Supporting information

Modular Synthesis of 5-Substituted Thiophen-2-yl C-2'-Deoxyribonucleosides

Jan Bárta,[†] *Radek Pohl,* [†] *Blanka Klepetářová,*[†] *Nikolaus P. Ernsting*[‡] *and Michal Hocek*[†]*

[†] Institute of Organic Chemistry and Biochemistry, Academy of Sciences of the Czech Republic, CZ-16610, Prague 6, Czech Republic

[‡] Institut für Chemie, Humboldt Universität zu Berlin, Brook-Taylor-Str. 2, D-12489 Berlin, Germany

hocek@uochb.cas.cz

List of contents:

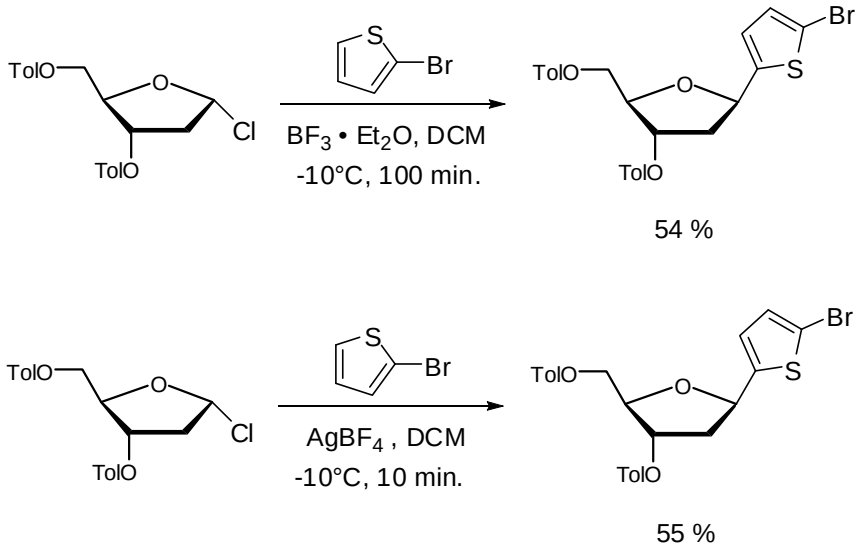
Experimental

General methods. Melting points were determined on a Kofler block. Optical rotations were measured at 25 °C, $[\alpha]_D^{20}$ values are given in 10^{-1} deg cm^2 g^{-1}. NMR spectra were measured at 400 MHz for ^{1}H and 100.6 MHz for ^{13}C nuclei, at 500 MHz for ^{1}H and 125.8 MHz for ^{13}C, or at 600 MHz for ^{1}H and 151 MHz for ^{13}C in $CDCl_3$ (TMS was used as internal standard), MeOH-d_4 (referenced to the residual solvent signal), or DMSO-d_6 (referenced to the residual solvent signal). Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) in Hz. Complete assignment of all NMR signals was performed using a combination of H,H-COSY, H,H-ROESY, H,C-HSQC and H,C-HMBC experiments. Mass spectra were measured using FAB (ionization by Xe, accelerating voltage 8 kV, glycerol + thioglycelor matrix) of EI (electron energy 70 eV). DMF was degassed *in vacuo* and stored over molecular sieves under argon.

1) Alternative ways of preparation of 4a

1*β*-(5-bromothiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-toluoyl-D-ribofuranose (4a) and 1*α*-(5-bromothiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-toluoyl-D-ribofuranose (5a).

Scheme S1:



A: *Using BF_3·Et_2O as Lewis acid*

BF_3·Et_2O (598 µL, 5.02 mmol) was added during 8 min to a dried flask containing a solution of the halogenol **1** (300 mg, 0.77 mmol) and 2-bromothiophene **3** (187 µL, 1.93 mmol) in dry dichloromethane (10 mL) at -10 °C under argon, and the mixture was stirred for 100 min. at -10 °C. Then the reaction was quenched by saturated Na_2CO_3, extracted with chloroform (3x 50 mL), dried over $MgSO_4$, and solvents were evaporated under vacuum. The crude product was purified by flash chromatography on silica gel in gradient hexane to hexane/EtOAc (19.5/0.5) to give the desired product **4a** (87 mg, 22 %) followed by α-anomer **5a** (86 mg, 22 %) as a colorless oil.

B: *Using $AgBF_4$·as Lewis acid*

$AgBF_4$ (490 mg, 2.50 mmol) was added in one portion to a dried flask containing a solution of the halogenol **1** (150 mg, 0.39 mmol) and 2-bromothiophene **3** (94 µL, 0.97 mmol) in dry dichloromethane (5 mL) at -10 °C under argon. The reaction mixture was stirred 10 min. at -10 °C, quenched by saturated Na_2CO_3, extracted with chloroform (3x 50 mL), dried on $MgSO_4$ and solvent was evaporated under vacuum. The crude product was purified by flash

chromatography on silica gel in gradient hexane to hexane/EtOAc (19.5/0.5) to give the desired product **4a** (108 mg, 55 %) followed by α-anomer **5a** (28 mg, 14 %) as a colorless oil.

Isomerization of *α*-Anomer:

A mixture of BSA (109 mg, 0.69 mmol) and TFA (254 μL, 3.31 mmol) was added to a solution of ***α***-anomer **5** (102 mg, 0.2 mmol) in dichloromethane (10 mL). The mixture was stirred at 40 °C for 22h and then poured onto ice containing $NaHCO_3$. Product was extracted to EtOAc (2x30 mL) and chromatographed on silica gel eluting hexane to hexane/EtOAc (19.5/0.5) to give the mixture of desired product **4a** (25 mg, 25 %) and starting material **5a**.

General procedure for catalytic hydrogenolysis of bromothiophene nucleosides: To a solution of the nucleoside **4a** (500 mg, 0.97 mmol) in a mixture of THF/EtOH/H_2O (10/10/1) (30 mL) at rt, 10% Pd/C (260 mg, 2.44 mmol) and Et_3N (1 mL) were added. The flask was evacuated and then filled with H_2. Then H_2 was bubbled through the solution at rt for 3-6 h. After the reaction was completed (checked by TLC), catalyst was filtered off and the solvents evaporated. The residue was chromatographed on silica gel in gradient hexane to hexane/EtOAc (9/1).

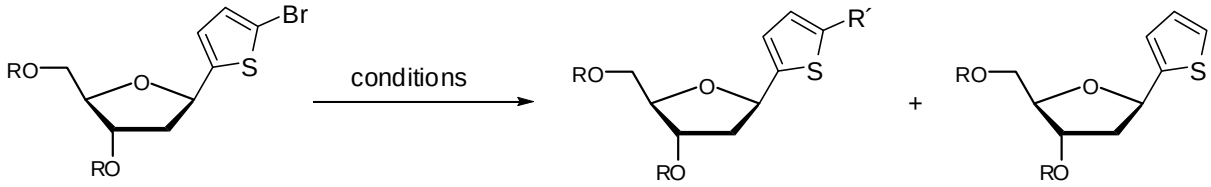
1*β*-(Thiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-toluoyl-D-ribofuranose (4b). Prepared from **4a** (500 mg, 0.97 mmol) by the general procedure, reaction time 3 h. **4b** (400 mg, 95%) was obtained as a colorless oil. MS (FAB) *m/z* 437 (M + H); HRMS (FAB) for $C_{25}H_{25}O_5S$: [M + H] calculated 437.1423, found 437.1416. ^{1}H NMR (600 MHz, $CDCl_3$): 2.41 (s, 3H, CH_3-Tol); 2.42 (ddd, 1H, J_{gem} = 13.8, $J_{2'b,1'}$ = 10.8, $J_{2'b,3'}$ = 6.0, H-2´b); 2.43 (s, 3H, CH_3-Tol); 2.58 (ddd, 1H, J_{gem} = 13.8, $J_{2'a,1'}$ = 5.1, $J_{2'a,3'}$ = 1.1, H-2´a); 4.51 (td, 1H, $J_{4',5'}$ = 4.1, $J_{4',3'}$ = 2.0, H-4´); 4.59 and 4.62 (2 × d, 2H, J_{gem} = 11.8, $J_{5',4'}$ = 4.1, H-5´); 5.51 (dd, 1H, $J_{1',2'}$ = 10.8, 5.1, H-1´); 5.62 (dddd, 1H, $J_{3',2'}$ = 6.0, 1.1, $J_{3',4'}$ = 2.0, $J_{3',1'}$ = 0.6, H-3´); 6.97 (dd, 1H, $J_{4,5}$ = 5.1, $J_{4,3}$ =

3.5, H-4); 7.06 (ddd, 1H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 1.3, $J_{3,1'}$ = 0.7, H-3); 7.24 (m, 2H, H-*m*-Tol); 7.26 (dd, 1H, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.3, H-5); 7.27 (m, 2H, H-*m*-Tol); 7.97 (m, 4H, H-*o*-Tol). ^{13}C NMR (151 MHz, $CDCl_3$): 21.67 and 21.71 (CH_3-Tol); 41.9 (CH_2-2´); 64.6 (CH_2-5´); 76.85 (CH-1´); 77.1 (CH-3´); 82.9 (CH-4´); 124.95 (CH-3); 125.3 (CH-5); 126.6 (CH-4); 126.9 and 127.1 (C-*i*-Tol); 129.1 and 129.2 (CH-*m*-Tol); 129.7 and 129.75 (CH-*o*-Tol); 143.8 (C-*p*-Tol); 143.8 (C-2); 144.2 (C-*p*-Tol); 166.05 and 166.35 (CO). IR spectrum (CCl_4): 3094, 3039, 1725, 1578, 1444, 1377, 1268, 1208, 1178, 1103, 1082, 1050, 939 cm^{-1}. $[\alpha]^{20}_D$ -14.5 (*c* 2.20, $CHCl_3$).

1*β*-(Thiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (7b). Prepared from **7a** (363 mg, 0.72 mmol) by the general procedure, reaction time 6 h. **7b** (300 mg, 98%) was obtained as a colorless oil. MS (FAB) *m/z* 429 (M + H); HRMS (FAB) for $C_{21}H_{41}O_3SSi_2$: [M + H] calculated 429.2315, found 429.2318. ^{1}H NMR (500 MHz, $CDCl_3$): 0.07 and 0.10 (4 × s, 4 × 3H, CH_3Si); 0.905 and 0.911 (2 × s, 2 × 9H, $(CH_3)_3C$); 2.04 (ddd, 1H, J_{gem} = 12.7, $J_{2'b,1'}$ = 10.5, $J_{2'b,3'}$ = 5.1, H-2´b); 2.16 (ddd, 1H, J_{gem} = 12.7, $J_{2'a,1'}$ = 5.1, $J_{2'a,3'}$ = 1.4, H-2´a); 3.53 (dd, 1H, J_{gem} = 10.6, $J_{5'b,4'}$ = 6.5, H-5´b); 3.73 (dd, 1H, J_{gem} = 10.6, $J_{5'a,4'}$ = 4.0, H-5´a); 3.94 (ddd, 1H, $J_{4',5'}$ = 6.5, 4.0, $J_{4',3'}$ = 1.7, H-4´); 4.44 (dddd, 1H, $J_{3',2'}$ = 5.1, 1.4, $J_{3',4'}$ = 1.7, $J_{3',1'}$ = 0.7, H-3´); 5.38 (dd, 1H, $J_{1',2'}$ = 10.5, 5.1, H-1´); 6.95 (dd, 1H, $J_{4,5}$ = 5.0, $J_{4,3}$ = 3.5, H-4); 7.00 (ddd, 1H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 1.3, $J_{3,1'}$ = 0.7, H-3); 7.23 (dd, 1H, $J_{5,4}$ = 5.0, $J_{5,3}$ = 1.3, H-5). ^{13}C NMR (125.7 MHz, $CDCl_3$): -5.45, -5.4 and -4.7 (CH_3Si); 18.0 and 18.4 (**C**$(CH_3)_3$); 25.8 and 25.95 ((**C**$H_3)_3$C); 44.3 (CH_2-2´); 63.9 (CH_2-5´); 74.4 (CH-3´); 76.0 (CH-1´); 88.1 (CH-4´); 124.4 (CH-3); 124.6 (CH-5); 126.45 (CH-4); 145.6 (C-2). IR spectrum (CCl_4): 2956, 2930, 1731, 1463, 1494, 1375, 1257, 1187, 1092, 1029, 969, 939 cm^{-1}. $[\alpha]^{20}_D$ +3.1 (*c* 4.53, $CHCl_3$).

2) Alkylations

Scheme S2:



R = Tol **4a**
R = TBS **7a**

R = Tol **4a**
R = TBS **7a**
R´= Me, Et, Bn

R = Tol **4a**
R = TBS **7a**

a) Methylation

1*β*-(5-Methylthiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-toluoyl-D-ribofuranose (4c).

A: *using Me_3Al:*

A solution of Me_3Al (980 µL, 2M in toluene, 1.96 mmol) in THF (15 mL) was added dropwise to a vigorously stirred solution of **4a** (505 mg, 0.98 mmol) and $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) in dry THF (18 mL). The mixture was stirred at 105 °C for 12h and then worked up by pouring into saturated NaH_2PO_4 (40 mL) and extracted to EtOAc (3x30mL). Crude product was chromatographed on silica gel in gradient hexane to hexane/EtOAc (19/0.5) to give inseparable mixture of the **4c/4b** (1:1) (209 mg, 24%/24%) as colorless oil.

B: *using MeZnCl:*

A solution of $ZnCl_2$ (4.57 mL, 0.5 M in THF, 2.33 mmol) was added dropwise to a stirred solution of MeMgCl (1.3 mL, 1.5 M in THF, 1.94 mmol) in THF (5 mL) during 5 min. at 0 °C under Ar, the stirring was continued for 20 min at 0 °C. This solution was transferred into **4a** (202 mg, 0.39 mmol), Pd_2dba_3 (18 mg, 0.02 mmol) and bdtbp (12 mg, 0.04 mmol) in THF (5 mL). The resulting reaction mixture was stirred at r.t. for 30 min. then at 70 °C for 24h. The mixture was cooled to rt and worked up with NH_4Cl solution (30 mL), and product was extracted with EtOAc (3 x 20 mL). Evaporation of the organic phase followed by a column

chromatography on silica gel in gradient hexane to hexane/EtOAc (19.5/0.5) afforded the inseparable mixture of products **4c/4b** (2:1) (139 mg, 51%/29%) as colorless oil.

C: *using $MeB(OH)_2$*:

1*β*-(5-Methylthiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-toluoyl-D-ribofuranose (4c). Dry toluene (15 mL) was added to an argon-purged flask containing **4a** (500 mg, 0.97 mmol), K_2CO_3 (200 mg, 1.44 mmol), methylboronic acid (116 mg, 1.94 mmol) and $Pd(PPh_3)_4$ (54 mg, 0.05 mmol), and the mixture was stirred under Ar at 115 °C for 43 h. After the mixture was cooled to rt and filtered through cellite. Evaporation of the solvent, followed by a column chromatography on silica gel in gradient hexane to hexane/toluene (9.7/0.3) afforded the mixture of products **4c/4b** (6:1) (260 mg, 60%) as a colorless oil. Compound **4c:** MS (FAB) *m/z* 451 (M + H); HRMS (FAB) for $C_{26}H_{27}O_5S$: [M + H] calculated 451.1579, found 451.1585. ^{1}H NMR (500 MHz, $CDCl_3$): 2.40 (ddd, 1H, J_{gem} = 13.8, $J_{2'b,1'}$ = 10.8, $J_{2'b,3'}$ = 6.0, H-2´b); 2.41 and 2.43 (2 × s, 2 × 3H, CH_3-Tol); 2.44 (d, 3H, ^4J = 1.1, CH_3); 2.53 (ddd, 1H, J_{gem} = 13.8, $J_{2'a,1'}$ = 5.0, $J_{2'a,3'}$ = 1.2, H-2´a); 4.48 (td, 1H, $J_{4',5'}$ = 4.2, $J_{4',3'}$ = 2.0, H-4´); 4.56 and 4.60 (2 × dd, 2H, J_{gem} = 11.7, $J_{5',4'}$ = 4.2, H-5´); 5.41 (dd, 1H, $J_{1',2'}$ = 10.8, 5.0, H-1´); 5.60 (dddd, 1H, $J_{3',2'}$ = 6.0, 1.2, $J_{3',4'}$ = 2.0, $J_{3',1'}$ = 0.5, H-3´); 6.60 (dq, 1H, $J_{4,3}$ = 3.4, ^4J = 1.1, H-4); 6.85 (d, 1H, $J_{3,4}$ = 3.4, H-3); 7.24 and 7.26 (2 × m, 2 × 2H, H-*m*-Tol); 7.96 and 7.97 (2 × m, 2 × 2H, H-*o*-Tol). ^{13}C NMR (125.7 MHz, $CDCl_3$): 15.4 (CH_3); 21.65 and 21.7 (CH_3-Tol); 41.5 (CH_2-2´); 64.6 (CH_2-5´); 77.0 (CH-1´); 77.0 (CH-3´); 82.7 (CH-4´); 124.6 (CH-4); 125.1 (CH-3); 126.9 and 127.15 (C-*i*-Tol); 129.1 and 129.2 (CH-*m*-Tol); 129.7 and 129.8 (CH-*o*-Tol); 140.0 (C-5); 141.1 (C-2); 143.7 and 144.1 (C-*p*-Tol); 166.0 and 166.3 (CO).

1*β*-(5-Methylthiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (7c).

*using $MeB(OH)_2$***:**

Dry toluene (20 mL) was added to an argon-purged flask containing the **7a** (700 mg, 1.36 mmol), K_2CO_3 (286 mg, 2.1 mmol), methylboronic acid (165 mg, 2.76 mmol), and $Pd(PPh_3)_4$ (80 mg, 0.07 mmol). The mixture was stirred under Ar at 70 °C for 19h. After the mixture was cooled to rt and filtered through cellite. Evaporation of the organic phase followed by a column chromatography on silica gel in gradient hexane to hexane/toluene (19.5/0.5) afforded the inseparable mixture of products **7c/7b** (9:1) (260 mg, 66%/7%) as colorless oil. Compound **7c**: MS (FAB) *m/z* 443 (M + H); $C_{22}H_{43}O_3SSi_2$ [M + H] calculated 443.2471, found 443.2482. ^{1}H NMR (500 MHz, $CDCl_3$): 0.08 and 0.09 (2 × s, 2 × 6H, CH_3Si); 0.908 and 0.909 (2 × s, 2 × 9H, $(CH_3)_3C$); 1.98 (ddd, 1H, J_{gem} = 12.7, $J_{2'b,1'}$ = 10.3, $J_{2'b,3'}$ = 5.2, H-2´b); 2.14 (ddd, 1H, J_{gem} = 12.7, $J_{2'a,1'}$ = 5.3, $J_{2'a,3'}$ = 1.6, H-2´a); 3.52 (dd, 1H, J_{gem} = 10.8, $J_{5'b,4'}$ = 6.4, H-5´b); 3.71 (dd, 1H, J_{gem} = 10.8, $J_{5'a,4'}$ = 4.0, H-5´a); 3.92 (ddd, 1H, $J_{4',5'}$ = 6.4, 4.0, $J_{4',3'}$ = 1.8, H-4´); 4.42 (dddd, 1H, $J_{3',2'}$ = 5.2, 1.6, $J_{3',4'}$ = 1.8, $J_{3',1'}$ = 0.6, H-3´); 5.28 (dddd, 1H, $J_{1',2'}$ = 10.3, 5.3, $J_{1',3}$ = 0.8, $J_{1',3'}$ = 0.6, H-1´); 6.73 (dd, 1H, $J_{3,4}$ = 3.8, $J_{3,1'}$ = 0.8, H-3); 6.88 (d, 1H, $J_{4,3}$ = 3.8, H-4). ^{13}C NMR (125.7 MHz, $CDCl_3$): -5.45, -5.4 and -4.7 (CH_3Si); 18.0 and 18.4 ($\mathbf{C}(CH_3)_3$); 25.8 and 25.95 (($\mathbf{C}H_3)_3C$); 44.15 (CH_2-2´); 63.8 (CH_2-5´); 74.3 (CH-3´); 76.2 (CH-1´); 88.2 (CH-4´); 111.4 (C-5); 124.45 (CH-3); 129.2 (CH-4); 147.7 (C-2).

1*β*-(Thiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (7b). MS (FAB) *m/z* 429 (M + H); $C_{21}H_{41}O_3SSi_2$: [M + H] calculated, 429.2315; found, 429.2322. ^{1}H NMR (500 MHz, $CDCl_3$): 0.07 and 0.10 (4 × s, 4 × 3H, CH_3Si); 0.905 and 0.911 (2 × s, 2 × 9H, $(CH_3)_3C$); 2.04 (ddd, 1H, J_{gem} = 12.7, $J_{2'b,1'}$ = 10.5, $J_{2'b,3'}$ = 5.1, H-2´b); 2.16 (ddd, 1H, J_{gem} = 12.7, $J_{2'a,1'}$ = 5.1, $J_{2'a,3'}$ = 1.4, H-2´a); 3.53 (dd, 1H, J_{gem} = 10.6, $J_{5'b,4'}$ = 6.5, H-5´b); 3.73 (dd, 1H, J_{gem} = 10.6, $J_{5'a,4'}$ = 4.0, H-5´a); 3.94 (ddd, 1H, $J_{4',5'}$ = 6.5, 4.0, $J_{4',3'}$ = 1.7, H-4´); 4.44 (dddd, 1H, $J_{3',2'}$ = 5.1, 1.4, $J_{3',4'}$ = 1.7, $J_{3',1'}$ = 0.7, H-3´); 5.38 (dd, 1H, $J_{1',2'}$ = 10.5,

5.1, H-1´); 6.95 (dd, 1H, $J_{4,5}$ = 5.0, $J_{4,3}$ = 3.5, H-4); 7.00 (ddd, 1H, $J_{3,4}$ = 3.5, $J_{3,5}$ = 1.3, $J_{3,1'}$ = 0.7, H-3); 7.23 (dd, 1H, $J_{5,4}$ = 5.0, $J_{5,3}$ = 1.3, H-5). ^{13}C NMR (125.7 MHz, $CDCl_3$): -5.45, -5.4 and -4.7 (CH_3Si); 18.0 and 18.4 (**C**$(CH_3)_3$); 25.8 and 25.95 ((**C**$H_3)_3$C); 44.3 (CH_2-2´); 63.9 (CH_2-5´); 74.4 (CH-3´); 76.0 (CH-1´); 88.1 (CH-4´); 124.4 (CH-3); 124.6 (CH-5); 126.45 (CH-4); 145.6 (C-2).

b) Ethylation

1*β*-(5-Ethylthiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-toluoyl-D-ribofuranose (4d).

A: *using Et_3Al:*

A solution of Et_3Al (1.96 mL, 1M in hexane, 1.96 mmol) in THF was dropwise added to a vigorously stirred solution of **4a** (505 mg, 0.98 mmol) and $Pd(PPh_3)_4$ (57 mg, 0.05 mmol) in THF (18 mL). The mixture was stirred at 105 °C for 12h. After the mixture was cooled to rt and filtered through cellite. Evaporation of the organic phase followed by a column chromatography on silica gel in gradient hexane to hexane/EtOAc (19/0.5) gave mixture of the **4a/4b** (1:4) (257 mg, 12%/46%) as colorless oil.

