), 119.5 (Nap-C), 97.6 (C≡N), 66.5 (Se-C), 45.2 (N-C), 31.3 (Se-C) ppm. ^{77}Se NMR (DMF-d_7, δ), 197.2 ppm. Mass spectrum [CI^+, m/z]: 412 $[M+H]^+$. Accurate mass measurement [CI^+, m/z]: 412.0670 $[M+H]^+$, calculated mass for $C_{19}H_{17}N_5OSeH$: 412.0671.

3.2.7. Synthesis of 1-((2-(6-Amino-9H-purin-9-yl)ethyl)selanyl)undecan-1-ol (9).

A mixture of potassium selenocyanate (2.88 g, 20 mmol) in dry acetone (50 mL) was heated to 60 °C, and 2-bromo-11undecanol (5.04 g, 20 mmol) in acetone (20 mL) was added dropwise to the mixture. The resulting mixture was stirred at 60 °C for another 5 h. Upon cooling to room temperature the mixture was hydrolysed by adding water (30 mL) and extracted with diethyl ether (2 x 50 mL). The ethereal layers were combined and dried over $MgSO_4$ overnight. The solvent was evaporated *in vacuo* and the residue was purified by silica gel column chromatography (dichloromethane as eluent) to give 5.50 g of 11-selenocyanatoundecan-1-ol as a pale yellow oil in 99% yield. Selected IR (KBr, cm^{-1}): 2927(s), 2854(s), 2151(m), 1463(m), 1056(m), 722(m), 628(m), 519(w). ^{1}H NMR (CD_2Cl_2, δ), 5.30 (s, 1H, OH), 3.53 (t, *J*(H,H) = 7.4 Hz, 2H, OCH_2), 3.02 (t, *J*(H,H) = 7.4 Hz, 2H, $SeCH_2$), 1.91-1.79 (m, 4H, CH_2), 1.55-1.28 (m, 14H, CH_2) ppm. ^{13}C NMR (CD_2Cl_2, δ), 101.7 (C≡N), 62.7 (OCH_2), 34.4 ($SeCH_2$), 32.9 (CH_2), 30.9 (CH_2), 29.9 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 29.1 (CH_2), 28.9 (CH_2), 25.8 (CH_2) ppm. ^{77}Se NMR (CD_2Cl_2, δ), 207.5 ppm. Mass spectrum [ES^+, m/z]: 300 $[M+Na]^+$. Mass spectrum [CI^+, m/z]: 278 $[M+H]^+$. Accurate mass measurement [CI^+, m/z]: 278.1018 $[M+H]^+$, calculated mass for $C_{12}H_{23}NOSeH$: 278.1018.

A suspension of 11-selenocyanatoundecan-1-ol (0.277 g, 1.0 mmol) and $NaBH_4$ (0.041 g, 1.1 mmol) in dry THF (30 mL) and dry EtOH (5 mL) 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 of the titled compound **9** as a white cream solid in 98% yield. M.p. 118-119°C. Two diastereoisomers were found in ca. 2 : 1 intensity ratio. Selected IR (KBr, cm^{-1}): 1674(m), 1642(m), 1601(s), 1575(m), 1470(s), 1419(m), 1305(s), 1253(m), 1059(s), 793(m), 716(m). ^{1}H NMR (DMF-d_7, δ), 8.24 (s, 1H, adenine-H), 8.21 (s, 1H, adenine-H), 7.32 (s, 1H, adenine-H), 7.26 (s, 1H, adenine-H), 6.81 (s, 2H, NH_2), 6.80 (s, 2H, NH_2), 4.92 (t, *J*(H,H) = 6.1 Hz, 2H, NCH_2), 4.50 (t, *J*(H,H) = 6.1 Hz, 2H, NCH_2), 4.39 (t, *J*(H,H) = 6.1 Hz, 2H, $SeCH_2$), 4.04 (t, *J*(H,H) = 6.1 Hz, 2H, $SeCH_2$), 3.49 (t, *J*(H,H) = 6.1 Hz, OCH_2), 3.11 (t, *J*(H,H) = 6.1 Hz, 2H, $SeCH_2$), 2.95 (t, *J*(H,H) = 6.1 Hz, OCH_2), 2.75 (s, 1Hx2, OH), 2.58 (t, *J*(H,H) = 6.1 Hz, 2H, $SeCH_2$), 1.76-1.30 (m, 18Hx2, CH_2) ppm. ^{13}C NMR (DMF-d_7, 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 (OCH_2), 45.2 ($SeCH_2$), 44.1 ($SeCH_2$), 33.2 (CH_2), 31.3 (CH_2), 30.9 (CH_2), 29.9 (CH_2), 29.8 (CH_2), 29.7 (CH_2), 29.6 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 26.1 (CH_2), 23.5 (CH_2), 22.3 (CH_2) ppm. ^{77}Se NMR (DMF-d_7, δ), 297.9, 140.0 ppm. Mass spectrum [CI^+, m/z]: 414 $[M+H]^+$. Accurate mass measurement [CI^+, m/z]: 414.1759 $[M+H]^+$, calculated mass for $C_{18}H_{31}N_5OSeH$: 414.1767.

3.2.8. Synthesis of 2-(6-Amino-9*H*-purin-9-yl)ethyl diselane (10).

To a suspension of 9-(2-bromoethyl)adenine (0.723 g, 3.0 mmol) in dry ethanol (50 mL) 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 $MgSO_4$. The organic residue was further purified by silica gel chromatography (1 : 5 ethyl acetate / dichloromethane as eluent) to give 0.420 g of the titled compound **10** as a off-white solid in 87% isolated yield. M.p. 159-161°C. Selected IR (KBr, cm^{-1}): 1688(s), 1648(s), 1603(s), 1570(m), 1513(m), 1477(m), 1419(m), 1370(m), 1332(m), 1296(s), 1248(m), 1219(m), 1079(m), 998(m), 970(m), 887(m), 793(m), 712(s), 641(s), 592(m), 344(m). ^{1}H NMR (DMF-d_7, δ), 8.57 (s, 2H, adenine-H), 8.30 (s, 2H, adenine-H), 7.54 (s, 4H, adenine-NH_2), 6.22 (t, *J*(H,H) = 6.9 Hz, 4H, NCH_2), 3.67 (s, 4H, $SeCH_2$) ppm. ^{13}C NMR (DMF-d_7, δ), 162.7 (adenine-C), 156.8 (adenine-C), 153.6 (adenine-C), 139.0 (adenine-C), 119.9 (adenine-C), 45.3 (NCH_2), 31.4 ($SeCH_2$) ppm. ^{77}Se NMR (DMF-d_7, δ), 282.8 ppm. Mass spectrum [CI^+, m/z]: 485 $[M+H]^+$. Accurate mass measurement [CI^+, m/z]: 484.9979 $[M+H]^+$, calculated mass for $C_{14}H_{16}N_{10}SeH$: 484.9965.

