Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Electronic Supporting Information

for

Direct C-H sulfenylation of purines and deazapurines

Martin Klečka,[a,b] Radek Pohl,[b] Jan Čejka [b] and Michal Hocek*[a,b]

[a] *Dept. of Organic Chemistry, Faculty of Science, Charles University in Prague, Hlavova 8, CZ-12843 Prague 2, Czech Republic.*

[b] *Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, Gilead Sciences & IOCB Research Center, Flemingovo nam. 2, CZ-16610 Prague 6, Czech Republic, Fax: (+420)220-183-559; Tel: (+420)220-183-324; E-mail: hocek@uochb.cas.cz*

Contents:

1. Experimental Section

General

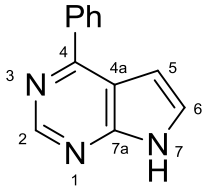
Deazapurines (**3** and **9**), disulfides, boronic acid and stannanes were purchased from commercial suppliers and used without any further purification. Dry DMF and THF were used as received from supplier. All compounds were fully characterized by NMR and spectra were recorded on a Bruker Avance II 600 (^{1}H at 600.1 MHz, ^{13}C at 150.9 MHz) or on a Bruker Avance II 500 (499.8 or 500.0 MHz for ^{1}H and 125.7 MHz for ^{13}C) spectrometer. ^{1}H and ^{13}C resonances were assigned using H,C-HSQC and H,C-HMBC spectra. The samples were measured in $CDCl_3$ and chemical shifts (in ppm, δ-scale) were referenced to solvent signal ($\delta(^{1}H)$ = 7.26 ppm, $\delta(^{1}H)$ = 77.0 ppm) or in or DMSO ($\delta(^{1}H)$ = 2.50 ppm, $\delta(^{1}H)$ = 39.43 ppm) Coupling constants (*J*) are given in Hz. IR spectra (wavenumbers in cm^{-1}) were recorded on Bruker Alpha FT-IR spectrometer using ATR technique. High resolution mass spectra were measured on a LTQ Orbitrap XL (Thermo Fisher Scientific) spectrometer using EI ionization technique. Melting points were determined on a Kofler block and are uncorrected. Elemental analyses were measured on PE 2400 Series II CHNS/O (Perkin Elmer, USA, 1999). X-ray diffraction experiment of single crystals was carried out on an X-ray diffractometer using CuKα radiation (λ=1.54180 Å).

Preparation of starting compounds:

7-Deazapurines

4-Phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine

(6-Phenyl-7-deazapurine) (1)

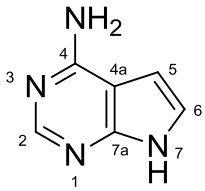


Dry toluene (250 ml) was added to a stirred solution of potassium carbonate (27.64 g, 200 mmol), 6-chloro-7-deazapurine **3** (15.36 g, 100 mmol), phenylboronic acid (18.29 g, 150 mmol) and $Pd(PPh_3)_4$ (4.62 g, 4 mmol) under Ar. The mixture was stirred for 18 h at temperature 100°C. After cooling to rt a brine was added and mixture were extracted with EtOAc 5x 250 mL and dried over Na_2SO_4. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 6:4) to give product **1** (17.57 g, 90 %) as white crystals.

M.p. 220-221 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 6.89 (d, 1H, $J_{5,6}$ = 3.6, H-5); 7.55 (m, 1H, H-*p*-Ph); 7.59 (m, 2H, H-*m*-Ph); 7.66 (d, 1H, $J_{6,5}$ = 3.5, H-6); 8.18 (m, 2H, H-*o*-Ph); 8.84 (s, 1H, H-2); 12.27 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 100.17 (CH-5); 114.71 (C-4a); 127.93 (CH-6); 128.76 (CH-*o*-Ph); 129.05 (CH-*m*-Ph); 130.23 (CH-*p*-Ph); 138.14 (C-*i*-Ph); 151.14 (CH-2); 152.80 (C-7a); 155.73 (C-4). IR (KBr): 3205, 3133, 3006, 2865, 1598, 1581, 1563, 1503, 1412, 1349. HRMS (ESI) calculated for $C_{12}H_{10}N_3$: 196.0869; found: 196.0869. Anal. calculated for $C_{12}H_9N_3$ (195.08): C 73.83%, H 4.65%, N 21.52%; found: C 73.59%, H 4.63%, N 21.19%.

4-Amino-7*H*-pyrrolo[2,3-*d*]pyrimidine

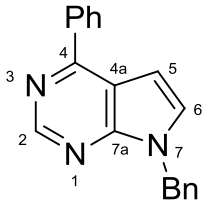
(6-Amino-7-deazapurine) (4)



6-chloro-7-deazapurine **3** (5 g; 31.73 mmol) was dissolved in 70 mL of mixture 1,4-dioxane/ aqueous ammonia (1:1) in a steel bomb and was heated at 130 °C for 19 h. After cooling, the mixture was evaporated. The crude mixture was separated by flash chromatography (gradient elution chloroform → chloroform/methanol 95:5) to give product **4** (4.25 g, 91 %) as white crystals.

7-Benzyl-4-phenyl-7*H*-pyrrolo[2,3-*d*]pyrimidine

(9-Benzyl-6-phenyl-7-deazapurine) (2)

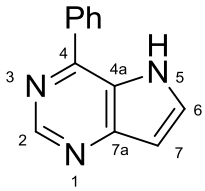


Dry toluene (250 ml) was added to a stirred solution of potassium carbonate (27.64 g, 200 mmol), 9-benzyl-6-chloro-7-deazapurine (23.4 g, 100 mmol), phenylboronic acid (18.29 g, 150 mmol) and $Pd(PPh_3)_4$ (4.62 g, 4 mmol) under Ar. The mixture was stirred for 18 h at temperature 100°C. After cooling to rt a brine was added and mixture were extracted with EtOAc 3x 250 mL and dried over Na_2SO_4. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 8:2) to give product **2** (25.9 g, 91 %) as white crystals.

9-Deazapurines

4-Phenyl-5H-pyrrolo[3,2-d]pyrimidine

(6-Phenyl-9-deazapurine) (7)

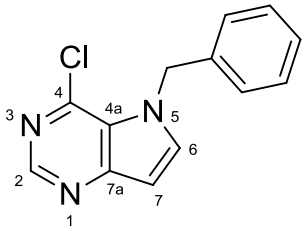


Dry toluene (250 ml) was added to a stirred solution of potassium carbonate (27.64 g, 200 mmol), 6-chloro-9-deazapurine **9** (15.36 g, 100 mmol), phenylboronic acid (18.29 g, 150 mmol) and $Pd(PPh_3)_4$ (4.62 g, 4 mmol) under Ar. The mixture was stirred for 18 h at temperature 100°C. After cooling to rt a brine was added and mixture were extracted with EtOAc 5x 250 mL and dried over Na_2SO_4. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 6:4) to give product **7** (16.59 g, 85 %) as yellowish crystals.

M.p. 136-142 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 6.71 (dd, 1H, $J_{7,6}$ = 3.1, $J_{7,NH}$ = 1.5, H-7); 7.58 (m, 1H, H-*p*-Ph); 7.62 (m, 2H, H-*m*-Ph); 7.91 (dd, 1H, $J_{6,7}$ = $J_{6,NH}$ = 3.1, H-6); 8.09 (m, 2H, H-*o*-Ph); 8.90 (s, 1H, H-2); 11.99 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 101.82 (CH-7); 123.70 (C-4a); 128.79 (CH-*o*-Ph); 129.11 (CH-*m*-Ph); 130.32 (CH-*p*-Ph); 134.20 (CH-6); 136.34 (C-*i*-Ph); 147.64 (C-4); 150.38 (CH-2); 151.45 (C-7a). IR (KBr): 3205, 3135, 3081, 3007, 2867, 1599, 1582, 1563,1503, 1438, 1412, 1350. HRMS (ESI) calculated for C_{12} H_{11} N_3: 196.0796; found: 196.0869. Anal. calculated for $C_{12}H_9N_3$ (195.08): C 73.83%, H 4.65%, N 21.52%; found: C 73.68%, H 4.54%, N 21.12%.

5-Benzyl-4-chloro-5H-pyrrolo[3,2-d]pyrimidine

(7-Benzyl-6-chloro-9-deazapurine)

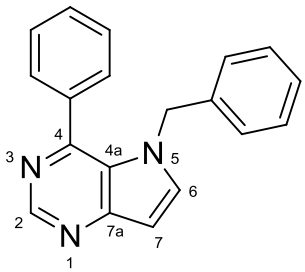


Dry DMF (150 ml) was added to a stirred solution of potassium carbonate (11.4 g, 82.5 mmol) and 6-choro-9-deazapurine **9** (11.5 g, 75 mmol) under Ar. After 20 min, benzyl chloride (9.2 ml, 78.75 mmol) was added and the resulting mixture was stirred overnight at rt.

After that brine was added and mixture were extracted with EtOAc 3x 250 mL and dried over Na_2SO_4. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 8:2) to give product 7-benzyl-6-chloro-9-deazapurine (16.63 g, 91 %) as yellowish crystals.

M.p. 122-126 °C. ^{1}H NMR (600.1 MHz, DMSO-d_6): 5.51 (s, 2H, CH_2Ph); 6.69 (d, 1H, $J_{7,6}$ = 3.6, H-7); 7.27 (m, 3H, H-*o*,*p*-Ph); 7.32 (m, 2H, H-*m*-Ph); 7.85 (d, 1H, $J_{6,7}$ = 3.6, H-6); 8.66 (s, 1H, H-2). ^{13}C NMR (150.9 MHz, DMSO-d_6): 47.99 (CH_2Ph); 99.01 (CH-7); 116.91 (C-4a); 127.54 (CH-*o*-Ph); 127.87 (CH-*p*-Ph); 128.84 (CH-*m*-Ph); 131.66 (CH-6); 137.33 (C-*i*-Ph); 150.65 (CH-2); 150.72, 150.90 (C-4,7a). IR(KBr): 3113, 3070, 3032, 1593, 1522, 1496, 1460, 1452, 1444, 1409, 1399, 1350. HRMS (ESI) calculated for $C_{18}H_{14}N_3S$: 243.0563; found: 243.0569.

5-Benzyl-4-phenyl-5H-pyrrolo[3,2-d]pyrimidine
(7-Benzyl-6-phenyl-9-deazapurine) (8)



Dry toluene (100 ml) was added to a stirred solution of potassium carbonate (11.06 g, 80 mmol), 7-benzyl-6-chloro-9-deazapurine (9.72 g, 40 mmol), phenylboronic acid (7.32 g, 60 mmol) and $Pd(PPh_3)_4$ (1.85 g, 1.6 mmol) under Ar. The mixture was stirred for 18 h at temperature 110°C. After cooling to rt a brine was added and mixture were extracted with EtOAc 5x 250 mL and dried over Na_2SO_4. The crude mixture was separated by flash chromatography (gradient elution hexanes → hexanes/ethyl acetate 7:3) to give product **8** (11.07 g, 97 %) as white crystals.

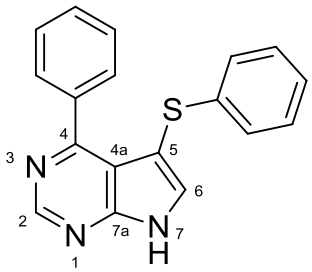
M.p. 110-111 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 5.21 (s, 2H, CH_2Ph); 6.37 (m, 2H, H-*o*-Bn); 6.81 (d, 1H, $J_{7,6}$ = 3.2, H-7); 7.07 (m, 2H, H-*m*-Bn); 7.10 (m, 1H, H-*p*-Bn); 7.41 (m, 2H, H-*o*-Ph); 7.45 (m, 2H, H-*m*-Ph); 7.53 (m, 1H, H-*p*-Ph); 8.10 (d, 1H, $J_{6,7}$ = 3.2, H-6); 8.85 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, DMSO-d_6): 51.85 (CH_2Ph); 101.83 (CH-7); 124.45 (C-4a);

125.97 (CH-*o*-Bn); 127.45 (CH-*p*-Bn); 128.21 (CH-*m*-Ph); 128.47 (CH-*m*-Bn); 129.32 (CH-*o*-Ph); 129.38 (CH-*p*-Ph); 137.35 (C-*i*-Ph); 137.44 (C-*i*-Bn); 138.99 (CH-6); 150.02 (CH-2); 150.37 (C-4); 152.14 (C-7a). IR(KBr): 3436, 3062, 3030, 1583, 1575, 1537, 1510, 1490, 1454, 1443, 1394, 1360. HRMS (ESI) calculated for $C_{19}H_{16}N_3$: 286.1339; found: 286.1339.

Sulfenytion of 7-deazapurines. General Procedure:

A mixture of 7-deazapurines **1-4** (2 mmol), disulphides (1.5 mmol), and CuI (0.2 mmol, 10 mol %) in DMF (20 mL) was stirred at 110°C under air atmosphere for 18 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (30 mL), washed with 1M solution of sodium salt of EDTA (20 mL). Aqueous solution was then extracted three times with EtOAc and combitated organic layers were dried over Na_2SO_4, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

4-Phenyl-5-(phenylsulfanyl)-7H-pyrrolo[2,3-d]pyrimidine
(6-Phenyl-7-(phenylsulfanyl)-7-deazapurine) (5a)

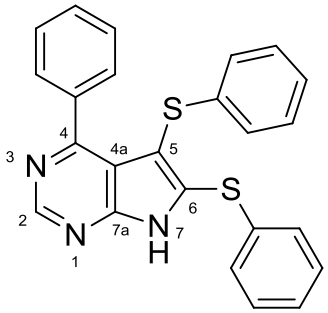


6-phenyl-7-deazapurine **1** (390 mg, 2 mmol) and diphenyldisulfide (328 mg , 1.5 mmol) were used as starting compounds to give products **5a** (582 mg, 96%) a **6a** (25 mg, 3%) as white solids after chromatography eluting with hexane/EtOAc 5:1 to 1:1. Crystalization in hexan/EtOAc gave white needles.

M.p. 184-186 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 6.70 (m, 2H, H-*o*-SPh); 6.99 (m, 1H, H-*p*-SPh); 7.06 (m, 2H, H-*m*-SPh); 7.27 (m, 2H, H-*m*-Ph); 7.38 (m, 1H, H-*p*-Ph); 7.53 (m, 2H, H-*o*-Ph); 8.05 (d, 1H, $J_{6,NH}$ = 2.5, H-6); 8.88 (s, 1H, H-2); 12.86 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 99.90 (C-5); 115.26 (C-4a); 125.25 (CH-*p*-SPh); 126.04 (CH-*o*-SPh); 127.29 (CH-*m*-Ph); 128.80 (CH-*m*-SPh); 129.23 (CH-*p*-Ph); 129.86 (CH-*o*-Ph); 135.69 (CH-6); 137.04 (C-*i*-Ph); 138.47 (C-*i*-SPh); 151.53 (CH-2); 153.55 (C-7a); 159.40 (C-4).

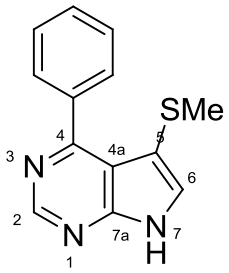
IR(KBr): 3104, 3059, 2988, 2862, 2818, 1598, 1581, 1551, 1478, 1435, 1322. HRMS (ESI) calculated for $C_{18}H_{14}N_3S$: 304.0902; found: 304.0901. Anal. calculated for $C_{18}H_{13}N_3S$ (303.08): C 71.26%, H 4.32%, N 13.85%, S 10.57%; found: C 71.07%, H 4.15%, N 13.57%, S 10.47%.

4-Phenyl-5,6-bis(phenylsulfanyl)-7H-pyrrolo[2,3-d]pyrimidine
(6-Phenyl-7,8-bis(phenylsulfanyl)-7-deazapurine) (6a)



M.p. 231-233 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 6.68 (m, 2H, H-*o*-SPh-5); 6.95 (m, 1H, H-*p*-SPh-5); 6.98 (m, 2H, H-*m*-SPh-5); 7.23 (m, 2H, H-*m*-Ph); 7.28-7.365 (m, 3H, H-*p*-Ph, H-*m*,*p*-SPh-6); 7.45 (m, 2H, H-*o*-SPh-6); 7.49 (m, 2H, H-*o*-Ph); 8.62 (s, 1H, H-2); 10.33 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 104.40 (C-5); 117.30 (C-4a); 125.40 (CH-*p*-SPh-5); 126.82 (CH-*o*-SPh-5); 127.46 (CH-*m*-Ph); 128.61 (CH-*m*-SPh-5); 129.04 (CH-*p*-Ph); 129.39 (CH-*p*-SPh-6); 129.87 (CH-*o*-Ph); 130.09 (CH-*m*-SPh-6); 131.02 (C-*i*-SPh-6); 132.24 (CH-*o*-SPh-6); 136.50 (C-*i*-Ph); 137.17 (C-*i*-SPh-5); 140.40 (C-6); 151.31 (CH-2); 153.27 (C-7a); 159.77 (C-4). IR(KBr): 3430, 3073, 2489, 1581, 1559, 1477, 1327. HRMS (ESI) calculated for $C_{24}H_{18}N_3S_2$: 412.0935; found: 412.0936.

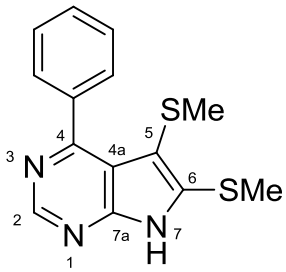
5-(Methylsulfanyl)-4-phenyl-7H-pyrrolo[2,3-d]pyrimidine
(7-(Methylsulfanyl)-6-phenyl-7-deazapurine) (5b)



6-phenyl-7-deazapurine **1** (390 mg, 2 mmol) and dimethyldisulfide (0.9 mL, 10 mmol) were used as starting compounds to give products **5b** (343 mg, 71%) a **6b** (86 mg, 15%) as yellow solids after chromatography with hexane/EtOAc 5:1 to 1:1.

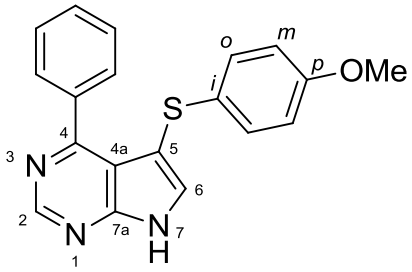
M.p. 174-175 °C. ^{1}H NMR (600.1 MHz, $CDCl_3$): 1.92 (s, 3H, CH_3S); 7.37 (d, 1H, J = 2.1, H-6); 7.53 (m, 3H, H-*m*,*p*-Ph); 7.91 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2); 11.12 (bs, 1H, NH). ^{13}C NMR (150.9 MHz, $CDCl_3$): 18.99 (CH_3S); 108.89 (C-5); 115.85 (C-4a); 126.78 (CH-6); 127.84 (CH-*m*-Ph); 129.76 (CH-*p*-Ph); 129.93 (CH-*o*-Ph); 137.27 (C-*i*-Ph); 151.29 (CH-2); 153.17 (C-7a); 160.54 (C-4). IR($CDCl_3$): 3452, 3114, 2924, 2855, 1579, 1553, 1453, 1442, 1325. HRMS (ESI) calculated for $C_{13}H_{12}N_3S$: 242.0746; found: 242.0746.

5,6-Bis(methylsulfanyl)-4-phenyl-7H-pyrrolo[2,3-d]pyrimidine (7,8-Bis(methylsulfanyl)-6-phenyl-7-deazapurine) (6b)



M.p. 139-141 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 1.70 (s, 3H, CH_3S-5); 2.66 (s, 3H, CH_3S-6); 7.48-7.55 (m, 3H, H-*m*,*p*-Ph); 7.80 (m, 2H, H-*o*-Ph); 8.81 (s, 1H, H-2); 12.86 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 15.74 (CH_3S-6); 19.33 (CH_3S-5); 103.91 (C-5); 116.72 (C-4a); 127.51 (CH-*m*-Ph); 129.49 (CH-*p*-Ph); 129.95 (CH-*m*-Ph); 136.69 (C-*i*-Ph); 142.14 (C-6); 149.87 (CH-2); 153.67 (C-7a); 156.20 (C-4). IR(KBr): 2920, 2857, 1739, 1577, 1550, 1464, 1458, 1437, 1317, 1254, 770, 704. HRMS (ESI) calculated for $C_{14}H_{14}N_3S_2$: 288.0624; found: 288.0624.

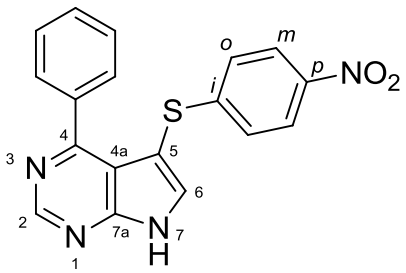
5-[(4-Methoxyphenyl)sulfanyl]-4-phenyl-7H-pyrrolo[2,3-d]pyrimidine
(7-[(4-Methoxyphenyl)sulfanyl]-6-phenyl-7-deazapurine) (5c)



6-phenyl-7-deazapurine **1** (390 mg, 2 mmol) and bis(4-methoxyphenyl) disulfide (418 mg, 1.5 mmol) were used as starting compounds to give product **5c** (608 mg, 91%) as white solids after chromatography eluting with hexane/EtOAc 5:1 to 1:1. Crystalization from hexan/EtOAc gave white needles.

M.p. 192-196 °C. ^{1}H NMR (499.8 MHz, $CDCl_3$): 3.71 (s, 3H, CH_3O); 6.59 (m, 2H, H-*m*-SC_6H_4OMe); 6.74 (m, 2H, H-*o*-SC_6H_4OMe); 7.42 (m, 2H, H-*m*-Ph); 7.47 (m, 1H, H-*p*-Ph); 7.54(s, 1H, H-6); 7.68 (m, 2H, H-*o*-Ph); 9.00 (s, 1H, H-2); 11.13 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, $CDCl_3$): 55.29 (CH_3O); 106.46 (C-5); 114.30 (CH-*m*-SC_6H_4OMe); 115.56 (C-4a); 127.29 (C-*i*-SC_6H_4OMe); 127.61 (CH-*m*-Ph); 129.53 (CH-*p*-Ph); 130.09 (CH-*o*-Ph); 130.67 (CH-*o*-SC_6H_4OMe); 131.02 (CH-6); 136.82 (C-*i*-Ph); 151.35 (CH-2); 153.33 (C-7a); 158.39 (C-*p*-SC_6H_4OMe); 160.94 (C-4). IR(KBr): 3099, 2982, 2959, 2835, 1595, 1552, 1493, 1249, 1026. HRMS (ESI) calculated for $C_{19}H_{16}ON_3S$: 334.1009; found: 334.1008.

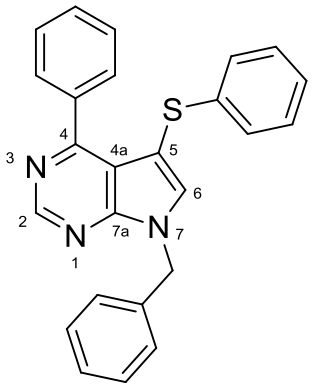
5-[(4-Nitrophenyl)sulfanyl]-4-phenyl-7H-pyrrolo[2,3-d]pyrimidine
(7-[(4-Nitrophenyl)sulfanyl]-6-phenyl-7-deazapurine) (5d)



6-phenyl-7-deazapurine **1** (390 mg, 2 mmol) and 4-nitrophenyl disulfide (463 mg, 1.5 mmol) were used as starting compounds to give product **5d** (328 mg, 47%) as green solids after chromatography eluting with hexane/EtOAc 5:1 to 1:1.

M.p. 253-261 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 6.88 (m, 2H, H-*o*-$SC_6H_4NO_2$); 7.22 (m, 2H, H-*m*-Ph); 7.32 (m, 1H, H-*p*-Ph); 7.47 (m, 2H, H-*o*-Ph); 7.88 (m, 2H, H-*m*-$SC_6H_4NO_2$); 8.16 (s, 1H, H-6); 8.92 (s, 1H, H-2); 13.03 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 97.21 (C-5); 115.06 (C-4a); 123.79 (CH-*m*-$SC_6H_4NO_2$); 125.47 (CH-*o*-$SC_6H_4NO_2$); 127.29 (CH-*m*-Ph); 129.28 (CH-*p*-Ph); 129.63 (CH-*o*-Ph); 136.31 (CH-6); 136.71 (C-*i*-Ph); 144.53 (C-*p*-$SC_6H_4NO_2$); 149.10 (C-*i*-$SC_6H_4NO_2$); 151.84 (CH-2); 153.69 (C-7a); 159.56 (C-4). IR(KBr): 2986, 2862, 2821, 1600, 1580, 1553, 1502, 1342, 1320, 1085. HRMS (ESI) calculated for $C_{18}H_{13}O_2N_4S$: 349.0754; found: 349.0753.

7-Benzyl-4-phenyl-5-(phenylsulfanyl)-7H-pyrrolo[2,3-d]pyrimidine
(9-Benzyl-6-phenyl-7-(phenylsulfanyl)-7-deazapurine) (5e)

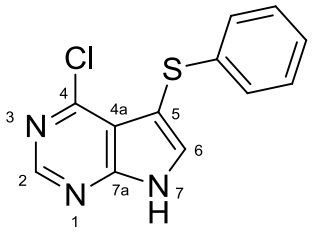


7-benzyl-6-phenyl-7-deazapurine **2** (570 mg, 2 mmol)) and diphenyldisulfide (1.1 g, 5 mmol) was used as starting compound to give product **5e** (157 mg, 20%) as white solids after chromatography eluting with hexane/EtOAc 10:1 to 4:1. Crystalization in hexan/EtOAc gave white crystals. Recovery of starting compound **2** (405 mg, 71%).

M.p. 91-94 °C ^{1}H NMR (500.0 MHz, $CDCl_3$): 5.55 (s, 2H, CH_2Ph); 6.71 (m, 2H, H-*o*-SPh); 6.98 (m, 1H, H-*p*-SPh); 6.99 (m, 2H, H-*m*-SPh); 7.29 (m, 2H, H-*m*-Bn); 7.33 (m, 2H, H-*o*-Bn); 7.35-7.40 (m, 4H, H-*m*,*p*-Ph, H-*p*-Bn); 7.48 (s, 1H, H-6); 7.52 (m, 2H, H-*o*-Ph); 9.01 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 48.23 (CH_2Ph); 102.82 (C-5); 115.90 (C-4a); 125.25 (CH-*p*-SPh); 126.80 (CH-*o*-SPh); 127.38 (CH-*m*-Bn); 127.85 (CH-*o*-Bn); 128.28 (CH-*p*-Bn); 128.45 (CH-*m*-SPh); 129.03 (CH-*m*-Ph); 129.20 (CH-*p*-Ph); 129.80 (CH-*o*-Ph); 135.25 (CH-6); 136.14 (C-*i*-Ph); 136.78 (C-*i*-Bn); 137.81 (C-*i*-SPh); 151.93 (CH-2); 152.66 (C-7a); 160.93 (C-4). IR(KBr): 1552, 1451, 1414, 1330, 983. HRMS (ESI) calculated for

$C_{25}H_{20}N_3S$: 394.1372; found: 394.1371. Anal. calculated for $C_{25}H_{19}N_3S$ (393.13): C 76.31%, H 4.87%, N 10.68%, S 8.15%; found: C 76.13%, H 4.69%, N 10.43%, S 8.02%.

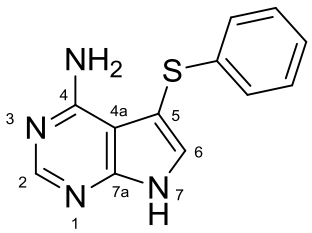
4-Chloro-5-(phenylsulfanyl)-7H-pyrrolo[2,3-d]pyrimidine
(6-Chloro-7-(phenylsulfanyl)-7-deazapurine) (5f)



6-chloro-7-deazapurine **3** (307 mg, 2 mmol) and diphenyldisulfide (2.2 g, 10 mmol) were used as starting compounds to give product **5f** (472 mg, 90%) as white solids. Diphenyldisulfide was divided into five portions and each one was added every 10 hours until complete consumption of staring material as monitored by TLC. Chromatography was started with pure hexane (to remove excess of diphenyldisulfide) and followed by hexane/EtOAc 5:1 to 1:1. Crystalization in hexan/EtOAc gave white crystals.