B: *using EtZnCl:*

1*β*-(5-Ethylthiophen-2-yl)-1,2-dideoxy-3,5-di-*O*-(*tert*-butyldimethylsilyl)-D-ribofuranose (7d). A solution of $ZnCl_2$ (5.7 mL, 0.5 M in THF, 2.84 mmol) was added dropwise to a stirred solution of EtMgBr (2.4 mL, 1 M in THF, 2.36 mmol) in THF (3 mL) during 5 min at 0 °C under Ar and the stirring was continued for 25 min at 0 °C. This solution was transferred into a solution of **7a** (400 mg, 0.79 mmol), Pd_2dba_3 (36 mg, 0.04 mmol) and bdtbp (24 mg, 0.08 mmol) in THF (5 mL) and the resulting reaction mixture was stirred at r.t. for 10 min and then at 85 °C for 23 h. The mixture was cooled to rt, poured into saturated NH_4Cl solution (20 mL), filtered through cellite and the products were extracted with EtOAc

(3x20 mL). Evaporation of the organic phase followed by a column chromatography on silica gel in gradient hexane to hexane/EtOAc (9.7/0.3) afforded the mixture of products **7d/7b** (4:1) (330 mg, 93%) as a colorless oil. Compound **7d**: MS (FAB) *m/z* 457 (M + H); HRMS (FAB) for $C_{23}H_{45}O_3SSi_2$: [M + H] calculated 457.2628, found 457.2623. ^{1}H NMR (500 MHz, $CDCl_3$): 0.068, 0.069, 0.089 and 0.090 (4 × s, 4 × 3H, CH_3Si); 0.905 and 0.907 (2 × s, 2 × 9H, $(CH_3)_3C$); 1.28 (t, 3H, J_{vic} = 7.6, C**H$_3$**CH_2); 2.03 (ddd, 1H, J_{gem} = 12.7, $J_{2'b,1'}$ = 10.4, $J_{2'b,3'}$ = 5.0, H-2′b); 2.12 (ddd, 1H, J_{gem} = 12.7, $J_{2'a,1'}$ = 5.2, $J_{2'a,3'}$ = 1.5, H-2′a); 2.80 (qd, 2H, J_{vic} = 7.6, ^4J = 1.0, C**H$_2$**CH_3); 3.50 (dd, 1H, J_{gem} = 10.6, $J_{5'b,4'}$ = 6.9, H-5′b); 3.72 (dd, 1H, J_{gem} = 10.6, $J_{5'a,4'}$ = 4.1, H-5′a); 3.91 (ddd, 1H, $J_{4',5'}$ = 6.9, 4.1, $J_{4',3'}$ = 1.5, H-4′); 4.43 (dtd, 1H, $J_{3',2'}$ = 5.0, 1.5, $J_{3',4'}$ = 1.5, $J_{3',1'}$ = 0.6, H-3′); 5.30 (dddd, 1H, $J_{1',2'}$ = 10.4, 5.2, $J_{1',3}$ = 0.7, $J_{1',3'}$ = 0.6, H-1′); 6.61 (dt, 1H, $J_{4,3}$ = 3.4, ^4J = 1.0, H-4); 6.81 (dd, 1H, $J_{3,4}$ = 3.8, $J_{3,1'}$ = 0.7, H-3). ^{13}C NMR (125.7 MHz, $CDCl_3$): -5.44, -5.36 and -4.7 (CH_3Si); 15.9 (**C**H_3CH_2); 18.0 and 18.4 (**C**$(CH_3)_3$); 23.6 (**C**H_2CH_3); 25.8 and 26.0 ((**C**$H_3)_3C$); 43.9 (CH_2-2′); 63.95 (CH_2-5′); 74.45 (CH-3′); 76.2 (CH-1′); 88.0 (CH-4′); 122.6 (CH-4); 124.4 (CH-3); 142.5 (C-2); 147.1 (C-5).

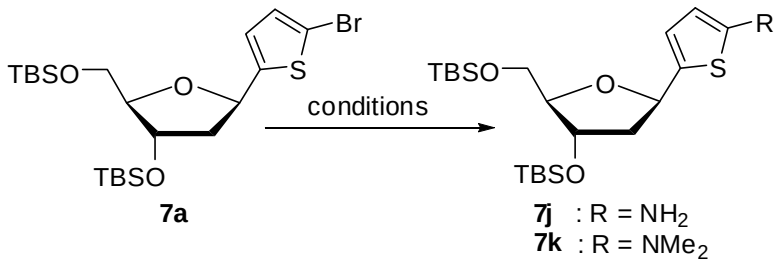
c) Benzylation

1*β*-(5-Benzylthiophen-2-yl)-1,2-dideoxy-D-ribofuranose (6e). A solution of BnMgCl (780 µL, 2 M in THF, 1.55 mmol) was added dropwise to a stirred solution of **4a** (400 mg, 0.78 mmol) and $NiCl_2$(dppp) (42 mg, 0.08 mmol) in THF (4 mL) during 40 min at -20 °C under Ar. The stirring was continued for 10 min to reach rt and then the mixture was stirred at 85 °C for 14 h. The mixture was cooled to rt and then filtered through cellite, extracted to EtOAc (20 mL) and evaporated. Crude mixture was treated with NaOMe (1M solution) in MeOH at rt for 24 h and the residue after evaporation of the solvent was flash-chromatographed on silica gel in gradient EtOAc to EtOAc/MeOH (8/2) to give **6e** (72 mg,

32% after two steps) followed by **6b** (26 mg, 17%) and **6a** (36 mg, 17%) as yellow oils. Compound **6e** was re-purified by flash chromatography on reverse phase and crystallized from isopropanol/heptan to obtain yellow crystals, mp 59-61 °C. MS (FAB) *m/z* 291 (M + H); HRMS (FAB) for $C_{16}H_{19}O_3S$: [M + H] calculated 291.1055, found 291.1046. ^{1}H NMR (500 MHz, CD_3OD): 2.06 (ddd, 1H, J_{gem} = 13.1, $J_{2'b,1'}$ = 10.2, $J_{2'b,3'}$ = 5.8, H-2´b); 2.17 (ddd, 1H, J_{gem} = 13.1, $J_{2'a,1'}$ = 5.4, $J_{2'a,3'}$ = 1.8, H-2´a); 3.54 (dd, 1H, J_{gem} = 11.6, $J_{5'b,4'}$ = 5.5, H-5´b); 3.58 (dd, 1H, J_{gem} = 11.6, $J_{5'a,4'}$ = 5.3, H-5´a); 3.87 (ddd, 1H, $J_{4',5'}$ = 5.5, 5.3, $J_{4',3'}$ = 2.4, H-4´); 4.09 (bs, 2H, CH_2Ph); 4.29 (dddd, 1H, $J_{3',2'}$ = 5.8, 1.8, $J_{3',4'}$ = 2.4, $J_{3',1'}$ = 0.6, H-3´); 5.26 (dddd, 1H, $J_{1',2'}$ = 10.2, 5.4, $J_{1',3}$ = 0.8, $J_{1',3'}$ = 0.6, H-1´); 6.67 (dt, 1H, $J_{4,3}$ = 3.5, ^4J = 1.0, H-4); 6.85 (dd, 1H, $J_{3,4}$ = 3.5, $J_{3,1'}$ = 0.8, H-3); 7.19 (m, 1H, H-*p*-Ph); 7.22 (m, 2H, H-*o*-Ph); 7.27 (m, 1H, H-*m*-Ph). ^{13}C NMR (125.7 MHz, CD_3OD): 37.15 (CH_2Ph); 44.6 (CH_2-2´); 64.1 (CH_2-5´); 74.3 (CH-3´); 77.6 (CH-1´); 89.05 (CH-4´); 125.5 (CH-4); 125.7 (CH-3); 127.45 (CH-*p*-Ph); 129.5 (CH-*m*-Ph); 129.6 (CH-*o*-Ph); 141.9 (C-*i*-Ph); 144.9 (C-2); 145.6 (C-5). IR spectrum (KBr): 3409, 3083, 3060, 2929, 2998, 2842, 1698, 1632, 1489, 1436, 1338, 1217, 1055, 1036, 968 cm^{-1}. $[\alpha]^{20}_D$ -12.5 (*c* 2.77, MeOH). Anal. Calcd $C_{16}H_{18}O_3S$ (290.4): C, 66.18; H, 6.25; found: C, 65.85; H, 6.25.

3) Amination

Scheme S3:



7a

7j : R = NH_2
7k : R = NMe_2

Attempted amination of 7a. $LiN(SiMe_3)_2$ (0.36 mL, 1 M solution in THF, 0.36 mmol) was added to a dried argon purged flask containing **7a** (100 mg, 0.20 mmol), tri-*tert*-butylphosphonium tetrafluoroborate (6.9 mg, 0.24 mol), and $Pd_2(dba)_3$ (11.9 mg, 6.6 mol %), and the mixture was stirred at rt for 24h and then 24h. at 80 °C. The reaction was quenched by the addition of Et_2O and 4 drops of 2 M aqueous solution of HCl and worked up. Chromatography on silica gel in gradient hexane to hexane / EtOAc to give only product of degradation as a yellow oil.

1*β*-(5-Dimethylaminothiophen-2-yl)-1,2-dideoxy-3,5-di-O-(*t*-butyldimethylsilyl)-D-ribofuranose (7k). A solution of Pd_2dba_3 (63 mg, 5 mol %), (2-biphenyl)-di-*tert*-butylphosphine (62 mg, 15 mol %) in toluene (9 mL) was added to an argon-purged dry flask containing **7a** (700 mg, 1.38 mmol), sodium *tert*-butoxide (663 mg, 6.89 mmol) in toluene (9 mL), and mixture was stirring for 2 min. then $Me_2NH.THF$ (3.44 mL, 2 M solution in THF, 6.89 mmol) was added in one portion. The mixture was stirred at 70 °C for 7h. After was reaction quenched by saturated NH_4Cl (30 ml) and, extracted EtOAc (2x 25 mL) and mixture was dried on $MgSO_4$, and solvent were evaporated under vacuum. and crude product **7k** was chromatographed on silica gel in gradient hexane to hexane / EtOAc to give **7k** (314 mg, 49 %) as a yellow oil which was unstable and spontaneously degraded. Compound **7k** : $C_{23}H_{45}NO_3SSi_2$: [M + H] calculated 472.2737, found 472.2728. ^{1}H NMR (500 MHz, $CDCl_3$): 0.069, 0.074, 0.086 and 0.087 (4 × s, 4 × 3H, CH_3Si); 0.90 and 0.91 (2 × s, 2 × 9H, $(CH_3)_3C$); 2.02 (ddd, 1H, J_{gem} = 12.7, $J_{2´b,1´}$ = 10.0, $J_{2´b,3´}$ = 4.9, H-2´b); 2.05 (ddd, 1H, J_{gem} = 12.7, $J_{2´a,1´}$ = 5.6, $J_{2´a,3´}$ = 1.5, H-2´a); 2.87 (s, 6H, CH_3N); 3.50 (dd, 1H, J_{gem} = 10.6, $J_{5´b,4´}$ = 6.8, H-5´b); 3.71 (dd, 1H, J_{gem} = 10.6, $J_{5´a,4´}$ = 4.0, H-5´a); 3.88 (ddd, 1H, $J_{4´,5´}$ = 6.8, 4.0, $J_{4´,3´}$ = 1.7, H-4´); 4.41 (dddd, 1H, $J_{3´,2´}$ = 4.9, 1.5, $J_{3´,4´}$ = 1.7, $J_{3´,1´}$ = 0.7, H-3´); 5.22 (ddt, 1H, $J_{1´,2´}$ = 10.0, 5.6, $J_{1´,3}$ = $J_{1´,3´}$ = 0.7, H-1´); 5.72 (d, 1H, $J_{4,3}$ = 3.7, H-4); 6.68 (dd, 1H, $J_{3,4}$ = 3.7, $J_{3,1´}$ = 0.7,

H-3). ^{13}C NMR (125.7 MHz, $CDCl_3$): -5.42, -5.34 and -4.66 (CH_3Si); 18.03 and 18.38 ($\mathbf{C}(CH_3)_3$); 25.84 and 25.98 (($\mathbf{C}H_3)_3C$); 43.08 (CH_3N); 43.48 (CH_2-2´); 64.06 (CH_2-5´); 74.49 (CH-3´); 76.63 (CH-1´); 87.75 (CH-4´); 101.75 (CH-4); 124.76 (CH-3); 129.47 (C-2); 159.29 (C-5).

4) Stille couplings

General procedure for the Stille cross-coupling reaction: 2-(Tributylstannyl)hetaryl (1.2-5 equiv.) was added dropwise under argon to a stirred solution of **4a** (1 equiv.) and $PdCl_2$dppf (5 mol. %) in DMF (5.0 mL). The mixture was stirred at 100-120 °C for 16-22 h. Crude reaction mixture was diluted with EtOAc (15 mL), filtered through cellite, washed with 2M HCl and brine. The water layers were extracted with EtOAc (3x20 mL). Then the collected organic layers were dried over $MgSO_4$ and solvents were evaporated under vacuum. The crude product was chromatographed on silica gel in gradient hexane to hexane / EtOAc (9.7/0.3).

1*β*-[5-(Thiophen-2-yl)thiophen-2-yl]-1,2-dideoxy-3,5-di-3,5-di-*O*-toluoyl-D-ribofuranose (4g). Prepared from **4a** (623 mg, 1.21 mmol) and 2-(tributylstannyl)thiophene (1.90 mL, 6 mmol), by the general procedure (110 °C, 16 h). Compound **4g** (560 mg, 90%) was obtained as a yellow oil. MS (FAB) *m/z* 519 (M + H); HRMS (FAB) for $C_{29}H_{27}O_5S_2$: [M + H] calculated 519.1222, found 519.1281. ^1H NMR (600 MHz, $CDCl_3$): 2.41 (s, 3H, CH_3-Tol); 2.42 (ddd, 1H, J_{gem} = 13.8, $J_{2´b,1´}$ = 10.7, $J_{2´b,3´}$ = 5.9, H-2´b); 2.44 (s, 3H, CH_3-Tol); 2.59 (ddd, 1H, J_{gem} = 13.8, $J_{2´a,1´}$ = 5.1, $J_{2´a,3´}$ = 1.2, H-2´a); 4.51 (td, 1H, $J_{4´,5´}$ = 4.2, 3.8, $J_{4´,3´}$ = 1.9, H-4´); 4.61 (dd, 1H, J_{gem} = 11.8, $J_{5´b,4´}$ = 3.8, H-5´b); 4.64 (dd, 1H, J_{gem} = 11.8, $J_{5´a,4´}$ = 4.2, H-5´a); 5.46 (ddt, 1H, $J_{1´,2´}$ = 10.7, 5.1, $J_{1´,3}$ = 0.7, $J_{1´,3´}$ = 0.6, H-1´); 5.63 (dddd, 1H, $J_{3´,2´}$ =

5.9, 1.2, $J_{3',4'}$ = 1.9, $J_{3',1'}$ = 0.6, H-3´); 6.95 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,1'}$ = 0.7, H-3); 6.99 (dd, 1H, $J_{4,5}$ = 5.1, $J_{4,3}$ = 3.6, H-4-thienyl); 7.00 (d, 1H, $J_{4,3}$ = 3.6, H-4); 7.05 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,5}$ = 1.2, H-3-thienyl); 7.20 (dd, 1H, $J_{5,4}$ = 5.1, $J_{5,3}$ = 1.2, H-5-thienyl); 7.24 and 7.27 (2 × m, 2 × 2H, H-*m*-Tol); 7.97 and 7.99 (2 × m, 2 × 2H, H-*o*-Tol). ^{13}C NMR (151 MHz, $CDCl_3$): 21.69 and 21.73 (CH_3-Tol); 41.8 (CH_2-2´); 64.5 (CH_2-5´); 77.0 (CH-1´); 77.1 (CH-3´); 83.0 (CH-4´); 123.1 (CH-4); 123.7 (CH-3-thienyl); 124.4 (CH-5-thienyl); 125.6 (CH-3); 126.8 and 127.1 (C-*i*-Tol); 127.7 (CH-4-thienyl); 129.1 and 129.2 (CH-*m*-Tol); 129.7 and 129.8 (CH-*o*-Tol); 137.28 and 137.29 (C-5 and C-2-thienyl); 142.8 (C-2); 143.8 and 144.2 (C-*p*-Tol); 166.05 and 166.4 (CO). IR spectrum (KBr): 3073, 1718, 1612, 1270, 1106, 1021 cm^{-1}. $[\alpha]^{20}_{D}$ = - 104 (*c* 2.23, , $CHCl_3$).

1*β*-[5-(Furan-2-yl)thiophen-2-yl]-1,2-dideoxy-3,5-di-3,5-di-*O*-toluoyl-D-ribofuranose (4h). Prepared from **4a** (773 mg, 1.5 mmol) and 2-(tributylstannyl)furan (570 µL, 1.80 mmol) by the general procedure (120 °C, 22 h). **4h** (672 mg, 89%) was obtained as a yellow oil. MS (FAB) *m/z* 503 (M + H); HRMS (FAB) for $C_{29}H_{27}O_6S$: [M + H] calculated 503.1528, found 503.1520. ^{1}H NMR (500 MHz, $CDCl_3$): 2.40 (s, 3H, CH_3-Tol); 2.41 (ddd, 1H, J_{gem} = 13.8, $J_{2'b,1'}$ = 10.6, $J_{2'b,3'}$ = 6.0, H-2´b); 2.43 (s, 3H, CH_3-Tol); 2.58 (ddd, 1H, J_{gem} = 13.8, $J_{2'a,1'}$ = 5.2, $J_{2'a,3'}$ = 1.2, H-2´a); 4.51 (td, 1H, $J_{4',5'}$ = 4.0, $J_{4',3'}$ = 2.1, H-4´); 4.61 (d, 2H, $J_{5',4'}$ = 4.0, H-5´); 5.46 (dddd, 1H, $J_{1',2'}$ = 10.6, 5.2, $J_{1',3}$ = 0.7, $J_{1',3'}$ = 0.5, H-1´); 5.62 (dddd, 1H, $J_{3',2'}$ = 6.0, 1.2, $J_{3',4'}$ = 2.1, $J_{3',1'}$ = 0.5, H-3´); 6.40 (dd, 1H, $J_{3,4}$ = 3.4, $J_{3,5}$ = 0.9, H-3-furyl); 6.41 (dd, 1H, $J_{4,3}$ = 3.4, $J_{4,5}$ = 1.8, H-4-furyl); 6.96 (dd, 1H, $J_{3,4}$ = 3.7, $J_{3,1'}$ = 0.7, H-3); 7.08 (d, 1H, $J_{4,3}$ = 3.7, H-4); 7.23 and 7.27 (2 × m, 2 × 2H, H-*m*-Tol); 7.38 (dd, 1H, $J_{5,4}$ = 1.8, $J_{5,3}$ = 0.9, H-5-furyl); 7.96 and 7.97 (2 × m, 2 × 2H, H-*o*-Tol). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.64 and 21.68 (CH_3-Tol); 41.7 (CH_2-2´); 64.5 (CH_2-5´); 76.9 (CH-1´); 77.0 (CH-3´); 83.0 (CH-4´); 105.1 (CH-3-furyl); 111.6 (CH-4-furyl); 122.0 (CH-4); 125.3 (CH-3); 126.9 and 127.2 (C-*i*-

Tol); 129.1 and 129.2 (CH-*m*-Tol); 129.7 and 129.8 (CH-*o*-Tol); 133.55 (C-5); 141.7 (CH-5-furyl); 141.7 (C-2); 143.8 and 144.2 (C-*p*-Tol); 149.3 (C-2-furyl); 166.0 and 166.4 (CO). IR spectrum (KBr): 3153, 3067, 1717, 1612, 1271, 1105, 1020 cm^{-1}. $[\alpha]^{20}_{D}$ = + 71.4 (*c* 2.06, $CHCl_3$).

1*β*-[5-([2,2´]Bipyridin-6-yl)thiophen-2-yl]-1,2-dideoxy-3,5-di-3,5-di-*O*-toluoyl-D-ribofuranose (4i). *n*-BuLi (1.7 mL, 1.6 M in hexane, 2.72 mmol,) was added dropwise into a solution of 6-bromo[2,2´]bipyridine (447 mg, 1.90 mmol) in THF (15 mL) under argon at -72 °C during 5 min, and mixture was stirred for 2 min followed by addition of Bu_3SnCl (740 µL, 1.90 mmol). After being stirred for 20 min at -72 °C, the reaction was allowed to warm to rt, and the solvent was carefully evaporated under vacuum. The crude 6-(tributylstannyl)[2,2´]bipyridine[Chyba! Záložka není definována.] was dissolved in DMF (4.5 mL) and added through septum to a flask containing **4a** (700 mg, 1.36 mmol) and $PdCl_2$dppf (50 mg, 0.07 mmol) seal under argon. The reaction mixture was stirred at 100 °C for 22 h. Chromatography on silica gel in gradient hexane to hexane/EtOAc (9.7/0.3) to gave only crude **4i** (358 mg) as a yellow oil. The crude product was stirred with Me_3Al (460 µL, 2M in toluene, 0.91 mmol) in toluene (13 mL) at rt for 24 h and worked up as in **4f**. Flash chromatography on silica gel eluting hexane to hexane/EtOAc (19.8/0.2) gave pure product **4i** (308 mg, 64%) as a colorless oil. MS (FAB) *m/z* 591 (M + H); HRMS (FAB) for $C_{35}H_{31}N_2O_5S$: [M + H] 591.1954 found, 591.1942. ^{1}H NMR (500 MHz, $CDCl_3$): 2.32 and 2.44 (2 × s, 2 × 3H, CH_3-Tol); 2.50 (ddd, 1H, J_{gem} = 13.9, $J_{2´b,1´}$ = 10.6, $J_{2´b,3´}$ = 6.0, H-2´b); 2.64 (ddd, 1H, J_{gem} = 13.9, $J_{2´a,1´}$ = 5.2, $J_{2´a,3´}$ = 1.2, H-2´a); 4.56 (ddd, 1H, $J_{4´,5´}$ = 4.2, 3.9, $J_{4´,3´}$ = 1.9, H-4´); 4.62 (dd, 1H, J_{gem} = 11.8, $J_{5´b,4´}$ = 4.2, H-5´b); 4.68 (dd, 1H, J_{gem} = 11.8, $J_{5´a,4´}$ = 3.9, H-5´a); 5.53 (dddd, 1H, $J_{1´,2´}$ = 10.6, 5.2, $J_{1´,3}$ = 0.8, $J_{1´,3´}$ = 0.5, H-1´); 5.65 (dddd, 1H, $J_{3´,2´}$ = 6.0, 1.2, $J_{3´,4´}$ = 1.9, $J_{3´,1´}$ = 0.5, H-3´); 7.08 (dd, 1H, $J_{3,4}$ = 3.7, $J_{3,1´}$ = 0.8, H-3);

7.20 and 7.28 (2 × m, 2 × 2H, H-*m*-Tol); 7.30 (ddd, 1H, $J_{5',4'}$ = 7.4, $J_{5',6'}$ = 4.8, $J_{5',3'}$ = 1.2, H-5´-bipy); 7.50 (d, 1H, $J_{4,3}$ = 3.7, H-4); 7.61 (dd, 1H, $J_{5,4}$ = 7.8, $J_{5,3}$ = 0.9, H-5-bipy); 7.74 (ddd, 1H, $J_{4',3'}$ = 8.0, $J_{4',5'}$ = 7.4, $J_{4',6'}$ = 1.8, H-4´-bipy); 7.80 (t, 1H, $J_{4,3}$ = $J_{4,5}$ = 7.8, H-4-bipy); 7.98 and 8.02 (2 × m, 2 × 2H, H-*o*-Tol); 8.28 (dd, 1H, $J_{3,4}$ = 7.8, $J_{3,5}$ = 0.9, H-3-bipy); 8.48 (ddd, 1H, $J_{3',4'}$ = 8.0, $J_{3',5'}$ = 1.2, $J_{3',6'}$ = 0.9, H-3´-bipy); 8.67 (ddd, 1H, $J_{6',5'}$ = 4.8, $J_{6',4'}$ = 1.8, $J_{6',3'}$ = 0.9, H-6´-bipy). ^{13}C NMR (125.7 MHz, $CDCl_3$): 21.6 and 21.7 (CH_3-Tol); 41.9 (CH_2-2´); 64.7 (CH_2-5´); 77.1 (CH-3´); 77.2 (CH-1´); 83.0 (CH-4´); 118.3 (CH-5-bipy); 119.0 (CH-3-bipy); 121.4 (CH-3´-bipy); 123.8 (CH-5´-bipy); 124.0 (CH-4); 125.7 (CH-3); 126.9 and 127.1 (C-*i*-Tol); 129.1 and 129.2 (CH-*m*-Tol); 129.7 and 129.8 (CH-*o*-Tol); 136.9 (CH-4´-bipy); 137.5 (CH-4-bipy); 143.7 and 144.2 (C-*p*-Tol); 144.9 (C-5); 146.1 (C-2); 148.95 (CH-6´-bipy); 151.65 (C-6-bipy); 155.55 (C-2-bipy); 155.8 (C-2´-bipy); 166.0 and 166.4 (CO). IR spectrum (KBr): 3066, 3039, 2954, 2926, 2858, 1725, 1613, 1475, 1430, 1268, 1178, 1103, 1021, 997 cm^{-1}. $[\alpha]^{20}_{D}$ = -105.5 (*c* 4.81, $CHCl_3$).

General procedure for the Suzuki cross-coupling: To an argon-purged flask containing TTPTS (36 mg, 0.06 mmol) and $Pd(OAc)_2$ (5.6 mg, 0.025 mmol), a mixture of H_2O/acetonitrile (2:1) (2.5 mL) was added and the mixture was sonicated for 2 min. This solution was added into a mixture of **6a** (140 mg, 0.5 mmol), boronic acid (0.75 mmol), Cs_2CO_3 (489 mg, 1.5 mmol) in H_2O/acetonitrile (2:1) (2 mL). The mixture was then stirred at 90 or 120 °C for 2-4 h. After evaporation, the crude product was purified by flash chromatography on silica gel in gradient $CHCl_3$ to $CHCl_3$/MeOH (9.5/0.5).