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

***Method 1*:** 1,2-Bis(2-bromobenzyl)diselane was prepared by a modified literature method.[26] A suspension of 1,2-bis(2-bromobenzyl)diselane (0.250 g, 0.5 mmol) and $NaBH_4$ (0.041 g, 1.1 mmol) in dry THF (30 mL) and dry EtOH (5 mL) 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 (1 : 4 methanol/dichloromethane as eluent) to give 0.354 g of the titled compound **11** as an yellowish white solid in 86% yield. ***Method 2*****:** A mixture of 1-bromo-2-(selenocyanatomethyl)benzene (0.275 g, 1.0 mmol) and $NaBH_4$ (0.041 g, 1.1 mmol) in dry THF (30 mL) and dry EtOH (5 mL) 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 of the titled compound **11** as an yellowish white solid in 61% yield. M.p. 118-119°C. Selected IR (KBr, cm^{-1}): 1669(s), 1599(vs), 1477(s), 1416(s), 1325(m), 1306(s), 1230(m), 1069(m), 1021(m), 797(m), 759(m), 657(m). ^{1}H NMR (DMF-d_7, δ), 8.26 (s, 1H, adenine-H), 8.23 (s, 1H, adenine-H), 7.65-7.33 (m, 4H, Ar-H), 7.54 (s, 2H, NH_2), 4.70 (t, *J*(H,H) = 6.9 Hz, 2H, CH_2), 4.05 (t, *J*(H,H) = 6.9 Hz, 2H, CH_2), 3.59 (s, 2H, CH_2) ppm. ^{13}C NMR (DMF-d_7, 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 (NCH_2), 31.3 ($SeCH_2$), 26.9 ($SeCH_2$) ppm. ^{77}Se NMR (DMF-d_7, δ), 225.4 ppm. Mass spectrum [CI^+, m/z]: 409 $[M+H]^+$. Accurate mass measurement [CI^+, m/z]: 408.9705 $[M+NH_4]^+$, calculated mass for $C_{14}H_{14}BrN_5SeH$: 408.9708.

3.2.10. General procedure for the synthesis of *Se*-(2-(6-amino-9*H*-purin-9-yl)ethyl) *O*-alkyl phenylphosphonodiselenoates 15 - 17.

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 Woollins' 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 THF (30 mL) 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-9*H*-purin-9-yl)ethyl) *O*-methyl 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). ^{1}H NMR (DMF-d_7, 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_2), 5.14 (d, J(P,H) = 12.0 Hz, 3H, OCH_3), 4.54-4.49 (m, 2H, NCH_2), 3.42-3.29 (m, 2H, $SeCH_2$) ppm. ^{13}C NMR (DMF-d_7, δ), 157.0 (adenine-C), 153.8 (adenine-C), 153.0 (adenine-C), 141.5 (adenine-C), 139.3 (Ar-C), 133.3 (Ar-C), 130.7 (Ar-C), 128.0 (Ar-C), 119.7 (adenine-C), 53.1 (OCH_2), 43.5 (NCH_2), 31.7 ($SeCH_2$) ppm. ^{31}P NMR (DMF-d_7, δ), 83.6 (s, *J*(P,Se) = 439 Hz, *J*(P,Se) = 831 Hz) ppm. ^{77}Se NMR (DMF-d_7, 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 $[M+NH_4]^+$, calculated mass for $C_{14}H_{16}N_5OPSe_2H$: 461.9498.

3.2.10.1. *Se*-(2-(6-Amino-9*H*-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}): 3333.9(m), 3147(m), 1649(vs), 1596(vs), 1576(s), 1483(s), 1437(m), 1416(m), 1354(m), 1326(m), 1309(m), 1223(s), 1105(m), 1015(s), 943(s), 796(m), 740(m), 685(m), 645(m), 601(m), 549(s), 493(s). ^{1}H NMR (DMF-d_7, 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, NH_2), 4.35 (dt, *J*(H,H) = 6.6 Hz, *J*(P,H) = 1.7 Hz, 2H, NCH_2), 4.14-3.90 (m, 2H, OCH_2), 3.27-3.18 (m, 2H, $SeCH_2$), 1.22 (t, *J*(H,H) = 7.0 Hz, 3H, CH_3) ppm. ^{13}C NMR (DMF-d_7, 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), 63.6 (OCH_2), 43.4 (NCH_2), 31.7 ($SeCH_2$), 15.6 (CH_3) ppm. ^{31}P NMR (DMF-d_7, δ), 79.3 (s, *J*(P,Se) = 436 Hz, *J*(P,Se) = 826 Hz) ppm. ^{77}Se NMR (DMF-d_7, δ), 319.7 (d, *J*(P,Se) = 434 Hz), -97.9 (d, *J*(P,Se) = 825 Hz) ppm. Mass spectrum [$APCI^+$, m/z]: 476 $[M+H]^+$. Accurate mass measurement [$APCI^+$, m/z]: 475.9652 $[M+NH_4]^+$, calculated mass for $C_{15}H_{18}N_5OPSe_2H$: 475.9655.

3.2.10.1. *Se*-(2-(6-Amino-9*H*-purin-9-yl)ethyl) *O*-isopropyl phenylphosphonodiselenoate (17).

0.335 g as white solid in 69% yield. M.p. 141-142°C. Selected IR (KBr, cm^{-1}): 3319(m), 3141(m), 1649(s), 1589(s), 1574(m), 1480(m), 1416(m), 1327(m), 1305(m), 1246(m), 1225(m), 1098(s), 962(s), 885(m), 795(m), 733(m), 687(m), 644(m), 546(s), 494(m). ^{1}H NMR (DMF-d_7, δ), 8.38 (s, 1H, adenine-H), 8.25 (s, 1H, adenine-H), 8.14-8.06 (m, 2H, Ar-H), 7.81-7.73 (m, 3H, Ar-H), 7.53 (s, 2H, NH_2), 5.16-5.03 (m, 1H, OCH), 4.74-4.58 (m, 2H, NCH_2), 3.70-3.47 (m, 2H, $SeCH_2$), 1.54 (dd, *J*(H,H) = 6.3 Hz, *J*(P,H) = 1.6 Hz, 6H, CH_3) ppm. ^{13}C NMR (DMF-d_7, δ), 157.1 (adenine-C), 153.3 (adenine-C), 150.5 (adenine-C), 141.7 (adenine-C), 138.3 (Ar-C), 137.0 (Ar-C), 130.6 (Ar-C), 129.3 (Ar-C), 119.9 (adenine-C), 73.9 (OCH), 43.5 (NCH_2), 32.1 ($SeCH_2$), 23.9 (CH_3) ppm. ^{31}P NMR (DMF-d_7, δ), 76.8 (s, *J*(P,Se) = 434 Hz, *J*(P,Se) = 825 Hz) ppm. ^{77}Se NMR (DMF-d_7, δ), 338.6 (d, *J*(P,Se) = 434 Hz), -92.1 (d, *J*(P,Se) = 825 Hz) ppm. Mass spectrum [ESI^+, m/z]: 490 $[M+H]^+$; 512 $[M+Na]^+$. Accurate mass measurement [ESI^+, m/z]: 489.9800 $[M+H]^+$, calculated mass for $C_{16}H_{20}N_5OPSe_2H$: 489.9814; Accurate mass measurement [ESI^+, m/z]: 511.9615 $[M+Na]^+$, calculated mass for $C_{16}H_{20}N_5OPSe_2Na$: 511.9634.

Acknowledgments

The authors are grateful to the University of St Andrews for financial support and the EPSRC National Mass Spectrometry Service Centre (Swansea) for mass spectral measurements.