M.p. 184-186 °C ^{1}H NMR (499.8 MHz, DMSO-d_6): 7.06 (m, 2H, H-*o*-Ph); 7.12 (m, 1H, H-*p*-Ph); 7.24 (m, 2H, H-*m*-Ph); 8.12 (d, 1H, J = 2.6, H-6); 8.65 (s, 1H, H-2); 13.11 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 99.70 (C-5); 116.29 (C-4a); 125.49 (CH-*p*-Ph); 125.90 (CH-*o*-Ph); 129.25 (CH-*m*-Ph); 136.32 (CH-6); 139.13 (C-*i*-Ph); 150.98 (C-4); 151.44 (CH-2); 153.31 (C-7a). IR(KBr): 3072, 2963, 2813, 1596, 1551, 1478, 1439, 1338, 1228, 975, 844, 734. HRMS (ESI) calculated for $C_{12}H_9N_3ClS$: 262.0200; found: 262.0200.

5-(Phenylsulfanyl)-7H-pyrrolo[2,3-d]pyrimidin-4-amine
(6-Amino-7-(phenylsulfanyl)-7-deazapurine) (5g)



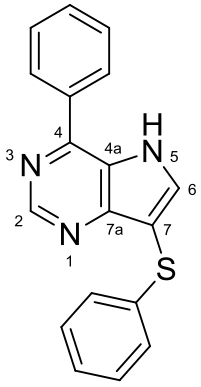
6-amino-7-deazapurine **4** (268 mg, 2 mmol) and diphenyldisulfide (1.1 g, 5 mmol) were used as starting compounds to give product **5g** (384 mg, 79%) as white solids after chromatography eluting DCM/MeOH 10:0 to 7:3 with 1% Et_3N

M.p. 268-299 °C ^{1}H NMR (500.0 MHz, DMSO-d_6): 6.52 (bs, 2H, NH_2); 7.09 (m, 2H, H-*o*-Ph); 7.13 (m, 1H, H-*p*-Ph); 7.27 (m, 2H, H-*m*-Ph); 7.58 (s, 1H, H-8); 8.10 (s, 1H, H-2); 12.16 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 98.03 (C-7); 102.87 (C-5); 125.67 (CH-*p*-Ph); 125.79 (CH-*o*-Ph); 129.35 (CH-*m*-Ph); 129.91 (CH-8); 138.94 (C-*i*-Ph); 151.83 (C-4); 152.79 (CH-2); 157.52 (C-6). IR(KBr):3456, 3100, 3066, 1644,1611, 1597, 1582, 1479, 1318. HRMS (ESI) calculated for $C_{12}H_{11}N_4S$: 243.0699; found: 243.0699

Sulfenytion of 9-deazapurines. General Procedure:

A mixture of CuI (0.2 mmol, 10 mol %) and 2,2'-bipyridine (0.4 mmol, 20 mol %) in DMF (10 mL) was stirred at rt for 15 minutes and then was added to mixture of 9-deazapurines **7-9** (2 mmol), disulphides (3 mmol) in DMF (20 mL) and then was stirred at 110°C under air atmosphere for 48 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (30 mL), washed with 1M solution of sodium salt of EDTA (20 mL). Aqueous solution was then extracted three times with EtOAc and combitated organic layers were dried over Na_2SO_4, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

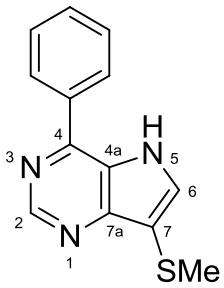
4-Phenyl-7-(phenylsulfanyl)-5H-pyrrolo[3,2-d]pyrimidine
(6-Phenyl-9-(phenylsulfanyl)-9-deazapurine) (10a)



6-phenyl-9-deazapurine **7** (390 mg, 2 mmol) and diphenyldisulfide (656 mg, 3 mmol) were used as starting compounds to give product **10a** (595 mg, 96%) as white solids after chromatography eluting with hexane/EtOAc 5:1 to 1:2. Crystalization in hexan/EtOAc gave white needles.

M.p. 210-216 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 7.10 (m, 3H, H-*o*,*p*-SPh); 7.22 (m, 2H, H-*m*-SPh); 7.61 (m, 1H, H-*p*-Ph); 7.63 (m, 2H, H-*m*-Ph); 8.11 (m, 2H, H-*o*-Ph); 8.29 (s, 1H, H-6); 8.95 (s, 1H, H-2); 12.56 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 101.28 (C-7); 124.83 (C-4a); 125.30 (CH-*p*-SPh); 126.02 (CH-*o*-SPh); 128.99 (CH-*o*-Ph); 129.10, 129.15 (CH-*m*-Ph, CH-*m*-SPh); 130.61 (CH-*p*-Ph); 135.77 (C-*i*-Ph); 138.63 (C-*i*-SPh); 140.37 (CH-6); 148.88 (C-4); 151.29 (CH-2); 151.43 (C-7a). IR(KBr): 3066, 2835, 1594, 1542, 1505, 1490, 1480, 1429. HRMS (ESI) calculated for $C_{18}H_{14}N_3S$: 304.0902; found: 304.0902.

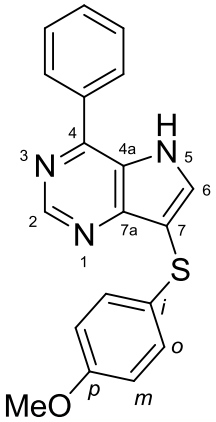
7-(Methylsulfanyl)-4-phenyl-5H-pyrrolo[3,2-d]pyrimidine
(9-(Methylsulfanyl)-6-phenyl-9-deazapurine) (10b)



6-phenyl-9-deazapurine **7** (390 mg, 2 mmol) and dimethyldisulfide (1.26 mL, 14 mmol) was used as starting compounds to give product **10b** (208 mg, 43%) as yellow solids after chromatography with hexane/EtOAc 5:1 to 1:2.

M.p. 196-206 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 2.46 (s, 3H, CH_3S); 7.59 (m, 1H, H-*p*-Ph); 7.61 (m, 2H, H-*m*-Ph); 7.94 (s, 1H, H-6); 8.07 (m, 2H, H-*o*-Ph); 8.94 (s, 1H, H-2); 12.15 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 18.12 (CH_3S); 107.46 (C-7); 124.55 (C-4a); 128.88 (CH-*o*-Ph); 129.17 (CH-*m*-Ph); 130.54 (CH-*p*-Ph); 135.06 (CH-6); 135.99 (C-*i*-Ph); 148.42 (C-4); 150.50 (CH-2); 150.54 (C-7a). IR(KBr): 3053, 2988, 2924, 2824, 1604, 1592, 1537, 1502, 1486, 1471, 1421, 1115, 866, 771. HRMS (ESI) calculated for $C_{13}H_{12}N_3S$: 242.0746; found: 242.0746.

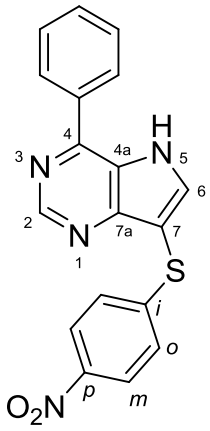
7-[(4-Methoxyphenyl)sulfanyl]-4-phenyl-5H-pyrrolo[3,2-d]pyrimidine
(9-[(4-Methoxyphenyl)sulfanyl]-6-phenyl-9-deazapurine) (10c)



6-phenyl-9-deazapurine **7** (390 mg, 2 mmol) and bis(4-methoxyphenyl) disulfide (836 mg, 3 mmol) were used as starting compounds to give product **10c** (566 mg, 85%) as yellow crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

M.p. 175-177 °C. ^{1}H NMR (600.1 MHz, $CDCl_3$): 3.63 (s, 3H, CH_3O); 6.63 (m, 2H, H-*m*-SC_6H_4OMe); 7.03 (m, 2H, H-*m*-SC_6H_4OMe); 7.20 (m, 2H, H-*m*-Ph); 7.26 (m, 1H, H-*p*-Ph); 7.72 (d, 1H, *J* = 3.0, H-6); 7.86 (m, 2H, H-*o*-Ph); 8.66 (s, 1H, H-2); 12.59 (bs, 1H, NH). ^{13}C NMR (150.9 MHz, $CDCl_3$): 55.10 (CH_3O); 104.13 (C-7); 114.33 (CH-*m*-SC_6H_4OMe); 125.56 (C-4a); 128.15 (C-*i*-SC_6H_4OMe); 128.50 (CH-*o*-Ph); 128.60 (CH-*m*-Ph); 128.71 (CH-*o*-SC_6H_4OMe); 130.16 (CH-*p*-Ph); 135.34 (C-*i*-Ph); 139.05 (CH-6); 149.91 (C-4); 150.56 (C-7a); 150.77 (CH-2); 157.91 (C-*p*-SC_6H_4OMe). IR($CDCl_3$): 3453, 3066, 2838, 2231, 1671, 1595, 1537, 1493, 1464, 1287, 1244, 1182, 1034. HRMS (ESI) calculated for $C_{19}H_{16}ON_3S$: 334.1009; found: 334.1008.

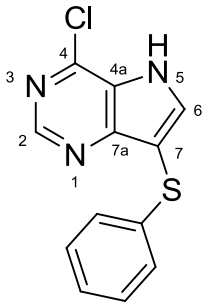
7-[(4-Nitrophenyl)sulfanyl]-4-phenyl-5H-pyrrolo[3,2-d]pyrimidine
(9-[(4-Nitrophenyl)sulfanyl]-6-phenyl-9-deazapurine) (10d)



6-phenyl-9-deazapurine **7** (390 mg, 2 mmol) and 4-nitrophenyl disulfide (926 mg, 3 mmol) were used as starting compounds to give product **10d** (348 mg, 50%) as yellow crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

M.p. 114-118 °C. ^{1}H NMR (600.1 MHz, DMSO-d_6): 7.25 (m, 2H, H-*o*-$SC_6H_4NO_2$); 7.64 (m, 1H, H-*p*-Ph); 7.65 (m, 2H, H-*m*-Ph); 8.07 (m, 2H, H-*m*-$SC_6H_4NO_2$); 8.13 (m, 2H, H-*o*-Ph); 8.41 (s, 1H, H-6); 8.96 (s, 1H, H-2); 12.75 (bs, 1H, NH). ^{13}C NMR (150.9 MHz, DMSO-d_6): 98.61 (C-7); 124.20 (CH-*m*-$SC_6H_4NO_2$); 125.11 (C-4a); 125.56 (CH-*o*-$SC_6H_4NO_2$); 129.01 (CH-*o*-Ph); 129.18 (CH-*m*-Ph); 130.72 (CH-*p*-Ph); 135.65 (C-*i*-Ph); 140.90 (CH-6); 144.80 (C-*p*-$SC_6H_4NO_2$); 149.09 (C-*i*-$SC_6H_4NO_2$); 149.17 (C-4); 151.18 (C-7a); 151.49 (CH-2). IR(KBr): 3095, 3065, 1596, 1580, 1540, 1506, 1322, 1115, 1089, 854. HRMS (ESI) calculated for $C_{18}H_{13}O_2N_4S$:349.0754; found: 349.0753.

4-Chloro-7-(phenylsulfanyl)-5H-pyrrolo[3,2-d]pyrimidine
(6-Chloro-9-(phenylsulfanyl)-9-deazapurine) (10e)



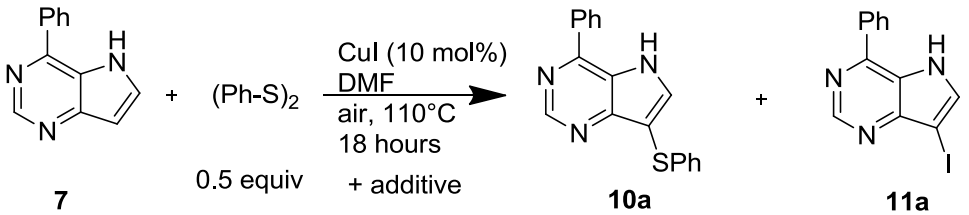
6-chloro-9-deazapurine **9** (307 mg, 2 mmol) and diphenyldisulfide (3.1 g, 14 mmol) were used as starting compounds to give product **10e** (471 mg, 90%) as white solids.

Diphenyldisulfide was divided into seven portions and each one was added every 10 hours until complete consumption of staring material as monitored by TLC. Chromatography was started with hexane (to remove excess of diphenyldisulfide) and followed by hexane/EtOAc 5:1 to 1:2. Crystalization in hexan/EtOAc gave white crystals.
[Do not excess the reaction time (80 hours) to avoid forming mixture of products.]

M.p. 224-226 °C ^{1}H NMR (499.8 MHz, DMSO-d_6):7.06 (m, 2H, H-*o*-Ph); 7.10 (m, 1H, H-*p*-Ph); 7.21 (m, 2H, H-*m*-Ph); 8.39 (s, 1H, H-6); 8.69 (s, 1H, H-2); 13.08 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 102.28 (C-7); 125.36 (C-4a); 125.48 (CH-*p*-Ph); 126.11 (CH-*o*-Ph); 129.16 (CH-*m*-Ph); 138.12 (C-*i*-Ph); 140.98 (CH-6); 142.99 (C-4); 150.43 (CH-2); 151.38 (C-7a). IR(KBr): 3072, 1796, 1612, 1584, 1524, 1494, 1478, 1422, 1393, 1215, 868. HRMS (ESI) calculated for $C_{12}H_9N_3ClS$: 262.0200; found: 262.0200.

Optimization of bypirydine ligand

A mixture of CuI (0.1 mmol, 10 mol %) and bypiridine ligand (10-100 mol%) in DMF (5 mL) was stirred at rt for 15 minutes and then was added to mixture of 9-deazapurines **7** (195 mg, 1 mmol) and diphenyldisulphides (110 mg, 0.5 mmol) in DMF (5 mL) and then was stirred at 110°C under air atmosphere for 18 hours. The solution was then cooled to room temperature, diluted with EtOAc (10 mL), washed with 1M solution of sodium salt of EDTA (5 mL). Aqueous solution was then extracted three times with EtOAc and combitated organic layers were dried over Na_2SO_4, filtered, and evaporated under vacuum and NMR of reaction mixture was measured.



NMR conversion

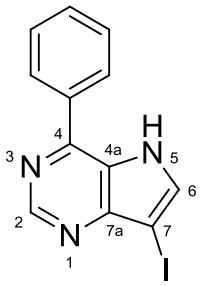
additive	**7**	**10a**	**11a**
bpy (10 mol%)	54%	43%	3%
bpy (20 mol%)	55%	45%	0%
bpy (50 mol%)	22%	78%	0%
bpy (100 mol%)	15%	85%	0%
dtbpy (10 mol%)	35%	63%	2%
dtbpy (20 mol%)	29%	71%	0%
dtbpy (50 mol%)	21%	79%	0%
dtbpy (100 mol%)	0%	100%	0%

As a the most economical ligand was chosen bpy (20 mol%) for the synthesis of **10a-d** and the time was prolonged until complete conversion (generally 48 hours). To avoid mixture of products in the synthesis of **10e ,** we used dtbpy (20 mol%) as a more effective ligand and prolonged reaction time up to 80 hours.

Halogenation of 9-deazapurines. General Procedure:

A mixture of 9-deazapurine **7** or **9** (0.5 mmol) and CuX, (I, Br_2) (0.6 mmol) in DMF (5 mL) was stirred at 110°C under air atmosphere for 18 hours until complete consumption of staring material as monitored by TLC. The solution was then cooled to room temperature, diluted with EtOAc (15 mL), washed with 1M solution of sodium salt of EDTA (10 mL). Aqueous solution was then extracted three times with EtOAc and combitated organic layers were dried over Na_2SO_4, filtered, and evaporated under vacuum. The crude product was purified by column chromatography on silica gel.

7-Iodo-4-phenyl-5H-pyrrolo[3,2-d]pyrimidine
(6-Phenyl-9-iodo-9-deazapurine) (11a)

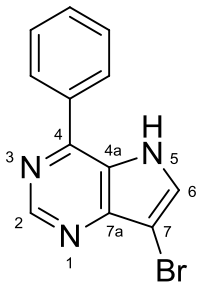


6-phenyl-9-deazapurine **7** (98 mg, 0.5 mmol) and CuI (115 mg, 0.6 mmol) were used as starting compound to give product **11 a** (130 mg, 81%) as white solid after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

^{1}H NMR (500.0 MHz, DMSO-d_6): 7.60 (m, 3H, H-*m*,*p*-Ph); 8.09 (m, 2H, H-*o*-Ph); 8.11 (s, 1H, H-6); 8.97 (s, 1H, H-2); 12.43 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 58.43 (C-7); 124.08 (C-4a); 128.90 (CH-*o*-Ph); 129.07 (CH-*m*-Ph); 130.54 (CH-*p*-Ph); 135.57 (C-*i*-Ph); 137.73 (CH-6); 148.48 (C-4); 150.95 (CH-2); 151.19 (C-7a). IR(KBr): 3434, 1605, 1595, 1539, 1504, 1486. HRMS (ESI) calculated for $C_{12}H_9N_3I$: 321.9836; found: 321.9835

7-Bromo-4-phenyl-5H-pyrrolo[3,2-d]pyrimidine

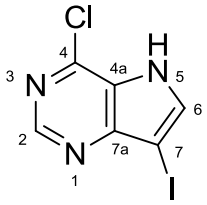
(6-Phenyl-9-bromo-9-deazapurine) (11b)



6-phenyl-9-deazapurine **7** (98 mg, 0.5 mmol) and $CuBr_2$ (134 mg, 0.6 mmol) were used as starting compound to give product **11b** (123 mg, 75%) as white solid after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

M.p. 264 - 294 °C. ^{1}H NMR (499.8 MHz, DMSO-d_6): 7.59 (m, 1H, H-*p*-Ph); 7.62 (m, 2H, H-*m*-Ph); 8.08 (m, 2H, H-*o*-Ph); 8.15 (d, 1H, J = 3.1, H-6); 8.98 (s, 1H, H-2); 12.40 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 89.68 (C-7); 123.66 (C-4a); 128.96 (CH-*o*-Ph); 129.14 (CH-*m*-Ph); 130.68 (CH-*p*-Ph); 133.44 (CH-6); 135.53 (C-*i*-Ph); 147.88 (C-7a); 148.77 (C-4); 150.98 (CH-2).
IR(KBr): 3438, 3054, 2929, 2788, 1607, 1597, 1545, 1508, 1490,1432, 1184. HRMS (ESI) calculated for $C_{12}H_9N_3Br$: 273.9974; found: 273.9974

4-Chloro-7-iodo-5H-pyrrolo[3,2-d]pyrimidine
(6-Chloro-9-iodo-9-deazapurine) (11c)



6-chloro-9-deazapurine **7** (77 mg, 0.5 mmol) and CuI (115 mg, 0.6 mmol) were used as starting compound to give product **11c** (91 mg, 65%) as white solid after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

^{1}H NMR (499.8 MHz, DMSO-d_6): 8.20 (s, 1H, H-6); 8.71 (s, 1H, H-2); 12.95 (bs, 1H, NH). ^{13}C NMR (125.7 MHz, DMSO-d_6): 58.68 (C-7); 124.59 (C-4a); 138.45 (CH-6); 142.30 (C-4); 150.00 (CH-2); 151.13 (C-7a).

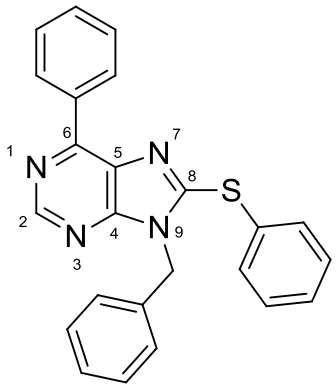
IR(KBr): 3436, 3120, 3092, 2972, 1609, 1527, 1494, 1417, 1354, 1245, 1177, 898, 860.

HRMS (ESI) calculated for $C_6H_4N_3ClI$: 279.9133; found: 279.9133

Sulfenytion of 9-benzyl-6-phenyl-9H-purine. General procedure

A 20 mL sealable tube equipped with a magnetic stirring bar was charged with all solid reaction components, 9-benzyl-6-phenyl-9H-purine **12** (286 mg, 1 mmol), disulfide (2.5 mmol), *t*BuOLi (240 mg, 3 mmol) and 1,4-dioxane (2 mL) via a syringe. The vessel was close by teflon-coated screw cap under Ar and was placed in a pre-heated oil bath at 130 °C and stirred until complete consumption of staring material as monitored by TLC, approx. 130 hours. It was cooled to room temperature and diluted with ethyl acetate (15 mL). The resulting solution was directly filtered through a filter paper and concentrated under reduced pressure.

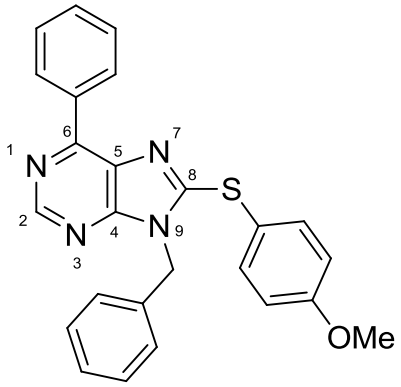
9-Benzyl-6-phenyl-8-(phenylsulfanyl)-9H-purine (13a)



Diphenyldisulfide (546 mg, 2.5 mmol) was used as starting compound to give product **13a** (237 mg, 60%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

M.p. 101 - 104 °C. ^{1}H NMR (499.8 MHz, $CDCl_3$): 5.50 (s, 2H, CH_2Ph); 7.27-7.35 (m, 5H, H-*o*,*m*,*p*-Bn); 7.37-7.41 (m, 5H, H-*m*,*p*-PhS); 7.45-7.50 (m, 3H, H-*m*,*p*-Ph); 7.59 (m, 2H, H-*o*-PhS); 8.74 (m, 2H, H-*o*-Ph); 8.96 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 46.59 (CH_2Ph); 127.75 (CH-*o*-Bn); 128.18 (CH-*p*-Bn); 128.50 (CH-*m*-Ph); 128.68 (C-*i*-PhS); 128.82 (CH-*m*-Bn); 129.03 (CH-*p*-PhS); 129.37 (CH-*m*-PhS); 129.68 (CH-*o*-Ph); 130.78 (CH-*p*-Ph); 131.16 (C-5); 132.91 (CH-*o*-PhS); 135.24 (C-*i*-Bn); 135.54 (C-*i*-Ph); 151.95 (CH-2); 152.37 (C-6); 152.92 (C-8); 154.46 (C-4). IR(KBr): 2921, 2851, 1580, 1561, 1495, 1459, 1429, 1258, 764. HRMS (ESI) calculated for $C_{24}H_{19}N_4S$: 395.1325; found: 395.1323.

9-Benzyl-8-[(4-methoxyphenyl)sulfanyl]-6-phenyl-9H-purine (13b)



Bis(4-methoxyphenyl) disulfide (696 mg, 2.5 mmol) was used as starting compound to give product **13b** (238 mg, 56%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 1:2.

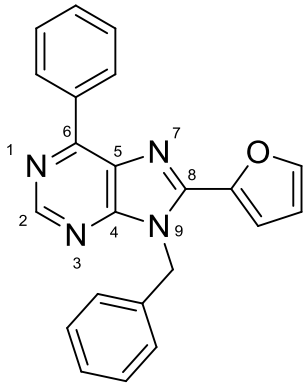
M.p. 124-127 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 3.85 (s, 3H, CH_3O); 5.49 (s, 2H, CH_2Ph); 6.94 (m, 2H, H-*m*-SC_6H_4OMe); 7.28-7.36 (m, 5H, H-*o*,*m*,*p*-Bn); 7.45-7.50 (m, 3H, H-*m*,*p*-Ph); 7.56 (m, 2H, H-*o*-SC_6H_4OMe); 8.73 (m, 2H, H-*o*-Ph); 8.95 (s, 1H, H-2).
^{13}C NMR (125.7 MHz, $CDCl_3$): 46.47 (CH_2Ph); 55.43 (CH_3O); 114.96 (CH-*m*-SC_6H_4OMe); 118.00 (C-*i*-SC_6H_4OMe); 127.73 (CH-*o*-Bn); 128.16 (CH-*p*-Bn); 128.47 (CH-*m*-Ph); 128.81 (CH-*m*-Bn); 129.65 (CH-*o*-Ph); 130.73 (CH-*p*-Ph); 131.10 (C-5); 135.21 (C-*i*-Bn); 135.39 (C-*i*-Ph); 135.84 (CH-*o*-SC_6H_4OMe); 151.47 (CH-2); 151.61 (C-6); 154.67 (C-4,8); 160.76 (C-*p*-SC_6H_4OMe). IR (KBr): 3066, 3022, 2953, 2923, 2854, 1586, 1559, 1494, 1542, 1443, 1323, 1302, 1245, 1171, 1030, 833, 770, 725, 692. HRMS (ESI) calculated for $C_{25}H_{21}ON_4S$: 425.1431; found: 425.1429.

Liebeskind-Srogl cross-coupling of 9-benzyl-6-phenyl-8-(phenylsulfanyl)-9H-purine

a) Reaction with stannanes

To the mixture of CuMeSal (47 mg, 0.22 mmol, 2.2 equiv), $Pd(PPh_3)_4$ (5.8 mg, 0.005 mmol, 0.05 equiv) and 9-benzyl-6-phenyl-8-(phenylthio)-9H-purine **13a** (39 mg, 0.1 mmol, 1.0 equiv) and stannane (0.12 mmol, 1.2 equiv) in THF (2 mL). The reaction mixture was stirred under nitrogen at 50 °C for 18 h, and then 10% aqueous NH_4OH (10 mL) was added and the mixture was stirred for an additional 10 min. The reaction mixture was filtered through a plug of Celite, and the filtrate was extracted with ethylacetate (3 × 15 mL). The organic layer was washed with brine (5 mL), dried over $NaSO_4$, and evaporated. The crude product was purified by column chromatography on silica gel.

9-Benzyl-8-(furan-2-yl)-6-phenyl-9H-purine (14a)

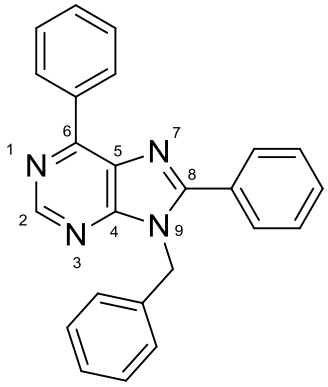


2-(tri-n-butylstannyl)furan (38 µL, 0.12 mmol, 1.2 equiv) was used as starting compound to give product **14a** (25 mg, 70%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 2:1.

M.p. 135 - 141 °C. ^{1}H NMR (500.0 MHz, $CDCl_3$): 5.86 (s, 2H, CH_2Ph); 6.59 (dd, 1H, $J_{4,3}$ = 3.6, $J_{4,5}$ = 1.8, H-4-furyl); 7.22 (m, 2H, H-*o*-Bn); 7.26 (m, 1H, H-*p*-Bn); 7.28 (m, 2H, H-*m*-Bn); 7.29 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,5}$ = 0.8, H-3-furyl); 7.52 (m, 1H, H-*p*-Ph); 7.58 (m, 2H, H-*m*-Ph); 7.64 (dd, 1H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.8, H-5-furyl); 8.88 (m, 2H, H-*o*-Ph); 9.02 (s, 1H, H-2). ^{13}C NMR (125.7 MHz, $CDCl_3$): 46.96 (CH_2Ph); 112.34 (CH-4-furyl); 114.88 (CH-3-furyl);126.85 (CH-*o*-Bn); 127.84 (CH-*p*-Bn); 128.62 (CH-*m*-Ph); 128.76 (CH-*m*-Bn); 129.79 (CH-*o*-Ph); 130.82 (CH-*p*-Ph); 131.05 (C-5); 135.75 (C-*i*-Ph); 136.16 (C-*i*-Bn); 144.70 (C-2-

furyl); 144.93 (CH-5-furyl); 145.47 (C-8); 152.27 (CH-2); 153.64 (C-6); 154.18 (C-4). IR(KBr): 3068, 1605, 1603, 1562, 1497, 1454, 1334, 1321, 1016. HRMS (ESI) calculated for $C_{22}H_{17}ON_4$: 353.1397; found: 353.1397

9-Benzyl-6,8-diphenyl-9H-purine (14b)



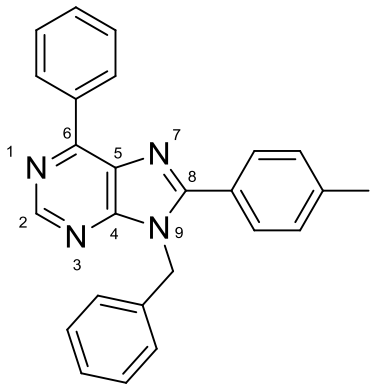
Tributylphenylstannane (39 μL, 0.12 mmol, 1.2 equiv) was used as starting compound to give product **14b** (30 mg, 83%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 2:1. ^{1}H NMR was compared with published data[1].