1*β*-[5-(4-Fluorophenyl)thiophen-2-yl]-1,2-dideoxy-D-ribofuranose (6m). Prepared from **6a** and 4-fluorophenylboronic acid (105 mg, 0.75 mmol) by the general procedure (120 °C, 4 h). **6m** (117 mg, 80%) was obtained as a brown oil which was crystallized from

isopropanol/heptan to give brown crystals, mp 106-108 ºC. MS (FAB) *m/z* 295 (M + H); HRMS (FAB) for $C_{15}H_{16}FO_3S$: [M + H] calculated 295.0804, found 295.0814. ^{1}H NMR (500 MHz, DMSO-d_6): 1.96 (ddd, 1H, J_{gem} = 12.8, $J_{2'b,1'}$ = 10.1, $J_{2'b,3'}$ = 5.5, H-2´b); 2.14 (ddd, 1H, J_{gem} = 12.8, $J_{2'a,1'}$ = 5.5, $J_{2'a,3'}$ = 1.8, H-2´a); 3.37 (dt, 1H, J_{gem} = 11.3, $J_{5'b,4'}$ = 6.2, $J_{5'b,OH}$ = 5.6, H-5´b); 3.45 (dt, 1H, J_{gem} = 11.3, $J_{5'a,OH}$ = 5.3, $J_{5'a,4'}$ = 5.0, H-5´a); 3.77 (ddd, 1H, $J_{4',5'}$ = 6.2, 5.0, $J_{4',3'}$ = 2.2, H-4´); 4.21 (m, 1H, $J_{3',2'}$ = 5.5, 1.8, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.2, $J_{3',1'}$ = 0.6, H-3´); 4.76 (t, 1H, $J_{OH,5'}$ = 5.6, 5.3, OH-5´); 5.12 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3´); 5.23 (ddt, 1H, $J_{1',2'}$ = 10.1, 5.5, $J_{1',3}$ = 0.8, $J_{1',3'}$ = 0.6, H-1´); 7.03 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,1'}$ = 0.8, H-3); 7.23 (m, 2H, H-*m*-C_6H_4F); 7.30 (d, 1H, $J_{4,3}$ = 3.6, H-4); 7.65 (m, 2H, H-*o*-C_6H_4F). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.6 (CH_2-2´); 62.7 (CH_2-5´); 72.5 (CH-3´); 75.4 (CH-1´); 88.0 (CH-4´); 116.2 (d, $J_{C,F}$ = 22, CH-*m*-C_6H_4F); 123.4 (CH-4); 125.9 (CH-3); 127.4 (d, $J_{C,F}$ = 8, CH-*o*-C_6H_4F); 130.7 (d, $J_{C,F}$ = 3, C-*i*-C_6H_4F); 141.3 (C-5); 146.1 (C-2); 161.8 (d, $J_{C,F}$ = 245, C-*p*-C_6H_4F). ^{19}F NMR (470.3 MHz, DMSO-d_6): -111.4. IR spectrum ($CHCl_3$): 3612, 3417, 3076, 1604, 1552, 1514, 1474, 1474, 1354, 1235, 1160, 1097, 1039, 960 cm^{-1}. $[\alpha]^{20}_D$ +10.0 (*c* 2.36, $CHCl_3$). Anal. Calcd $C_{15}H_{15}FO_3S$ (294.3): C, 61.21; H, 5.14; F, 6.45; S, 10.89; found: C, 60.88; H, 5.15; F, 6.50; S 10.64.

1*β*-[5-(Thiophen-3-yl)thiophen-2-yl]-1,2-dideoxy-D-ribofuranose (6n). Compound **6n** was prepared from **6a** and 3-thienylboronic acid (96 mg, 0.75 mmol) by the general procedure (120 °C, 4 h). **6n** (99 mg, 70%) was obtained as a yellow oil which was was crystallized from isopropanol/heptan to give yellow crystals, mp 123-125 ºC. MS (FAB) *m/z* 283 (M + H); HRMS (FAB) for $C_{13}H_{15}O_3S_2$: [M + H] calculated 283.0463, found 283.0469. ^{1}H NMR (500 MHz, DMSO-d_6): 1.96 (ddd, 1H, J_{gem} = 12.8, $J_{2'b,1'}$ = 10.2, $J_{2'b,3'}$ = 5.6, H-2´b); 2.13 (ddd, 1H, J_{gem} = 12.8, $J_{2'a,1'}$ = 5.5, $J_{2'a,3'}$ = 1.8, H-2´a); 3.37 (dt, 1H, J_{gem} = 11.3, $J_{5'b,4'}$ = 6.3, $J_{5'b,OH}$ = 6.1, H-5´b); 3.45 (dt, 1H, J_{gem} = 11.3, $J_{5'a,OH}$ = 5.4, $J_{5'a,4'}$ = 5.0, H-5´a); 3.76 (ddd, 1H, $J_{4',5'}$ =

6.0, 5.0, $J_{4',3'}$ = 2.2, H-4´); 4.20 (m, 1H, $J_{3',2'}$ = 5.6, 1.8, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.2, $J_{3',1'}$ = 0.6, H-3´); 4.76 (t, 1H, $J_{OH,5'}$ = 6.1, 5.4, OH-5´); 5.11 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3´); 5.21 (ddt, 1H, $J_{1',2'}$ = 10.2, 5.5, $J_{1',3}$ = 0.8, $J_{1',3'}$ = 0.6, H-1´); 6.99 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,1'}$ = 0.8, H-3); 7.34 (d, 1H, $J_{4,3}$ = 3.6, H-4); 7.39 (dd, 1H, $J_{4,5}$ = 5.0, $J_{4,2}$ = 1.4, H-4-thienyl); 7.61 (dd, 1H, $J_{5,4}$ = 5.0, $J_{5,2}$ = 2.9, H-5-thienyl); 7.65 (dd, 1H, $J_{2,5}$ = 2.9, $J_{2,4}$ = 1.4, H-2-thienyl). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.62 (CH_2-2´); 62.66 (CH_2-5´); 72.5 (CH-3´); 75.4 (CH-1´); 88.0 (CH-4´); 120.0 (CH-2-thienyl); 123.2 (CH-4); 125.4 (CH-3); 126.05 (CH-4-thienyl); 127.55 (CH-5-thienyl); 135.4 (C-3-thienyl); 137.7 (C-5); 144.8 (C-2). IR spectrum (KBr): 3402, 3327, 3085, 2981, 1478, 1426, 1359, 1346, 1090, 1080, 1045, 1036 cm^{-1}. $[\alpha]^{20}_D$ +2.1 (*c* 2.81, $CHCl_3$). Anal. Calcd $C_{13}H_{14}O_3S_2$ (282.4): C, 55.29; H, 5.00; S, 22.71; found: C, 55.25; H, 5.09; S 22.30.

1*β*-[5-(Furan-3-yl)thiophen-2-yl]-1,2-dideoxy-D-ribofuranose (6o). Prepared from **6a** and 3-furylboronic acid (84 mg, 0.75 mmol) by the general procedure (90 °C, 2 h). **6o** (103 mg, 78%) was obtained as a yellow oil which was crystallized from isopropanol/heptan to give yellow crystals, mp 107-110 ºC. MS (FAB) *m/z* 267 (M + H); HRMS (FAB) for $C_{13}H_{15}O_4S$: [M + H] calculated 267.0691, found 267.0696. ^{1}H NMR (500 MHz, DMSO-d_6): 1.92 (ddd, 1H, J_{gem} = 12.8, $J_{2'b,1'}$ = 10.2, $J_{2'b,3'}$ = 5.6, H-2´b); 2.11 (ddd, 1H, J_{gem} = 12.8, $J_{2'a,1'}$ = 5.5, $J_{2'a,3'}$ = 1.8, H-2´a); 3.36 (dt, 1H, J_{gem} = 11.2, $J_{5'b,4'}$ = 6.2, $J_{5'b,OH}$ = 6.9, H-5´b); 3.44 (dt, 1H, J_{gem} = 11.2, $J_{5'a,OH}$ = 5.3, $J_{5'a,4'}$ = 5.1, H-5´a); 3.75 (ddd, 1H, $J_{4',5'}$ = 6.2, 5.1, $J_{4',3'}$ = 2.2, H-4´); 4.19 (m, 1H, $J_{3',2'}$ = 5.6, 1.8, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.2, $J_{3',1'}$ = 0.5, H-3´); 4.75 (t, 1H, $J_{OH,5'}$ = 5.9, 5.3, OH-5´); 5.11 (d, 1H, $J_{OH,3'}$ = 3.9, OH-3´); 5.21 (ddt, 1H, $J_{1',2'}$ = 10.2, 5.5, $J_{1',3}$ = 0.8, $J_{1',3'}$ = 0.5, H-1´); 6.80 (dd, 1H, $J_{4,5}$ = 1.9, $J_{4,2}$ = 0.9, H-4-furyl); 6.97 (dd, 1H, $J_{3,4}$ = 3.6, $J_{3,1'}$ = 0.8, H-3); 7.09 (d, 1H, $J_{4,3}$ = 3.6, H-4); 7.72 (t, 1H, $J_{5,4}$ = 1.9, $J_{5,2}$ = 1.6, H-5-furyl); 8.01 (dd, 1H, $J_{2,5}$ = 1.6, $J_{2,4}$ = 0.9, H-2-furyl). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.65 (CH_2-2´); 62.68 (CH_2-5´); 72.5 (CH-3´); 75.4 (CH-1´); 88.0 (CH-4´); 126.05 (CH-4-furyl); 120.5 (C-3-

furyl); 123.4 (CH-4); 125.25 (CH-3); 133.5 (C-5); 138.6 (CH-2-furyl); 144.5 (C-2); 144.5 (CH-5-furyl). IR spectrum (KBr): 3408, 3135, 2940, 1031, 1511, 1360, 1349, 1206, 1044, 3325 cm^{-1}. $[\alpha]^{20}_D$ +12.0 (*c* 2.35, $CHCl_3$). Anal. Calcd for $C_{13}H_{14}O_4S$ (266.3): C, 58.63; H, 5.30; found: C 58.32; H 5.32.

1*β*-[(3-Nitrophenyl)thiophen-2-yl]-1,2-dideoxy-D-ribofuranose (6p). Prepared from **6a** (140 mg, 0.5 mmol) and 3-nitrophenylboronic acid (126 mg, 0.75 mmol) by the general procedure (90 °C, 2 h). **6p** (119 mg, 74%) was obtained as a yellow oil which was crystallized from isopropanol/heptan to give yellow crystals, mp 123-124 ºC. MS (FAB) *m/z* 322 (M + H); HRMS (FAB) for $C_{15}H_{16}NO_5S$: [M + H] calculated 322.07492, found 322.0738. ^{1}H NMR (500 MHz, DMSO-d_6): 1.97 (ddd, 1H, J_{gem} = 12.8, $J_{2'b,1'}$ = 10.1, $J_{2'b,3'}$ = 5.5, H-2´b); 2.17 (ddd, 1H, J_{gem} = 12.8, $J_{2'a,1'}$ = 5.5, $J_{2'a,3'}$ = 1.8, H-2´a); 3.39 (dt, 1H, J_{gem} = 11.3, $J_{5'b,4'}$ = 6.1, $J_{5'b,OH}$ = 5.8, H-5´b); 3.47 (dt, 1H, J_{gem} = 11.3, $J_{5'a,OH}$ = 5.3, $J_{5'a,4'}$ = 5.0, H-5´a); 3.79 (ddd, 1H, $J_{4',5'}$ = 6.1, 5.0, $J_{4',3'}$ = 2.1, H-4´); 4.22 (m, 1H, $J_{3',2'}$ = 5.5, 1.8, $J_{3',OH}$ = 3.9, $J_{3',4'}$ = 2.1, $J_{3',1'}$ = 0.6, H-3´); 4.78 (t, 1H, $J_{OH,5'}$ = 5.8, 5.3, OH-5´); 5.14 (t, 1H, $J_{OH,3'}$ = 3.9, OH-3´); 5.27 (ddt, 1H, $J_{1',2'}$ = 10.1, 5.5, $J_{1',3}$ = 0.8, $J_{1',3'}$ = 0.6, H-1´); 7.11 (dd, 1H, $J_{3,4}$ = 3.7, $J_{3,1'}$ = 0.8, H-3); 7.60 (d, 1H, $J_{4,3}$ = 3.7, H-4); 7.69 (t, 1H, $J_{5,4}$ = 8.2, $J_{5,6}$ = 7.8, H-5-$C_6H_4NO_2$); 8.07 (ddd, 1H, $J_{6,5}$ = 7.8, $J_{6,2}$ = 1.9, $J_{6,4}$ = 1.0, H-6-$C_6H_4NO_2$); 8.12 (ddd, 1H, $J_{4,5}$ = 8.2, $J_{4,2}$ = 2.3, $J_{4,6}$ = 1.0, H-4-$C_6H_4NO_2$); 8.37 (t, 1H, $J_{2,4}$ = 2.3, $J_{2,6}$ = 1.9, H-2-$C_6H_4NO_2$). ^{13}C NMR (125.7 MHz, DMSO-d_6): 43.7 (CH_2-2´); 62.6 (CH_2-5´); 72.5 (CH-3´); 75.4 (CH-1´); 88.1 (CH-4´); 119.3 (CH-2-$C_6H_4NO_2$); 122.0 (CH-4-$C_6H_4NO_2$); 125.5 (CH-4); 126.1 (CH-3); 130.9 (CH-5-$C_6H_4NO_2$); 131.6 (CH-6-$C_6H_4NO_2$); 135.7 (C-1-$C_6H_4NO_2$); 141.5 (C-5); 148.1 (C-2); 148.6 (C-3-$C_6H_4NO_2$). IR spectrum (KBr): 3351, 3094, 1615, 1551, 1529, 1353, 1201, 1173, 1085, 1078, 1042, 998cm^{-1}. $[\alpha]^{20}_D$ +2.7 (*c* 2.69, $CHCl_3$). Anal. Calcd for $C_{15}H_{15}NO_5S$ (321.3): C, 56.06; H, 4.70; N, 4.36; found: C 56.22; H 4.50; N 4.82.

General procedure for the deprotection of TBDMS-Group: $Et_3N•3HF$ (363 μL, 2.25 mmol) was added to a solution of compounds **7b-7d** (0.45 mmol) in THF (4 mL) and the mixture was stirred at room temperature for 48 h. After the reaction was completed (TLC hexane/EtOAc (9/1)), the solvent was evaporated under reduced pressure. Then the crude product was dissolved in MeOH (2 mL), and a 1M aqueous solution of sodium hydroxide (2 mL) was added to neutralize the mixture. The solvent was evaporated and products were purified by flash chromatography on silica gel in gradient chloroform to chloroform/methanol (19.5/0.5). Compounds **6c** and **6d** were re-purified by flash chromatography on reverse phase (C18 column, with linear gradient of H_2O to MeOH).

1*β*-(5-Thiophen-2-yl)-1,2-dideoxy-D-ribofuranose (6b). Yield (69 mg, 78%).

1*β*-(5-Methylthiophen-2-yl)-1,2-dideoxy-D-ribofuranose (6c). Prepared from mixture **7c/7b** (390 mg, 0.88 mmol) by the general procedure. The crude product was chromatographed to give **6c** (94 mg, 50%) and **6b** (14 mg, 8%) as yellow oils.

1*β*-(5-Ethylthiophen-2-yl)-1,2-dideoxy-D-ribofuranose (6d). Prepared from mixture **7d/7b** (330 mg, 0.73 mmol) by the general procedure. The crude product was chromatographed to give **6d** (95 mg, 73%) and **6b** (20 mg, 14%) as yellow oils. Product did not crystallized, lyophilization gave yellow amorphous solid, mp 28-31 ºC. MS (FAB) *m/z* 229 (M + H); HRMS (FAB) for $C_{11}H_{17}O_3S$: [M + H] calculated 229.0898, found 229.0902. ^{1}H NMR (500 MHz, DMSO-d_6): 1.20 (t, 3H, J_{vic} = 7.6, C**H**$_3$CH$_2$); 1.90 (ddd, 1H, J_{gem} = 12.8, $J_{2'b,1'}$ = 10.2, $J_{2'b,3'}$ = 5.6, H-2´b); 2.06 (ddd, 1H, J_{gem} = 12.8, $J_{2'a,1'}$ = 5.5, $J_{2'a,3'}$ = 1.7, H-2´a);

2.75 (qd, 2H, J_{vic} = 7.6, $J_{CH2,4}$ = 1.1, C**H$_2$**CH$_3$); 3.33 (ddd, 1H, J_{gem} = 11.3, $J_{5´b,4´}$ = 6.2, $J_{5´b,OH}$ = 5.4, H-5´b); 3.41 (ddd, 1H, J_{gem} = 11.3, $J_{5´a,OH}$ = 5.4, $J_{5´a,4´}$ = 5.1, H-5´a); 3.72 (ddd, 1H, $J_{4´,5´}$ = 6.2, 5.1, $J_{4´,3´}$ = 2.2, H-4´); 4.17 (bm, 1H, H-3´); 4.71 (t, 1H, $J_{OH,5´}$ = 5.4, OH-5´); 5.07 (bd, 1H, $J_{OH,3´}$ = 3.7, OH-3´); 5.14 (dddd, 1H, $J_{1´,2´}$ = 10.2, 5.5, $J_{1´,3}$ = 0.8, $J_{1´,3´}$ = 0.5, H-1´); 6.65 (dt, 1H, $J_{4,3}$ = 3.4, $J_{4,CH2}$ = 1.1, H-4); 6.82 (dd, 1H, $J_{3,4}$ = 3.4, $J_{3,1´}$ = 0.8, H-3). ^{13}C NMR (125.7 MHz, DMSO-d_6): 16.1 (**C**H$_3$CH$_2$); 23.0 (**C**H$_2$CH$_3$); 43.5 (CH$_2$-2´); 62.7 (CH$_2$-5´); 72.5 (CH-3´); 75.4 (CH-1´); 87.8 (CH-4´); 123.0 (CH-4); 124.4 (CH-3); 143.2 (C-2); 146.2 (C-5). IR spectrum (KBr): 3379, 3340, 3083, 2966, 2915, 2875, 1390, 959, 806, 155 cm^{-1}. $[\alpha]^{20}_{D}$ +7.1 (*c* 3.70, MeOH). Anal. Calcd $C_{11}H_{16}O_3S$ (228.3): C, 57.87; H, 7.06; found: C, 57.68; H, 7.01.

UV-vis and fluorescence spectroscopy

Absorption spectra $\varepsilon(\lambda)$ were measured with a UV-vis scanning spectrophotometer. Fluorescence spectra were recorded upon excitation at the peak of the absorption band (absorbance ≤ 0.05). The collected photon flux Φ was dispersed in a double monochromator and registered by photon counting. Signal from the acetonitrile solvent was measured separately and subtracted. Photometric calibration was performed by comparison with a secondary standard lamp (GIGAHERTZ OPTIC Model BN9701). Thus the relative number of photons per wavelength, $\partial\Phi/\partial\lambda$, is obtained in each case. Fluorescence spectra are represented as relative number of photons per energy interval $\partial\Phi/\partial\tilde{\nu} \equiv F(\tilde{\nu})$ however. This representation allows a direct comparison of absorption and emission band shapes for given compound, or of fluorescence bandshapes from several compounds whose fluorescence ranges across the UV/vis region. The broad first absorption band of **6i** was also examined by fluorescence excitation but no difference to the absorption spectrum was observed. Fluorescence spectra $F(\tilde{\nu})$ were fitted by a lognormal function.

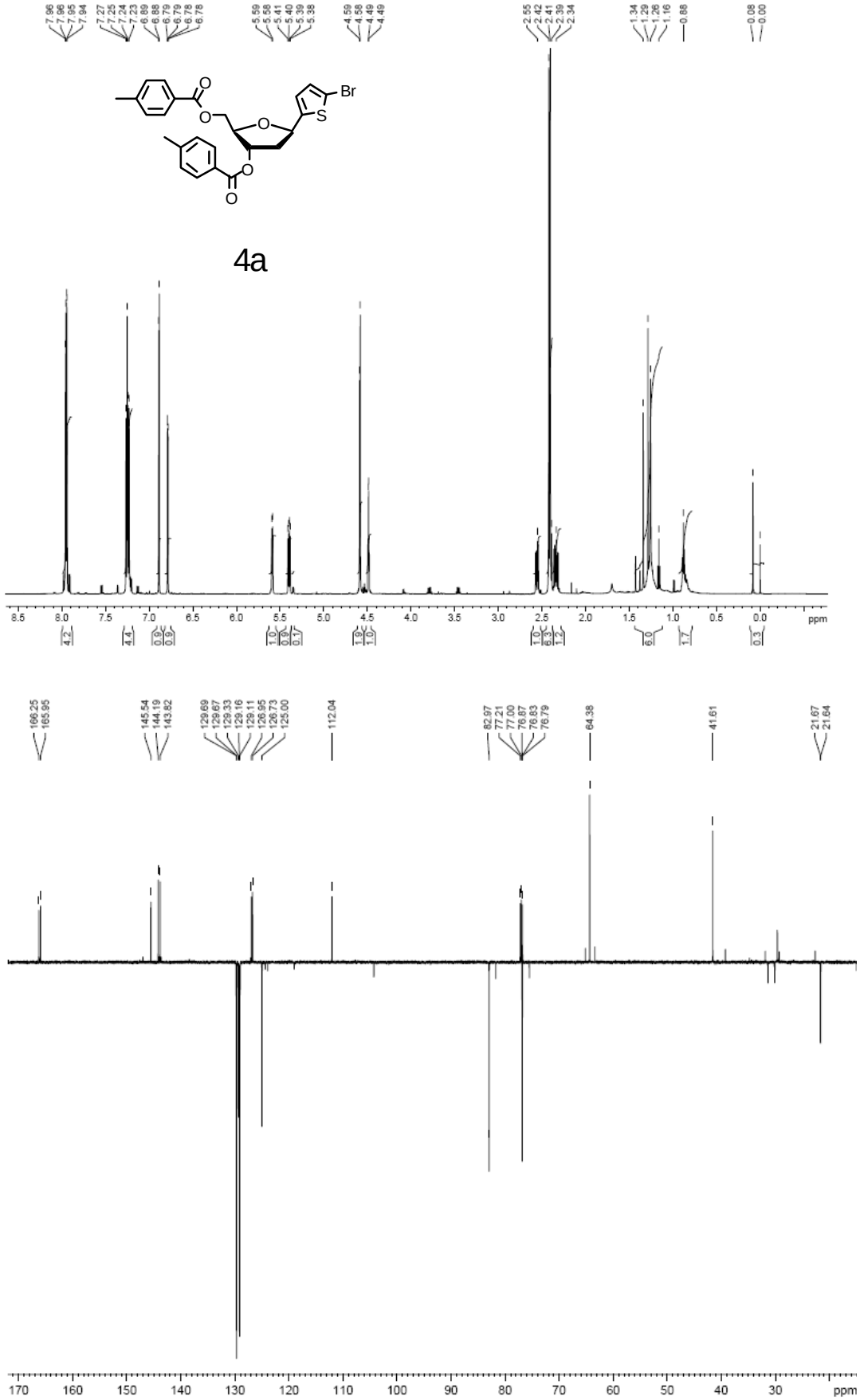
$$\log\mathrm{norm}(\tilde{\nu}) = \exp\left\{-\ln 2\left(\frac{\ln\left[1+2\gamma\,(\tilde{\nu}-\tilde{\nu}_P)/\tilde{\Delta}\right]}{\gamma}\right)^2\right\} \qquad (1)$$

with peak wavenumber $\tilde{\nu}_P$, width parameter $\tilde{\Delta}$, and asymmetry parameter γ in Table 1. Band positions (wavelengths) are indicated in Figure 2 and collected in Table 2.

