

Supporting Information

Improving the affinity of SL0101 for RSK using structure-based design

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***In vivo* studies**

Absorption Systems LP (Exton, PA) performed the pharmacokinetic evaluation of SL0101 in male CD-1 mice according to their established protocol.

Purified Recombinant RSK2

Baculovirus containing RSK2 cDNA was prepared using the Bac-to-Bac baculovirus expression system (Invitrogen, Carlsbad, California). His-tagged active RSK2 was expressed in Sf9 cells and purified using NiNTA resin (Qiagen, Valencia, California).

In Vitro Kinase Assay

The assays were performed as previously described.¹ Briefly, Glutathione-S-transferase (GST)-fusion protein (1 mg) containing the ER α -Ser167 sequence-RLASTND was adsorbed in the wells of LumiNunc 96-well polystyrene plates (MaxiSorp surface treatment). The wells were blocked with 3% tryptone in phosphate-buffered saline. Kinase (5 nM) in 50 μ L of kinase buffer (5 mM b-glycerophosphate, pH 7.4, 25 mM HEPES, pH 7.4, 1.5 mM DTT, 30 mM MgCl₂, 0.15 M NaCl) and 25 μ L of the compound at the indicated concentrations or vehicle was added to each well. Reactions were initiated by ATP (10 mM) and were terminated after 120 min by 500 mM EDTA, pH 7.5. All assays measured the initial velocity of reaction. After extensive washing of wells, a polyclonal anti-ER α -pSer167 antibody¹ and HRP-conjugated anti-rabbit antibody (211-035-109, Jackson ImmunoResearch Laboratories, West Grove, Pennsylvania) were used to detect serine phosphorylation of the substrate. HRP activity was measured using Western Lightning Chemiluminescence Reagent (NEL102, PerkinElmer Life Sciences) according to the manufacturer's protocol. Maximum responses and the concentrations at half the inhibitory response (IC₅₀) were determined by performing a best-fit analysis of the data (GraphPad Prism).

Proliferation Assays

The assays were performed as previously described.¹ Briefly, cells were seeded at 2000 cells per well in 96-well tissue culture plates in the appropriate medium as described by American Type Culture Collection. After 24 h, compound or vehicle was added. Cell number was measured 48 h later using CellTiter-GloTM assay reagent (Promega, Madison, Wisconsin) according to the manufacturer's protocol. Maximum responses and the concentrations of half the effective response (EC₅₀) were determined by performing a best-fit analysis of the data (GraphPad Prism).

Cell-based inhibition assays

The assays were performed as described previously¹. Briefly, 250,000 cells were seeded onto 60 mm dishes and after 24 hours the inhibitor treatments were commenced. Compound **7** was used at 25 μ M for 24 h, and SL0101 (**1**) was used at 100 μ M for 2 hours. 20 minutes before lysing the cells phorbol myristate acetate (PMA) at 500 nM was added to the media. Lysis was performed as described previously². The lysates were normalized to total protein, electrophoresed and immunoblotted. Antibodies used on cell lysates include anti-(Lys/Arg)X(Lys/Arg)XX(pSer/pThr) motif (9611), anti-eEF2 (2332), anti-peEF2 (2331), monoclonal anti-cyclin D1 (2926) from Cell Signaling Technology (Danvers, MA), and monoclonal anti-Ran (610341) from BD Transduction Laboratories (Franklin Lakes, NJ). Secondary antibodies used were donkey anti-rabbit and goat anti-mouse conjugated with horseradish peroxidase (HRP) from Jackson ImmunoResearch Laboratories (West Grove, PA).

