New affinity-based probes for capture of flavonoid-binding proteins

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Supporting information

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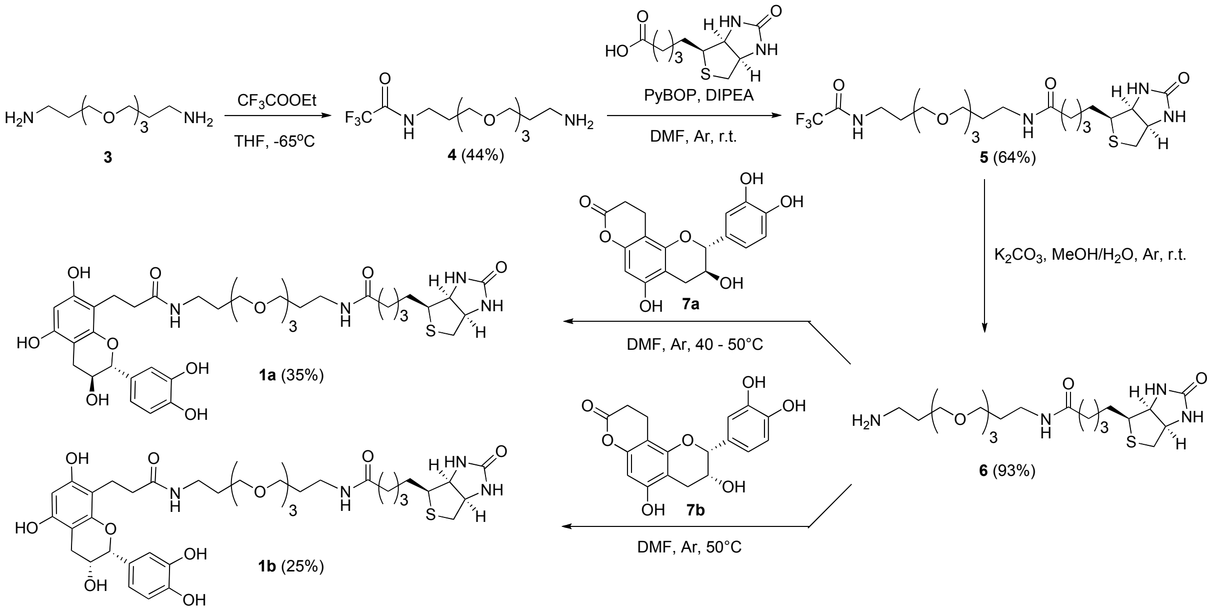
General

All moisture and oxygen sensitive reactions were carried out in flame-dried glassware under inert atmosphere with dry solvents. Dichloromethane (CH_2Cl_2) and dioxane were distilled from CaH_2 under nitrogen prior to use. Tetrahydrofurane (THF) was distilled from sodium and benzophenon under nitrogen immediately before use. Dimethylformamide (DMF) was distilled from CaH_2 or 4 Å molecular thieves under reduced pressure prior to use. Methanol (MeOH), ethyl acetate (EtOAc), acetone, acetonitrile, *n*-hexane, ethanol, trifluoroacetic acid (TFA), ammonium hydroxide solution 28-30% in water (NH_4OH) and cyclohexane were used as received. Evaporations were conducted under reduced pressure at temperatures less than 40 °C except for DMF which was evaporated at 50 °C. Reactions were monitored by thin layer chromatography (TLC) carried out on 0.25 mm E. Merck silica plates (60 F_{254}) using UV light for visualization and a phosphomolybdic acid solution or a cerium molybdate solution and heat as the developing agent. Column chromatography was carried out under positive pressure using 40-63 µm silica gel (Merck) and the indicated solvents. Melting points were recorded in open capillary tubes on a Buchi B-540 apparatus and are uncorrected. IR spectra were recorded with a Bruker IFS55 FT-IR spectrometer. Solution phase NMR spectra of samples in the indicated solvent were run at 300 MHz or 400 MHz and calibrated using residual solvent as an internal standard. Coupling constant (*J*) are given in Hertz (Hz). Splitting patterns are abbreviated as follow: s (singlet), bs (broad singlet), d (doublet), t (triplet), q (quartet), p (pentet) and m (multiplet). Carbon multiplicities were determined by DEPT 135 experiments. Electrospray (ESIMS, positive mode unless otherwise noted) and high resolution mass spectrometric analysis (HRMS, positive mode unless otherwise noted) were obtained from the mass spectrometry laboratory of the Institut Européen de Chimie et Biologie (IECB) and from the Centre d'Etude Structurale et d'Analyse des Molécules Organiques (CESAMO, Université Bordeaux 1).

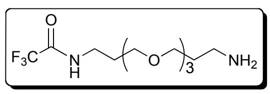
Experimental Procedures

Synthesis of catechin- and epicatechin-bearing probes (**1a-b**):



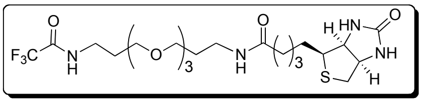
Scheme S1: synthesis of probes **1a** and **1b**

Compound 4



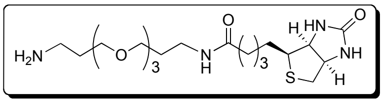
Adapted from the procedure described by Fixon-Owoo *et al.*,[1] commercially available 4,7,10-trioxa-1,13-tridecanediamine (**3**, 3.0 g, 13.6 mmol) was dissolved in anhydrous THF (9 mL) under nitrogen atmosphere and cooled to –65 °C. To this solution, ethyltrifluoroacetate (1.9 g, 13.6 mmol) was added dropwise and the resulting solution was stirred for 1 h at –65 °C under nitrogen atmosphere. The solution was then slowly warmed to room temperature. Solvent and volatiles were removed *in vacuo* and the remainder taken up in water (10 mL). The resulting aqueous solution was then extracted with CH_2Cl_2 (6 × 15 mL). The combined organic layers were dried over Na_2SO_4, filtered and concentrated *in vacuo* to give a yellow oil, which was purified by column chromatography, eluted with CH_2Cl_2/MeOH/NH_4OH (9.8:0.8:0.2) to remove by-products and then CH_2Cl_2/MeOH/NH_4OH (9:1:0.2) to furnish the product **4** as pale yellowish oil (1.88 g, 44%): R_f = 0.31 [CH_2Cl_2/MeOH/NH_4OH (8.8:0.8:0.2)]; IR (ZnSe) ν_{max} 3363, 2876, 1714, 1188, 1156 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 1.56 (bs, 2H), 1.70 (p, *J* = 6.2 Hz, 2H), 1.80-1.88 (m, 2H), 2.79 (t, *J* = 6.5 Hz, 2H), 3.45 (t, *J* = 6.0 Hz, 2H), 3.54-3.64 (m, 12H), 8.79 (bs, 1H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 157.2 (q, *J* = 36.6 Hz, $COCF_3$), 116.1 (q, *J* = 287.8 Hz, CF_3), 70.5 (CH_2), 70.4 (CH_2), 70.0 (CH_2), 69.7 (CH_2), 69.7 (CH_2), 39.8 (CH_2), 38.2 (CH_2), 32.9 (CH_2), 28.0 (CH_2); ESIMS *m/z* (rel. intensity) 317 (100) $[M+H]^+$; HRMS (ESI-TOF) calcd for $C_{12}H_{24}F_3N_2O_4$ $[M+H]^+$ 317.1683, found 317.1697.

Compound 5



To a stirred solution of commercially available biotin (0.77 mg, 3.16 mmol) in anhydrous DMF (25 mL) were added *N*,*N*-Diisopropylethylamine (DIPEA, 0.55 mL, 3.16 mmol) and benzotriazol-1-yl-oxytripyrrolidinophosphonium hexafluorophosphate (PyBOP, 2.14 g, 4.11 mmol). After stirring at room temperature for 30 minutes under argon atmosphere, a solution of **4** (1.30 g, 4.11 mmol) and DIPEA (0.72 mL, 4.11 mmol) in anhydrous DMF (12 mL) was added. The resulting mixture was stirred at room temperature for 24 h under argon atmosphere. The solution was then diluted with water (15 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organics layers were washed with an aqueous saturated solution of NH_4Cl (50 mL), brine (2 × 50 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo* to give a yellowish sticky solid, which was purified by column chromatography, eluted with CH_2Cl_2/MeOH/NH_4OH (9.5:0.5:0.2 to remove impurities, then 9:1:0.2) to furnish the product **5** as a white translucent wax (1.10 g, 64%): R_f = 0.39 [CH_2Cl_2/MeOH/NH_4OH (9:1:0.2)]; IR (ZnSe) ν_{max} 3286, 2928, 2871, 1697, 1156 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.41-1.49 (m, 2H), 1.54-1.85 (m, 8H), 2.20 (t, J = 7.3 Hz, 2H), 2.71 (d, J = 12.7 Hz, 1H), 2.93 (dd, J = 12.7, 5.0 Hz, 1H), 3.18-3.24 (m, 1H), 3.26 (t, J = 6.8 Hz, 2H), 3.38 (t, J = 6.9 Hz, 2H), 3.50-3.55 (m, 4H), 3.57-3.66 (m, 8H), 4.30 (dd, J = 7.9, 4.5 Hz, 1H), 4.47-4.51 (m, 1H); ^{13}C-NMR (75.5 MHz, CD_3OD) δ 175.9 (CO), 166.0 (CO), 158.8 (q, J = 36.6 Hz, $COCF_3$), 117.5 (q, J = 286.8 Hz, CF_3), 71.5 (2 CH_2), 71.2 (CH_2), 71.2 (CH_2), 69.9 (CH_2), 69.5 (CH_2), 63.3 (CH), 61.6 (CH), 57.0 (CH), 41.0 (CH_2), 38.3 (CH_2), 37.8 (CH_2), 36.8 (CH_2), 30.4 (CH_2), 29.8 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 26.9 (CH_2); ESIMS *m/z* (rel. intensity) 543 (45) $[M+H]^+$, 565 (100) $[M+Na]^+$; HRMS (ESI-TOF) calcd for $C_{22}H_{37}F_3N_4O_6NaS$ $[M+Na]^+$ 565.2278, found 565.2272.

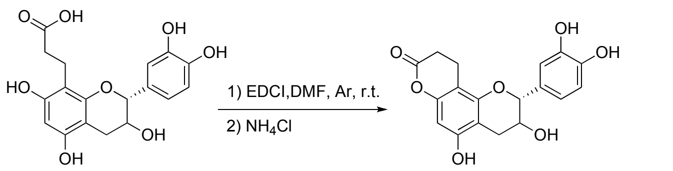
Compound 6



To a stirred solution of **5** (0.91 g, 1.68 mmol) in methanol (6 mL) was added dropwise a solution of K_2CO_3 (0.70 g, 5.04 mmol) in a mixture of methanol (12 mL) and water (5 mL). The resulting mixture was stirred at room temperature for 16 h under argon atmosphere. The solvents were then removed *in vacuo* and the crude was taken up in MeOH (10 mL), filtered to remove K_2CO_3 and concentrated *in vacuo* to give a yellow gel, which was purified by column chromatography, eluted with CH_2Cl_2/MeOH/NH_4OH (9:1:0.2 to remove impurities, and then 8:2:0.2) to furnish the product **6** as a yellow sticky oil (698 mg, 93%): R_f = 0.18 [CH_2Cl_2/MeOH/NH_4OH

(7:3:0.2)]; IR (ZnSe) ν_{max} 3313, 2933, 2877, 1683, 1202, 1133 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.41-1.49 (m, 2H), 1.54-1.80 (m, 6H), 1.88 (p, J = 6.3 Hz, 2H), 2.21 (t, J = 7.3 Hz, 2H), 2.71 (d, J = 12.7 Hz, 1H), 2.93 (dd, J = 12.8, 4.9 Hz, 1H), 3.01 (t, J = 6.5 Hz, 2H), 3.18-3.24 (m, 1H), 3.26 (t, J = 6.9 Hz, 2H), 3.52 (t, J = 6.1 Hz, 2H), 3.57-3.66 (m, 10H), 4.30 (dd, J = 7.9, 4.5 Hz, 1H), 4.48-4.52 (m, 1H); ^{13}C-NMR (75.5 MHz, CD_3OD) δ 176.0 (CO), 166.1 (CO), 71.4 (CH_2), 71.2 (CH_2), 71.1 (CH_2), 71.1 (CH_2), 70.4 (CH_2), 69.8 (CH_2), 63.4 (CH), 61.6 (CH), 57.0 (CH), 41.0 (CH_2), 40.1 (CH_2), 37.7 (CH_2), 36.8 (CH_2), 30.5 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 29.4 (CH_2), 26.9 (CH_2); ESIMS *m/z* (rel. intensity) 447 (100) $[M+H]^+$; HRMS (ESI-TOF) calcd for $C_{20}H_{39}N_4O_5S$ $[M+H]^+$ 447.2635, found 447.2632.

Synthesis of (*2R*,*3S*)-8-lactone-catechin (7a) and -epicatechin (7b) :



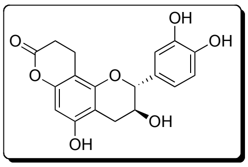
8a: (*2R*,*3S*)-catechin derivative
8b: (*2R*,*3R*)-epicatechin derivative

7a: (*2R*,*3S*)-lactone-8-catechin; 93 %
7b: (*2R*,*3R*)-lactone-8-epicatechin; 74 %

Scheme S2: synthesis of compounds **7a** and **7b**

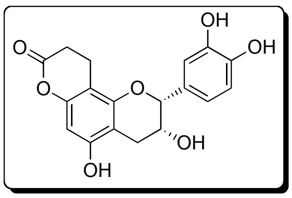
The A-ring-modified catechin (**8a**) or epicatechin (**8b**) were prepared according to the procedure described in a previous study.[2]

(2*R*,3*S*)-8-lactone-catechin (7a)



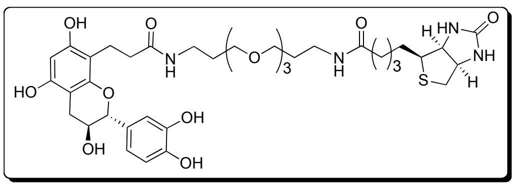
To a stirred solution of **8a** (79 mg, 0.22 mmol) in anhydrous DMF (3 mL) was added EDCI (46 mg, 0.24 mmol). The reaction mixture was stirred for 19 h at room temperature under argon atmosphere. The solution was evaporated until dryness, taken up in ethyl acetate (80 mL), washed twice with a saturated aqueous solution of NH_4Cl (2 × 15 mL), brine (15 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to furnish the product **7a** as a white powder (70 mg, 93%): mp 222-223 °C; R_f = 0.51 [CH_2Cl_2/MeOH (8:2)]; IR (ZnSe) ν_{max} 3395, 1739, 1618, 1272, 1168, 1114 cm^{-1}; ^{1}H-NMR (300 MHz, acetone-d_6) δ 2.57-2.71 (m, 3H), 2.81-2.98 (m, 3H + H_2O), 4.02-4.12 (m, 1H + OH), 4.71 (d, J = 7.4 Hz, 1H), 6.16 (s, 1H), 6.76 (dd, J = 8.2, 1.8 Hz, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.90 (d, J = 1.8 Hz, 1H), 7.97-8.44 (m, 3H, ArOH); ^{13}C-NMR (75.5 MHz, acetone-d_6) δ 168.9 (CO), 155.7 (ArC), 152.8 (ArC), 152.1 (ArC), 145.8 (ArC), 145.7 (ArC), 131.8 (ArC), 119.8 (ArCH), 115.8 (ArCH), 115.0 (ArCH), 105.3 (ArC), 102.3 (ArC), 96.2 (ArCH), 82.8 (CH), 67.8 (CH), 29.4 (CH_2), 28.6 (CH_2), 18.0 (CH_2).

(2*R*,3*R*)-8-lactone-epicatechin (7b)



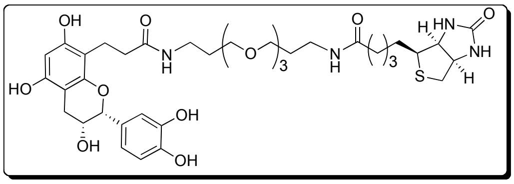
To a stirred solution of **8b** (114 mg, 0.32 mmol) in anhydrous DMF (9 mL) was added EDCI (66 mg, 0.35 mmol). The reaction mixture stirred for 18 h at room temperature under argon atmosphere. The solution was evaporated until dryness, taken up in ethyl acetate (120 mL), washed twice with a saturated aqueous solution of NH_4Cl (2 × 20 mL), brine (20 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to furnish the product **7b** as a beige foam (80 mg, 74%): mp 216-217 °C; R_f = 0.75 [CH_2Cl_2/MeOH (8:2)]; IR (ZnSe) ν_{max} 3367, 2361, 1619, 1112 cm^{-1}; ^{1}H-NMR (300 MHz, acetone-d_6) δ 2.67-2.72 (m, 2H), 2.87-2.92 (m, 4H), 4.30-4.32 (m, 1H), 4.98 (s, 1H), 6.15 (s, 1H), 6.81 (d, J = 8.1 Hz, 1H), 6.87 (dd, J = 8.2, 1.6 Hz, 1H), 7.09 (d, J = 1.9 Hz, 1H), 8.02 (bs, 3H); ^{13}C-NMR (75.5 MHz, acetone-d_6) δ 169.0 (CO), 156.0 (ArC), 153.0 (ArC), 151.9 (ArC), 145.5 (ArC), 145.3 (ArC), 131.9 (ArC), 119.0 (ArCH), 115.6 (ArCH), 114.9 (ArCH), 104.4 (ArC), 102.3 (ArC), 96.1 (ArCH), 79.5 (CH), 66.3 (CH), 29.4 (CH_2), 29.2 (CH_2), 17.9 (CH_2).

Probe 1a



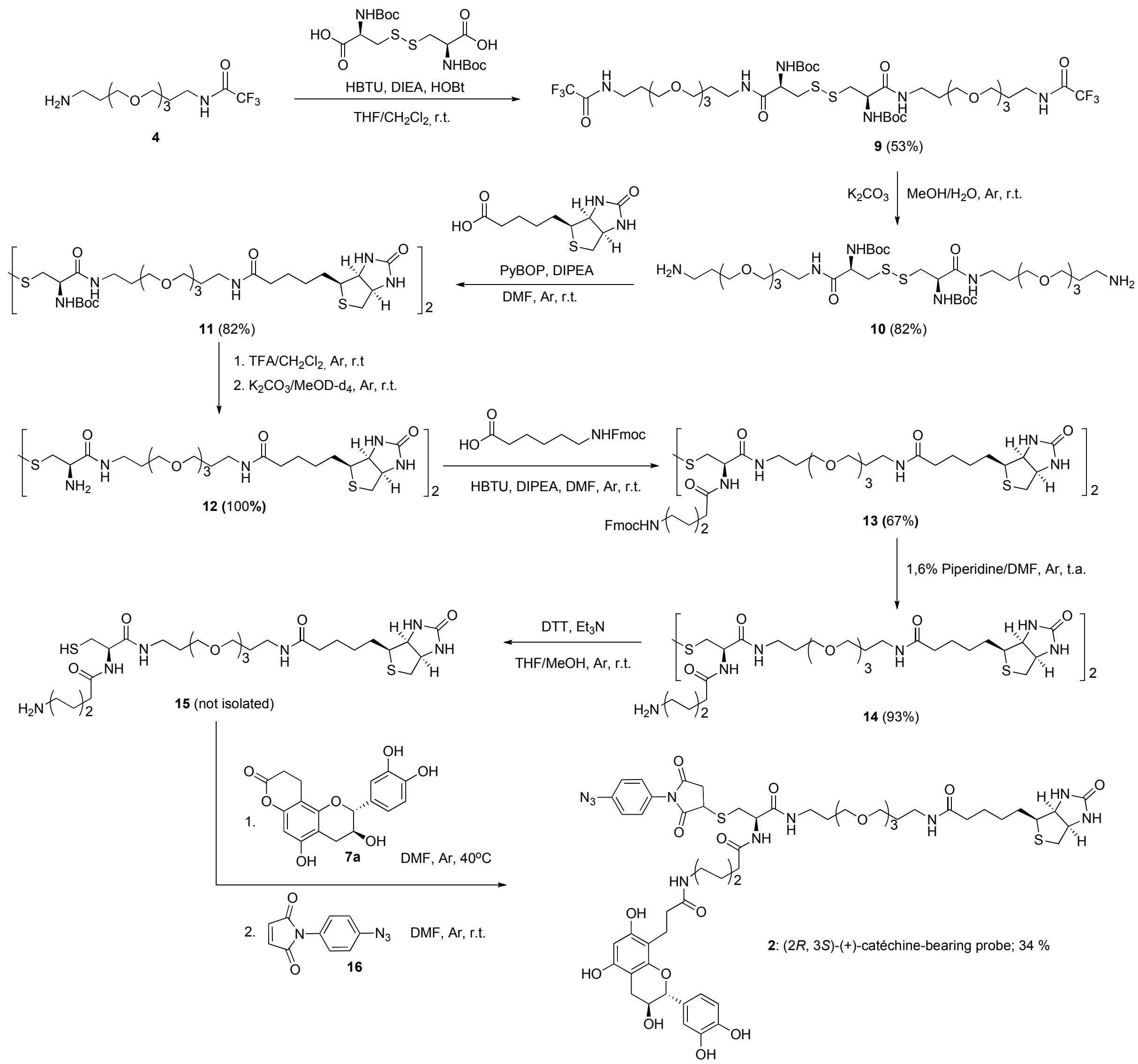
To a stirred solution of **6** (0.259 g, 0.58 mmol) in anhydrous DMF (6.6 mL) was added (2*R*,3*S*)-8-lactone-catechin (**7a**, 0.100 g, 0.29 mmol). The reaction mixture was stirred for 24 h at 40 °C under argon atmosphere and then heated at 50 °C for 24 h. The reaction mixture was then concentrated *in vacuo* to give an orange foam, which was purified by column chromatography, eluted with CH_2Cl_2/MeOH (9:1 to remove impurities and then 8.5:1.5) to furnish the probe **1a** as a yellowish sticky oil (80 mg, 35%): R_f = 0.29 [CH_2Cl_2/MeOH (8:2)]; IR (ZnSe) ν_{max} 3386, 1618, 1449, 1103 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.39-1.46 (m, 2H), 1.54-1.78 (m, 8H), 2.21 (t, J = 7.3 Hz, 2H), 2.41-2.58 (m, 3H), 2.72 (d, J = 12.8 Hz, 1H), 2.78-2.95 (m, 4H), 3.15-3.26 (m, 5H), 3.41 (t, J = 6.1 Hz, 2H), 3.47-3.61 (m, 10H), 3.93-4.00 (m, 1H), 4.31 (dd, J = 7.8, 4.3 Hz, 1H), 4.51 (dd, J = 7.6, 4.8 Hz, 1H), 4.65 (d, J = 7.3 Hz, 1H), 6.03 (s, 1H), 6.73 (dd, J = 8.2, 1.7 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.87 (d, J = 1.7 Hz, 1H); ^{13}C-NMR (100 MHz, CD_3OD) δ 176.6 (CO), 176.0 (CO), 165.5 (CO), 155.3 (ArC), 155.1 (ArC), 154.5 (ArC), 146.2 (ArC), 146,1 (ArC), 132.5 (ArC), 119.8 (ArCH), 116.2 (ArCH), 115.2 (ArCH), 107.1 (ArC), 101.0 (ArC), 96.7 (ArCH), 82.7 (CH), 71.4 (CH_2), 71.1 (CH_2), 69.9 (CH_2), 69.8 (CH_2), 68.7 (CH), 63.4 (CH), 61.7 (CH), 56.8 (CH), 40.9 (CH_2), 37.9 (CH_2), 37.8 (CH_2), 36.9 (CH_2), 36.8 (CH_2), 30.3 (CH_2), 30.1 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 28.5 (CH_2), 26.8 (CH_2), 20.0 (CH_2); ESIMS *m/z* (rel. intensity) 813 (100) $[M+Na]^+$; HRMS (ESI-TOF) calcd for $C_{38}H_{54}N_4O_{12}NaS$ $[M+Na]^+$ 813.3351, found 813.3376.

Probe 1b



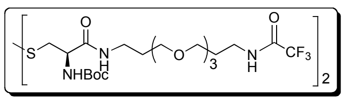
To a solution of **6** (0.128 g, 0.29 mmol) in anhydrous DMF (4 mL) was added (2*R*,3*R*)-8-lactone-epicatechin (**7b**, 0.070 g, 0.20 mmol). The resulting solution was stirred for 96 h at 50 °C under argon atmosphere. The reaction mixture was then concentrated *in vacuo* to give an orange foam, which was purified by column chromatography, eluted with CH_2Cl_2/MeOH (9:1 to remove impurities and then 8.7:1.3) to furnish the probe **1b** as a beige foam (40 mg, 25%): R_f = 0.36 [CH_2Cl_2/MeOH (8:2)]; IR (ZnSe) ν_{max} 3369, 1679, 1631, 1204, 1137, 1025 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.38-1.45 (m, 2H), 1.52-1.77 (m, 8H), 2.18 (t, *J* = 7.1 Hz, 2H), 2.50 (t, *J* = 7.2 Hz, 2H), 2.67 (d, *J* = 12.7 Hz, 1H), 2.77 (dd, *J* =16.9, 2.2 Hz, 1H), 2.84-2.96 (m, 4H), 3.13-3.26 (m, 5H), 3.39 (t, *J* = 6.2 Hz, 2H), 3.47-3.61 (m, 10H), 4.23-4.28 (m, 2H), 4.44-4.48 (m, 1H), 4.85 (bs, 1H), 6.02 (s, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.84 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.03 (d, *J* = 1.6 Hz, 1H); ^{13}C-NMR (75.5 MHz, CD_3OD) δ 176.8 (CO), 176.0 (CO), 166.1 (CO), 155.8 (ArC), 155.2 (ArC), 154.9 (ArC), 146.1 (ArC), 145.7 (ArC), 132.5 (ArC), 119.1 (ArCH), 116.0 (ArCH), 115.1 (ArCH), 107.4 (ArC), 100.2 (ArC), 96.7 (ArCH), 79.7 (CH), 71.5 (CH_2), 71.2 (CH_2), 71.1 (CH_2), 69.9 (CH_2), 69.8 (CH_2), 67.2 (CH), 63.4 (CH), 61.6 (CH), 57.0 (CH), 41.0 (CH_2), 37.8 (CH_2), 37.0 (CH_2), 36.9 (CH_2), 30.4 (CH_2), 30.2 (CH_2), 29.8 (CH_2), 29.6 (CH_2), 29.5 (CH_2), 26.9 (CH_2), 20.1 (CH_2); ESIMS *m/z* (rel. intensity) 813 (100) $[M+Na]^+$; HRMS (ESI-TOF) calcd for $C_{38}H_{54}N_4O_{12}SNa$ $[M+Na]^+$ 813.3351, found 813.3349.

Synthesis of catechin-bearing probe 2:



Scheme S3: synthesis of probe **2**

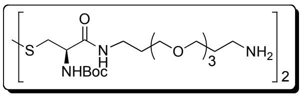
Compound 9



To a solution of Boc$_2$-cystine (3.44 g, 7.81 mmol) in anhydrous THF (80 mL) was added *O*-Benzotriazole-*N*,*N*,*N*',*N*'-tetramethyl-uronium-hexafluorophosphate (HBTU, 6.22 g, 16.40 mmol) and hydroxybenzotriazole (HOBt, 2.22 g, 16.40 mmol). To the resulting suspension was added a solution of **4** (5.19 g, 16.40 mmol) and *N*-diisopropylethylamine (DIPEA, 4.6 mL, 26.56 mmol) in anhydrous CH_2Cl_2 (80 mL). The resulting mixture was stirred at room temperature in the dark for 48 h under argon atmosphere. Then, CH_2Cl_2 (200 mL) was added and the organic layer was successively washed with an aqueous solution of HCl 0.5 M (3 × 30 mL), $NaHCO_3$ (3 × 30 mL) and brine (50 mL), dried over anhydrous

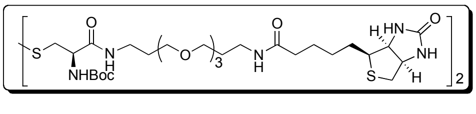
$MgSO_4$, filtrated and then evaporated. The resulting yellowish oil was purified by column chromatography, eluted with CH_2Cl_2/EtOAc/MeOH (4.8:5:0.2) to give the product **9** as a white translucent wax (4.16 g, 53%); R*f* = 0.44 [CH_2Cl_2/EtOAc/MeOH (4.2:5:0.8)]; IR (ZnSe) ν_{max} 3338, 2930, 2872, 1714, 1686, 1659, 1455, 1162 cm^{-1}; ^{1}H-NMR (300 MHz, acetone-*d*$_6$) δ 1.44 (bs, 18H), 1.72-1.88 (m, 8H), 2.97-3.04 (m, 2H), 3.17-3.22 (m, 2H), 3.28-3.35 (m, 4H), 3.43 (q, *J* = 6.4 Hz, 4H), 3.50-3.62 (m, 24H), 4.46-4.48 (m, 2H), 6.28 (d, *J* = 8.2 Hz, 2H), 7.58 (bs, 2H), 8.41 (bs, 2H); ^{13}C-NMR (100 MHz, acetone-*d*$_6$) δ 171.0 (CO), 157.4 (q, *J* = 36.1 Hz, $COCF_3$), 156.4 (CO), 117.1 (q, *J* = 287.6 Hz, CF_3), 79.8 (Cq), 71.1 (CH_2), 71.0 (CH_2), 70.9 (CH_2), 70.8 (CH_2), 69.5 (CH_2), 69.3 (CH_2), 55.1 (CH), 43.4 (CH_2), 38.3 (CH_2), 37.7 (CH_2), 30.2 (CH_2), 29.5 (CH_2), 28.6 (CH_3); ESIMS *m/z* (rel. intensity) 1037 (100) $[M+H]^+$; HRMS (ESI-TOF) calcd for $C_{40}H_{70}N_6O_{14}F_6S_2Na$ $[M+Na]^+$ 1059.4170, found 1059.4187.

Compound 10



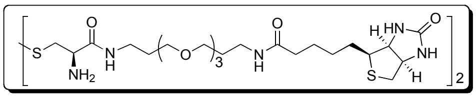
K_2CO_3 (0.624 g, 4.5 mmol) was dissolved in deionized water (6 ml). This solution was diluted with inerted MeOH (30 ml) and then added to the compound **9** (1.50 g, 1.45 mmol). The resulting solution was stirred for 48 h at room temperature under argon atmosphere. After this time, solvents were removed *in vacuo* and the resulting residue was purified by column chromatography, eluted with CH_2Cl_2/MeOH/NH_4OH (9.8:0.2:0.2 to remove impurities and then 8.8:1:0.2) to give the product **10** as pale yellowish oil (984 mg, 82%); R*f* = [CH_2Cl_2/MeOH/NH_4OH (8.8:0.8:0.2)]; IR (ZnSe) ν_{max} 3343, 2934, 2869, 1659, 1520, 1045, 1021, 844 cm^{-1}; ^{1}H-NMR (300 MHz, acetone-*d*$_6$) δ 1.43 (bs, 18H), 1.74-1.95 (m, 8H + 2 NH_2), 2.97-3.37 (m, 12 H), 3.47-3.61 (m, 24H), 4.46 (bs, 2H), 6.39 (d, *J* = 8.5 Hz, 2 NH), 7.68 (bs, 2 NH); ^{13}C-NMR (75,5 MHz, acetone-*d*$_6$) δ 170.8 (CO), 156.4 (CO), 79.7 (Cq), 71.1 (CH_2), 70.9 (CH_2), 69.6 (CH_2), 69.6 (CH_2), 55.0 (CH), 48.4 (CH_2), 43.4 (CH_2), 37.6 (CH_2), 31.8 (CH_2), 30.3 (CH_2), 28.6 (CH_3); ESIMS *m/z* (rel. intensity) 845 (100) $[M+H]^+$; HRMS (ESI-TOF) calcd for $C_{36}H_{73}N_6O_{12}S_2$ $[M+H]^+$ 845.4722, found 845.4725.