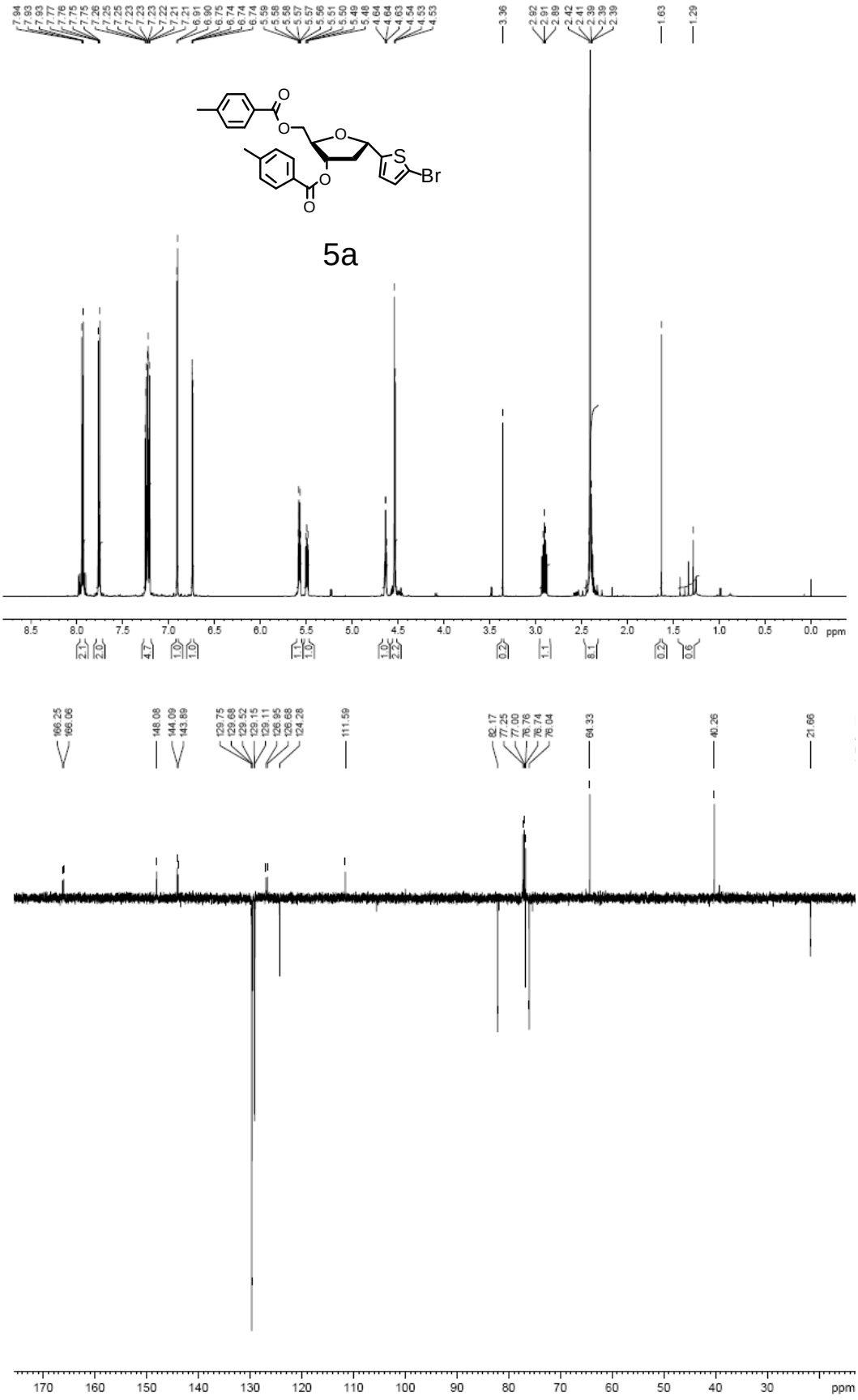
Table S1: Lognormal parameters (eq. 1) for fluorescence spectra in acetonitrile.

Compound	$\tilde{\nu}_P$ / cm^{-1}	$\tilde{\Delta}$ / cm^{-1}	γ
6f	27250	4120	-0.24
6g	26760	4060	-0.26
6h	27730	4520	-0.30
6i	25270	4575	-0.18
6l	28790	4110	-0.30
6m	28890	4170	-0.30
6n	28980	4175	-0.29
6o	29460	5520	-0.30

