Electronic Supplementary Information

Synthesis and Properties of a Cu(II) complexing Pyrazol Ligandoside in DNA

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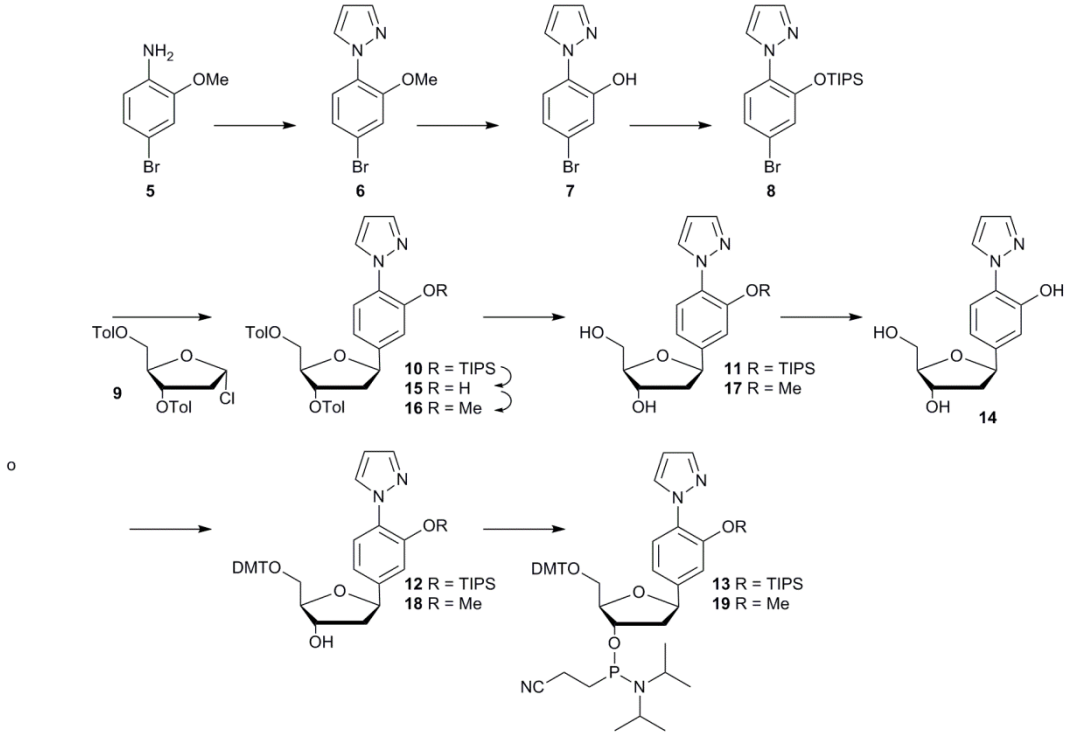
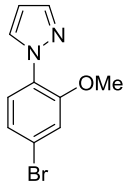
I. General methods and materials for synthesis

All experiments involving air and/or moisture sensitive compounds were performed using flame- or oven-dried glassware under argon atmosphere. Chemicals were purchased from *Sigma-Aldrich*, *TCI* and *Alfa-Aesar* and used without further purification unless otherwise noted. The solvents for organic synthesis were of reagent grade and purified by distillation. Solutions were concentrated *in vacuu*m a *Heidolph* rotary evaporator with a *Vario PC2001* diphragm pump by *Vacuubrand*. All mixed solvent systems are reported as v/v solutions. All reactions were monitored by thin layer chromatography (TLC), performed on *Merck* 60 (silica gel F_{254}) plates. Chromatographic purification of products was accomplished using flash column chromatography on silica gel (230-400 mesh) purchased from Merck. ^{1}H-, ^{13}C- and ^{31}P-NMR spectra were recorded in deuterated solvents on *Bruker ARX 300*, *Varian VXR400S*, *Varian Inova 400* and *Bruker AMX 600* spectrometers and calibrated to the residual solvent peak. Chemical shifts (δ, ppm) are quoted relative to the residual solvent peak as internal standard and coupling constants (*J*) are corrected and quoted to the nearest 0.1 Hz. Multiplicities are abbreviated as follows: s = singlet, d = doublet, dd = doublet doublet, ddd = doublet doublet doublet, dt = doublet triplet, t = triplet, td = triplet doublet, m = multiplet, br = broad.

II. Procedures, analytical and spectroscopic data



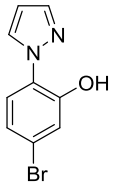
Scheme S1. Synthesis of **Pz** (**13**) and **Pm** (**19**) monomers**.**



1-(4-bromo-2-methoxyphenyl)-1*H*-pyrazole (6)

4-bromo-2-methoxyaniline **5** (5.00 g, 24.7 mmol) was dissolved in 20% HCl (25 mL). The solution was stirred and cooled in an ice bath while a solution of sodium nitrite (1.79 g, 26.0 mmol) in 4 mL of H_2O was added dropwise. The mixture was stirred 1 h at 0 °C. Stannous chloride dihydrate (11.2 g, 49.5 mmol) in 35% HCl (15 mL) was then slowly added. The mixture was allowed to reach room temperature whilst stirring for another 2 h before being filtered. The residue was washed with 35% HCl twice and dried under vacuum. The resulted diazonium salt was dissolved in ethanol (100 mL) and transferred to a solution of 1,1,3,3-tetramethoxypropane (8.15 mL 49.5 mmol) in ethanol (50 mL) and 35% HCl (5.0 mL) at room temperature. The reaction was refluxed for 4 h and then concentrated. The residue was dissolved in water (100 mL). The aqueous phase was extracted three times with ethyl acetate (3×100 mL). The combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/ethyl acetate 10:1) to give **6** as yellow oil (5.36 g, 21.2 mmol, 86% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.74–7.67 (m, 1H), 7.63 (dd, *J* = 8.3, 0.4 Hz, 1H), 7.19 (dt, *J* = 2.8, 1.9 Hz, 2H), 6.43 (dd, *J* = 2.5, 1.8 Hz, 1H), 3.89 (s, 3H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 151.6 (C), 140.3 (CH), 131.4 (CH), 128.9 (C), 126.2 (CH), 124.2 (CH), 120.7 (C), 115.8 (CH), 106.5 (CH), 56.3 (CH_3).
HRMS (ESI+): calculated for $C_{10}H_{10}BrN_2O^+$ $[M+H^+]^+$: 252.9971; found: 252.9972.

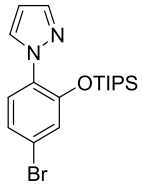


1-(4-bromo-2-hydroxyphenyl)-1*H*-pyrazole (7)

1-(4-bromo-2-methoxyphenyl)-1*H*-pyrazole (**6**) (5.08 g, 20.1 mmol) was dissolved in dichloromethane (100 mL) at -78 °C. BBr_3 (1M solution in dichloromethane, 24.1 mL) was added dropwise, and then stirred for 12 h. The reaction was quenched with methanol and warmed to room temperature. The solution was diluted with dichloromethane (300 mL), washed twice with water (2×300 mL), and then dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/dichloromethane 3:1) to give **7** as a white amorphous powder (3.25 g, 13.6 mmol, 68% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.58 (br, 1H), 7.97 (d, *J* = 2.6 Hz, 1H), 7.73 (d, *J* = 1.9 Hz, 1H), 7.27 (d, *J* = 2.2 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 7.06 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.53 (t, *J* = 2.2 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 150.2 (C), 139.0 (CH), 126.6 (CH), 124.1 (C), 122.4 (CH),

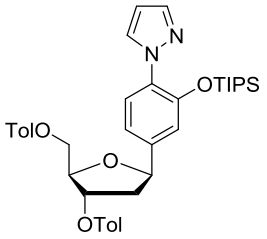
122.1 (CH), 120.1 (C), 118.7 (CH), 107.1 (CH).
HRMS (ESI+): calculated for $C_9H_8BrN_2O^+$ $[M+H^+]^+$: 238.9815; found: 238.9815.



1-{4-bromo-2-[(triisopropylsilyl)oxy]phenyl}-1*H*-pyrazole (8)

1-(4-bromo-2-hydroxyphenyl)-1*H*-pyrazole (**7**) (2.41 g, 10.1 mmol) was dissolved in dichloromethane (50 mL) and *N*,*N*-diisopropylethylamine was added (4.18 mL, 25.2 mmol) at 0 °C. Triisopropylsilyl trifluoromethanesulfonate (4.06 mL, 15.1 mmol) was added dropwise. The mixture was allowed to reach room temperature while stirring for 1 h, diluted with dichloromethane (150 mL), washed twice with water (2×300 mL), dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/ethyl acetate 20:1) to give **8** as a yellowish oil (4.39 g, 10.0 mmol, 99% yield).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.67 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 7.21–7.15 (m, 1H), 7.13 (d, *J* = 1.9 Hz, 1H), 6.41 (dd, *J* = 2.4, 1.8 Hz, 1H), 1.30–1.11 (m, 3H), 1.09–0.92 (m, 18H).
^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.0 (C), 140.2 (CH), 131.3 (CH), 131.0 (C), 127.2 (CH), 124.7 (CH), 123.2 (CH), 120.5 (C), 106.3 (CH), 17.71 (6×CH_3), 12.85 (3×CH).
HRMS (ESI+): calculated for $C_{18}H_{28}BrN_2OSi^+$ $[M+H^+]^+$: 395.1154; found: 395.1148.

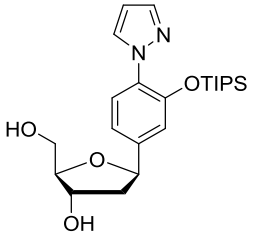


5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-{[(4-methylbenzoyl)oxy]methyl}tetrahydrofuran-3-yl 4-methylbenzoate (10)

1-{4-bromo-2-[(triisopropylsilyl)oxy]phenyl}-1*H*-pyrazole (**8**) (3.52 g, 8.04 mmol) was dissolved in anhydrous diethylether (40 mL) and cooled to -78 °C. *t*BuLi in pentane (1.6 M, 10.05 mL, 16.1mmol) was added dropwise over 1 h. The reaction was kept at -78 °C for another 2 h and then transferred to a precooled (-78 °C) suspension of copper(I) bromide-disulfide complex (826mg, 4.20 mmol) in diethyl ether (20 mL). The mixture was slowed warmed to -30 °C and stirred for 20 min as all the copper dissolved. The resulted clear yellow solution was cooled down to -78 °C and transferred to a precooled solution of 3',5'-O-bis(toluoyl)-2'-deoxy-alpha-D-erythropentofuranosyl chloride (**9**, 1.04 g, 2.68 mmol) in anhydrous dichloromethane (20 mL). The reaction mixture was allowed to warm up to room temperature for 12 h. The reaction was quenched by sat. NH_4Cl solution and ammonia (2 M, 1 mL). The aqueous phases were extracted three times with ether (3×100 mL). The combined organic phases were washed twice with water (2×300 mL), brine (300 mL), then dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on

silica gel (hexanes/ethyl acetate 10:1) to give **10** as yellowish oil (944 mg, 1.41 mmol, 53% yield).