Compound 11



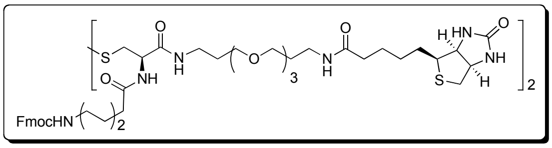
To a stirred solution of biotin (0.260 g, 1.07 mmol) in dry inerted DMF (12.5 ml) was added DIPEA (0.165 g, 1.28 mmol) and PyBOP (0.554 g, 1.07 mmol). The resulting mixture was stirred 5 min at room temperature, in the dark under argon atmosphere. To this mixture, a solution of **10** (360 mg, 0.43 mmol) in dry DMF (12.5 ml) was added dropwise. After stirring at room temperature for 24 h under argon, the mixture was evaporated until dryness to afford a sticky orange oil, which was purified by column chromatography, eluted with CH_2Cl_2/MeOH/NH_4OH (9:1:0.1) to give the product **11** as a translucent lacquer (455 mg, 82%); R_f = 0.38 [CH_2Cl_2/MeOH/NH_4OH (9:1:0.2)]; IR (ZnSe) ν_{max} 3344, 2935-2867, 1660, 1520, 1045, 845 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.39-1.49 (m, 4H), 1.46 (bs, 18H), 1.54-1.83 (m, 16H), 2.20 (t, J = 7.3 Hz, 4H), 2.71 (d, J = 12.7 Hz, 2H), 2.86-2.96 (m, 4H), 3.13-3.29 (m, 12H), 3.51-3.67 (m, 24H), 4.31 (dd, J = 7.9, 4.5 Hz, 2H), 4.35-4.38 (m, 2H), 4.48-4.52 (m, 2H); ^{13}C-NMR (75,5 MHz, CD_3OD) δ 175.9 (CO), 173.0 (CO), 166.1 (CO), 157.6 (CO), 80.9 (Cq), 71.5 (CH_2), 71.2 (CH_2), 69.9 (CH_2), 63.4 (CH), 61.6 (CH), 57.0 (CH), 55.5 (CH), 42.0 (CH_2), 41.1 (CH_2), 38.1 (CH_2), 37.8 (CH_2), 36.9 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 28.8 (CH_3), 26.9 (CH_2); ESIMS *m/z* (rel. intensity) 1298.3 (100): $[M+H]^+$; HRMS (ESI-TOF) calcd for $C_{56}H_{100}N_{10}O_{16}S_4Na$ $[M+Na]^+$ 1319.6093, found 1319.6089.

Compound 12



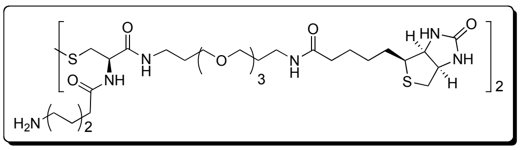
To a solution of **11** (453 mg, 0.349 mmol) in anhydrous CH_2Cl_2 (15 mL) was added trifluoroacetic acid (TFA, 1.5 mL). The resulting mixture was stirred at room temperature for 5 h under argon atmosphere. Solvent and volatiles were removed *in vacuo* and the resulting residue was dried overnight under high vacuum. The mixture was then taken up in methanol (5 mL), stirred with powdered K_2CO_3 (145 mg, 1.047 mmol) at room temperature for 1 h under argon. After this time, the suspension was filtered and the filtrate was evaporated to give the expected product **12** as a pale yellowish foam in quantitative yield (400 mg) without further purification: R_f = 0.05 [CH_2Cl_2/MeOH (85:15)]; IR (ZnSe) ν 3351, 2930, 1684, 1561, 1433, 1338, 1206, 1183, 1133, 838, 802, 723 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.41-1.49 (m, 4H), 1.58-1.84 (m, 16H), 2.21 (t, J = 7.3 Hz, 4H), 2.71 (d, J = 12.7 Hz, 2H), 2.86 (dd, J = 13.6, 7.4 Hz, 2H), 2.93 (dd, J = 12.8, 4.9 Hz, 2H), 3.11 (dd, J = 13.5, 5.5 Hz, 2H), 3.18-3.35 (m, 10 H), 3.50-3.66 (m, 26H), 4.31 (dd, J = 7.9, 4.4 Hz, 2H), 4.48-4.52 (m, 2H); ^{13}C-NMR (100 MHz, CD_3OD) δ 175.9 (CO), 175.3 (CO), 166.1 (CO), 71.5 (CH_2), 71.3 (CH_2), 70.1 (CH_2), 70.0 (CH_2), 63.4 (CH), 61.6 (CH), 57.0 (CH), 55.3 (CH), 44.4 (CH_2), 41.1 (CH_2), 38.1 (CH_2), 37.8 (CH_2), 36.9 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 26.9 (CH_2); ESIMS *m/z* (rel. intensity) 1098.3 (100) $[M+H]^+$; HRMS (ESI-TOF) calcd for $C_{46}H_{84}N_{10}O_{12}S_4Na$ $[M+Na]^+$ 1119.5045, found 1119.5099.

Compound 13



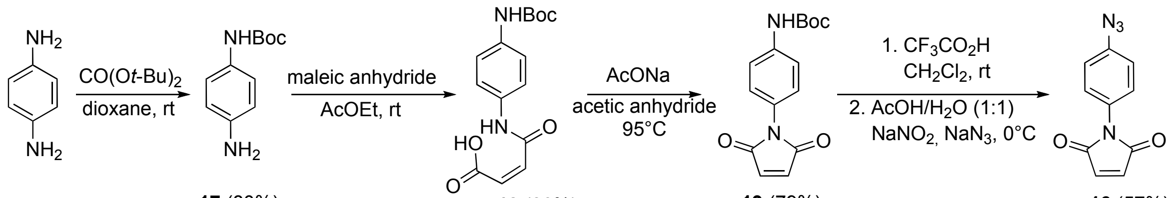
To a stirred solution of 6-(Fmoc-amino)hexanoic acid (240 mg, 0.68 mmol) in anhydrous DMF (10 mL), was added DIPEA (120 μL, 0.68 mmol) and HBTU (296 mg, 0.78 mmol). The resulting solution was stirred at room temperature for 1 h. A solution of **12** (373 mg, 0.34 mmol) and DIPEA (117 μL, 0.68 mmol) in anhydrous DMF (12 mL) was then added dropwise. After stirring at room temperature under argon atmosphere for 14 h, the solution was concentrated under reduced pressure at 50 ^{o}C. The residue was purified by column chromatography, eluted with CH_2Cl_2/NH_4OH (100:1) to remove impurities and then $CH_2Cl_2/MeOH/NH_4OH$ (98:2:1) to give the expected product **13** as a white foam (400 mg, 67%): R_f = 0.38 [$CH_2Cl_2/MeOH/NH_4OH$ (90:10:2)]; IR (ZnSe) ν 3305, 2932, 2865, 2413, 2361, 1643, 1540, 1451, 1354, 1251, 1104, 913, 760, 741, 646 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.29-1.78 (m, 32H), 2.18 (t, J = 7.3 Hz, 4H), 2.27 (t, J = 7.3 Hz, 4H), 2.69 (d, J = 12.7 Hz, 2H), 2.86-2.96 (m, 4H), 3.07-3.28 (m, 16H), 3.49 (t, J = 6.2 Hz, 8H), 3.54-3.62 (m, 16H), 4.18 (t, J = 6.8 Hz, 2H), 4.27 (dd, J = 7.9, 4.5 Hz, 2H), 4.33 (d, J = 6.9 Hz, 4H), 4.44-4.48 (m, 2H), 4.69-4.73 (m, 2H), 7.28-7.41 (m, 8H), 7.64 (d, J = 7.3 Hz, 4H), 7.79 (d, J = 7.5 Hz, 4H); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 174.0 (CO), 173.2 (CO), 170.9 (CO), 164.4 (CO), 156.6 (CO), 144.0 (ArC), 141.3 (ArC), 127.6 (ArCH), 127.0 (ArCH), 125.1 (ArCH), 119.9 (ArCH), 70.4 (CH_2), 70.0 (CH_2), 69.9 (CH_2), 68.8 (CH_2), 66.4 (CH_2), 61.9 (CH), 60.1 (CH), 55.6 (CH), 53.0 (CH), 47.3 (CH), 44.3 (CH_2), 40.8 (CH_2), 40.6 (CH_2), 37.7 (CH_2), 37.0 (CH_2), 35.9 (CH_2), 35.9 (CH_2), 29.3 (CH_2), 29.1 (CH_2), 28.7 (CH_2), 28.2 (CH_2), 28.0 (CH_2), 26.1 (CH_2), 25.5 (CH_2), 25.2 (CH_2); ESIMS *m/z* (rel. intensity) 907.6 (100) $[M+2Na]^{2+}$, 1791.5 (65) $[M+Na]^{+}$; HRMS (ESI-TOF) calcd for $C_{88}H_{126}N_{12}O_{18}S_4Na_2$ $[M+2Na]^{2+}$ 906.3990, found 906.4060.

Compound 14



To a solution of **13** (365 mg, 0.206 mmol) in anhydrous DMF (7.5 mL) was added piperidine (123 μL, 1.24 mmol). After stirring at room temperature for 2 h under argon atmosphere, inerted MeOH (7.5 mL) was added and the resulting solution was washed with *n*-hexane (10 × 15 mL) to remove the dibenzofulvene. After evaporation of the solvent under reduced pressure at 50 ^{o}C and then under high vacuum at room temperature, the expected product **14** was obtained without further purification as a yellow plastic-like compound (254 mg, 93%): IR (ZnSe) ν 3286, 3081, 2930, 2865, 1650, 1549, 1460, 1332, 1264, 1102, 845 cm^{-1}; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.35-1.80 (m, 32H), 2.20 (t, J = 7.3 Hz, 4H), 2.29 (t, J = 7.4 Hz, 4H), 2.66-2.73 (m, 6H), 2.86-3.00 (m, 4H), 3.13-3.30 (m, 12H), 3.53 (t, J = 6.1 Hz, 8H), 3.59-3.66 (m, 16H), 4.31 (dd, J = 7.8, 4.5 Hz, 2H), 4.48-4.52 (m, 2H), 4.70 (dd, J = 8.9, 5.4 Hz, 2H); ^{13}C-NMR (75.5 MHz, CD_3OD) δ 176.0 (CO), 175.9 (CO), 172.4 (CO), 166.1 (CO), 71.5 (CH_2), 71.2 (CH_2), 70.0 (CH_2), 69.8 (CH_2), 63.4 (CH), 61.6 (CH), 57.0 (CH), 54.0 (CH), 42.1 (CH_2), 41.7 (CH_2), 41.1 (CH_2), 38.0 (CH_2), 37.8 (CH_2), 36.9 (CH_2), 36.7 (CH_2), 32.5 (CH_2), 30.4 (CH_2), 30.3 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 27.4 (CH_2), 26.9 (CH_2), 26.6 (CH_2); ESIMS *m/z* (rel. intensity) 662.6 (100) $[M+2H]^{2+}$; HRMS (ESI-TOF) calcd for $C_{58}H_{108}N_{12}O_{14}S_4$ $[M+2H]^{2+}$ 662.3489, found 662.3562.

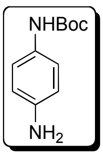
Synthesis of 1-(4-azidophenyl)-1*H*-pyrrole-2,5-dione (16)



17 (80%) **18** (86%) **19** (79%) **16** (57%)

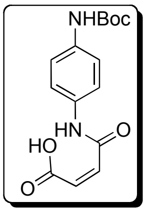
Scheme S4: synthesis of compound **16**

Compound 17



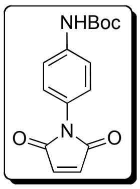
According to the procedure described in the literature,[3] to a solution of *p*-phenylenediamine (7.57 g, 70 mmol) in anhydrous dioxane (35 mL) was added dropwise a solution of di-*tert*-butyl dicarbonate (1.97 g, 9 mmol) in anhydrous dioxane (40 mL). After stirring at room temperature under argon atmosphere for 21 h, the solvent was removed *in vacuo* and the resulting mixture was suspended in water (90 mL). The resulting precipitate was filtrated on a Büchner funnel and then dissolved in CH_2Cl_2 (100 mL). The organic extract was washed with water (10 × 100 mL), dried over anhydrous $MgSO_4$, filtrated and evaporated to give the product **17** as a brownish powder (1.51 g, 80%): R_f = 0.64 [EtOAc/hexane/NH_4OH (2:1:0.1)]; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.43 (s, 9H), 4.72 (s, 2H), 6.45 (d, J = 8.7 Hz, 2H), 7.05 (d, J = 8.1 Hz, 2H), 8.77 (bs, 1H); ESIMS *m/z* (rel. intensity) 209.0 (100) $[M+H]^{+}$.

Compound 18



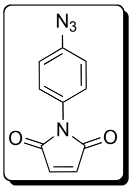
According to the procedure described in the literature,[4] to a stirred solution of *tert*-butyl 4-aminophenylcarbamate **17** (0.700 g, 3.36 mmol) in ethyl acetate (6 mL) was added a solution of maleic anhydride (0.395 g, 4.03 mmol) in ethyl acetate (2 mL). The resulting suspension was stirred for 12 min at room temperature. The resulting solids were filtered off on a Büchner funnel, rinsed with ethyl acetate, resuspended in CH_2Cl_2 (15 mL) and dried *in vacuo* to give the product **18** as a yellow powder (0.88 g, 86%): IR (ZnSe) ν_{max} 3286, 1712, 1519, 1238, 1160 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.47 (s, 9H), 6.30 (d, J = 12.1 Hz, 1H), 6.44 (d, J = 12.1 Hz, 1H), 7.40 (d, J = 8.9 Hz, 2H), 7.50 (d, J = 8.9 Hz, 2H), 9.32 (bs, 1H), 10.40 (bs, 1H), 13.37 (bs, 1H, COOH); ^{13}C-NMR (75,5 MHz, DMSO-d_6) δ 166.7 (CO), 162.9 (CO), 152.8 (CO), 135.8 (ArC), 132.8 (ArC), 131.5 (CH), 131.0 (CH), 120.2 (ArCH), 118.5 (ArCH), 79.0 (Cq), 28.2 (CH_3); ESIMS *m/z* (rel. intensity) 329.2 (100) $[M+Na]^+$; m.p. 177-179 °C (lit.[4] 173-175 °C).

Compound 19



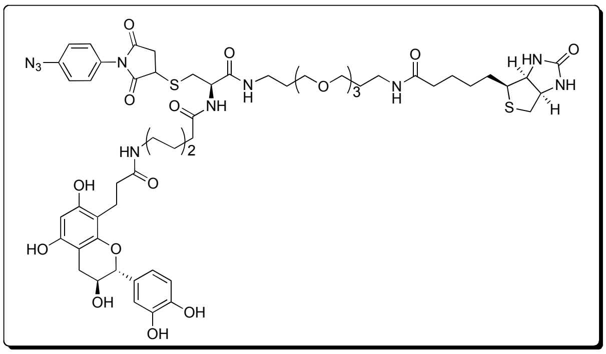
A stirred suspension of acid **18** (0.890 g, 2.91 mmol) in acetic anhydride (9 mL) was heated to 95 °C. Anhydrous sodium acetate (0.263 g, 3.20 mmol) was then added and the resulting solution was stirred for 2 h 30. The solution was allowed to stand overnight to give a yellow crystalline precipitate. Water (60 mL) was added and the resulting suspension was stirred for few minutes. The precipitate was filtered on a Büchner funnel and washed with saturated $NaHCO_3$ (4 × 15 mL) and then with water (4 × 15 mL). The solid obtained was redissolved in CH_2Cl_2 (15 mL), dried over anhydrous Na_2SO_4, filtrated and concentrated *in vacuo* to give the product **19** as a pale yellow powder (0.667 g, 79%): IR (ZnSe) ν_{max} 3368, 1707, 1600, 1530, 1234, 1155 cm^{-1}; ^{1}H-NMR (300 MHz, DMSO-d_6) δ 1.48 (s, 9H), 7.15 (s, 2H), 7.18 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 8.8 Hz, 2H), 9.51 (bs, 1H); ^{13}C-NMR (75,5 MHz, DMSO-d_6) δ 170.1 (CO), 152.7 (CO), 139.1 (ArC), 134.6 (CH), 127.3 (ArC), 125.3 (ArCH), 118.2 (ArCH), 79.3 (Cq), 28.1 (CH_3); ESIMS *m/z* (rel. intensity) 311.1 (100) $[M+Na]^+$; m.p. 181-184 °C (lit.[4] 182-184 °C).

Compound 16



To a suspension of compound **18** (0.616 g, 2.14 mmol) in anhydrous CH_2Cl_2 (6 mL) was added dropwise trifluoroacetic acid at 0 °C. The resulting solution was warmed to room temperature and stirred for 2 h. The solvents were then evaporated and the remainder taken up in a mixture of concentrated acetic acid (7 mL) and water (7 mL). The solution obtained was cooled to 0 °C and sodium nitrite (0.215 g, 3.11 mmol) was added in one portion. After stirring for 1 h 50 at 0 °C, sodium azide (0.205 g, 3.15 mmol) was added slowly. When the evolution of nitrogen gas had ceased, the reaction mixture was extracted with CH_2Cl_2 (3 × 14 mL). The organic layers were combined and washed with $NaHCO_3$ (3 × 14 mL), dried over anhydrous Na_2SO_4, filtered and evaporated. The brownish residue was purified by column chromatography, eluted with cyclohexane/EtOAc (75:25) to give the product **16** as yellow needles (0.261 g, 57%); R*f* = 0.33 [cyclohexane/EtOAc (2:1)]; IR (ZnSe) ν_{max} 3106, 2130-2097, 1713, 1508, 1394, 1294 cm^{-1}; **^{1}H**-NMR (300 MHz, acetone-*d*$_6$) *δ* 7.04 (s, 2H), 7.19-7.22 (m, 2H), 7.42-7.44 (m, 2H); ^{13}C-NMR (75,5 MHz, acetone-*d*$_6$) *δ* 170.4 (CO), 140.1 (ArC), 135.3 (CH), 129.8 (ArC), 128.9 (ArCH), 120.2 (ArCH); ESIMS *m/z* (rel. intensity) 237.2 (100) $[M+Na]^+$; m.p. 116-118 °C (lit.[4] 116-118 °C).

Probe 2



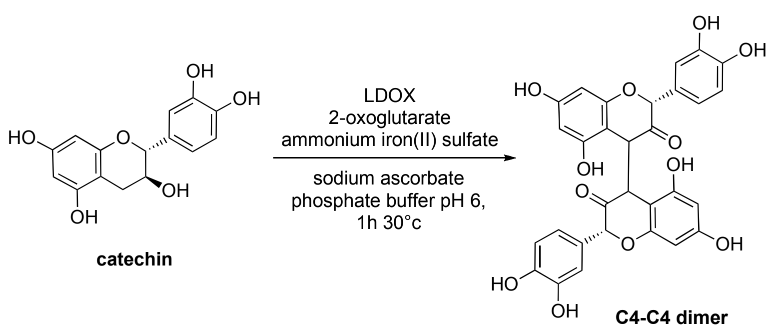
To a stirred solution of **14** (95 mg, 0.072 mmol) in 4 mL of an anhydrous mixture of THF/MeOH (3:1), was added DL-dithiothreitol (DTT, 22 mg, 0.144 mmol) and Et_3N (20 µL, 0.144 mmol). The resulting solution was stirred at room temperature for 3 h under argon atmosphere. Solvents and volatiles were then removed *in vacuo* and the crude product **15** was taken up in dry DMF (4 mL). To this resulting solution was added (2*R*,3*S*)-8-lactone catechin **7a** (38 mg, 0.110 mmol) under argon atmosphere. The reaction mixture was stirred at 40 °C for 30 h under argon atmosphere. After complete consumption of the lactone monitored by TLC, the mixture was allowed to room temperature and 1-(4-azidophenyl)-1*H*-pyrrole-2,5-dione (**16**, 36 mg, 0.167 mmol) was added in one portion in the dark. The reaction mixture was then stirred at room temperature for an additional 3 h under argon atmosphere and in the dark. After evaporation of the solvents under reduced pressure at 50 °C, the residue was subjected to column chromatography, eluting with CH_2Cl_2/MeOH/HCl 0.1M (95:5:2) to remove impurities, and then CH_2Cl_2/MeOH/HCl 0.1M (90:10:2) to furnish the expected probe **2** as an inseparable mixture of diastereoismers, and as a yellowish foam (44 mg, 34%): R_f = 0.5 [CH_2Cl_2/MeOH/HCl 0.1M (80:20:2)]; IR (ZnSe) ν 3366, 3328, 3285, 3091-2511, 2126, 1707, 1659, 1642, 1283, 1175, 669; ^{1}H-NMR (300 MHz, CD_3OD) δ 1.25-1.79 (m, 16H), 2.16-2.26 (m, 4H), 2.40-2.44 (m, 2H), 2.54 (dd, J = 16.2, 8.0 Hz, 1H), 2.61-2.72 (m, 1H), 2.69 (d, J = 12.2 Hz, 1H), 2.78-2.83 (m, 2H), 2.90 (dd, J = 12.9, 5.0 Hz, 1H), 2.86-3.01 (m, 2H), 3.07-3.28 (m, 8H), 3.37-3.41 (m, 1H), 3.48-3.63 (m, 12H), 3.92-3.99 (m, 1H), 4.11 (dd, J = 9.1, 4.0 Hz, 1H), 4.27 (dd, J = 7.8, 4.4 Hz, 1H), 4.44-4.48 (m, 1H), 4.58-4.68 (m, 1H), 4.64 (d, J = 7.3 Hz, 1H), 6.00 (s, 1H), 6.73 (dd, J = 8.2, 1.5 Hz, 1H), 6.78 (d, J = 8.1 Hz, 1H), 6.86 (d, J = 1.2 Hz, 1H), 7.14-7.20 (m, 2H), 7.31-7.36 (m, 2H); ^{13}C-NMR (100 MHz, CD_3OD) δ 178.0 (CO), 177.9 (CO), 176.6 (CO), 176.3 (CO), 176.2 (CO), 176.0 (CO), 175.8 (CO), 172.3 (CO), 166.1 (CO), 155.3 (ArC), 155.2 (ArC), 154.6 (ArC), 146.2 (ArC), 146.2 (ArC), 141.8 (ArC), 132.5 (ArC), 130.2 (ArC), 129.6 (ArCH), 122.6 (ArCH), 120.6 (ArCH), 120.4 (ArCH), 119.9 (ArCH), 116.2 (ArCH), 115.1 (ArCH), 107.1 (ArC), 101.0 (ArC), 96.6 (ArCH), 82.7 (CH), 71.5 (CH_2), 71.2 (CH_2), 69.9 (CH_2), 69.7 (CH_2), 68.8 (CH), 63.4 (CH), 61.6 (CH), 57.0 (CH), 54.3 (CH), 53.9 (CH), 41.1 (CH_2), 40.3 (CH_2), 38.0 (CH_2), 37.9 (CH_2), 37.0 (CH_2), 36.9 (CH_2), 36.7 (CH_2), 35.0 (CH_2), 34.6 (CH_2), 30.4 (CH_2), 30.2 (CH_2), 30.0 (CH_2), 29.8 (CH_2), 29.5 (CH_2), 28.7 (CH_2), 27.4 (CH_2), 26.9 (CH_2), 26.5 (CH_2), 20.0 (CH_2); ESIMS *m/z* (rel. intensity) 1243.3 (100) $[M+Na]^+$; HRMS (ESI-TOF) calcd for $C_{57}H_{76}N_{10}O_{16}S_2Na$ $[M+Na]^+$ 1243.4774, found 1243.4807.

<u>**Biological part**</u>

Production and purification of recombinant LDOX

The pQE-30Xa vector containing the full-length coding region of LDOX in frame with an N-terminal His_6, amplified with a post veraison DNA library from *Vitis vinifera* cabernet sauvignon as template, was obtained from Dr. Bernard Gallois (UMR 5248, University of Bordeaux 1, France). Bacteria *E. coli* Origami™ cells (Novagen) were transformed with pQE-30Xa / LDOX constructs and grown at 37°C under agitation (220 rpm) in LB broth medium supplemented with 50 µg/ml of ampicillin until OD_{600} reached 1.1. Expression of fusion proteins was thereafter induced with 1 mM isopropyl-β-D-1-thiogalactopyranoside (IPTG) and bacteria were incubated at 15°C overnight under agitation. Bacterial cells were harvested by centrifugation (4500 g, 15 min, 4°C) and stored at –20°C until extraction and purification of recombinant LDOX. Bacteria containing His-tagged LDOX were resuspended in non-denaturing buffer (20 mM Tris-HCl, 0.5 M NaCl and 5 mM imidazole, pH 7.9) and emulsified. Cell debris were removed by centrifugation at 45000g for 45 min at 4°C and supernatant containing fusion protein was applied on His·bind® resin affinity chromatography (Novabiochem) for 2 h. Resin was washed with a large volume of wash buffer (20 mM Tris-HCl, 0.5 M NaCl and 20 mM imidazole, pH 7.9) and recombinant LDOX protein was eluted with wash buffer containing 250 mM imidazole. Finally, imidazole was removed from sample by dialysis and purified His-tagged LDOX was preserved in 0.2 M phosphate buffer pH 6 with 10% (vol/vol) of glycerol at –20°C until use. Protein concentration was measured by Bradford method using a protein-dye reagent (Bio-Rad) and BSA as a standard.[5]

LDOX enzyme assays with (+)-catechin[2]



Scheme S5

In order to evaluate LDOX enzyme activity, catechin (150 µM) was submitted to the enzymatic test with the partially purified LDOX (200 µg) in a reaction mixture (500 µL) containing 2-oxoglutarate (100 μM), ammonium iron (II) sulfate (50 μM) and sodium ascorbate (2.5 mM) and in 200 mM potassium phosphate buffer pH 6.0. The incubations were carried out in open vials under gentle shaking at 30°C for 1 h. After two extractions with 500 μL of EtOAc (HPLC grade), and solvent evaporation, the residue was diluted in 200 μL of MeOH (HPLC grade) and then submitted to LC/MS analysis. C4-C4 dimer was detected by UV at 280 nm and caracterized by single ion monitoring at m/z 575 $[M+H]^+$.[2]

Capture assays with probes 1a-b, 2 and LDOX enzyme

LDOX enzyme affinity assays were performed using a flavanol-bearing probes **1a**, **1b** or **2** (8 μL of 113.6 μM aqueous solution, final concentration 9.1 μM) in the presence of partially purified LDOX (21 μL of 25 μM in 0.2 M phosphate buffer solution, final concentration 5.3 μM) in 100 μL of capture buffer (0.2 M phosphate buffer, pH 7, 0.5 mM dithiothrietol (DTT) and 0.05% (wt/vol) octyl-β-D-glucopyranoside). For negative controls, sodium ascorbate was added (1 μL of 50 mM solution, final concentration 0.5 mM) to avoid oxygen-mediated autooxidation of the probes due to potential presence of residual oxygen in the buffer solution. Incubations were carried out in 1.5 mL Eppendorf tubes under gentle shaking (1150 rpm) at 23 °C for 30 min. Chemical oxidative activation of probes **1a** and **1b** was performed using an aqueous solution of $NaIO_4$ (5 μL of 100 mM, final concentration of 5 mM). For activation of probe **2**, sample in open vial placed at 2 cm from the UV lamp was irradiated at 312 nm (VL-215.MC, Vilbert Lourmat, irradiance 1.8 $mW.cm^{-2}$ at 15 cm) at 10 °C during 20 min. In all cases, the reaction was then left for 20 min after which the reaction was quenched by addition of 105 μL of buffer containing 0.2 M phosphate buffer, pH 7, 100 mM dithiothrietol (DTT) and 0.05% (wt/vol) octyl-β-D-glucopyranoside. Sample were gently shaked for 1 minute and then 22 μL of 5 M sodium chloride solution was added to a final concentration of 0.5 M and the resulting solution was incubated with streptavidin-coated magnetic beads (50 μL, Dynabeads®MyOne™ Streptavidin C_1) for 1 hour at room temperature under shaking (1400 rpm). The beads were collected using a magnetic device and washed first with washing buffer (300 μL, 50 mM Tris-HCl, 0.5 mM DTT, 0.05% (wt/vol) octyl-β-D-glucopyranoside, 0.5 M NaCl, pH 7.5), then one time with washing buffer supplemented with 10 μM, four times with an aqueous solution of SDS 0.1% (300 μL × 4), three times with an acetonitrile/water mixture ([80:20], 300 μl × 3) and finally two times with MS grade water (300 μL × 2). A denaturing Laemmli buffer (30 μL) was then added to the beads, and the resulting solution was heated to 95°C for 10 minutes prior to electrophoretic analysis.

SDS-Polyacrylamide Gel Electrophoresis (PAGE)

SDS-PAGE was performed according to Laemmli on 0.75 mm thick gels (12.5% acrylamide in running gel, 4% acrylamide in stacking gel). Proteins were visualized by Coomassie blue staining procedure. A volume of 10 µL was applied from each elution fractions.

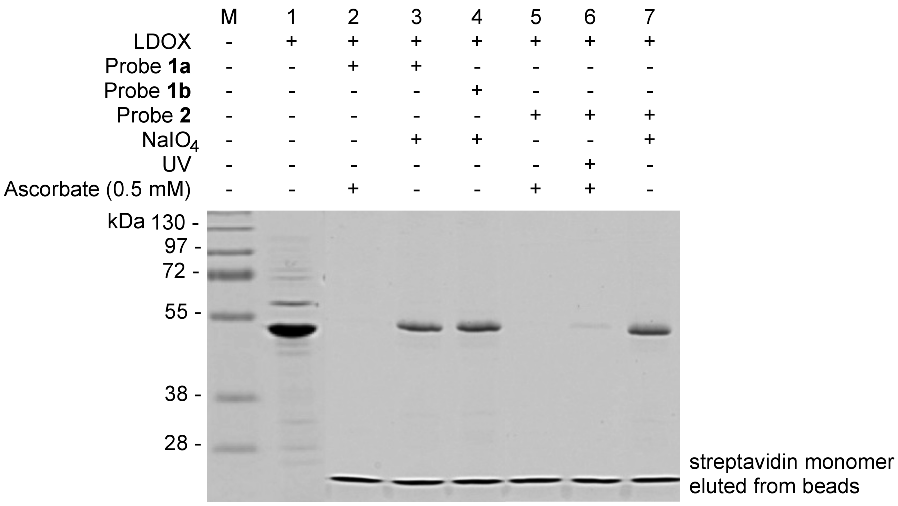


Figure S1. Analysis of Coomassie blue stained SDS-PAGE for comparison of oxidative- and photo-activated cross-linking of probes **1a-b** and **2** to LDOX enzyme.