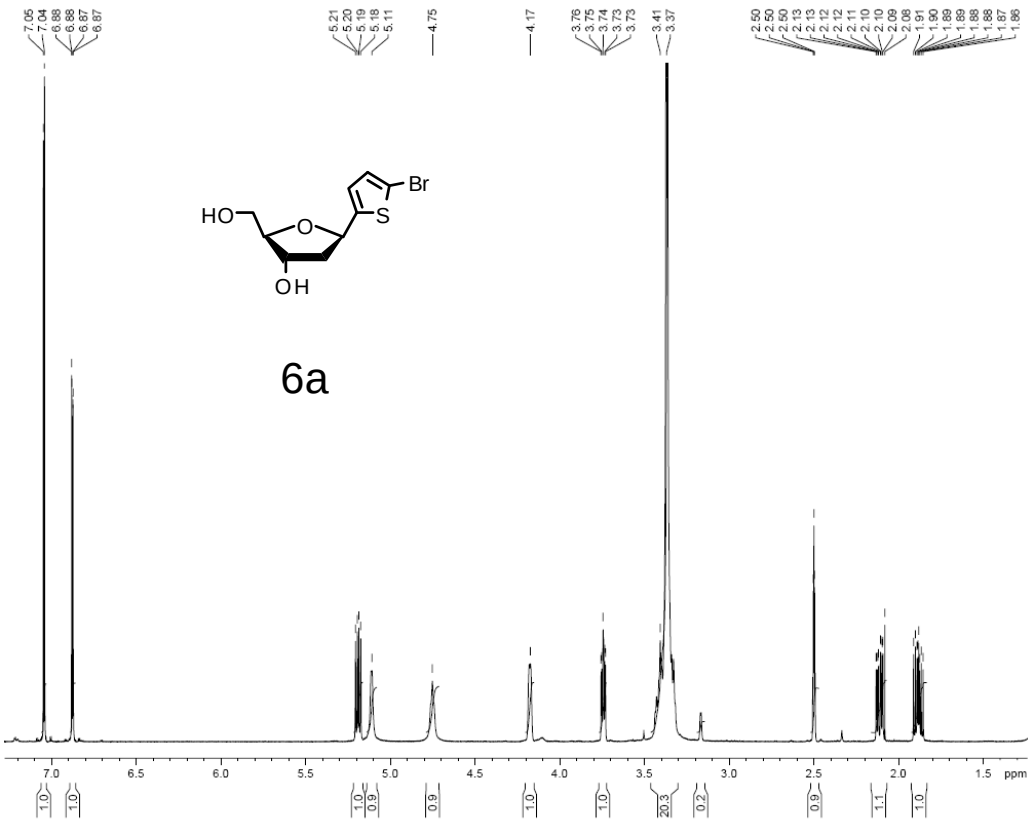
NMR spectra of 4a

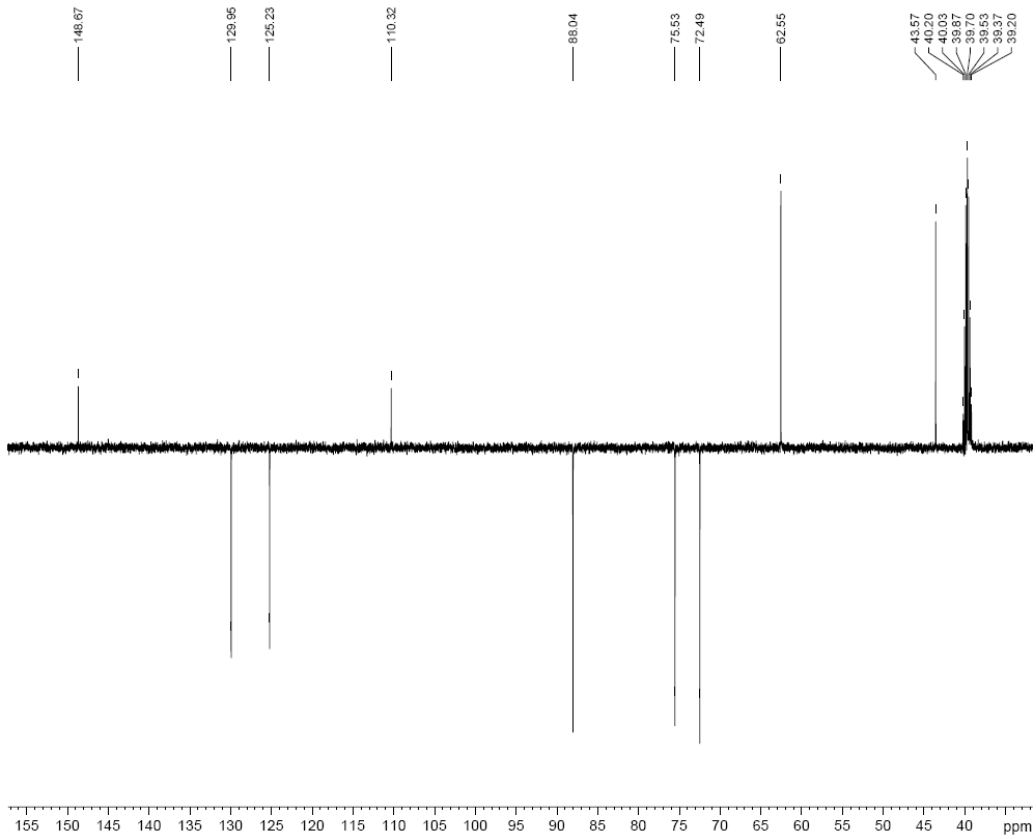


NMR spectra of 5a

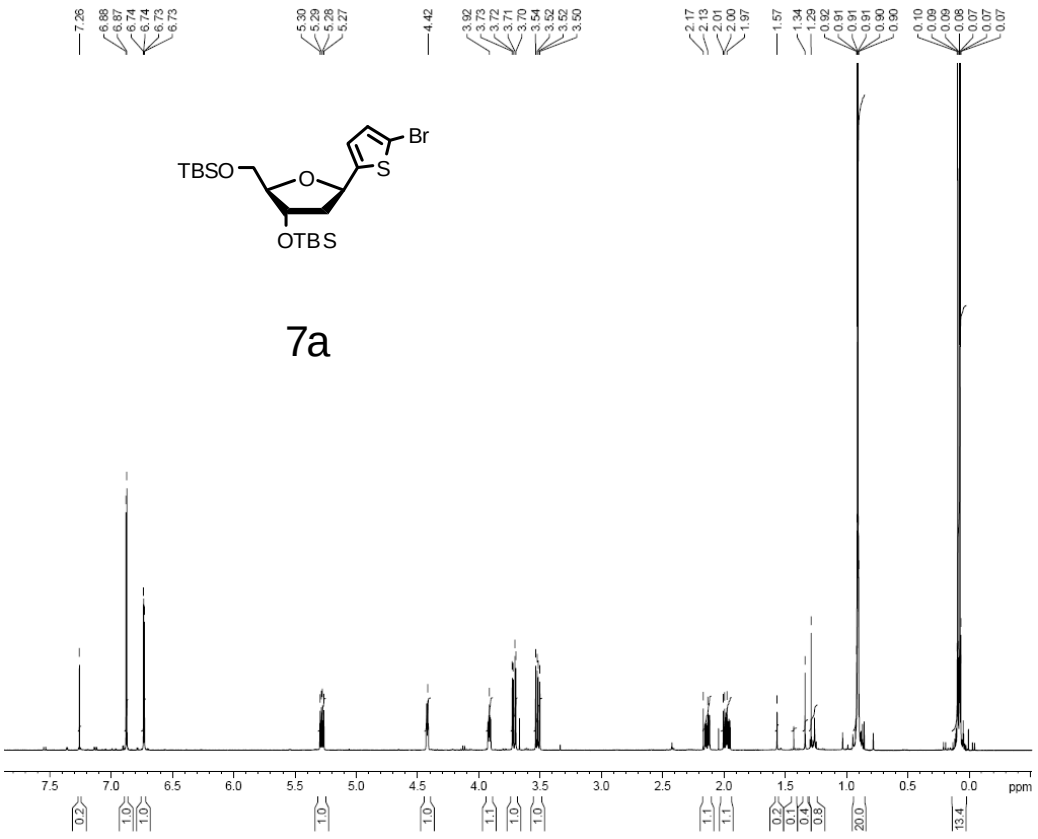


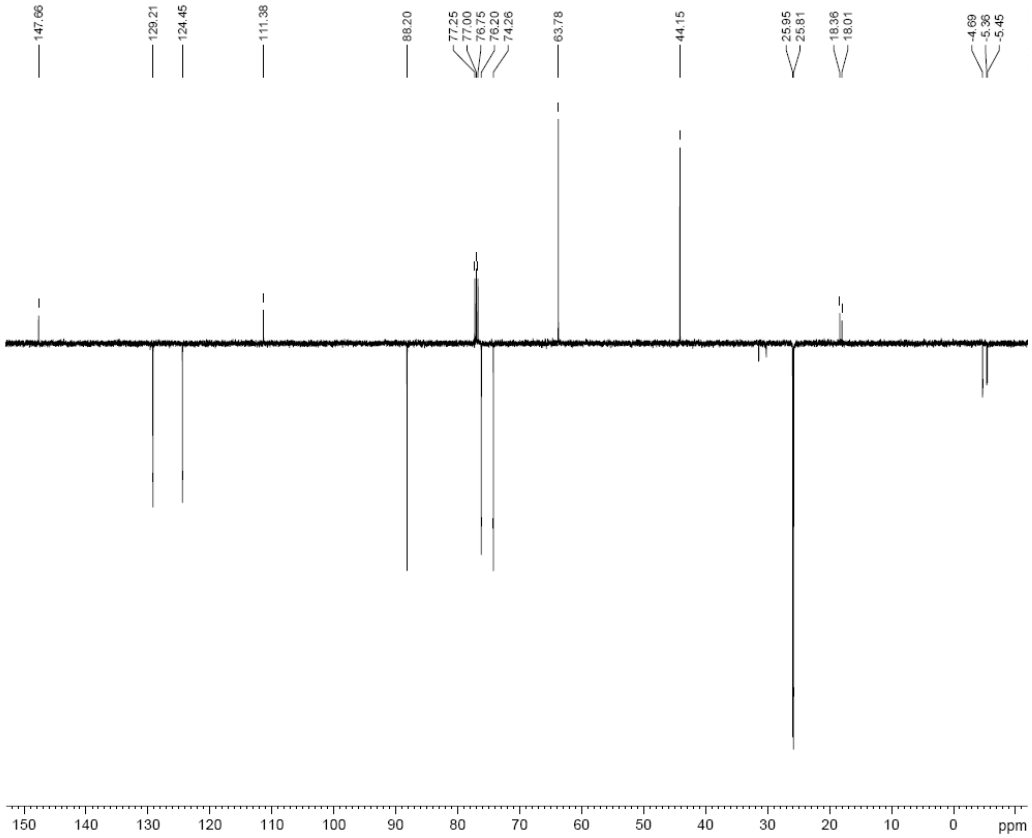
NMR spectra of 6a



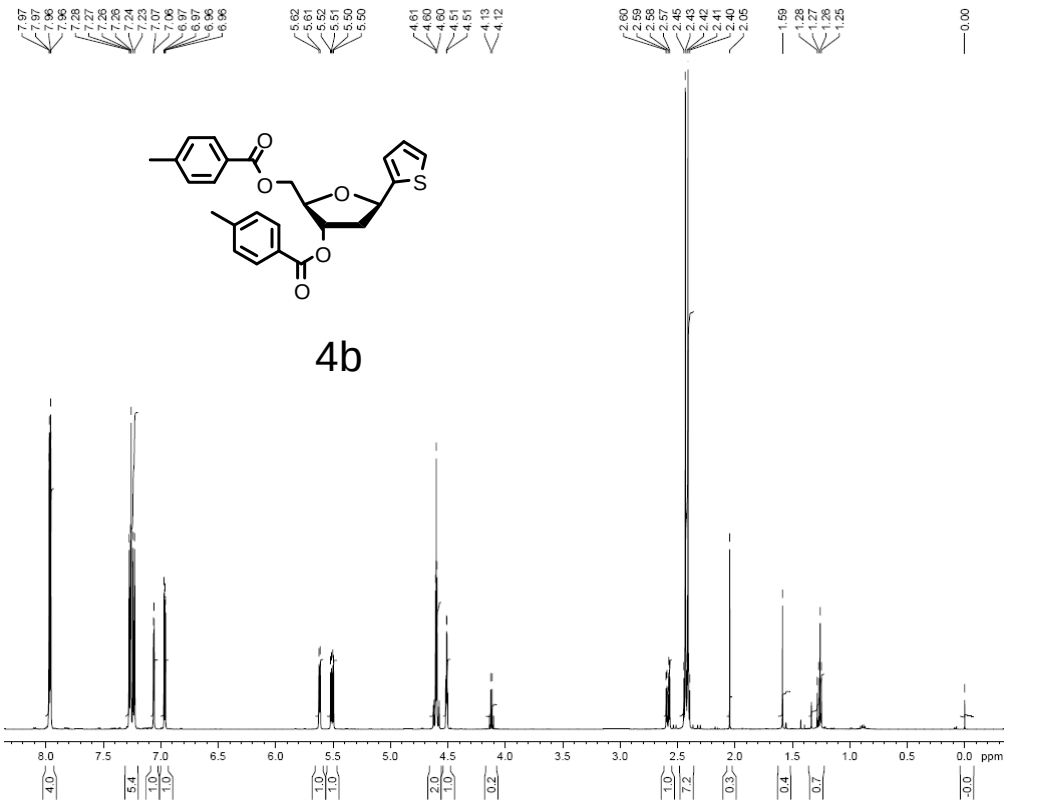


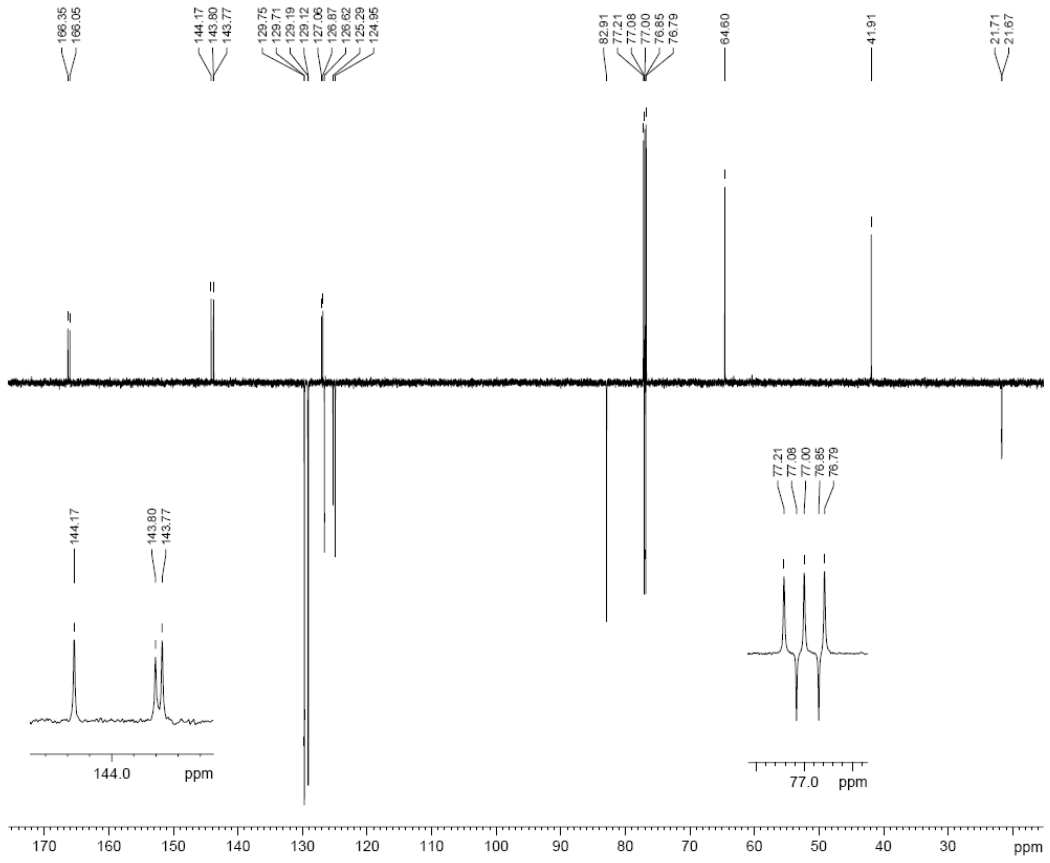
NMR spectra of 7a



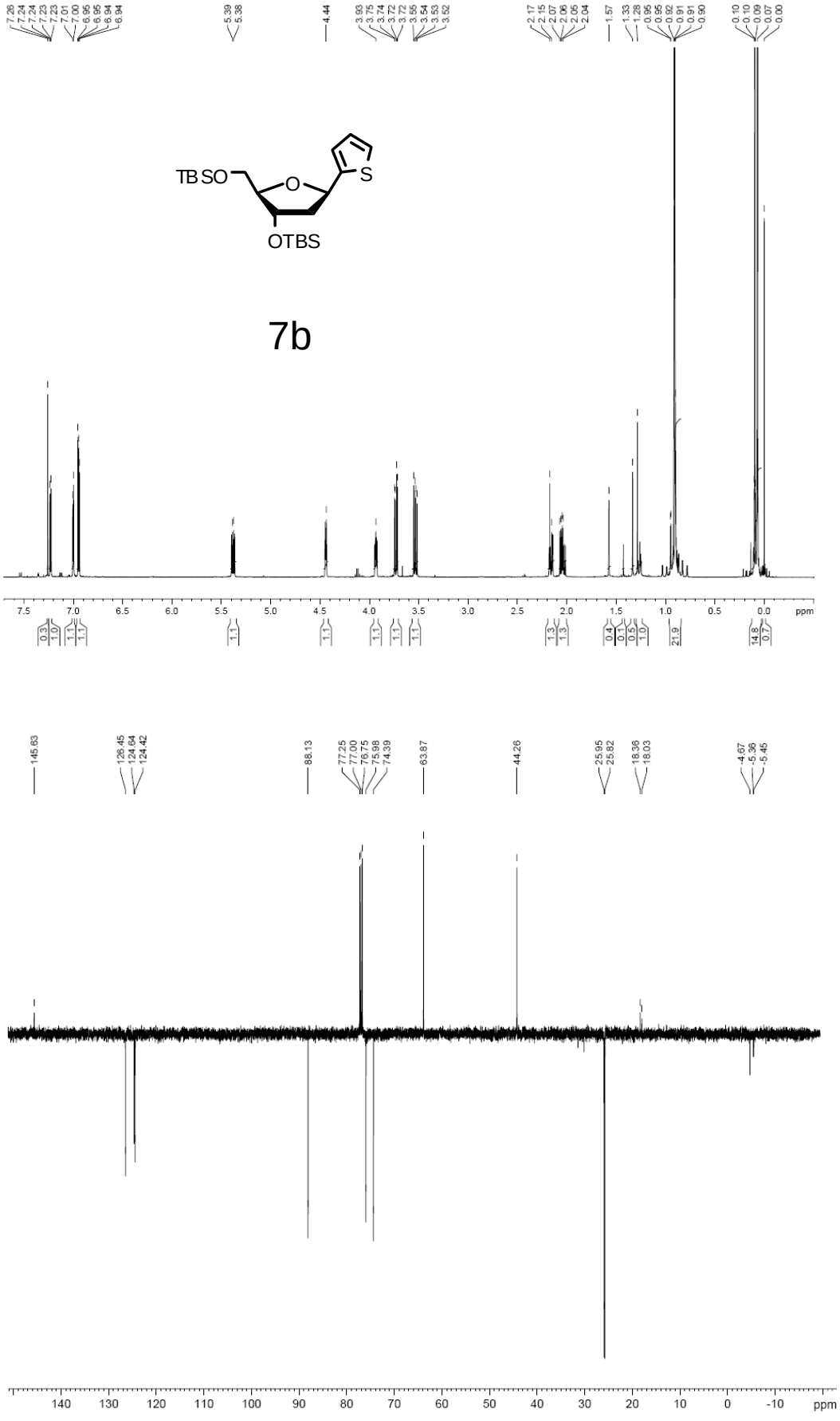


NMR spectra of 4b

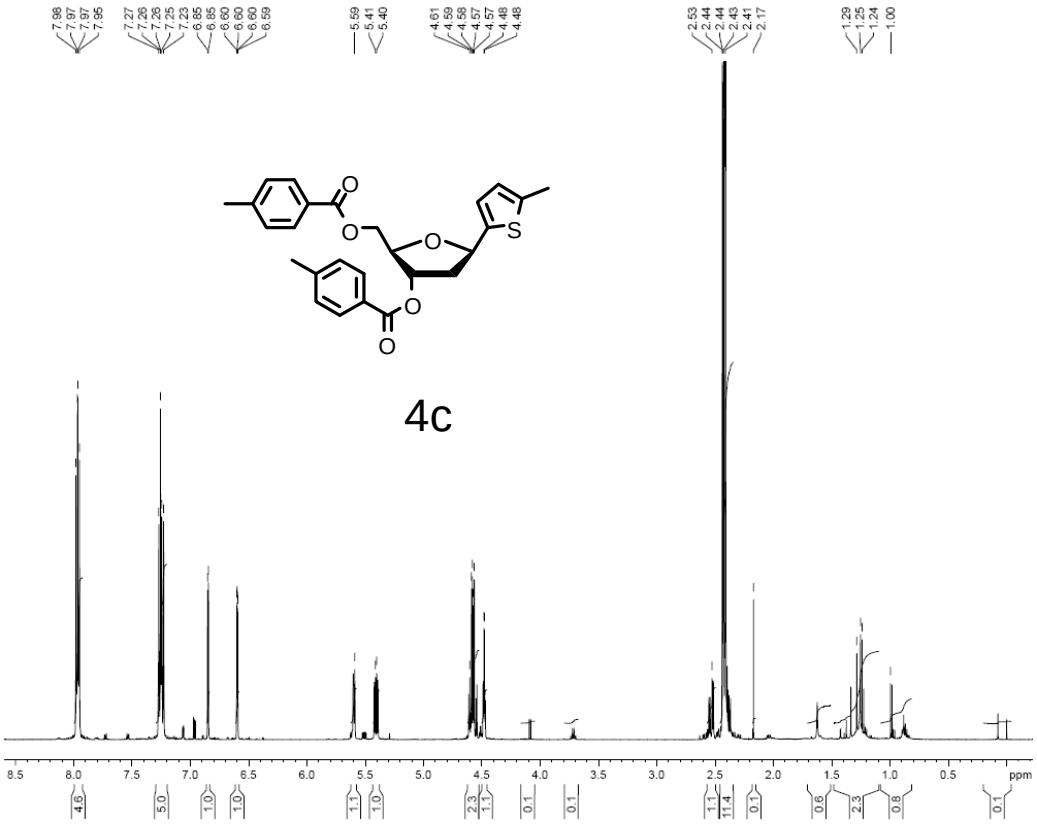


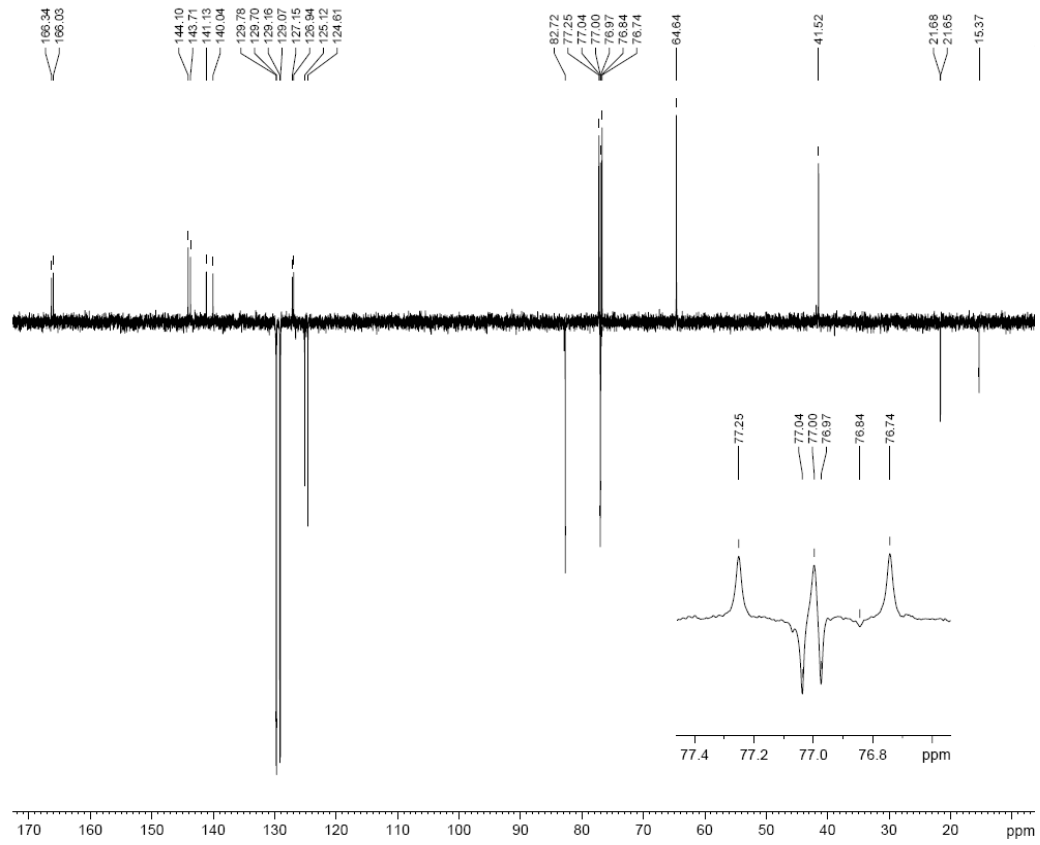


NMR spectra of 7b

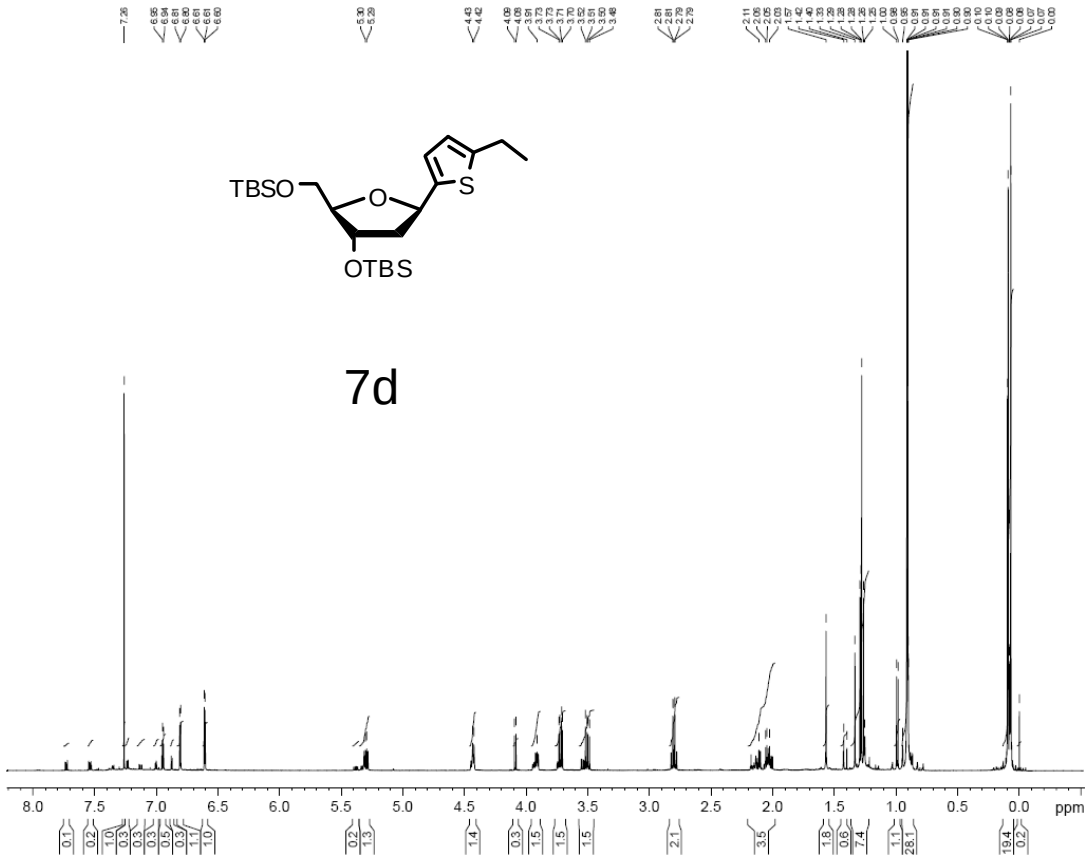


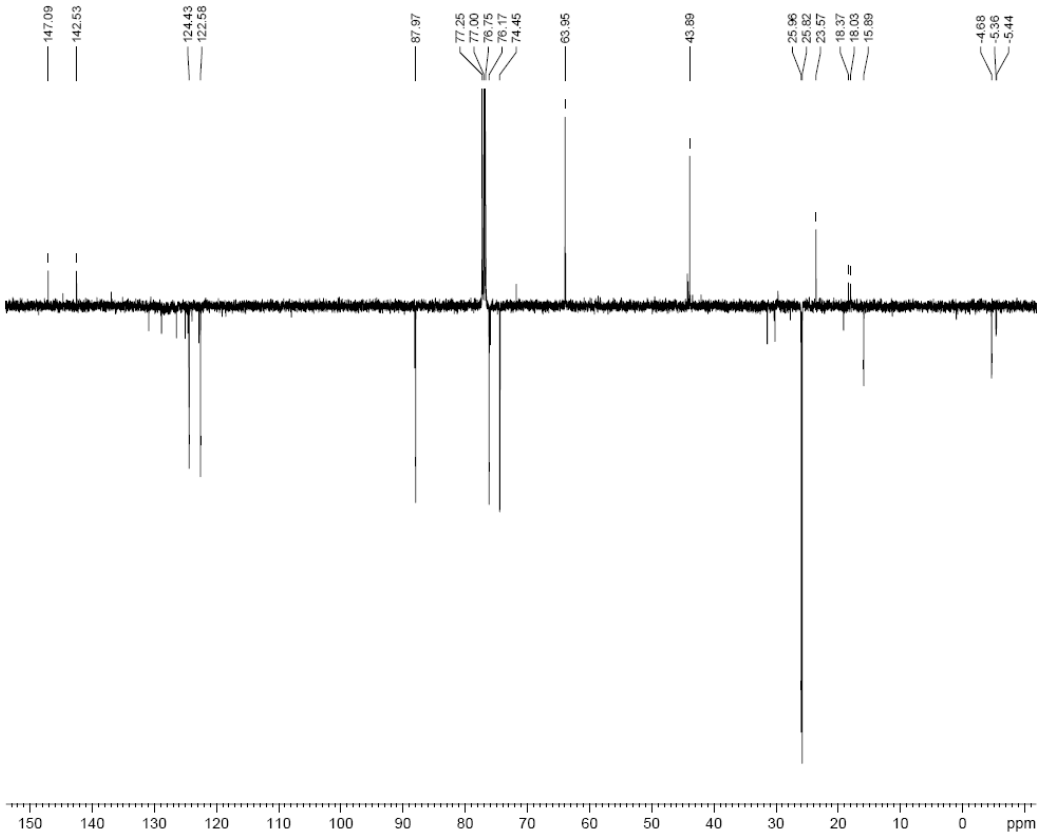