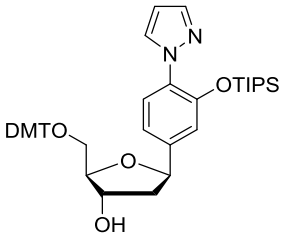
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 2.4 Hz, 1H), 7.91 (d, *J* = 8.6 Hz, 2H), 7.67 (dd, *J* = 1.8, 0.5 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.31–7.27 (m, 2H), 7.22–7.19 (m, 2H), 7.09 (d, *J* = 1.7 Hz, 1H), 7.05–7.01 (m, 1H), 6.41–6.37 (m, 1H), 5.61 (dd, *J* = 6.0, 0.8 Hz, 1H), 5.25 (dd, *J* = 10.9, 5.0 Hz, 1H), 4.60 (dd, *J* = 4.2, 2.7 Hz, 2H), 4.57 (dd, *J* = 4.2, 1.9 Hz, 1H), 2.58 (dd, *J* = 13.7, 5.1 Hz, 1H), 2.43 (s, 3H), 2.41 (s, 3H), 2.20 (ddd, *J* = 13.8, 11.0, 6.0 Hz, 1H), 1.18–1.10 (m, 3H), 1.00–0.91 (m, 18H).
^{13}C NMR (151 MHz, $CDCl_3$): δ = 166.3 (COO), 166.1 (COO), 148.3 (C), 144.2 (C), 143.8 (C), 141.0 (C), 139.9 (CH), 131.4 (CH), 131.0 (C), 129.7 (4×CH), 129.2 (4×CH), 129.0 (C), 127.0 (C), 126.0 (CH), 118.7 (CH), 117.1 (CH), 105.9 (CH), 82.9 (C4'), 80.0 (C1'), 77.1 (C3'), 65.0 (C5'), 41.7 (C2'), 21.7 (CH_3), 21.6 (CH_3), 17.7 (6×CH_3), 12.9 (3×CH).
HRMS (ESI+): calculated for $C_{39}H_{49}N_2O_6Si^+$ $[M+H^+]^+$: 669.3360; found: 669.3339.



5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-(hydroxymethyl)tetrahydrofuran-3-ol (11)

A suspension of 5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-{[(4-methylbenzoyl)oxy]methyl}tetrahydrofuran-3-yl 4-methylbenzoate (**10**) (1.68 g, 2.52 mmol) and potassium carbonate (764 mg, 5.53 mmol) in methanol (20 mL) was stirred at room temperature for 1 h. The reaction was diluted with water (100 mL) and the aqueous phases were extracted three times with chloroform (3×100 mL). The combined organic phases were dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (chloroform/methanol 20:1) to give **11** as a colorless oil (712 mg, 1.65 mmol, 65% yield).

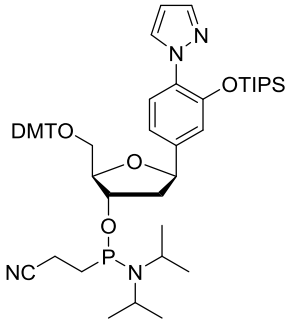
^{1}H NMR (400 MHz, CD_3OD): δ = 7.96–7.87 (m, 1H), 7.67 (dd, *J* = 1.9, 0.6 Hz, 1H), 7.43 (d, *J* = 8.1 Hz, 1H), 7.15 (d, *J* = 1.8 Hz, 1H), 7.08 (ddd, *J* = 8.1, 1.8, 0.5 Hz, 1H), 6.48 (dd, *J* = 2.4, 2.0 Hz, 1H), 5.14 (dd, *J* = 10.5, 5.5 Hz, 1H), 4.34 (dt, *J* = 3.9, 1.7 Hz, 1H), 4.03–3.95 (m, 1H), 3.69 (dd, *J* = 11.4, 5.1 Hz, 1H), 3.60 (ddd, *J* = 9.2, 6.4, 3.9 Hz, 1H), 2.24 (ddd, *J* = 13.1, 5.5, 1.7 Hz, 1H), 1.96–1.84 (m, 1H), 1.28–1.12 (m, 3H), 1.01 (dt, *J* = 7.8, 3.9 Hz, 18H).
^{13}C NMR (100 MHz, CD_3OD): δ = 150.5 (C), 145.2 (C), 141.0 (CH), 133.4 (CH), 131.7 (C), 127.5 (CH), 120.2 (CH), 118.5 (CH), 107.2 (CH), 89.2 (C4'), 80.7 (C1'), 74.5 (C3'), 64.2 (C5'), 45.0 (C2'), 18.3 (6×CH_3), 14.1 (3×CH).
HRMS (ESI+): calculated for $C_{23}H_{37}N_2O_4Si^+$ $[M+H^+]^+$: 433.2523; found: 433.2513.



5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-{[bis(4-methoxyphenyl)(phenyl)methoxy]methyl}tetrahydrofuran-3-ol (12)

5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-(hydroxymethyl)tetrahydrofuran-3-ol (**11**) (712 mg, 1.65 mmol) and 4,4'-dimethoxytrityl chloride (613 mg, 1.81 mmol) were dissolved in anhydrous dichloromethane (30 mL) and stirred at 0 °C. Then *N*,*N*-diisopropylethylamine (683 µL, 4.11 mmol) was added dropwise. The reaction was allowed to warm to room temperature for 1 h and diluted with dichloromethane (200 mL). The organic phase was washed two times with sat. $NaHCO_3$ solution (2×200 mL), then dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/ethyl acetate 2:1+3% triethylamine) to give **12** as yellowish foam (893 mg, 1.22 mmol, 74% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 2.4, 0.7 Hz, 1H), 7.66 (dd, *J* = 1.8, 0.6 Hz, 1H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.48–7.41 (m, 2H), 7.38–7.15 (m, 7H), 7.09–6.98 (m, 1H), 6.91 (d, *J* = 1.8 Hz, 1H), 6.87–6.78 (m, 4H), 6.39 (dd, *J* = 2.4, 1.8 Hz, 1H), 5.12 (dd, *J* = 10.1, 5.6 Hz, 1H), 4.40 (dd, *J* = 5.4, 2.8 Hz, 1H), 4.06 (ddd, *J* = 7.1, 4.6, 2.6 Hz, 1H), 3.79 (t, *J* = 2.4 Hz, 5H), 3.42 (dd, *J* = 9.6, 4.7 Hz, 1H), 3.19 (dd, *J* = 9.6, 6.7 Hz, 1H), 2.28–2.15 (m, 1H), 1.92 (ddd, *J* = 13.1, 10.1, 6.0 Hz, 2H), 1.20–1.07 (m, 3H), 1.01–0.83 (m, 18H).
^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.5 (2×C), 148.1 (C), 144.7 (C), 142.1 (C), 139.8 (CH), 135.9 (2×C), 131.4 (CH), 130.8 (C), 130.0 (2×CH), 128.1 (2×CH), 127.8 (4×CH), 126.8 (CH), 126.0 (CH), 118.7 (CH), 117.5 (CH), 113.1 (4×CH), 105.8 (CH), 86.3 (C4'), 86.2 (C), 79.2 (C1'), 74.7 (C3'), 64.4 (C5'), 55.2 (2×OCH_3), 43.5 (C2'), 17.7 (6×CH_3), 12.8 (3×CH).
HRMS (ESI+): calculated for $C_{44}H_{55}N_2O_6Si^+$ $[M+H^+]^+$: 735.3829; found: 735.3820.

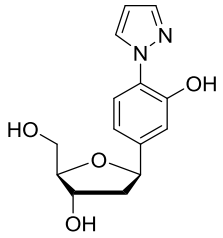


5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-{[bis(4-methoxyphenyl)(phenyl)methoxy]methyl}tetrahydrofuran-3-yl (2-cyanoethyl) diisopropylphosphoramidite (13)

In a Schlenck tube the DMT-protected nucleoside **12** (237 mg, 322 µmol) and diisopropylammonium tetrazolide (221 mg, 1.29 mmol) were dissolved in rigorously degassed dichloromethane (2 mL). The solution was then degassed three more times. Bis(diisopropylamino)(2-cyanoethoxy)phosphine (205 µL, 645 µmol) was added to the solution. The reaction mixture was stirred at room temperature

for 1 h under argon atmosphere, then directly purified by flash chromatography on silica gel (hexanes/ethyl acetate 2:1+3% triethylamine) to give **13** as a yellowish foam (301 mg, 322 μmol, quant.).

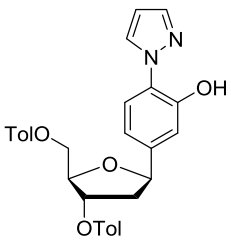
^{31}P NMR (81 MHz, $CDCl_3$): δ = 149.25, 149.07.
HRMS (ESI+): calculated for $C_{53}H_{72}N_4O_7PSi^+$ $[M+H^+]^+$: 935.4908; found: 935.4902.



5-[3-hydroxy-4-(1*H*-pyrazol-1-yl)phenyl]-2-(hydroxymethyl) tetrahydrofuran-3-ol (14)

A suspension of 5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-{[(4-methylbenzoyl)oxy] methyl}tetrahydrofuran-3-yl 4-methylbenzoate (**10**) (393 mg, 588 μmol) and potassium carbonate (233 mg, 1.69 mmol) in methanol (10 mL) was stirred at room temperature. A solution of TBAF in THF (1 M, 0.60 mL) was added to the mixture and then stirred at room temperature for 2 h. Solvents were removed under reduced pressure. The residue was purified by flash chromatography on silica gel (chloroform/methanol 20:1) to give **14** as a white amorphous solid (141 mg, 511 mmol, 87% yield). Further crystallization was achieved in ethyl acetate solution of **14**.

^{1}H NMR (400 MHz, CD_3OD): δ = 8.24 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.72 (dd, *J* = 1.9, 0.5 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 1H), 7.11–7.03 (m, 1H), 6.97 (ddd, *J* = 8.3, 1.9, 0.5 Hz, 1H), 6.51 (dd, *J* = 2.5, 2.0 Hz, 1H), 5.10 (dd, *J* = 10.4, 5.4 Hz, 1H), 4.32 (dt, *J* = 4.1, 1.9 Hz, 1H), 3.96 (td, *J* = 5.2, 2.4 Hz, 1H), 3.79–3.59 (m, 2H), 2.21 (ddd, *J* = 13.1, 5.5, 1.7 Hz, 1H), 1.95 (ddd, *J* = 13.1, 10.4, 5.9 Hz, 1H).
^{13}C NMR (100 MHz, CD_3OD) δ = 150.5 (C), 143.6 (C), 140.3 (CH), 130.7 (CH), 126.8 (C), 122.4 (CH), 118.4 (CH), 116.2 (CH), 107.4 (CH), 89.2 (C4'), 80.9 (C1'), 74.4 (C3'), 64.1 (C5'), 44.8 (C2').
HRMS (ESI+): calculated for $C_{14}H_{17}N_2O_4^+$[$M+H^+$]$^+$: 277.1183; found: 277.1186.
UV λ_{max}= 284.5, 246.0 nm.