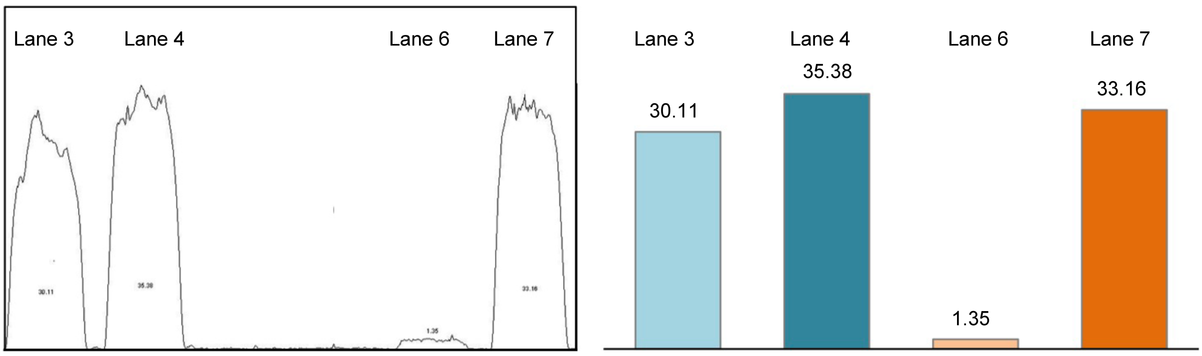


Figure S2. Band densities of SDS-PAGE (Fig. S1) quantified using ImageJ software t.38X (National Institutes of Health, Bethesda, MD) and expressed in percentage of total band density of lanes 3-7.

Evaluation of the autooxidation and effect of incubation times of probe 1a on the capturing process

For this assays, (+)-catechin-bearing probe **1a** (8 µL of 113.6 µM solution, final concentration 9.1 µM) was incubated in the presence of partially purified LDOX (15 µL of 32 µM in 0.2 M phosphate buffer solution, final concentration 4.8 µM) in 100 µL of reaction capture buffer. Incubations were carried out in 1.5 mL Eppendorf tubes under gentle stirring (1150 rpm) at 23 °C for 30, 60, 120 and 180 min.

For autooxidation evaluation (lanes a, Figure S3), no addition of $NaIO_4$ was performed and enrichment protocol was the same as described for the capture assays (see p. S18).

For incubation time evaluation (lanes b, Figure S3), activation and enrichment protocol were the same as described for the capture assays (see p. S18).

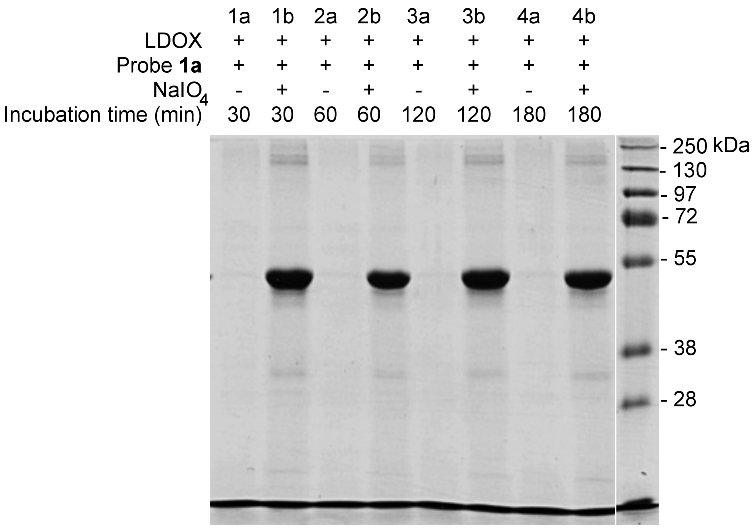
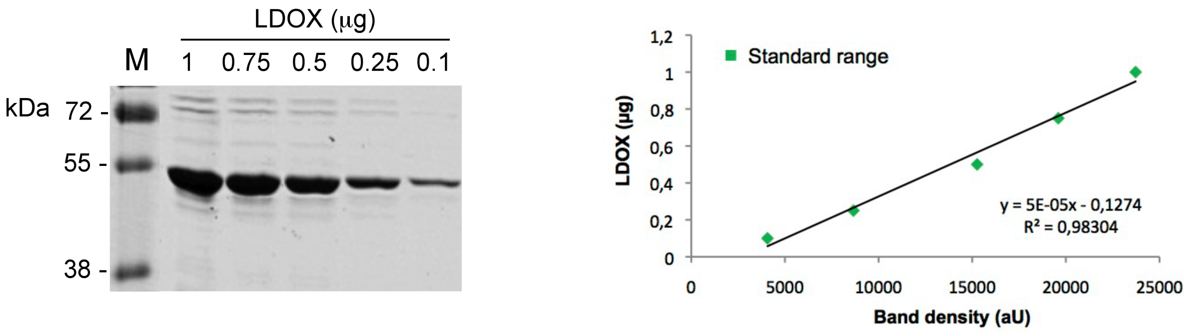


Figure S3. Analysis of Coomassie blue stained SDS-PAGE for the evaluation of autooxidation of the probe **1a** (lanes 1a-4a) and incubation times (lanes 1b-4b).

Evaluation of the capture efficiency

Quantitative determination of captured LDOX enzyme by probe **1a** was performed by means of SDS-PAGE, using a standard curve. Coomassie blue stained SDS-PAGE (gel A, Figure S4) was obtained with 10 µL of solutions of recombinant LDOX enzyme, ranging from 0.1 to 0.01 µg/µL from a stock solution of LDOX. The standard curve (B, Figure S4) was established from densitometric analysis of gel A (Figure S4).



A **B**

Figure S4. (A) SDS-Page obtained with solutions of recombinant LDOX enzyme with 1, 0.75, 0.5, 0.25, 0.1 µg of LDOX enzyme. (**B**) Standar curve for the LDOX obtained from densitometric analysis of gel A.

Application of the standard curve to assays 1b, 2b, 3b and 4b (SDS-PAGE, Figure S3) provided quantitative capturated LDOX enzyme in 10 µL of the initial 30 µL Laemmli buffer denaturing for each assays (Table S1). Capture efficiencies were calculated from the total quantitative amount of capturated LDOX enzyme in this 30 µL and the 21 µg of LDOX ($[M+H]^+$ 43 653 Da; 32 µM in 15 µL) initially present in captured assays (Table S1).

Table S1: capture efficiency of LDOX analysis

	color density (aU)	Capturated LDOX (µg) in 10 µL from standard curve	Total of captured LDOX (µg) in 30 µL	Capture efficency
1b	24721	0.99	2.96	14.1%
2b	19053	0.73	2.19	10.4%
3b	24792	0.99	2.97	14.1%
4b	22109	0.87	2.60	12.4%

Competitive affinity assays with free catechin

Competitive enzymatic affinity assays was performed using (+)-catechin-bearing probe **1a** (8 µL of 113.6 µM solution, final concentration 9.1 µM) in the presence of partially purified LDOX (15 µL of 32 µM in phosphate buffer solution, final concentration 4.8 µM) and (+)-catechin (10 µL of 9.1 mM solution, final concentration 910 µM) in 100 µL of capture buffer. Incubations were carried out in 1.5 mL Eppendorf tubes under gentle stirring (1150 rpm) at 23 °C for 30 min. The activation and enrichment protocol were the same as described for the capture assays (see p. S18).

Competitive affinity assays with BSA

Competitive enzymatic affinity assays were performed using (+)-catechin-bearing probe **1a** or (–)-epicatechin-bearing probe **1b** (8 µL of 113.6 µM solution, final concentration 9.1 µM) in the presence of partially purified LDOX (15 µL of 32 µM in phosphate buffer solution, final concentration 4.8 µM) and/or commercial BSA (sigma-Aldrich) (31 µl of 16 µM in phosphate buffer solution, final concentration 5.0 µM) in 100 µL of reaction buffer containing 0.2 M phosphate buffer, 0.5 mM DTT and 0.05% (wt/vol) octyl-β-D-glucopyranoside. Incubations were carried out in 1.5 mL Eppendorf tubes under gentle stirring (1150 rpm) at 23 °C for 30 min. The activation and enrichment protocol were the same as described for the capture assays (see p. S18).

Western blot analysis

Western blot were carried out according to standard procedures.[6] After separation by SDS-PAGE, the proteins were transfered to nitrocellulose membrane (Wathman 0.2 µm nitrocellulose transfert membrane, PROTAN®, Germany). After tranfer, the proteins on the membrane were stained with Ponceau S, then the membrane was washed with distillated water and 1X Tris buffer saline (Euromedex, Souffel Weyersheim) supplemented with 0.05% (vol/vol) Tween 20 (TBS-T). The membrane was blocked for 15 min at room temperature with a solution of 5% (wt/vol) skimmed milk powder in TBS-T (20 mL). Incubation with the primary antibody was performed over-night at 4 °C, followed by two wash steps with a solution of 5% skimmed milk powder in TBS-T and incubation with the secondary antibody for 2 h at room temperature. Antibodies were diluted in 5% skimmed milk powder in TBS-T as follow: monoclonal anti-biotin from mouse (Santa Cruz Biotechnology, Inc., Heidelberg, Germany) 1:1000, secondary anti-mouse antibody conjugated to horseradish peroxidase (Sigma-Aldrich, St Louis, Missouri, USA) 1:10000. After three washes in TBS-T (25 mL) and one in PBS (25 mL), membrane was treated with the Super Signal West Pico Chemoluminescent Substrate (Thermo Scientific, Rockford, USA) according to the manufacturer's instructions. Kodak fotographic film (Sigma-Aldrich, St. Louis, Missouri, USA) was used to detect the chemiluminescence.

As shown in Figure S5, only the LDOX enzyme covalently tagged with the biotinylated probes **1a/b** or **2** are observed (lanes 3, 4, 6 and 7). The much higher efficiency of capture of the LDOX enzyme by oxidative activation of probes **1a/b** and **2** over that by photo-activation of probe **2** is also clearly demonstrated (see lanes 3, 4 and 7 as compared to lane 6).

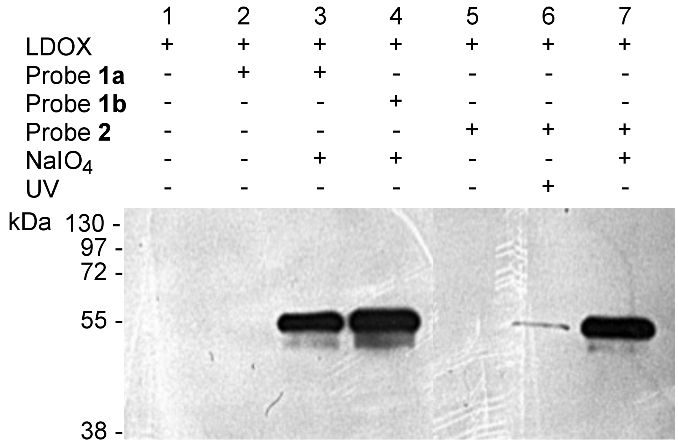


Figure S5. Western blot analysis (using a mouse anti-biotin antibody) of the biotinylated flavanol-bearing probes (**1a**/**b** and **2**) covalently bound to the LDOX enzyme.

MALDI-TOF analysis of the reaction capture of the LDOX by probe 1a.

Mass spectrometry analyses were performed on a MALDI-TOFTOF Ultraflex III mass spectrometer (Bruker) in linear mode with sinapinic acid (Sigma-Aldrich) used as a matrix (10 mg.mL^{-1} solution in 50% acetonitrile in 0.1% aqueous trifluoroacetic acid) and MCP detector. Average masses were measured using an internal calibration with a mixture of trypsinogen, protein A, bovine serum albumin (simply and doubly charged) (respective theoretical average masses: 23981 Da, 44612 Da, 33215 Da and 66430 Da) (Sigma-Aldrich).

A solution of probe **1a** (14.8 µM) and partially purified LDOX (8 µM) in 100 µl of phosphate buffer (0.2 M, pH 7) containing 0.5 mM dithiothrietol (DTT) was incubated in Eppendorf tube (1.5 mL). After stirring (1150 rpm) 30 min at 23 °C, $NaIO_4$ (7.4 µL of 100 mM solution) was added and the reaction was stirred for 5 min at 23 °C. The reaction was then quenched by addition of 74 µL of phosphate buffer (0.2 M, pH 7) containing 200 mM DTT. The sample was gentlely shaked for 1 min and then sodium chloride (20.2 µL of 5 M solution) was added to a final concentration of 0.5 M. The resulting solution (201.6 µL) was concentrated four times by centrifugal filtration through a 10.000 MW Microcon (Millipore) at 14.000g for 10 min at 4 ^{o}C to obtain a 100 µL solution used for for MALDI-TOF analysis. A sample reaction (1 µL) was mixed with 1 µL of matrix solution. The mixture was then spotted onto the MALDI sample stage and air-dried prior to analysis. The dried droplet method was used for sample loading on MALDI stainless steel targets (mix of 1µL of sample with 1µL of matrix solution).

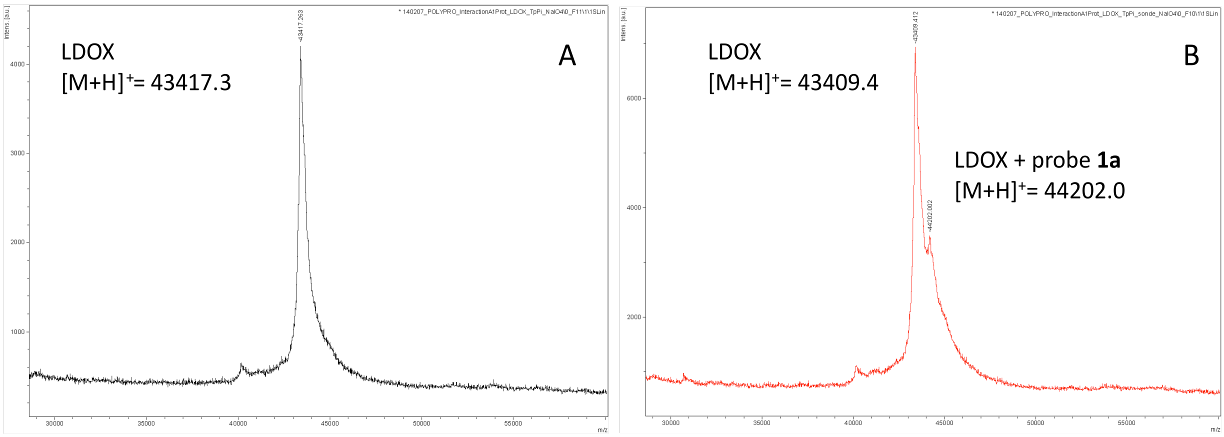


Figure S6. MALDI-TOF analysis of (**A**) Partially purified LDOX (0.14 mg/mL in phosphate buffer 0.2 M, pH 7) diluted at one centesimal in MS grade water, desalted on ZipTip C18 microcolumn (0.6 µL of C_{18} resin, Millipore) before MALDI-TOF analysis. (**B**) Oxidative cross-linking reaction between probe **1a** (14.8 µM) and the LDOX enzyme (8 µM) showing a 793 Da mass shift corresponding to the monoadduct LDOX - probe **1a**.

Production and extraction of *E. coli* proteins

Bacteria *E. coli* Origami^{TM} cells (Novagen) were grown at 37°C under agitation (220 rpm) in LB broth medium supplemented with 50 µg/ml of ampicillin. Expression of proteins was thereafter induced with 1 mM isopropyl-β-D-1-thiogalactopyranoside (IPTG) and bacteria were incubated at 15°C overnight under agitation. Bacterial cells were harvested by centrifugation (8000 g, 15 min, 4°C). The pellet was resuspended in 1 mL of non-denaturing buffer (phosphate 0.2 M, pH 7) and sonicated with a Sonifier® Cell Disruptor (Branson Ultrasonics). Cell debris were removed by centrifugation at 8000 g for 20 min at 4°C and supernatant containing crude proteins was collected. Protein concentration (0.973 µg/µL) was measured by Bradford method using a protein-dye reagent (Bio-Rad) and BSA as a standard and kept at -20°C until further use.

Competitive affinity assays with LDOX and *E. coli* proteome

The *E. coli* protein mixture was first submitted to a depletion step in the aim of removing the maximum of proteins having an affinity for streptavidin or the capacity to be non-specifically retained by beads in the conditions used for capture and washing steps. Thus, *E. coli* proteins (1.5 mL at a concentration of 0.973 µg/µL) were incubated with 50 µL of streptavidin-coated magnetic beads (Dynabeads®MyOne™ Streptavidin C_1) for 1 h at 23 °C with stirring. The supernatant was collected and incubated 2 more times with the same quantity of beads until the final protein concentration remains constant, i.e., 0.847 µg/µL). Competitive affinity assays were then performed in triplicate using 100 µg of a protein mixture composed of 99.5 µg of *E. coli* proteins (117.5 µL at 0.847 µg/µL in phosphate buffer solution 0.2 M, pH = 7) and 0.5 µg of partially purified LDOX (4.7 µL of 2.43 µM solution) in the presence of the (+)-catechin-bearing probe **1a** (1.8 µL of 11.3 µM solution) in 150 µL of capture buffer (0.2 M phosphate buffer, pH 7, 0.5 mM DTT and 0.05% (wt/vol) octyl-β-D-glucopyranoside). Incubations were carried out in 1.5 mL Eppendorf tubes under gentle stirring (1150 rpm) at 23 °C for 30 min, after which time $NaIO_4$ (16.7 µL of 10 mM solution, final concentration 1.0 mM) was added and the reaction was run for 15 min at 23 °C (1150 rpm). The reaction mixture was then quenched by addition of 41.7 µL of buffer containing 0.2 M phosphate buffer, pH 7, 50 mM DTT and 0.05% (wt/vol) octyl-β-D-glucopyranoside. The samples were gently stirred for 1 min and then sodium chloride (23.1 µL of 5 M solution) was added to a final concentration of 0.5 M and the resulting solution was incubated with streptavidin-coated magnetic beads (25 µL, Dynabeads®MyOne™ Streptavidin C_1) for 1 h at 23 °C under stirring (1400 rpm). The enrichment protocol was the same as described for the capture assays (see p. S18). Finally, 30 µL of 2X denaturing Laemmli buffer (100 mM Tris-HCl, pH 6.8, 2% SDS, 20% glycerol, 4% β-mercaptoethanol) were added to the beads, and the resulting solution was heated to 95 °C for 10 min under stirring (1400 rpm) prior to electrophoretic analysis.

Sample preparation and protein digestion prior to electrophoretic analysis

The proteins samples solubilized in Laemmli buffer were loaded onto 10% acrylamide SDS-PAGE. After a short migration limited to the first centimeter of the separation gel, the gel was revealed by colloidal blue staining. Bands were cut in slices of equal volume. Gel slices were distained in 25 mM ammonium bicarbonate, 50% acetonitrile (ACN) in water, rinsed twice with ultrapure water and shrunk in ACN for 10 min. After ACN removal, gel slices were dried at room temperature, resuspended in 30 mM DTT for 30 min at 56 °C followed by incubation in 100 mM iodoacetamide for 30 min at room temperature. After solution removal, gel slices were dried again in ACN and subsequently covered with the trypsin solution (10 ng/µl in 40 mM NH_4HCO_3 and 10% ACN), rehydrated at 4 °C for 10 min, and finally incubated overnight at 37 °C. Slices were then incubated for 15 min after addition of 40 mM NH_4HCO_3 and 10% ACN at room temperature with rotary shaking. The supernatant was collected, and an H_2O/ACN/HCOOH (47.5:47.5:5) extraction solution was added onto gel slices for 15 min. The extraction step was repeated twice. All supernatants were pooled and concentrated in a vacuum centrifuge to a final volume of 45 µL. Digests were finally acidified by addition of 1.5 µL of formic acid (5%, v/v) and stored at -20 °C.

nLC-MS/MS analysis

The resulting peptide digests were analyzed on an Ultimate 3000 nanoLC system (Dionex) coupled to a nanospray LTQ-Orbitrap XL mass spectrometer (ThermoFinnigan, San Jose, CA). Ten microliters of peptide digests were loaded onto a 300-µm-inner diameter (id) x 5-mm C18 PepMapTM trap column (LC Packings) at a flow rate of 30 µL/min. The peptides were eluted from the trap column onto an analytical 75-mm id x 15-cm C18 Pep-Map column (LC Packings) with a 2-40% linear gradient of solvent B in 48 min (solvent A was 0.1% formic acid in 5% ACN, and solvent B was 0.1% formic acid in 80% ACN). The separation flow rate was set at 200 nL/min. The mass spectrometer operated in positive ion mode at a 1.8-kV needle voltage and a 46-V capillary voltage. Data were acquired in a data-dependent mode, alternating an FTMS scan survey over the range m/z 300–1700 and six ion trap MS/MS scans with CID (Collision Induced Dissociation) as activation mode. MS/MS spectra were acquired using a 3-m/z unit ion isolation window and normalized collision energy of 35. Mono-charged ions and unassigned charge-state ions were rejected from fragmentation. Dynamic exclusion duration was set to 30 s.

Database search and results processing

Data were searched by SEQUEST through Proteome Discoverer 1.4 (Thermo Fisher Scientific Inc.) against the LDOX sequence embedded in the Reference Proteome Set of *Escherichia coli* (2014-05: 4270 entries). Spectra from peptides higher than 5000 Da or lower than 350 Da were rejected. The search parameters were as follows: mass accuracy of the monoisotopic peptide precursor and peptide fragments was set to 10 ppm and 0.6 Da respectively. Only b- and y-ions were considered for mass calculation. Oxidation of methionines (+16 Da) and carabamidomethylation of cysteines (+57 Da) were considered as variable modification. Two missed trypsin cleavages were allowed. Peptide validation was performed using Percolator algorithm[7] and only "high confidence" peptides were retained corresponding to a 1% False Positive Rate at peptide level. Results are given as "grouped" listing so as to present the minimal number of proteins covering all detected peptides. Hits with score below 1.6 and identified by one peptide only were not included in the final list of proteins. LDOX was unambiguously identified in each competitive affinity assay and the following results processing (Tables S2 and S3) are representative of the triplicate analyses thus performed.

Table S2. Sequence of unique peptides of LDOX identified by LC-MS/MS analysis of the fraction captured by the affinity strategy carried out over depleted *E.coli* proteome supplemented by 0.5 %/wt LDOX and corresponding identification scores (XCorr).

Sequence	XCorr
VESLSSSGIQSIPK	2.86
MVTSVAPR	2.02
IILKPLPETVSETEPPLFPPR	1.91
TQEALLSK	1.48
KINYYPK	1.31

Table S3. Proteins identified by LC-MS/MS analysis of the fraction captured by the affinity strategy carried out over depleted *E. coli* proteome supplemented by 0.5 %/wt LDOX: accession number, description of the protein, protein score, number of unique peptides and deduced sequence coverage.

Accession	Description	Protein sscore	Sequence coverage	Unique peptides
P0A853	Tryptophanase OS=Escherichia coli (strain K12) GN=tnaA PE=1 SV=1 - [TNAA_ECOLI]	99,25	35,88	18
P0ABT2	DNA protection during starvation protein OS=Escherichia coli (strain K12) GN=dps PE=1 SV=2 - [DPS_ECOLI]	47,56	49,10	8
P0ABD8	Biotin carboxyl carrier protein of acetyl-CoA carboxylase OS=Escherichia coli (strain K12) GN=accB PE=1 SV=1 - [BCCP_ECOLI]	32,25	39,10	4
P06959	Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex OS=Escherichia coli (strain K12) GN=aceF PE=1 SV=3 - [ODP2_ECOLI]	29,02	17,30	9
P0AB71	Fructose-bisphosphate aldolase class 2 OS=Escherichia coli (strain K12) GN=fbaA PE=1 SV=2 - [ALF_ECOLI]	14,75	15,04	4
P35340	Alkyl hydroperoxide reductase subunit F OS=Escherichia coli (strain K12) GN=ahpF PE=1 SV=2 - [AHPF_ECOLI]	12,17	14,01	6
P0CE47	Elongation factor Tu 1 OS=Escherichia coli (strain K12) GN=tufA PE=1 SV=1 - [EFTU1_ECOLI]	11,30	16,24	6
P51093	**LDOX [LDOX_VITVI]**	**8,13**	**15,03**	**5**
P0ADY7	50S ribosomal protein L16 OS=Escherichia coli (strain K12) GN=rplP PE=1 SV=1 - [RL16_ECOLI]	7,97	13,24	2
P60422	50S ribosomal protein L2 OS=Escherichia coli (strain K12) GN=rplB PE=1 SV=2 - [RL2_ECOLI]	6,37	12,09	2
P04982	D-ribose pyranase OS=Escherichia coli (strain K12) GN=rbsD PE=1 SV=3 - [RBSD_ECOLI]	6,10	10,07	1
P0A9Q7	Aldehyde-alcohol dehydrogenase OS=Escherichia coli (strain K12) GN=adhE PE=1 SV=2 - [ADHE_ECOLI]	5,84	3,25	2
P0AE08	Alkyl hydroperoxide reductase subunit C OS=Escherichia coli (strain K12) GN=ahpC PE=1 SV=2 - [AHPC_ECOLI]	5,31	21,39	3
P0A9G6	Isocitrate lyase OS=Escherichia coli (strain K12) GN=aceA PE=1 SV=1 - [ACEA_ECOLI]	5,02	5,99	2
P0A7X3	30S ribosomal protein S9 OS=Escherichia coli (strain K12) GN=rpsI PE=1 SV=2 - [RS9_ECOLI]	4,53	15,38	2
P0A7L3	50S ribosomal protein L20 OS=Escherichia coli (strain K12) GN=rplT PE=1 SV=2 - [RL20_ECOLI]	3,74	12,71	2
P21599	Pyruvate kinase II OS=Escherichia coli (strain K12) GN=pykA PE=1 SV=3 - [KPYK2_ECOLI]	2,77	3,54	1
P0AFG6	Dihydrolipoyllysine-residue succinyltransferase component of 2-oxoglutarate dehydrogenase complex OS=Escherichia coli (strain K12) GN=sucB PE=1 SV=2 - [ODO2_ECOLI]	2,74	4,44	1
P0AG55	50S ribosomal protein L6 OS=Escherichia coli (strain K12) GN=rplF PE=1 SV=2 - [RL6_ECOLI]	2,22	3,95	1
P0AG44	50S ribosomal protein L17 OS=Escherichia coli (strain K12) GN=rplQ PE=1 SV=1 - [RL17_ECOLI]	2,08	6,30	1
P0ADZ4	30S ribosomal protein S15 OS=Escherichia coli (strain K12) GN=rpsO PE=1 SV=2 - [RS15_ECOLI]	1,96	15,73	2
P08839	Phosphoenolpyruvate-protein phosphotransferase OS=Escherichia coli (strain K12) GN=ptsI	1,94	1,91	1

	PE=1 SV=1 - [PT1_ECOLI]			
P0A7S9	30S ribosomal protein S13 OS=Escherichia coli (strain K12) GN=rpsM PE=1 SV=2 - [RS13_ECOLI]	1,90	7,63	1
P31057	3-methyl-2-oxobutanoate hydroxymethyltransferase OS=Escherichia coli (strain K12) GN=panB PE=1 SV=1 - [PANB_ECOLI]	1,75	3,79	1
P0A799	Phosphoglycerate kinase OS=Escherichia coli (strain K12) GN=pgk PE=1 SV=2 - [PGK_ECOLI]	1,71	3,62	1

Additional references

[1] S. Fixon-Owoo, F. Levasseur, K. Williams, T. N. Sabado, M. Lowe, M. Klose, A. J. Mercier, P. Fields, J. Atkinson. *Phytochemistry*, **2003**, *63*, 315-334.

[2] C. Chalumeau, D. Deffieux, S. Chaignepain, S. Quideau. *ChemBioChem*, **2011**, *12*, 1193-1197.

[3] A. Barazza, M. Götz, S. A. Cadamuro, P. Goetting, M. Willem, H. Steuber, T. Kohler, A. Jestel, L. Moroder. *ChemBioChem*, **2007**, *8*, 2078-2091.

[4] D. Rotili, M. Altun, R.B. Hamed, C. Loenarz, C.J. Schofield. *ChemComm.,* **2011**, *47*, 1488-1490.

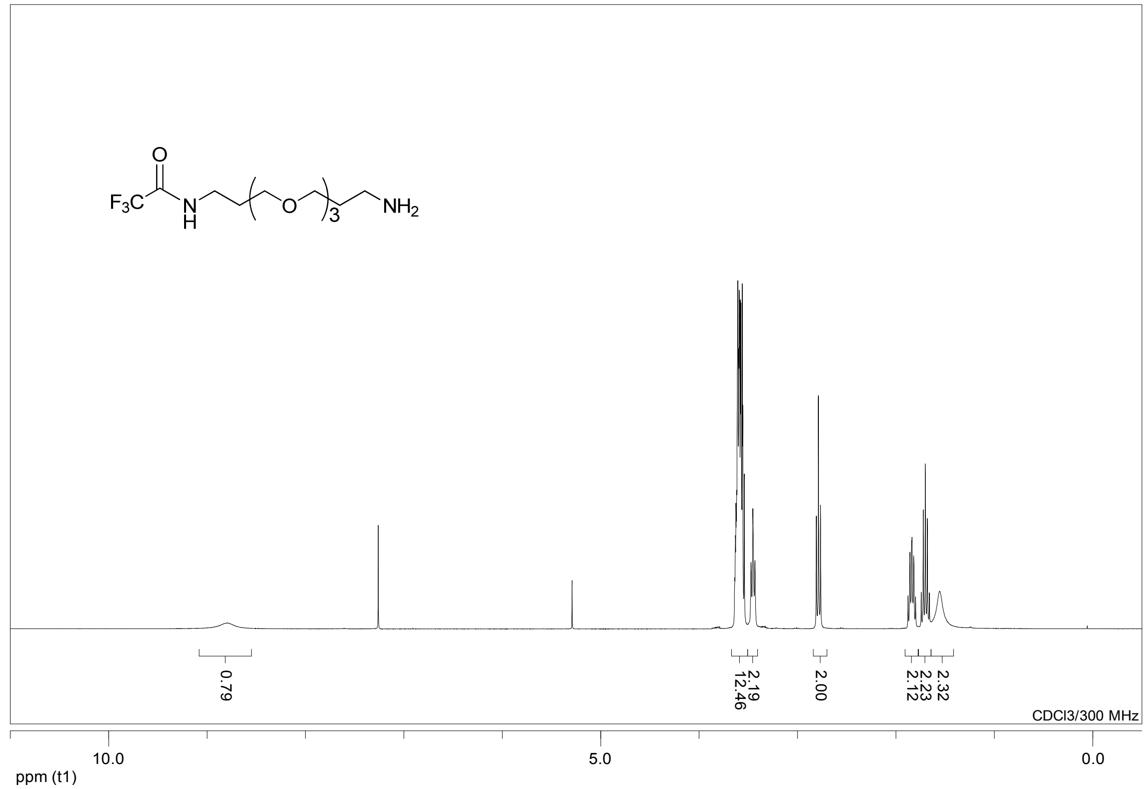
[5] M. M. Bradford. *Anal. Biochem*., **1976**, *72*, 248-54.