Supplementary data

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

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Supporting Information

Efficient Synthesis of Novel Chalcogen-Containing Derivatives of DNA Nucleobases

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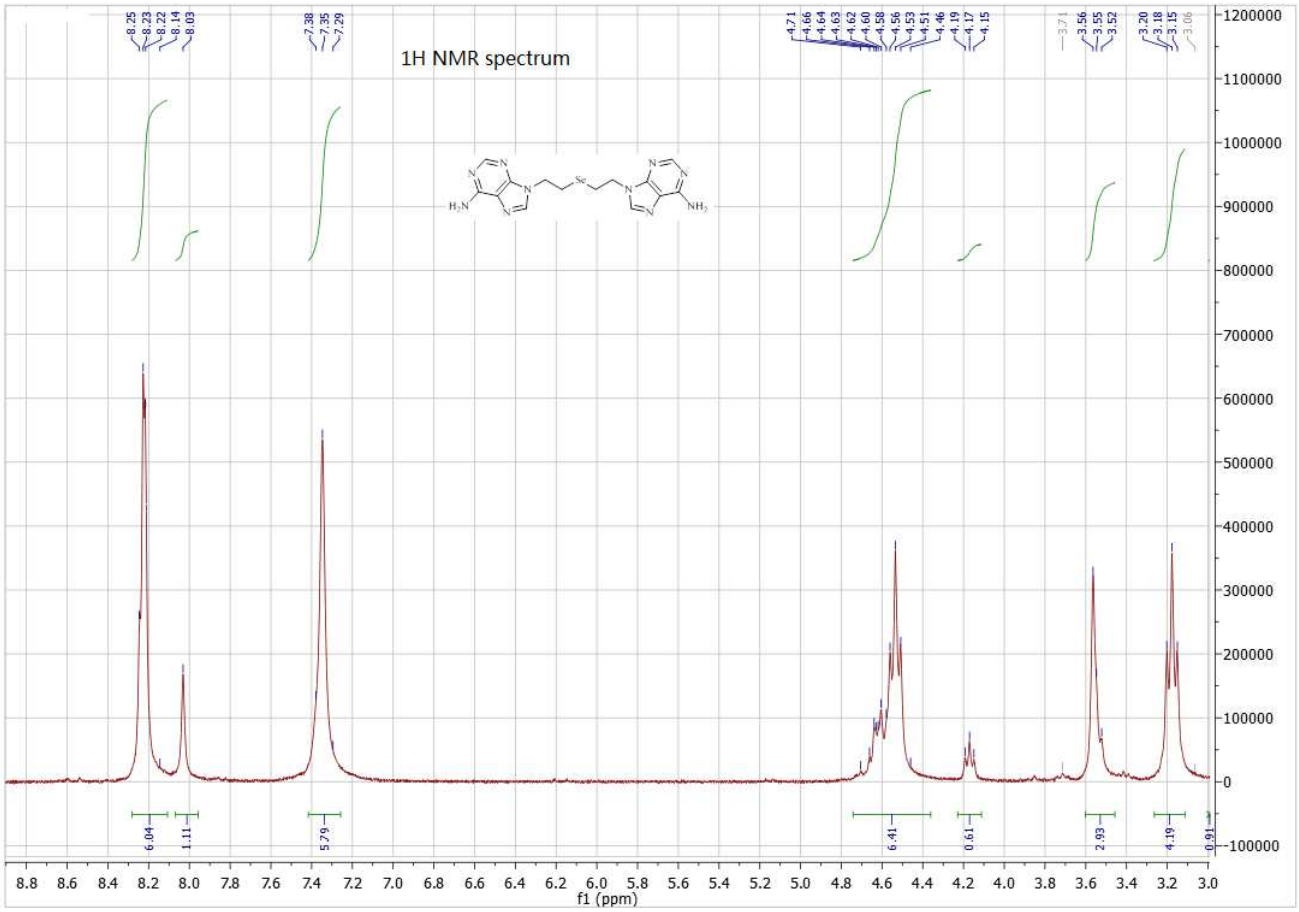
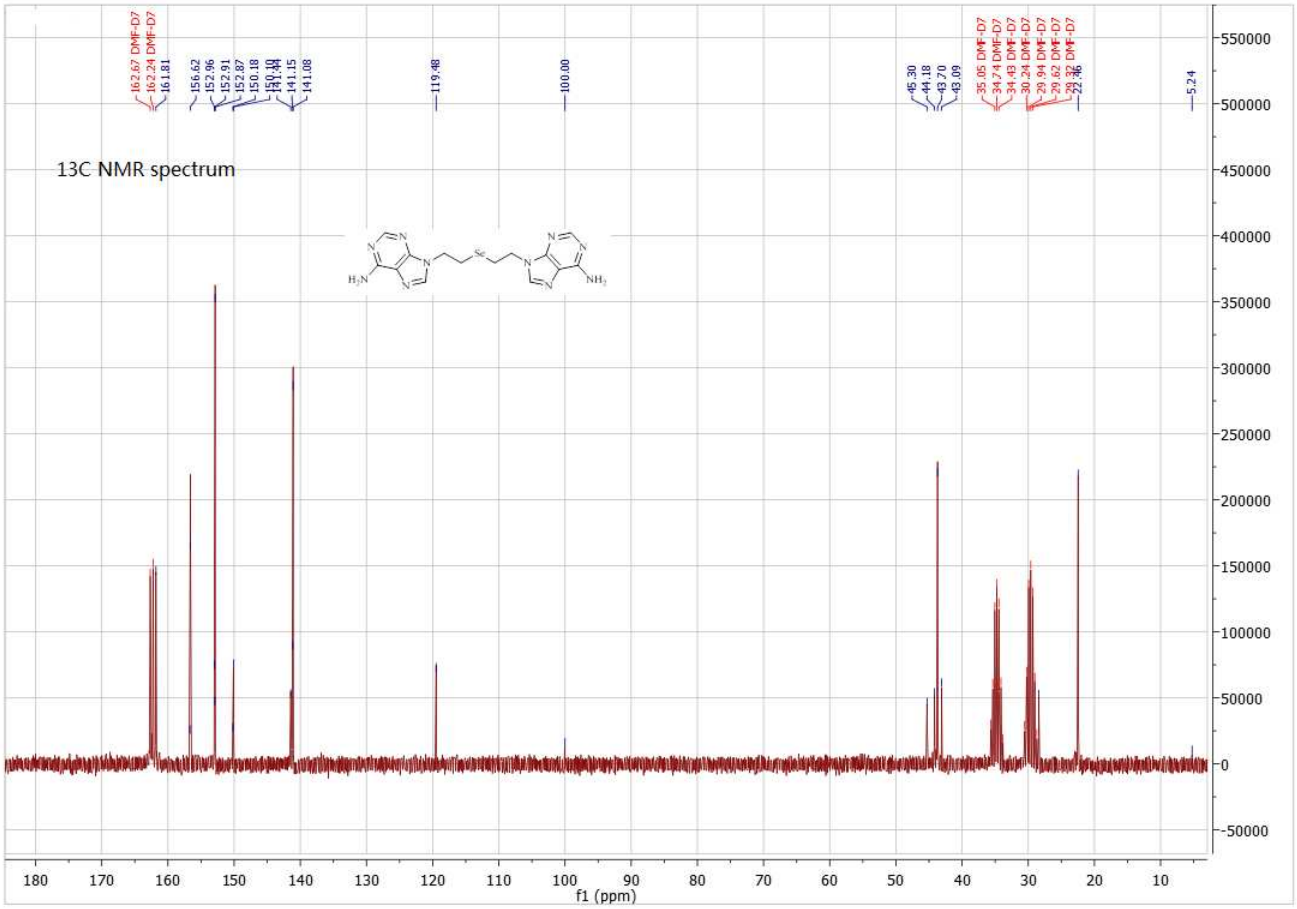
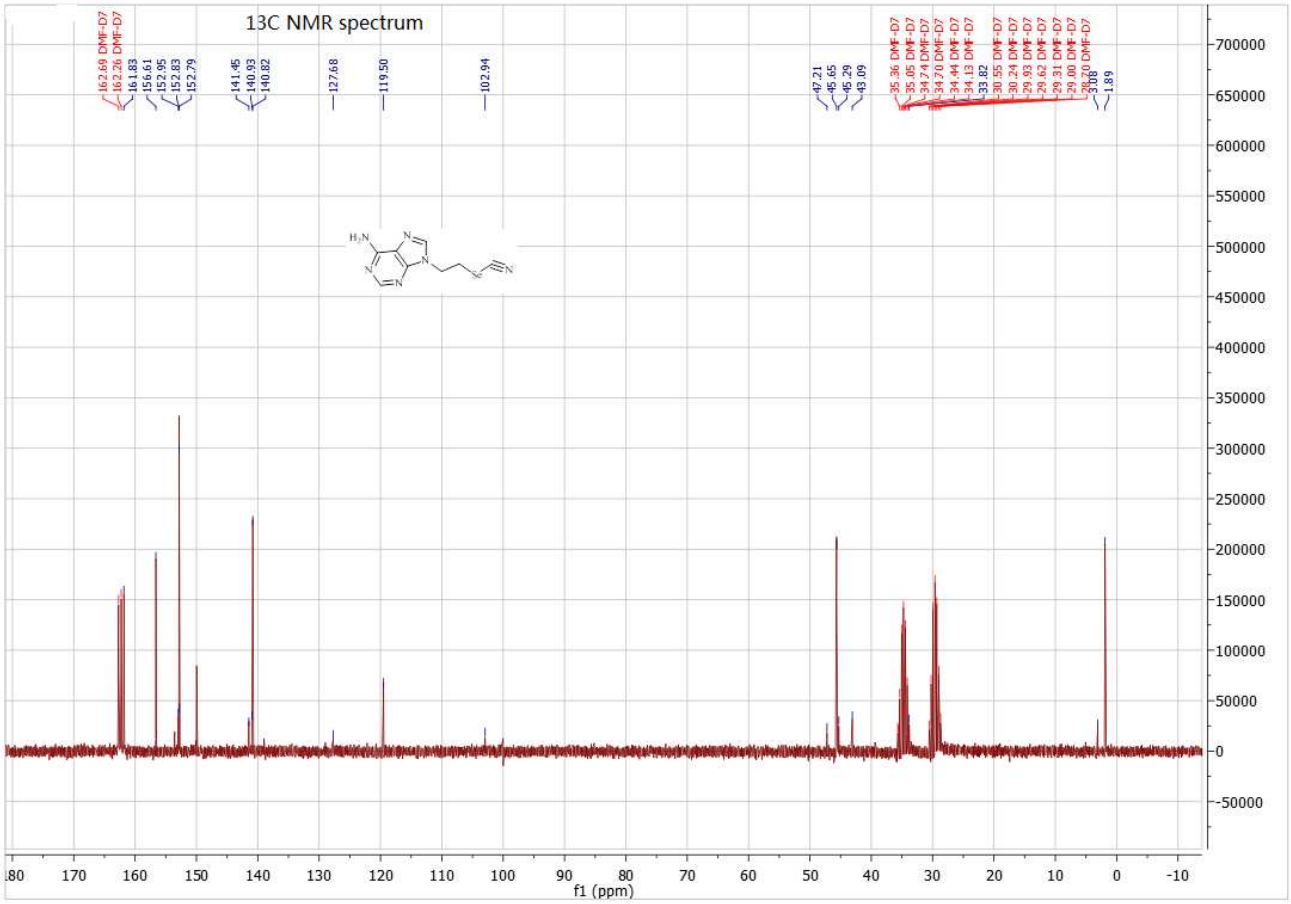
1. ^{1}H and ^{13}C NMR spectra of compounds **3** - **11** and **15** - **17**