NMR spectra of 4c



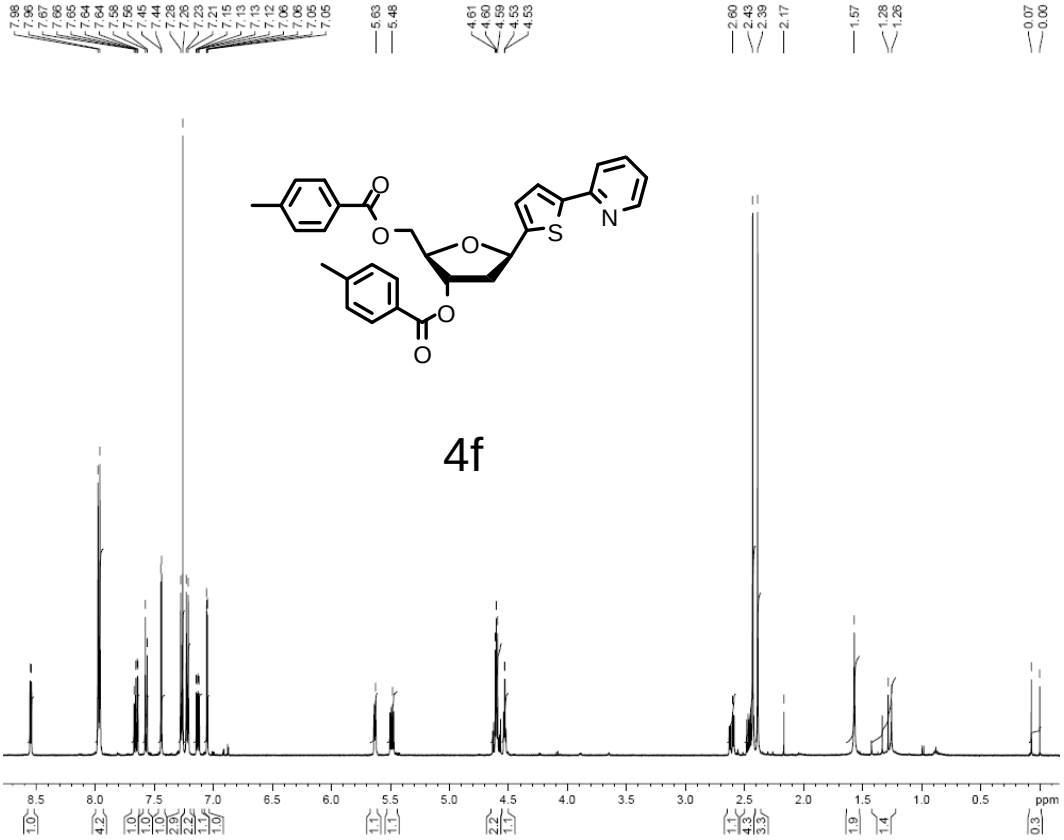


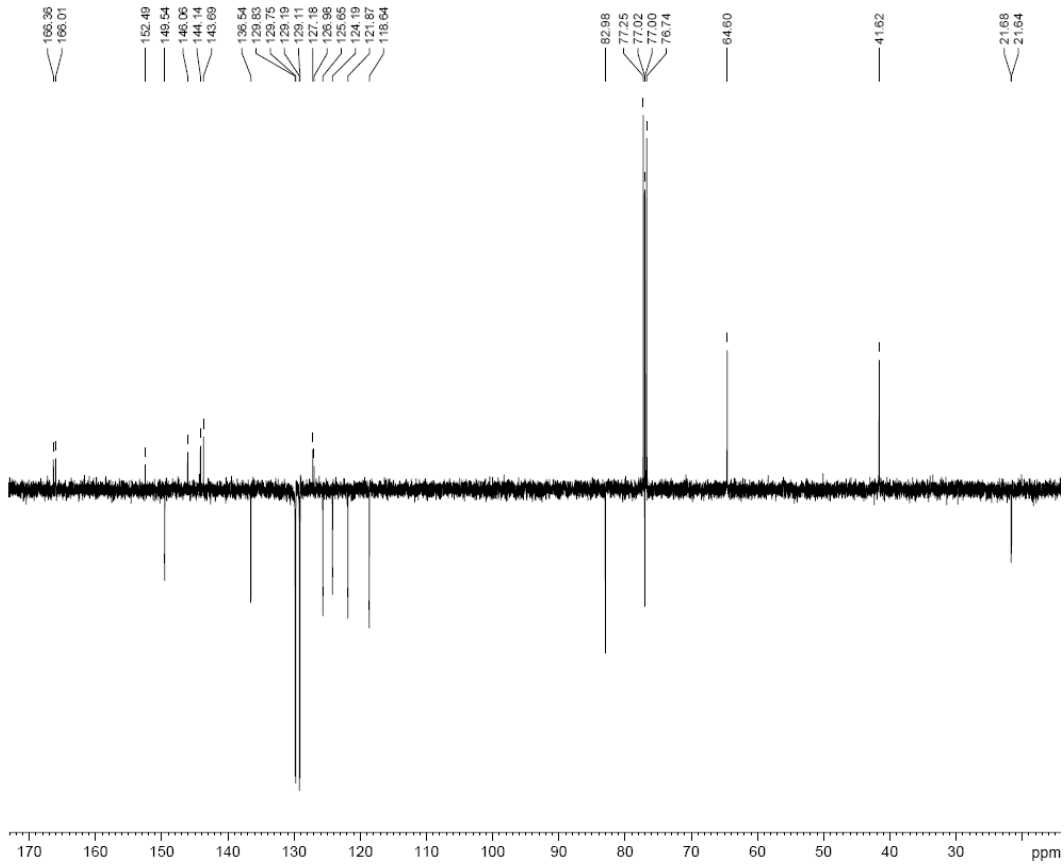
NMR spectra of 7d



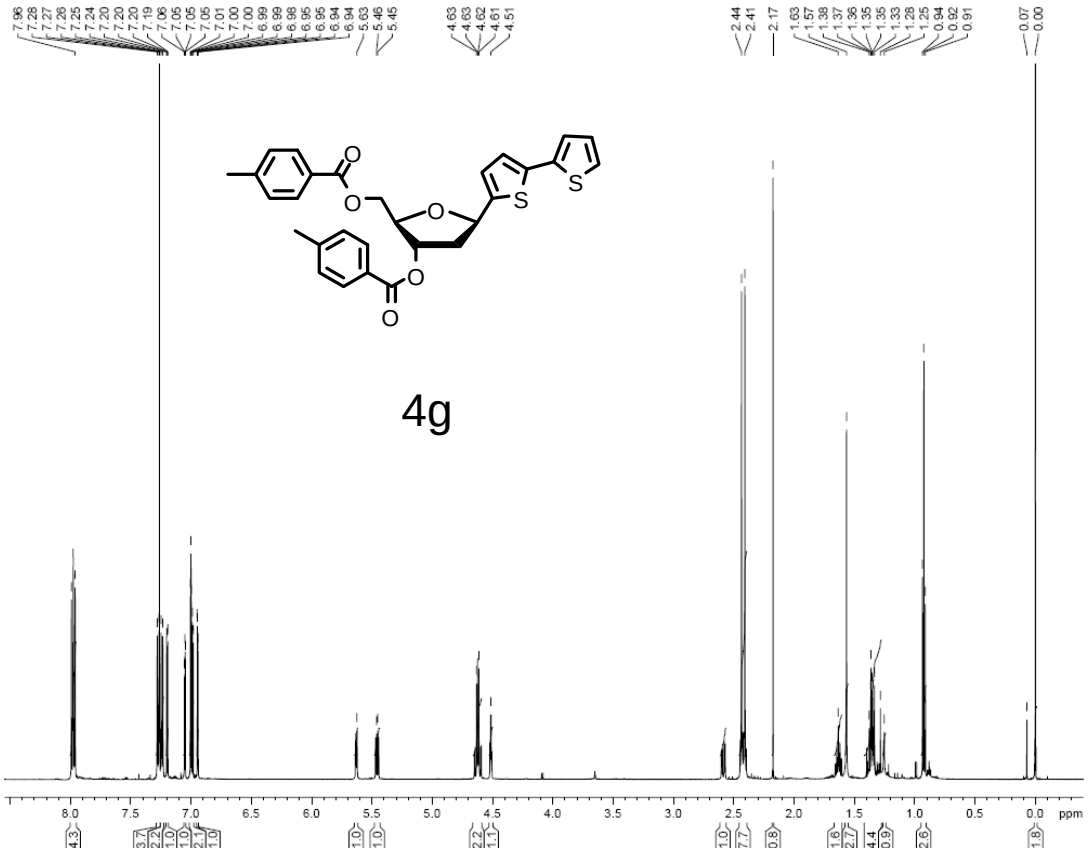


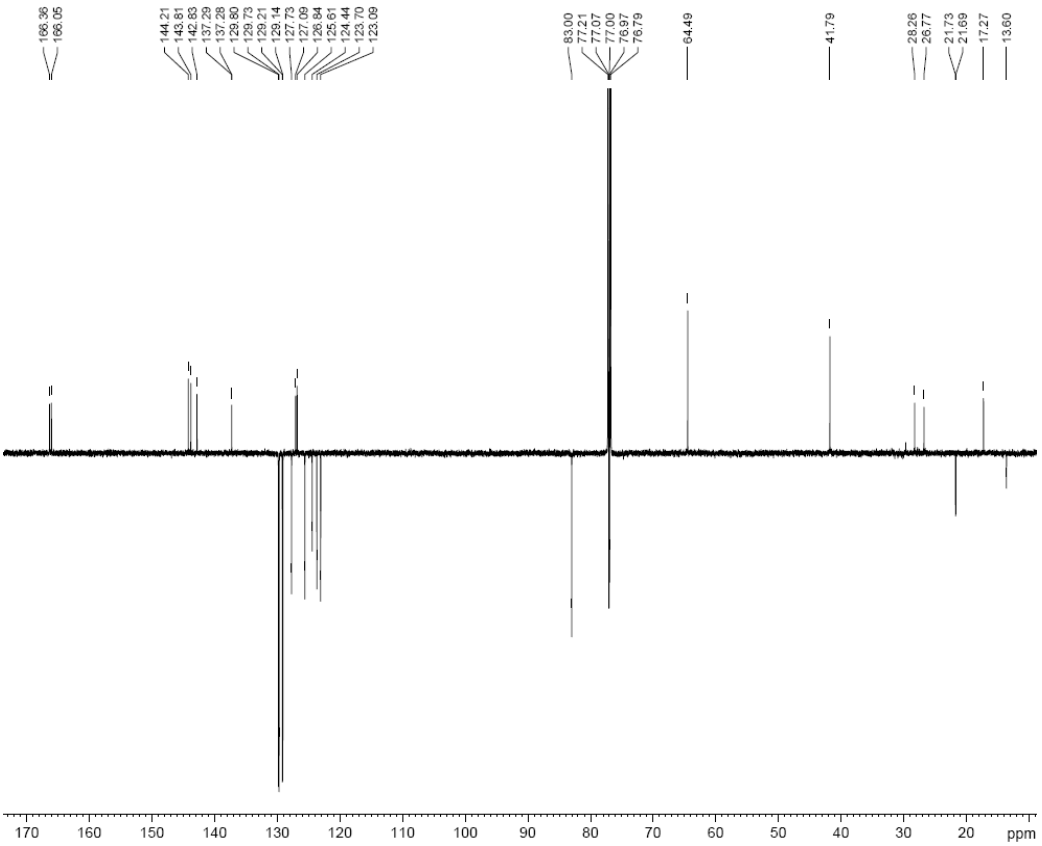
NMR spectra of 4f



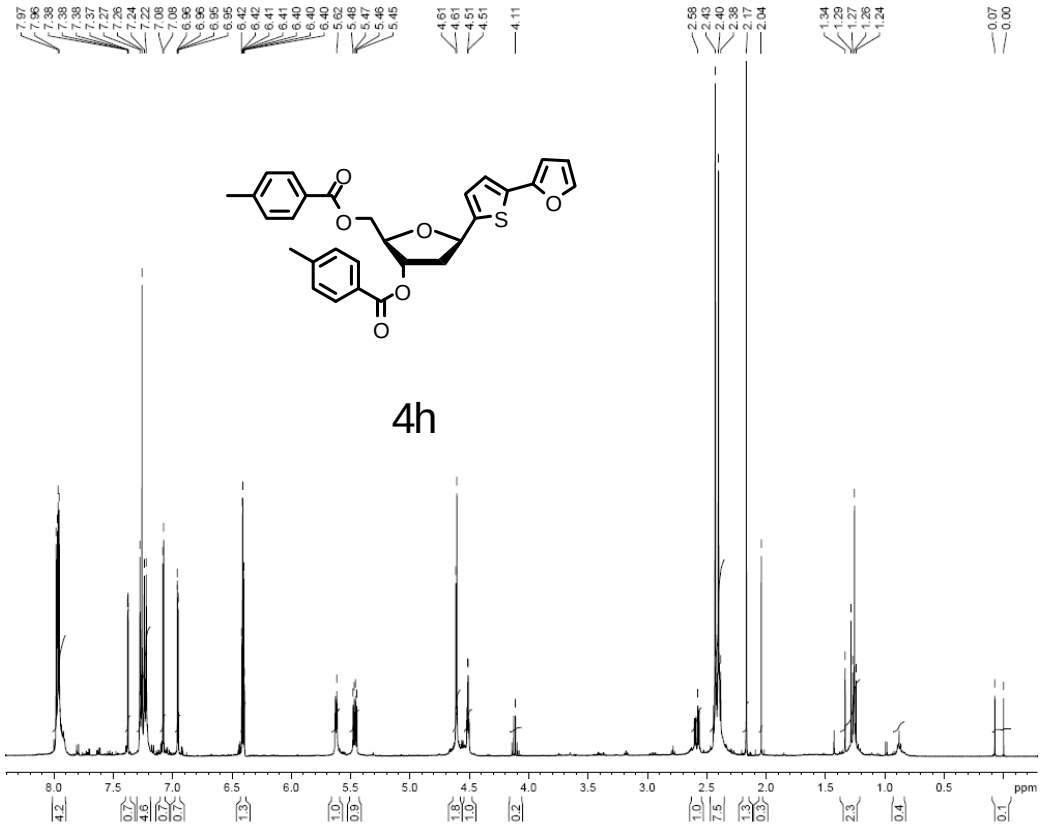


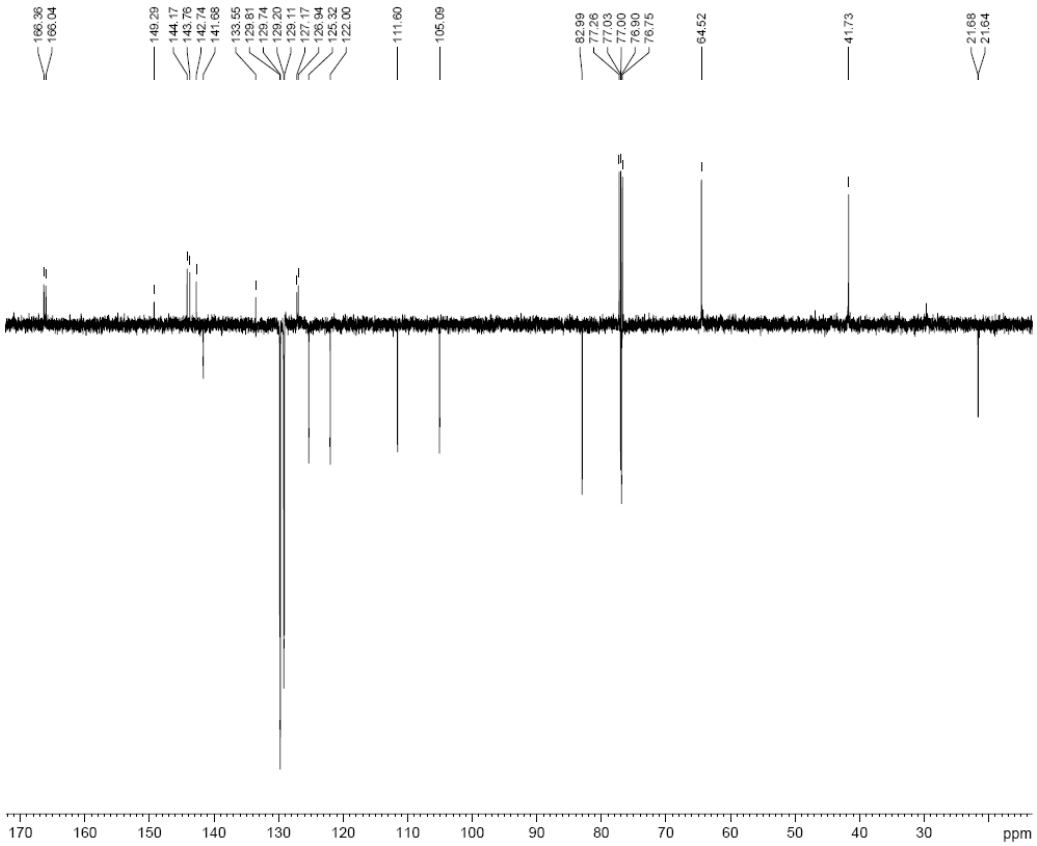
NMR spectra of 4g



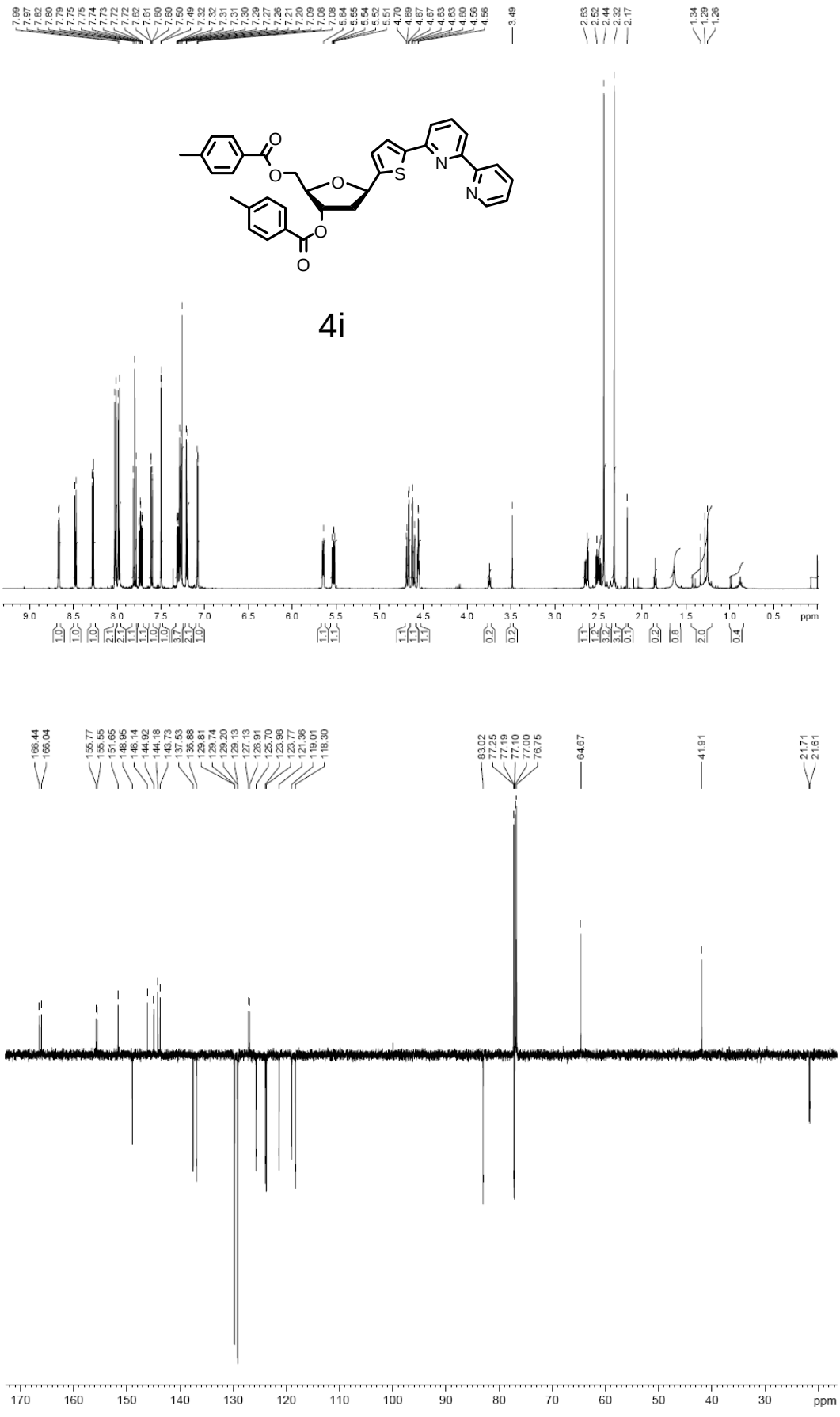


NMR spectra of 4h

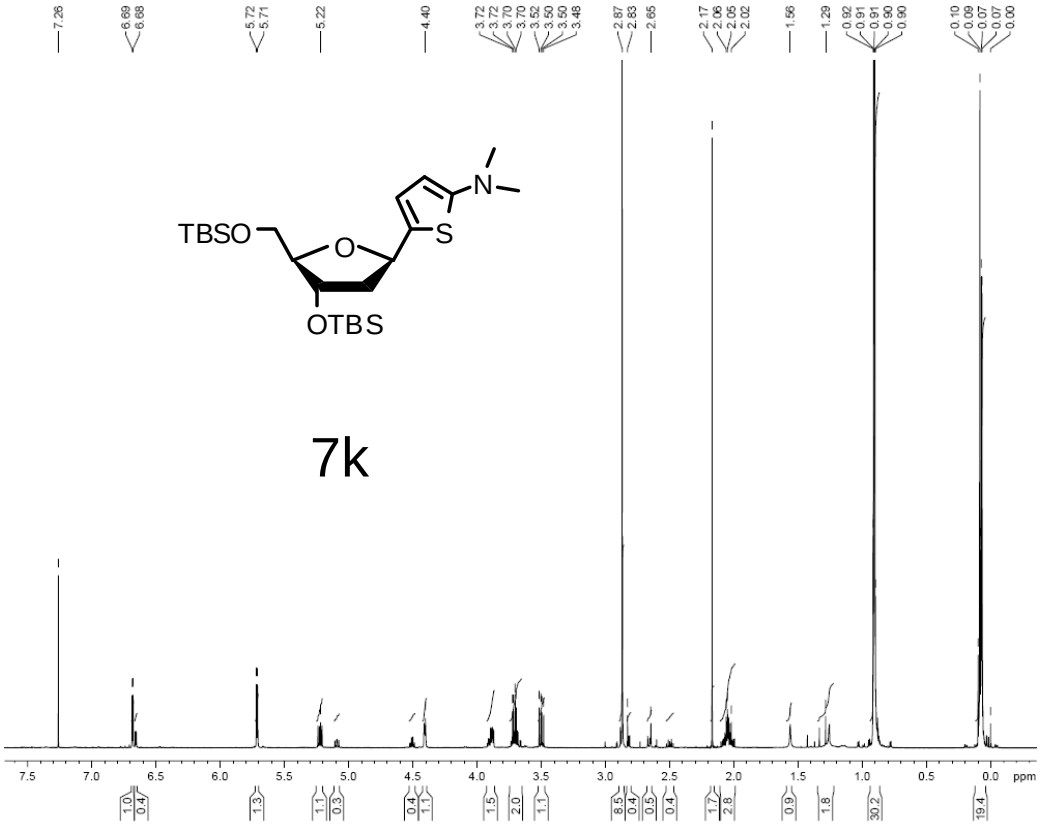


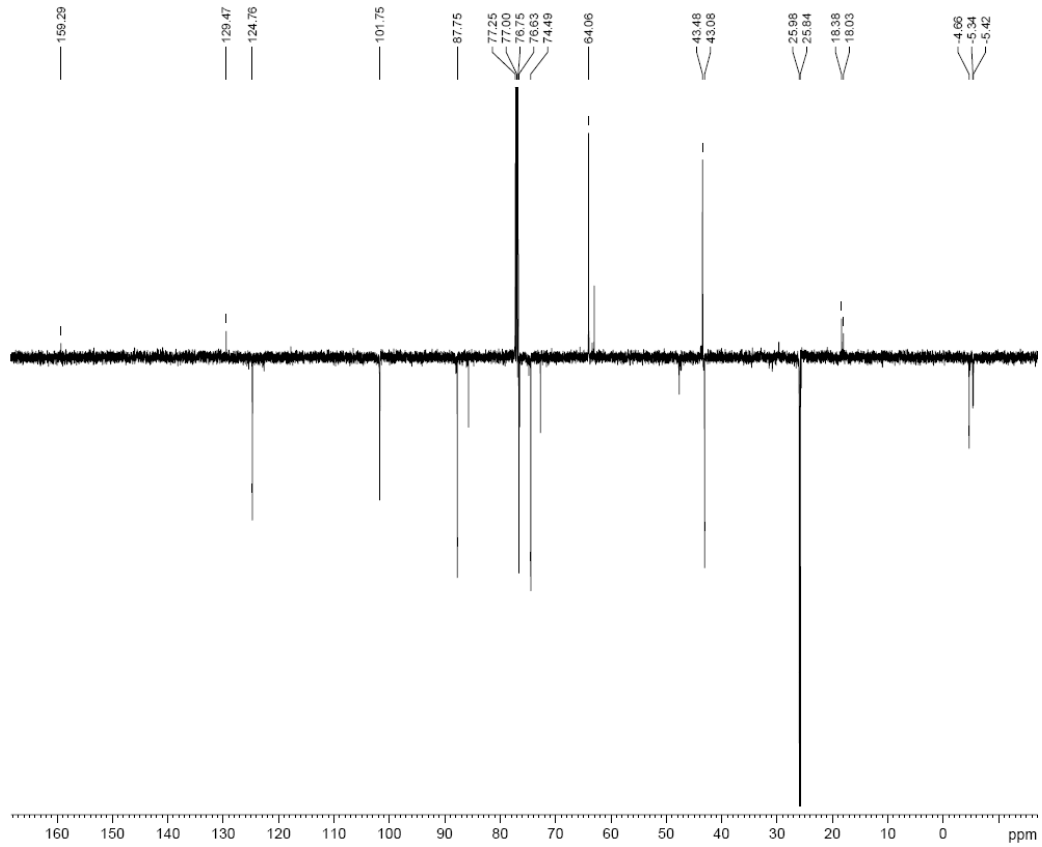


NMR spectra of 4i

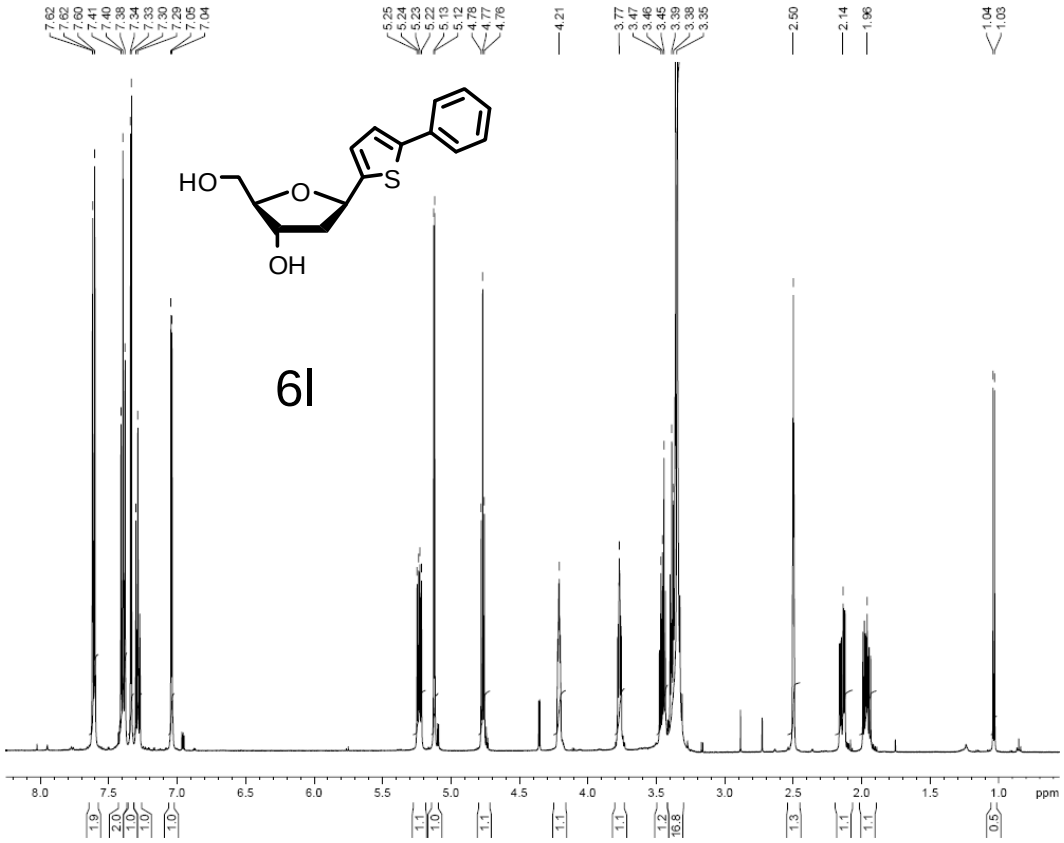


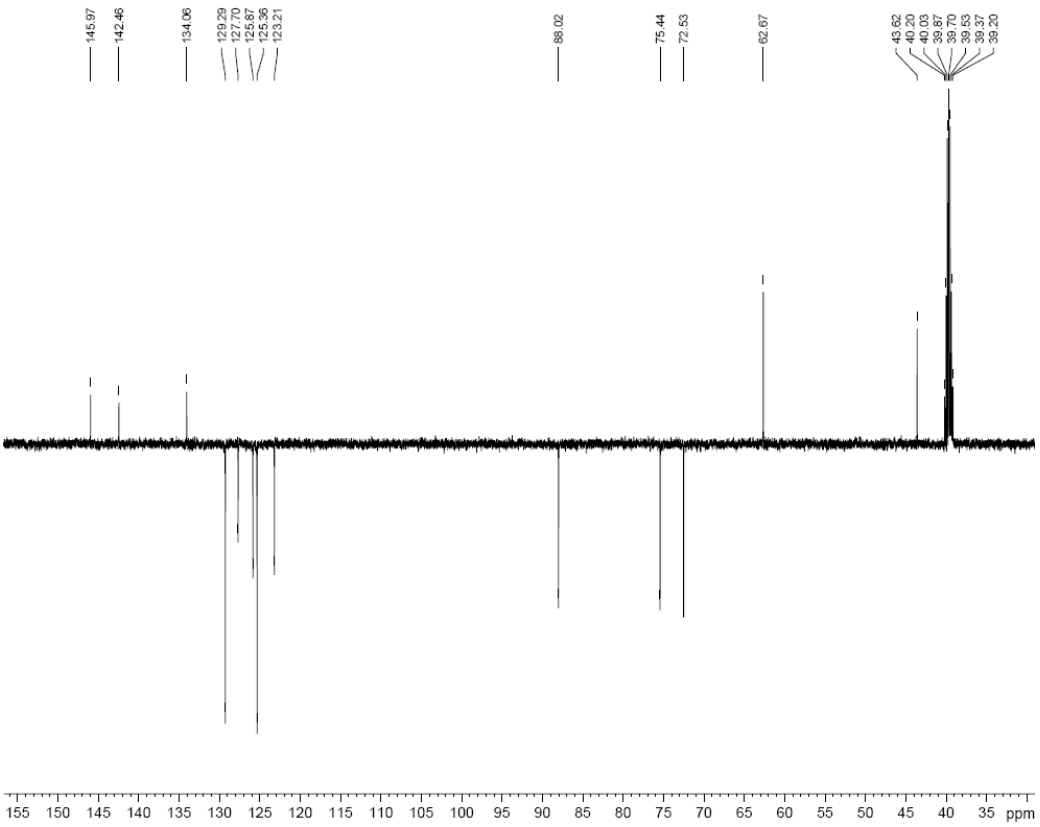