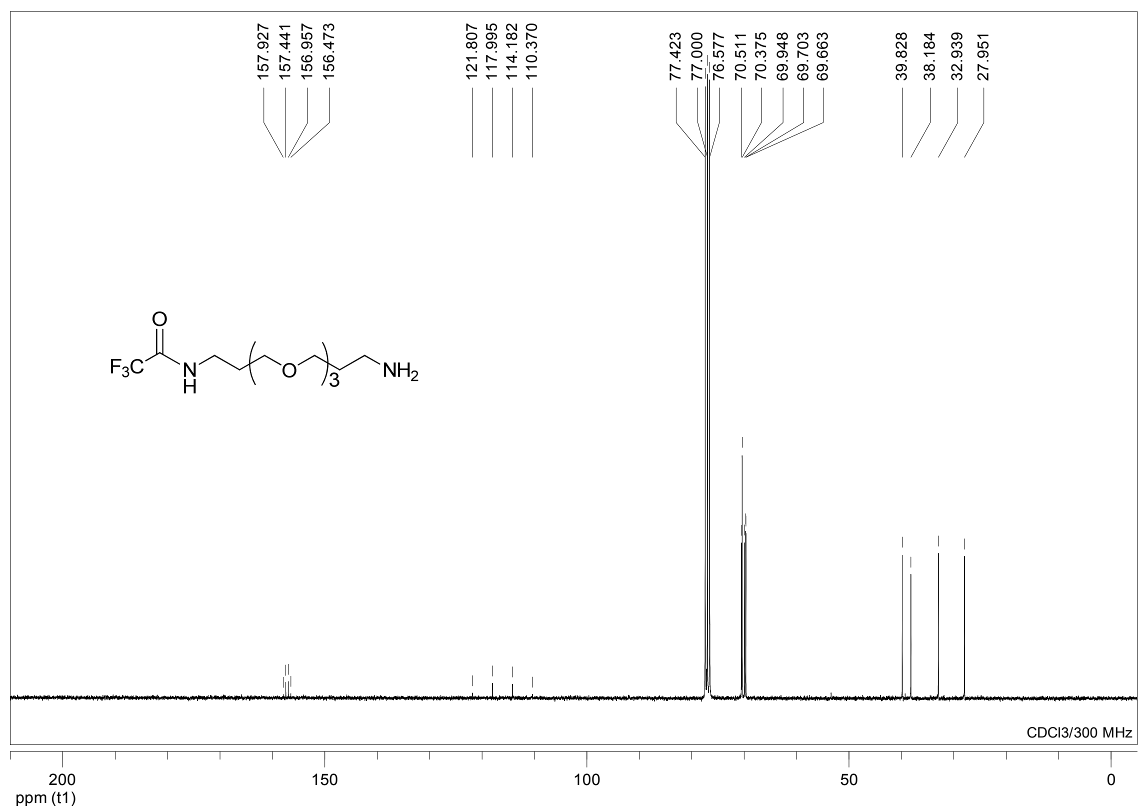
[6] H. Towbin, T. Staehelin, J. Gordon. *PNAS*., **1979**, *76*, 4350-4353.

[7] L. Käll, J. D. Canterbury, J. Weston, W. Stafford Noble, M. J. MacCross, *Nat. Methods*, **2007**, 4, 923-925.

^1H and ^{13}C spectra for all compounds

Compound 6

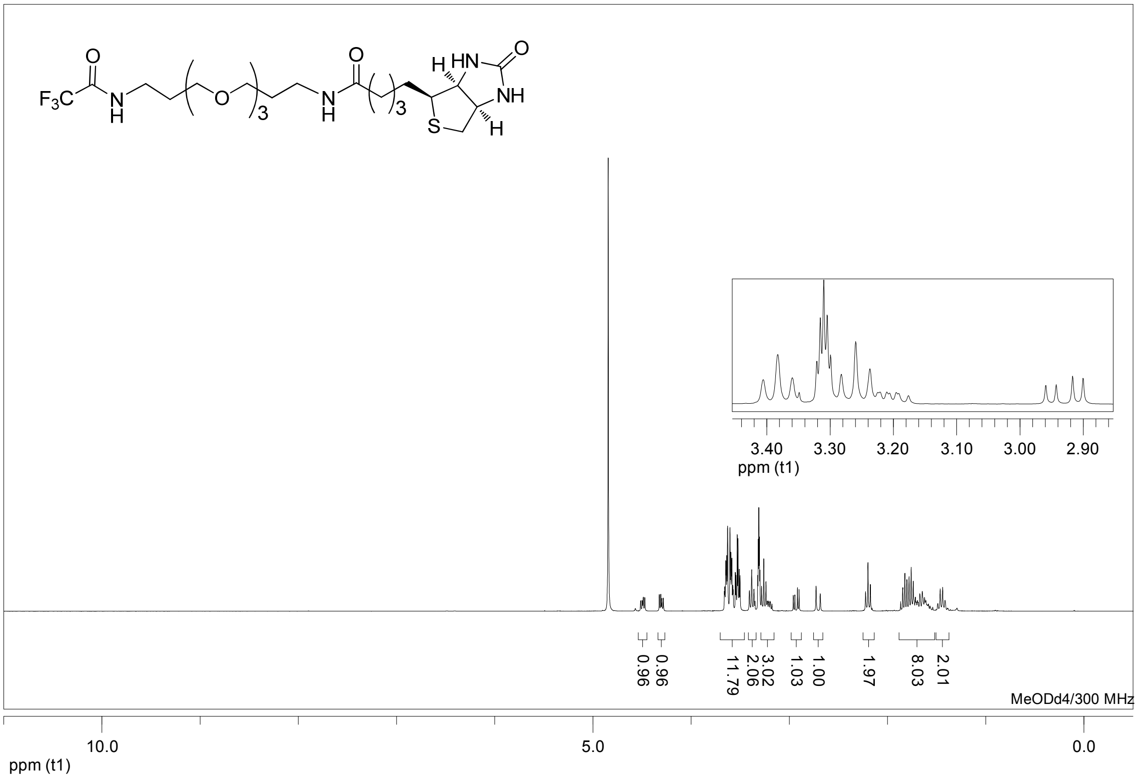




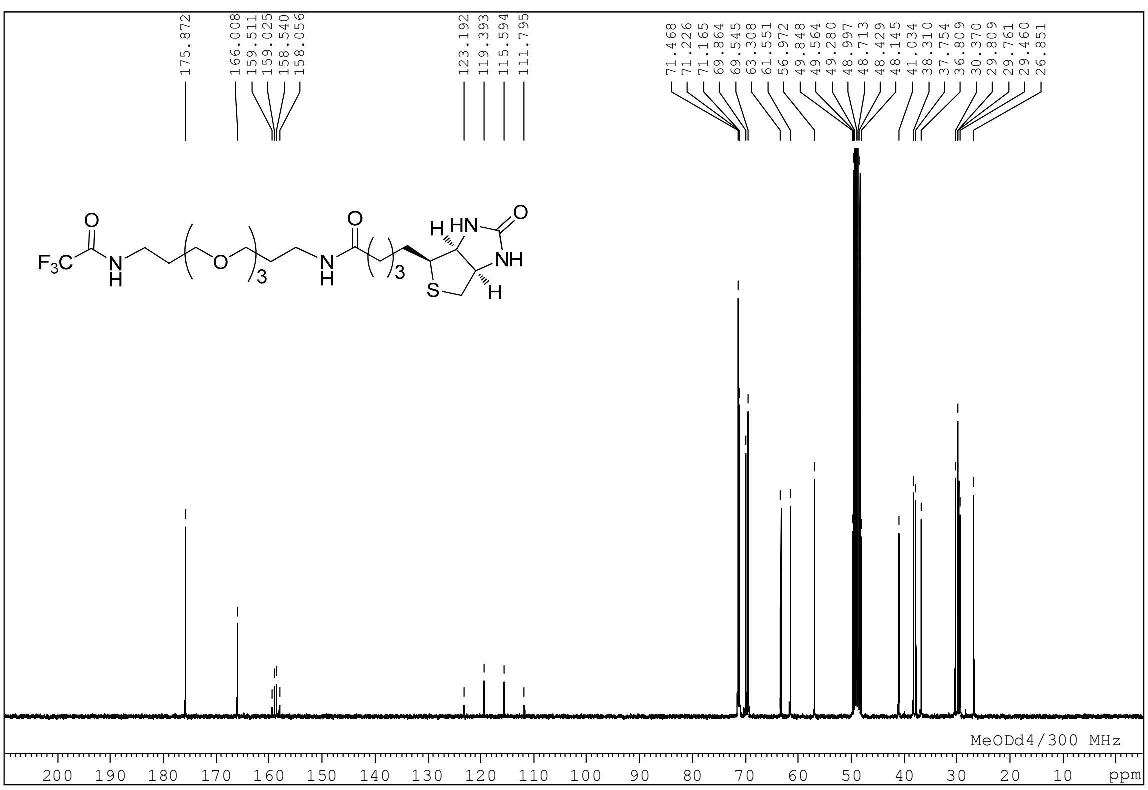
Compound 6

Index	ppm	Hz	Point	Height
1	8.794	2639.620	12162.974	126.326
2	7.260	2179.131	14601.404	2306.010
3	5.290	1587.942	17731.931	1066.392
4	3.636	1091.436	20361.083	1161.439
5	3.630	1089.583	20370.900	2085.755
6	3.625	1088.090	20378.804	2800.603
7	3.621	1087.059	20384.261	2616.687
8	3.606	1082.397	20408.949	7709.724
9	3.596	1079.288	20425.412	6206.423
10	3.591	1077.920	20432.656	7488.491
11	3.580	1074.679	20449.820	7263.871
12	3.574	1072.939	20459.033	7191.081
13	3.560	1068.642	20481.785	7609.947
14	3.556	1067.297	20488.910	4917.660
15	3.540	1062.611	20513.722	3410.553
16	3.471	1041.983	20622.955	1466.468
17	3.453	1036.526	20651.853	2653.016
18	3.432	1030.037	20686.210	1497.146
19	2.808	842.860	21677.375	2507.820
20	2.786	836.396	21711.599	5169.433
21	2.765	829.950	21745.734	2730.842
22	1.876	563.081	23158.890	740.475
23	1.857	557.251	23189.761	1700.977
24	1.839	552.036	23217.376	1957.305
25	1.836	551.080	23222.437	2024.770
26	1.819	545.868	23250.037	1614.989
27	1.799	540.061	23280.789	707.034
28	1.742	522.864	23371.849	813.621
29	1.721	516.641	23404.800	2631.396
30	1.700	510.398	23437.861	3645.693
31	1.680	504.229	23470.529	2438.989
32	1.659	497.936	23503.853	790.580
33	1.555	466.702	23669.246	825.644

Compound 7



F3C
O
N
H
O
3
N
H
O
3
H
HN
O
NH
S
H
3.40
3.30
3.20
3.10
3.00
2.90
ppm (t1)
0.96
0.96
11.79
2.06
3.02
1.03
1.00
1.97
8.03
2.01
MeODd4/300 MHz
10.0
5.0
0.0
ppm (t1)



175.872
166.008
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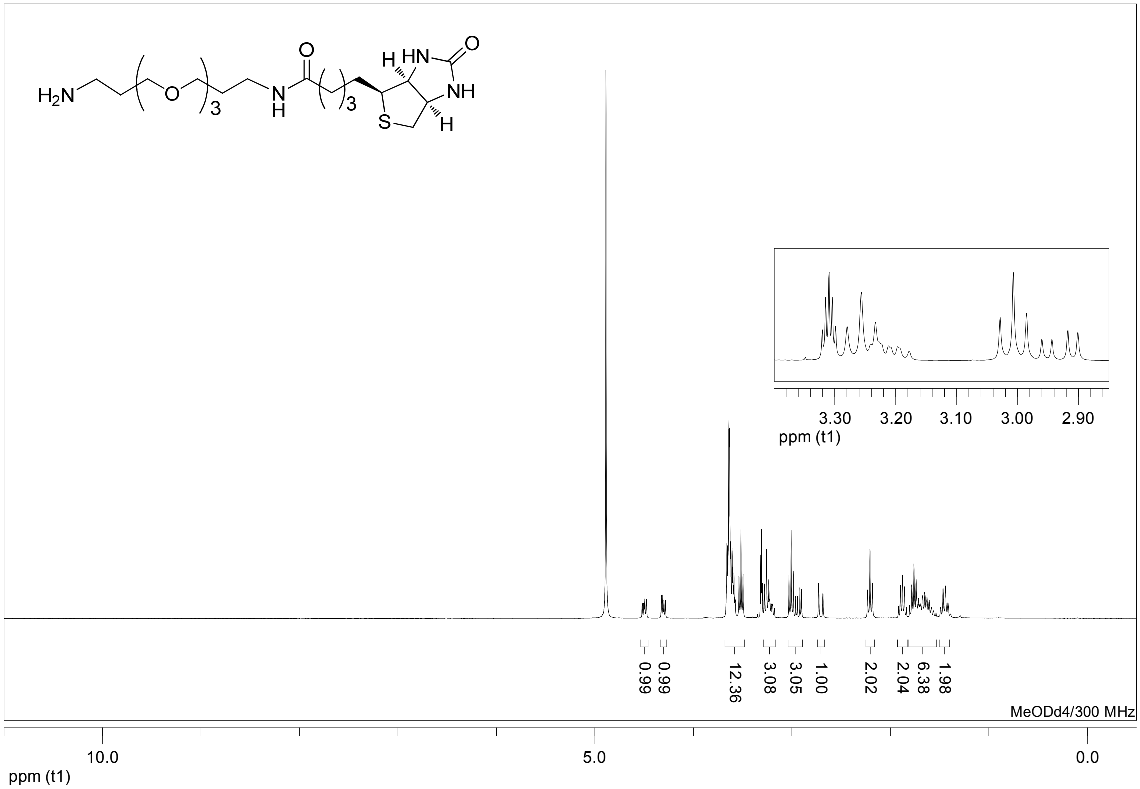
158.540
158.056
123.192
119.393
115.594
111.795
71.468
71.226
71.165
69.864
69.545
63.308
61.551
56.972
49.848
49.564
49.280
48.997
48.713
48.429
48.145
41.034
38.310
37.754
36.809
30.370
29.809
29.761
29.460
26.851
MeODd4/300 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Compound 7

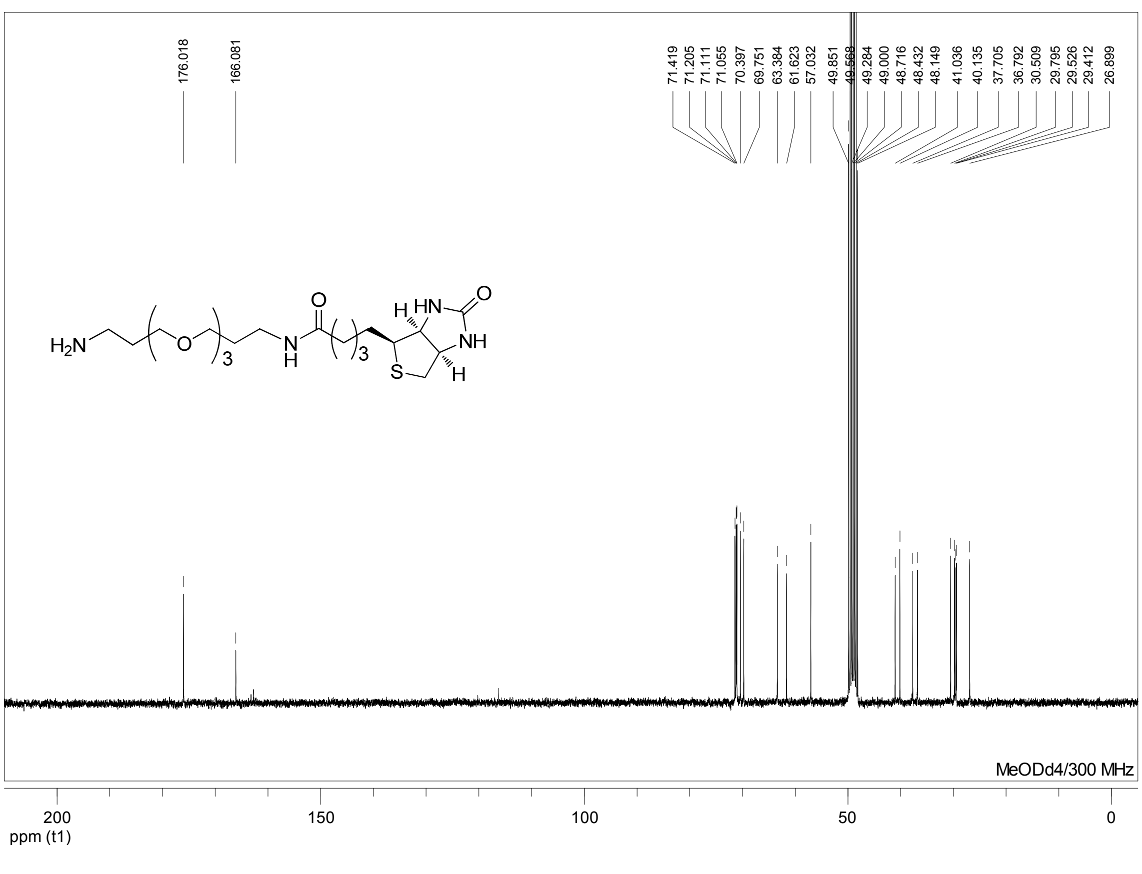
Index	ppm	Hz	Point	Height
1	4.844	1453.963	18450.068	67220.601
2	4.514	1354.993	18974.144	1354.014
3	4.511	1354.205	18978.316	1558.948
4	4.498	1350.071	19000.205	1596.805
5	4.495	1349.286	19004.361	1497.619
6	4.488	1347.100	19015.937	1839.511
7	4.485	1346.336	19019.982	2081.791
8	4.471	1342.190	19041.937	2041.275
9	4.469	1341.432	19045.955	1865.629
10	4.323	1297.558	19278.281	2475.222
11	4.308	1293.103	19301.869	2516.722
12	4.296	1289.683	19319.980	1930.969
13	4.282	1285.220	19343.613	1961.166
14	3.660	1098.702	20331.283	2964.874
15	3.655	1097.271	20338.861	3626.305
16	3.646	1094.538	20353.333	7519.771
17	3.642	1093.209	20360.371	6031.885
18	3.636	1091.330	20370.322	8284.728
19	3.627	1088.809	20383.667	12640.755
20	3.603	1081.438	20422.699	12403.603
21	3.595	1079.104	20435.058	8734.953
22	3.589	1077.258	20444.833	6158.796
23	3.584	1075.915	20451.947	7878.540
24	3.575	1073.184	20466.406	3849.078
25	3.570	1071.712	20474.201	3235.040
26	3.549	1065.346	20507.914	5769.771
27	3.542	1063.103	20519.789	5328.570
28	3.529	1059.329	20539.773	11366.467
29	3.521	1056.913	20552.566	10817.418
30	3.509	1053.311	20571.642	6249.723
31	3.501	1050.754	20585.183	5314.507
32	3.405	1022.144	20736.683	3051.941
33	3.382	1015.236	20773.263	6162.462
34	3.359	1008.325	20809.857	3285.281
35	3.320	996.681	20871.517	5349.354
36	3.315	995.051	20880.146	10715.560
37	3.310	993.412	20888.824	15390.318
38	3.304	991.787	20897.429	11076.835
39	3.299	990.165	20906.021	6104.879
40	3.282	985.084	20932.923	3713.454
41	3.259	978.245	20969.140	7761.496
42	3.236	971.483	21004.949	4394.740
43	3.224	967.730	21024.822	1471.149
44	3.220	966.692	21030.318	1523.192
45	3.210	963.494	21047.250	1519.473
46	3.206	962.197	21054.117	1389.121
47	3.195	959.007	21071.011	1473.610
48	3.191	957.847	21077.154	1352.604
49	3.176	953.239	21101.556	1065.423
50	2.959	888.081	21446.583	2358.145
51	2.942	883.118	21472.865	2430.725
52	2.916	875.335	21514.082	3498.443
53	2.900	870.376	21540.339	3240.674
54	2.726	818.347	21815.851	3720.034
55	2.684	805.637	21883.152	2582.196
56	2.222	667.051	22617.007	2868.312
57	2.198	659.753	22655.654	7197.749

Index	ppm	Hz	Point	Height
58	2.173	652.375	22694.724	3974.652
59	1.845	553.847	23216.458	3410.381
60	1.843	553.178	23220.003	3480.768
61	1.822	547.021	23252.603	5642.855
62	1.802	540.870	23285.175	4689.618
63	1.780	534.193	23320.533	5140.242
64	1.759	527.851	23354.115	6521.988
65	1.737	521.385	23388.357	4464.024
66	1.715	514.783	23423.312	2082.762
67	1.670	501.292	23494.753	2587.781
68	1.645	493.859	23534.113	2955.878
69	1.622	486.796	23571.513	2043.573
70	1.538	461.783	23703.964	593.326
71	1.486	446.115	23786.935	1156.512
72	1.463	439.087	23824.146	3304.881
73	1.438	431.490	23864.378	3547.750
74	1.414	424.285	23902.527	1622.569

Compound 3



H2N
O
3
N
H
O
3
H
HN
O
NH
S
H
3.30
3.20
3.10
3.00
2.90
ppm (t1)
0.99
0.99
12.36
3.08
3.05
1.00
2.02
2.04
6.38
1.98
MeODd4/300 MHz
10.0
5.0
0.0
ppm (t1)



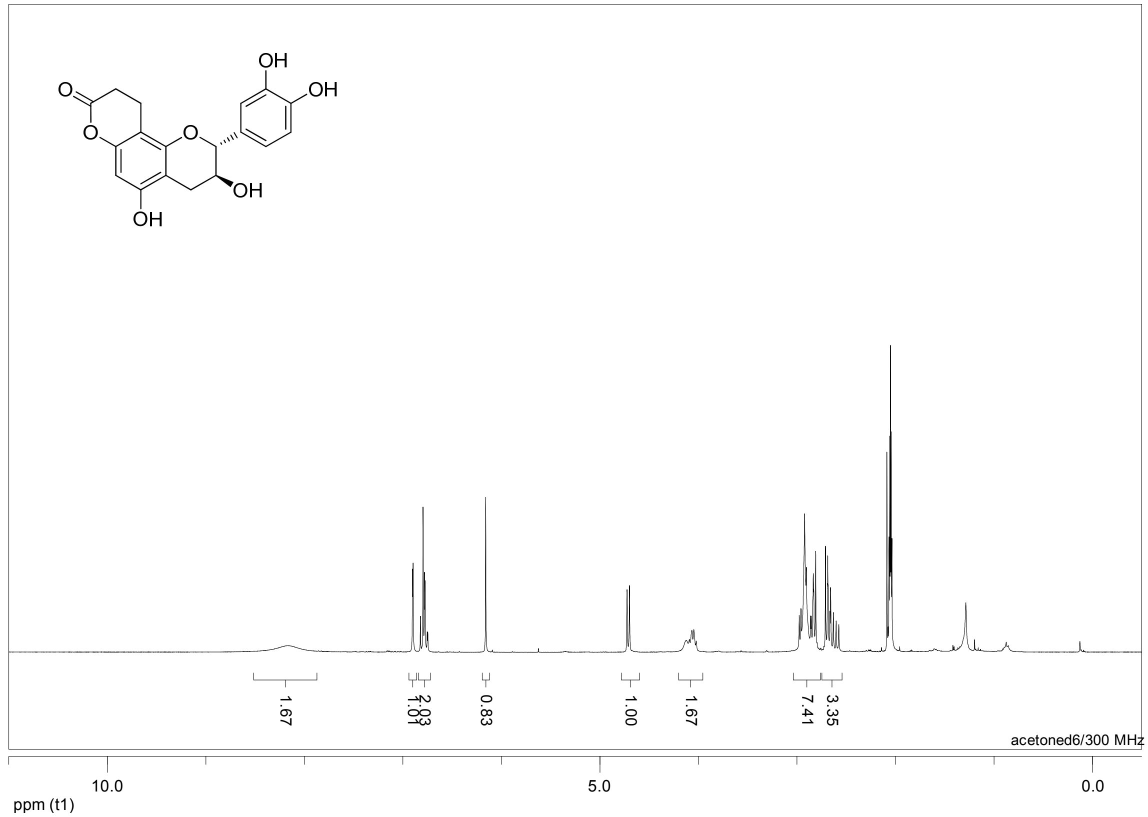
176.018
166.081
71.419
71.205
71.111
71.055
70.397
69.751
63.384
61.623
57.032
49.851
49.568
49.284
49.000
48.716
48.432
48.149
41.036
40.135
37.705
36.792
30.509
29.795
29.526
29.412
26.899
H2N
O
3
N
H
O
3
H
HN
O
NH
S
H
MeODd4/300 MHz
200
150
100
50
0
ppm (t1)

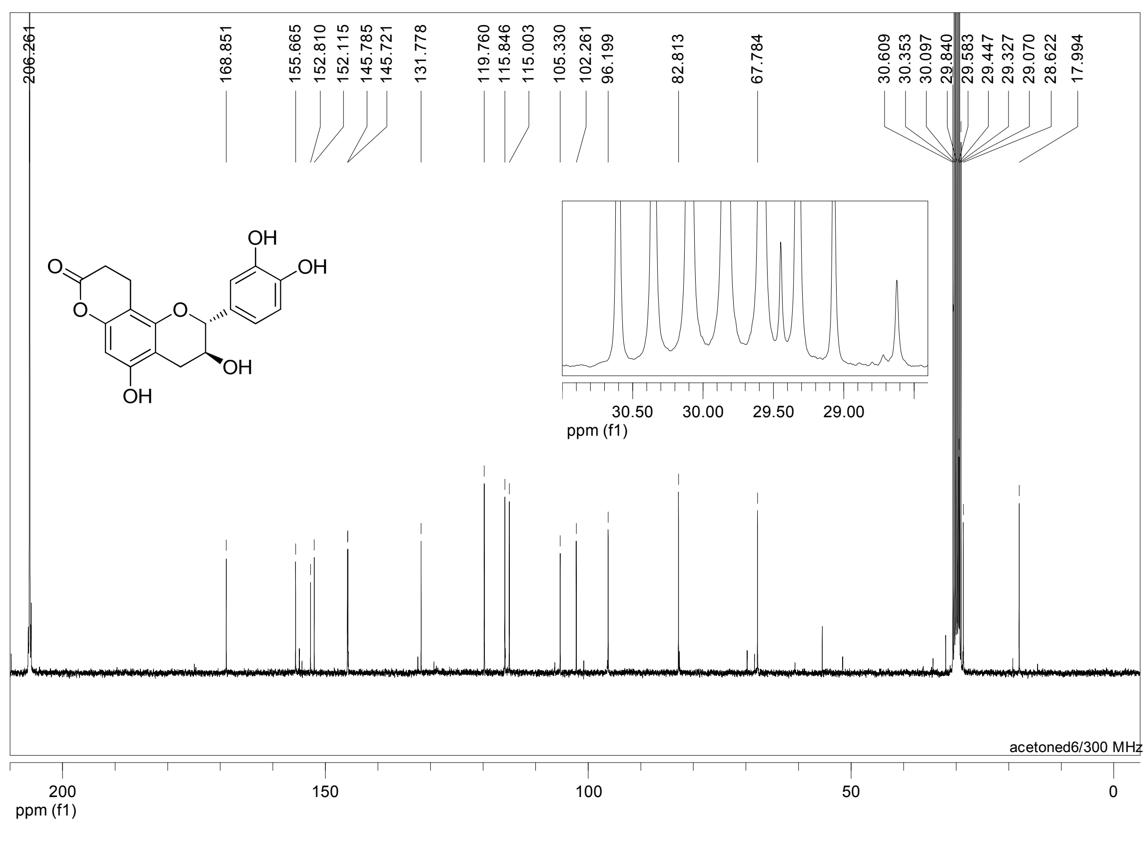
Compound 3

Index	ppm	Hz	Point	Height
1	4.887	1467.006	18380.853	27041.970
2	4.518	1356.092	18968.177	731.114
3	4.504	1351.892	18990.417	752.204
4	4.502	1351.245	18993.845	720.569
5	4.491	1348.223	19009.847	966.151
6	4.477	1344.010	19032.158	946.880
7	4.475	1343.373	19035.529	874.046
8	4.325	1298.112	19275.199	1139.445
9	4.310	1293.656	19298.796	1157.840
10	4.298	1290.235	19316.910	891.663
11	4.283	1285.774	19340.533	901.105
12	3.658	1098.174	20333.935	3689.893
13	3.652	1096.320	20343.751	3580.272
14	3.638	1091.998	20366.640	9793.784
15	3.632	1090.313	20375.560	9388.134
16	3.621	1086.820	20394.058	3788.408
17	3.607	1082.737	20415.675	3470.610
18	3.599	1080.199	20429.117	2514.757
19	3.592	1078.227	20439.560	1631.447
20	3.587	1076.710	20447.591	2249.932
21	3.579	1074.164	20461.074	1059.045
22	3.574	1072.859	20467.986	919.079
23	3.536	1061.455	20528.375	2075.062
24	3.516	1055.337	20560.771	4386.745
25	3.495	1049.238	20593.064	2164.758
26	3.320	996.712	20871.208	1548.849
27	3.315	995.061	20879.949	3131.059
28	3.310	993.413	20888.677	4414.013
29	3.304	991.789	20897.275	3152.754
30	3.299	990.145	20905.982	1723.449
31	3.280	984.452	20936.126	1698.545
32	3.256	977.501	20972.937	3401.250
33	3.241	972.850	20997.564	835.069
34	3.233	970.529	21009.851	1908.848
35	3.227	968.767	21019.183	939.910
36	3.212	964.080	21044.003	748.305
37	3.197	959.603	21067.712	707.749
38	3.178	953.891	21097.955	494.915
39	3.029	909.132	21334.968	2144.192
40	3.007	902.608	21369.517	4384.611
41	2.985	896.099	21403.982	2343.531
42	2.960	888.535	21444.035	1083.379
43	2.944	883.591	21470.216	1079.960
44	2.918	875.774	21511.613	1517.648
45	2.901	870.832	21537.779	1429.627
46	2.727	818.487	21814.960	1743.659
47	2.684	805.769	21882.306	1221.200
48	2.231	669.584	22603.449	1403.553
49	2.206	662.278	22642.138	3400.166
50	2.182	654.951	22680.939	1746.556
51	1.918	575.684	23100.681	590.657
52	1.897	569.387	23134.027	1626.249
53	1.877	563.361	23165.933	2133.924
54	1.858	557.663	23196.109	1566.619
55	1.837	551.324	23229.673	563.506
56	1.803	541.216	23283.197	633.601
57	1.782	534.806	23317.140	1653.120

Index	ppm	Hz	Point	Height
58	1.759	528.060	23352.863	2690.914
59	1.738	521.540	23387.388	1911.421
60	1.716	515.055	23421.730	988.346
61	1.707	512.432	23435.621	696.065
62	1.697	509.316	23452.117	731.895
63	1.687	506.454	23467.275	617.869
64	1.674	502.442	23488.521	1121.250
65	1.650	495.230	23526.707	1282.632
66	1.627	488.314	23563.333	1037.050
67	1.605	481.698	23598.367	885.009
68	1.580	474.176	23638.195	534.074
69	1.564	469.462	23663.158	383.604
70	1.559	468.004	23670.880	330.217
71	1.535	460.877	23708.621	282.477
72	1.488	446.486	23784.826	547.995
73	1.464	439.435	23822.162	1488.794
74	1.439	431.867	23862.236	1604.761
75	1.414	424.455	23901.486	774.889