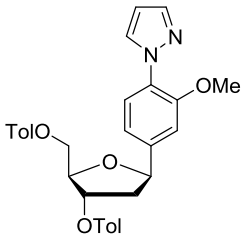


5-[3-hydroxy-4-(1*H*-pyrazol-1-yl)phenyl]-2-{[(4-methylbenzoyl)oxy] methyl}tetrahydrofuran-3-yl 4-methylbenzoate (15)

5-{4-(1*H*-pyrazol-1-yl)-3-[(triisopropylsilyl)oxy]phenyl}-2-{[(4-methylbenzoyl)oxy]methyl}tetrahydro furan-3-yl 4-methylbenzoate (**10**) (1.19 g, 1.78 mmol) was dissolved in THF (10 mL) and tetrabutylammonium fluoride solution (1.0 M in THF, 2 mL) was added dropwise at room temperature.

The mixture was stirred for 30 min and then diluted with dichloromethane (200 mL). The organic phase was washed three times with water (3×200 mL), then dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/ethyl acetate 4:1) to give **15** as white foam (760 mg, 1.48 mmol, 83% yield).

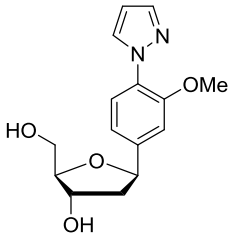
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.99 (m, 3H), 7.92 (m, 2H), 7.72 (dd, *J* = 1.8, 0.5 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.29–7.27 (m, 2H), 7.22–7.21 (m, 2H), 7.14 (d, *J* = 1.7 Hz, 1H), 6.98-6.97 (m, 1H), 6.50 (dd, 1H), 5.60 (m, 1H), 5.23 (dd, *J* = 10.9, 5.0 Hz, 1H), 4.64 (dd, *J* = 4.2, 2.7 Hz, 2H), 4.54 (dd, *J* = 4.2, 1.9 Hz, 1H), 2.55 (dd, *J* = 13.8, 5.2, 0.9 Hz, 1H), 2.43 (s, 3H), 2.41 (s, 3H), 2.24 (ddd, *J* = 13.8, 11.0, 6.0 Hz, 1H).
^{13}C NMR (151 MHz, $CDCl_3$): δ = 166.4 (COO), 166.1 (COO), 149.3 (C), 144.1 (C), 143.8 (C), 140.6 (C), 138.8 (CH), 129.7 (4×CH), 129.2 (4×CH), 127.0 (2×C), 126.6 (CH), 124.3 (C), 118.0 (CH), 116.7 (CH), 116.4 (CH), 106.8 (CH), 83.0 (C4'), 80.1 (C1'), 77.1 (C3'), 64.7 (C5'), 41.5 (C2'), 21.7 (CH_3), 21.6 (CH_3).
HRMS (ESI+): calculated for $C_{30}H_{29}N_2O_6^+$ $[M+H^+]^+$: 513.2026; found: 513.2028.



5-[3-methoxy-4-(1*H*-pyrazol-1-yl)phenyl]-2-{[(4-methylbenzoyl)oxy]methyl}tetrahydrofuran-3-yl 4-methylbenzoate (16)

5-[3-hydroxy-4-(1*H*-pyrazol-1-yl)phenyl]-2-{[(4-methylbenzoyl)oxy]methyl}tetrahydrofuran-3-yl-4-methylbenzoate (**15**) (741 mg, 1.446 mmol) was dissolved in anhydrous DMF (10 mL) at 0 °C and sodium hydride (60% dispersion in mineral oil, 116 mg, 2.89 mmol) was added slowly. The mixture was stirred for 30 min before the addition of CH_3I (108 μL, 1.74 mmol). The system was allowed to reach room temperature gradually for further 2 h, and then diluted with dichloromethane (150 mL). The organic phase was washed with brine (150 mL), water (2×100 mL), and then dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **16** as colorless oil (582 mg, 1.10 mmol, 76% yield).

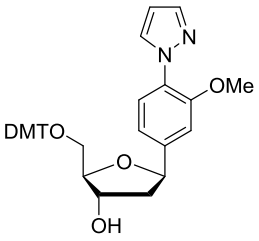
^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.99 (m, 2H), 7.92 (m, 2H), 7.70 (dd, *J* = 1.8, 0.5 Hz, 1H), 7.66 (s, 1H), 7.65 (s, 1H), 7.29–7.27 (m, 2H), 7.22–7.21 (m, 2H), 7.11 (d, *J* = 1.7 Hz, 1H), 7.02 (m, 1H), 6.41 (dd, *J* = 2.4, 1.9 Hz, 1H), 5.65 (m, 1H), 5.28 (m, 1H), 4.79 (dd, *J* = 11.8, 3.5 Hz, 1H), 4.63 (dd, *J* = 11.8, 3.7 Hz, 1H), 4.56 (td, *J* = 3.6, 1.9 Hz, 1H), 3.70 (s, 3H), 2.59 (dd, *J* = 13.8, 5.1 Hz, 1H), 2.44 (s, 3H), 2.39 (s, 3H), 2.24 (ddd, *J* = 13.8, 11.0, 6.0 Hz, 1H).
^{13}C NMR (151 MHz, $CDCl_3$): δ = 166.3 (COO), 166.2 (COO), 151.4 (C), 144.2 (C), 144.0 (C), 141.0 (C), 139.9 (CH), 131.5 (CH), 129.7 (2×CH), 129.6 (2×CH), 129.2 (4×CH), 128.9 (C), 127.0 (2×C), 125.1 (CH), 118.5 (CH), 109.3 (CH), 106.1 (CH), 83.3 (C4'), 80.4 (C1'), 77.3 (C3'), 64.6 (C5'), 55.7 (OCH_3), 42.1 (C2'), 21.7 (2×CH_3).
HRMS (ESI+): calculated for $C_{31}H_{31}N_2O_6^+$ $[M+H^+]^+$: 527.2182; found: 527.2185.



2-(hydroxymethyl)-5-[3-methoxy-4-(1*H*-pyrazol-1-yl) phenyl]tetrahydrofuran-3-ol (17)

A suspension of 5-[3-methoxy-4-(1*H*-pyrazol-1-yl)phenyl]-2-{[(4-methylbenzoyl)oxy]methyl}tetrahydrofuran-3-yl-4-methylbenzoate (**16**) (570 mg, 1.08 mmol) and potassium carbonate (329 mg, 2.38 mmol) in methanol (5 mL) was stirred at room temperature for 2 h and then diluted with water (50 mL). The aqueous phase was extracted four times with chloroform (4×50 mL). The combined organic layers were dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (chloroform/methanol 20:1) to give **17** as white foam (283 mg, 975 µmol, 90% yield).

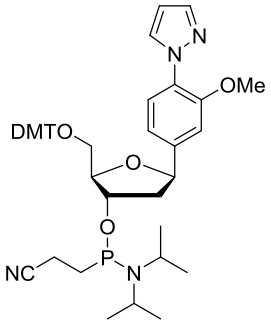
^{1}H NMR (600 MHz, CD_3OD): δ = 8.01 (dd, *J* = 2.5, 0.6 Hz, 1H), 7.67 (dd, *J* = 1.9, 0.5 Hz, 1H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.29 (d, *J* = 1.6 Hz, 1H), 7.09 (ddd, *J* = 8.2, 1.7, 0.6 Hz, 1H), 6.46 (dd, *J* = 2.4, 2.0 Hz, 1H), 5.19 (dd, *J* = 10.3, 5.6 Hz, 1H), 4.34 (dt, *J* = 5.9, 2.1 Hz, 1H), 3.98 (td, *J* = 4.9, 2.6 Hz, 1H), 3.89 (s, 3H), 3.71 (d, *J* = 4.9 Hz, 2H), 2.26 (ddd, *J* = 13.1, 5.6, 1.8 Hz, 1H), 2.07–1.94 (m, 1H).
^{13}C NMR (151 MHz, CD_3OD): δ = 153.4 (C), 145.0 (C), 140.9 (CH), 133.4 (CH), 129.7 (C), 126.4 (CH), 119.4 (CH), 111.3 (CH), 107.2 (CH), 89.3 (C4'), 81.1 (C1'), 74.3 (C3'), 64.0 (C5'), 56.5 (OCH_3), 45.1 (C2').
HRMS (ESI+): calculated for $C_{15}H_{19}N_2O_4^+$ $[M+H^+]^+$: 291.1339, found: 291.1345.
UV λ_{max}= 284.5, 248.7 nm.



2-[(bis(4-methoxyphenyl)(phenyl)methoxy]methyl}-5-[3-methoxy-4-(1*H*-pyrazol-1-yl)phenyl]tetrahydrofuran-3-ol (18)

2-(hydroxymethyl)-5-[3-methoxy-4-(1*H*-pyrazol-1-yl)phenyl]tetrahydrofuran-3-ol (**17**) (265 mg, 913 µmol) and 4,4'-dimethoxytrityl chloride (340 mg, 1.00 mmol) were dissolved in anhydrous dichloromethane (10 mL) and stirred at 0 °C. Then *N*,*N*-diisopropylethylamine (378 µL, 2.28 mmol) was added dropwise. The reaction was allowed to reach room temperature for 3 h, and then diluted with dichloromethane (150 mL). The organic phase was washed twice with sat. aqueous $NaHCO_3$ (2×150 mL), then dried over $MgSO_4$ and filtered. Solvent was removed under reduced pressure. The crude was purified by flash chromatography on silica gel (hexanes/ethyl acetate 1:2+3% triethylamine) to give **18** as white foam (408 mg, 688 µmol, 75% yield).

^{1}H NMR (600 MHz, $CDCl_3$): δ = 8.00 (dd, *J* = 2.4, 0.6 Hz, 1H), 7.69 (dd, *J* = 1.8, 0.5 Hz, 1H), 7.66 (d, *J* = 8.1 Hz, 1H), 7.49–7.43 (m, 2H), 7.39–7.31 (m, 3H), 7.30–7.25 (m, 3H), 7.21 (dt, *J* = 9.2, 4.3 Hz, 1H), 7.15 (d, *J* = 1.6 Hz, 1H), 7.06–6.99 (m, 1H), 6.86–6.76 (m, 4H), 6.41 (dd, *J* = 2.4, 1.9 Hz, 1H), 5.20 (dd, *J* = 10.2, 5.5 Hz, 1H), 4.67–4.36 (m, 1H), 4.11–4.06 (m, 1H), 3.78 (s, 6H), 3.68 (s, 3H), 3.36 (ddd, *J* = 13.8, 9.9, 4.5 Hz, 2H), 2.30–2.24 (m, 1H), 2.11 (ddd, *J* = 13.1, 10.2, 6.0 Hz, 1H).
^{13}C NMR (151 MHz, $CDCl_3$): δ = 158.5 (2×C), 151.4 (C), 144.8 (C), 142.2 (C), 140.0 (CH), 136.0 (2×C), 131.4 (CH), 130.1 (4×CH), 128.9 (C), 128.2 (2×CH), 127.8 (2×CH), 126.8 (C), 125.0 (CH), 118.7 (CH), 113.1 (4×CH), 113.1 (CH), 109.7 (CH), 106.1 (CH), 86.5 (C4'), 86.2 (C), 79.8 (C1'), 74.6 (C3'), 64.2 (C5'), 55.8 (2xOCH_3), 55.2 (CH_3), 44.3 (C2').
HRMS (ESI+): calculated for $C_{36}H_{37}N_2O_6^+$ $[M+H^+]^+$: 593.2652; found: 593.2653.