13C NMR spectrum
162.60 DMF-D7
162.26 DMF-D7
161.83
156.61
152.95
152.83
152.79
141.45
140.93
140.82
127.68
119.50
102.94
47.21
45.65
45.29
45.09
35.36 DMF-D7
35.05 DMF-D7
34.74 DMF-D7
34.70 DMF-D7
34.44 DMF-D7
34.13 DMF-D7
33.82
30.55 DMF-D7
30.24 DMF-D7
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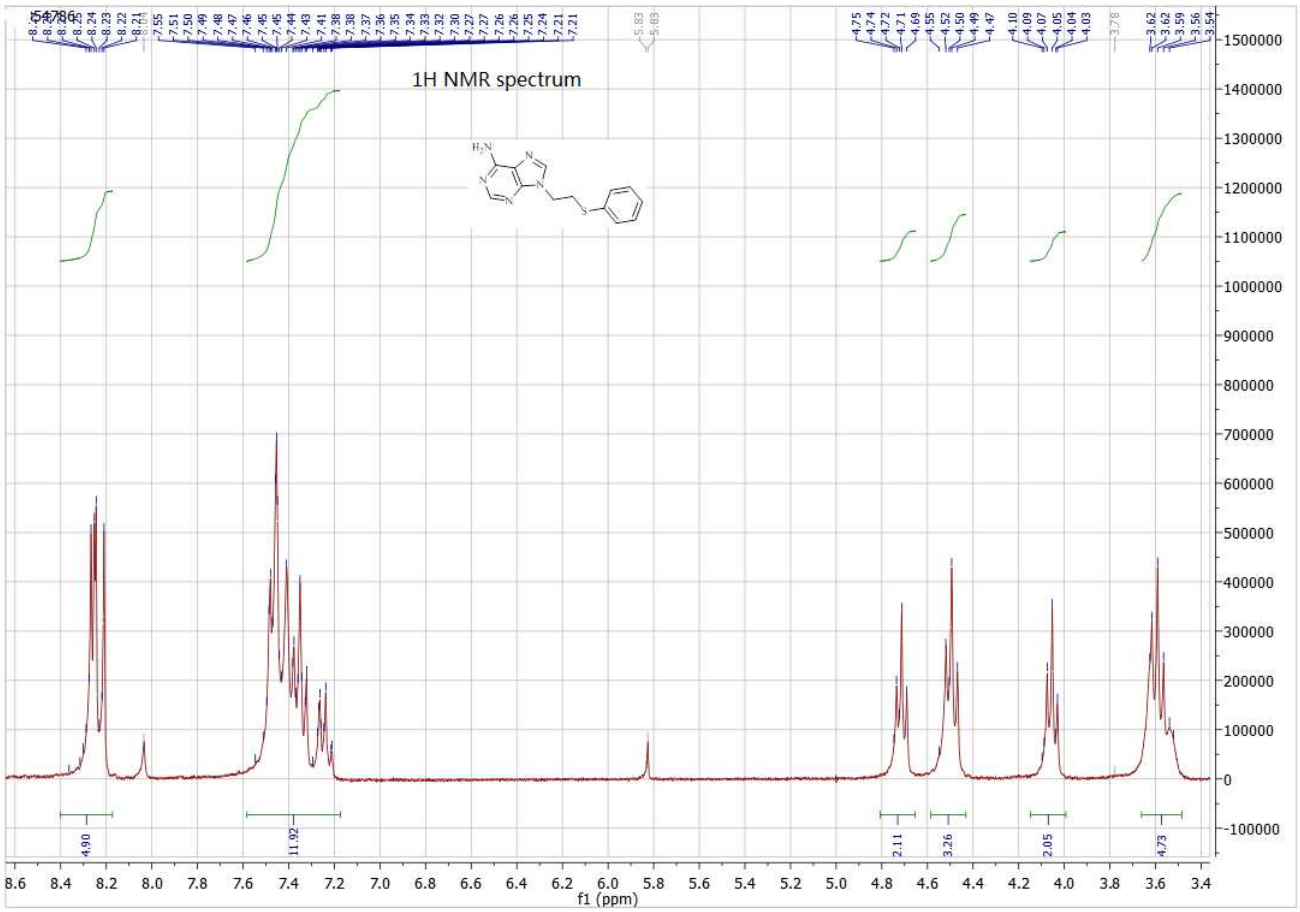
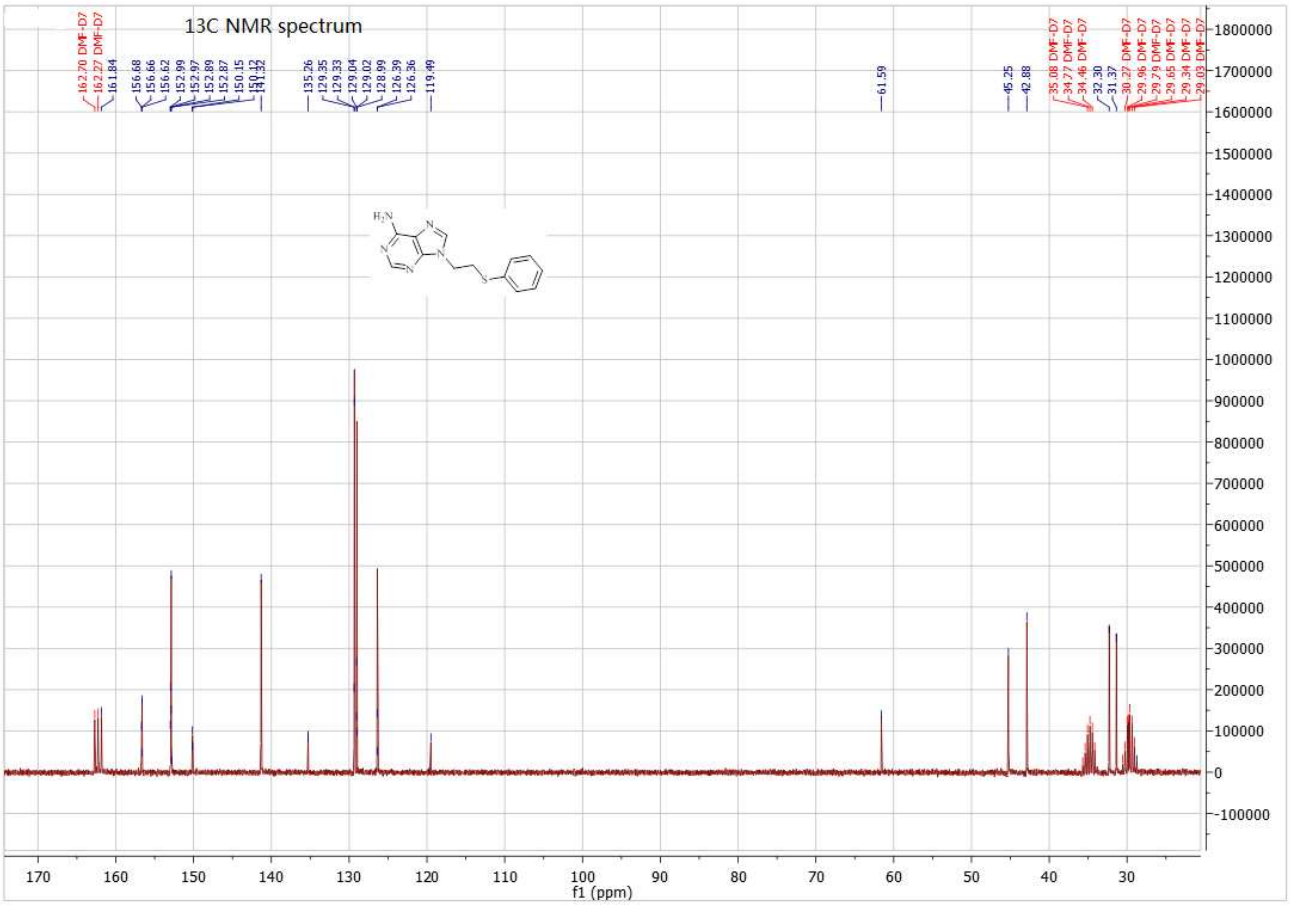