Compound 4a

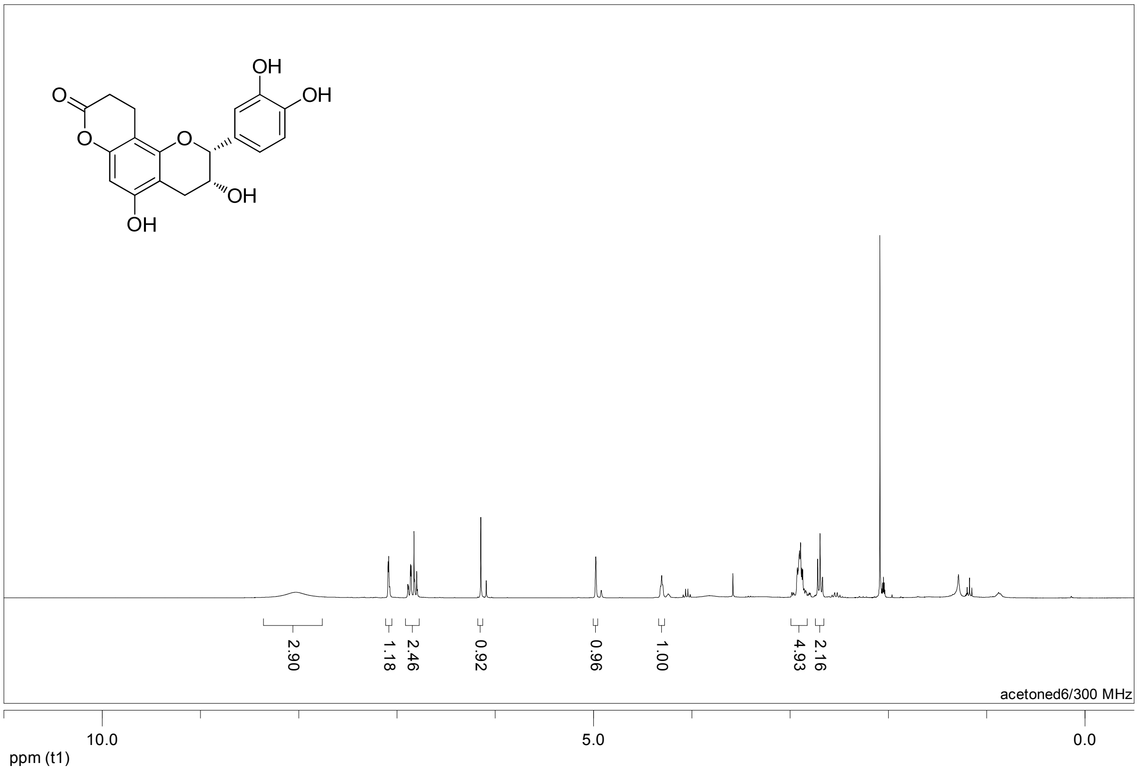




Compound 4a

Index	ppm	Hz	Point	Height
1	8.441	2533.914	12735.027	32.940
2	7.965	2390.907	13492.291	56.185
3	6.901	2071.577	15183.244	3009.926
4	6.895	2069.743	15192.958	3225.358
5	6.821	2047.545	15310.499	1299.601
6	6.794	2039.474	15353.238	5271.714
7	6.779	2035.009	15376.881	2896.877
8	6.773	2033.204	15386.440	2594.844
9	6.752	2026.784	15420.434	724.774
10	6.746	2025.059	15429.570	720.074
11	6.158	1848.599	16363.979	5620.647
12	4.724	1417.887	18644.736	2259.215
13	4.699	1410.490	18683.902	2415.435
14	4.122	1237.446	19600.226	419.227
15	4.091	1227.899	19650.781	451.406
16	4.065	1220.265	19691.203	782.203
17	4.046	1214.353	19722.509	813.935
18	4.021	1206.969	19761.609	393.115
19	2.976	893.256	21422.816	1324.626
20	2.958	887.903	21451.162	1572.447
21	2.921	876.769	21510.123	5019.410
22	2.903	871.479	21538.134	3074.322
23	2.861	858.636	21606.140	1305.076
24	2.853	856.424	21617.855	1299.776
25	2.833	850.369	21649.916	2848.147
26	2.828	848.881	21657.796	2279.400
27	2.809	843.147	21688.160	3656.849
28	2.709	813.301	21846.205	3847.255
29	2.686	806.264	21883.466	3502.426
30	2.683	805.308	21888.531	2447.316
31	2.664	799.788	21917.757	1479.176
32	2.658	797.847	21928.039	2337.076
33	2.629	789.233	21973.652	1429.023
34	2.601	780.792	22018.351	1121.854
35	2.574	772.732	22061.031	989.737
36	2.086	626.033	22837.847	7283.403
37	2.064	619.587	22871.982	4182.388
38	2.057	617.377	22883.683	7870.651
39	2.050	615.184	22895.296	11184.789
40	2.042	612.981	22906.958	8010.547
41	2.035	610.775	22918.640	4131.034
42	1.285	385.582	24111.109	1784.826

Compound 4b


OH
OH
O
O
O
OH
OH
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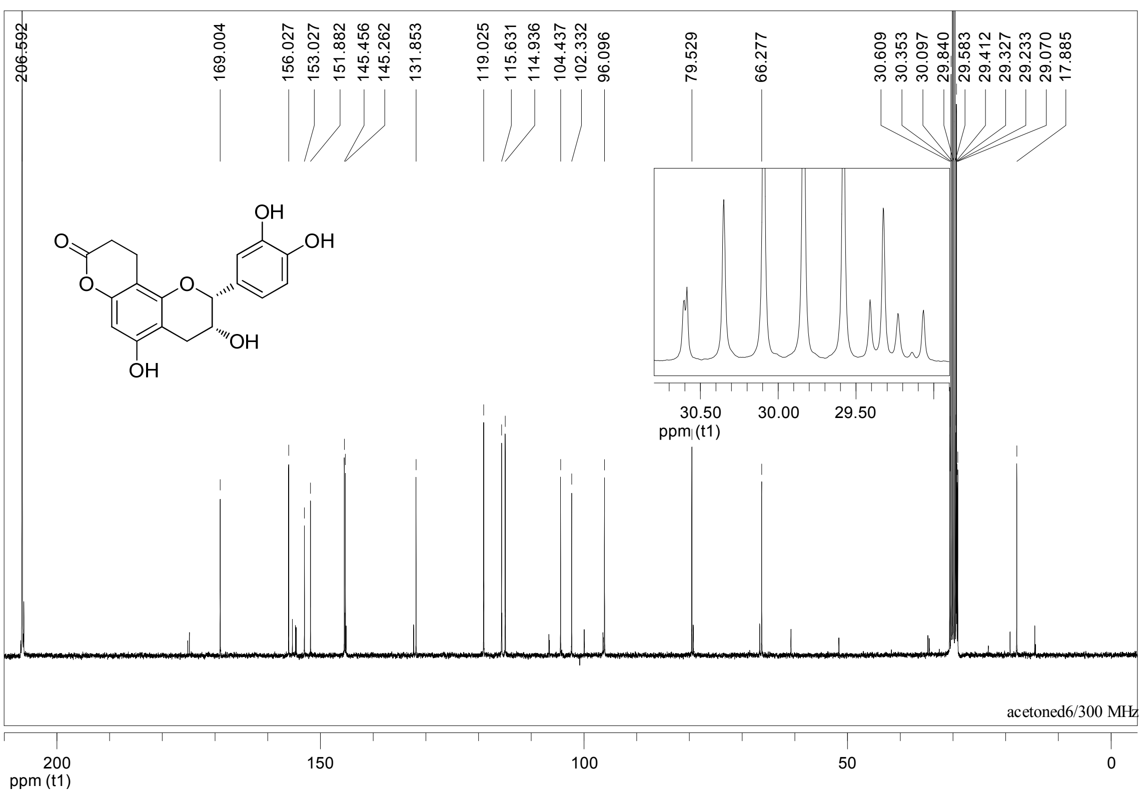
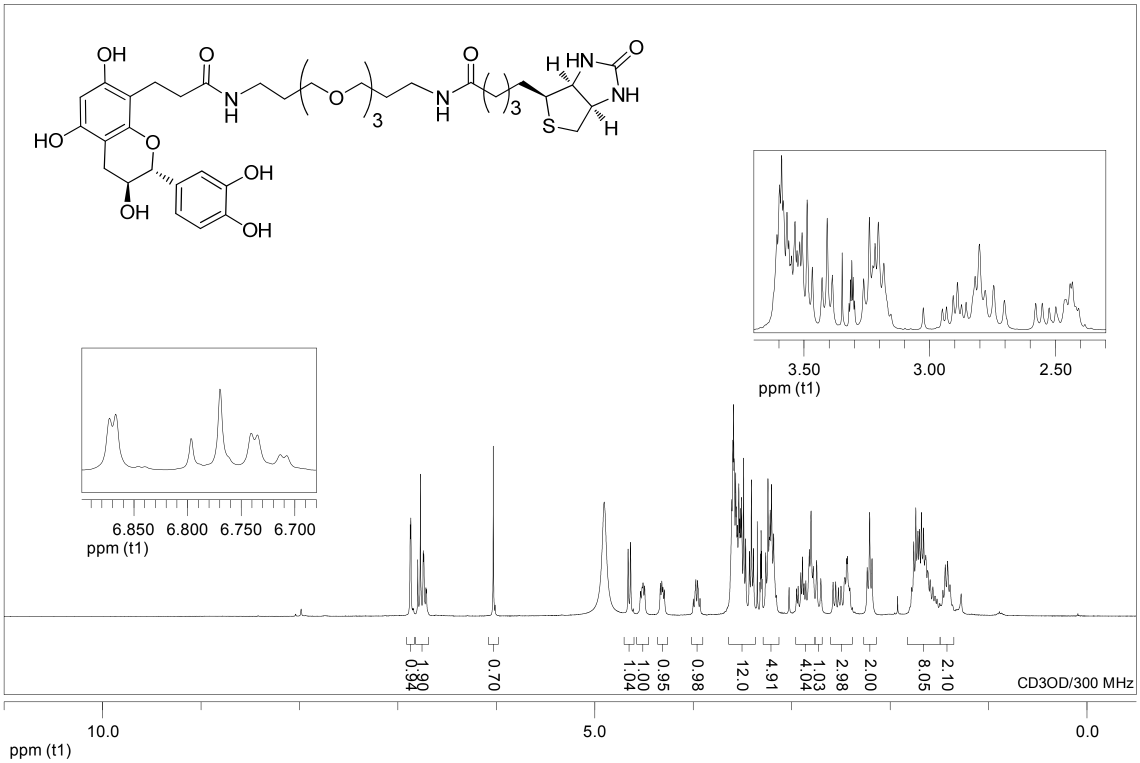
1.18
2.46
0.92
0.96
1.00
4.93
2.16
acetoned6/300 MHz
10.0
5.0
0.0
ppm (t1)

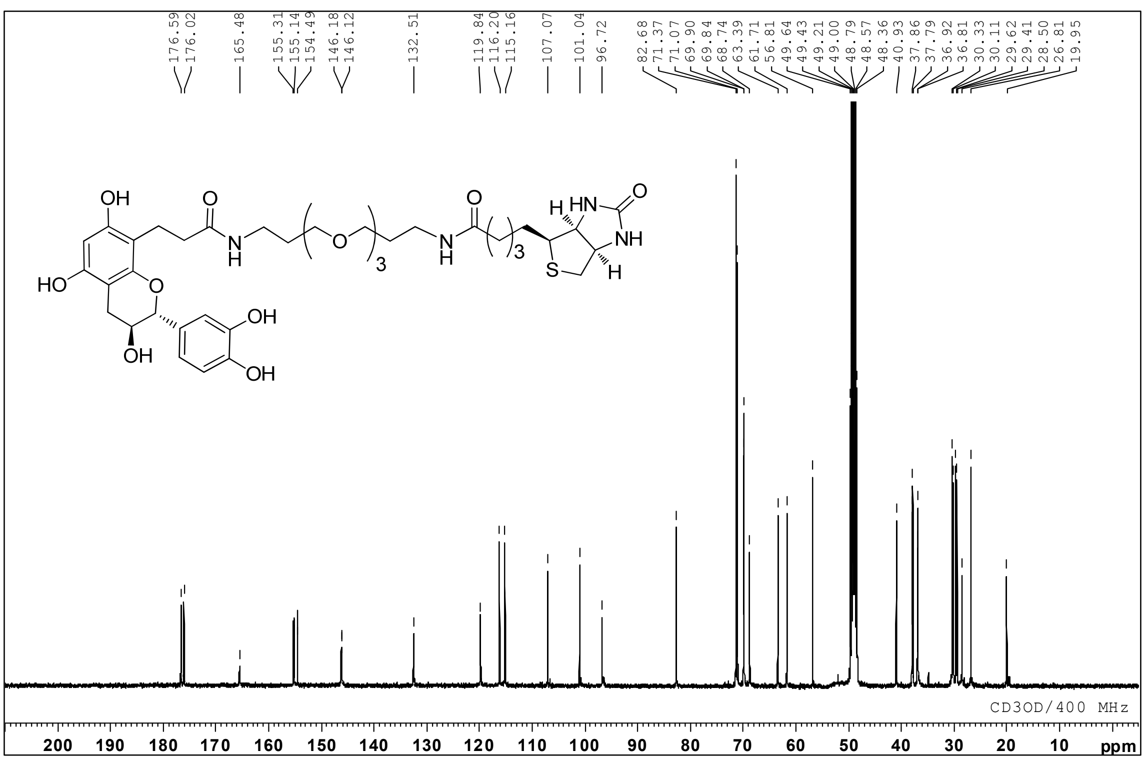

206.592
169.004
156.027
153.027
151.882
145.456
145.262
131.853
119.025
115.631
114.936
104.437
102.332
96.096
79.529
66.277
30.609
30.353
30.097
29.840
29.583
29.412
29.327
29.233
29.070
17.885
OH
OH
O
O
O
OH
OH
30.50
30.00
29.50
ppm (t1)
acetoned6/300 MHz
200
150
100
50
0
ppm (t1)

Compound 4b

Index	ppm	Hz	Point	Height
1	8.023	2408.351	13399.956	358.109
2	7.090	2128.204	14883.416	2359.167
3	7.084	2126.328	14893.354	2718.557
4	6.888	2067.567	15204.512	881.698
5	6.861	2059.396	15247.777	2194.478
6	6.855	2057.798	15256.241	2101.762
7	6.826	2048.940	15303.148	4345.032
8	6.819	2046.924	15313.819	1216.469
9	6.799	2040.800	15346.249	1723.380
10	6.146	1844.873	16383.742	5276.296
11	6.091	1828.362	16471.173	1125.453
12	4.976	1493.720	18243.208	2686.721
13	4.315	1295.356	19293.607	777.838
14	4.306	1292.452	19308.984	1452.731
15	4.296	1289.634	19323.908	866.605
16	3.581	1074.898	20461.000	1578.395
17	2.925	877.968	21503.802	1975.930
18	2.917	875.576	21516.472	1810.887
19	2.904	871.700	21536.996	3078.243
20	2.893	868.292	21555.041	3612.000
21	2.880	864.560	21574.802	1952.002
22	2.871	861.857	21589.115	1861.070
23	2.718	815.974	21832.083	2538.150
24	2.695	808.972	21869.158	4204.691
25	2.671	801.857	21906.837	1325.320
26	2.669	801.064	21911.037	1356.129
27	2.085	625.976	22838.181	23783.408
28	2.064	619.600	22871.943	606.787
29	2.057	617.383	22883.681	985.399
30	2.050	615.184	22895.328	1366.998
31	2.042	612.983	22906.982	996.003
32	2.035	610.776	22918.667	524.721
33	1.286	386.014	24108.853	1530.040
34	1.197	359.423	24249.662	697.456
35	1.174	352.313	24287.308	1320.005
36	1.150	345.182	24325.072	652.496

Probe 1a



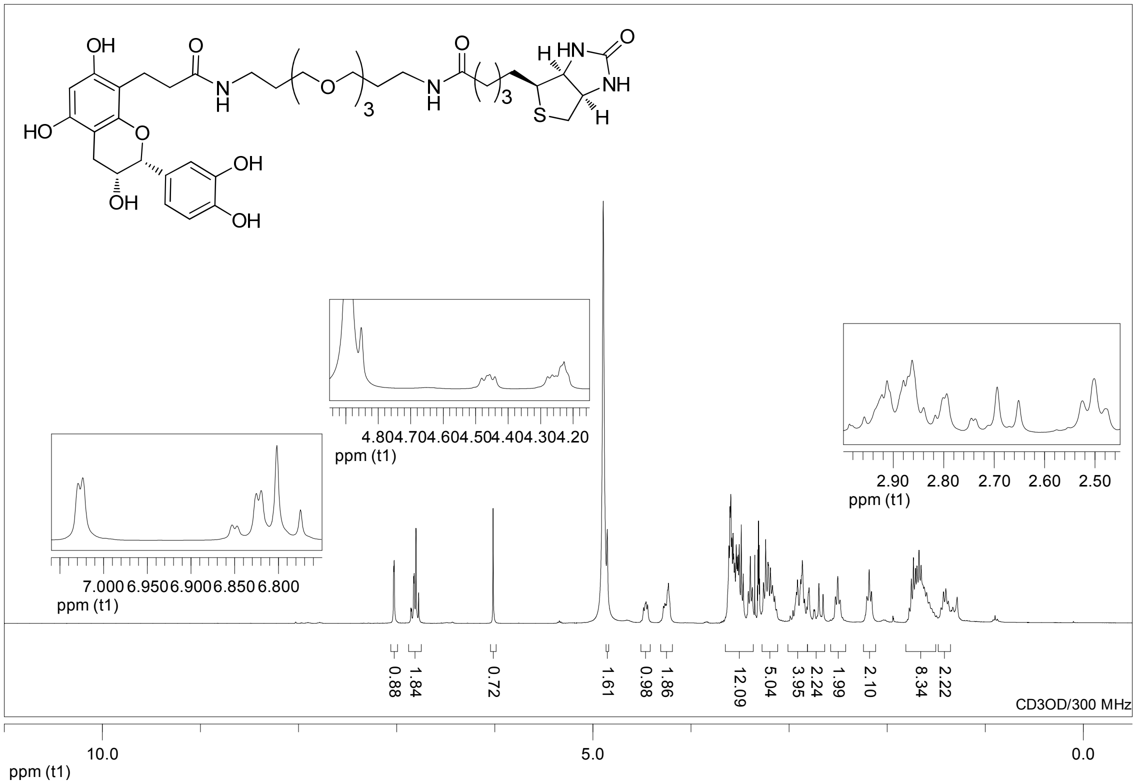


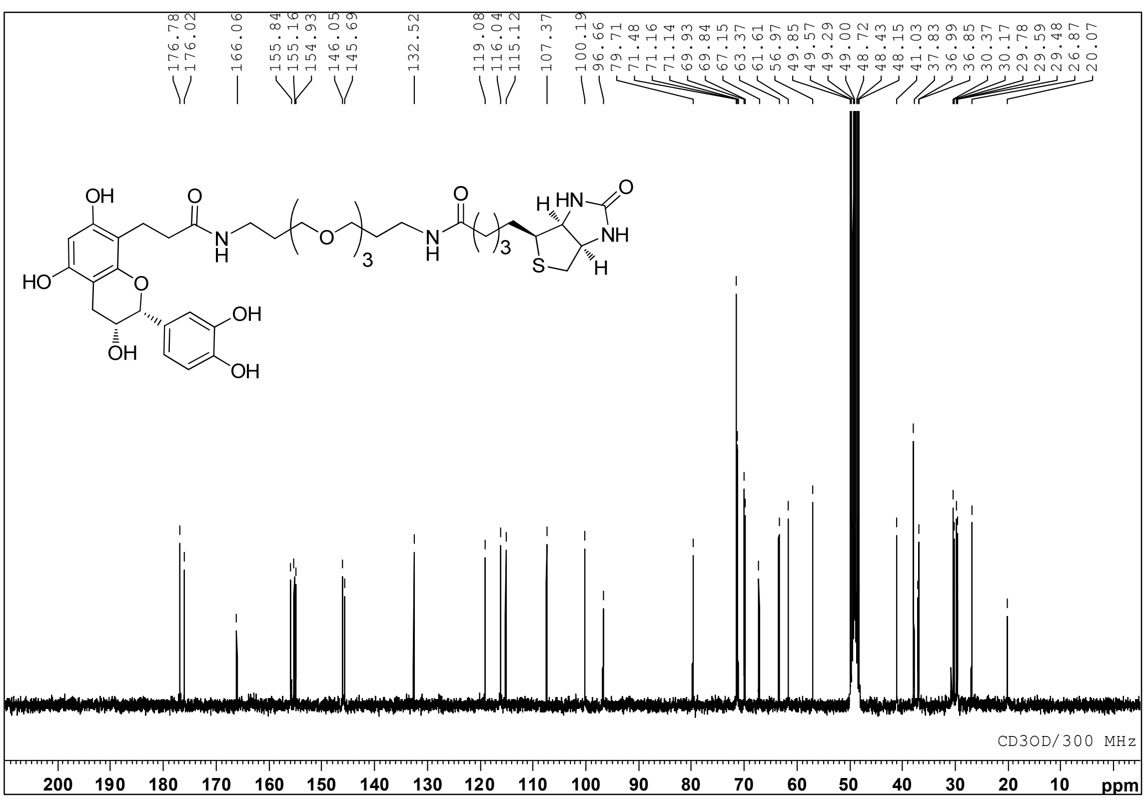
Probe 1a

Index	ppm	Hz	Point	Height
1	6.873	2063.255	15223.207	941.707
2	6.868	2061.533	15232.321	1012.040
3	6.797	2040.383	15344.321	579.702
4	6.770	2032.282	15387.217	1463.759
5	6.741	2023.588	15433.255	673.823
6	6.736	2021.859	15442.407	640.736
7	6.714	2015.433	15476.438	289.648
8	6.708	2013.651	15485.873	272.270
9	6.030	1809.954	16564.509	1763.942
10	4.903	1471.696	18355.693	1175.363
11	4.660	1398.808	18741.658	690.086
12	4.636	1391.542	18780.132	759.276
13	4.534	1361.054	18941.574	254.754
14	4.518	1356.184	18967.363	299.235
15	4.509	1353.380	18982.210	341.135
16	4.493	1348.669	19007.156	308.259
17	4.333	1300.515	19262.146	336.177
18	4.318	1296.172	19285.148	360.407
19	4.307	1292.737	19303.333	294.532
20	4.292	1288.306	19326.798	269.168
21	3.998	1200.053	19794.125	174.320
22	3.973	1192.464	19834.310	375.296
23	3.955	1187.112	19862.652	364.507
24	3.930	1179.572	19902.580	179.992
25	3.608	1082.888	20414.550	1200.743
26	3.597	1079.638	20431.761	1815.458
27	3.589	1077.357	20443.839	2181.985
28	3.582	1075.312	20454.667	1622.553
29	3.568	1070.901	20478.025	1476.014
30	3.561	1068.769	20489.314	1126.940
31	3.554	1066.920	20499.105	832.685
32	3.550	1065.514	20506.552	936.071
33	3.536	1061.307	20528.830	1361.727
34	3.527	1058.821	20541.990	999.850
35	3.517	1055.676	20558.644	1109.770
36	3.508	1052.868	20573.513	1223.998
37	3.487	1046.725	20606.044	1628.343
38	3.467	1040.577	20638.601	796.869
39	3.428	1028.951	20700.166	667.145
40	3.408	1022.836	20732.546	1406.188
41	3.387	1016.732	20764.869	696.775
42	3.348	1004.960	20827.201	975.695
43	3.320	996.668	20871.111	346.404
44	3.315	995.033	20879.769	640.280
45	3.310	993.412	20888.351	883.373
46	3.304	991.775	20897.019	669.009
47	3.299	990.139	20905.687	377.94
48	3.262	979.302	20963.068	651.403
49	3.240	972.478	20999.203	1415.116
50	3.226	968.305	21021.300	814.627
51	3.217	965.655	21035.333	1091.033
52	3.204	961.727	21056.134	1356.393
53	3.182	955.255	21090.404	846.901
54	3.154	946.783	21135.267	214.680
55	3.025	908.076	21340.236	294.153
56	2.949	885.243	21461.144	279.071
57	2.933	880.341	21487.099	305.769

Index	ppm	Hz	Point	Height
58	2.906	872.376	21529.275	446.359
59	2.889	867.264	21556.345	609.429
60	2.873	862.452	21581.828	332.470
61	2.855	857.014	21610.621	362.916
62	2.819	846.197	21667.900	684.533
63	2.802	841.040	21695.212	1082.206
64	2.779	834.064	21732.150	509.802
65	2.745	824.026	21785.302	572.454
66	2.703	811.249	21852.960	385.591
67	2.578	773.906	22050.705	348.376
68	2.552	765.944	22092.867	350.632
69	2.524	757.710	22136.470	292.534
70	2.498	749.789	22178.412	305.984
71	2.462	739.087	22235.083	392.810
72	2.457	737.633	22242.785	396.343
73	2.441	732.718	22268.810	592.820
74	2.432	730.079	22282.783	614.070
75	2.419	726.073	22303.998	307.716
76	2.407	722.614	22322.314	287.989
77	2.231	669.789	22602.039	500.357
78	2.207	662.458	22640.855	1070.793
79	2.183	655.170	22679.451	590.830
80	1.923	577.067	23093.029	201.438
81	1.781	534.493	23318.472	293.835
82	1.759	528.073	23352.464	764.585
83	1.738	521.667	23386.386	1114.295
84	1.717	515.231	23420.470	874.944
85	1.701	510.708	23444.421	894.205
86	1.680	504.352	23478.080	1067.498
87	1.659	497.945	23512.005	907.397
88	1.637	491.289	23547.248	627.948
89	1.618	485.568	23577.542	470.764
90	1.592	477.808	23618.634	374.174
91	1.564	469.581	23662.201	298.693
92	1.544	463.418	23694.837	204.397
93	1.539	462.036	23702.156	203.336
94	1.463	439.080	23823.710	265.809
95	1.439	431.789	23862.320	528.144
96	1.415	424.735	23899.673	563.398
97	1.391	417.471	23938.140	320.524
98	1.277	383.319	24118.986	227.179

Probe 1b


OH
O
H
N
O
3
N
H
O
3
H
HN
O
NH
S
H
HO
O
OH
OH
OH
4.80 4.70 4.60 4.50 4.40 4.30 4.20
ppm (t1)
7.000 6.950 6.900 6.850 6.800
ppm (t1)
2.90 2.80 2.70 2.60 2.50
ppm (t1)
0.88
1.84
0.72
1.61
0.98
1.86
12.09
5.04
3.95
2.24
1.99
2.10
8.34
2.22
CD3OD/300 MHz
10.0
5.0
0.0
ppm (t1)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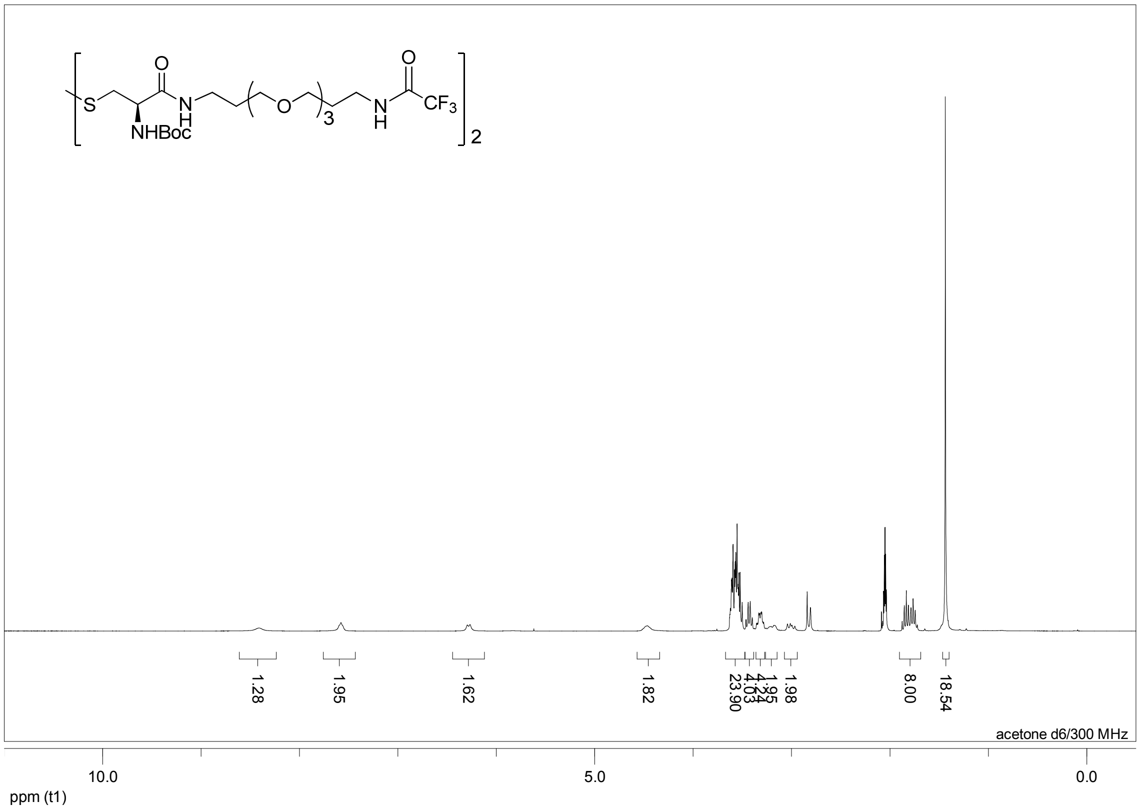
100.19
96.66
79.71
71.48
71.16
71.14
69.93
69.84
67.15
63.37
61.61
56.97
49.85
49.57
49.29
49.00
48.72
48.43
48.15
41.03
37.83
36.99
36.85
30.37
30.17
29.78
29.59
29.48
26.87
20.07
CD3OD/300 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Probe 1b

Index	ppm	Hz	Point	Height
1	7.029	2109.995	14975.631	4890.112
2	7.024	2108.395	14984.104	5371.706
3	6.853	2057.148	15255.469	1310.052
4	6.847	2055.421	15264.618	1223.097
5	6.825	2048.808	15299.636	4008.230
6	6.820	2047.152	15308.404	4265.188
7	6.802	2041.771	15336.900	8117.301
8	6.775	2033.623	15380.041	2609.604
9	6.016	1805.796	16586.458	9861.997
10	4.893	1468.673	18371.626	36134.960
11	4.852	1456.494	18436.121	8028.104
12	4.481	1345.146	19025.740	1324.042
13	4.464	1340.070	19052.621	1669.985
14	4.457	1337.734	19064.992	1820.692
15	4.441	1332.935	19090.404	1578.442
16	4.278	1284.153	19348.718	1453.469
17	4.264	1279.922	19371.125	1698.140
18	4.253	1276.538	19389.041	1582.245
19	4.228	1269.075	19428.560	3428.090
20	3.611	1084.028	20408.445	6620.954
21	3.600	1080.733	20425.890	9986.801
22	3.592	1078.216	20439.216	11024.445
23	3.583	1075.400	20454.130	7295.293
24	3.569	1071.458	20475.005	7698.231
25	3.562	1069.331	20486.267	5921.157
26	3.556	1067.467	20496.136	4406.205
27	3.551	1065.964	20504.097	5152.892
28	3.536	1061.544	20527.503	6730.144
29	3.528	1058.888	20541.568	5684.994
30	3.517	1055.714	20558.373	5839.902
31	3.506	1052.509	20575.343	6742.395
32	3.486	1046.296	20608.246	8409.338
33	3.465	1040.168	20640.697	4204.144
34	3.414	1024.683	20722.693	2722.703
35	3.393	1018.478	20755.548	5726.270
36	3.373	1012.342	20788.042	3048.276
37	3.348	1005.012	20826.857	5826.871
38	3.320	996.662	20871.074	3229.886
39	3.315	995.012	20879.808	6289.863
40	3.309	993.392	20888.388	8796.808
41	3.304	991.753	20897.068	6679.518
42	3.298	990.106	20905.789	3793.641
43	3.259	978.399	20967.779	3482.415
44	3.237	971.600	21003.783	7169.319
45	3.213	964.509	21041.333	5217.369
46	3.208	962.809	21050.335	5014.195
47	3.188	957.027	21080.951	4732.510
48	3.167	950.611	21114.927	3237.588
49	3.144	943.816	21150.908	2311.198
50	3.126	938.410	21179.535	1178.865
51	2.958	887.838	21447.332	1089.620
52	2.923	877.355	21502.839	2644.365
53	2.913	874.291	21519.066	3709.968
54	2.880	864.525	21570.781	3732.889
55	2.870	861.627	21586.125	4079.116
56	2.863	859.381	21598.019	5367.224
57	2.840	852.555	21634.164	2069.840