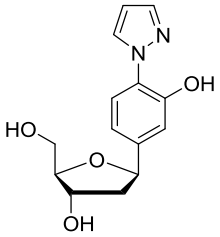


2-{[bis(4-methoxyphenyl)(phenyl)methoxy]methyl}-5-[3-methoxy-4-(1*H*-pyrazol-1-yl)phenyl]tetrahydrofuran-3-yl (2-cyanoethyl) diisopropylphosphoramidite (19)

In a Schlenck tube the DMT-protected nucleoside **12** (93 mg, 157 μmol) and diisopropylammonium tetrazolide (107 mg, 628 μmol) were dissolved in rigorously degassed dichloromethane (2 mL). The solution was then degassed three more times. Bis(diisopropylamino)(2-cyanoethoxy)phosphine (100 μL, 314 μmol) was added to the solution. The reaction mixture was stirred at room temperature for 30 min under argon atmosphere, then directly purified by flash chromatography on silica gel (hexanes/ethyl acetate 2:1+3% triethylamine) to give **19** as a white foam (123 mg, 157 μmol, quant.).

^{31}P NMR (81 MHz, $CDCl_3$): δ = 149.01, 148.87.
HRMS (ESI+): calculated for $C_{45}H_{53}N_4O_7P^+$ $[M+H^+]^+$:793.3730; found: 793.3731.

Crystallographic data $C_{14}H_{16}N_2O_4$_rv186_carell



net formula	$C_{14}H_{16}N_2O_4$
M_r/g mol^{-1}	276.288
crystal size/mm	0.195 × 0.127 × 0.051
T/K	173(2)
Radiation	'Mo Kα
Diffractometer	'Bruker D8Venture'
crystal system	Monoclinic
space group	$P2_1$
a/Å	11.8630(13)
b/Å	4.8437(7)
c/Å	12.6119(16)
α/°	90
β/°	116.802(3)
γ/°	90
V/Å^3	646.84(14)
Z	2
calc. density/g cm^{-3}	1.4186(3)
μ/mm^{-1}	0.105
absorption correction	multi-scan
transmission factor range	0.9043–0.9580
refls. Measured	8079
R_{int}	0.0407
mean σ(I)/I	0.0390
θ range	3.18–25.41
observed refls.	2117
x, y (weighting scheme)	0.0376, 0.1254
hydrogen refinement	Mixed
Flack parameter	1.7(11)
refls in refinement	2358
Parameters	193
Restraints	1
$R(F_{obs})$	0.0327
$R_w(F^2)$	0.0809
S	1.059
shift/error$_{max}$	0.001

max electron density/e $Å^{-3}$	0.154
min electron density/e $Å^{-3}$	−0.168

C-bound H: constr, O-bound H: refall.

Correct structure derived from synthesis (Flack parameter meaningless).

III. General method for oligonucleotide synthesis

DNA Oligonucleotide synthesis was performed on an Applied Biosystems Incorporated 394 automated synthesizer. Phosphoramidites and LV-PS (Low Volume Polystyrene) columns were purchased from *Glen Research Corporation*. All oligodeoxynucleotides were synthesized on a 200 nmol scale with standard DNA synthesis cycles (trityl off mode). For the pyrazole monomer, the coupling time was extended to 600 s. The efficiency of oligomers synthesis was monitored by trityl absorbance. Cleavage from the solid support and deprotection were achieved by incubation in a 28% ammonium hydroxide solution and 40% mono-methylamine solution (1/1) at 65 °C for 5 min.

The solvents were removed in a *SpeedVac* concentrator and the pellet redissolved in bidest water. Semi-preparative HPLC was achieved using a *Macherey-Nagel* C18 column (5 mm, 9.4×250 mm) on *Waters* Breeze 2487 Dual λ Array Detector, 1525 Binary HPLC Pump.

Conditions:

Buffer A, 0.01M TEAA.

Buffer B, 0.01M TEAA in 80% acetonitrile.

Started at 0% B; linear gradient to 30% B over 45 min, flow rate: 5 mL/min.

The purified fractions were concentrated, desalted on *Waters* Sepac-C18 cartridges and concentrated again. The obtained oligomers were characterized by Matrix Assisted Laser Desorption Ionization Time of Flight (MALDI-TOF) on Bruker Daltonics Autoflex II. Concentration of oligonucleotide solutions was calculated from the UV absorbance at 260 nm on a Nanodrop ND-1000 spectrophotometer with the following molar extinction coefficients: ε(Pz) = 7600, ε(Pm) = 5685, ε(A) = 15200, ε(G) = 12000, ε(C) = 7100, ε(T) = 8400.

IV. Procedures and selected spectroscopic data for melting curves and CD experiments

Table S1. Sequence of synthesized DNA oligonucleotides for melting point and CD experiments **(X=Pz)**

Entry	Strands	Sequence of oligonucleotides	Calc. mass	Exptl. mass
1	**X1**	5’-CAC ATT A***Pz***T GTT GTA-3’	4588.8	4585.0
2	**Y1**	5’-TAC AAC A***Pz***T AAT GTG-3’	4606.8	4602.9
3	**X2**	5’-CAC ATT A***Pm***T GTT GTA-3’	4602.8	4597.9
4	**Y2**	5’-TAC AAC A***Pm***T AAT GTG-3’	4620.8	4616.3
5	**X3**	5’-GCG CG**X XXX X**GG CCG-3’	4758.9	4757.6
6	**Y3**	5’-CGG CC**X XXX X**CG CGC-3’	4678.9	4676.6

Melting point experiments

Melting profiles were measured on a *JASCO V-650* spectrometer using quartz glass cuvettes with 10.00 mm path length. The samples contained 150 mM NaCl, 10 mM CHES buffer pH 9 and 1 μM of each strand in a final volume of 200 μL. The measurement was repeated at least three times with independent sample. Before the measurement, the oligonucleotides were hybridized with specific metal ion by slowly cooling down the samples from 85 °C to room temperature overnight. For the addition of metal source see table S1. The solutions were covered with silicon oil and tightly plugged. Absorbance was recorded in the forward and reverse direction at temperatures of 20 °C to 80 °C with a slope of 1 °C/min. At least 3 denaturing and renaturing ramps were performed and averaged for evaluation of the melting point. T_M values were calculated as the zero-crossing of 2nd derivate of the 349 nm background corrected change in hyperchromicity at 260 nm.

Circular dichroism spectra measurements

CD spectra were measured on a *JASCO J-810* spectrometer using quartz glass cuvettes with 10.00 mm path length. The sample preparation was identical with the procedures used for the T_M measurements. Five spectra from 320 nm to 210 nm were accumulated in each case with scanning speed of 50 nm/min. Blank correction was made of aqueous solution of buffer and salt and measured for every individual cuvette separately. The obtained CD curves were then smoothed using the JASCO built-in software.

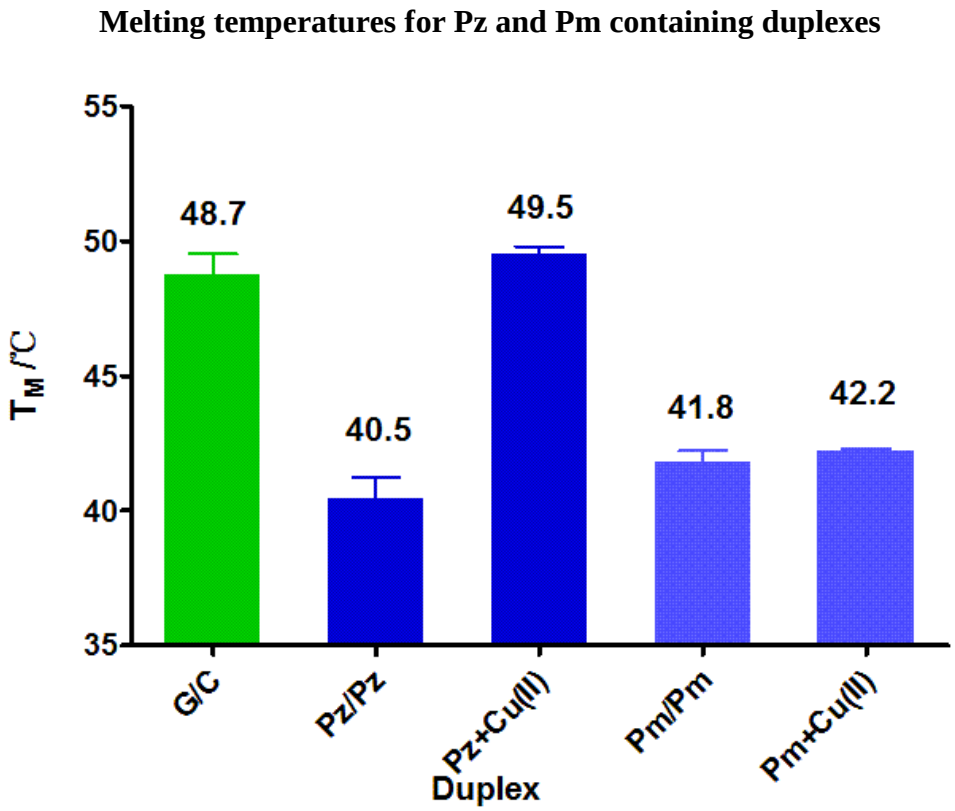


Fig. S1. Graphical comparison of the thermal stability of duplexes X1/Y1 and X2/Y2 without any additives and with Cu^{2+}, compared to canonical dsDNA. Conditions: 150 mM NaCl, 10 mM CHES buffer pH 9.0, 1 μM of each strand and 1 μM $CuSO_4$ when required.