NMR spectra of 7k



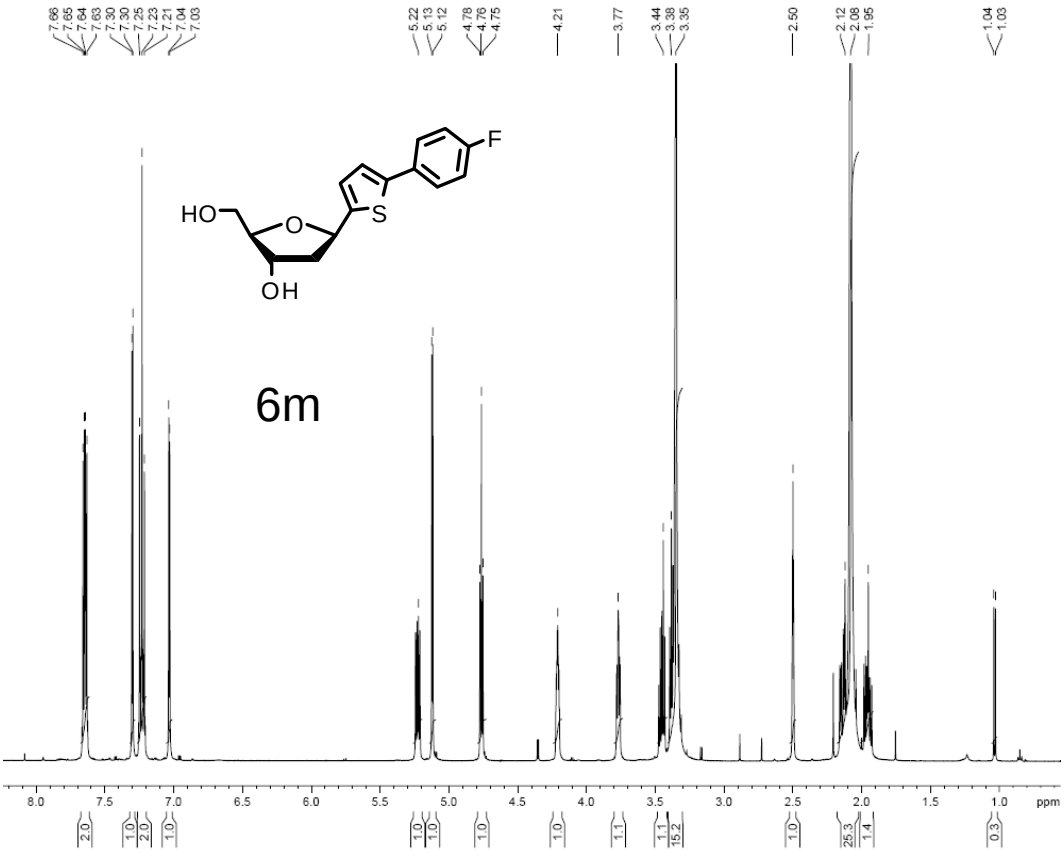


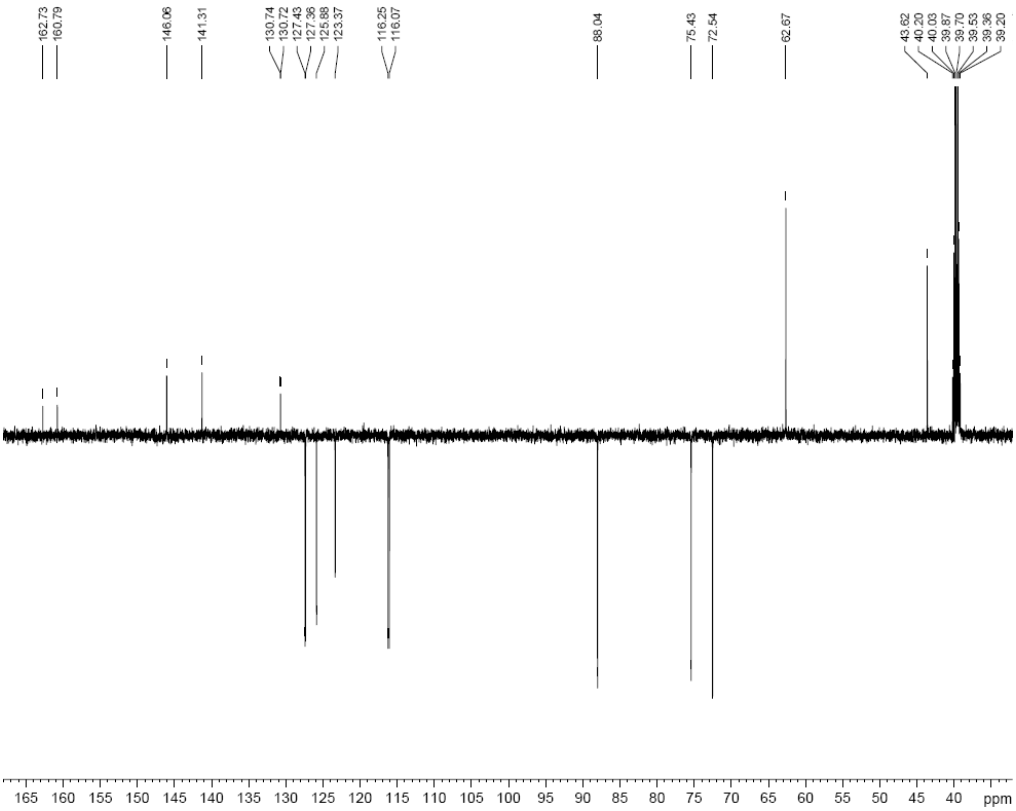
NMR spectra of 6l



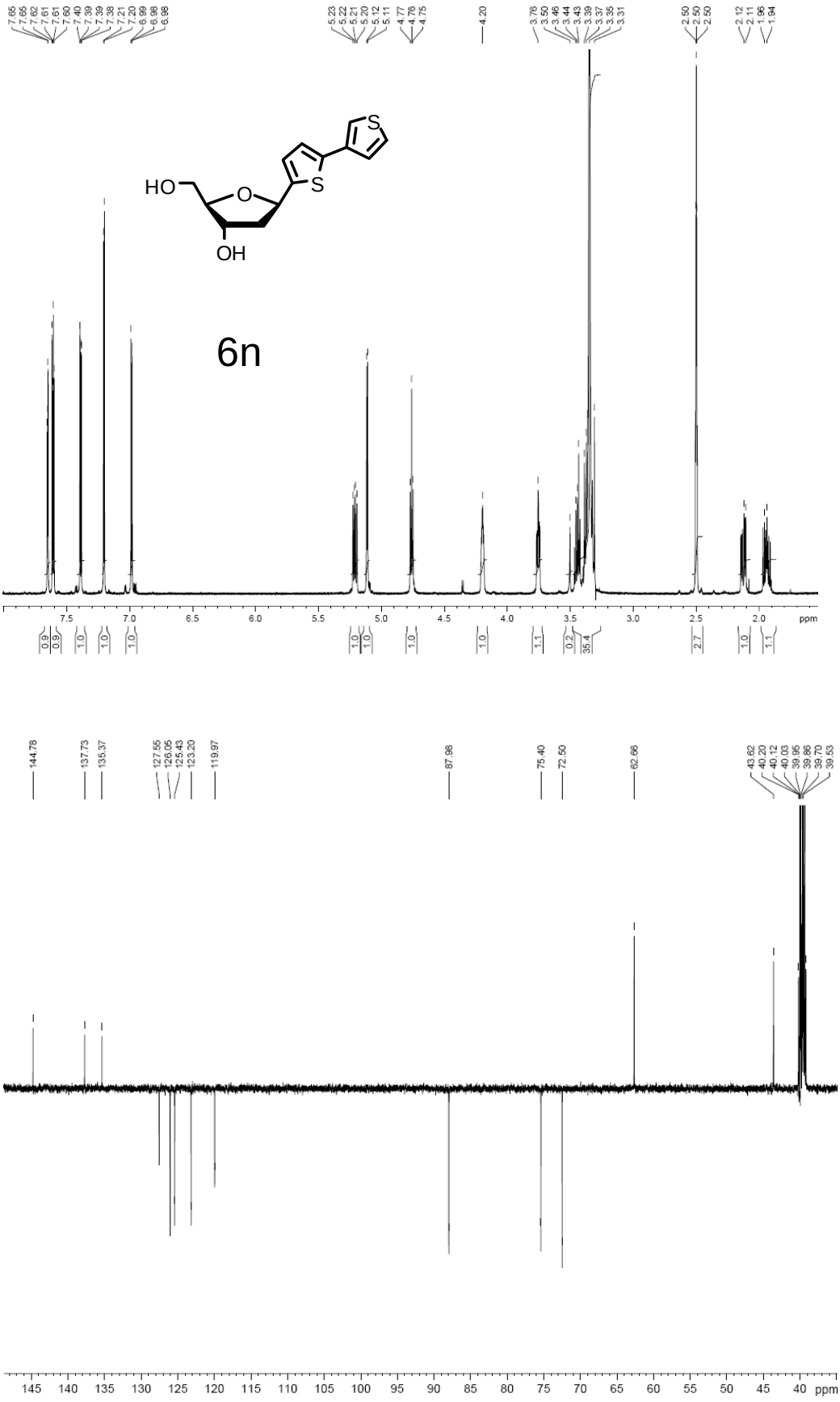


NMR spectra of 6m

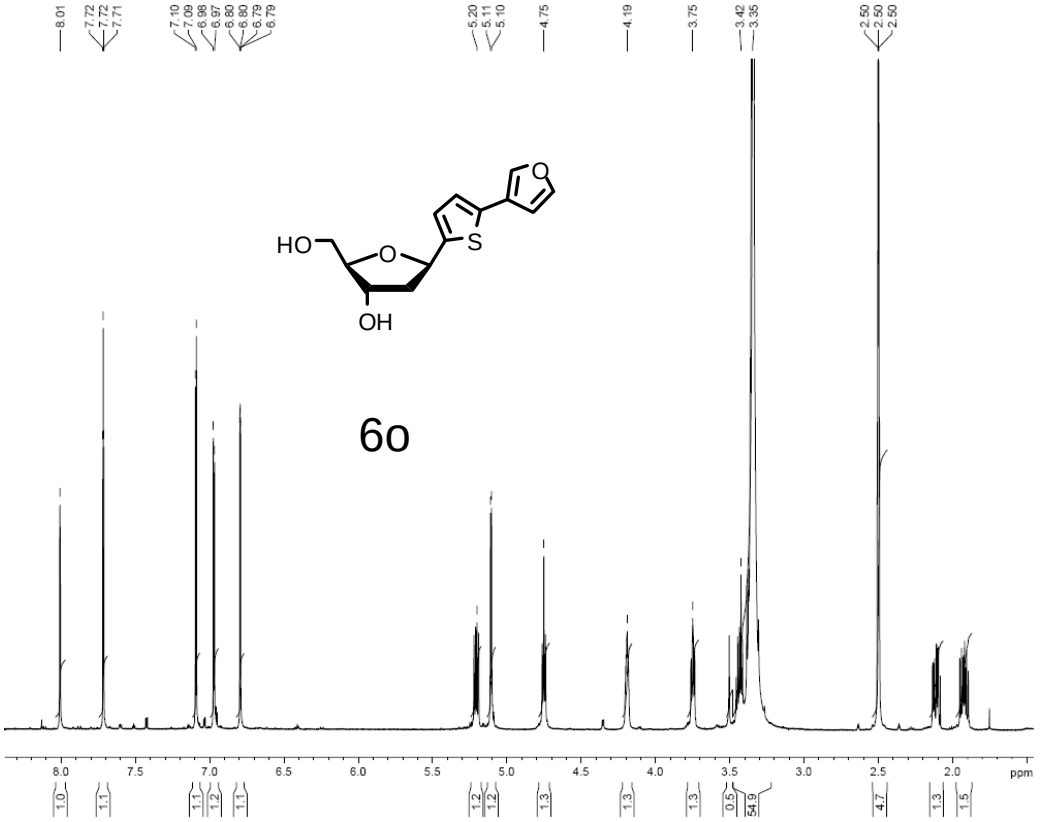


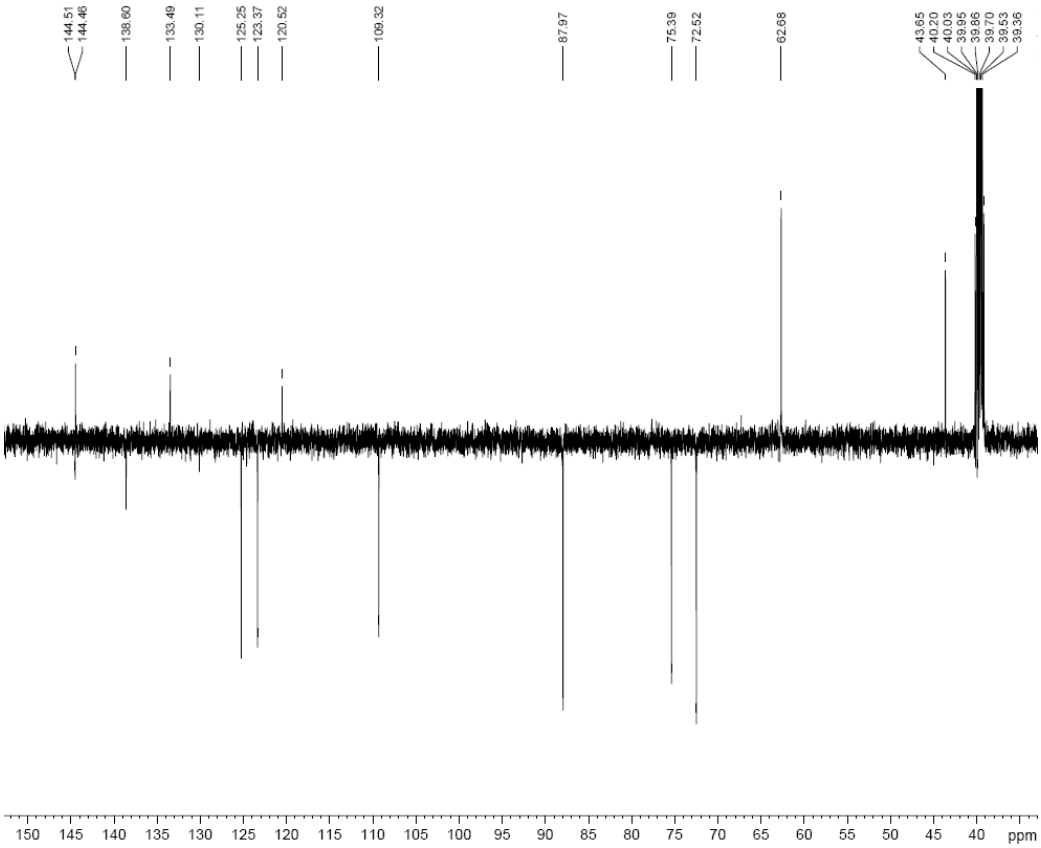


NMR spectra of 6n

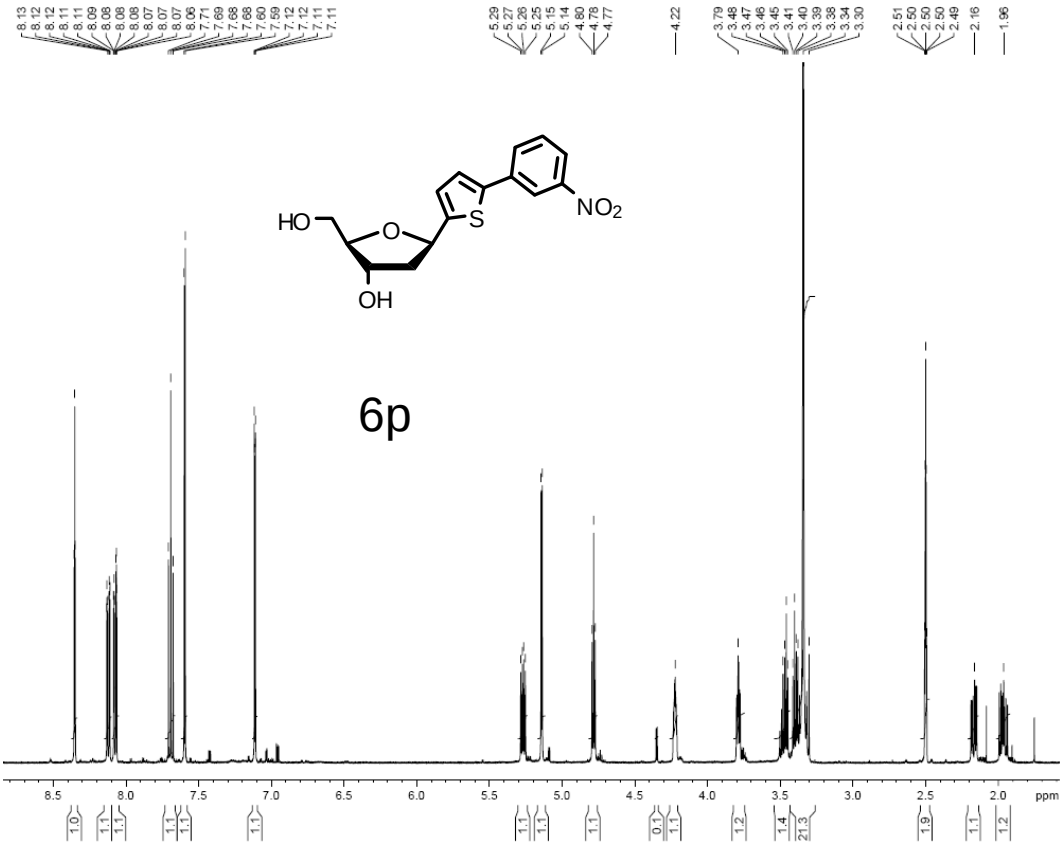


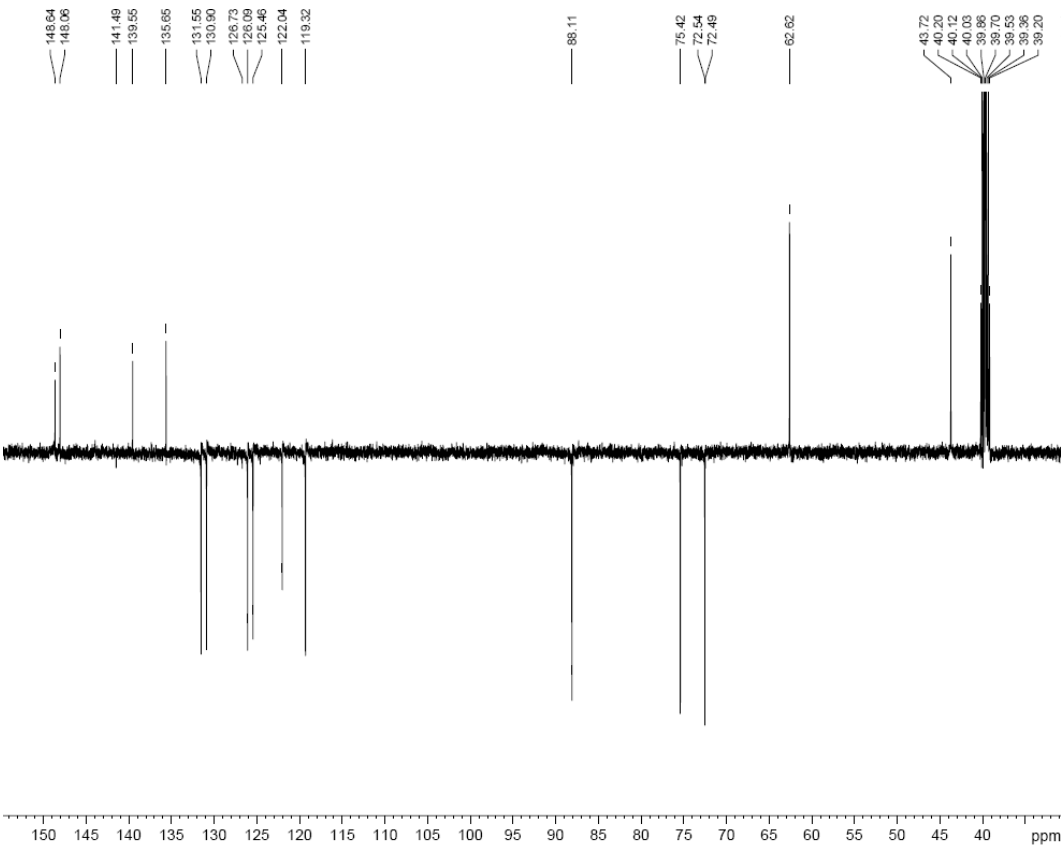
NMR spectra of 6o



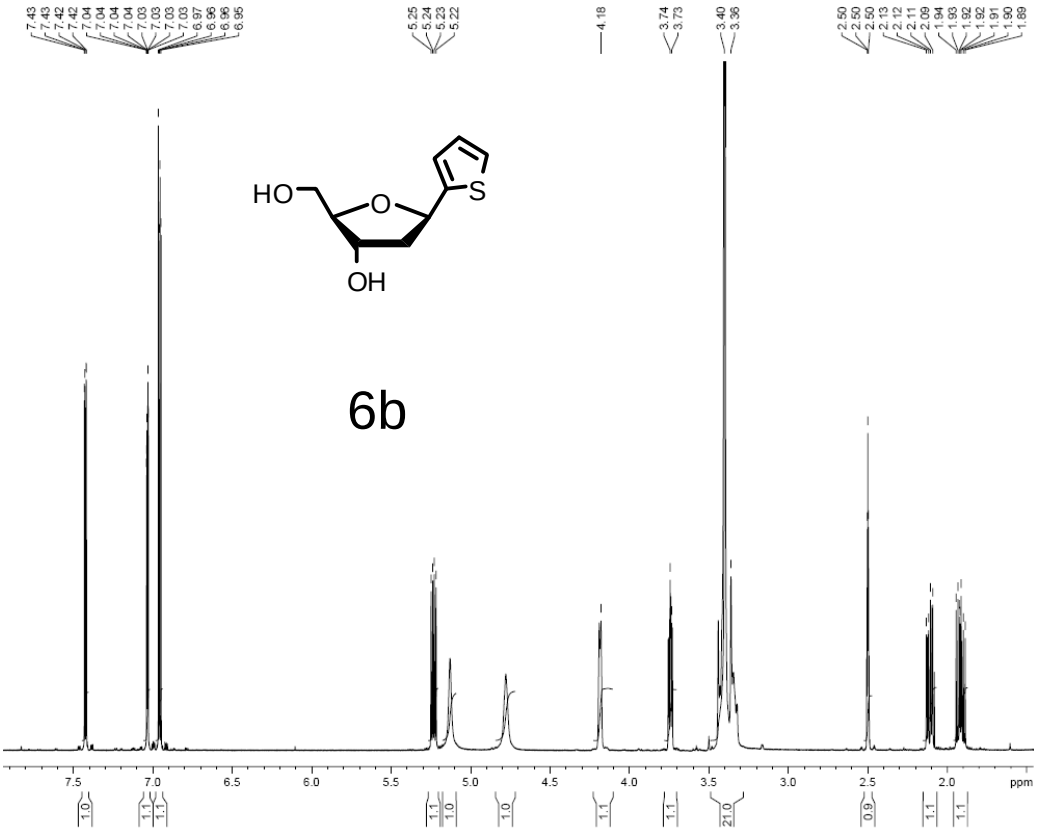


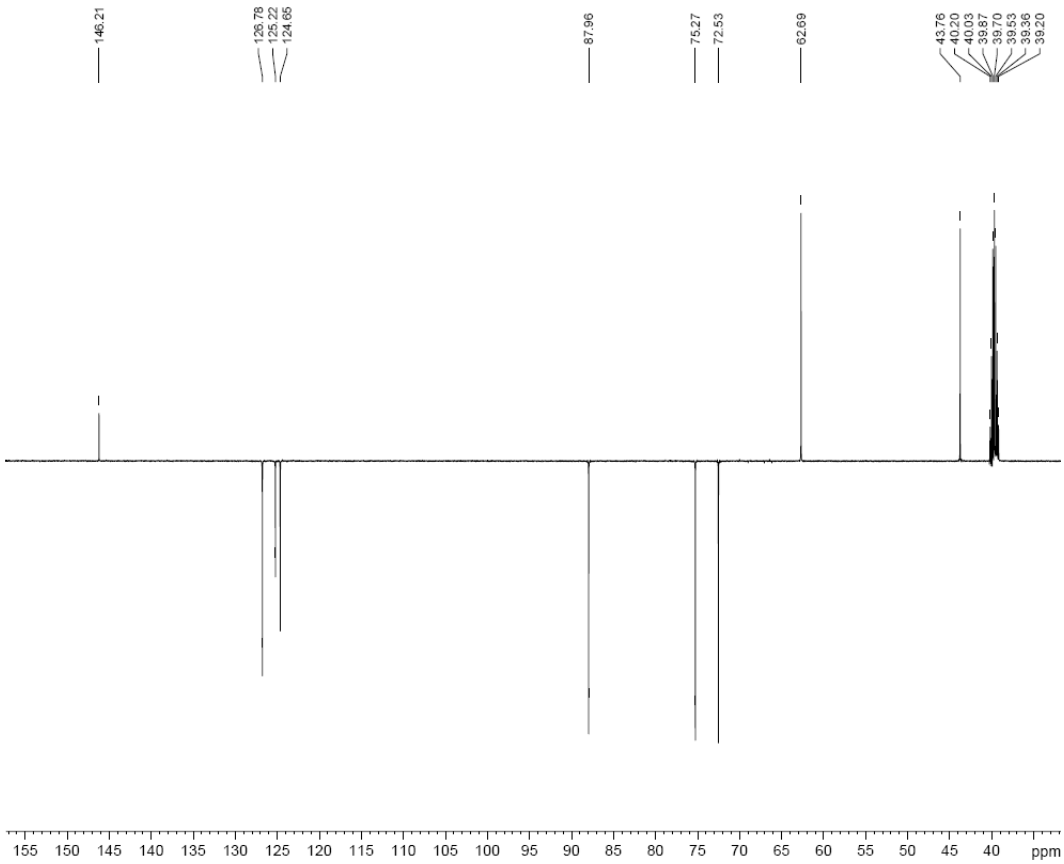
NMR spectra of 6p



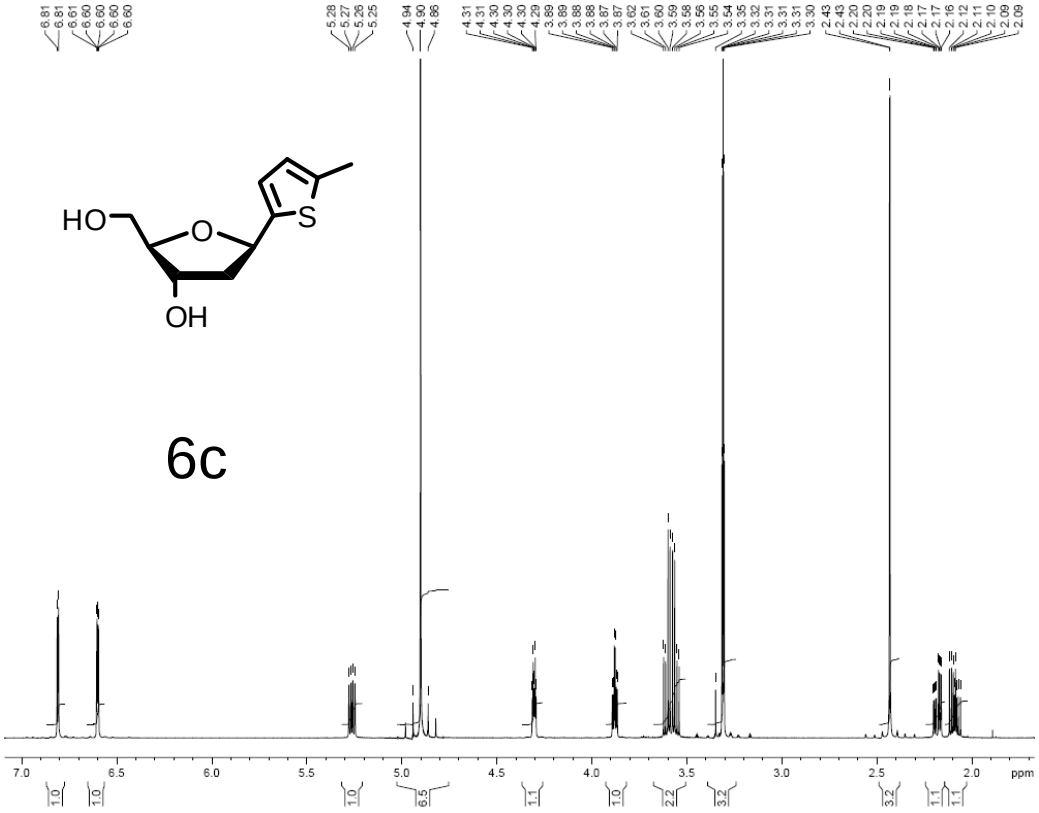