^{1}H NMR (300 MHz, $CDCl_3$): 5.61 (s, 2H, CH_2Ph); 7.10 (m, 2H, H-*o*-Bn); 7.25-7.33 (m, 3H, H-*m*,*p*-Bn); 7.46-7.60 (m, 6H, H-m,*p*-Ph-6 and H-m,*p*-Ph-8); 7.73 (m, 2H, H-*o*-Ph-8); 8.92 (m, 2H, H-*o*-Ph-6); 9.05 (s, 1H, H-2).

b) Reaction with boronic acid

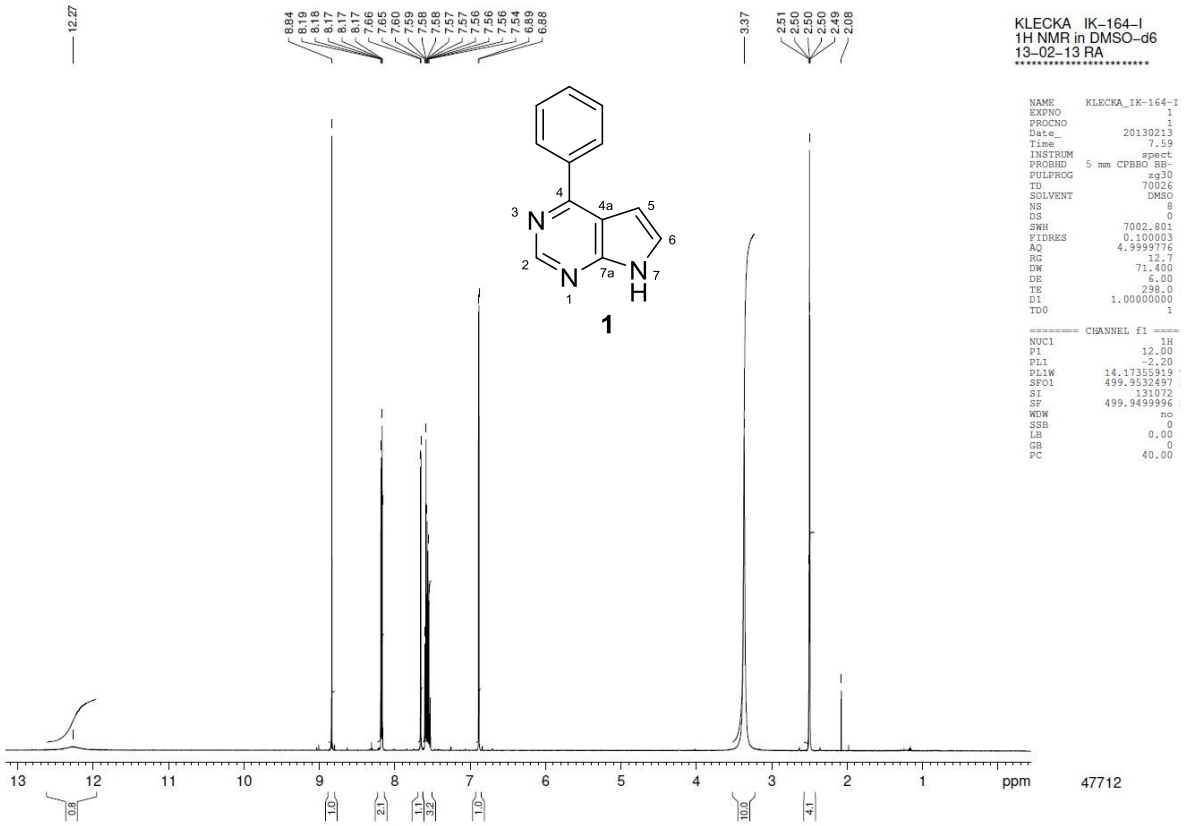
9-benzyl-6-phenyl-8-(phenylsulfanyl)-9H-purine **13a** (39 mg, 0.1 mmol), Cu (I) thiophene-2-carboxylate (23 mg, 0.12 mmol), *p*-tolylboronic acid (21 mg, 0.15 mmol), Pd_2dba_3 (4 mg, 0.004 mmol) and tris-2-furylphosphine (4 mg, 0.016 mmol) were placed in reaction vessel that was flushed with argon. THF (1 mL) was added and the mixture was stirred for 18 h at 50 °C. EtOAc (5 mL) was added and the suspension was washed with 10% aq. NH_4OH (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and filtered, and all of the volatiles were removed under reduced pressure. The crude product was purified by column chromatography on silica gel to give product **14c** (20 mg, 54%) as white crystals after chromatography eluting with hexane/EtOAc 5:1 to 2:1. ^{1}H NMR was compared with published data[1].

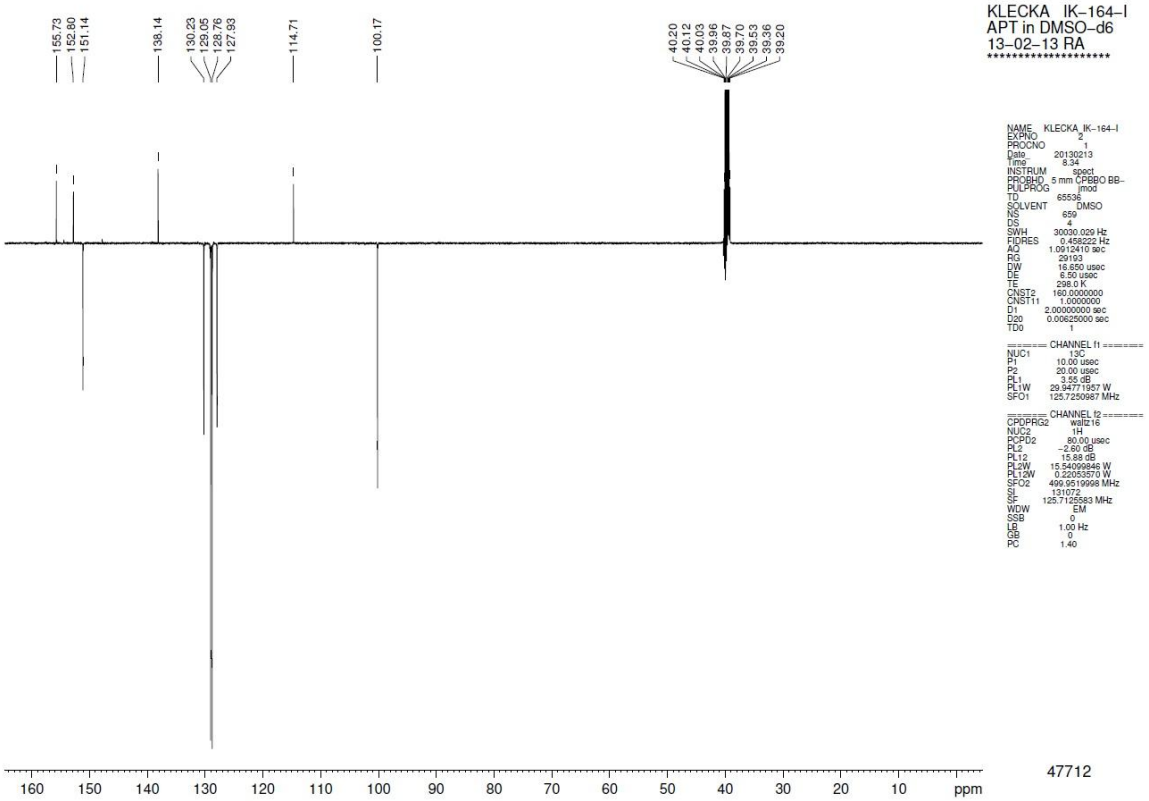
9-Benzyl-6-phenyl-8-(p-tolyl)-9H-purine (14c)

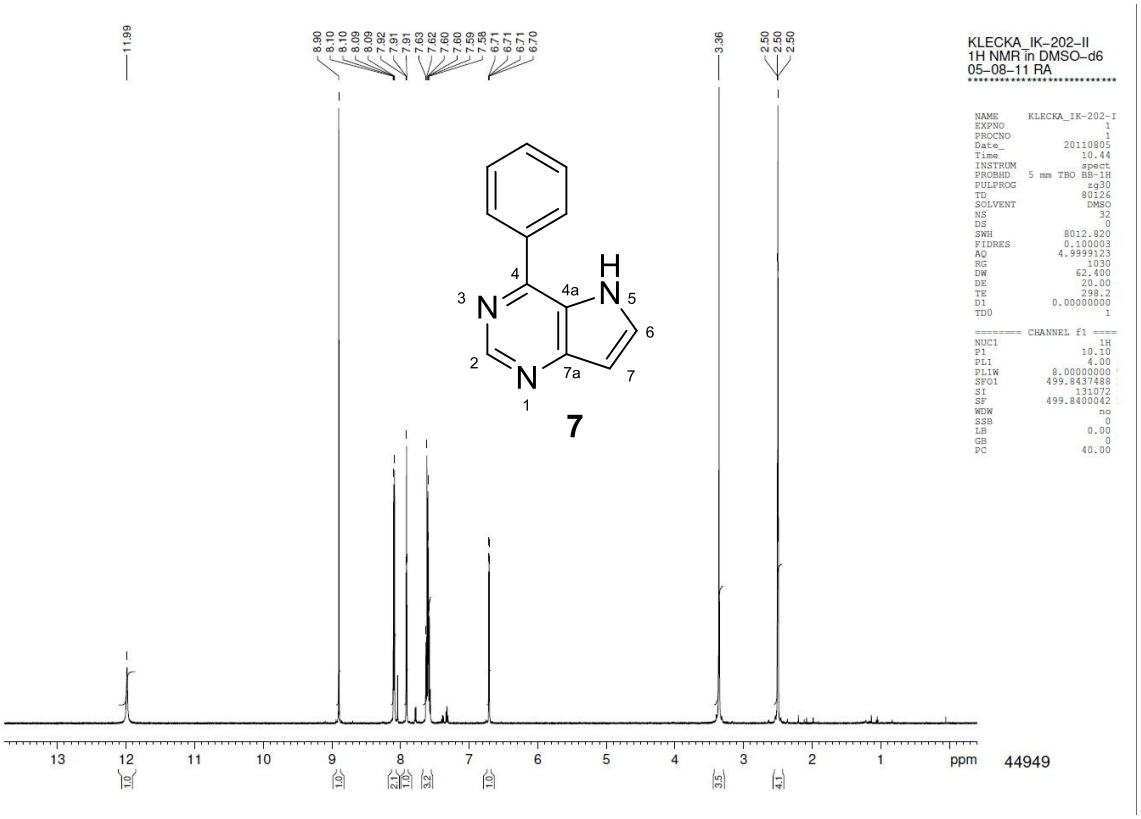


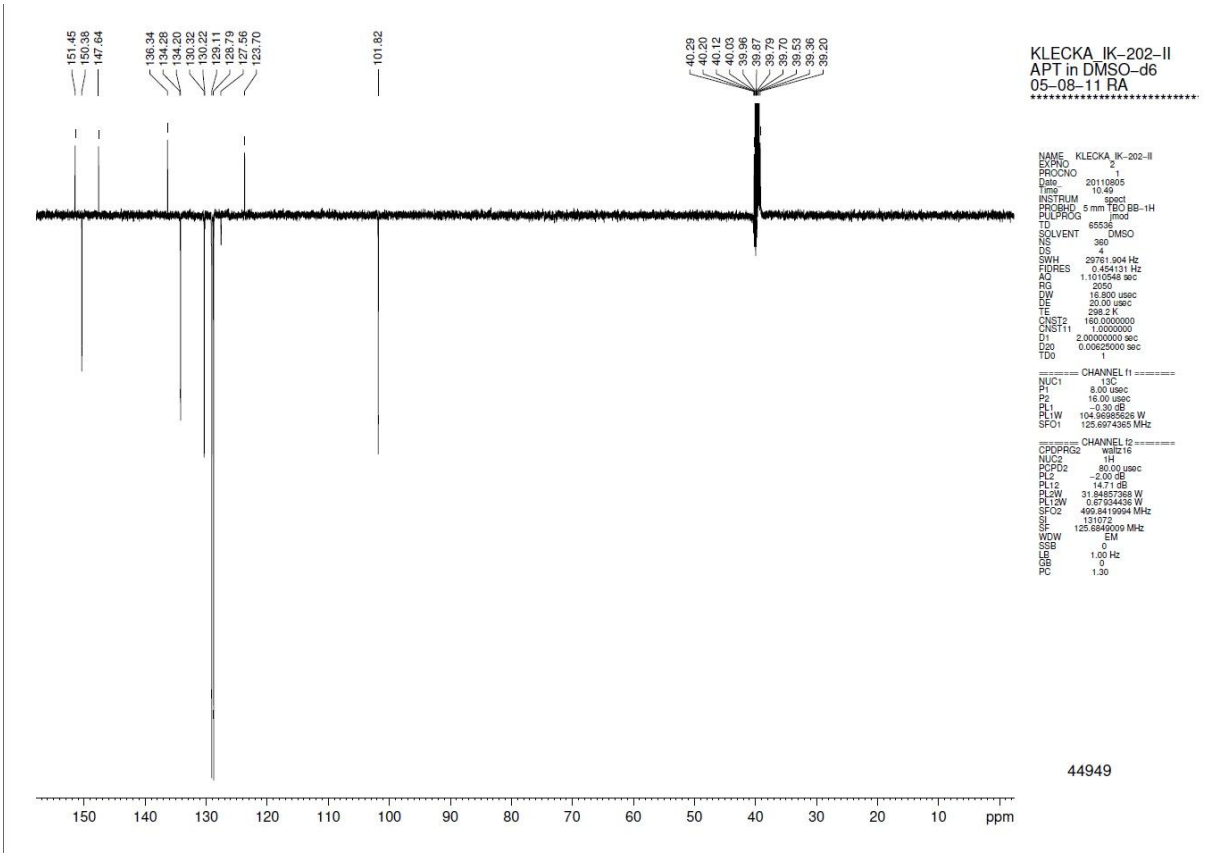
^{1}H NMR (300 MHz, $CDCl_3$): 2.43 (s, 3H, CH_3); 5.59 (s, 2H, CH_2Ph); 7.11 (m, 2H, H-*o*-Bn); 7.25-7.34 (m, 5H, H-*m*-Tol and H-*m*,*p*-Bn); 7.51 (m, 1H, H-*p*-Ph); 7.57 (m, 2H, H-*m*-Ph); 7.64 (m, 2H, H-*o*-Tol); 8.92 (m, 2H, H-*o*-Ph); 9.03 (s, 1H, H-2).