Melting temperatures of duplex X1/Y1 with 1 equivalent of different metal ions

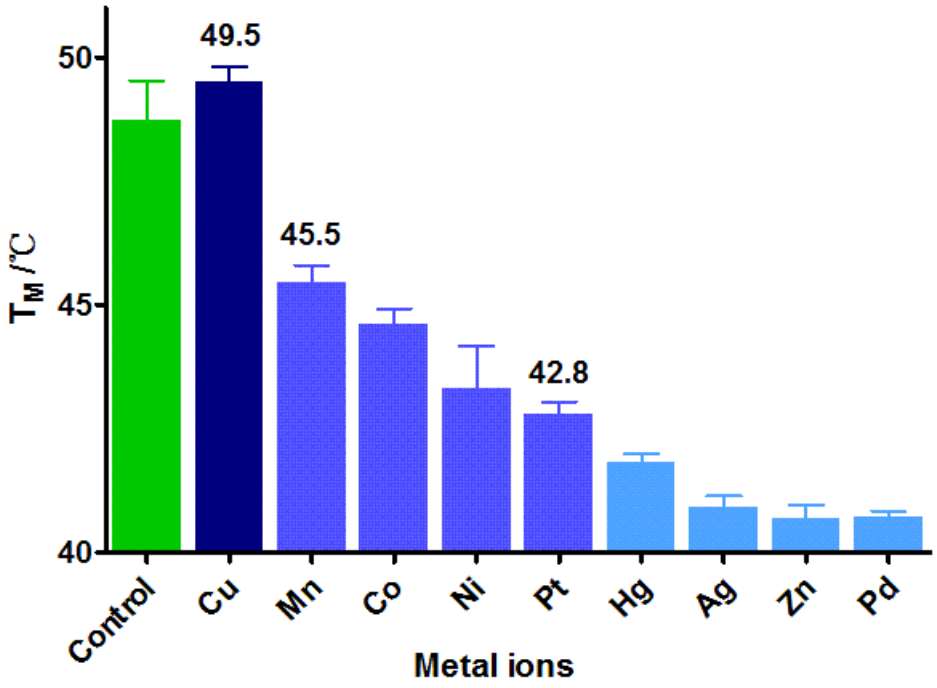


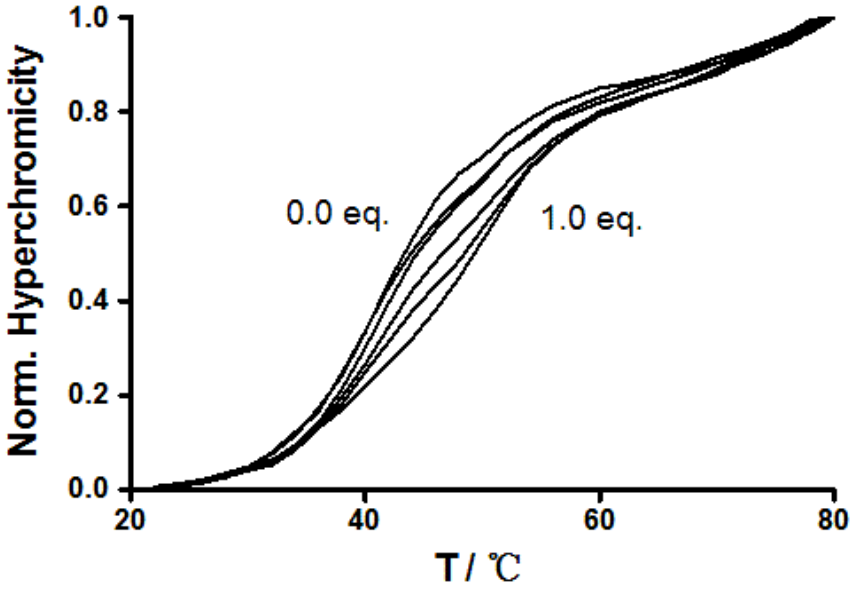
Fig. S2. Graphical comparison of the thermal stability of duplex X1/Y1 with different metal ions. Conditions: 150 mM NaCl, 10 mM CHES buffer pH 9.0, 1 μM of each strand and 1μM [metal ion].

Table S2. Melting temperatures for duplex X1/Y1 with different metal ions

Entry	Metal / Metal source	T_M (°C)
1	- (Control duplex with G/C base pair)	48.7
2	Cu (II) / $CuSO_4$	49.5
3	Mn (II/III) / $MnSO_4$	45.5
4	Co (II) / $CoCl_2$	44.6
5	Ni (II) / $NiCl_2$	43.3
6	Pt (II) / K_2PtCl_4	42.8
7	Hg (II) / $HgCl_2$	41.8
8	Ag (I) / $AgNO_3$	40.9
9	Zn (II) / $ZnCl_2$	40.7
10	Pd (II) / $PdCl_2$	40.7

Melting curves for Cu(II) and Mn(II) titration (0.0 - 1.0 eq)

a)



b)

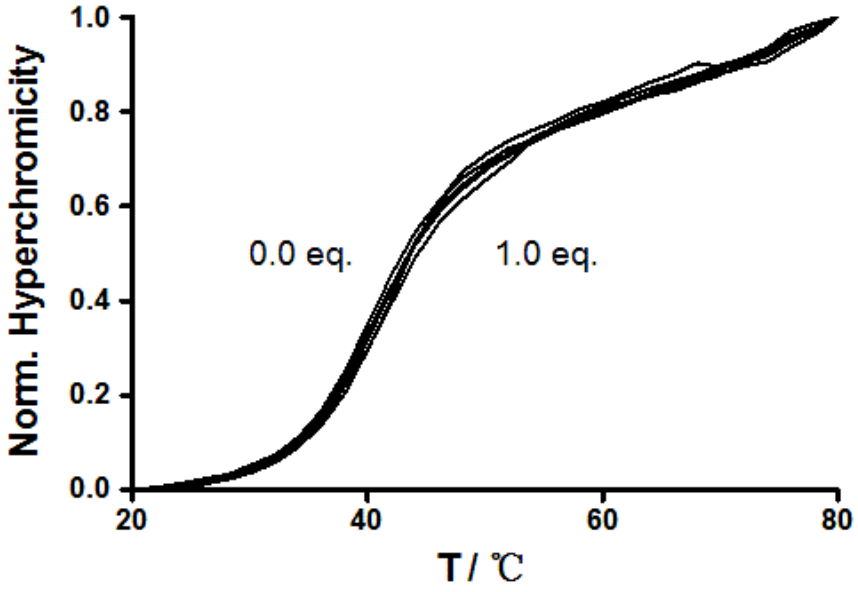


Fig. S3. Comparison of melting curves of duplex X1/Y1 in the presence of different equivalents of a) Cu^{2+} (0.0-1.0 eq, 0.2 eq per titration) and b) Mn^{2+} (0.0-1.0 eq, 0.2 eq per titration).Conditions: 150 mM NaCl, 10 mM CHES buffer pH 9.0, 1 μM of each strand.

Melting curves for duplex X3/Y3

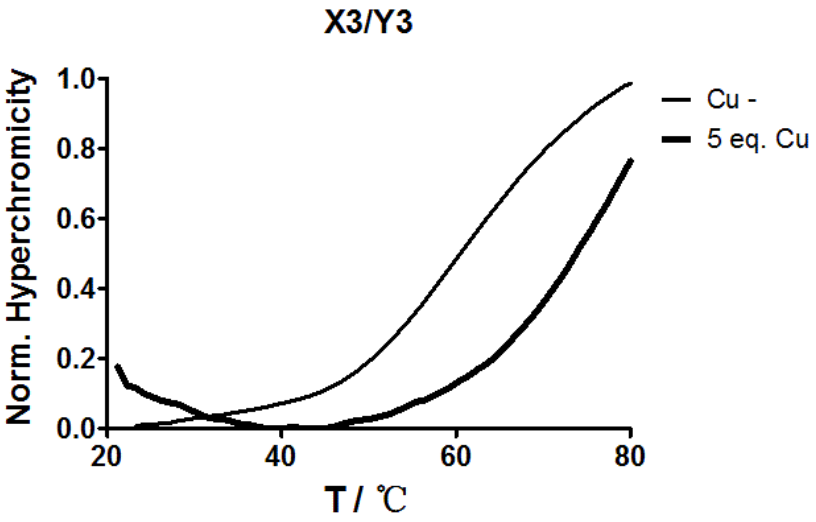


Fig. S4. Comparison of melting curves of duplex X3/Y3 in the presence and in the absence of 5 eq of Cu^{2+}. Conditions: 150 mM NaCl, 10 mM CHES buffer pH 9.0, 1 μM of each strand.

UV absorption changes of duplex X3Y3 at various concentrations of Cu^{2+}

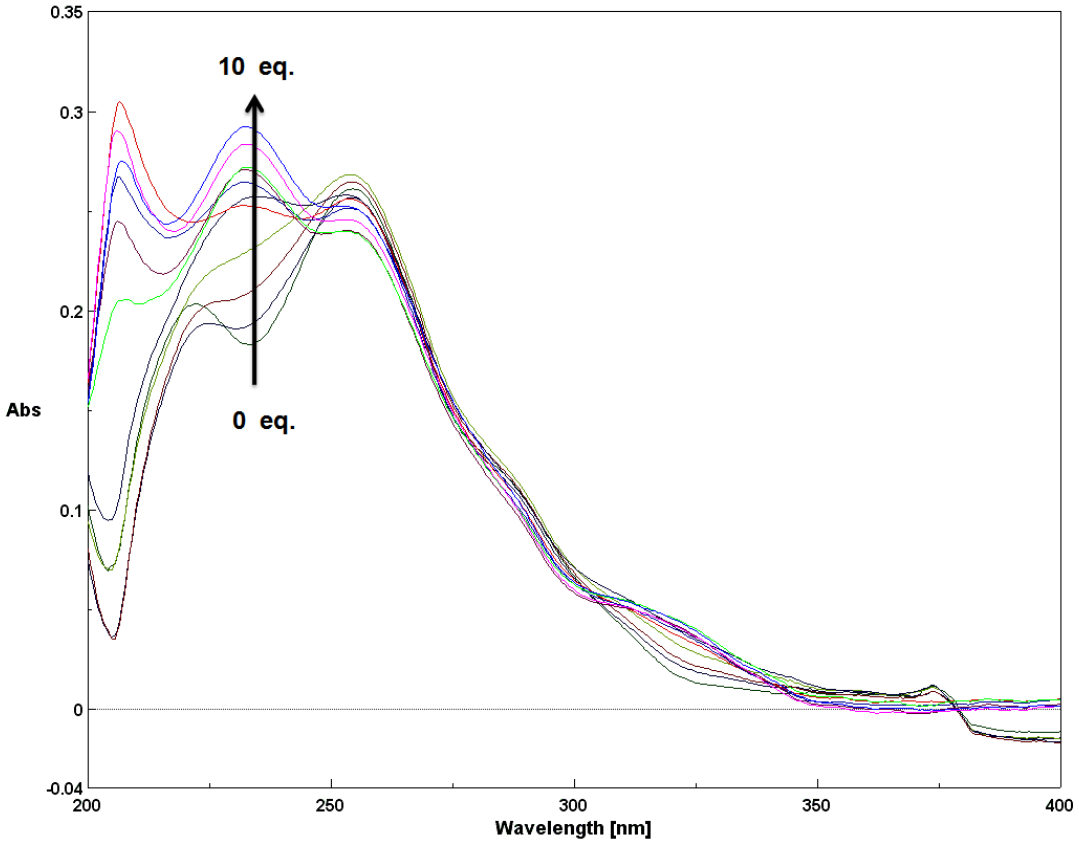
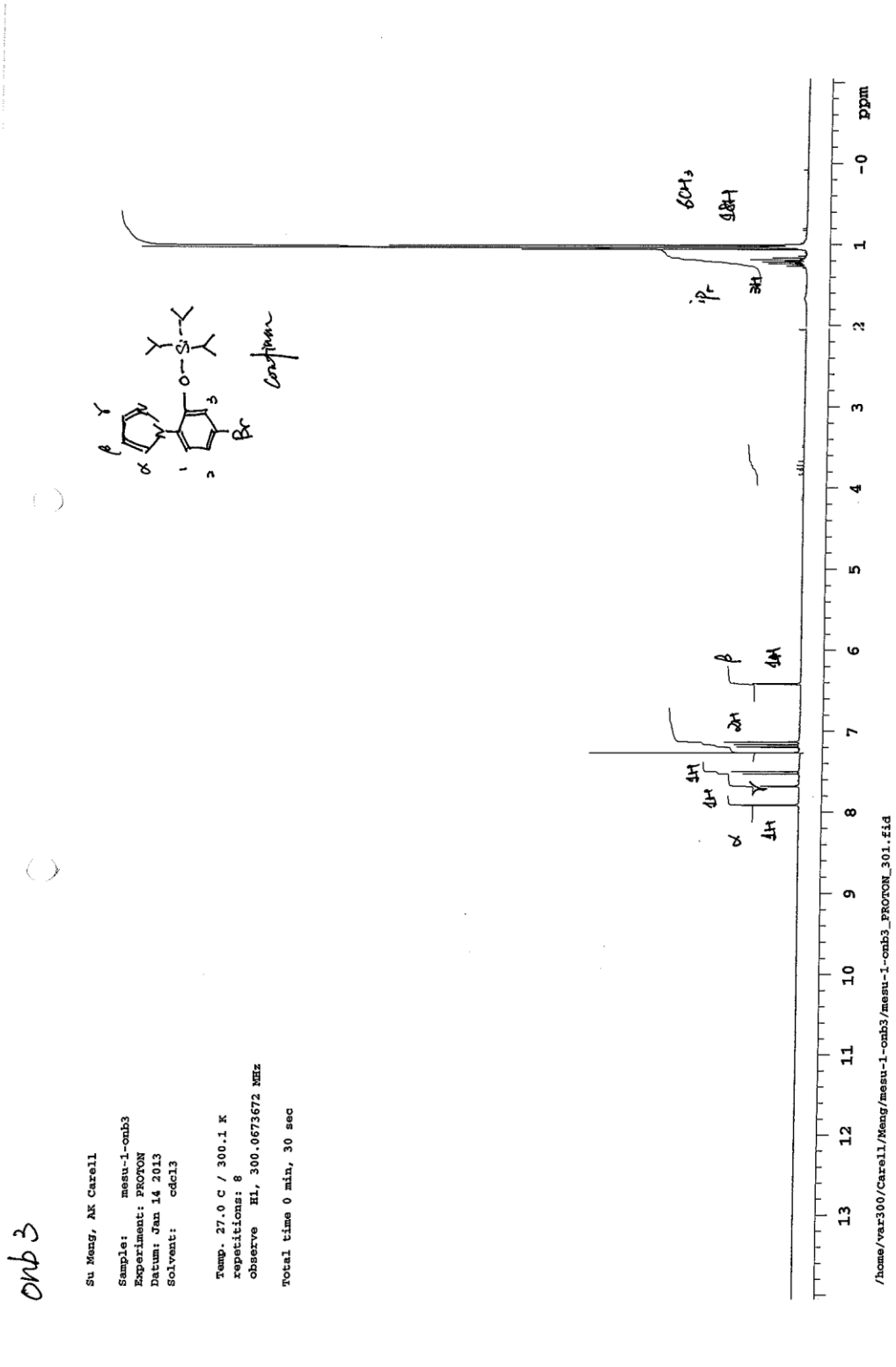