Index	ppm	Hz	Point	Height
58	2.801	840.818	21696.312	2657.026
59	2.794	838.771	21707.152	3030.926
60	2.745	824.055	21785.078	1166.857
61	2.738	821.777	21797.142	1153.719
62	2.694	808.712	21866.328	3396.015
63	2.652	795.991	21933.685	2474.556
64	2.525	757.971	22135.017	2265.545
65	2.501	750.852	22172.714	4003.022
66	2.477	743.522	22211.527	1975.809
67	2.205	661.894	22643.775	2281.782
68	2.182	654.869	22680.972	4585.676
69	2.158	647.693	22718.972	2705.871
70	1.773	532.219	23330.441	1307.196
71	1.752	525.822	23364.318	3783.002
72	1.731	519.441	23398.107	5613.757
73	1.709	512.997	23432.226	4695.256
74	1.695	508.621	23455.402	4906.483
75	1.673	502.288	23488.935	6248.065
76	1.652	495.879	23522.873	4956.518
77	1.620	486.386	23573.142	3090.663
78	1.595	478.897	23612.798	2626.126
79	1.569	470.846	23655.429	1789.230
80	1.546	464.158	23690.843	1244.669
81	1.524	457.296	23727.183	937.692
82	1.448	434.563	23847.562	1320.393
83	1.424	427.417	23885.402	2678.813
84	1.400	420.231	23923.453	2957.232
85	1.375	412.848	23962.548	1888.763

Compound 9



S
O
N
H
O
3
N
H
O
CF3
NHBoc
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1.95
1.62
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23.90
4.03
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18.54
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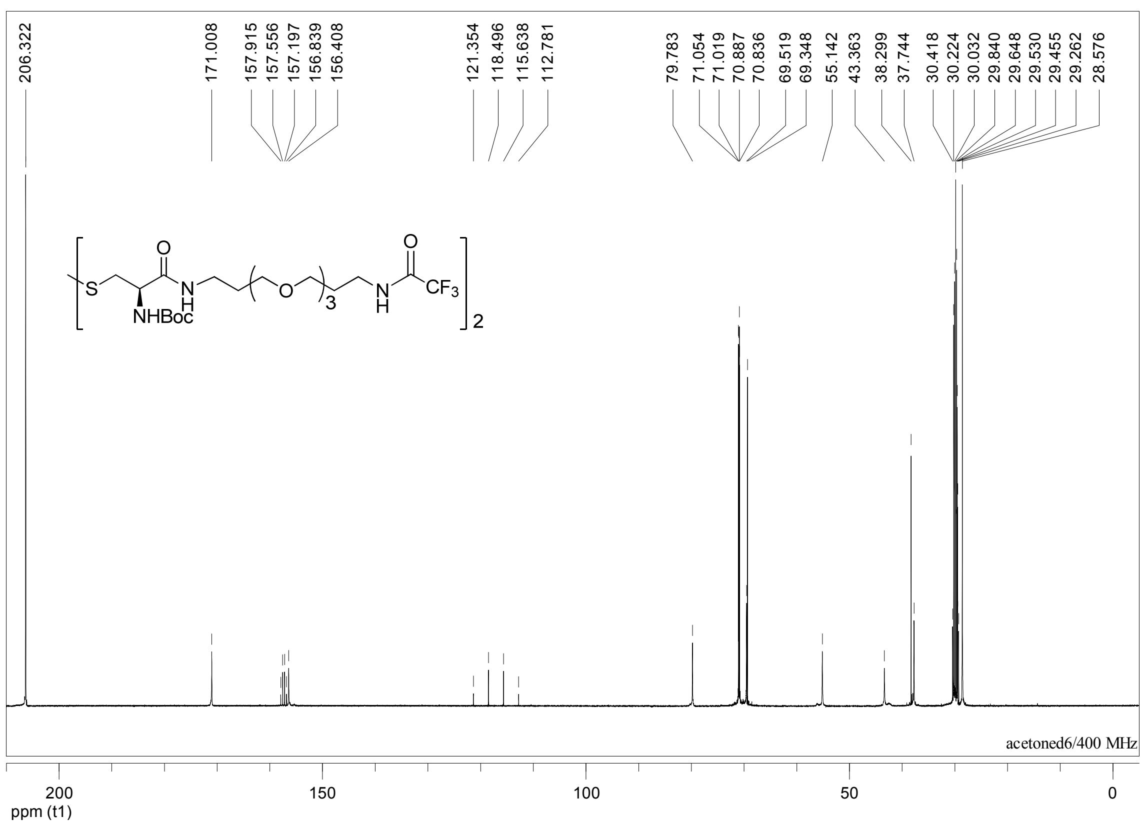
ppm (t1)



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115.638
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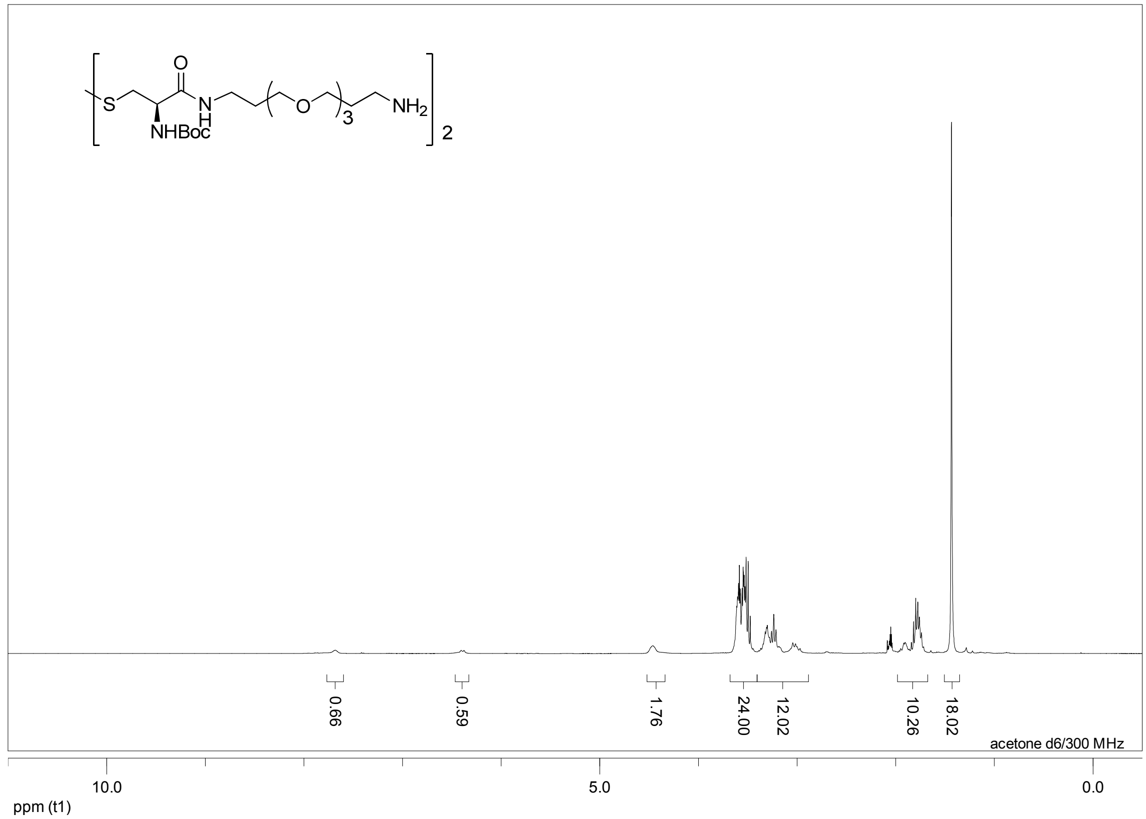
71.054
71.019
70.887
70.836
69.519
69.348
55.142
43.363
38.299
37.744
30.418
30.224
30.032
29.840
29.648
29.530
29.455
29.262
28.576
S
O
N
H
O
3
N
H
O
CF3
NHBoc
2
acetoned6/400 MHz
200
150
100
50
0
ppm (t1)

Compound 9

Index	ppm	Hz	Point	Height
1	8.410	2524.521	12784.989	725.006
2	7.578	2274.672	14108.016	2104.959
3	6.293	1889.148	16149.487	1496.470
4	6.266	1880.966	16192.811	1604.198
5	4.477	1343.791	19037.322	1204.808
6	4.464	1340.104	19056.843	1285.048
7	3.620	1086.632	20399.058	5673.844
8	3.609	1083.228	20417.082	12813.636
9	3.603	1081.642	20425.482	13228.220
10	3.593	1078.592	20441.632	21619.496
11	3.578	1073.863	20466.671	15456.057
12	3.571	1071.915	20476.990	17371.833
13	3.565	1070.208	20486.027	19646.750
14	3.553	1066.390	20506.246	26713.898
15	3.545	1064.068	20518.542	11691.060
16	3.542	1063.054	20523.908	10849.587
17	3.533	1060.483	20537.523	14574.983
18	3.521	1056.837	20556.830	14672.643
19	3.501	1050.752	20589.052	7114.729
20	3.462	1039.111	20650.695	2840.779
21	3.440	1032.619	20685.070	7134.083
22	3.419	1026.313	20718.464	7408.180
23	3.398	1019.905	20752.396	3311.492
24	3.354	1006.859	20821.480	1988.913
25	3.346	1004.354	20834.744	1996.935
26	3.332	1000.108	20857.228	4554.139
27	3.324	997.786	20869.523	4391.879
28	3.312	994.236	20888.324	4600.561
29	3.304	991.827	20901.080	4809.609
30	3.290	987.693	20922.970	2336.267
31	3.282	985.240	20935.958	2180.535
32	3.218	965.826	21038.759	1058.010
33	3.176	953.486	21104.105	1416.062
34	3.170	951.685	21113.640	1388.329
35	3.040	912.652	21320.335	1765.799
36	3.012	904.053	21365.867	1882.343
37	2.995	898.985	21392.705	1442.609
38	2.966	890.252	21438.951	1205.154
39	2.840	852.585	21638.406	9825.777
40	2.807	842.582	21691.378	5865.570
41	2.086	626.084	22837.800	4832.114
42	2.073	622.375	22857.441	2442.482
43	2.064	619.601	22872.130	9958.049
44	2.057	617.388	22883.851	18920.958
45	2.050	615.183	22895.523	26139.576
46	2.042	612.988	22907.146	19183.841
47	2.035	610.781	22918.835	10313.840
48	1.876	562.960	23172.060	2398.104
49	1.853	556.229	23207.705	6393.153
50	1.833	550.163	23239.828	10068.701
51	1.813	544.069	23272.093	6494.190
52	1.785	535.908	23315.312	5791.833
53	1.764	529.488	23349.308	8089.176
54	1.743	523.107	23383.093	5223.687
55	1.721	516.652	23417.279	1541.691
56	1.437	431.220	23869.666	133512.796

Compound 10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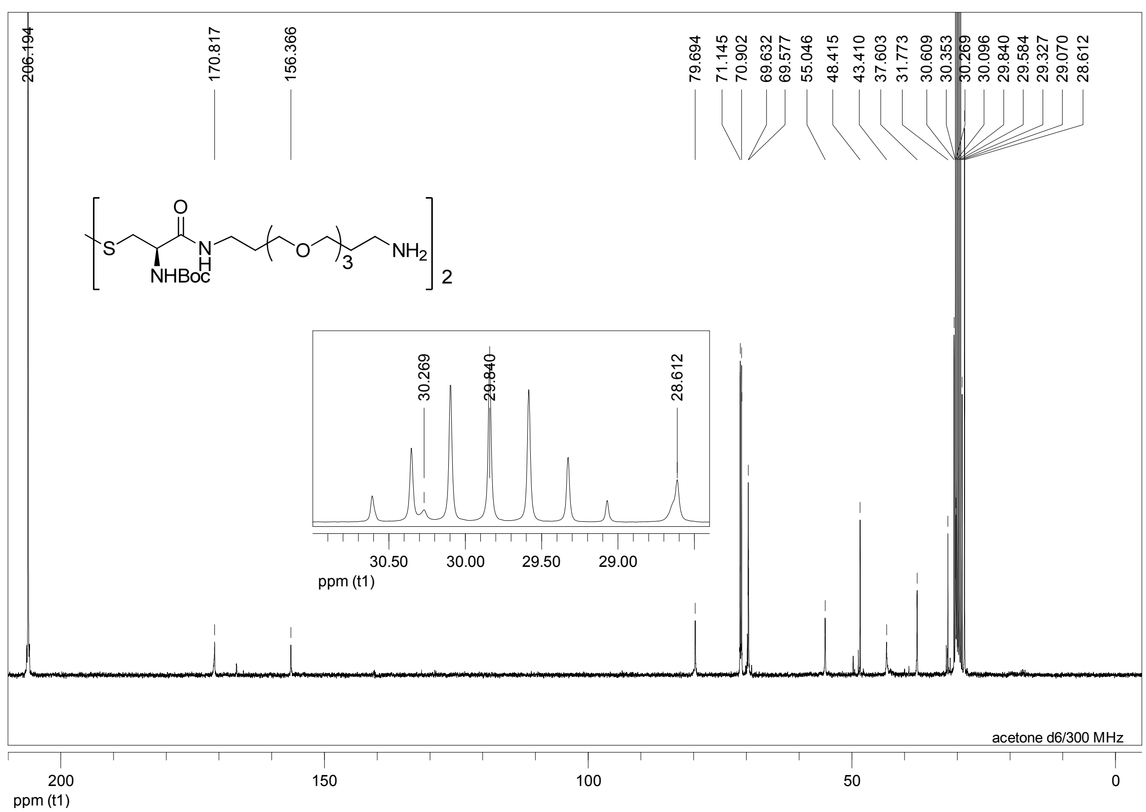
ppm (t1)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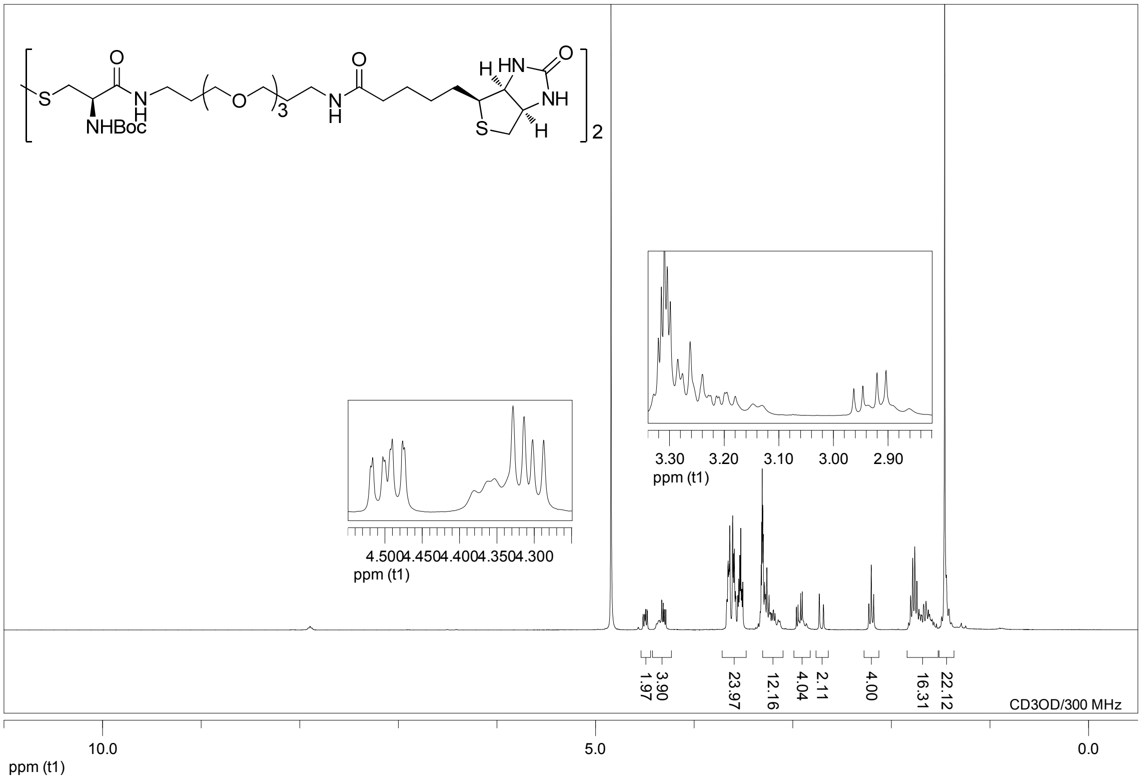
30.609
30.353
30.269
30.096
29.840
29.584
29.327
29.070
28.612
NH2
NHBoc
30.269
29.840
28.612
30.50
30.00
29.50
29.00
ppm (t1)
acetone d6/300 MHz
200
150
100
50
0
ppm (t1)

Compound 10

Index	ppm	Hz	Point	Height
1	7.681	2305.582	13943.959	440.684
2	6.405	1922.477	15972.617	420.507
3	6.376	1913.983	16017.596	398.700
4	4.460	1338.742	19063.675	1010.121
5	3.609	1083.440	20415.580	6199.045
6	3.604	1081.789	20424.322	7424.825
7	3.600	1080.609	20430.568	7297.696
8	3.593	1078.404	20442.246	9178.108
9	3.584	1075.778	20456.150	11532.220
10	3.576	1073.306	20469.242	8455.607
11	3.556	1067.513	20499.916	8511.042
12	3.546	1064.331	20516.767	11294.297
13	3.535	1061.212	20533.283	10267.837
14	3.527	1058.798	20546.064	8718.437
15	3.516	1055.414	20563.984	12593.030
16	3.495	1049.159	20597.109	12056.713
17	3.474	1042.769	20630.943	4896.676
18	3.366	1010.519	20801.716	688.312
19	3.344	1003.710	20837.777	1245.798
20	3.322	997.275	20871.851	2857.604
21	3.309	993.239	20893.222	3426.549
22	3.301	990.805	20906.113	3704.185
23	3.280	984.410	20939.972	2109.718
24	3.258	977.963	20974.115	2922.864
25	3.235	971.128	21010.308	5106.601
26	3.213	964.356	21046.164	3104.049
27	3.183	955.504	21093.042	922.095
28	3.065	919.915	21281.496	615.913
29	3.043	913.321	21316.412	1406.846
30	3.015	905.094	21359.974	1287.086
31	2.999	900.104	21386.402	898.152
32	2.969	891.271	21433.173	661.837
33	2.085	625.887	22838.464	1724.447
34	2.064	619.573	22871.896	1617.818
35	2.057	617.390	22883.458	2509.959
36	2.049	615.180	22895.162	3471.813
37	2.042	612.968	22906.876	2504.938
38	2.035	610.768	22918.521	1382.616
39	1.948	584.699	23056.566	646.353
40	1.917	575.472	23105.425	1370.668
41	1.905	571.762	23125.072	1453.896
42	1.840	552.329	23227.974	1473.654
43	1.818	545.770	23262.710	4174.896
44	1.796	539.153	23297.748	7230.304
45	1.775	532.644	23332.212	6716.998
46	1.759	527.843	23357.638	4785.565
47	1.738	521.565	23390.880	2736.606
48	1.433	430.207	23874.648	69436.101

Compound 11



NHBoc
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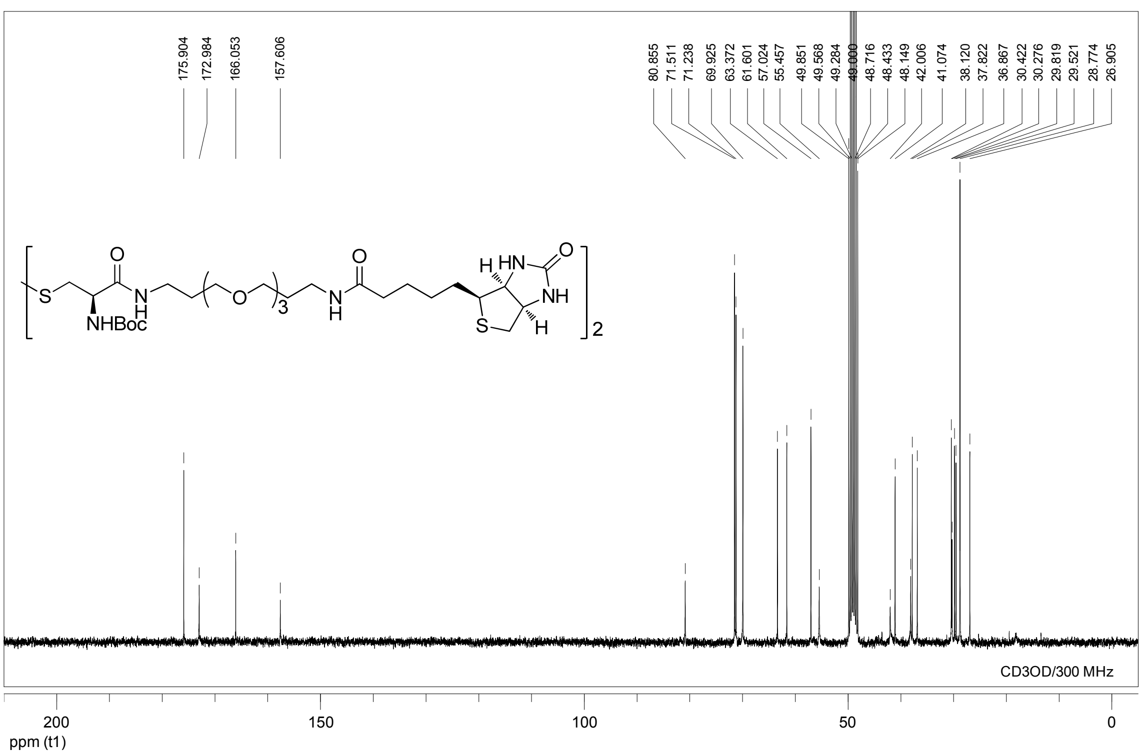
4.500 4.450 4.400 4.350 4.300
ppm (t1)
3.30 3.20 3.10 3.00 2.90
ppm (t1)
1.97 3.90 23.97 12.16 4.04 2.11 4.00 16.31 22.12
CD3OD/300 MHz
10.0 5.0 0.0
ppm (t1)



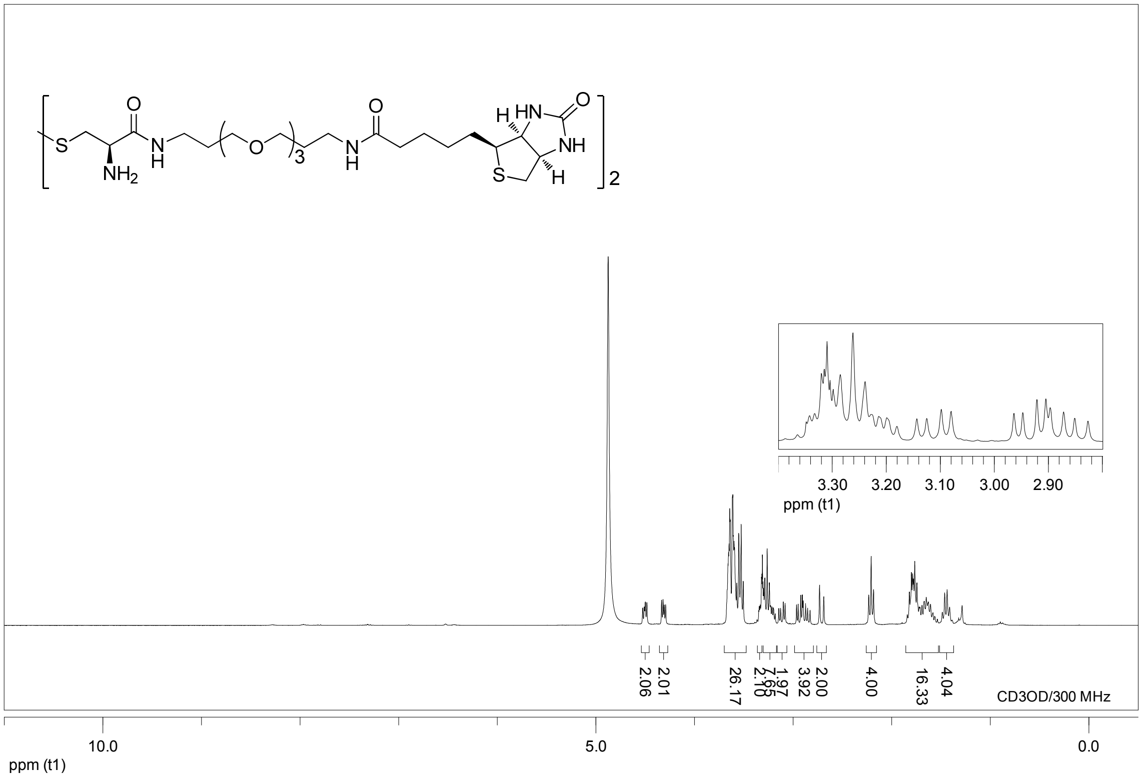
175.904 172.984 166.053 157.606
80.855 71.511 71.238 69.925 63.372 61.601 57.024 55.457 49.851 49.568 49.284 49.000 48.716 48.433 48.149 42.006 41.074 38.120 37.822 36.867 30.422 30.276 29.819 29.521 28.774 26.905
NHBoc
3
2
CD3OD/300 MHz
200 150 100 50 0
ppm (t1)

Compound 11

Index	ppm	Hz	Point	Height
1	4.843	1453.630	18451.830	57162.687
2	4.517	1355.732	18970.232	1419.456
3	4.503	1351.584	18992.197	1442.476
4	4.500	1350.843	18996.123	1357.807
5	4.490	1347.863	19011.900	1885.667
6	4.476	1343.707	19033.908	1836.227
7	4.381	1314.947	19186.201	585.384
8	4.362	1309.247	19216.382	821.917
9	4.353	1306.734	19229.693	882.432
10	4.329	1299.314	19268.984	2726.593
11	4.314	1294.847	19292.636	2453.761
12	4.302	1291.415	19310.812	1870.079
13	4.287	1286.959	19334.404	1861.085
14	3.668	1101.005	20319.091	2755.820
15	3.665	1100.185	20323.433	2781.866
16	3.656	1097.296	20338.730	6244.422
17	3.649	1095.197	20349.843	5453.029
18	3.645	1094.173	20355.267	5962.778
19	3.639	1092.271	20365.341	9444.737
20	3.609	1083.348	20412.589	10339.723
21	3.601	1081.060	20424.703	6911.063
22	3.591	1077.956	20441.144	7336.331
23	3.582	1075.104	20456.246	3502.861
24	3.577	1073.753	20463.398	3074.888
25	3.557	1067.684	20495.535	3129.291
26	3.548	1064.895	20510.304	4614.662
27	3.537	1061.595	20527.781	6765.694
28	3.527	1058.712	20543.044	9208.734
29	3.516	1055.546	20559.808	3709.719
30	3.506	1052.546	20575.697	4347.828
31	3.329	999.261	20857.857	1679.258
32	3.321	996.718	20871.324	5912.342
33	3.315	995.069	20880.052	9752.614
34	3.310	993.413	20888.826	14586.725
35	3.304	991.819	20897.261	11299.973
36	3.299	990.175	20905.970	8653.464
37	3.285	986.047	20927.830	4307.021
38	3.276	983.476	20941.441	3229.450
39	3.262	979.251	20963.814	5633.783
40	3.240	972.503	20999.550	3174.875
41	3.229	969.134	21017.388	1594.508
42	3.225	968.049	21023.132	1573.989
43	3.214	964.766	21040.519	1539.010
44	3.210	963.490	21047.275	1473.161
45	3.199	960.194	21064.728	1788.074
46	3.195	959.073	21070.662	1820.910
47	3.180	954.481	21094.982	1513.521
48	3.147	944.695	21146.798	932.594
49	3.131	939.738	21173.048	822.996
50	2.963	889.304	21440.115	2086.552
51	2.946	884.329	21466.457	2300.849
52	2.937	881.480	21481.541	838.085
53	2.920	876.546	21507.671	3303.108
54	2.904	871.599	21533.865	3462.904
55	2.861	858.907	21601.072	575.885
56	2.731	819.649	21808.958	3275.759
57	2.688	806.949	21876.207	2300.567

Index	ppm	Hz	Point	Height
58	2.228	668.769	22607.912	2372.150
59	2.204	661.473	22646.548	5897.418
60	2.179	654.106	22685.556	3236.984
61	1.825	547.771	23248.636	672.028
62	1.805	541.675	23280.914	3109.862
63	1.783	535.254	23314.917	6517.570
64	1.762	528.986	23348.105	7522.756
65	1.741	522.532	23382.281	4430.413
66	1.719	516.024	23416.748	1881.840
67	1.711	513.660	23429.265	1374.302
68	1.698	509.528	23451.146	1408.135
69	1.690	507.373	23462.554	1319.071
70	1.672	502.011	23490.949	2347.437
71	1.648	494.749	23529.404	2606.187
72	1.625	487.753	23566.449	1819.760
73	1.612	483.750	23587.648	1444.721
74	1.602	480.788	23603.330	950.582
75	1.593	478.094	23617.597	867.987
76	1.586	476.067	23628.328	996.527
77	1.570	471.373	23653.187	739.088
78	1.542	462.782	23698.679	550.282
79	1.489	446.943	23782.550	1223.406
80	1.459	438.026	23829.769	68385.007
81	1.441	432.615	23858.423	4973.495
82	1.417	425.219	23897.585	1905.488
83	1.392	417.901	23936.339	675.832

Compound 12



CD3OD/300 MHz
ppm (t1)
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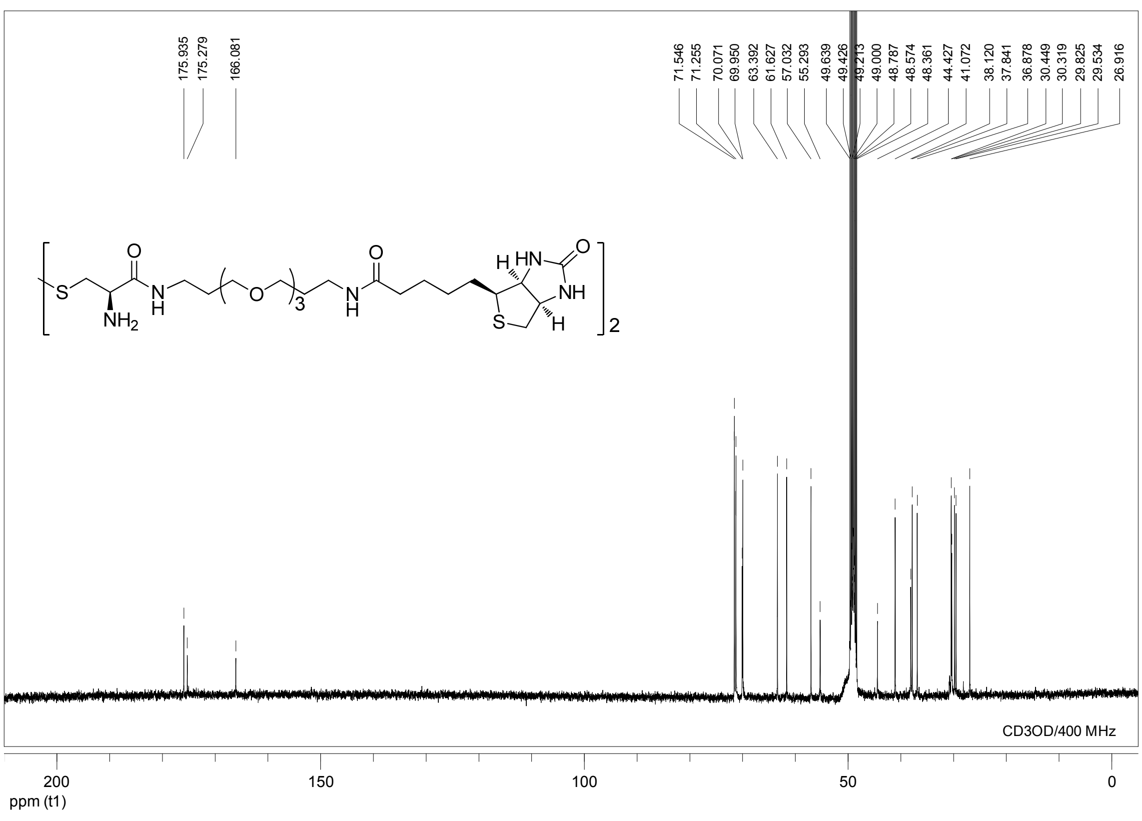
2.01
26.17
2.10
7.65
1.97
3.92
2.00
4.00
16.33
4.04
10.0
5.0
0.0
3.30
3.20
3.10
3.00
2.90