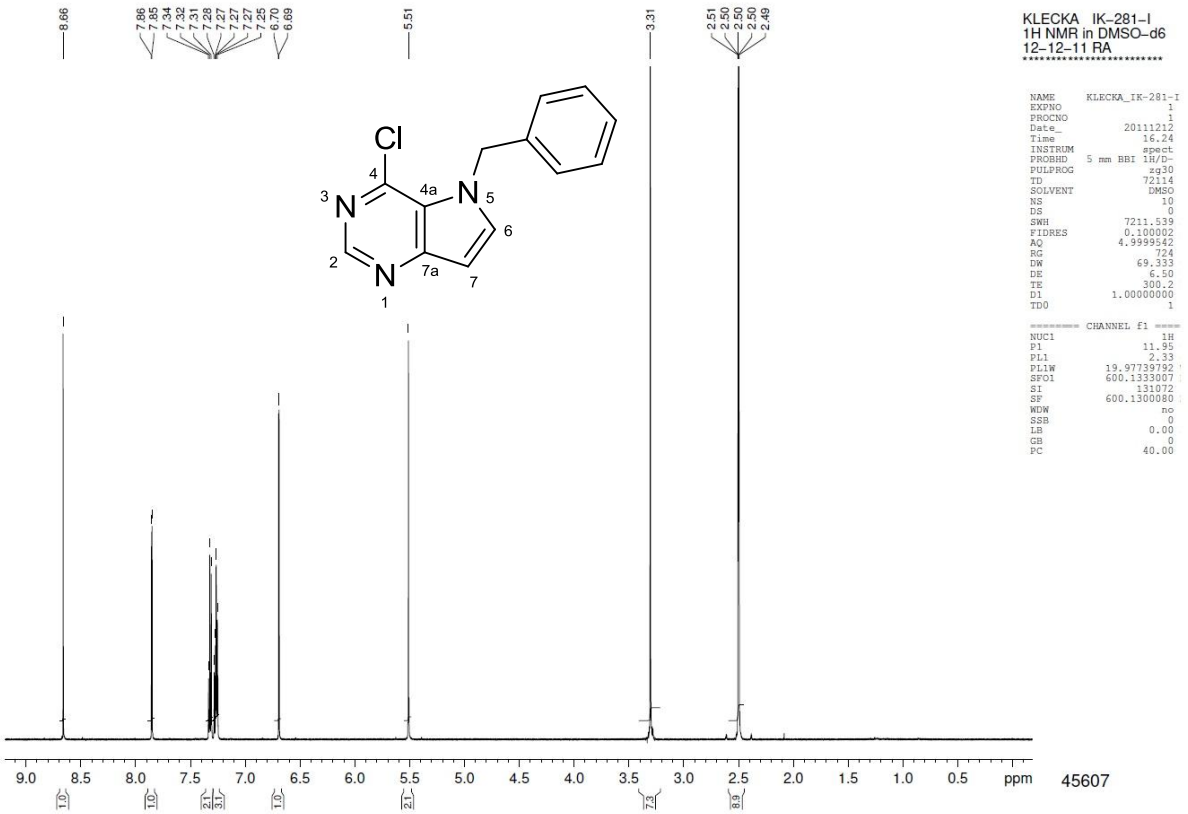
2. Copies of NMR spectra

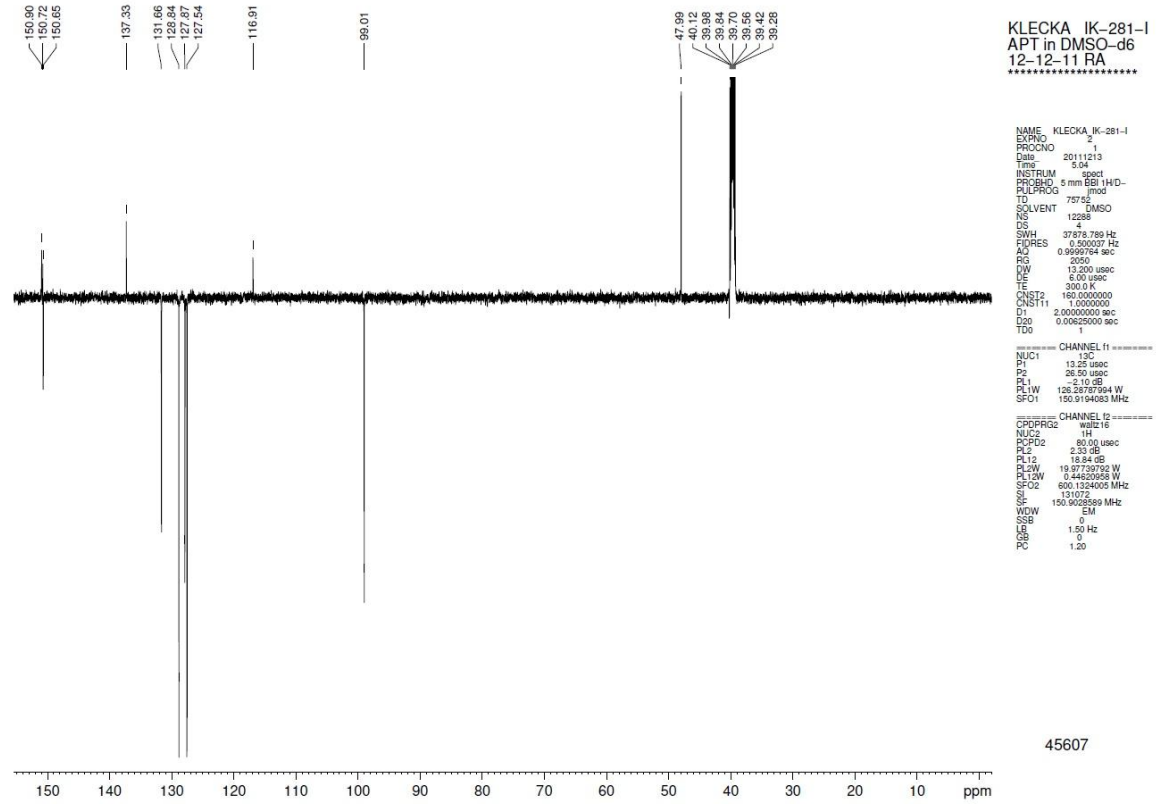


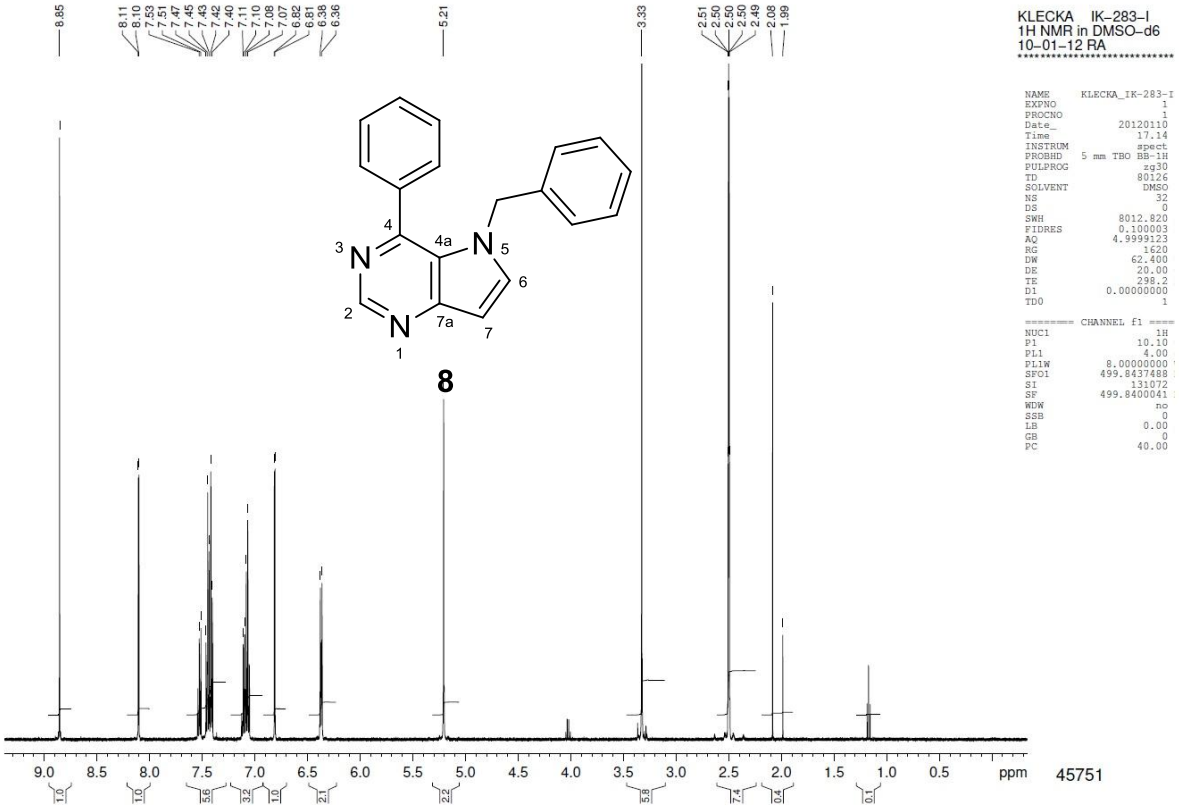


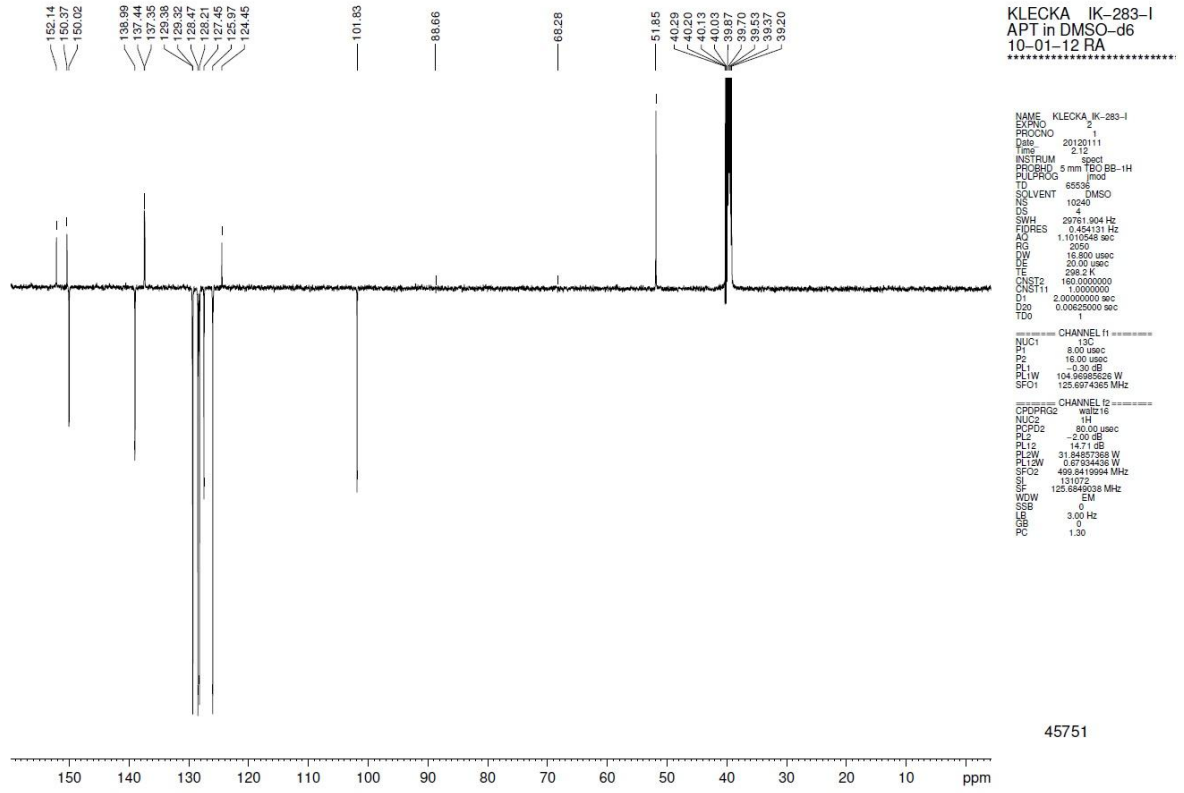

KLECKA_IK-202-II
1H NMR in DMSO-d6
05-08-11 RA
7
44949

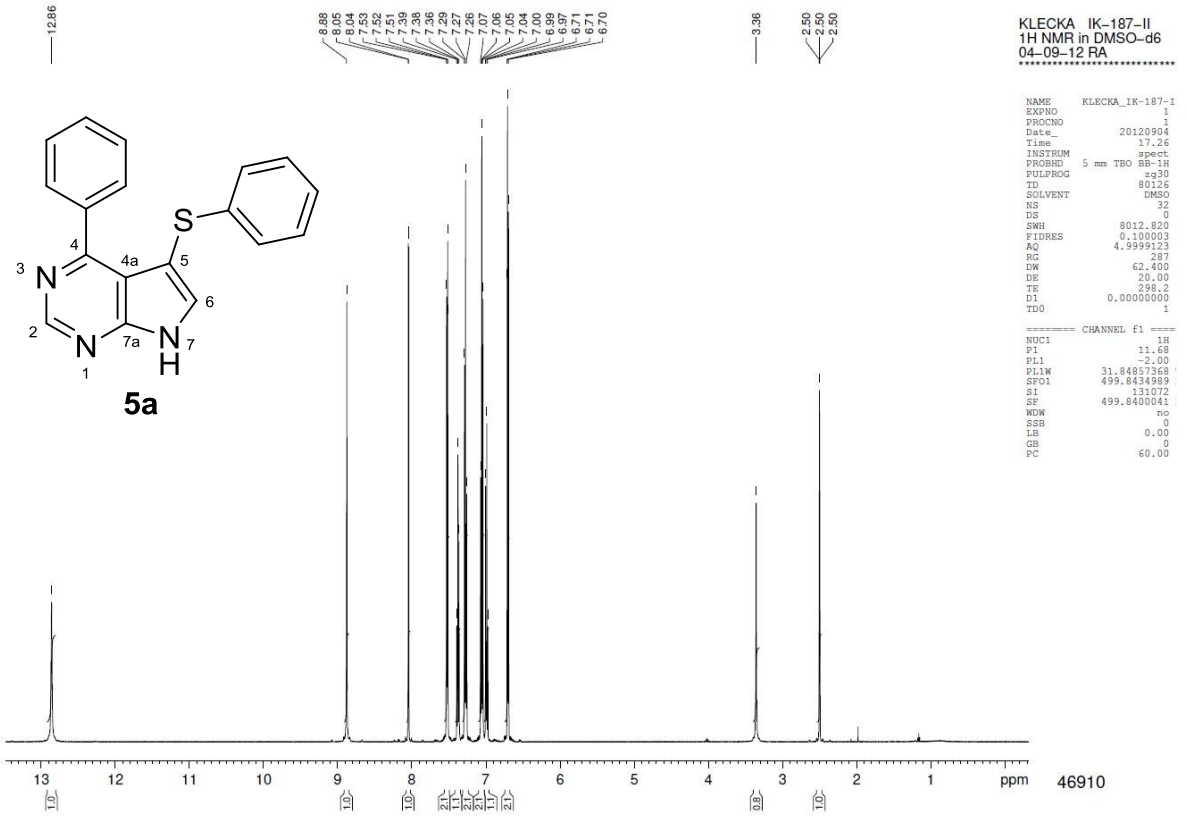

KLECKA_IK-202-II
APT in DMSO-d6
05-08-11 RA
44949

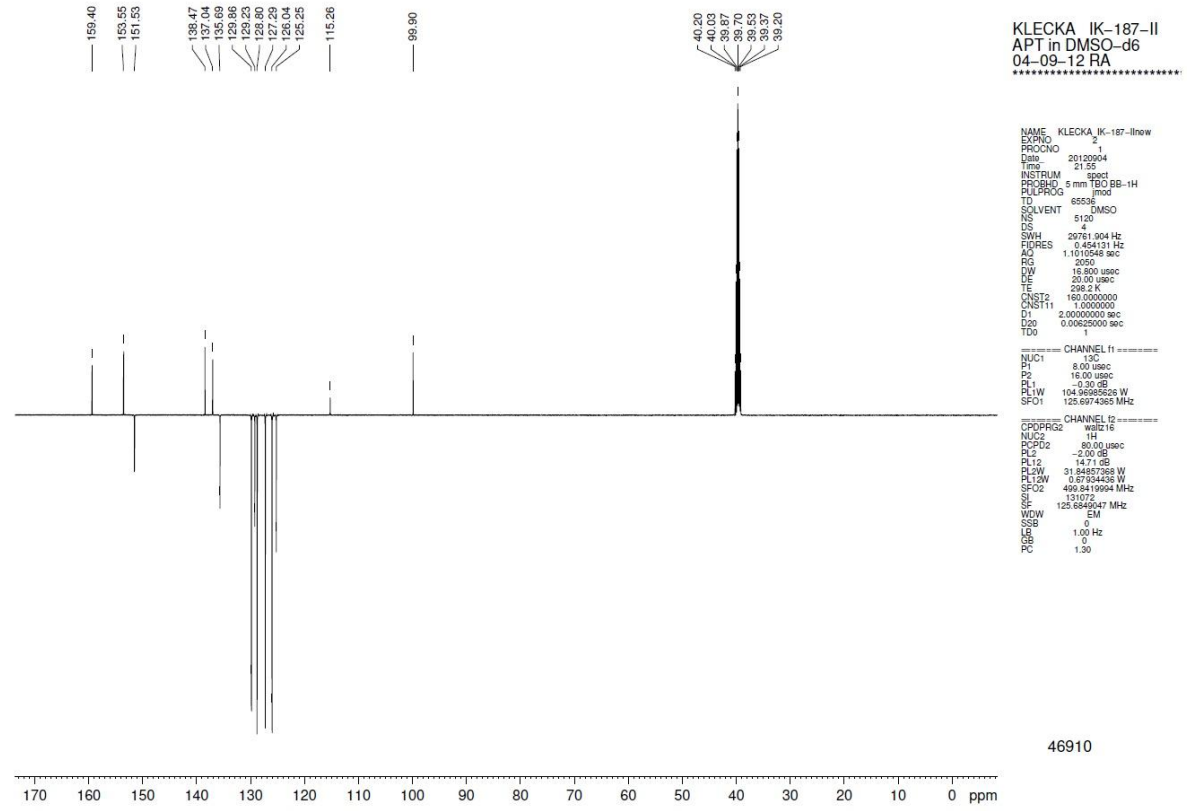


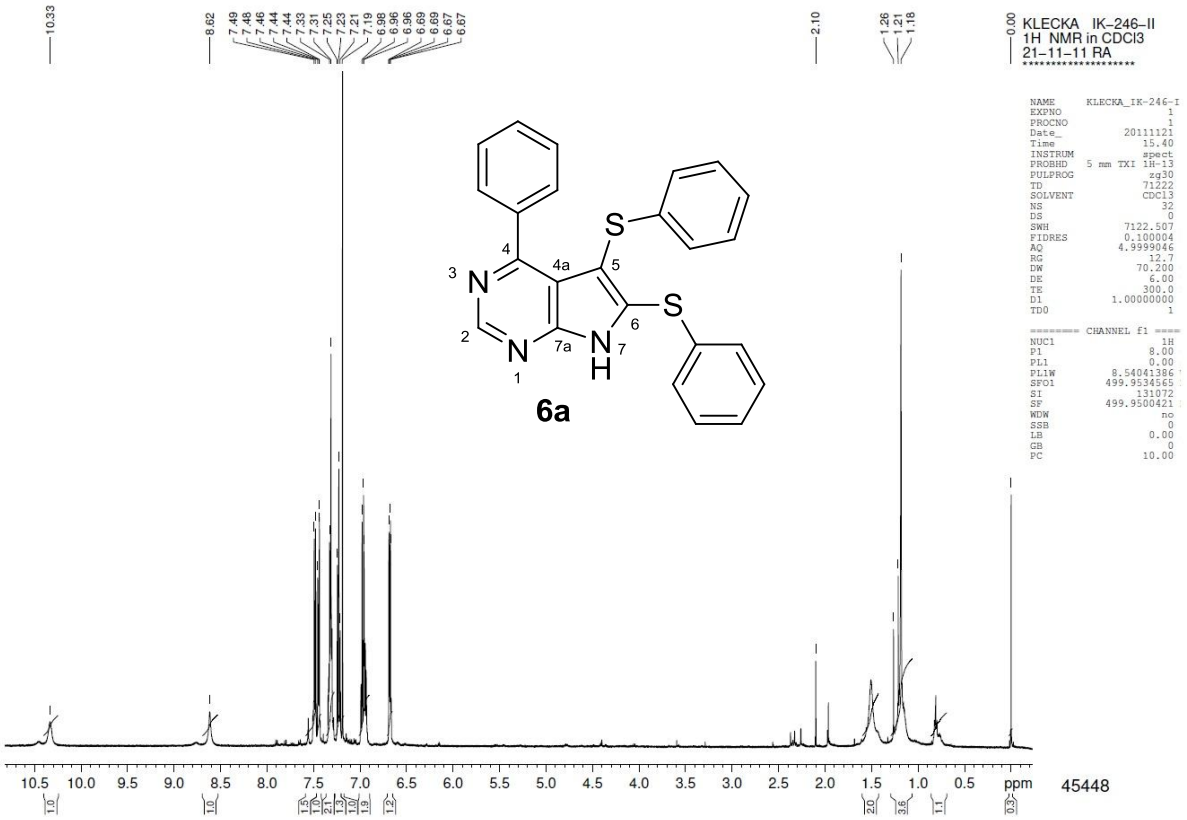


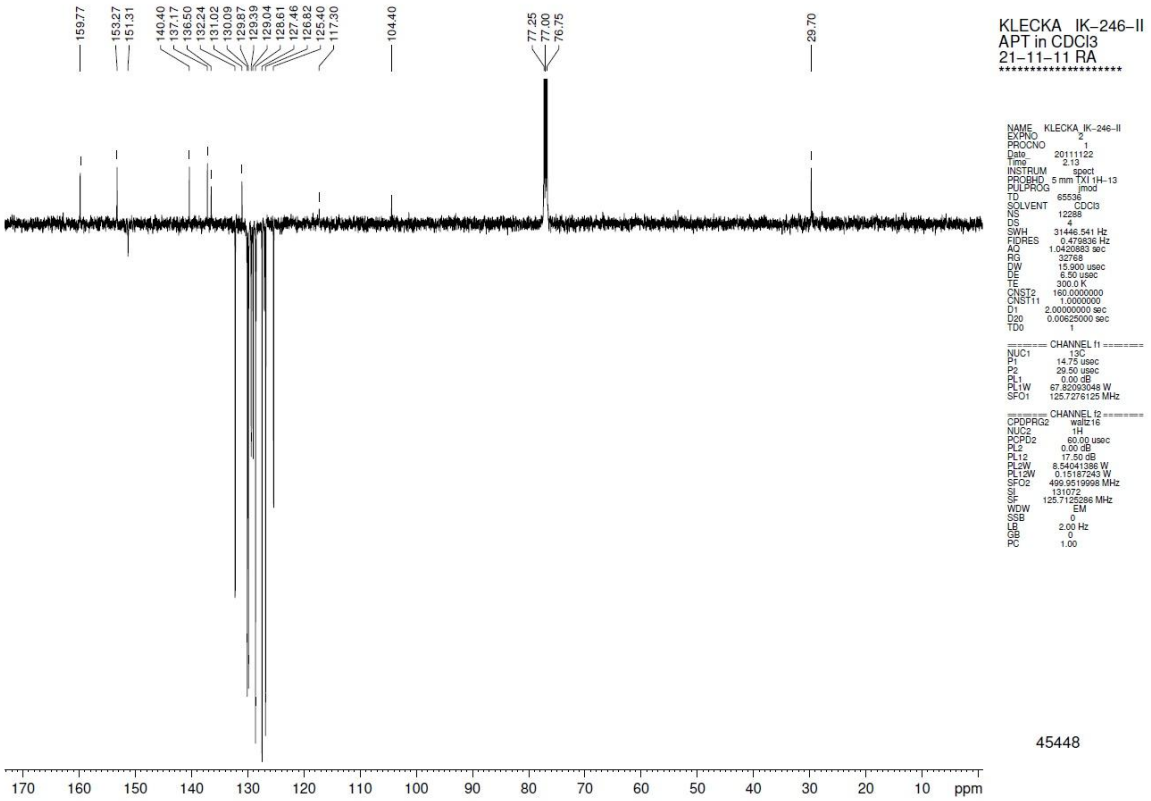

8.85
8.11
8.10
7.53
7.51
7.47
7.45
7.43
7.42
7.40
7.11
7.10
7.08
7.07
6.82
6.81
6.38
6.36
5.21
3.33
2.51
2.50
2.50
2.50
2.49
2.08
1.99
KLECKA IK-283-I
1H NMR in DMSO-d6
10-01-12 RA
NAME KLECKA_IK-283-I
EXPNO 1
PROCNO 1
Date_ 20120110
Time 17.14
INSTRUM spect
PROBHD 5 mm TBO BB-1H
PULPROG zg30
TD 80126
SOLVENT DMSO
NS 32
DS 0
SWH 8012.820
FIDRES 0.100003
AQ 4.9999123
RG 1620
DW 62.400
DE 20.00
TE 298.2
D1 0.00000000
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 10.10
PL1 4.00
PL1W 8.00000000
SFO1 499.8437488
SI 131072
SF 499.8400041
WDW no
SSB 0
LB 0.00
GB 0
PC 40.00
8
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
45751

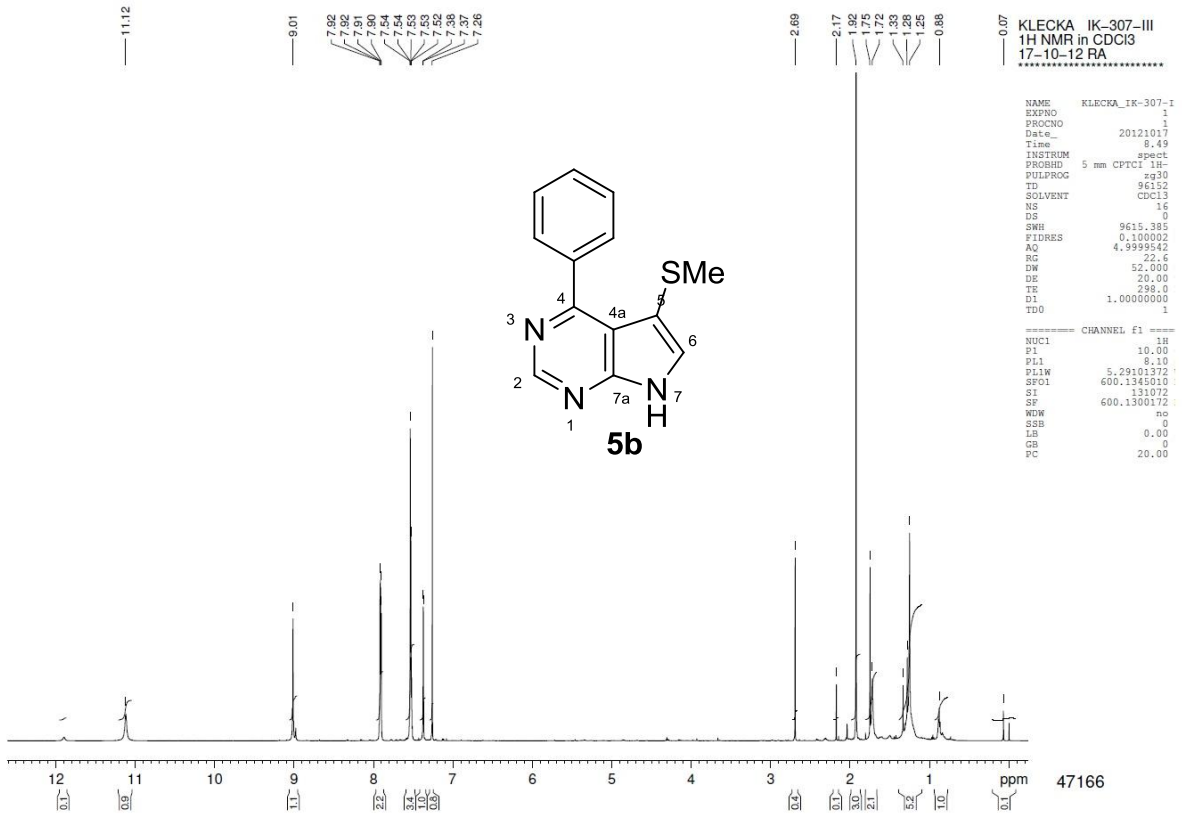

152.14
150.37
150.02
138.99
137.44
137.35
129.38
129.32
128.47
128.21
127.45
125.97
124.45
101.83
88.66
68.28
51.85
40.29
40.20
40.13
40.03
39.87
39.70
39.53
39.37
39.20
KLECKA IK-283-I
APT in DMSO-d6
10-01-12 RA
NAME KLECKA_IK-283-I
EXPNO 2
PROCNO 1
Date_ 20120111
Time 2.12
INSTRUM spect
PROBHD 5 mm TBO BB-1H
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 10240
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010548 sec
RG 2050
DW 16.800 usec
DE 20.00 usec
TE 298.2 K
CNST2 160.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00625000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 8.00 usec
P2 16.00 usec
PL1 -0.30 dB
PL1W 104.96985626 W
SFO1 125.6974365 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.71 dB
PL2W 31.84857368 W
PL12W 0.67934438 W
SFO2 499.8419994 MHz
SI 131072
SF 125.6849038 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.30
45751
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