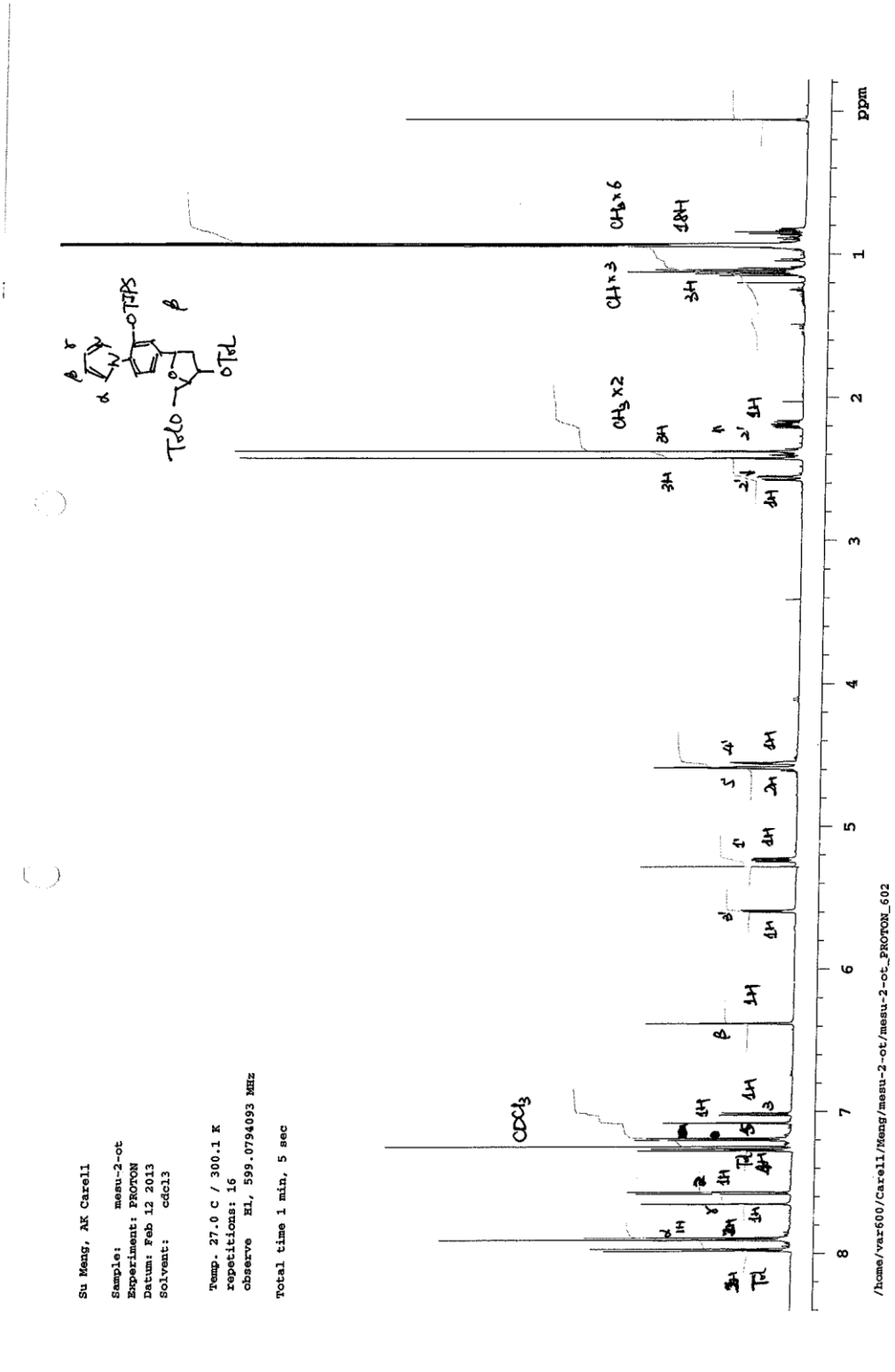
Fig. S5. UV spectra of Cu(II) titration of X3/Y3, [Cu^{2+}]/[duplex] from 0 to 10. Condition: 150 mM NaCl, 10 mM CHES buffer pH 9.0, 1 μM of each strand, Cu^{2+} (0.0-10.0 eq, per titration).