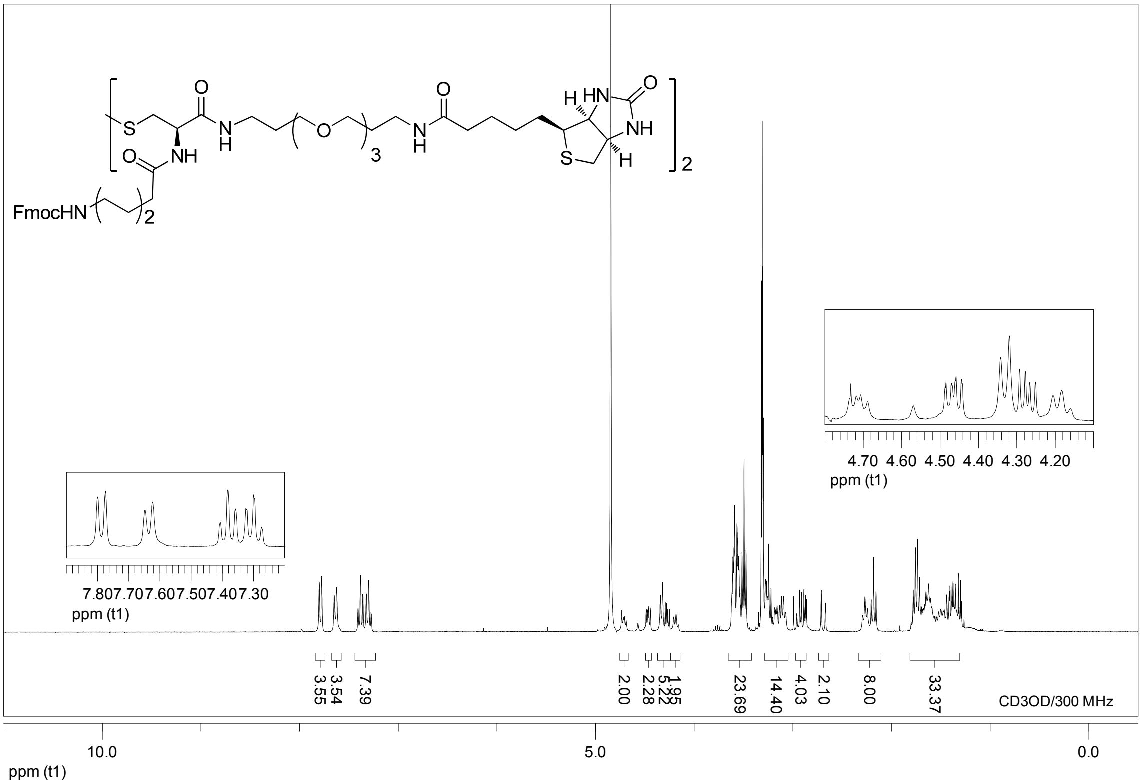
175.935
175.279
166.081
71.546
71.255
70.071
69.950
63.392
61.627
57.032
55.293
49.639
49.426
49.213
49.000
48.787
48.574
48.361
44.427
41.072
38.120
37.841
36.878
30.449
30.319
29.825
29.534
26.916
CD3OD/400 MHz
200
150
100
50
0
ppm (t1)

Compound 12

Index	ppm	Hz	Point	Height
1	4.874	1463.142	18400.720	6871.504
2	4.523	1357.782	18958.632	316.643
3	4.508	1353.124	18983.296	337.684
4	4.497	1349.964	19000.029	426.139
5	4.482	1345.374	19024.337	414.129
6	4.332	1300.327	19262.876	463.455
7	4.317	1295.899	19286.322	475.777
8	4.306	1292.474	19304.457	371.819
9	4.291	1288.030	19327.992	375.731
10	3.659	1098.358	20332.365	1138.686
11	3.653	1096.655	20341.382	1357.088
12	3.648	1095.154	20349.330	1514.320
13	3.642	1093.084	20360.289	2171.584
14	3.636	1091.326	20369.599	1961.528
15	3.614	1084.728	20404.539	2399.162
16	3.610	1083.623	20410.386	2432.833
17	3.598	1079.919	20430.003	1559.545
18	3.593	1078.519	20437.414	1445.557
19	3.571	1071.800	20472.994	778.317
20	3.550	1065.593	20505.861	1707.938
21	3.525	1058.151	20545.269	1878.438
22	3.504	1051.944	20578.140	813.978
23	3.348	1004.938	20827.050	266.338
24	3.342	1003.166	20836.433	345.154
25	3.333	1000.342	20851.388	372.541
26	3.320	996.558	20871.425	893.579
27	3.315	994.990	20879.728	950.721
28	3.310	993.412	20888.082	1307.812
29	3.304	991.753	20896.869	803.095
30	3.298	990.029	20905.998	686.276
31	3.285	986.083	20926.892	878.246
32	3.262	979.067	20964.042	1419.754
33	3.239	972.313	20999.812	787.672
34	3.228	968.987	21017.423	360.786
35	3.214	964.682	21040.216	336.706
36	3.199	960.231	21063.787	318.701
37	3.180	954.630	21093.449	207.247
38	3.143	943.554	21152.095	305.260
39	3.125	938.045	21181.271	309.480
40	3.098	930.003	21223.855	428.868
41	3.080	924.517	21252.904	402.750
42	2.964	889.609	21437.753	376.555
43	2.947	884.679	21463.857	387.272
44	2.921	876.852	21505.304	554.389
45	2.905	871.905	21531.503	562.429
46	2.896	869.435	21544.582	450.069
47	2.872	862.006	21583.919	395.605
48	2.851	855.864	21616.445	312.055
49	2.827	848.484	21655.523	274.924
50	2.730	819.510	21808.949	743.252
51	2.688	806.784	21876.335	525.003
52	2.232	669.833	22601.537	556.738
53	2.207	662.541	22640.150	1277.508
54	2.183	655.210	22678.968	660.487
55	1.841	552.591	23222.367	189.118
56	1.820	546.163	23256.408	614.820
57	1.798	539.815	23290.021	977.649

Index	ppm	Hz	Point	Height
58	1.787	536.299	23308.640	953.385
59	1.778	533.623	23322.810	860.327
60	1.765	529.838	23342.853	1182.716
61	1.743	523.311	23377.414	785.322
62	1.721	516.504	23413.458	337.272
63	1.711	513.683	23428.398	329.555
64	1.691	507.589	23460.667	365.936
65	1.668	500.763	23496.812	439.360
66	1.649	494.816	23528.306	516.523
67	1.626	488.103	23563.853	430.257
68	1.605	481.715	23597.677	385.166
69	1.580	474.270	23637.103	225.956
70	1.485	445.852	23787.582	234.416
71	1.462	438.678	23825.572	597.327
72	1.437	431.255	23864.878	656.839
73	1.412	423.757	23904.585	330.020
74	1.285	385.679	24106.220	359.036

Compound 13



FmocHN
CD3OD/300 MHz
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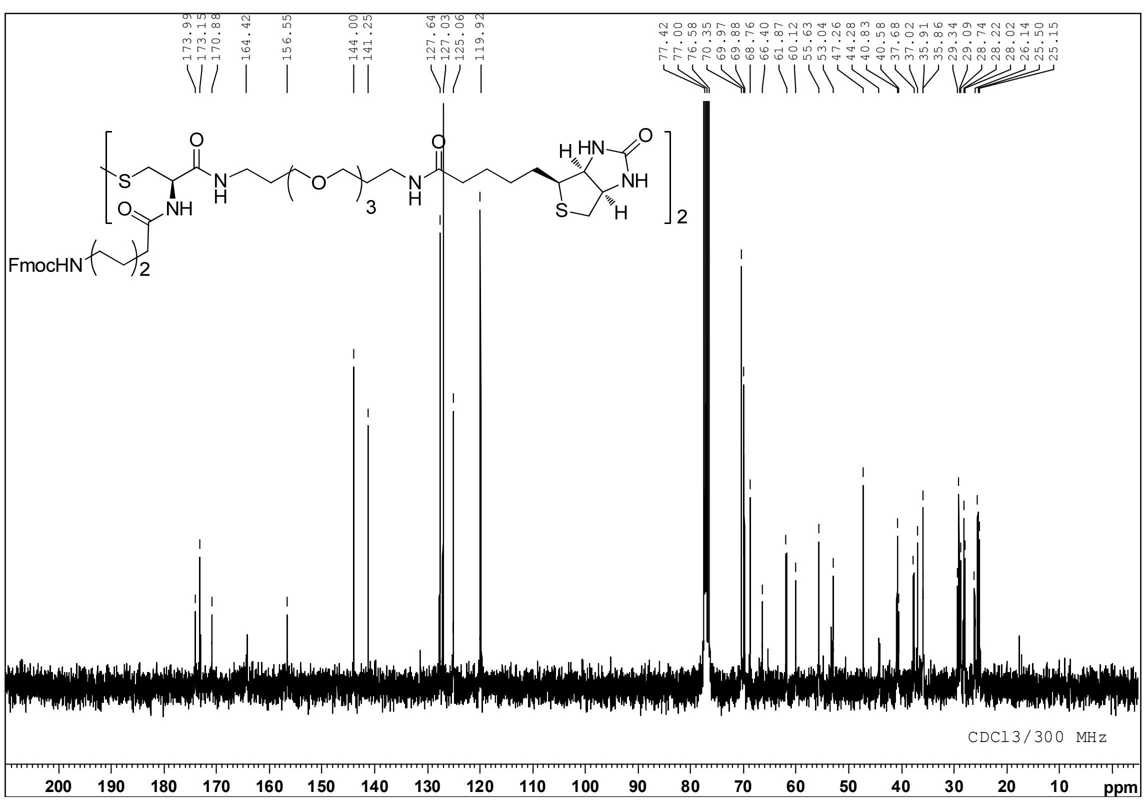
ppm (t1)
4.70 4.60 4.50 4.40 4.30 4.20
ppm (t1)
3.55 3.54 7.39 2.00 2.28 5.22 1.95 23.69 14.40 4.03 2.10 8.00 33.37
10.0 5.0 0.0
ppm (t1)



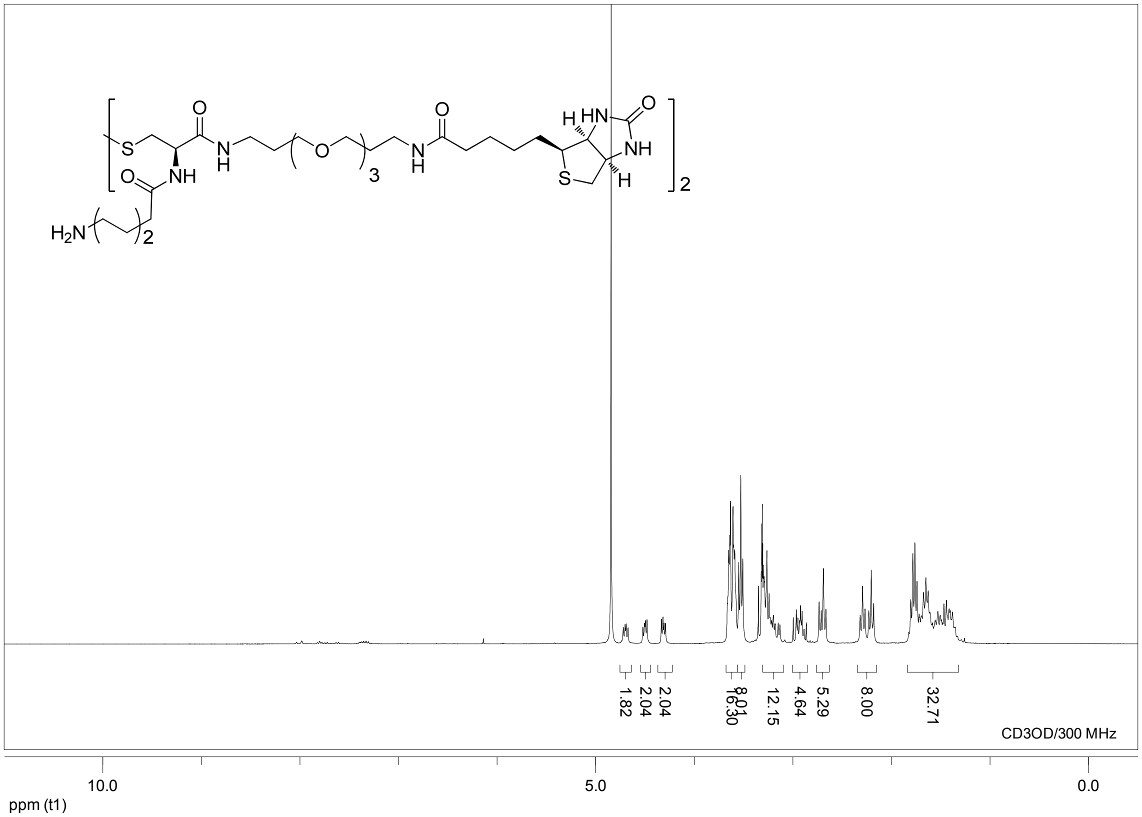
173.99 173.15 170.88 164.42 156.55 144.00 141.25 127.64 127.03 125.06 119.92
77.42 77.00 76.58 70.35 69.97 69.88 68.76 66.40 61.87 60.12 55.63 53.04 47.26 44.28 40.83 40.58 37.68 37.02 35.91 35.86 29.34 29.09 28.74 28.22 28.02 26.14 25.50 25.15
FmocHN
CDCl3/300 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Compound 13

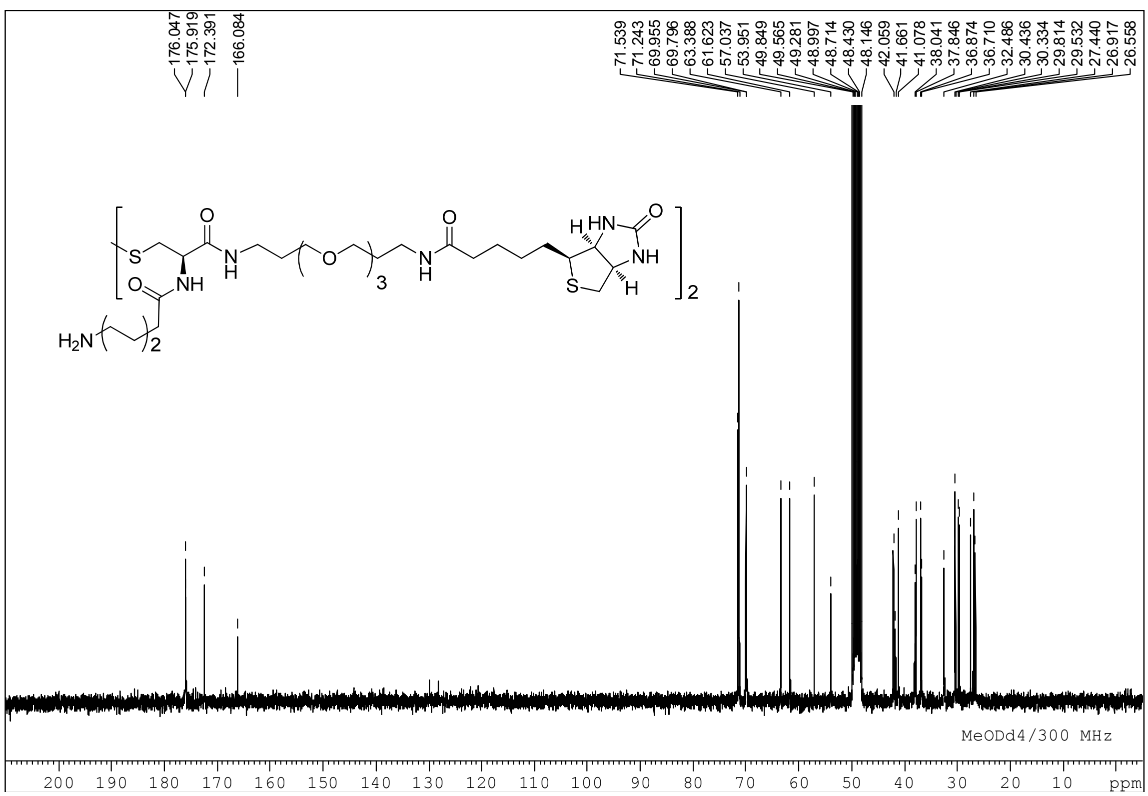
Index	ppm	Hz	Point	Height
1	7.800	2341.261	13751.596	1790.253
2	7.775	2333.793	13791.141	1999.980
3	7.648	2295.663	13993.048	1318.604
4	7.623	2288.341	14031.822	1611.230
5	7.406	2223.184	14376.851	871.741
6	7.383	2216.065	14414.548	2043.171
7	7.358	2208.735	14453.359	1363.004
8	7.324	2198.511	14507.500	1390.405
9	7.321	2197.555	14512.564	1359.711
10	7.299	2191.082	14546.838	1869.704
11	7.275	2183.661	14586.137	710.825
12	4.846	1454.685	18446.291	94572.156
13	4.732	1420.484	18627.396	789.905
14	4.718	1416.188	18650.142	539.585
15	4.707	1412.829	18667.931	561.147
16	4.689	1407.416	18696.591	418.046
17	4.484	1346.099	19021.283	812.076
18	4.471	1341.947	19043.271	805.888
19	4.458	1338.243	19062.884	946.305
20	4.444	1334.068	19084.994	881.088
21	4.342	1303.392	19247.433	1333.246
22	4.319	1296.535	19283.742	1788.450
23	4.293	1288.516	19326.205	1088.342
24	4.278	1284.066	19349.767	1044.698
25	4.266	1280.646	19367.878	814.444
26	4.251	1276.177	19391.544	829.450
27	4.206	1262.417	19464.410	548.125
28	4.183	1255.636	19500.316	656.698
29	4.160	1248.782	19536.607	272.288
30	3.616	1085.307	20402.259	1421.224
31	3.607	1082.698	20416.074	2710.958
32	3.596	1079.327	20433.923	3042.539
33	3.588	1077.099	20445.724	4557.594
34	3.565	1070.075	20482.916	3909.466
35	3.554	1066.884	20499.816	2791.680
36	3.549	1065.172	20508.878	2719.643
37	3.535	1060.983	20531.062	1387.642
38	3.514	1054.853	20563.521	2875.685
39	3.494	1048.692	20596.146	6221.402
40	3.473	1042.542	20628.712	2961.164
41	3.348	1005.118	20826.886	716.607
42	3.320	996.702	20871.449	6214.688
43	3.315	995.062	20880.132	12636.319
44	3.310	993.413	20888.869	18364.152
45	3.304	991.775	20897.541	13208.595
46	3.299	990.152	20906.136	7699.406
47	3.279	984.240	20937.439	1756.880
48	3.275	982.954	20944.251	1907.451
49	3.265	980.183	20958.923	1842.051
50	3.252	976.202	20980.001	1290.717
51	3.243	973.363	20995.037	3171.769
52	3.220	966.571	21031.003	1577.899
53	3.202	961.162	21059.644	544.364
54	3.182	955.017	21092.187	900.190
55	3.173	952.374	21106.181	807.996
56	3.168	950.934	21113.806	744.062
57	3.158	948.081	21128.914	939.383

Index	ppm	Hz	Point	Height
58	3.134	940.734	21167.818	959.947
59	3.116	935.259	21196.808	1284.583
60	3.094	928.768	21231.183	1288.586
61	3.071	921.891	21267.595	725.859
62	2.992	898.107	21393.542	1282.458
63	2.958	888.041	21446.841	682.449
64	2.929	879.290	21493.185	1510.750
65	2.913	874.367	21519.251	1437.715
66	2.887	866.556	21560.615	1535.173
67	2.871	861.638	21586.656	1320.731
68	2.862	859.090	21600.148	1176.667
69	2.711	813.756	21840.205	1507.856
70	2.669	801.066	21907.404	1040.228
71	2.292	688.066	22505.771	613.583
72	2.268	680.768	22544.419	1278.382
73	2.244	673.454	22583.146	846.920
74	2.205	661.775	22644.992	1166.485
75	2.180	654.466	22683.697	2686.284
76	2.156	647.077	22722.822	1478.654
77	1.779	533.920	23322.023	1512.975
78	1.757	527.478	23356.134	3039.318
79	1.736	521.128	23389.759	3344.655
80	1.715	514.664	23423.990	1958.748
81	1.693	508.091	23458.796	910.644
82	1.682	504.938	23475.490	817.218
83	1.675	502.692	23487.388	858.875
84	1.661	498.707	23508.486	999.759
85	1.650	495.175	23527.191	1456.482
86	1.625	487.818	23566.150	1740.769
87	1.602	480.768	23603.482	1216.988
88	1.589	476.963	23623.626	923.113
89	1.519	456.012	23734.572	744.358
90	1.499	449.876	23767.062	832.493
91	1.474	442.350	23806.916	766.865
92	1.464	439.554	23821.720	811.322
93	1.439	432.006	23861.689	1347.490
94	1.414	424.333	23902.322	1481.118
95	1.406	422.163	23913.812	1675.109
96	1.385	415.591	23948.615	1825.776
97	1.375	412.632	23964.279	1762.691
98	1.367	410.179	23977.271	911.912
99	1.353	405.986	23999.474	1737.048
100	1.322	396.843	24047.890	2112.922
101	1.313	394.189	24061.943	887.675
102	1.300	390.340	24082.324	1879.922
103	1.289	386.753	24101.318	1111.245

Compound 14



1.82
2.04
2.04
16.30
8.01
12.15
4.64
5.29
8.00
32.71
CD3OD/300 MHz
10.0
5.0
0.0
ppm (t1)



176.047
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71.243
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69.796
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61.623
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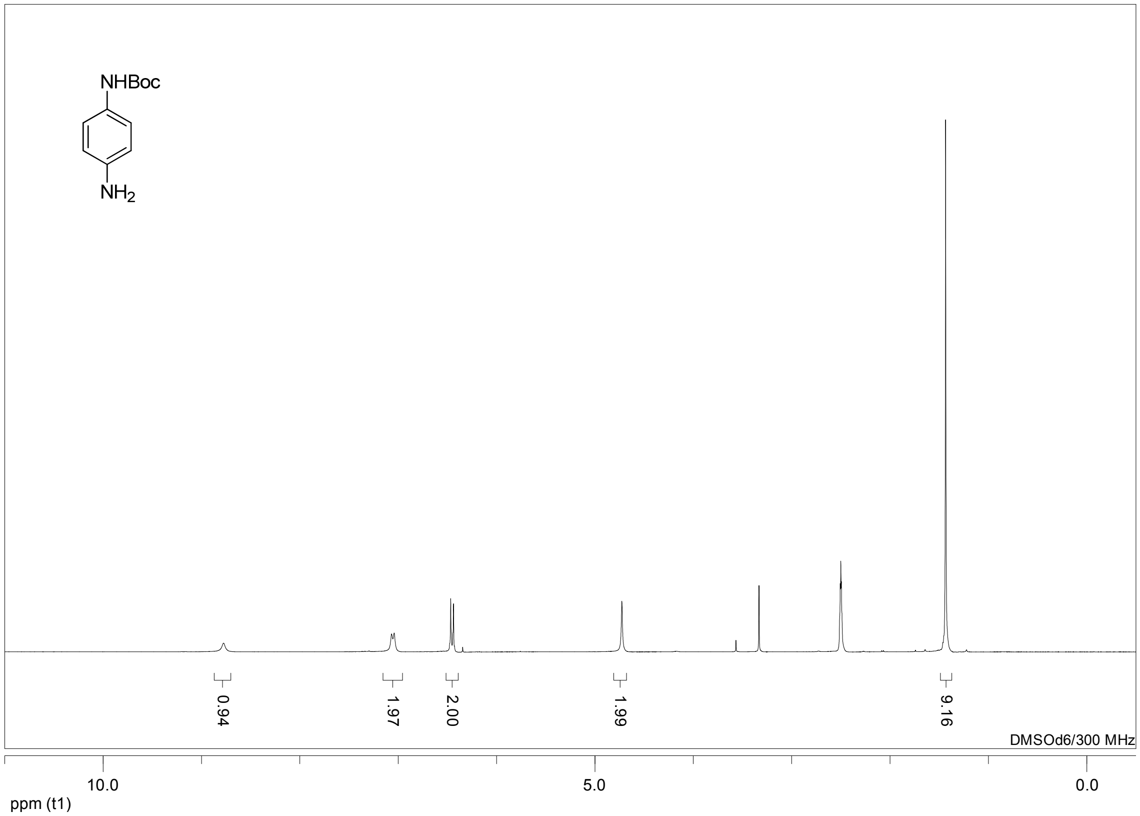
38.041
37.846
36.874
36.710
32.486
30.436
30.334
29.814
29.532
27.440
26.917
26.558
MeODd4/300 MHz
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Compound 14

Index	ppm	Hz	Point	Height
1	4.842	1453.376	18453.119	64679.652
2	4.719	1416.413	18648.851	1650.774
3	4.701	1410.967	18677.689	1967.506
4	4.689	1407.500	18696.048	2007.899
5	4.671	1402.068	18724.812	1613.919
6	4.519	1356.568	18965.750	1689.277
7	4.505	1352.146	18989.164	2062.765
8	4.495	1349.222	19004.644	2341.225
9	4.479	1344.375	19030.310	2418.817
10	4.331	1300.153	19264.482	2492.070
11	4.317	1295.702	19288.052	2687.862
12	4.305	1292.320	19305.960	2096.299
13	4.290	1287.857	19329.593	2055.583
14	3.659	1098.278	20333.474	4745.406
15	3.650	1095.612	20347.591	9416.668
16	3.645	1094.252	20354.789	8378.129
17	3.639	1092.422	20364.480	10925.048
18	3.632	1090.321	20375.607	14331.196
19	3.606	1082.464	20417.212	13810.569
20	3.599	1080.396	20428.162	9948.895
21	3.589	1077.251	20444.818	9462.713
22	3.548	1064.857	20510.447	8188.481
23	3.527	1058.698	20543.058	16938.017
24	3.507	1052.581	20575.451	8546.954
25	3.348	1005.086	20826.955	5803.958
26	3.320	996.617	20871.800	7288.467
27	3.315	995.038	20880.158	12056.946
28	3.310	993.414	20888.757	14047.368
29	3.304	991.768	20897.478	10107.786
30	3.298	990.103	20906.291	7934.440
31	3.295	988.980	20912.240	6671.510
32	3.291	987.772	20918.638	6764.102
33	3.286	986.240	20926.748	6273.043
34	3.262	979.236	20963.837	9369.872
35	3.240	972.469	20999.669	5043.659
36	3.230	969.543	21015.162	2682.130
37	3.215	965.177	21038.285	2348.856
38	3.195	959.187	21070.001	2880.606
39	3.180	954.684	21093.845	2015.487
40	3.176	953.389	21100.707	2002.908
41	3.148	944.890	21145.708	2098.139
42	3.130	939.524	21174.123	1922.090
43	2.995	899.023	21388.589	2659.527
44	2.964	889.604	21438.466	3413.470
45	2.948	884.772	21464.054	2616.283
46	2.931	879.762	21490.583	2346.524
47	2.922	876.941	21505.521	3852.547
48	2.905	872.050	21531.421	3292.168
49	2.886	866.153	21562.646	1475.617
50	2.863	859.360	21598.617	2124.481
51	2.733	820.309	21805.402	4227.803
52	2.711	813.803	21839.855	3348.307
53	2.689	807.016	21875.792	7564.526
54	2.663	799.472	21915.740	3501.522
55	2.316	695.241	22467.675	2888.739
56	2.292	687.970	22506.179	5788.340
57	2.267	680.490	22545.787	3511.274

Index	ppm	Hz	Point	Height
58	2.228	668.871	22607.316	3334.027
59	2.204	661.536	22646.158	7423.213
60	2.179	654.187	22685.072	4057.441
61	1.803	541.267	23283.017	4452.561
62	1.782	534.838	23317.060	9079.474
63	1.761	528.600	23350.091	10167.311
64	1.740	522.221	23383.875	6276.667
65	1.718	515.720	23418.296	2994.291
66	1.696	509.156	23453.054	2819.124
67	1.674	502.512	23488.238	5163.266
68	1.650	495.213	23526.888	6650.865
69	1.626	488.090	23564.605	5336.806
70	1.610	483.381	23589.541	3189.444
71	1.583	475.143	23633.166	2114.291
72	1.555	466.843	23677.115	2396.658
73	1.528	458.652	23720.492	3274.940
74	1.504	451.285	23759.498	2870.293
75	1.492	447.725	23778.353	2437.913
76	1.480	444.176	23797.142	2138.168
77	1.467	440.236	23818.005	4011.820
78	1.441	432.613	23858.373	4380.411
79	1.414	424.519	23901.232	3523.693
80	1.403	420.996	23919.890	3352.723
81	1.392	417.822	23936.699	2455.424
82	1.380	414.123	23956.283	3209.955
83	1.362	408.899	23983.945	1701.130
84	1.350	405.324	24002.880	1677.584