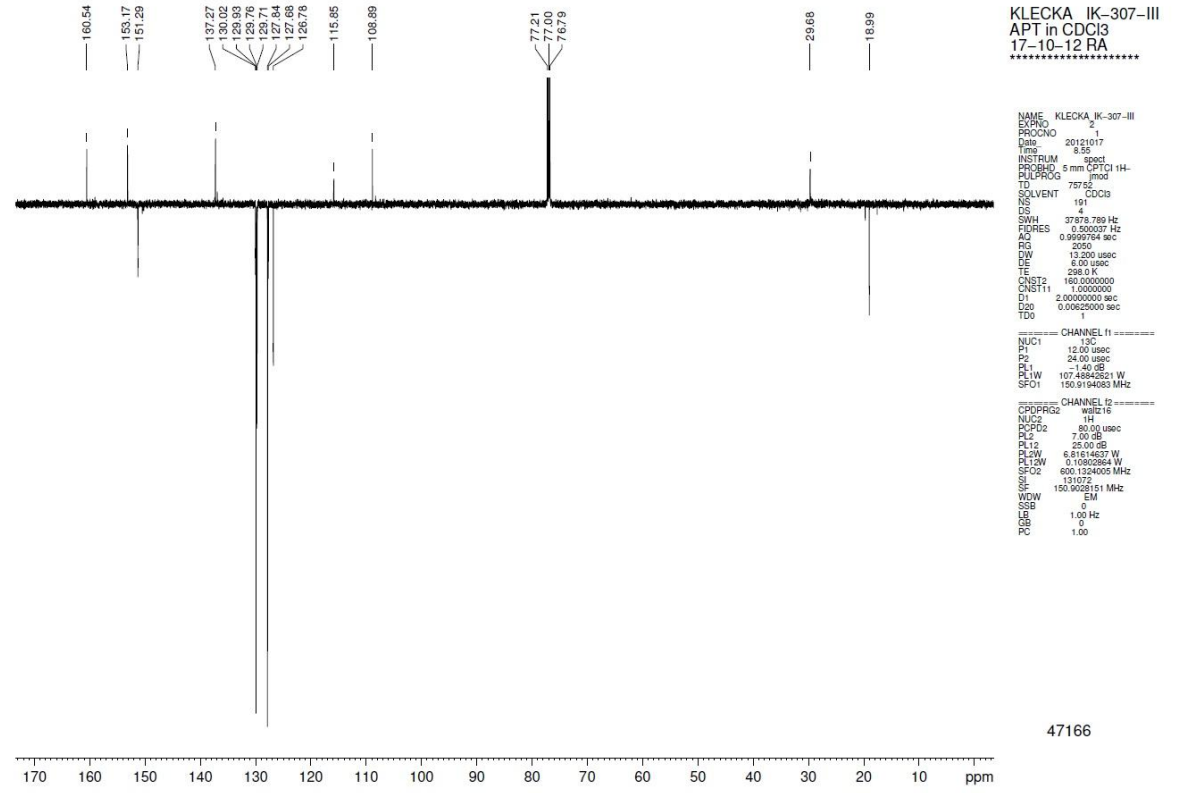


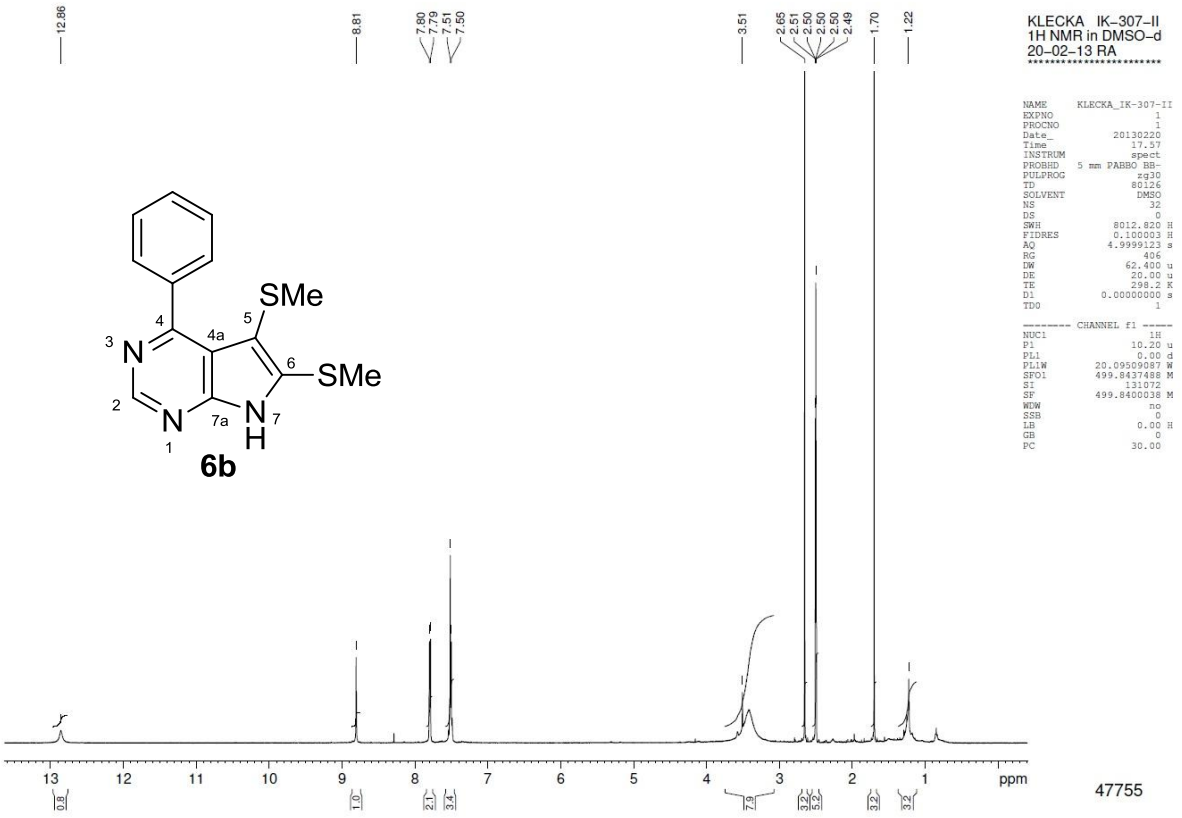


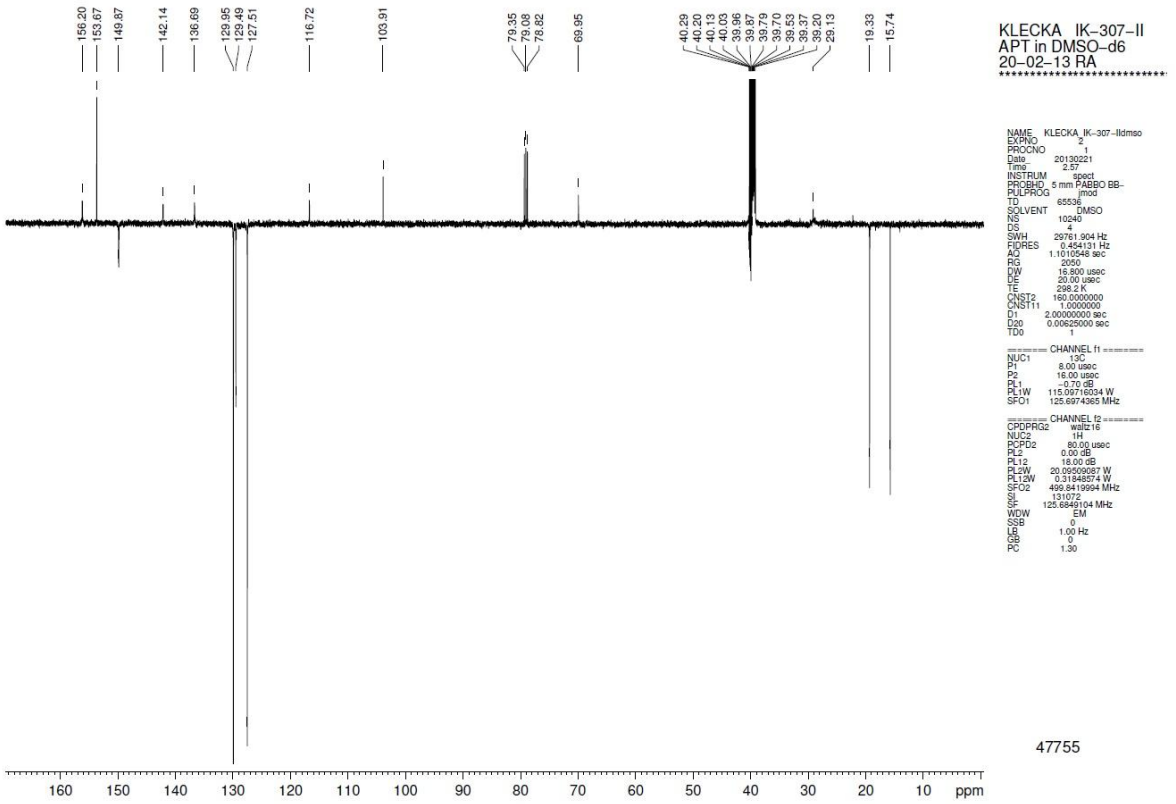


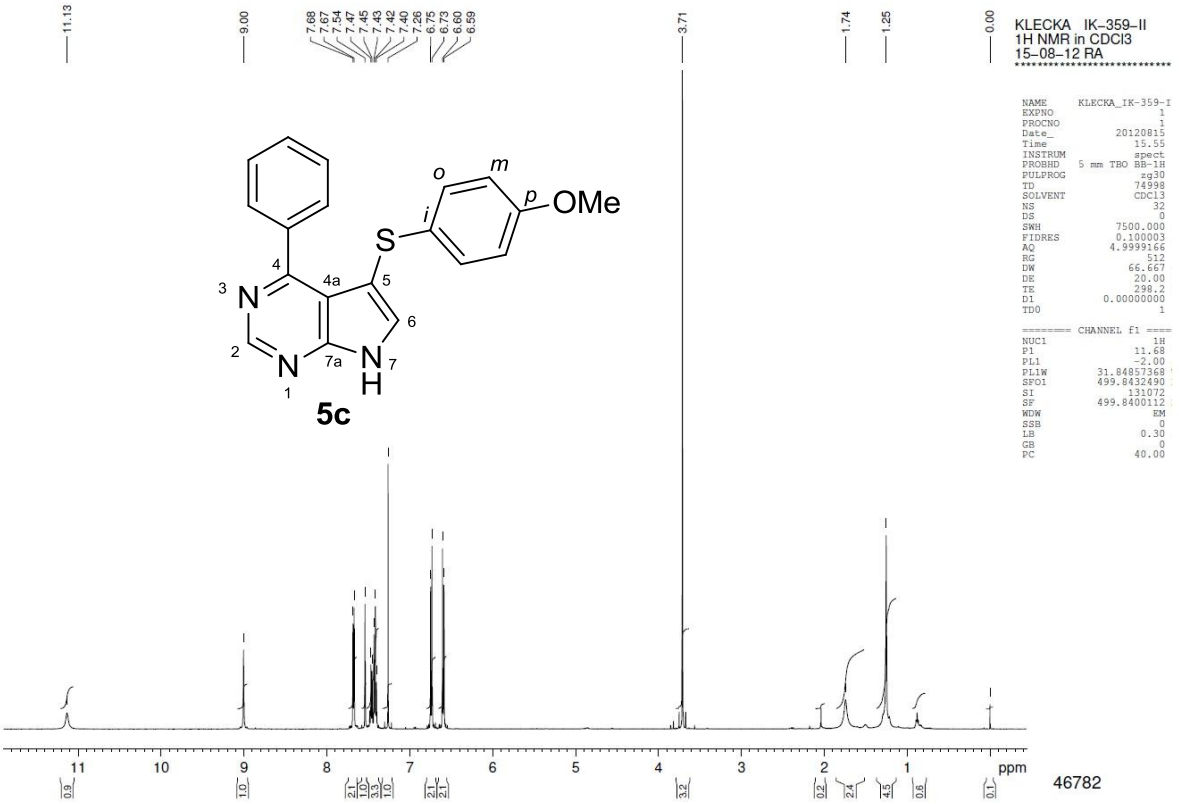


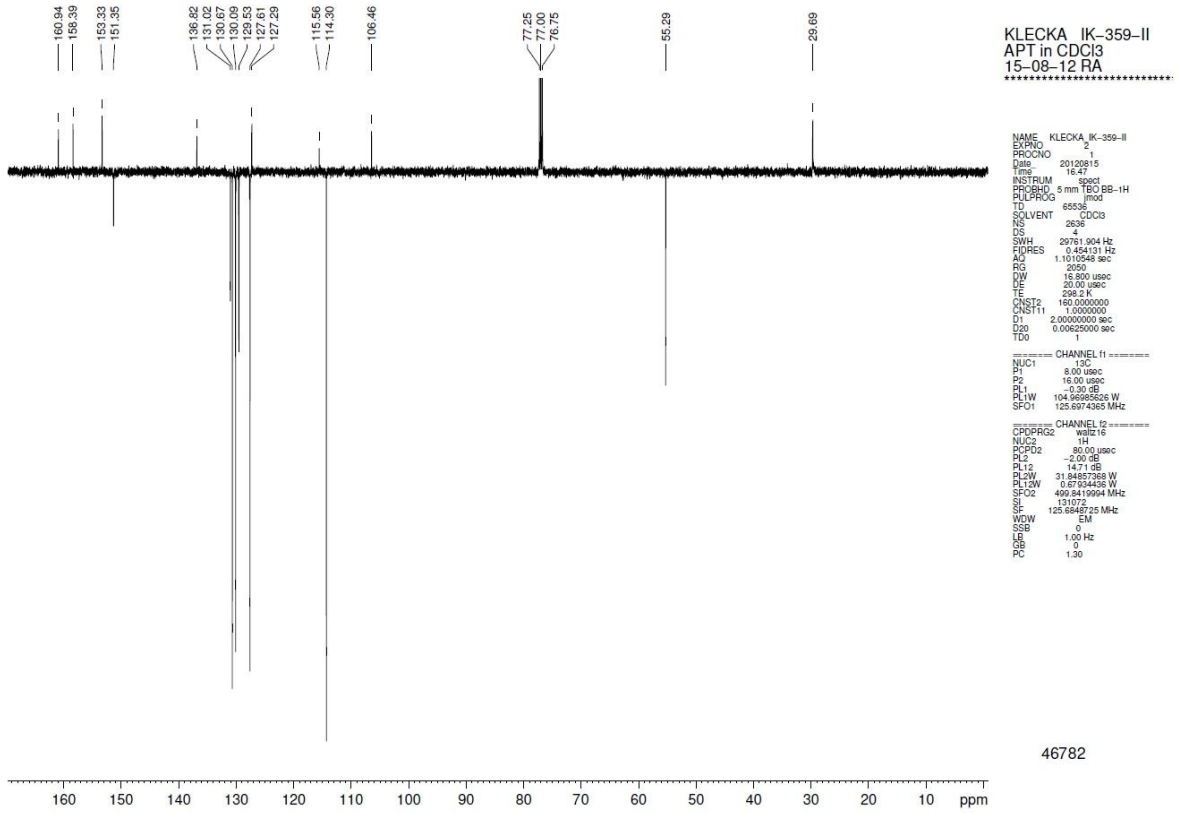


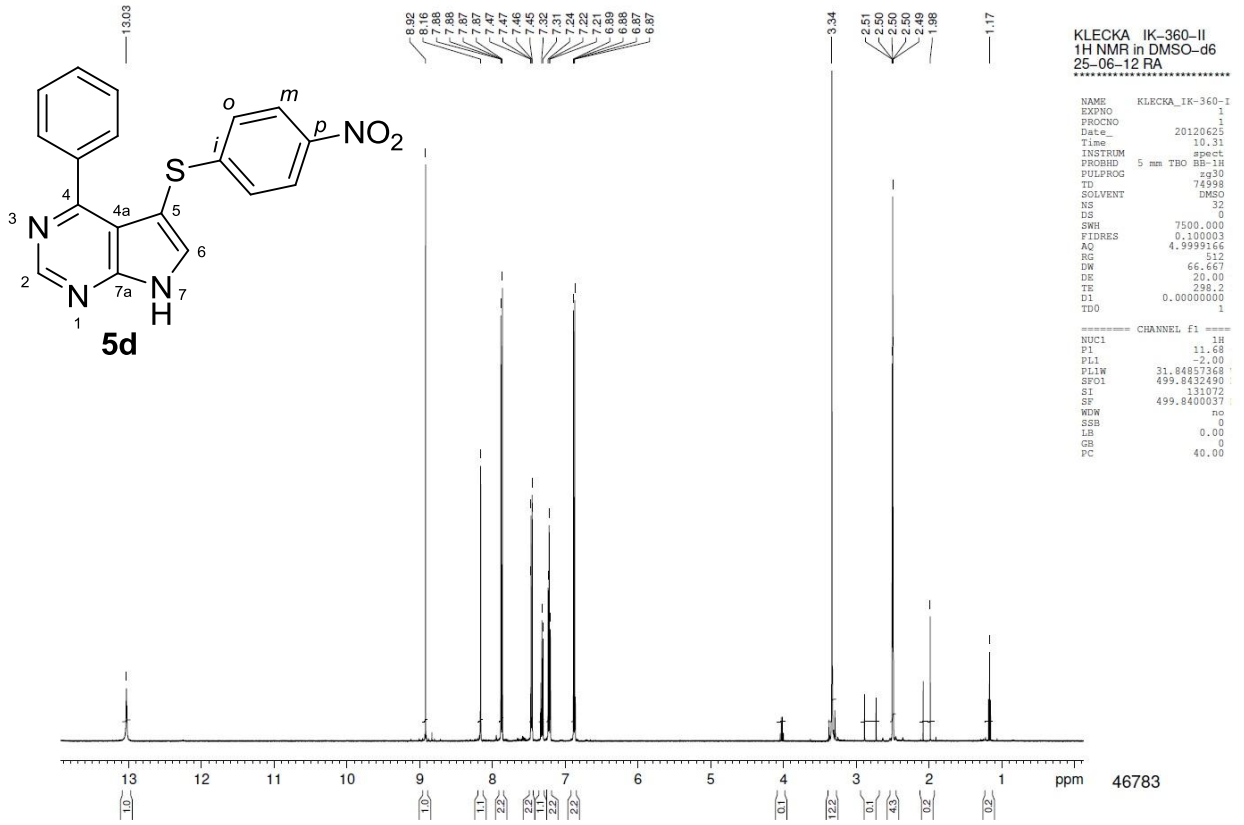


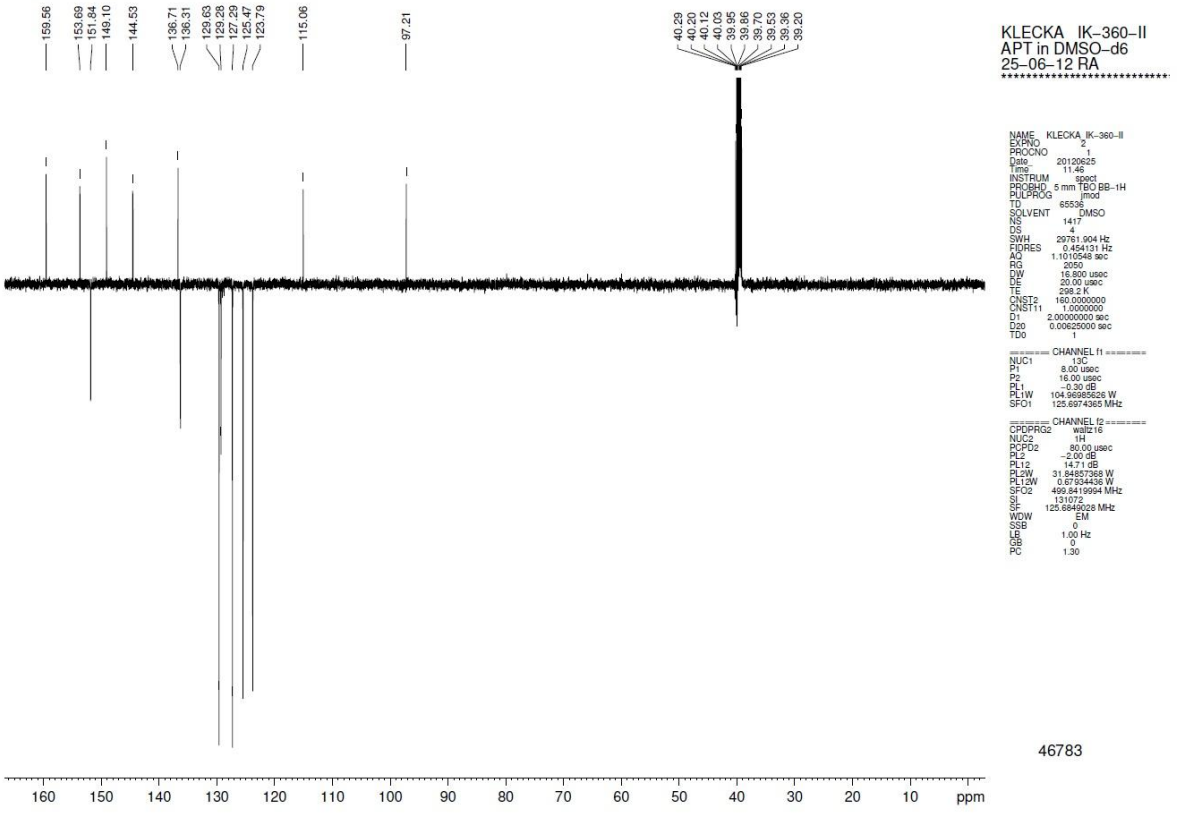


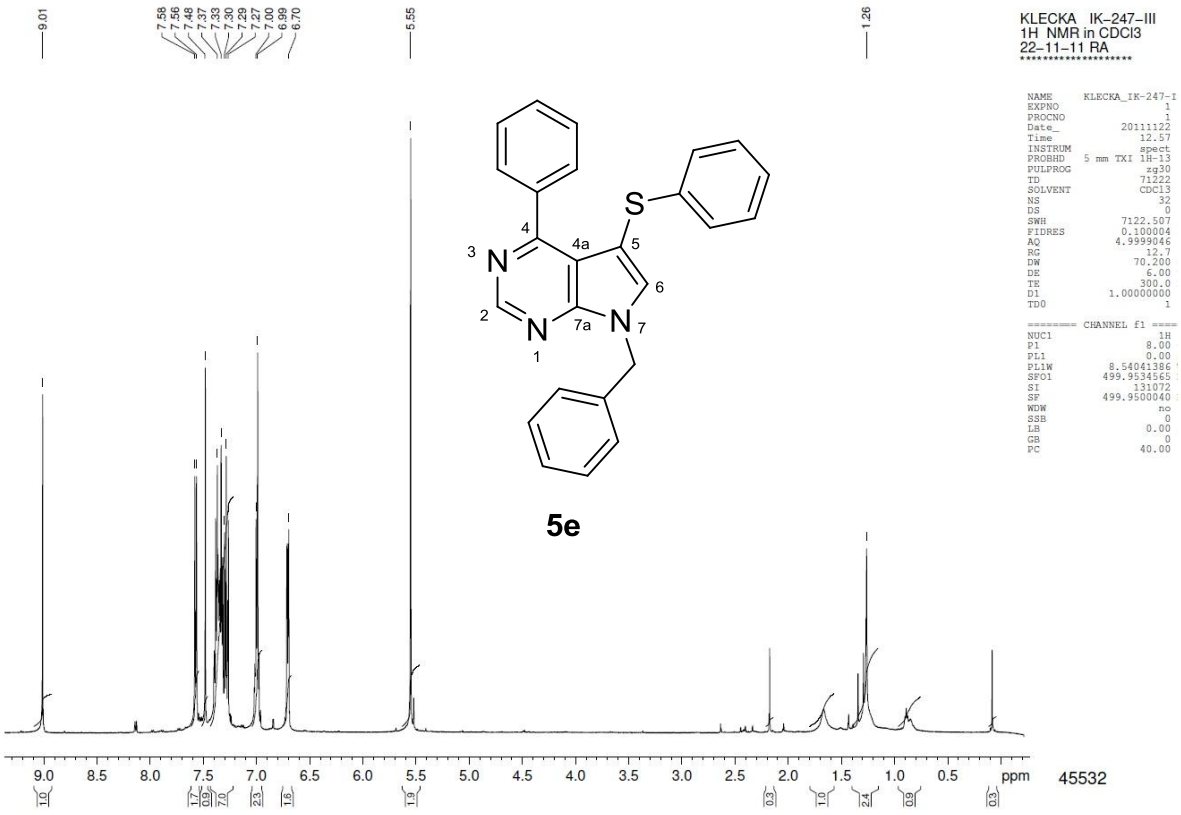


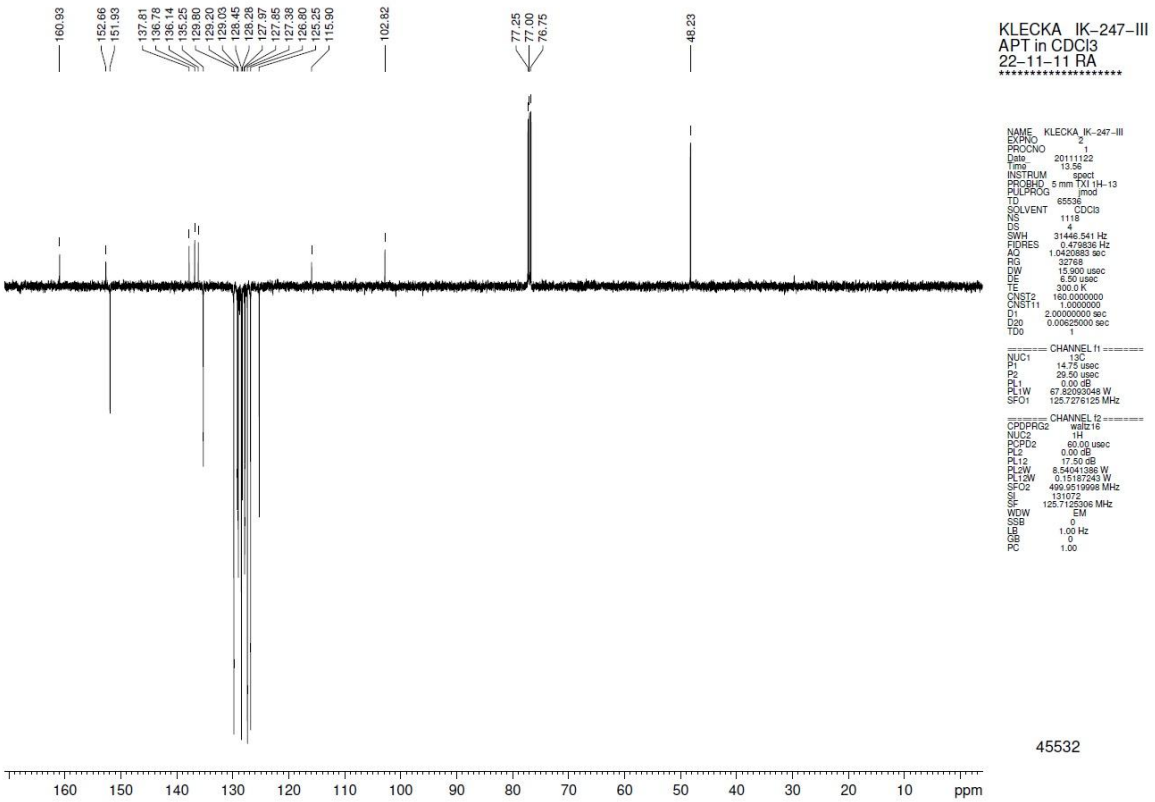

11.13
9.00
7.68
7.67
7.54
7.47
7.45
7.43
7.42
7.40
7.26
6.75
6.73
6.60
6.59
3.71
1.74
1.25
0.00
KLECKA IK-359-II
1H NMR in CDCl3
15-08-12 RA
5c
46782
ppm

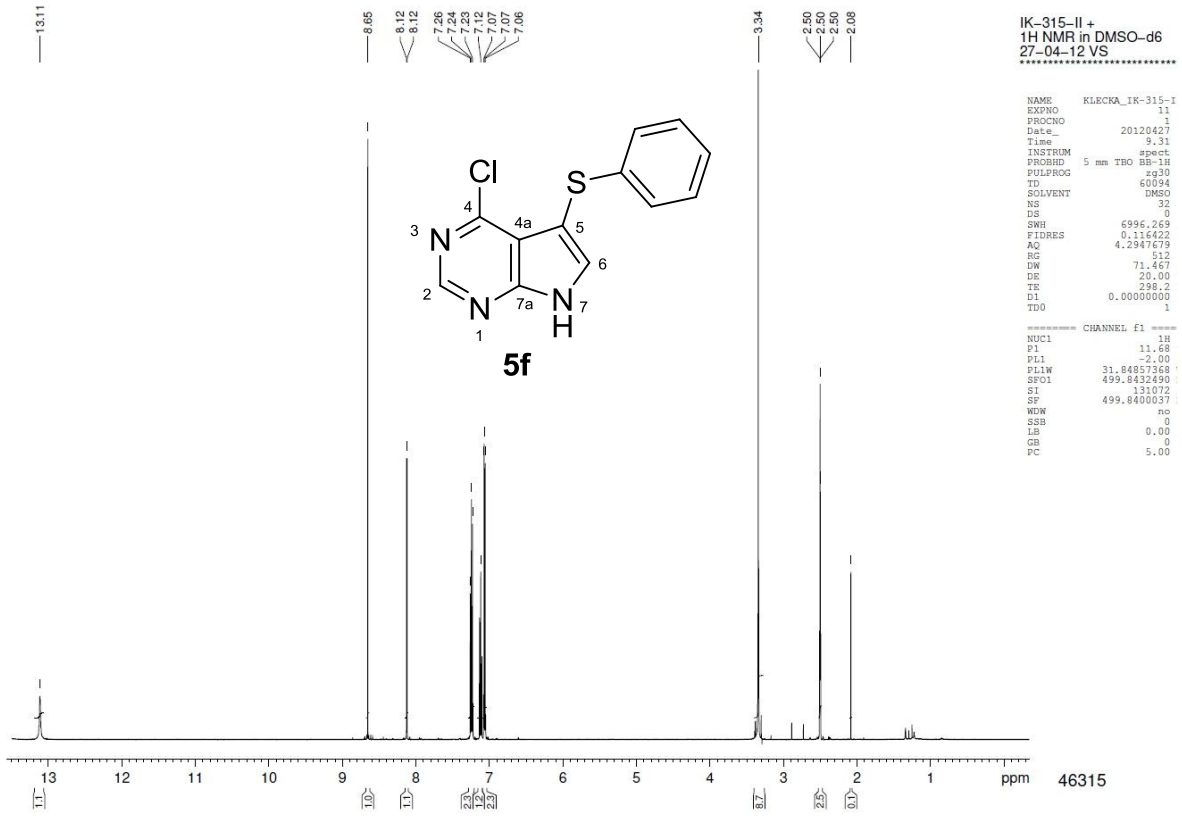

160.94
158.39
153.33
151.35
136.82
131.02
130.67
130.09
129.53
127.61
127.29
115.56
114.30
106.46
77.25
77.00
76.75
55.29
29.69
KLECKA IK-359-II
APT in CDCl3
15-08-12 RA
46782
ppm