V. Selected ^{1}H NMR spectra for the synthesized compounds

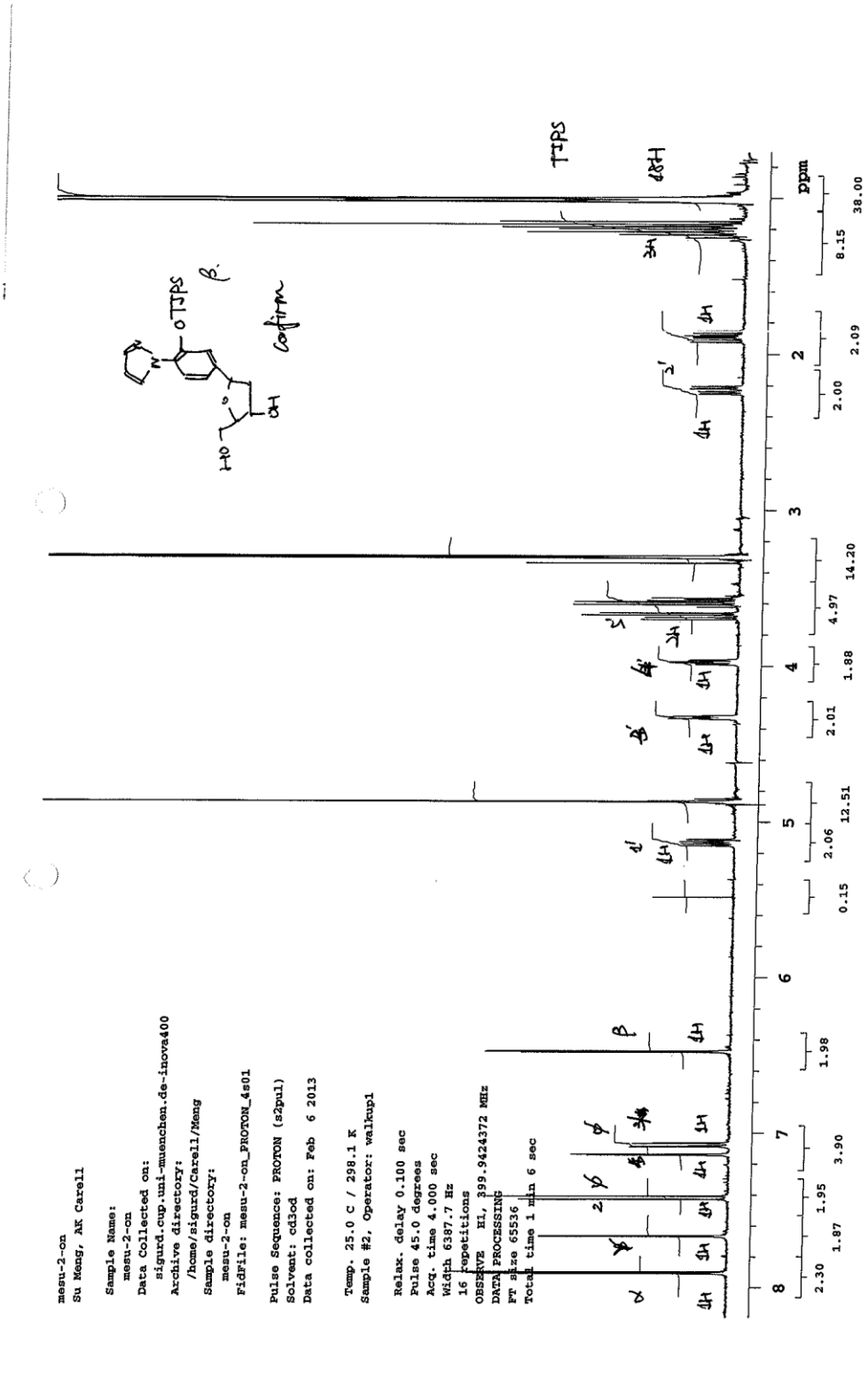
Compound **8**



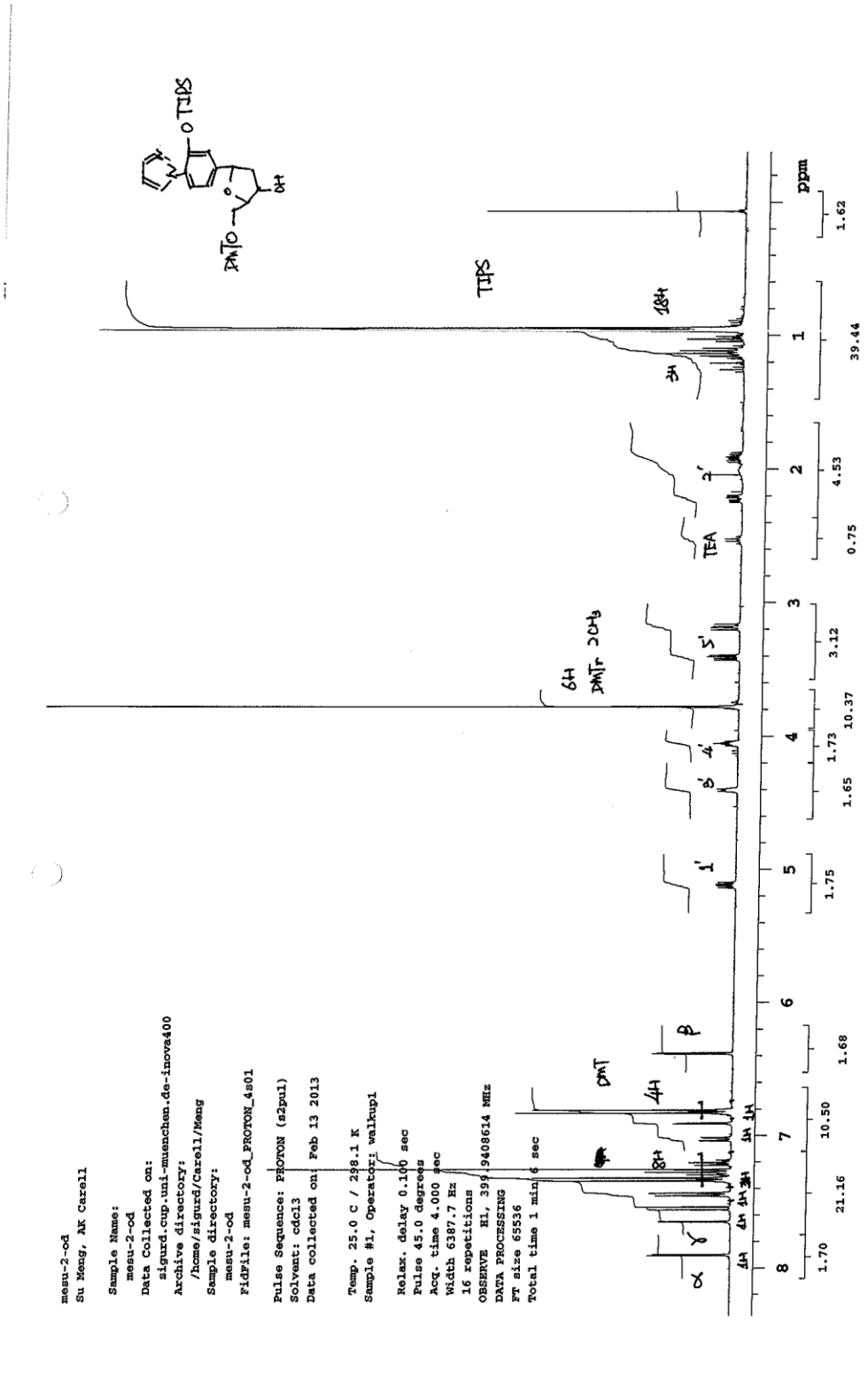
Compound **10**


Su Meng, AK Carell
Sample: mesu-2-ot
Experiment: PROTON
Datum: Feb 12 2013
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
repetitions: 16
observe H1, 599.0794093 MHz
Total time 1 min, 5 sec
/home/varx600/Carell/Meng/mesu-2-ot/mesu-2-ot_PROTON_602
ppm

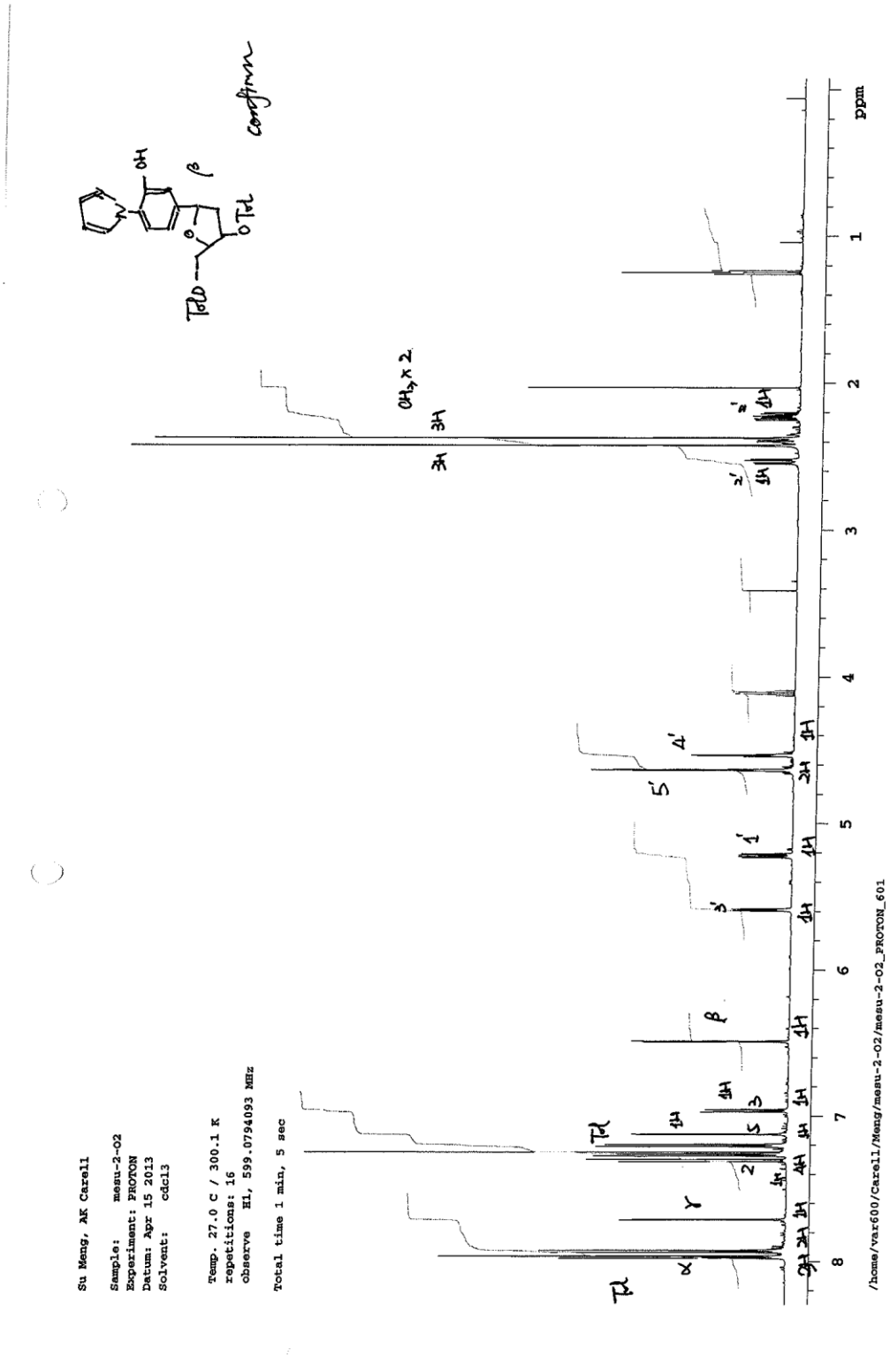
Compound**11**


mesu-2-on
Su Meng, AK Carell
Sample Name:
mesu-2-on
Data Collected on:
sigurd.cup.uni-muenchen.de-inova400
Archive directory:
/home/sigurd/Carell/Meng
Sample directory:
mesu-2-on
FidFile: mesu-2-on_PROTON_4s01
Pulse Sequence: PROTON (s2pul)
Solvent: cd3od
Data collected on: Feb 6 2013
Temp. 25.0 C / 298.1 K
Sample #2, Operator: walkup1
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 6387.7 Hz
16 repetitions
OBSERVE H1, 399.9424372 MHz
DATA PROCESSING
FT size 65536
Total time 1 min 6 sec
TIPS
OH
ppm