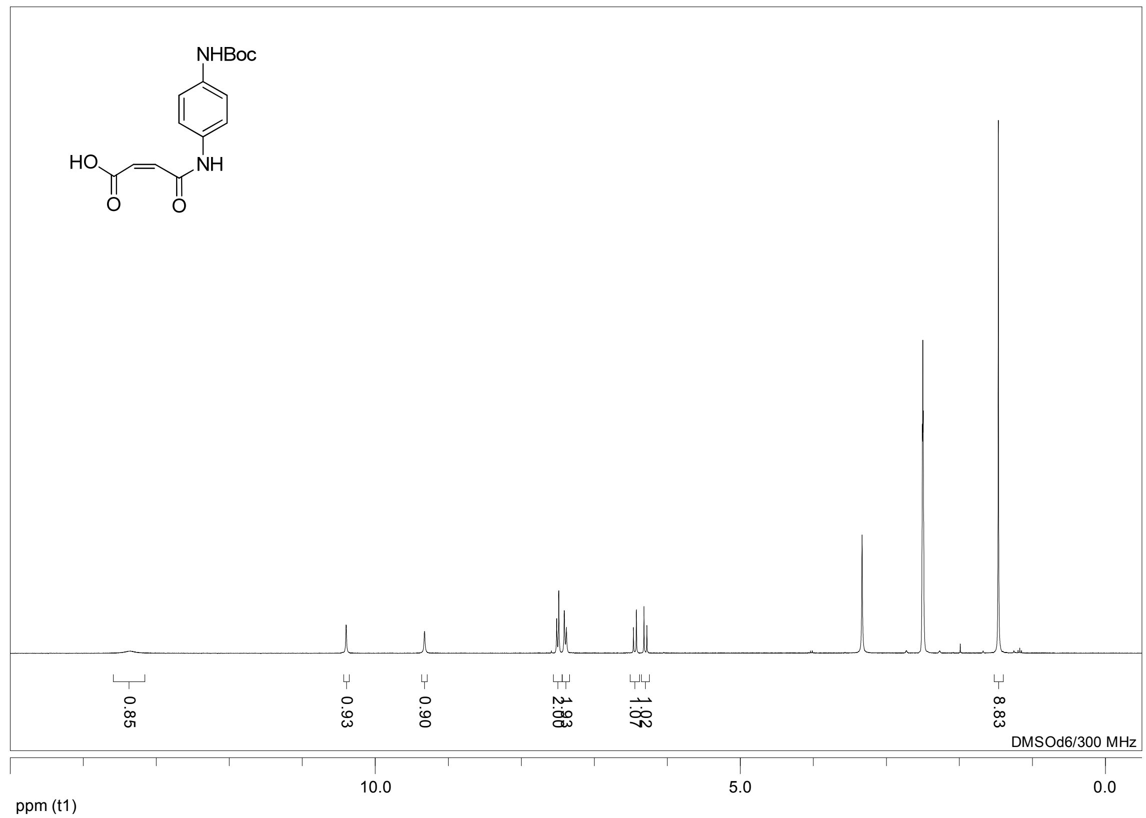
Compound 17

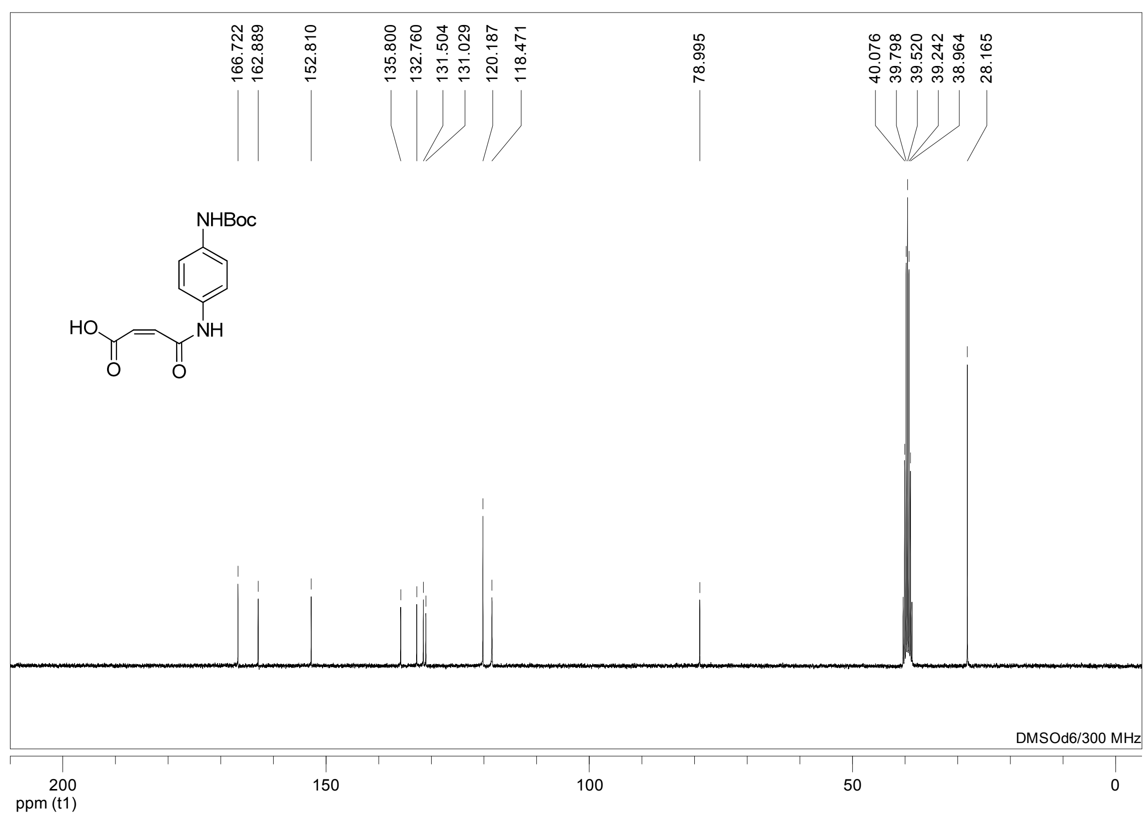


Compound 17

Index	ppm	Hz	Point	Height
1	8.773	2633.601	12217.817	455.804
2	7.067	2121.197	14931.154	929.211
3	7.040	2113.129	14973.875	978.493
4	6.466	1940.799	15886.414	2741.898
5	6.437	1932.085	15932.559	2479.587
6	4.725	1418.365	18652.867	2609.408
7	3.565	1070.251	20496.234	603.632
8	3.331	999.915	20868.685	3413.692
9	2.505	752.018	22181.376	3509.693
10	2.500	750.266	22190.658	4670.448
11	2.494	748.515	22199.925	3615.735
12	1.434	430.386	23884.517	27387.158

Compound 18

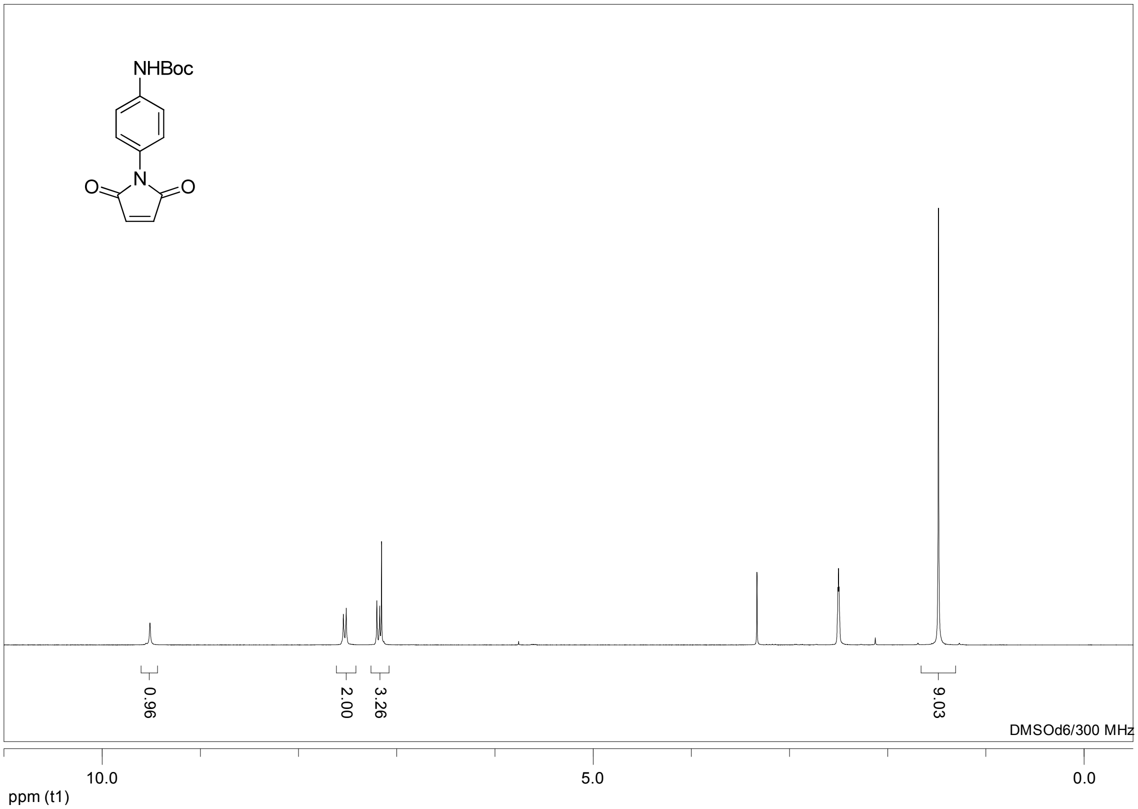

NHBoc
HO
NH
O
O
0.85
0.93
0.90
2.00
1.83
1.07
1.02
8.83
DMSOd6/300 MHz
10.0
5.0
0.0
ppm (t1)

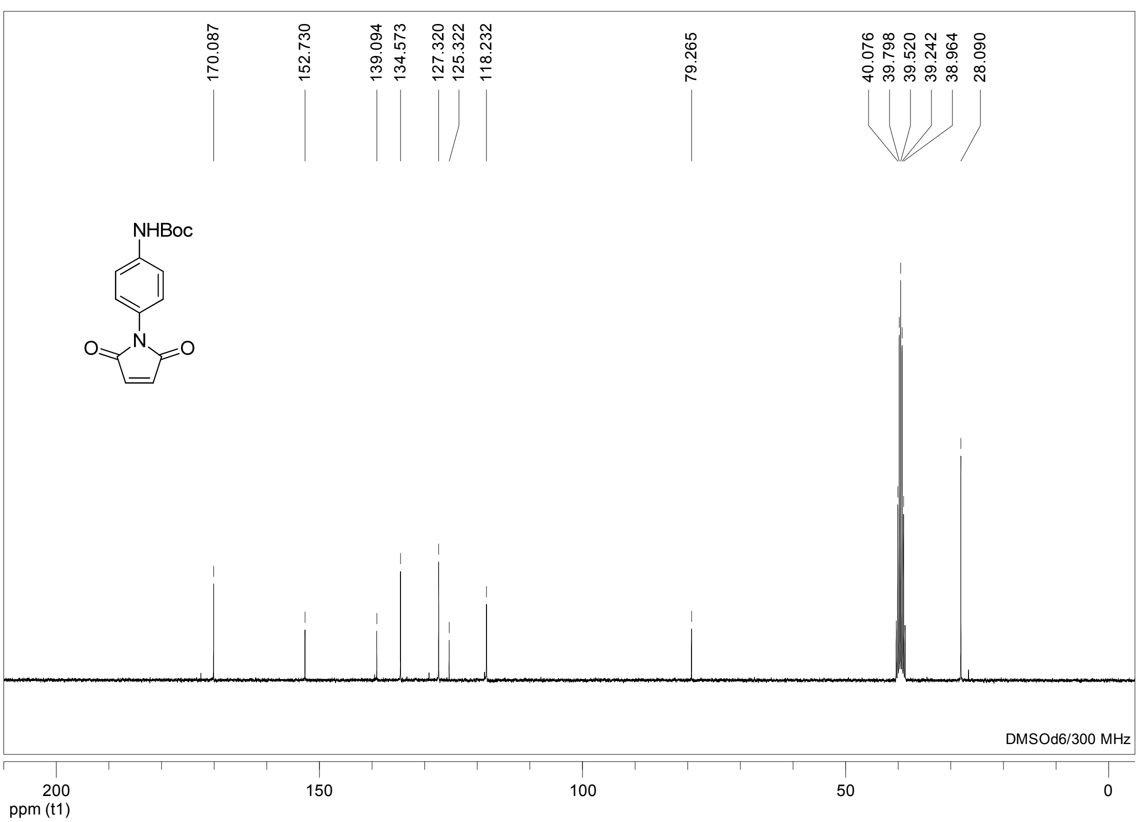

166.722
162.889
152.810
135.800
132.760
131.504
131.029
120.187
118.471
78.995
40.076
39.798
39.520
39.242
38.964
28.165
NHBoc
HO
NH
O
O
DMSOd6/300 MHz
200
150
100
50
0
ppm (t1)

Compound 18

Index	ppm	Hz	Point	Height
1	13.368	4012.713	4915.331	48.153
2	10.398	3121.270	9635.796	592.320
3	9.324	2798.904	11342.823	459.427
4	7.515	2255.763	14218.925	724.150
5	7.485	2246.755	14266.626	1306.365
6	7.410	2224.279	14385.643	892.452
7	7.380	2215.370	14432.818	543.300
8	6.463	1940.033	15890.811	538.778
9	6.423	1927.887	15955.129	908.972
10	6.319	1896.720	16120.167	975.034
11	6.278	1884.622	16184.230	582.464
12	3.332	1000.025	20868.445	2465.948
13	2.505	752.020	22181.708	4777.953
14	2.500	750.265	22191.000	6509.698
15	2.494	748.515	22200.267	5046.389
16	1.465	439.832	23834.839	11081.704

Compound 19

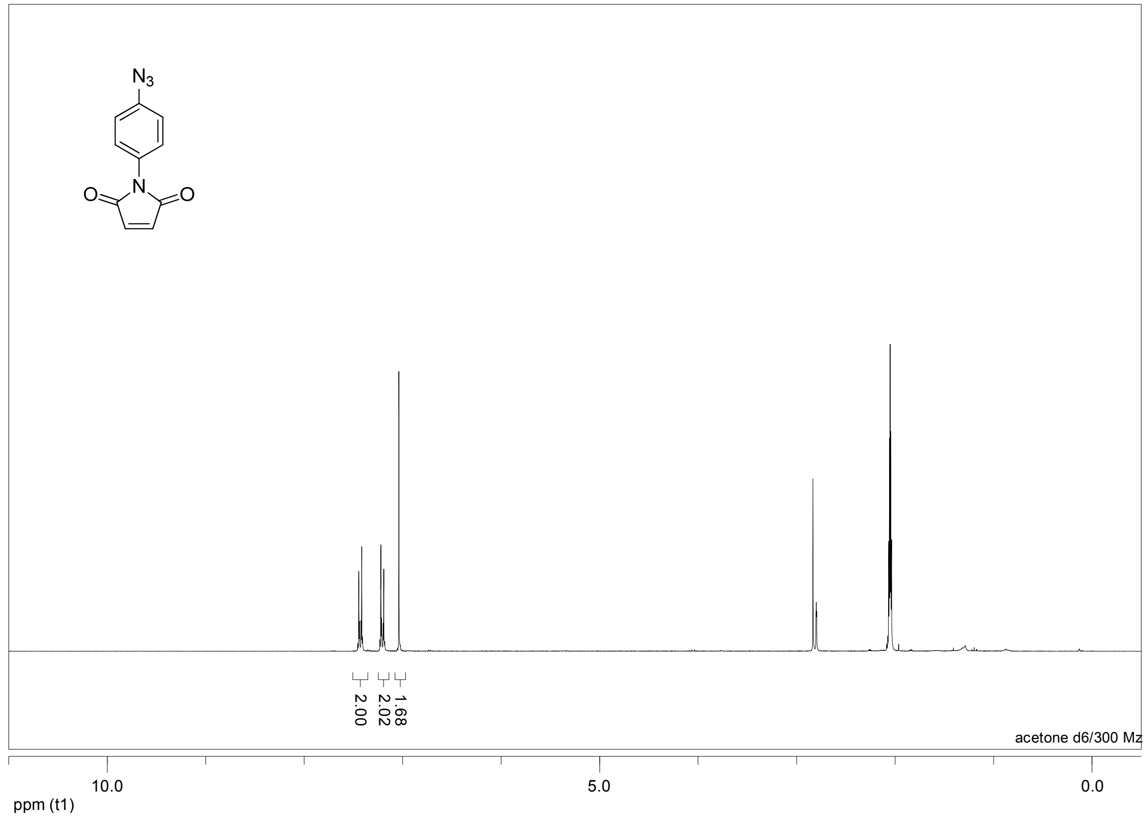

NHBoc
O
N
O
0.96
2.00
3.26
9.03
DMSOd6/300 MHz
10.0
5.0
0.0
ppm (t1)


170.087
152.730
139.094
134.573
127.320
125.322
118.232
79.265
40.076
39.798
39.520
39.242
38.964
28.090
NHBoc
O
N
O
DMSOd6/300 MHz
200
150
100
50
0
ppm (t1)

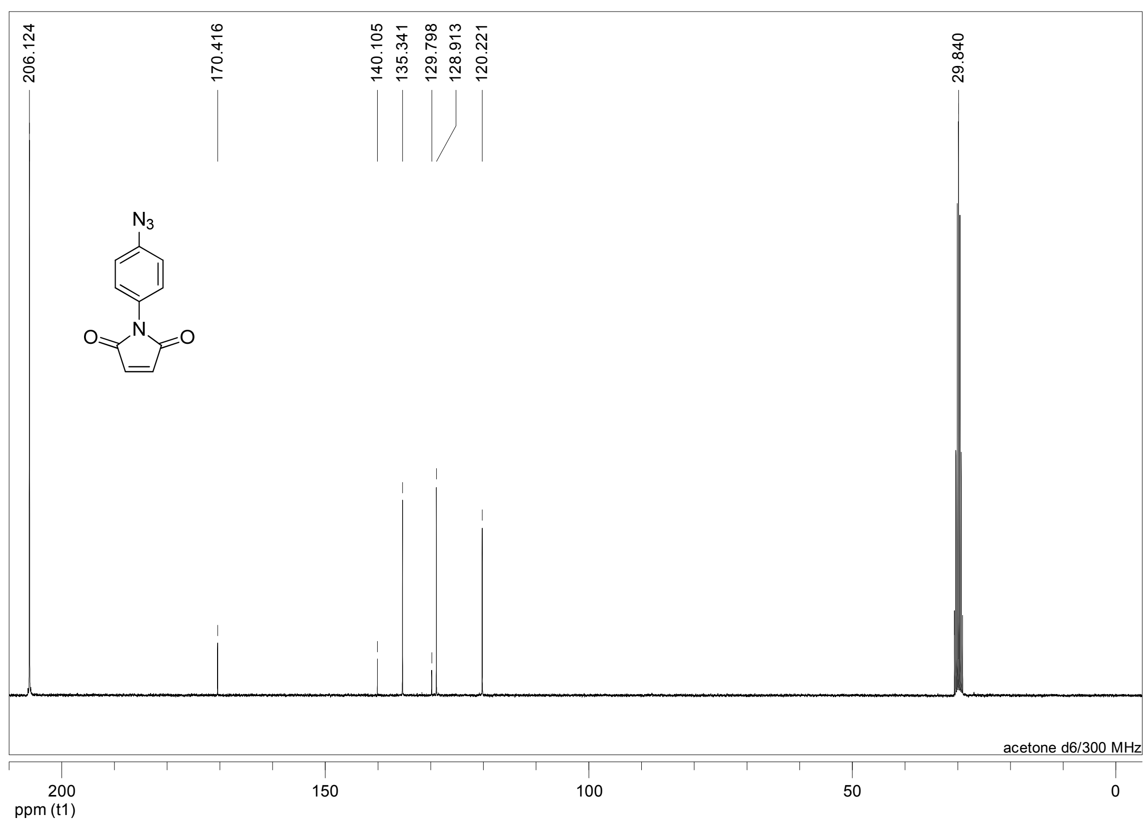
Compound 19

Index	ppm	Hz	Point	Height
1	9.512	2855.394	11043.500	1356.297
2	7.543	2264.097	14174.604	1909.855
3	7.513	2255.284	14221.272	2278.782
4	7.202	2161.734	14716.648	2738.988
5	7.172	2152.897	14763.439	2413.739
6	7.153	2147.256	14793.309	6415.645
7	3.330	999.663	20870.169	4500.157
8	2.505	752.006	22181.591	3565.419
9	2.500	750.265	22190.808	4729.350
10	2.494	748.534	22199.978	3584.869
11	1.482	444.797	23808.359	27050.599

Compound 16



N3
O
N
O
2.00
2.02
1.68
acetone d6/300 Mz
10.0
5.0
0.0
ppm (t1)

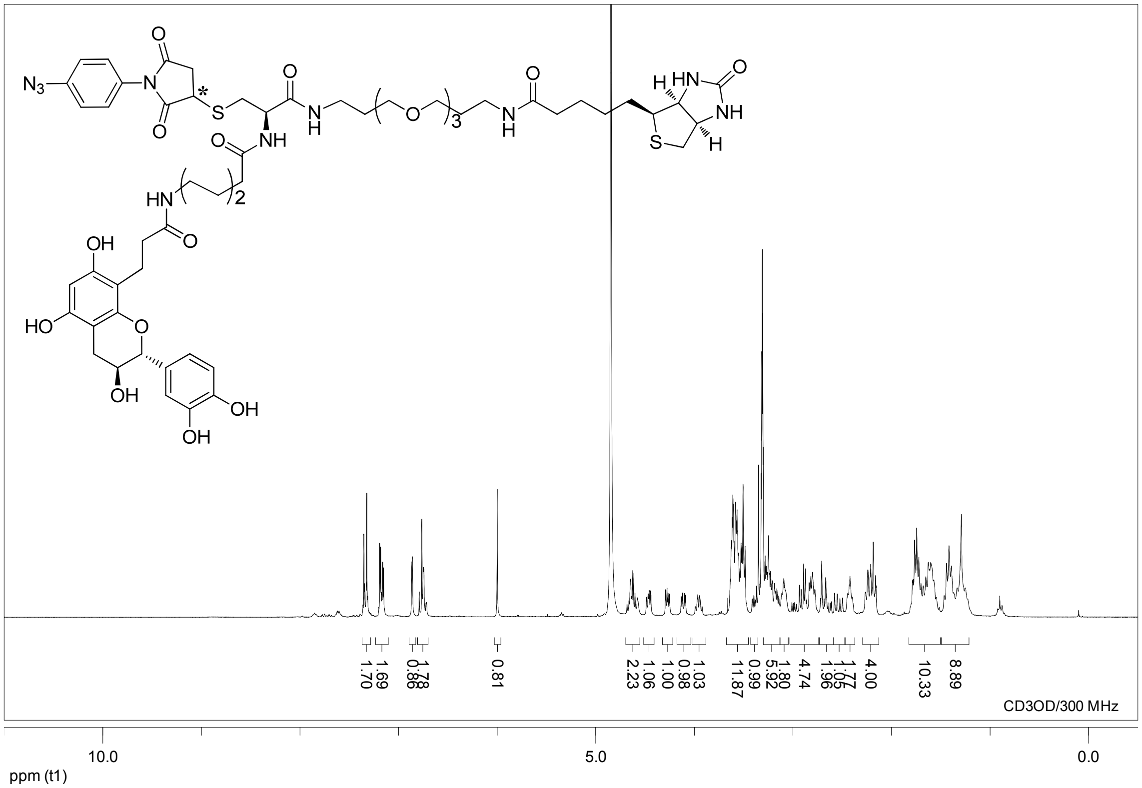


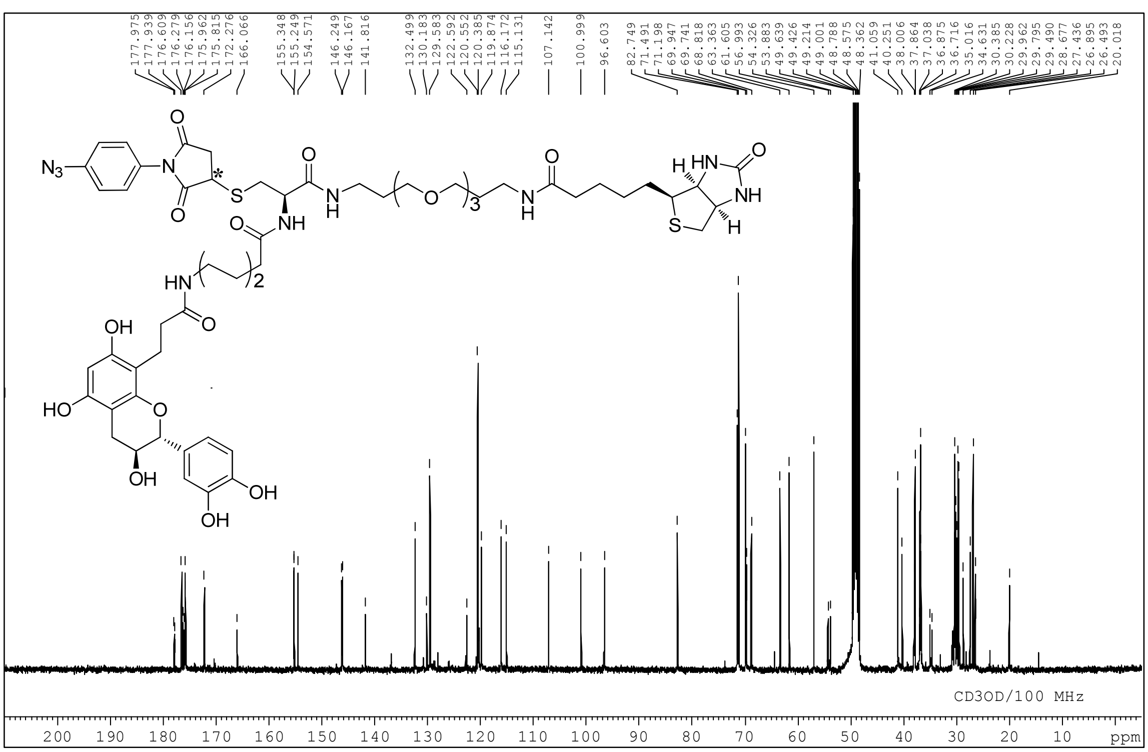
206.124
170.416
140.105
135.341
129.798
128.913
120.221
29.840
N3
O
N
O
acetone d6/300 MHz
200
150
100
50
0
ppm (t1)

Compound 16

Index	ppm	Hz	Point	Height
1	7.445	2234.945	14318.183	2417.953
2	7.438	2232.737	14329.878	905.557
3	7.423	2228.233	14353.729	934.345
4	7.416	2225.976	14365.677	3166.591
5	7.221	2167.614	14674.726	3221.951
6	7.214	2165.362	14686.650	1022.860
7	7.199	2160.884	14710.362	854.551
8	7.191	2158.676	14722.053	2472.202
9	7.038	2112.572	14966.190	8453.264
10	2.833	850.418	21649.683	5232.964
11	2.803	841.224	21698.369	1175.874
12	2.799	840.233	21703.619	1484.270
13	2.064	619.586	22872.011	3310.330
14	2.057	617.376	22883.714	6434.808
15	2.050	615.182	22895.330	9291.780
16	2.042	612.978	22907.001	6621.477
17	2.035	610.771	22918.687	3373.335

Probe 2





Probe 2

Index	ppm	Hz	Point	Height
1	7.360	2209.284	14450.384	459.891
2	7.351	2206.450	14465.392	3295.137
3	7.343	2204.316	14476.695	1306.714
4	7.328	2199.742	14500.913	1383.423
5	7.321	2197.536	14512.595	4935.043
6	7.312	2194.810	14527.028	803.166
7	7.199	2160.892	14706.637	375.170
8	7.190	2158.123	14721.297	2922.024
9	7.180	2155.375	14735.853	2763.763
10	7.173	2153.189	14747.426	964.562
11	7.167	2151.391	14756.950	873.862
12	7.160	2149.187	14768.620	2169.693
13	7.151	2146.455	14783.083	1944.316
14	7.141	2143.674	14797.812	305.876
15	6.864	2060.313	15239.236	2170.292
16	6.860	2059.112	15245.594	2380.171
17	6.789	2038.009	15357.341	986.842
18	6.762	2029.922	15400.164	3882.097
19	6.748	2025.436	15423.916	1961.280
20	6.743	2024.022	15431.405	1896.931
21	6.720	2017.309	15466.955	532.559
22	6.715	2015.696	15475.494	556.015
23	5.998	1800.569	16614.658	5081.116
24	4.846	1454.603	18446.656	110991.187
25	4.681	1405.199	18708.265	486.363
26	4.662	1399.361	18739.179	639.159
27	4.647	1394.939	18762.595	1488.271
28	4.634	1390.983	18783.544	793.466
29	4.623	1387.600	18801.458	1835.895
30	4.601	1381.045	18836.169	938.276
31	4.577	1373.920	18873.894	745.658
32	4.483	1345.530	19024.228	770.099
33	4.467	1340.843	19049.050	900.713
34	4.456	1337.714	19065.621	1043.682
35	4.442	1333.255	19089.230	1019.679
36	4.291	1287.913	19329.328	1068.066
37	4.276	1283.475	19352.832	1127.581
38	4.265	1280.093	19370.738	923.266
39	4.250	1275.628	19394.384	893.835
40	4.131	1240.139	19582.310	795.458
41	4.118	1236.138	19603.496	934.380
42	4.101	1230.992	19630.742	918.578
43	4.088	1227.006	19651.853	848.430
44	3.988	1197.125	19810.080	393.875
45	3.964	1189.824	19848.740	867.958
46	3.945	1184.181	19878.625	832.481
47	3.920	1176.804	19917.689	396.948
48	3.634	1090.735	20373.447	1461.463
49	3.625	1088.053	20387.650	2764.869
50	3.620	1086.644	20395.111	3028.101
51	3.614	1084.872	20404.496	3950.038
52	3.608	1083.011	20414.347	4854.712
53	3.595	1079.247	20434.281	3013.503
54	3.581	1074.978	20456.888	4552.648
55	3.565	1070.231	20482.025	4257.875
56	3.550	1065.566	20506.728	2536.534
57	3.536	1061.527	20528.115	1903.455

Index	ppm	Hz	Point	Height
58	3.525	1058.065	20546.449	2932.832
59	3.516	1055.384	20560.644	2837.230
60	3.505	1052.030	20578.402	5278.653
61	3.484	1045.835	20611.208	2797.356
62	3.410	1023.728	20728.273	697.202
63	3.395	1019.006	20753.277	840.194
64	3.379	1014.201	20778.722	658.700
65	3.366	1010.432	20798.675	1215.050
66	3.348	1005.064	20827.103	6043.161
67	3.320	996.679	20871.503	5716.311
68	3.315	995.054	20880.111	10559.720
69	3.310	993.413	20888.800	14627.424
70	3.304	991.789	20897.396	12084.090
71	3.299	990.211	20905.751	6747.597
72	3.281	984.747	20934.689	2418.255
73	3.269	981.295	20952.968	2002.328
74	3.258	978.052	20970.140	1759.922
75	3.247	974.503	20988.933	3217.767
76	3.236	971.250	21006.158	1726.903
77	3.224	967.747	21024.707	1802.701
78	3.207	962.579	21052.074	1428.905
79	3.186	956.290	21085.375	1320.751
80	3.177	953.544	21099.917	1013.433
81	3.173	952.372	21106.125	945.568
82	3.161	948.940	21124.298	1115.574
83	3.142	943.131	21155.056	821.176
84	3.112	934.073	21203.023	918.172
85	3.091	927.684	21236.853	1521.837
86	3.080	924.627	21253.041	1156.457
87	3.074	922.820	21262.609	1031.867
88	3.009	903.057	21367.259	563.934
89	2.980	894.560	21412.257	558.599
90	2.932	880.149	21488.564	1250.442
91	2.915	875.132	21515.134	1086.359
92	2.889	867.261	21556.814	2103.122
93	2.873	862.236	21583.419	1905.619
94	2.861	858.704	21602.123	650.445
95	2.834	850.723	21644.386	1348.866
96	2.817	845.461	21672.251	1604.292
97	2.799	840.140	21700.425	1761.064
98	2.776	833.366	21736.298	1089.487
99	2.718	815.991	21828.302	718.513
100	2.706	812.296	21847.867	2216.639
101	2.683	805.215	21885.367	701.337
102	2.666	800.134	21912.271	1549.023
103	2.643	793.356	21948.162	577.072
104	2.607	782.512	22005.583	592.445
105	2.576	773.187	22054.962	926.041
106	2.549	765.127	22097.642	894.971
107	2.522	757.015	22140.599	722.761
108	2.495	748.988	22183.107	737.992
109	2.442	732.996	22267.789	924.732
110	2.420	726.346	22303.001	1605.115
111	2.396	719.180	22340.947	768.254
112	2.261	678.543	22556.130	973.546
113	2.237	671.484	22593.513	1857.469
114	2.209	663.131	22637.746	2079.936
115	2.184	655.530	22677.996	2960.530
116	2.167	650.589	22704.160	904.815

Index	ppm	Hz	Point	Height
117	2.159	648.184	22716.892	1630.237
118	1.786	535.951	23311.199	1433.853
119	1.779	533.914	23321.988	1475.149
120	1.764	529.566	23345.013	3042.872
121	1.743	523.062	23379.453	3527.798
122	1.721	516.598	23413.681	2360.144
123	1.700	510.248	23447.308	1322.272
124	1.677	503.448	23483.314	1218.523
125	1.650	495.329	23526.306	1587.880
126	1.626	487.939	23565.439	2157.430
127	1.615	484.628	23582.974	1888.812
128	1.601	480.505	23604.802	2149.738
129	1.570	471.238	23653.876	1447.660
130	1.544	463.545	23694.615	759.733
131	1.464	439.525	23821.806	830.654
132	1.440	432.348	23859.810	2116.160
133	1.415	424.859	23899.466	2822.836
134	1.392	417.665	23937.560	2015.117
135	1.332	399.806	24032.132	1137.305
136	1.290	387.110	24099.363	4062.897
137	1.254	376.362	24156.275	1135.597
138	1.248	374.602	24165.591	1133.352