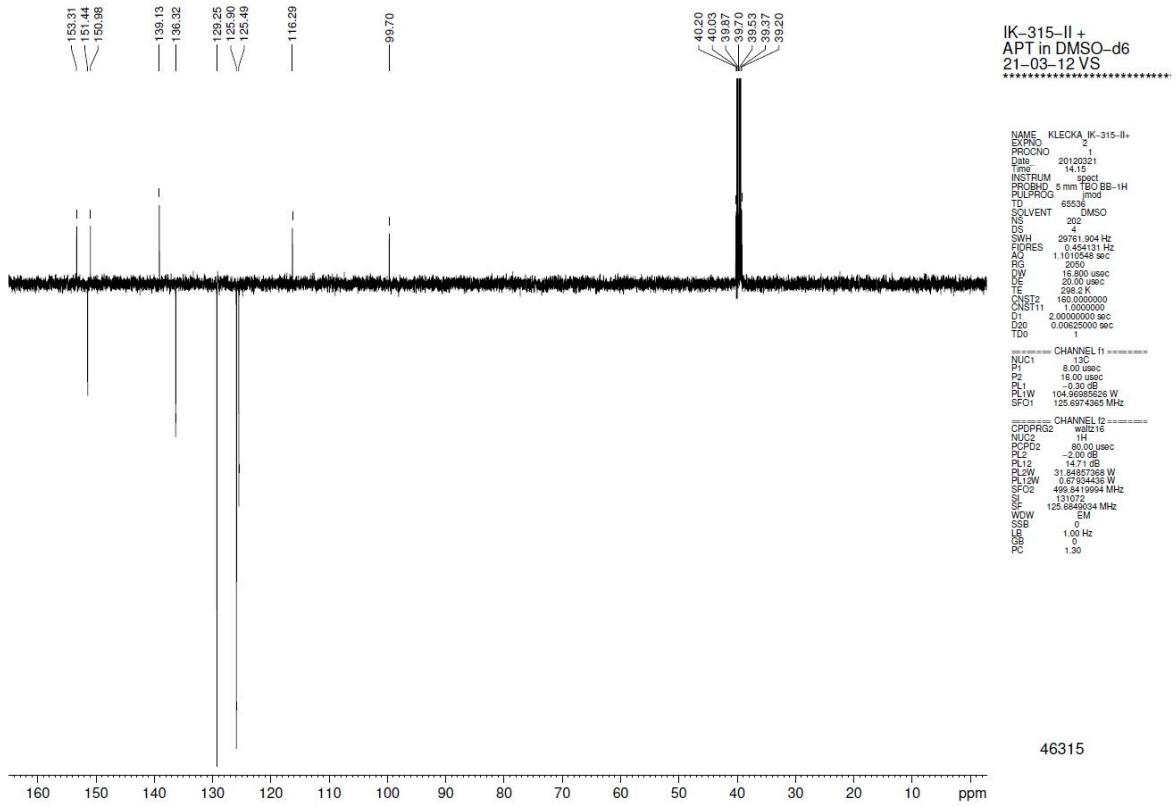


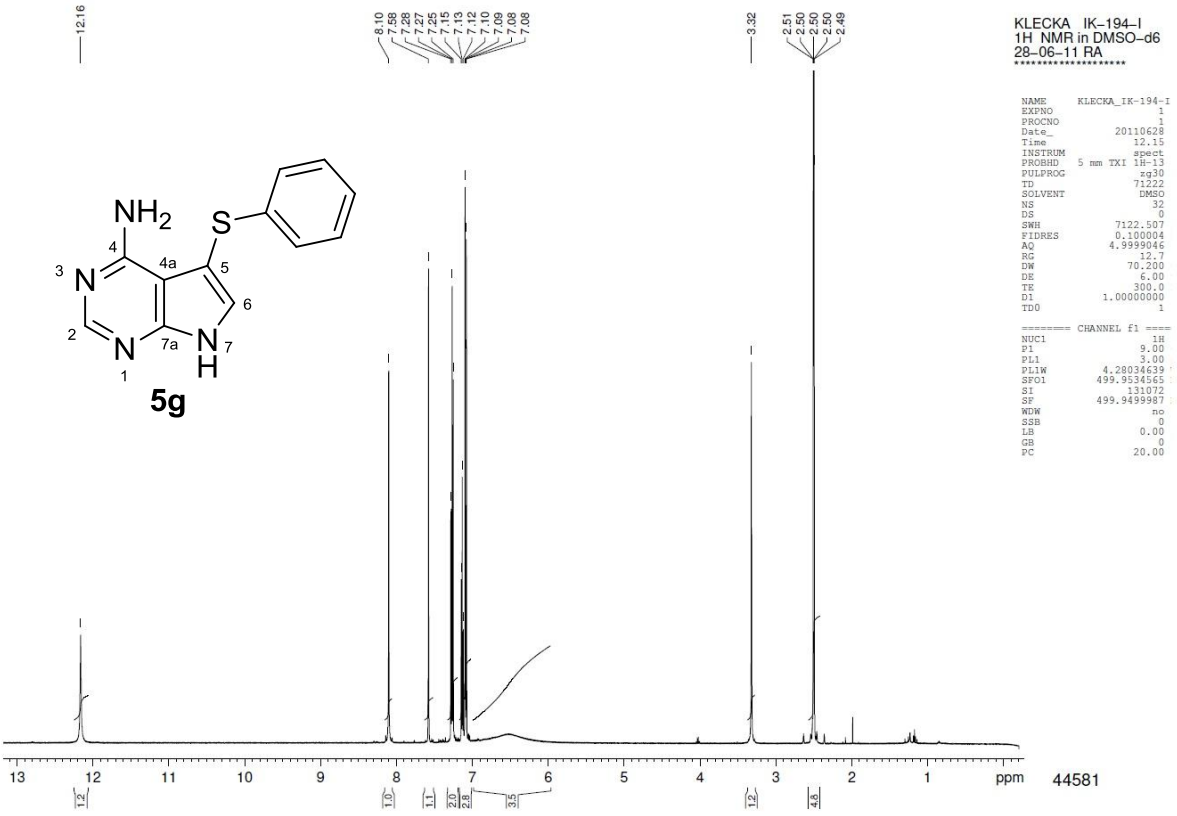


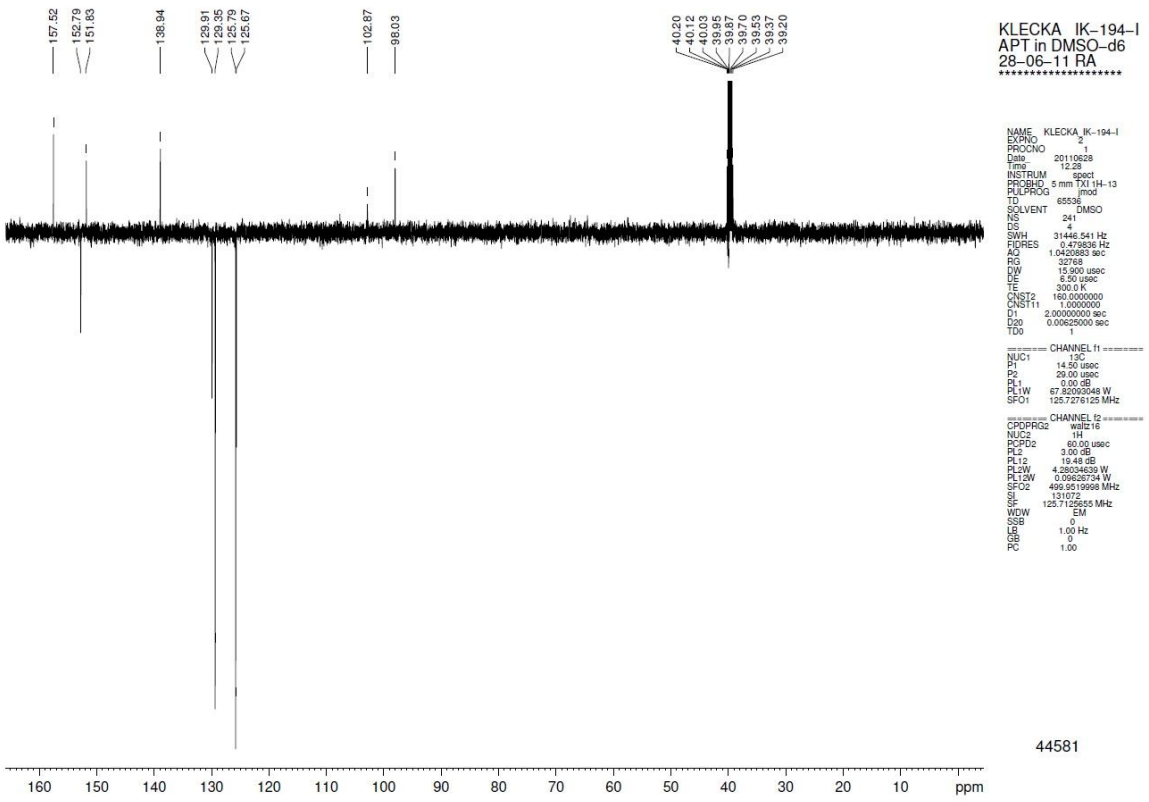


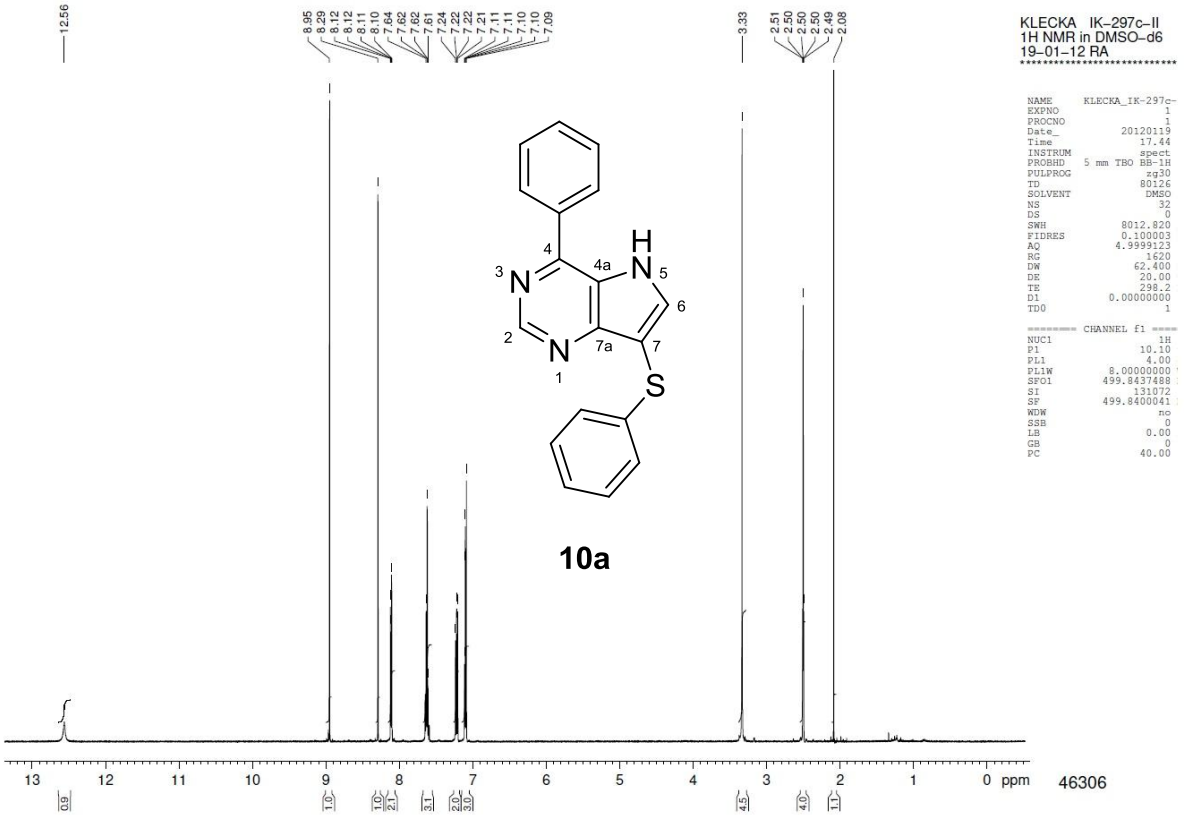


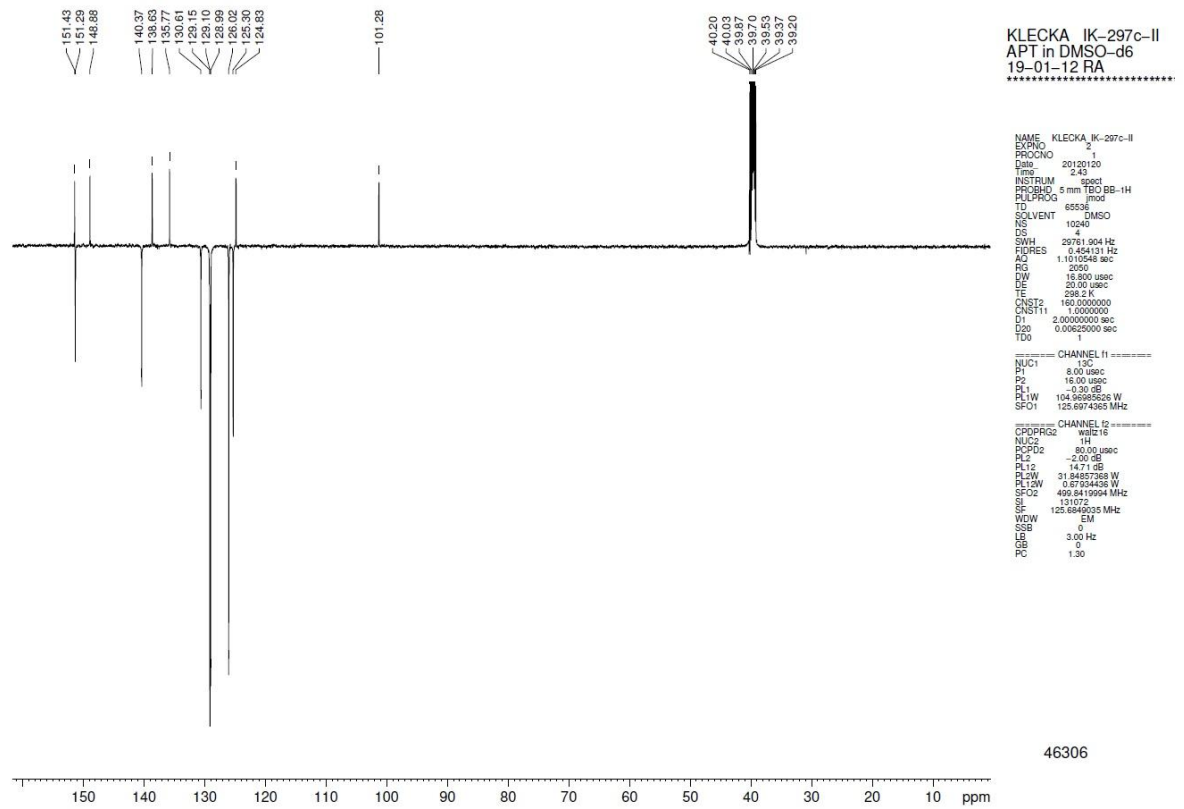


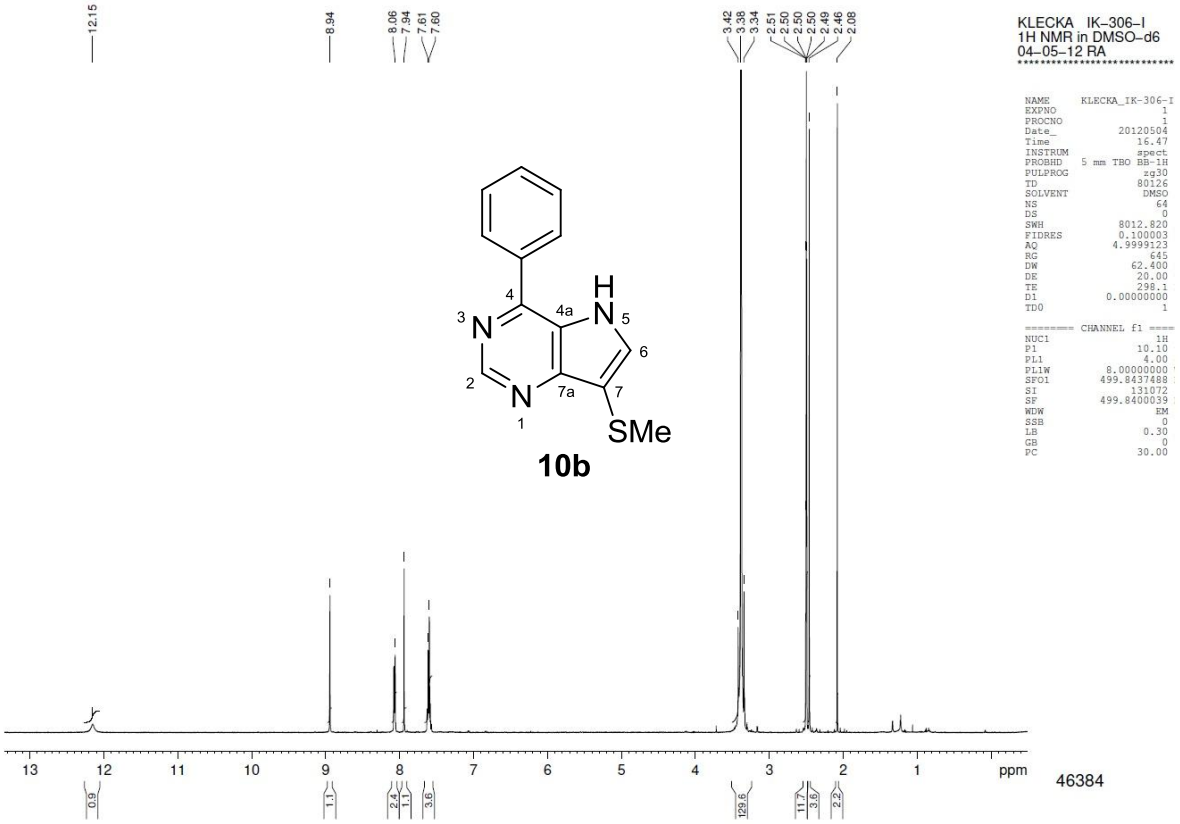


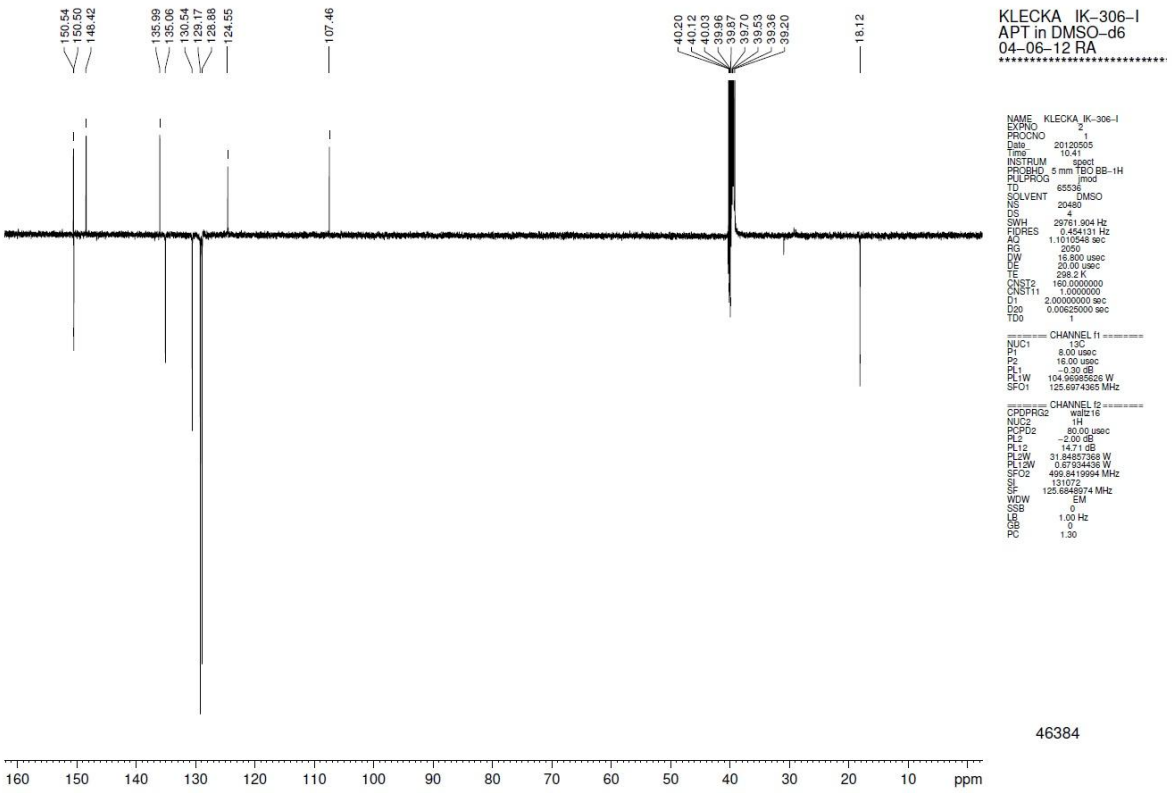


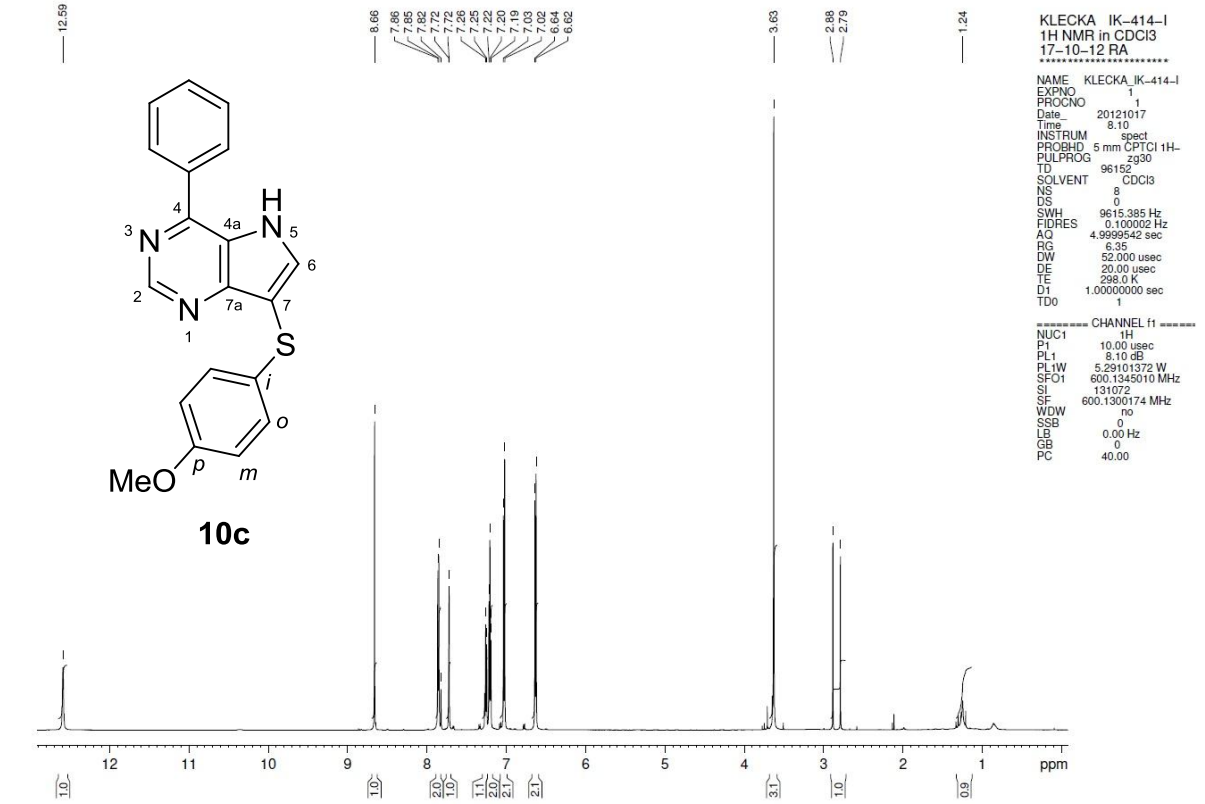


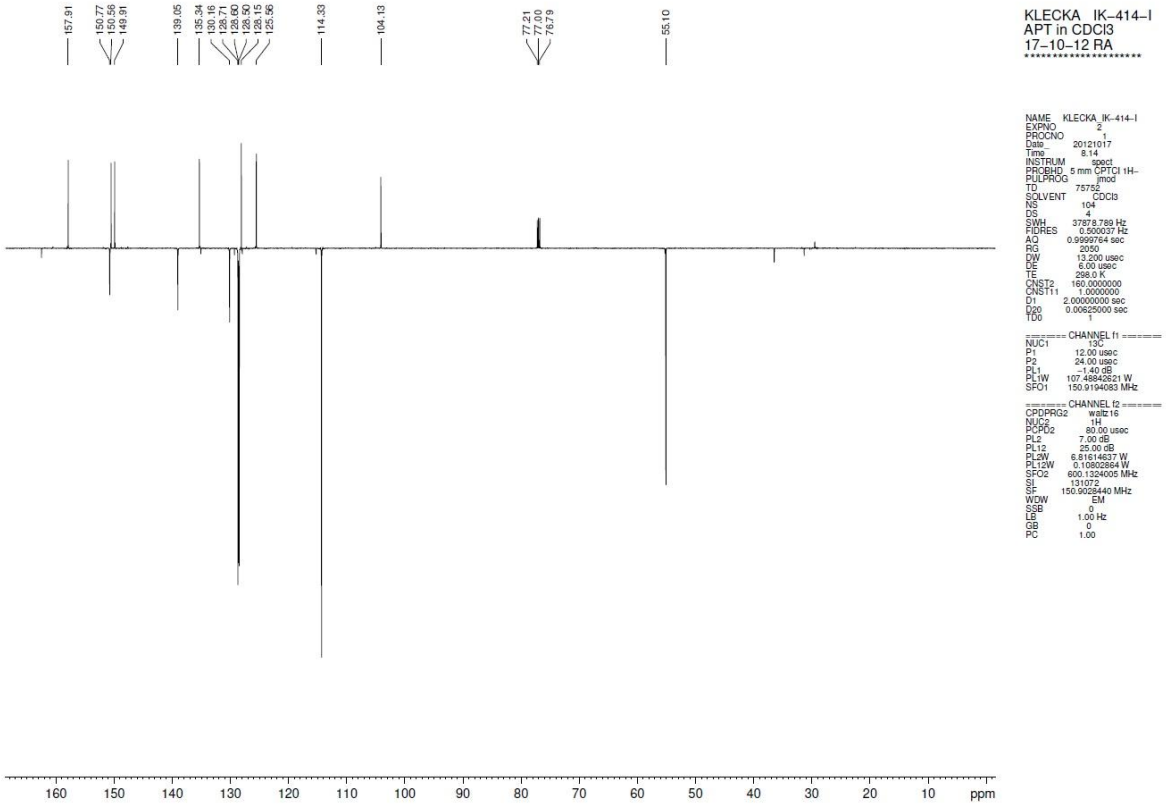

12.56
8.95
8.29
8.12
8.12
8.11
8.10
7.64
7.62
7.62
7.61
7.24
7.22
7.22
7.21
7.11
7.11
7.10
7.10
7.09
3.33
2.51
2.50
2.50
2.50
2.49
2.08
KLECKA IK-297c-II
1H NMR in DMSO-d6
19-01-12 RA
NAME KLECKA_IK-297c-
EXPNO 1
PROCNO 1
Date_ 20120119
Time 17.44
INSTRUM spect
PROBHD 5 mm TBO BB-1H
PULPROG zg30
TD 80126
SOLVENT DMSO
NS 32
DS 0
SWH 8012.820
FIDRES 0.100003
AQ 4.9999123
RG 1620
DW 62.400
DE 20.00
TE 298.2
D1 0.00000000
TD0 1
CHANNEL f1
NUC1 1H
P1 10.10
PL1 4.00
PL1W 8.00000000
SFO1 499.8437488
SI 131072
SF 499.8400041
WDW no
SSB 0
LB 0.00
GB 0
PC 40.00
10a
13 12 11 10 9 8 7 6 5 4 3 2 1 0 ppm
46306

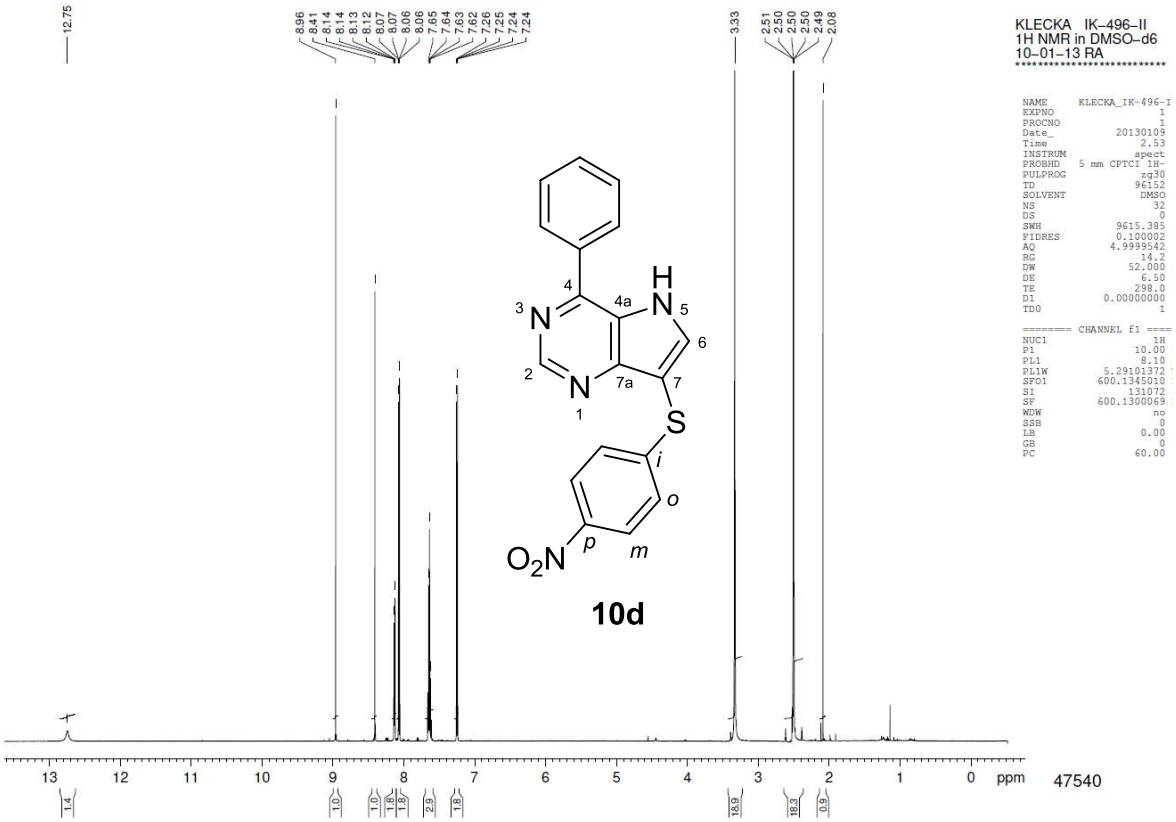

151.43
151.29
148.88
140.37
138.63
135.77
130.61
129.15
129.10
128.99
126.02
125.30
124.83
101.28
40.20
40.03
39.87
39.70
39.53
39.37
39.20
KLECKA IK-297c-II
APT in DMSO-d6
19-01-12 RA
NAME KLECKA_IK-297c-II
EXPNO 2
PROCNO 1
Date_ 20120120
Time 2.43
INSTRUM spect
PROBHD 5 mm TBO BB-1H
PULPROG jmod
TD 65536
SOLVENT DMSO
NS 10240
DS 4
SWH 29761.904 Hz
FIDRES 0.454131 Hz
AQ 1.1010548 sec
RG 2050
DW 16.800 usec
DE 20.00 usec
TE 298.2 K
CNST2 160.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00625000 sec
TD0 1
CHANNEL f1
NUC1 13C
P1 8.00 usec
P2 16.00 usec
PL1 -0.30 dB
PL1W 104.99985626 W
SFO1 125.6974365 MHz
CHANNEL f2
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.00 dB
PL12 14.71 dB
PL2W 31.84857368 W
PL12W 0.67934436 W
SFO2 499.8419994 MHz
SI 131072
SF 125.6849035 MHz
WDW EM
SSB 0
LB 3.00 Hz
GB 0
PC 1.30
46306
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