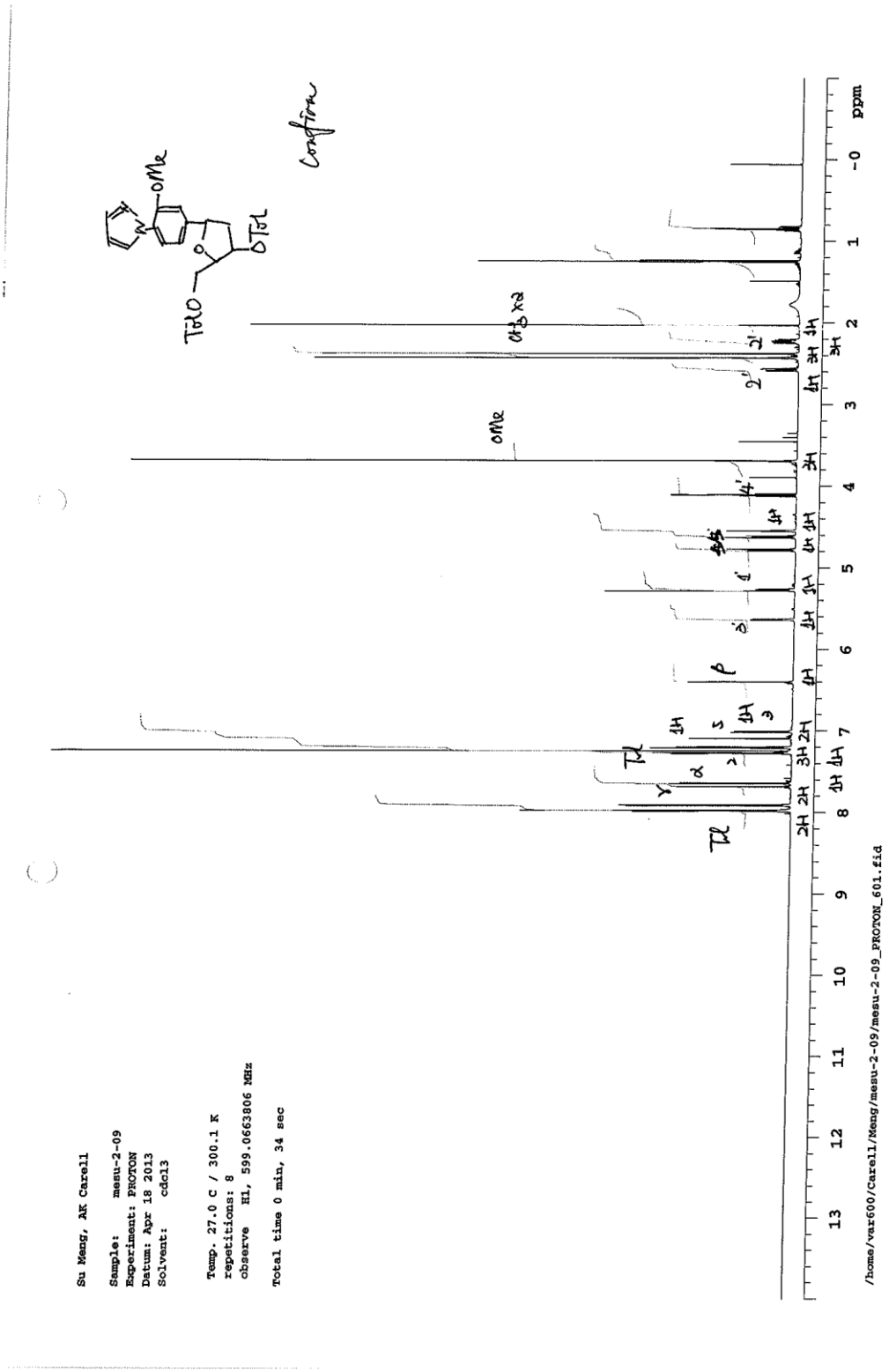
Compound**12**


mesu-2-od
Su Meng, AK Carell
Sample Name:
mesu-2-od
Data Collected on:
sigurd.cup.uni-muenchen.de-inova400
Archive directory:
/home/sigurd/Carell/Meng
Sample directory:
mesu-2-od
FidFile: mesu-2-od_PROTON_4s01
Pulse Sequence: PROTON (s2pul)
Solvent: cdcl3
Data collected on: Feb 13 2013
Temp. 25.0 C / 298.1 K
Sample #1, Operator: walkup1
Relax. delay 0.100 sec
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 6387.7 Hz
16 repetitions
OBSERVE H1, 399.9408614 MHz
DATA PROCESSING
FT size 65536
Total time 1 min, 6 sec
TIPS
TEA
ppm

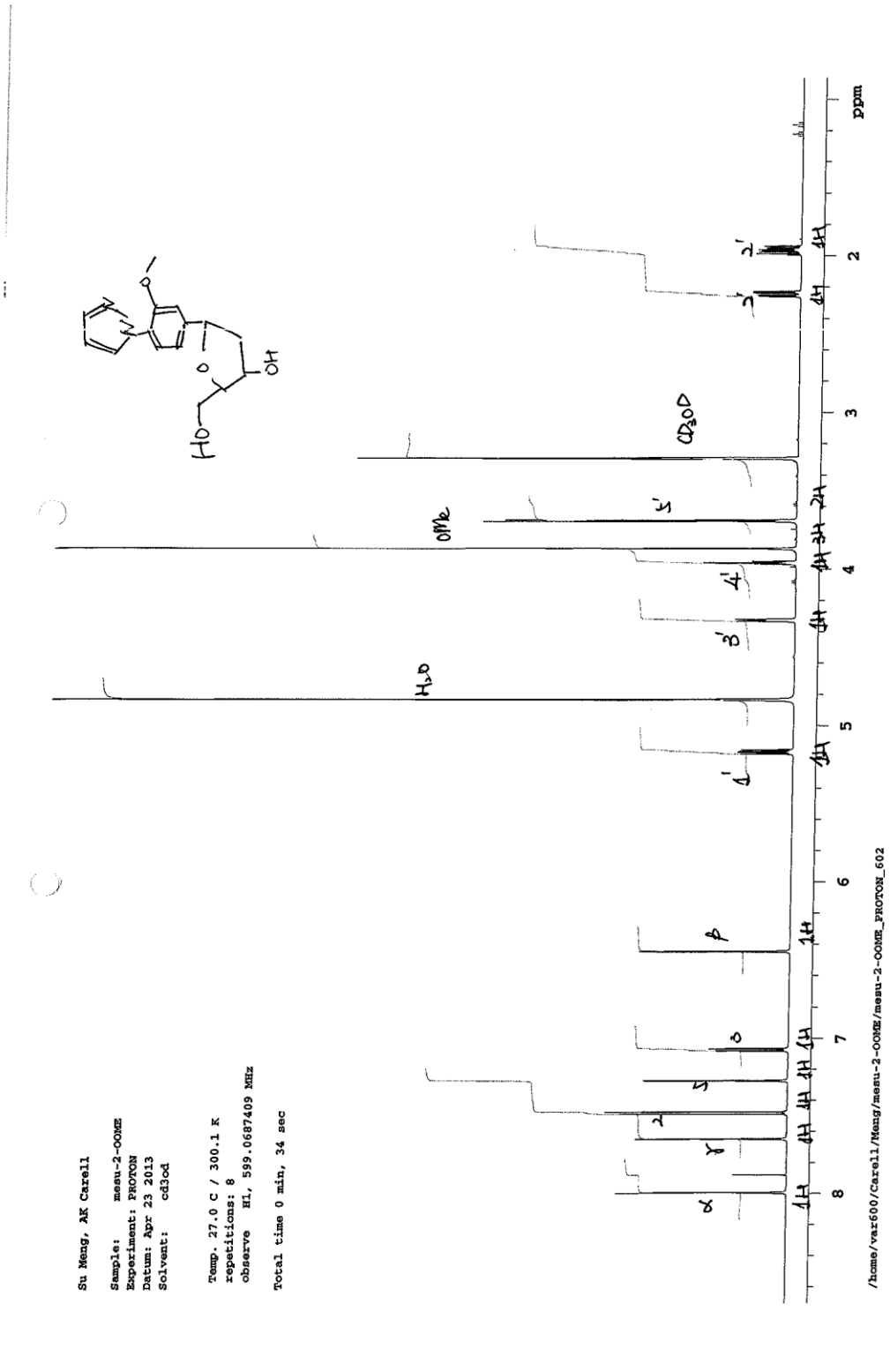
Compound **15**


Su Meng, AK Carell
Sample: mesu-2-02
Experiment: PROTON
Datum: Apr 15 2013
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
repetitions: 16
observe H1, 599.0794093 MHz
Total time 1 min, 5 sec
/home/var600/Carell/Meng/mesu-2-02/mesu-2-02_PROTON_601
ppm

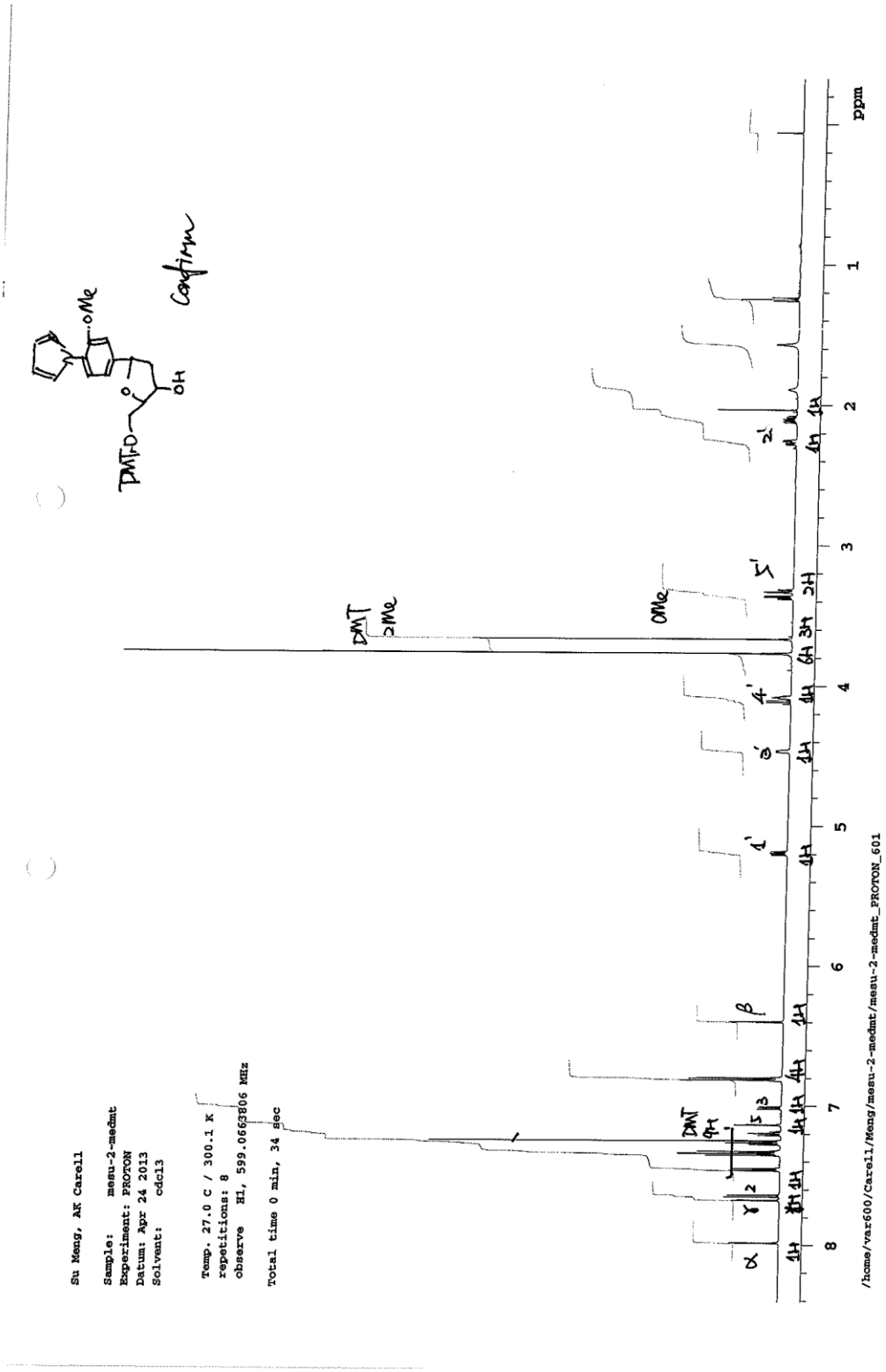
Compound **16**


Su Meng, AK Carell
Sample: mesu-2-09
Experiment: PROTON
Datum: Apr 18 2013
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
repetitions: 8
observe H1, 599.0663806 MHz
Total time 0 min, 34 sec
/home/var600/Carell/Meng/mesu-2-09/mesu-2-09_PROTON_601.fid
ppm

Compound **17**


Su Meng, AK Carell
Sample: mesu-2-OOME
Experiment: PROTON
Datum: Apr 23 2013
Solvent: cd3od
Temp. 27.0 C / 300.1 K
repetitions: 8
observe H1, 599.0687409 MHz
Total time 0 min, 34 sec
HO
OH
O
OMe
CD3OD
H2O
ppm
/home/vxr600/Carell/Meng/mesu-2-OOME/mesu-2-OOME_PROTON_602

Compound **18**


Confirm
OMe
OH
DMTrO
Su Meng, AK Carell
Sample: mesu-2-medmt
Experiment: PROTON
Datum: Apr 24 2013
Solvent: cdcl3
Temp. 27.0 C / 300.1 K
repetitions: 8
observe H1, 599.0663806 MHz
Total time 0 min, 34 sec
/home/vxr600/Carell/Meng/mesu-2-medmt/mesu-2-medmt_PROTON_601
ppm