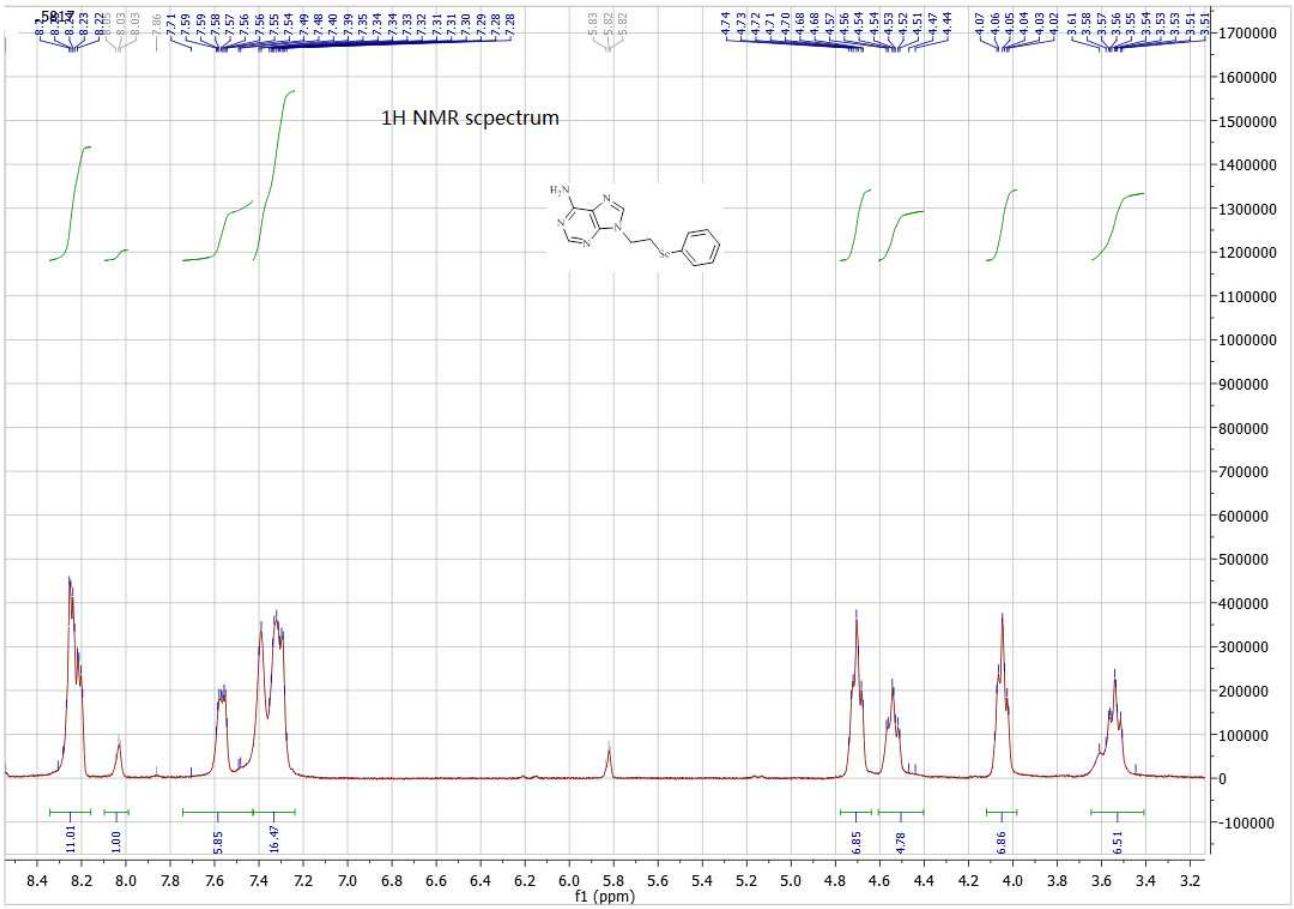
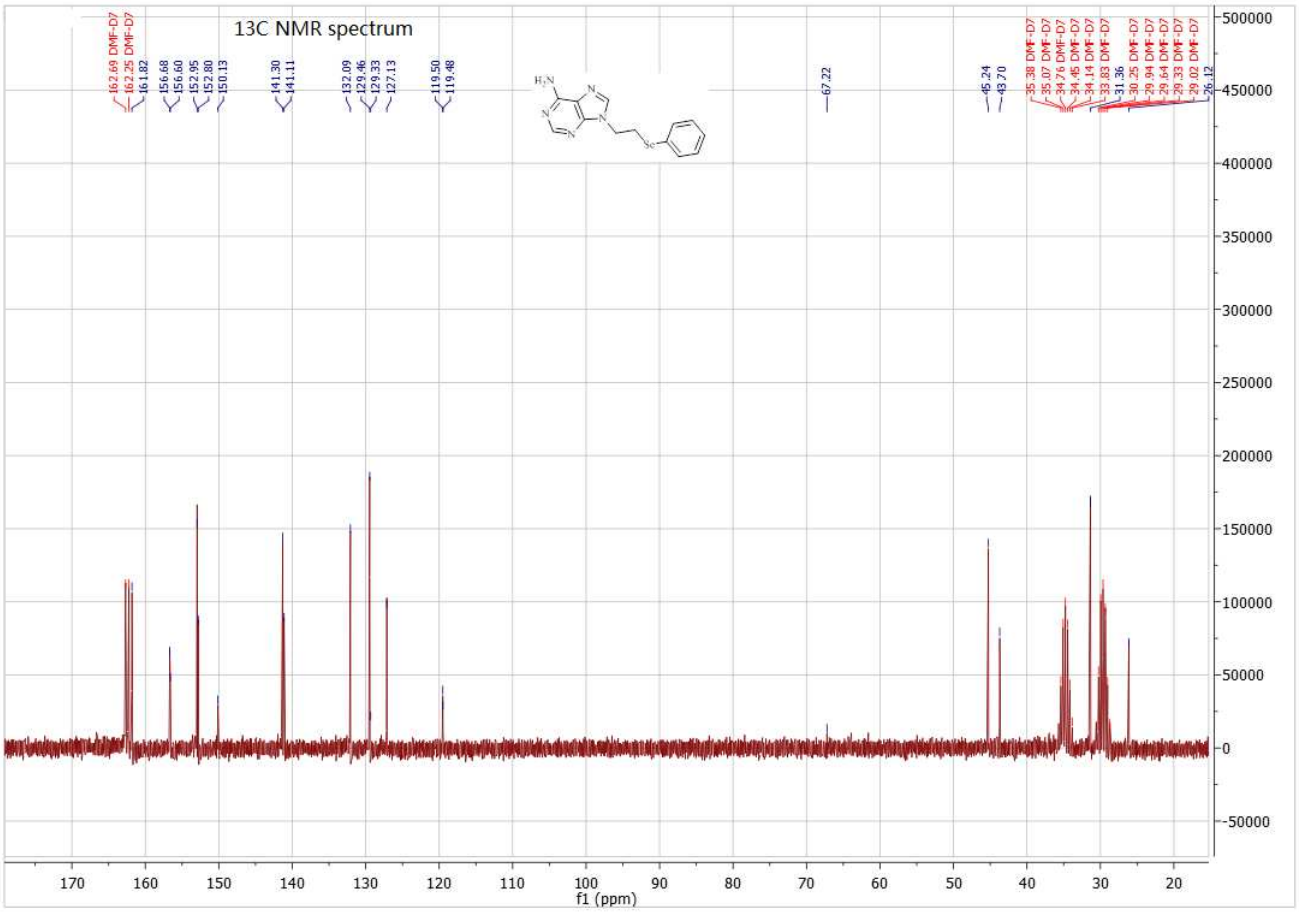
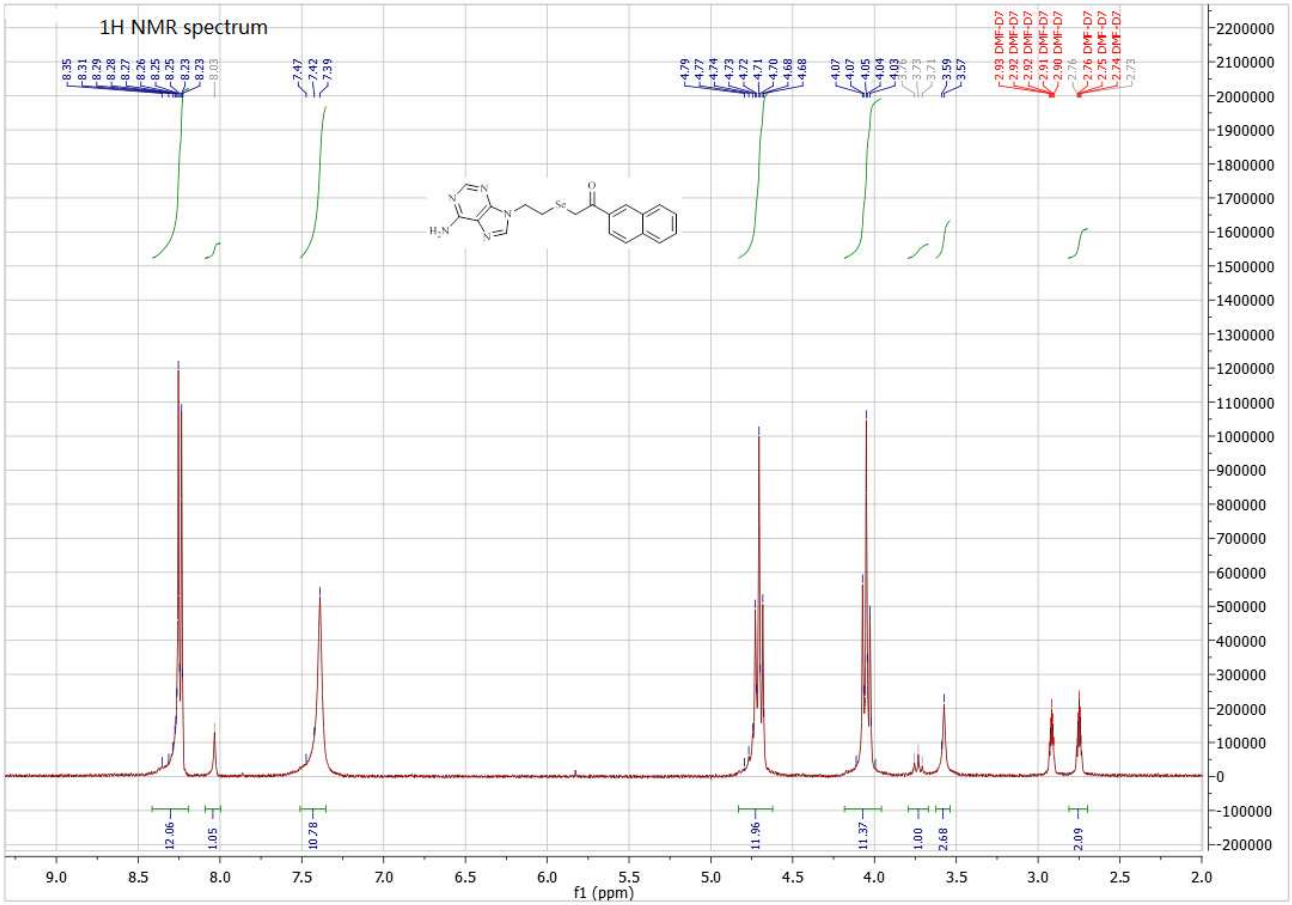
29.31 DMF-D7
29.00 DMF-D7
3.08
1.89
f1 (ppm)