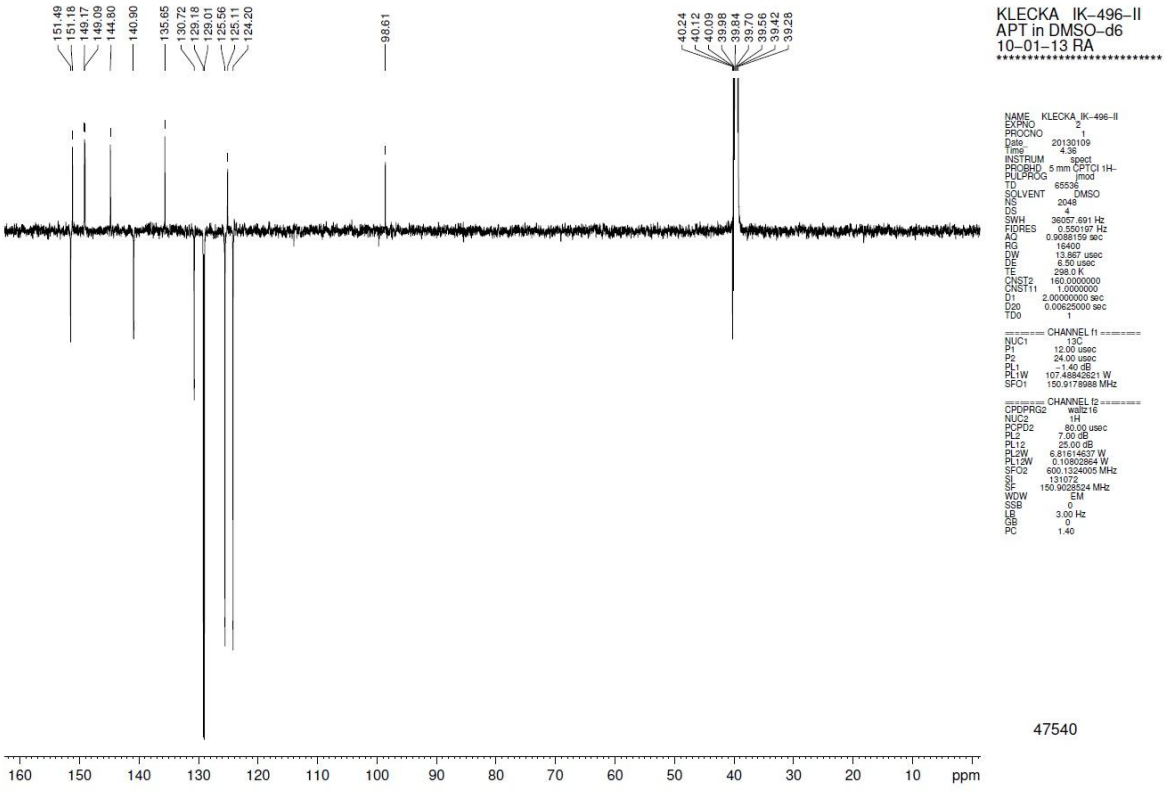


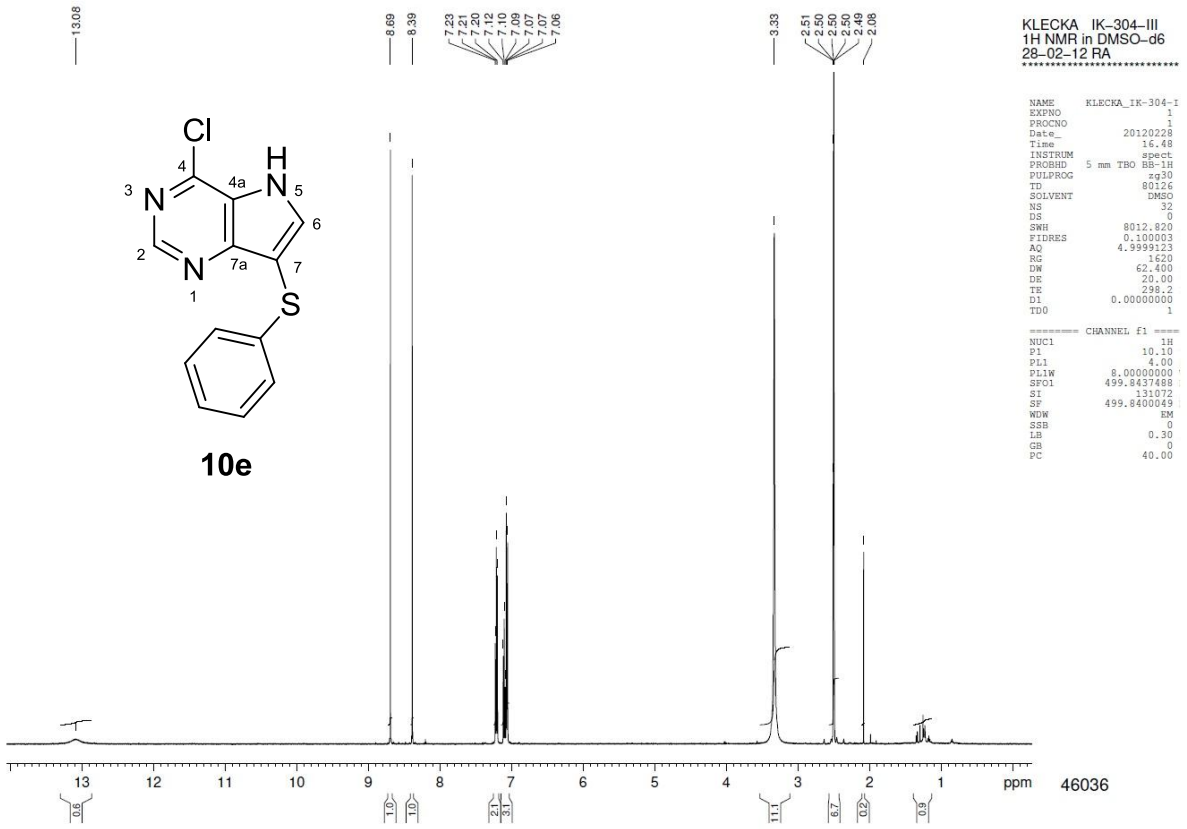


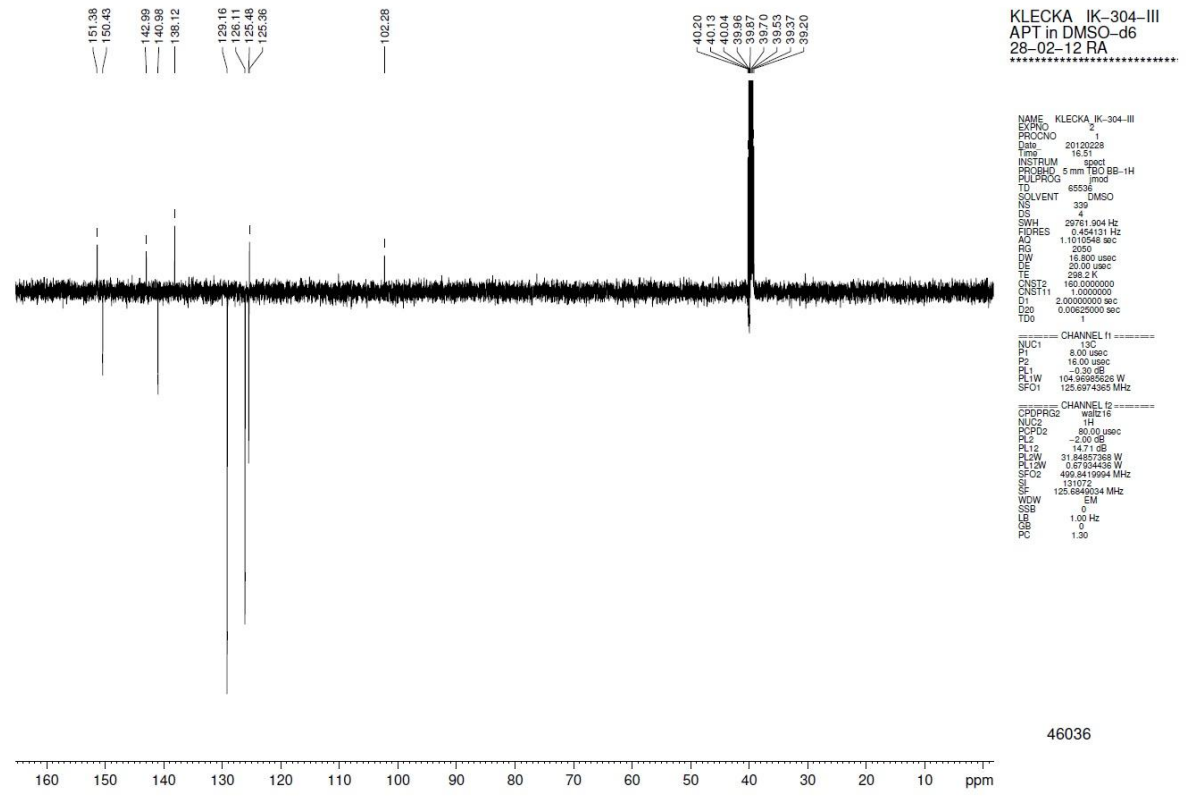

12.59
8.66
7.86
7.85
7.82
7.72
7.72
7.26
7.25
7.22
7.20
7.19
7.03
7.02
6.64
6.62
3.63
2.88
2.79
1.24
KLECKA IK–414–I
1H NMR in CDCl3
17–10–12 RA
NAME KLECKA_IK–414–I
EXPNO 1
PROCNO 1
Date_ 20121017
Time 8.10
INSTRUM spect
PROBHD 5 mm CPTCI 1H–
PULPROG zg30
TD 96152
SOLVENT CDCl3
NS 8
DS 0
SWH 9615.385 Hz
FIDRES 0.100002 Hz
AQ 4.9999542 sec
RG 6.35
DW 52.000 usec
DE 20.00 usec
TE 298.0 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 1H
P1 10.00 usec
PL1 8.10 dB
PL1W 5.29101372 W
SFO1 600.1345010 MHz
SI 131072
SF 600.1300174 MHz
WDW no
SSB 0
LB 0.00 Hz
GB 0
PC 40.00
4
4a
5
6
3
2
7a
7
1
S
i
o
p
m
MeO
10c
12
11
10
9
8
7
6
5
4
3
2
1
ppm
1.0
1.0
2.0
1.0
1.1
2.0
2.1
2.1
3.1
1.0
0.9

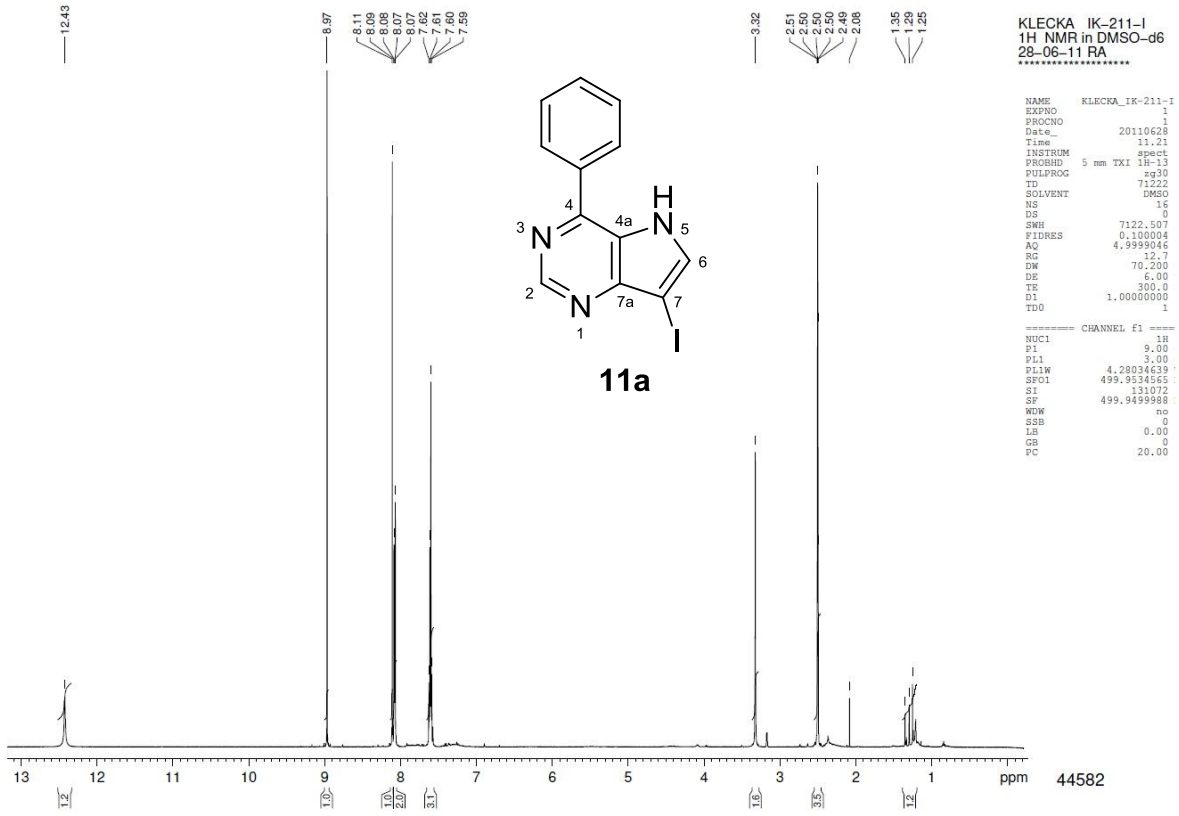

157.91
150.77
150.56
149.91
139.05
135.34
130.16
128.71
128.60
128.55
128.15
125.56
114.33
104.13
77.21
77.00
76.79
55.10
KLECKA IK–414–I
APT in CDCl3
17–10–12 RA
NAME KLECKA_IK–414–I
EXPNO 2
PROCNO 1
Date_ 20121017
Time 8.14
INSTRUM spect
PROBHD 5 mm CPTCI 1H–
PULPROG jmod
TD 75752
SOLVENT CDCl3
NS 104
DS 4
SWH 37878.789 Hz
FIDRES 0.500037 Hz
AQ 0.9999764 sec
RG 2050
DW 13.200 usec
DE 6.00 usec
TE 298.0 K
CNST2 160.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00625000 sec
TD0 1
======== CHANNEL f1 ======
NUC1 13C
P1 12.00 usec
P2 24.00 usec
PL1 -1.40 dB
PL1W 107.48842621 W
SFO1 150.9194083 MHz
======== CHANNEL f2 ======
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 7.00 dB
PL12 25.00 dB
PL2W 6.81614637 W
PL12W 0.10802664 W
SFO2 600.1324005 MHz
SI 131072
SF 150.9028440 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.00
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