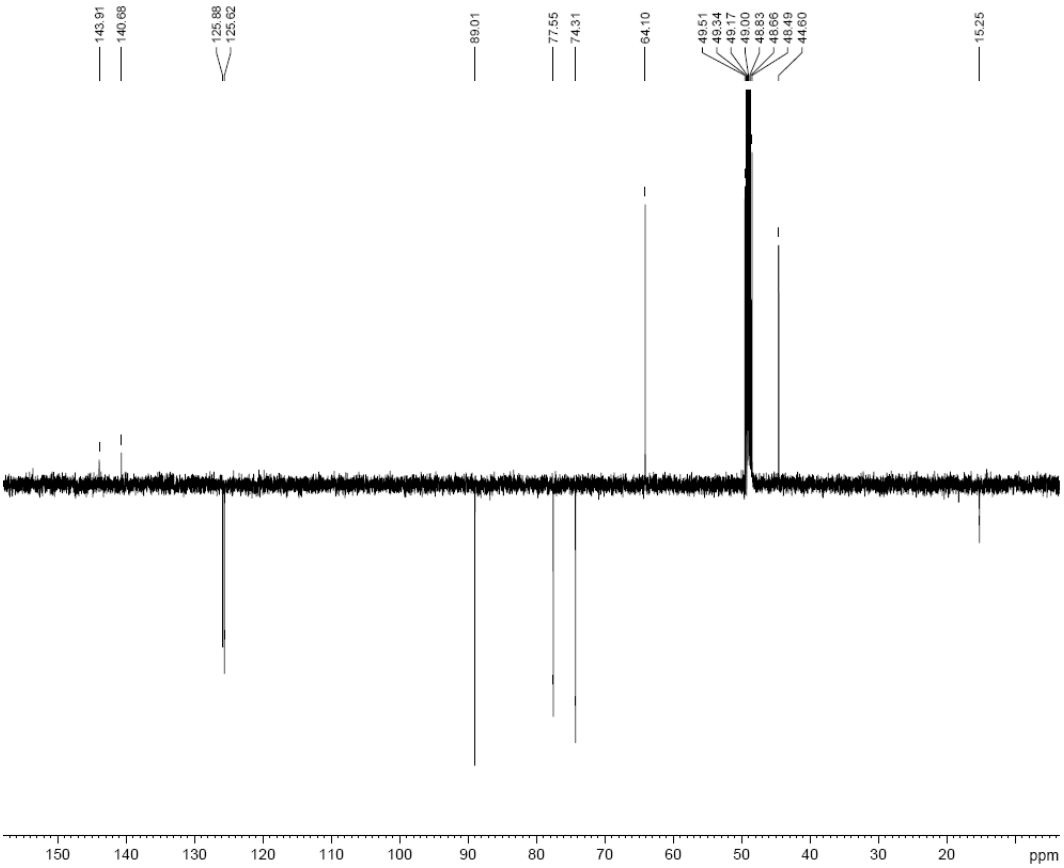
NMR spectra of 6b



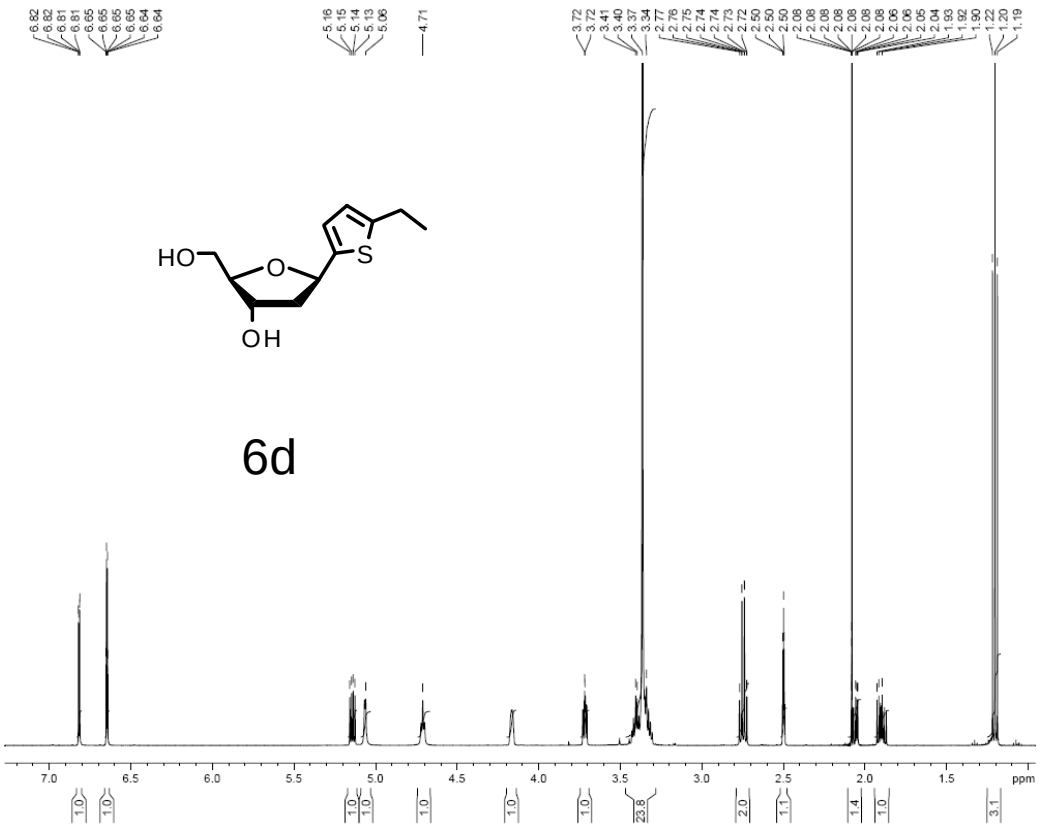


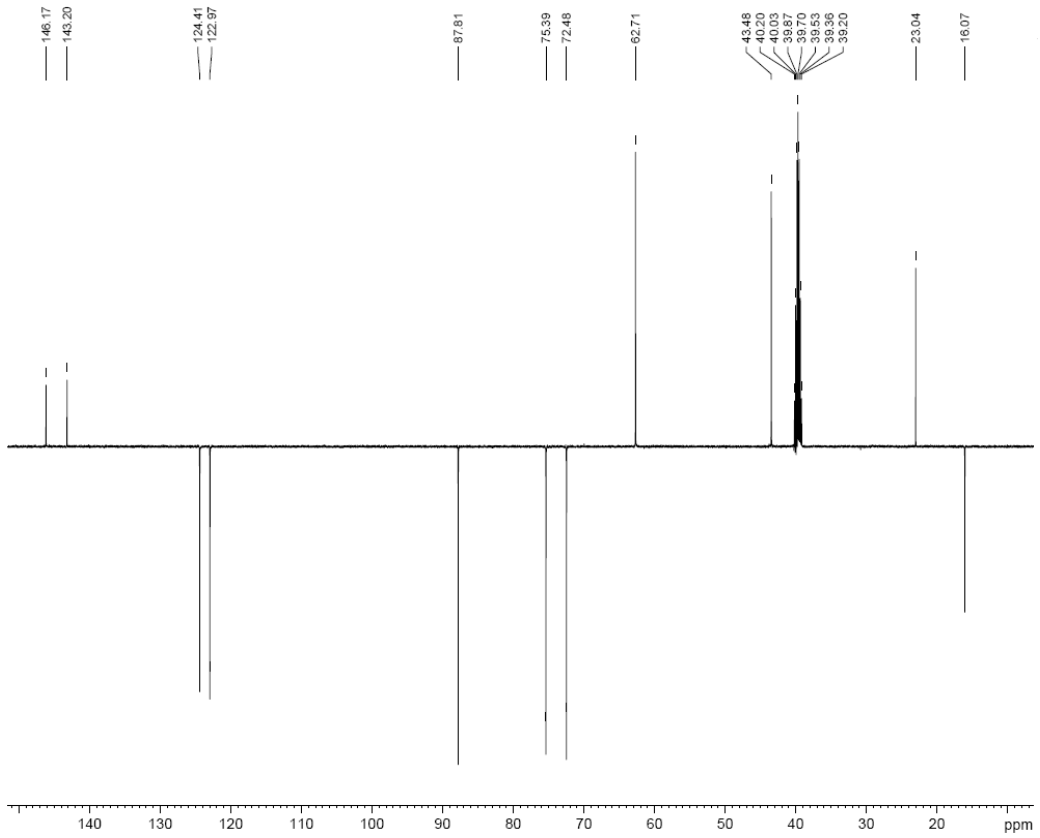
NMR spectra of 6c



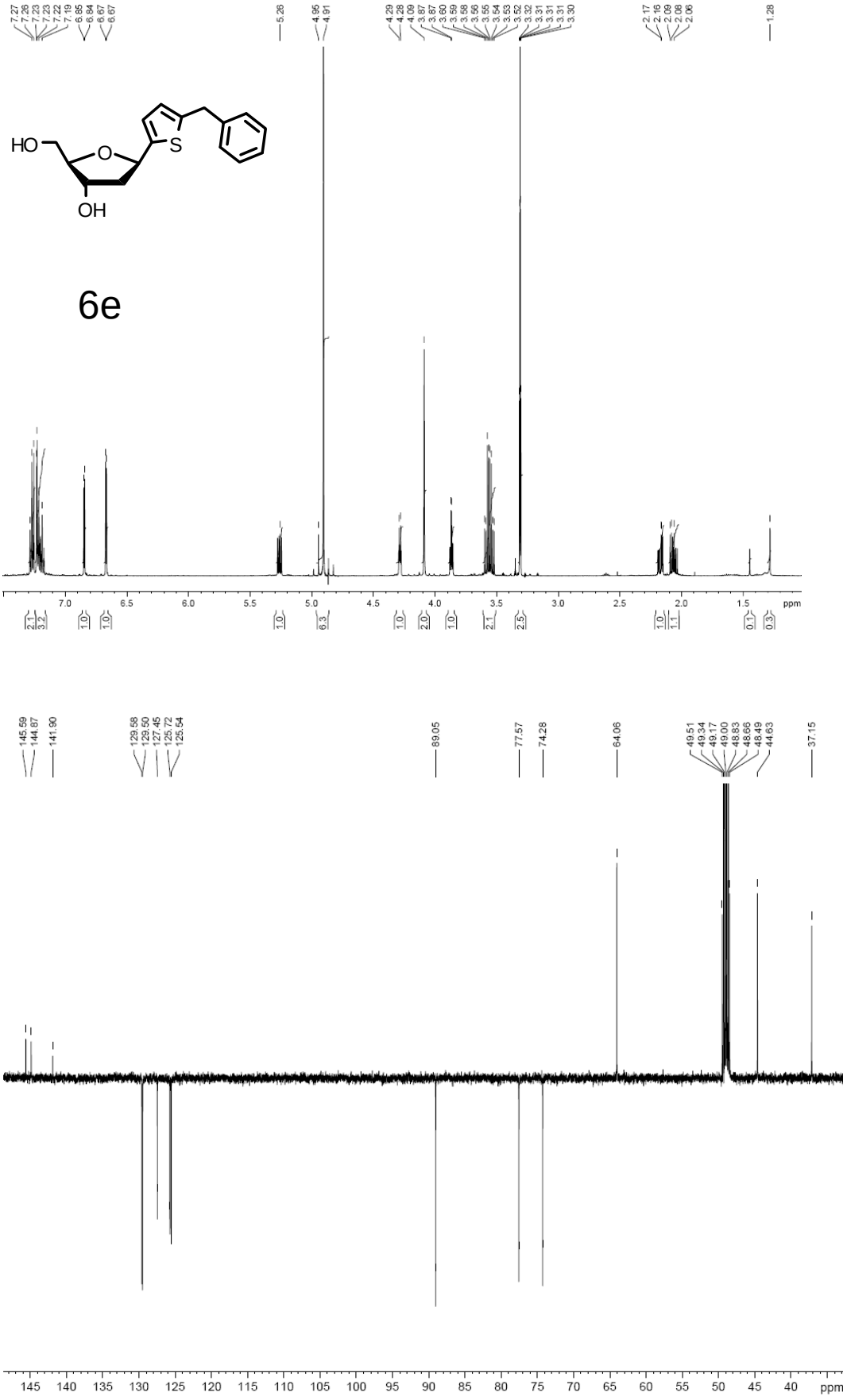


NMR spectra of 6d

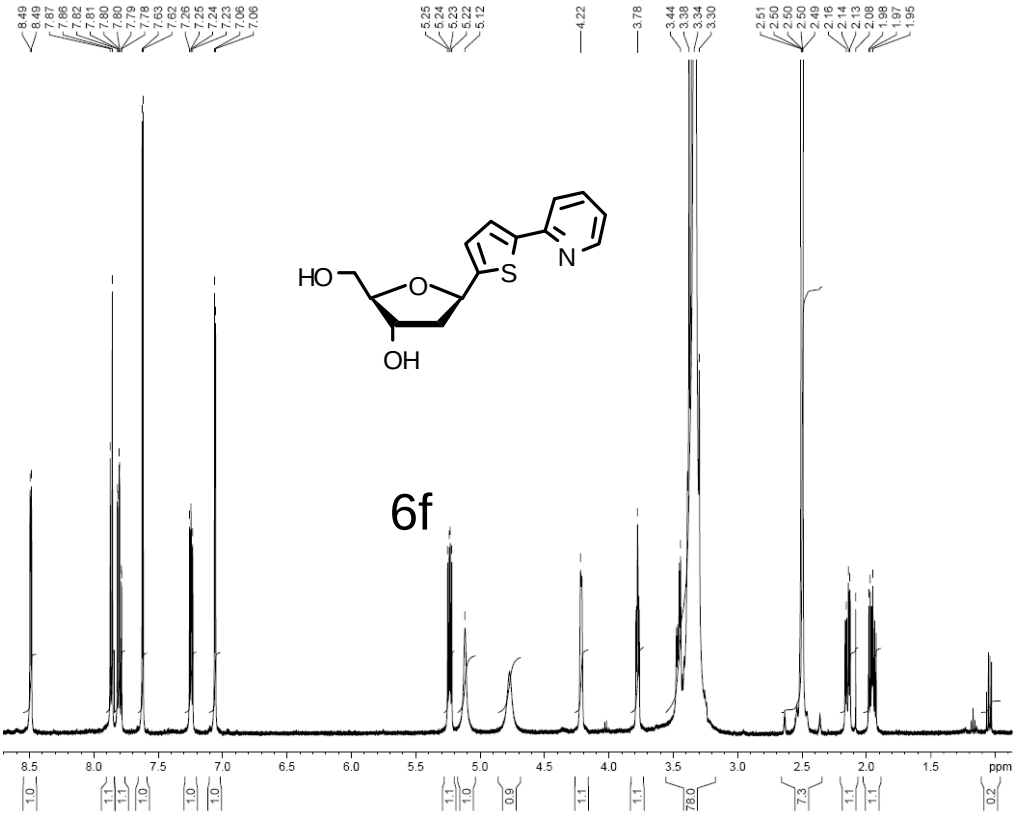


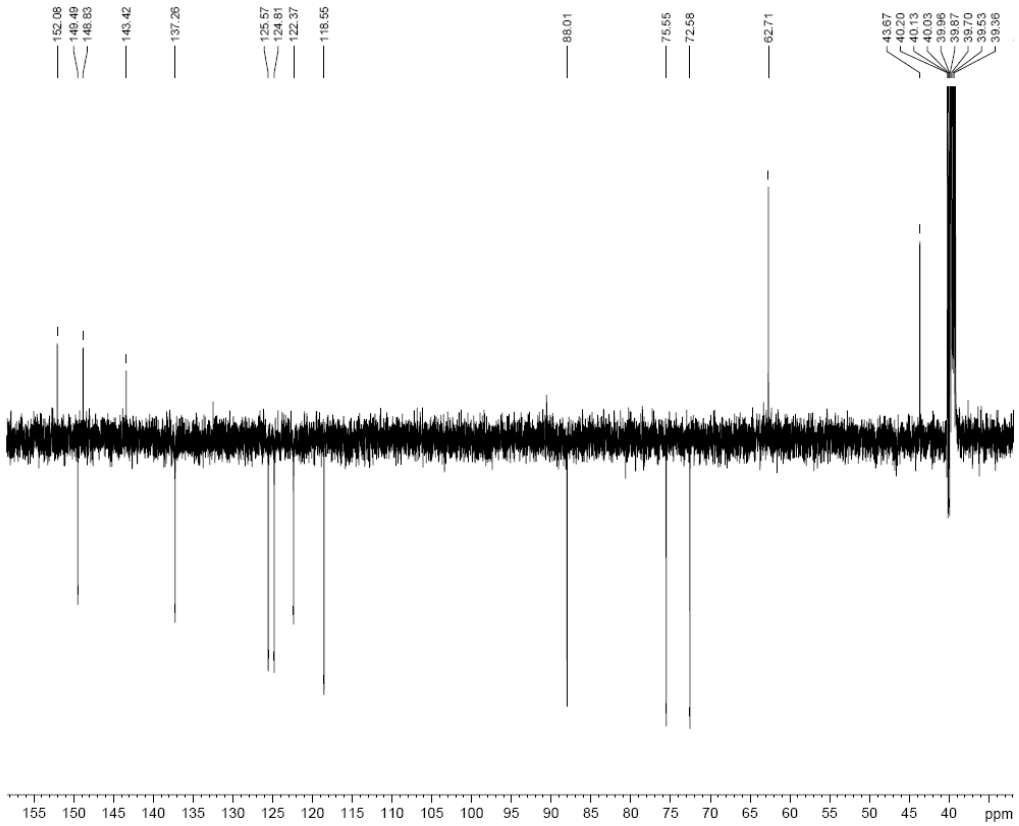


NMR spectra of 6e

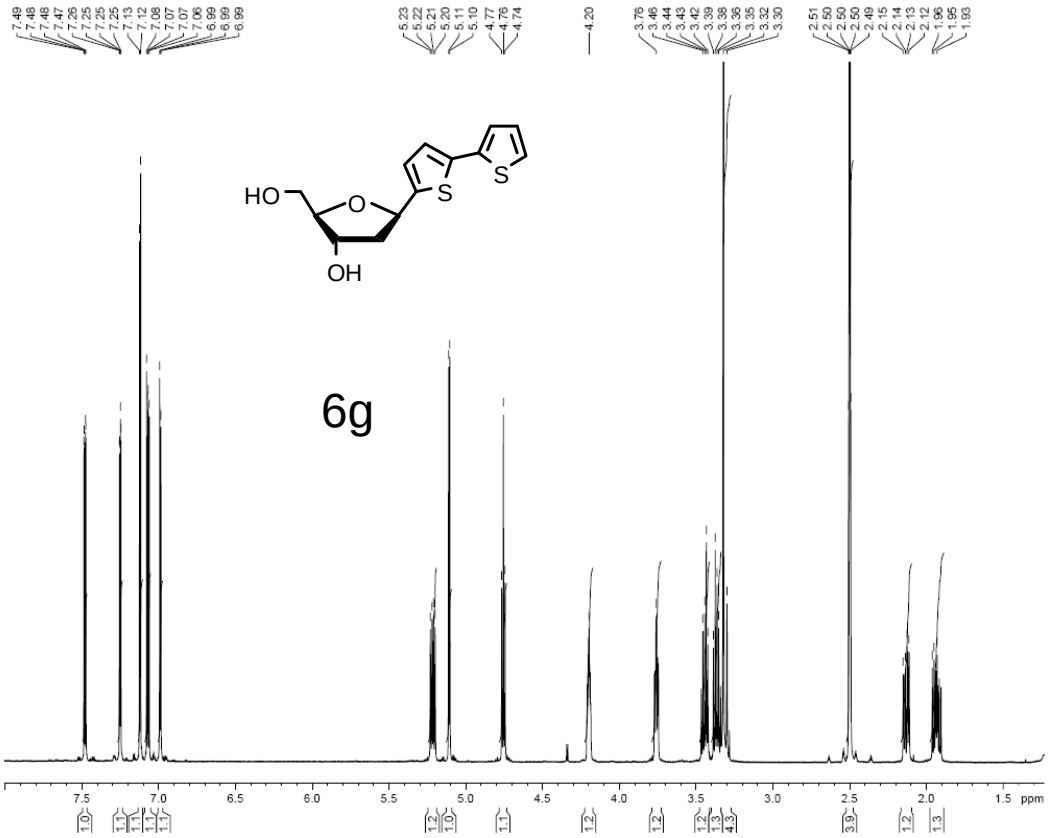


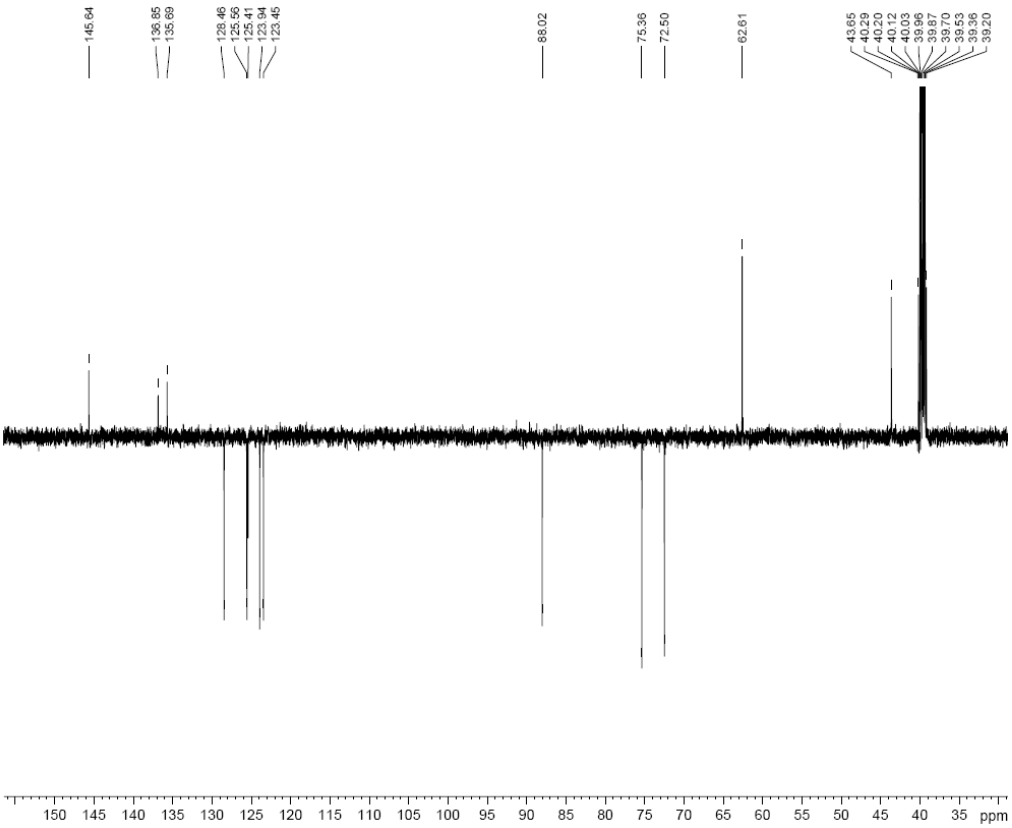
NMR spectra of 6f



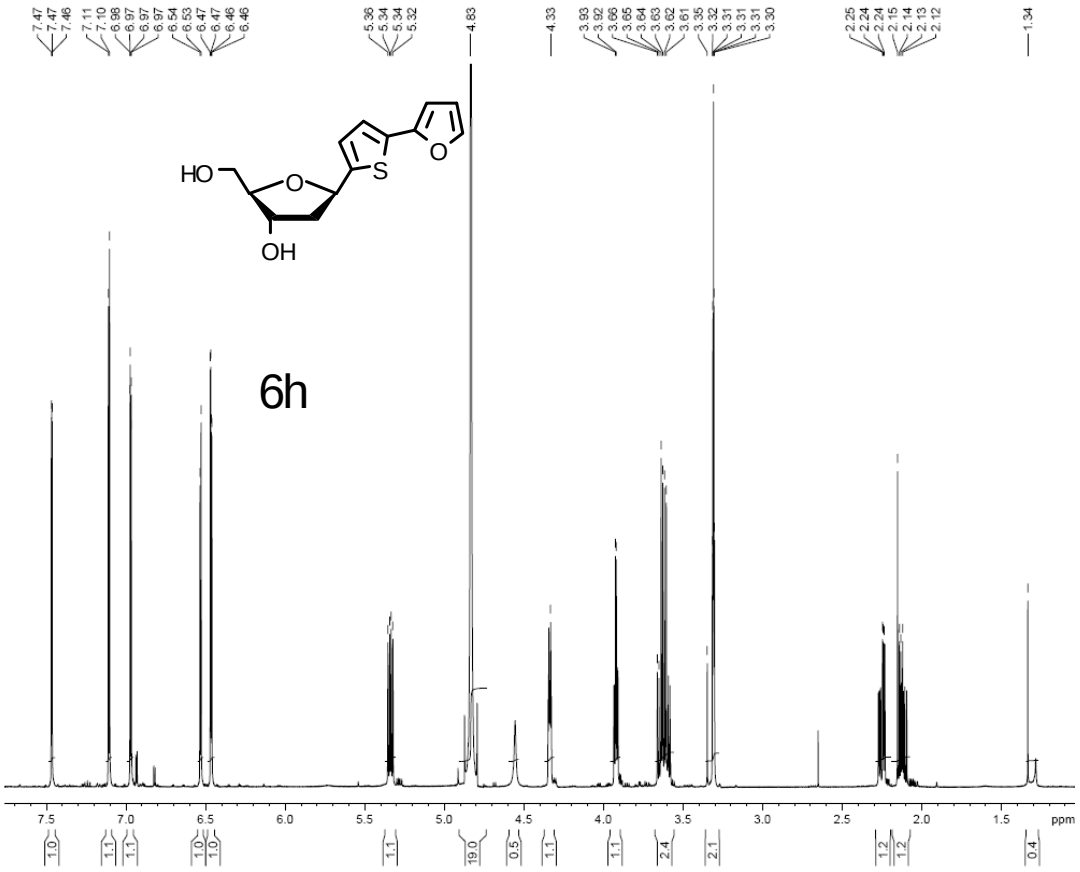


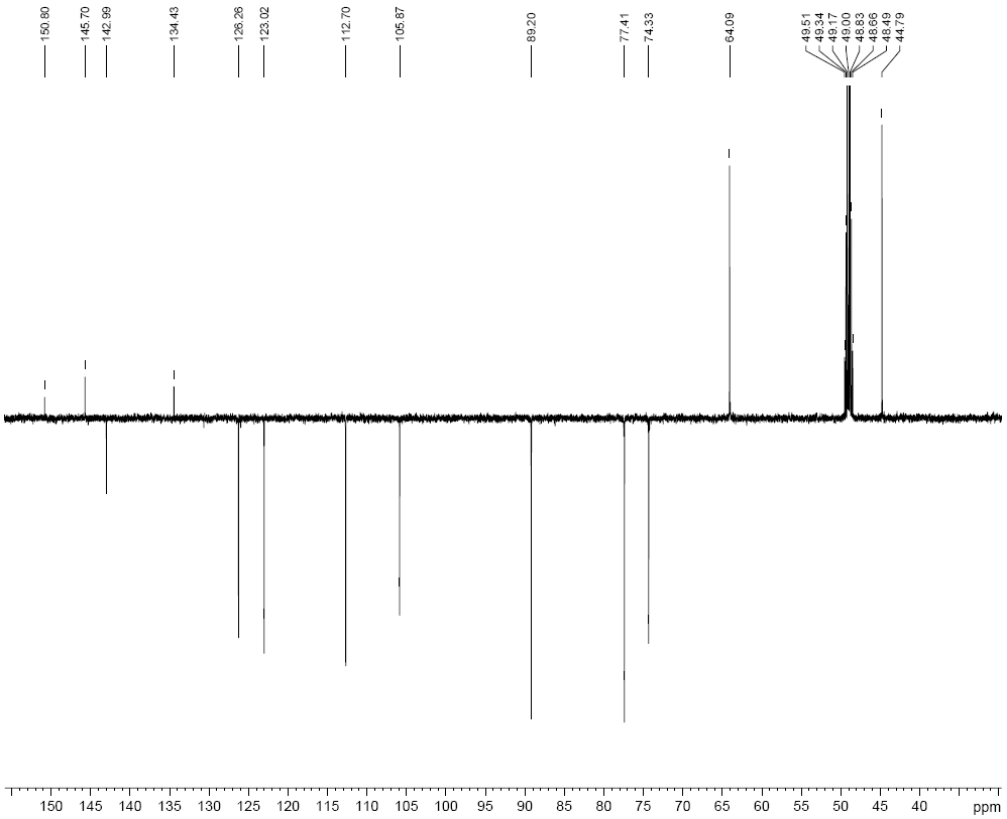
NMR spectra of 6g





NMR spectra of 6h





NMR spectra of 6i