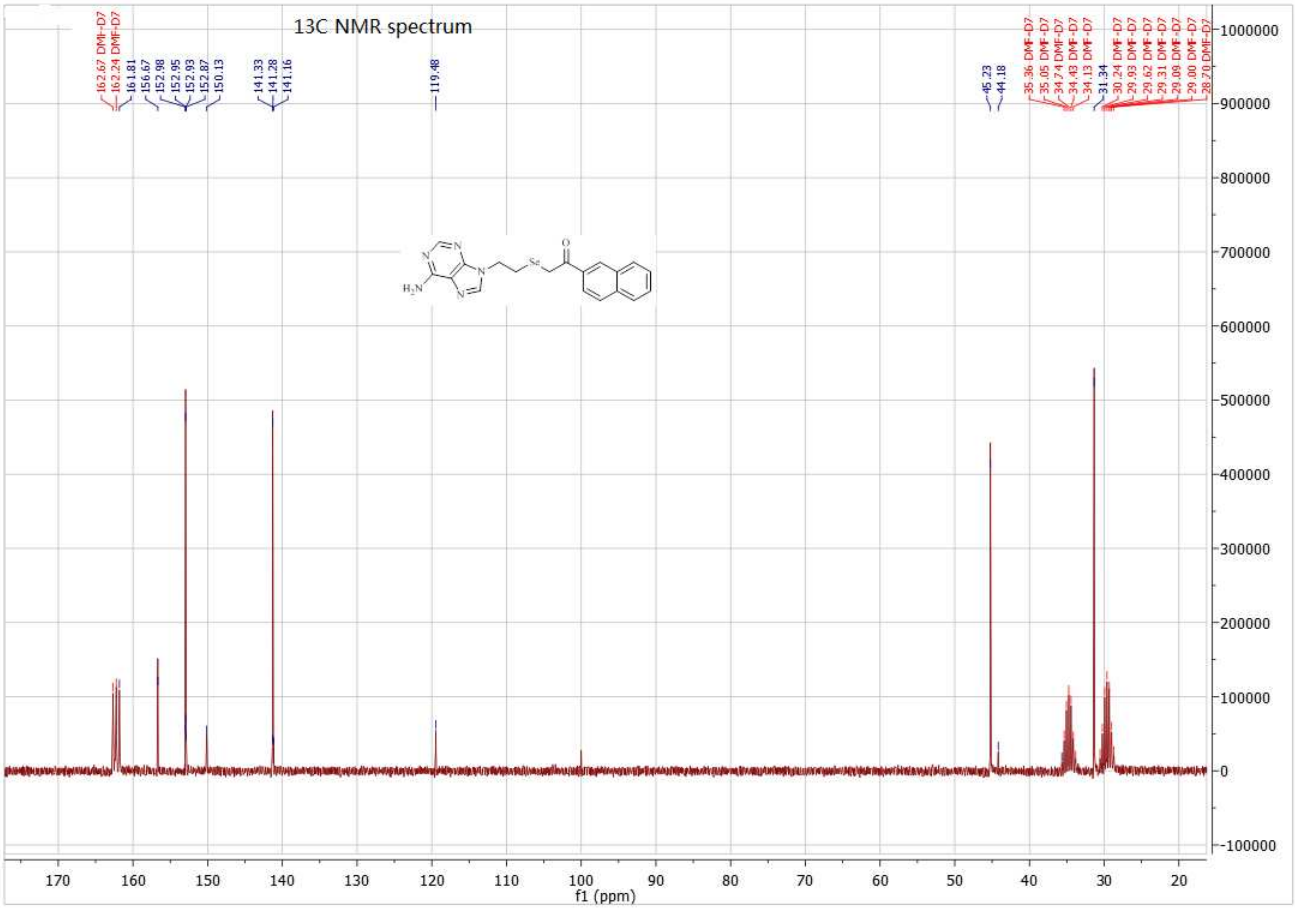


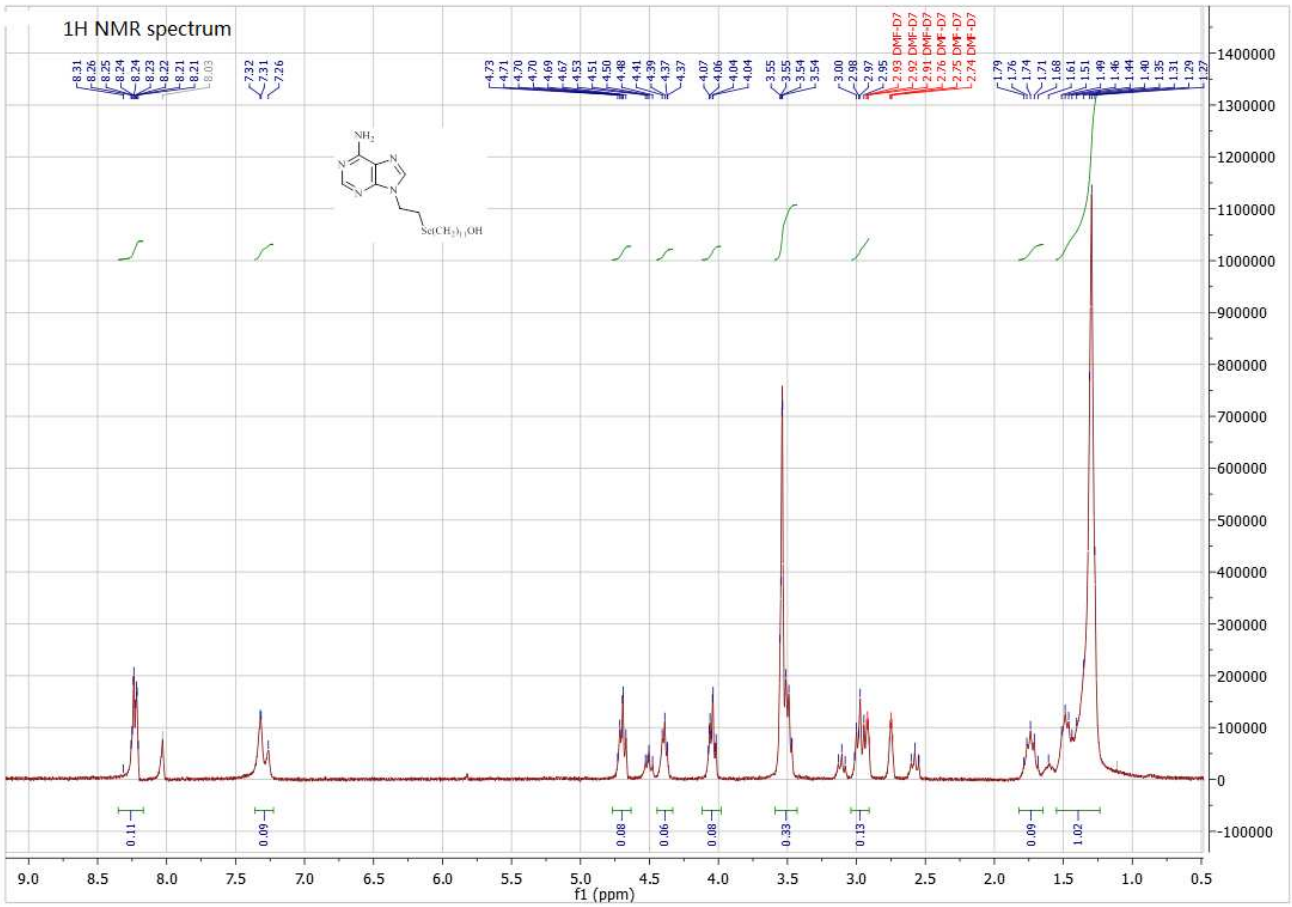

13C NMR spectrum
162.70 DMF-D7
162.27 DMF-D7
161.84
156.68
156.66
156.62
152.99
152.97
152.89
152.87
150.15
150.12
141.32
135.26
129.35
129.33
129.04
129.02
128.99
126.39
126.36
119.49
61.59
45.25
42.88
35.08 DMF-D7
34.77 DMF-D7
34.46 DMF-D7
32.30
31.37
30.27 DMF-D7
29.96 DMF-D7
29.79 DMF-D7