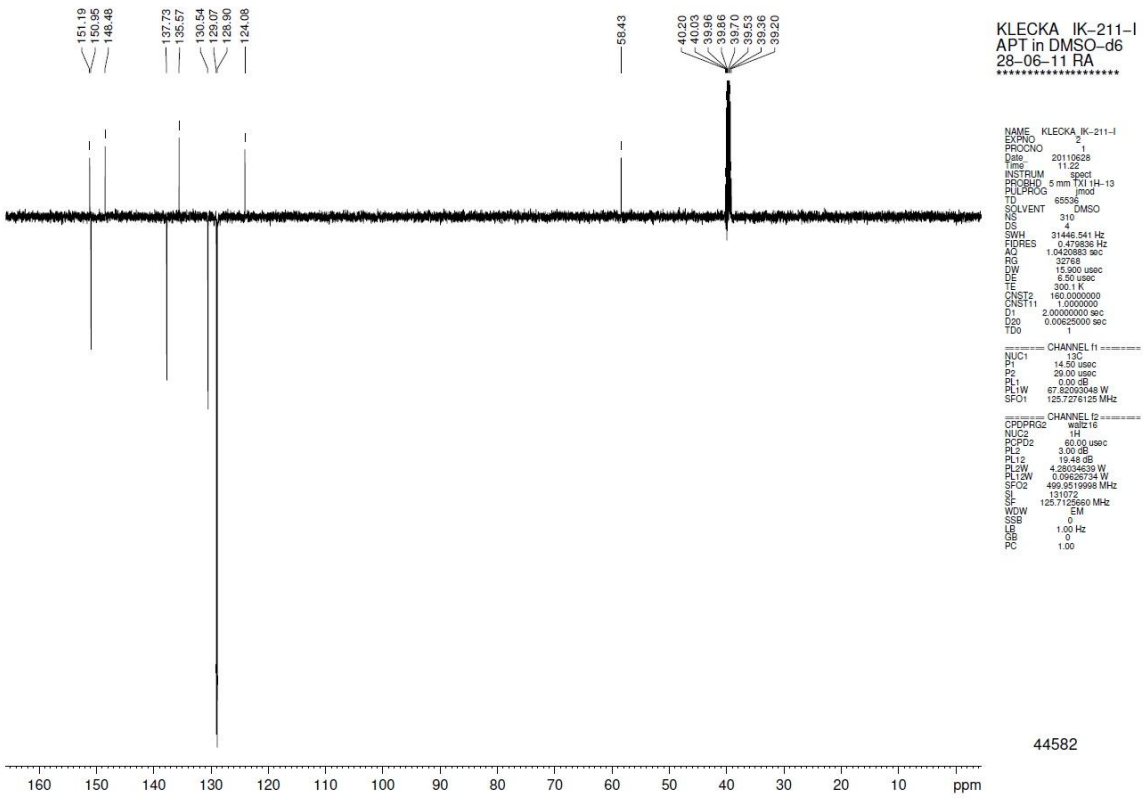


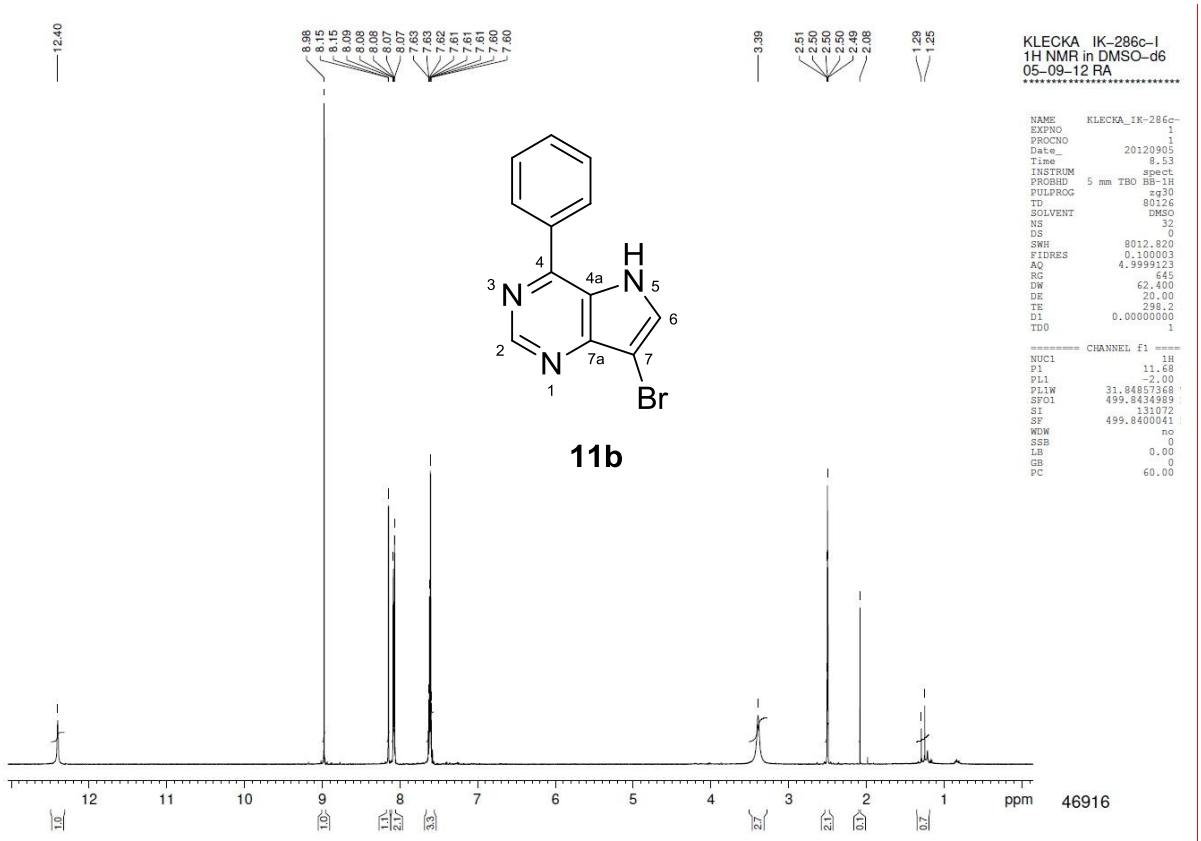


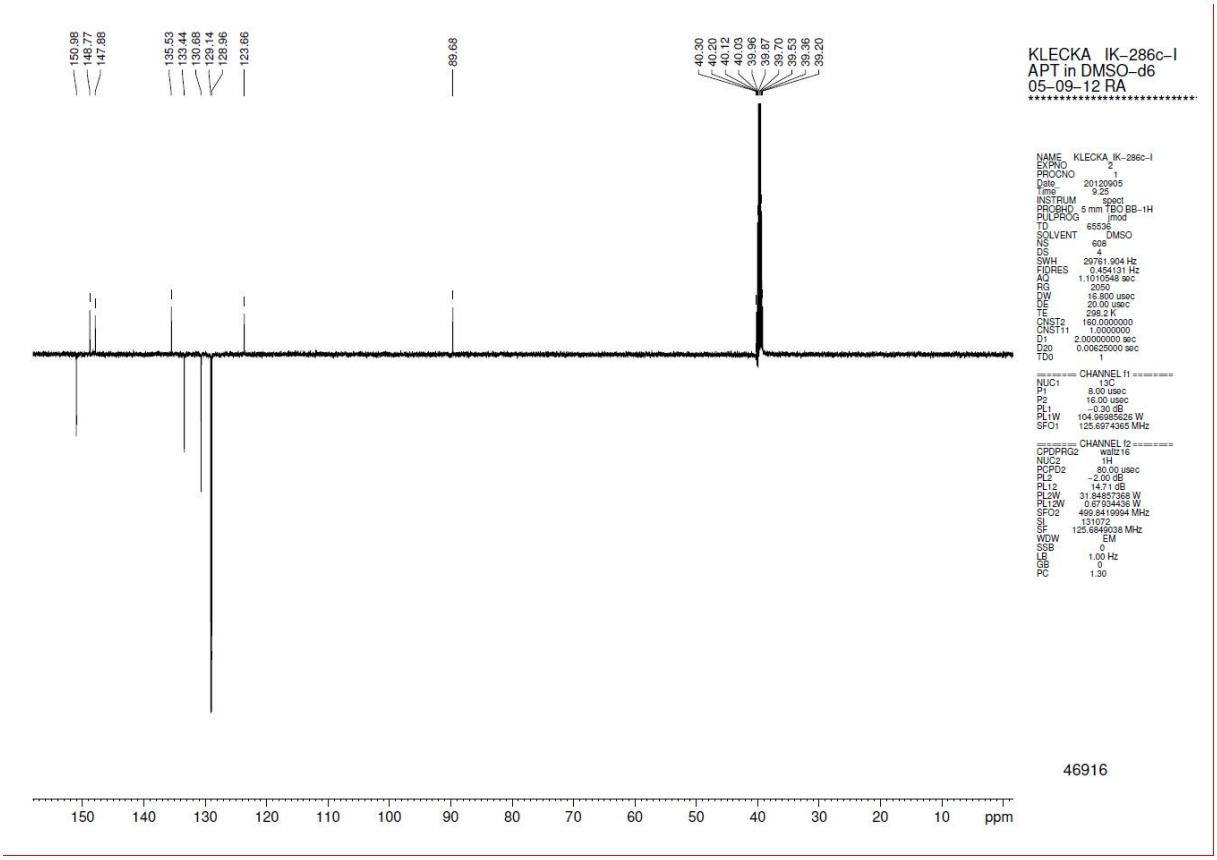


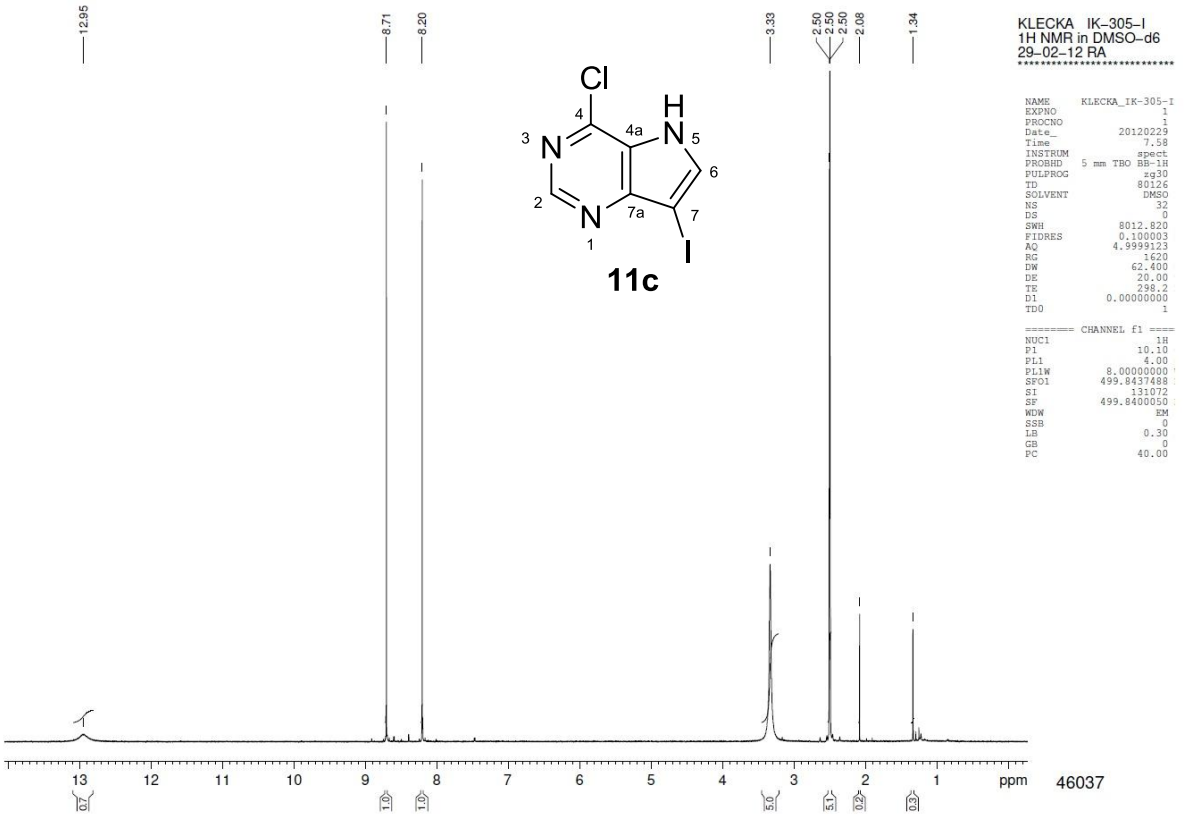


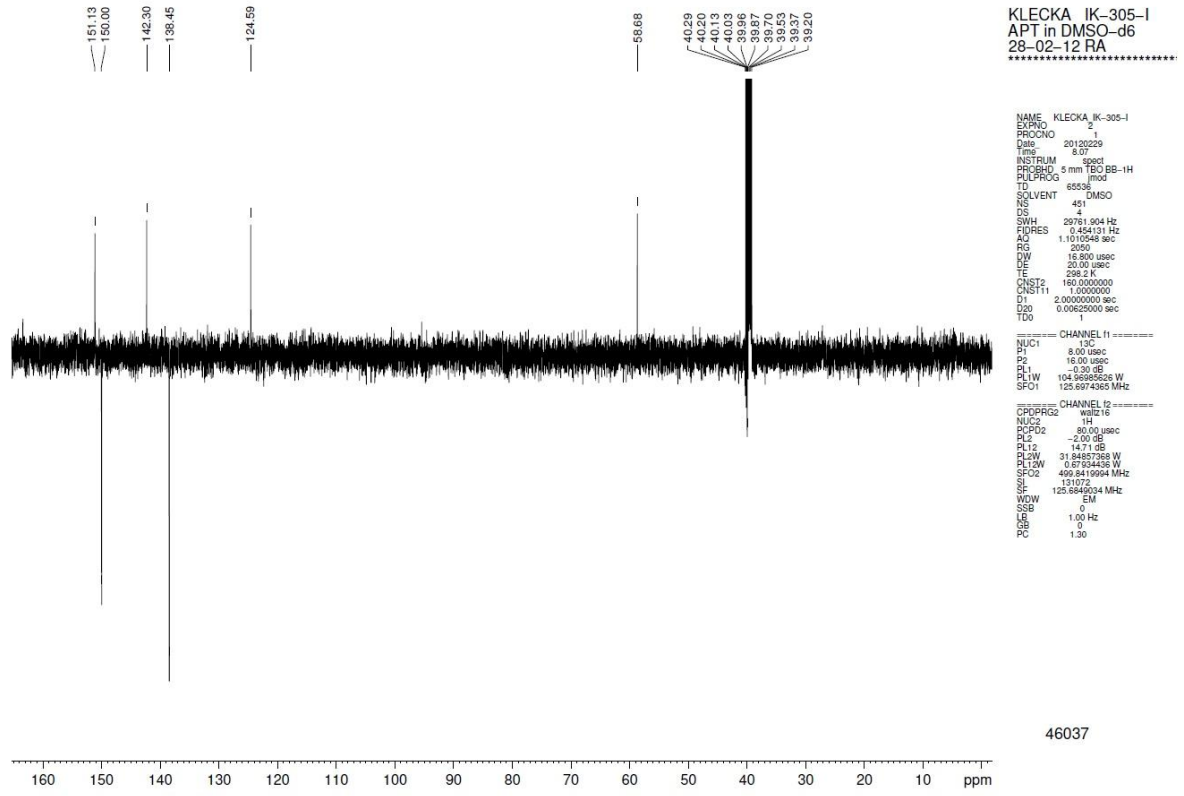


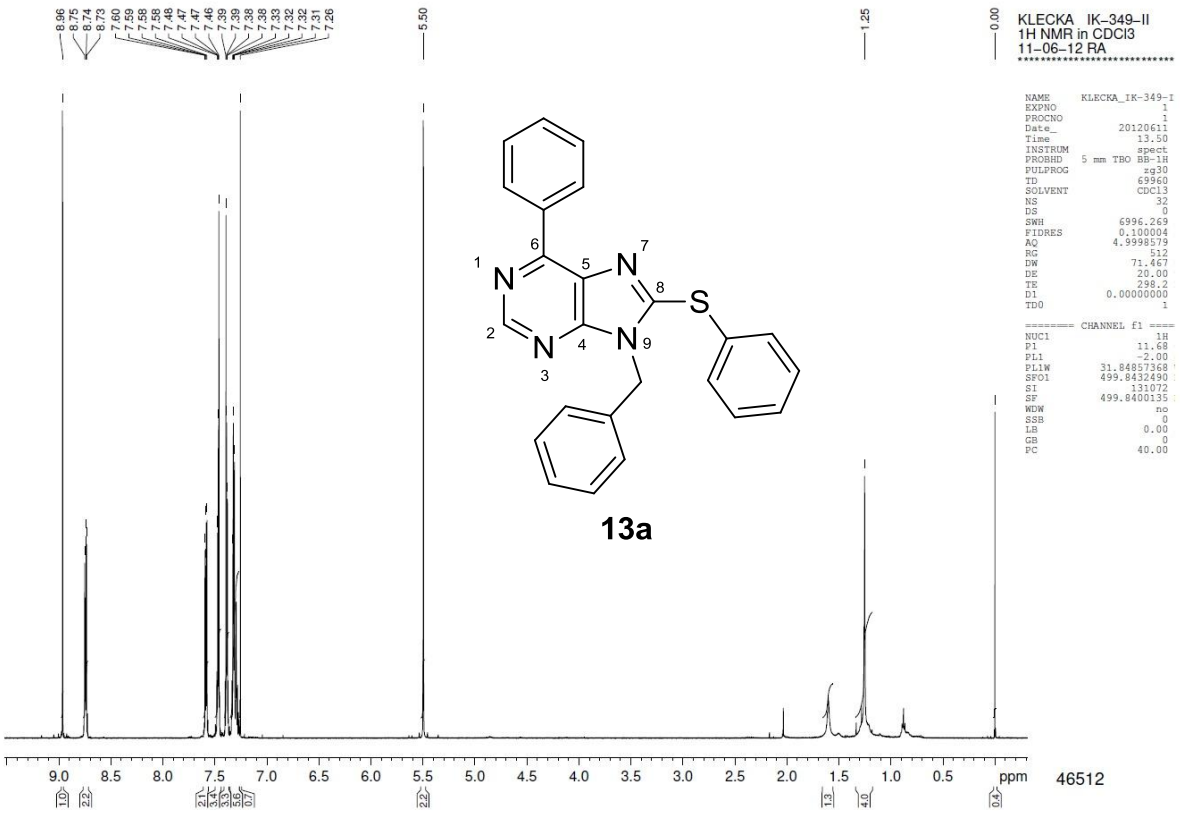


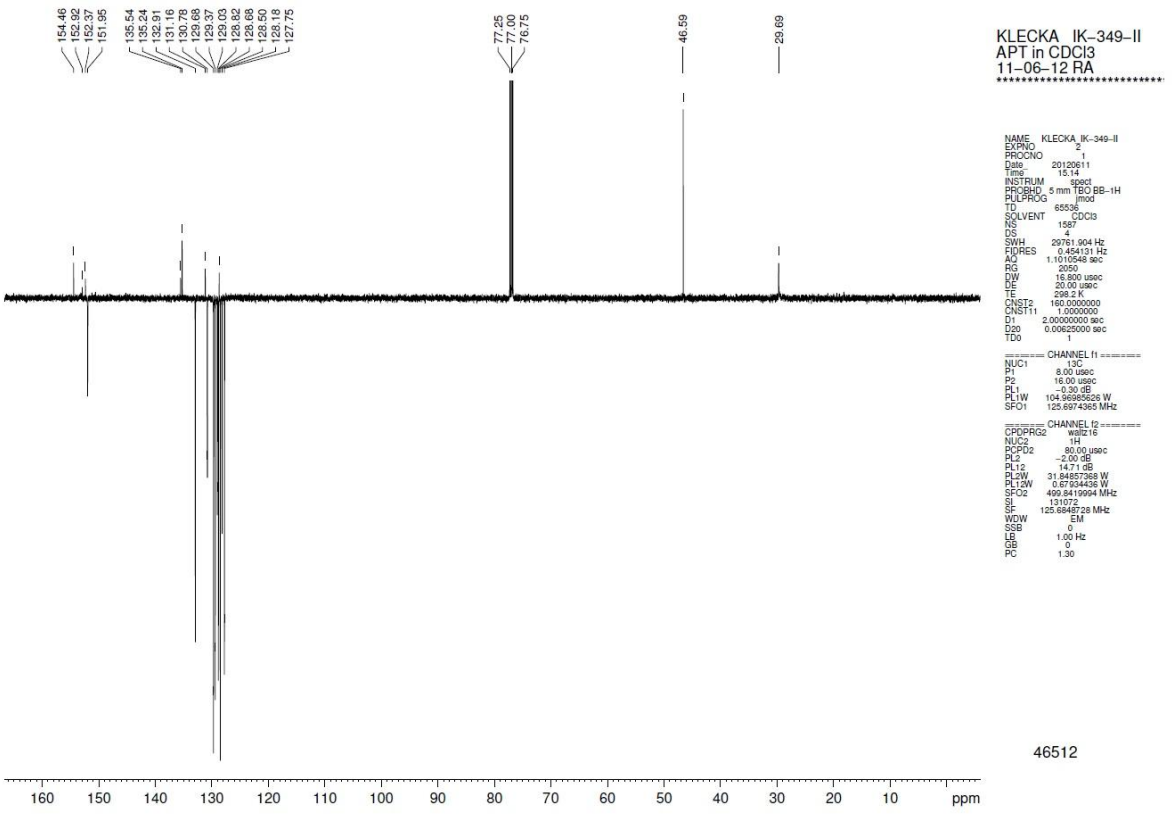


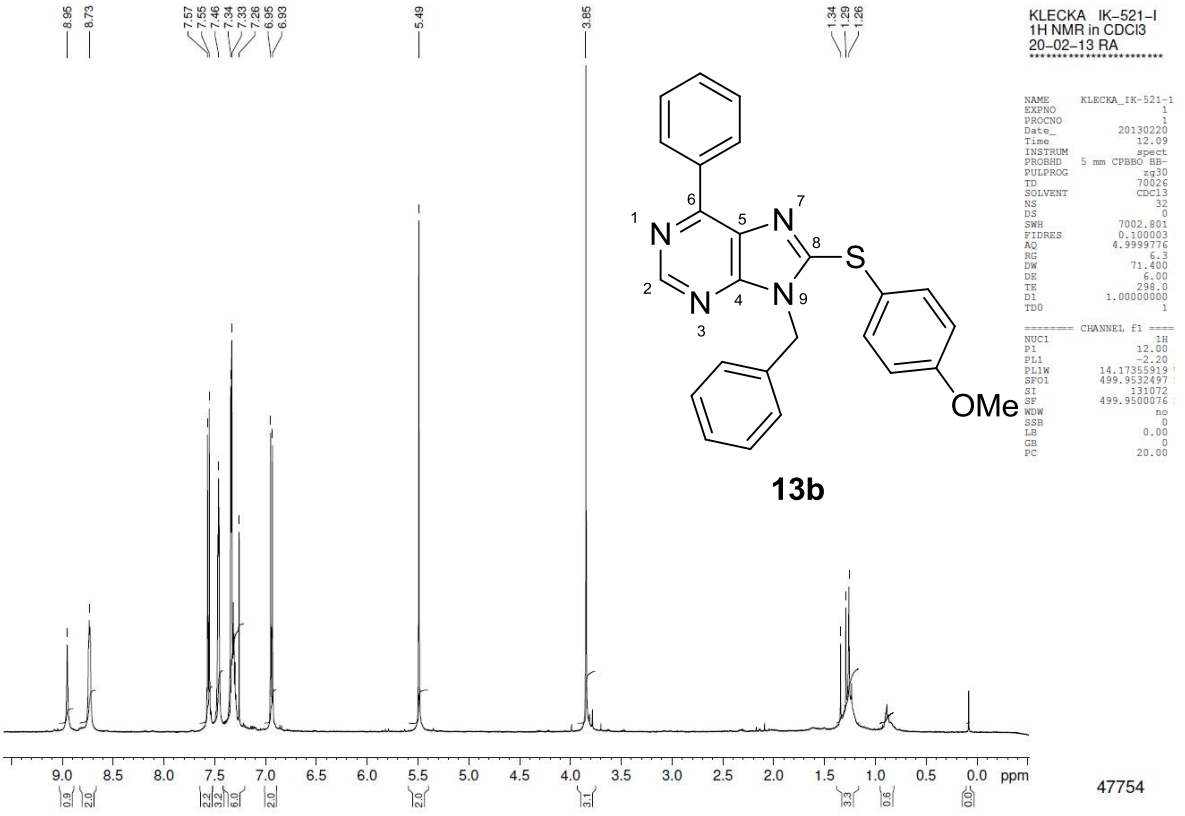


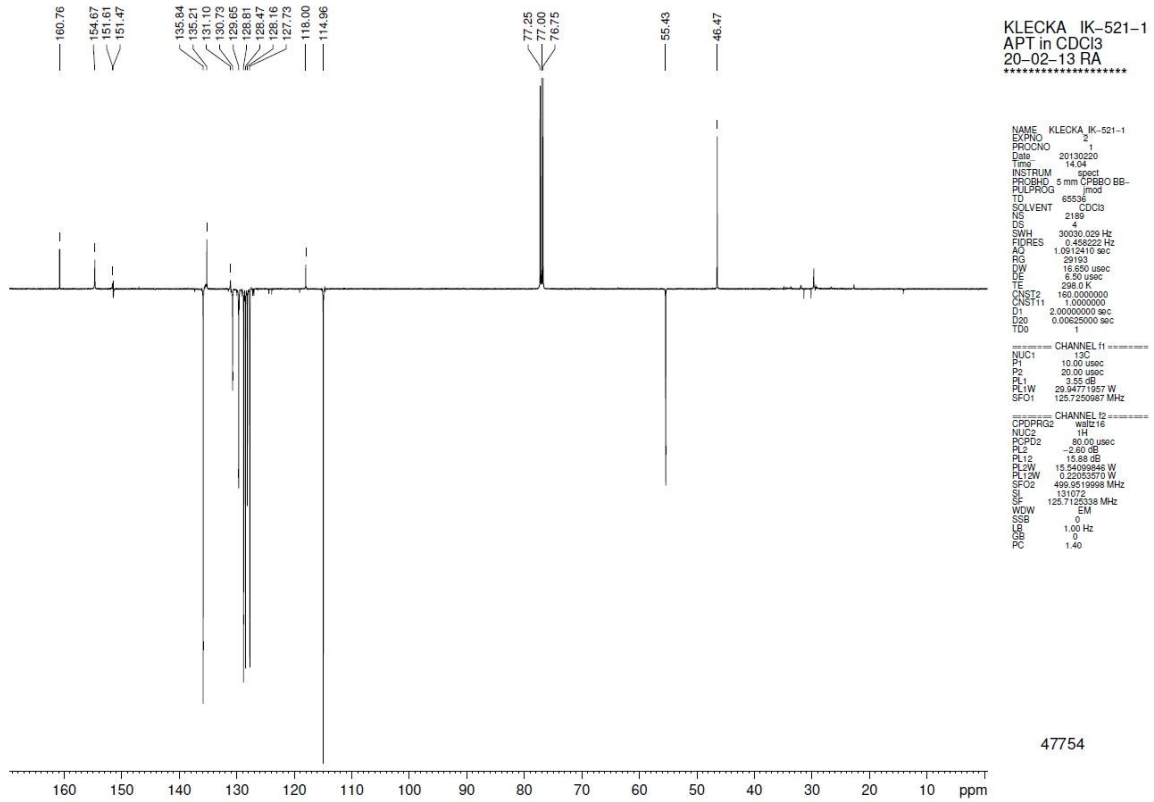


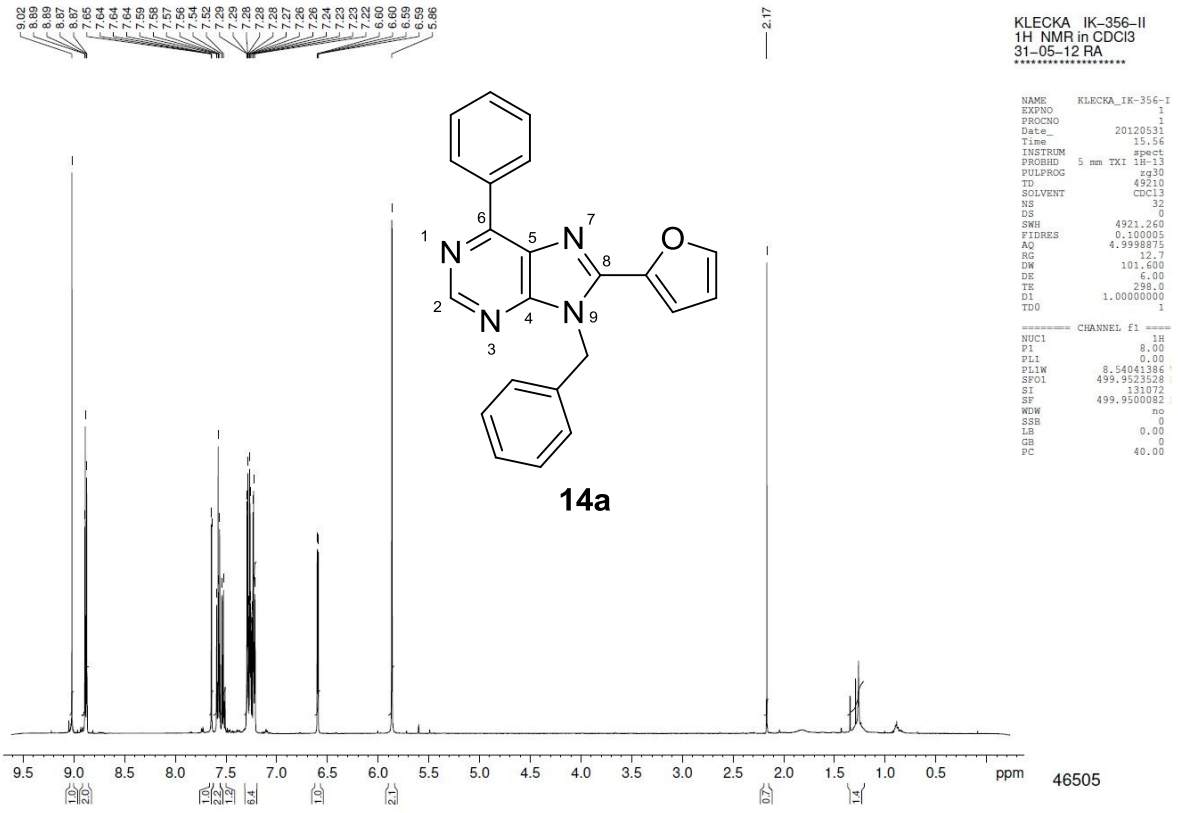


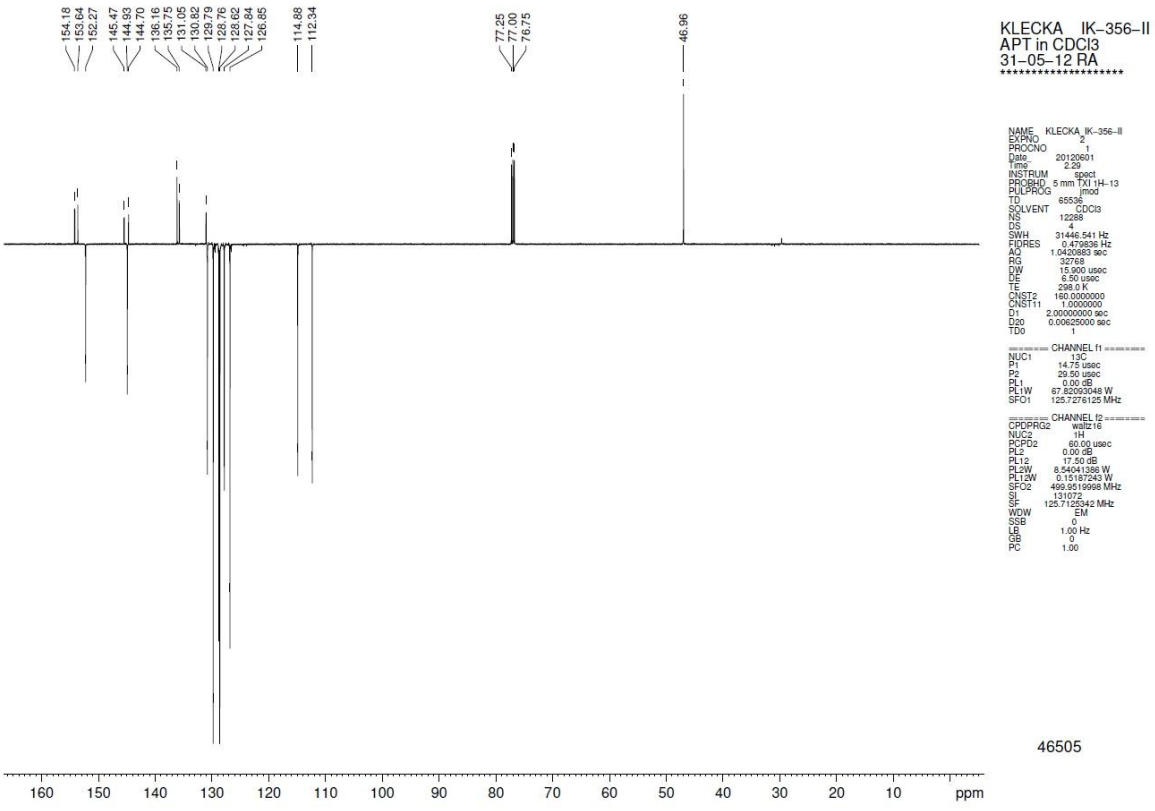

KLECKA IK–349–II
1H NMR in CDCl3
11–06–12 RA
13a
46512

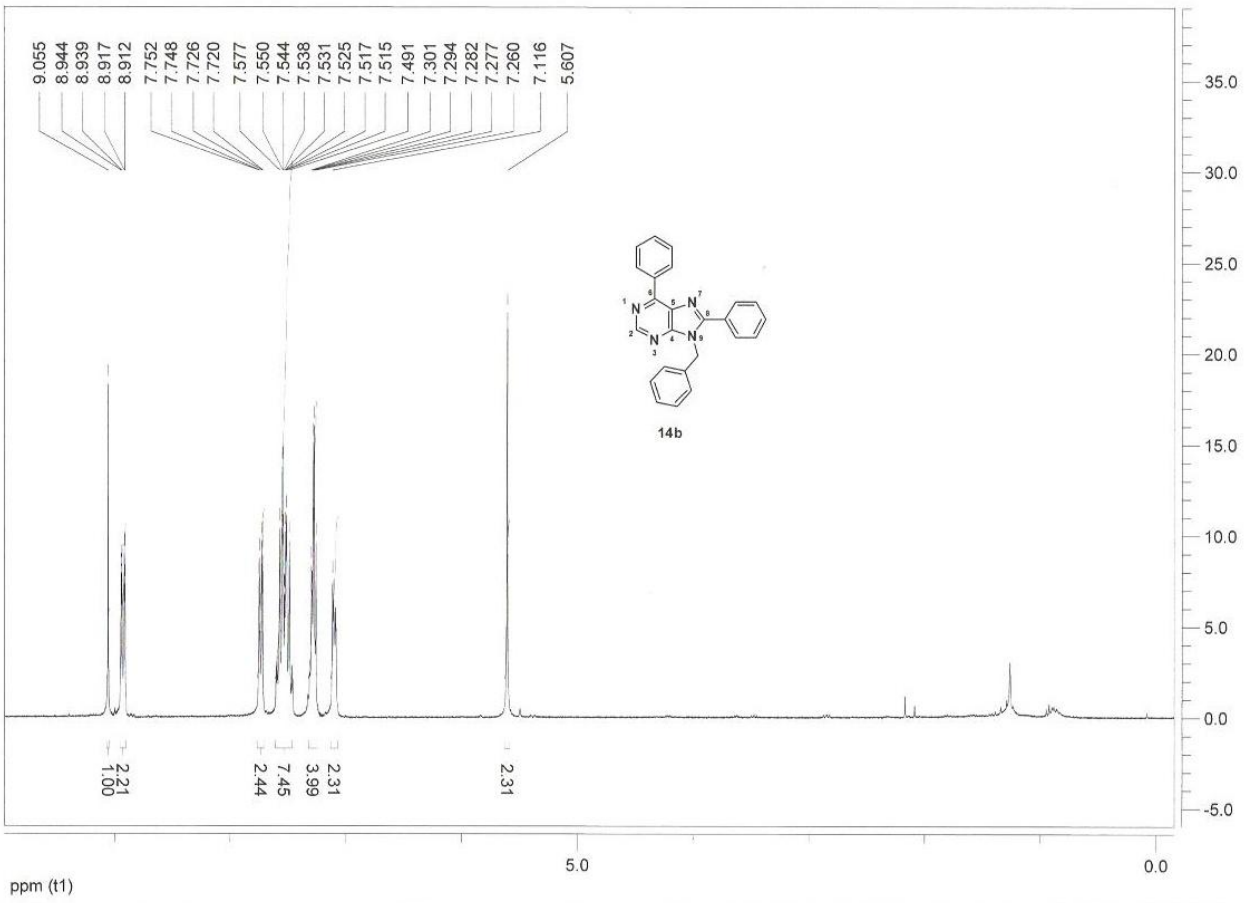

KLECKA IK–349–II
APT in CDCl3
11–06–12 RA
46512

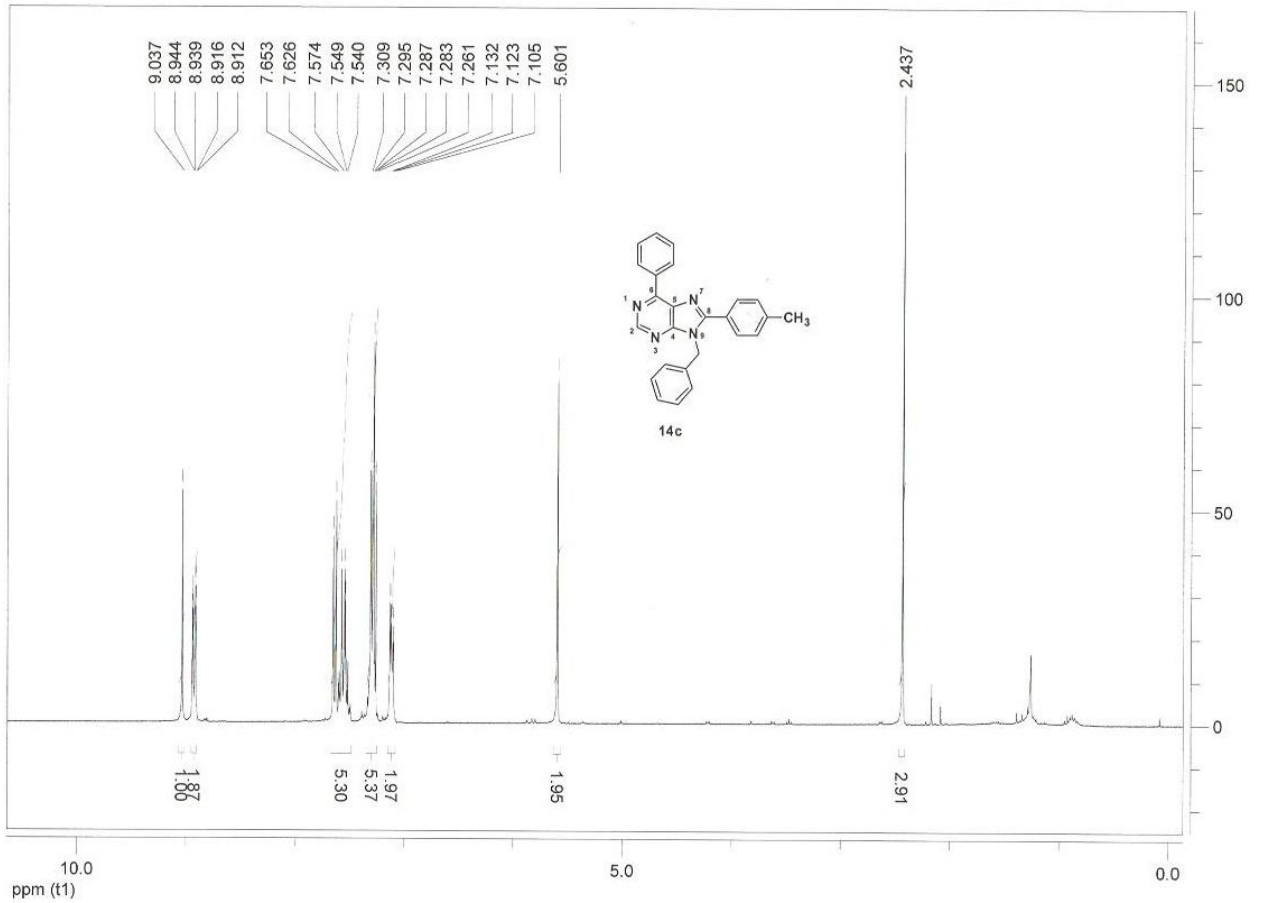

8.95
8.73
7.57
7.55
7.46
7.34
7.33
7.26
6.95
6.93
5.49
3.85
1.34
1.29
1.26
KLECKA IK-521-I
1H NMR in CDCl3
20-02-13 RA
NAME KLECKA_IK-521-1
EXPNO 1
PROCNO 1
Date_ 20130220
Time 12.09
INSTRUM spect
PROBHD 5 mm CPBBO BB-
PULPROG zg30
TD 70026
SOLVENT CDCl3
NS 32
DS 0
SWH 7002.801
FIDRES 0.100003
AQ 4.9999776
RG 6.3
DW 71.400
DE 6.00
TE 298.0
D1 1.00000000
TD0 1
======== CHANNEL f1 ====
NUC1 1H
P1 12.00
PL1 -2.20
PL1W 14.17355919
SFO1 499.9532497
SI 131072
SF 499.9500076
WDW no
SSB 0
LB 0.00
GB 0
PC 20.00
OMe
13b
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
47754


160.76
154.67
151.61
151.47
135.84
135.21
131.10
130.73
129.65
128.81
128.47
128.16
127.73
118.00
114.96
77.25
77.00
76.75
55.43
46.47
KLECKA IK-521-1
APT in CDCl3
20-02-13 RA
NAME KLECKA_IK-521-1
EXPNO 2
PROCNO 1
Date_ 20130220
Time 14.04
INSTRUM spect
PROBHD 5 mm CPBBO BB-
PULPROG jmod
TD 65536
SOLVENT CDCl3
NS 2189
DS 4
SWH 30030.029 Hz
FIDRES 0.458222 Hz
AQ 1.0912410 sec
RG 29193
DW 16.650 usec
DE 6.50 usec
TE 298.0 K
CNST2 160.0000000
CNST11 1.0000000
D1 2.00000000 sec
D20 0.00625000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 10.00 usec
P2 20.00 usec
PL1 3.55 dB
PL1W 29.94771957 W
SFO1 125.7250987 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 80.00 usec
PL2 -2.60 dB
PL12 15.88 dB
PL2W 15.54099846 W
PL12W 0.22053570 W
SFO2 499.9519998 MHz
SI 131072
SF 125.7125338 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40
160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm
47754


KLECKA IK–356–II
1H NMR in CDCl3
31–05–12 RA
14a
46505


KLECKA IK–356–II
APT in CDCl3
31–05–12 RA
46505





3. Single crystal X-ray structure analysis

Crystallographic data for **5e** and **10a** were obtained from Xcalibur X-ray diffractometer by monochromatized CuK_α radiation (λ=1.54180 Å) at 190 K. The structures were solved by direct methods (SIR92)[2] and refined by full-matrix least-squares based on F with (CRYSTALS)[3]. The hydrogen atoms were found on difference Fourier map, those on carbon atoms were recalculated into idealized positions. All hydrogen atoms were refined with riding constraints, while all other atoms were refined anisotropically in both cases.

Crystal data for 5e (0.05 x 0.13 x 0.21 mm)**:**

$C_{25}H_{19}N_3S_1$, monoclinic, space group $P2_1/n$, a = 5.9059(3) Å, b = 13.5680(5) Å, c = 24.5309(9) Å, β = 91.499(4)°, V = 1965.01(13) Å^3, Z = 4, M = 393.51, 9133 reflections measured, 4031 independent reflections. Final R = 0.039, wR = 0.050, GoF = 1.089 for 3473 reflections with $I > 2\sigma(I)$ and 263 parameters. CCDC 926544.

Crystal data for 10a:

$C_{18}H_{13}N_3S_1$, monoclinic, space group $P2_1/n$, a = 6.8659(2) Å, b = 18.4844(5) Å, c = 11.9993(4) Å, β = 103.118(3)°, V = 1483.11(8) Å^3, Z = 4, M = 303.39, 6709 reflections measured, 3014 independent reflections. Final R = 0.037, wR = 0.047, GoF = 1.004 for 2707 reflections with $I > 2\sigma(I)$ and 200 parameters. CCDC 926543.

References:

1. Čerňa, I.; Pohl, R.; Klepetářová, B; Hocek, M. *Org. Lett*, **2006**, *8*, 5389-5392.

2. Altomare A., Cascarano G., Giacovazzo C., Guagliardi A., Burla M. C., Polidori G., Camalli M. *J. Appl. Cryst.* **1994**, *27*, 435-436.

3. Betteridge P. W., Carruthers J. R., Cooper R. I., Prout K., Watkin D. J. *J. Appl. Cryst.* **2003**, *36*, 1487.