29.65 DMF-D7
29.34 DMF-D7
29.03 DMF-D7
f1 (ppm)

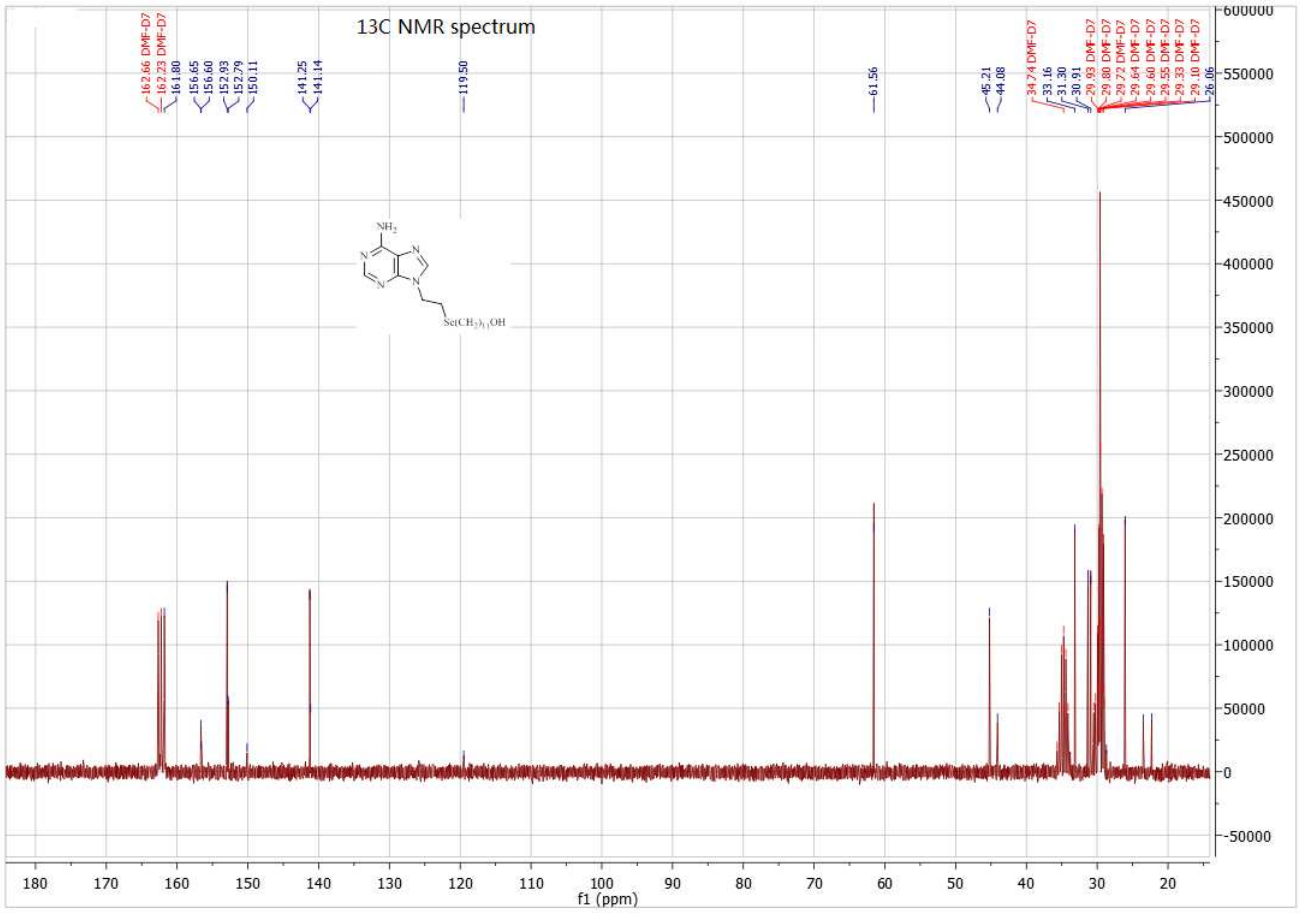











13C NMR spectrum
162.66 DMF-D7
162.23 DMF-D7
161.80
156.65
156.60
152.93
152.79
150.11
141.25
141.14
119.50
61.56
45.21
44.08
34.74 DMF-D7
33.16
31.30
30.91
29.93 DMF-D7
29.80 DMF-D7
29.72 DMF-D7
29.64 DMF-D7
29.60 DMF-D7
29.55 DMF-D7
29.33 DMF-D7
29.10 DMF-D7
26.06
f1 (ppm)