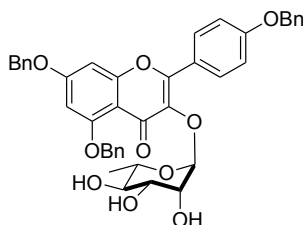
General chemistry methods and materials

^1H and ^{13}C spectra were recorded on 270 MHz, 400 MHz and 600 MHz spectrometers. Chemical shifts were reported relative to benzene- d_6 (δ 7.16 ppm), CDCl_3 (δ 7.26 ppm), CD_3OD (δ 3.31 ppm), acetone- d_6 (δ 2.05 ppm), D_2O (δ 4.80 ppm) for ^1H , and benzene- d_6 (δ 127.68 ppm), CDCl_3 (δ 77.0 ppm), CD_3OD (δ 49.15 ppm), acetone- d_6 (δ 29.92 ppm) for ^{13}C . Optical rotations were measured with a digital polarimeter at sodium D line (589 nm) and were reported in concentration of g / 100 mL at 25 °C in the solvent specified. Infrared (IR) spectra were obtained on a FT-IR spectrometer. Flash chromatography was performed using the indicated solvent system on silica gel standard grade 60 (230-400 mesh). R_f values are reported for analytical TLC using the specified solvents and 0.25 mm silica gel 60 F254 plates that were visualized by UV irradiation (254 nm) or by staining with KMnO_4 stain or *p*-anisaldehyde stain. Ether, tetrahydrofuran, methylene chloride, toluene, and triethylamine were dried by passing through activated alumina (8 x 14 mesh) column with argon gas pressure. Commercial reagents were used without purification unless otherwise noted. Air and/or moisture-sensitive reactions were carried out under an atmosphere of argon/nitrogen using oven/flamed-dried glassware and standard syringe/septum techniques. Melting points are uncorrected.

General Synthetic Procedures

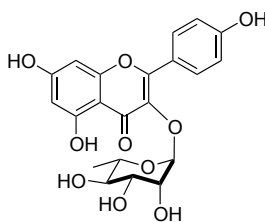
To a solution of tri-benzyl protected compounds (0.08 mmol) in 2 mL THF-EtOH (1:1) was added 20 mg Pearlman's catalyst (Pd-C, 10%). The reaction mixture was degassed using vacuum at -90 °C and refilling with H_2 . This procedure was repeated three times, then the bath was removed and the reaction was warmed up to room temperature. The reaction mixture was stirred under a H_2 atmosphere for 3-4 hours. The reaction mixture was loaded onto silica gel and elution with hexane-EtOAc (7:3 to 1:3) to give deprotected products **1-8** (54 to 91 % yield).

5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4*H*-chromen-4-one (A)



White solid, mp: 105-107 °C; $R_f = 0.56$ (10:1 (v/v) Et₂O/MeOH); $[\alpha]_D^{25} = -112$ ($c = 1.3$, MeOH); IR (thin film, cm⁻¹) 3418 (broad), 2924, 1606, 1506, 1453, 1354, 1299, 1255, 1177, 1141, 1102, 1058, 998, 953; ¹H NMR (acetone-d₆, 600 MHz) δ 7.91 (d, $J = 9.0$ Hz, 2H), 7.68 (d, $J = 7.8$ Hz, 2H), 7.50 (d, $J = 7.8$ Hz, 4H), 7.43-7.39 (m, 6H), 7.38-7.29 (m, 3H), 7.19 (d, $J = 8.4$ Hz, 2H), 6.80 (d, $J = 1.8$ Hz, 1H), 6.67 (d, $J = 2.4$ Hz, 1H), 5.57 (d, $J = 1.8$ Hz, 1H), 5.29 (d, $J = 13.2$ Hz, 1H), 5.28 (d, $J = 13.2$ Hz, 1H), 5.24 (s, 2H), 5.23 (s, 2H), 4.28 (dd, $J = 3.6, 1.8$ Hz, 1H), 3.70 (dd, $J = 9.0, 3.6$ Hz, 1H), 3.33 (dd, $J = 9.6, 9.6$ Hz, 1H), 3.21 (dq, $J = 9.6, 6.0$ Hz, 1H), 2.91 (brs, 1H), 0.87 (d, $J = 6.0$ Hz, 3H); ¹³C NMR (acetone-d₆, 150 MHz) δ 173.5, 164.1, 161.5, 160.8, 159.8, 154.8, 138.4, 138.1, 138.0, 137.4, 131.4, 129.5, 129.4, 129.3, 129.1, 128.9, 128.7, 128.5, 128.4, 127.9, 124.4, 115.7, 110.6, 102.2, 98.9, 95.1, 73.2, 72.2, 71.5, 71.4, 71.3, 71.2, 70.8, 17.9; HRMS (ESI) calcd. for [C₄₂H₃₈O₁₀+H]⁺: 703.2543, Found: 703.2537.

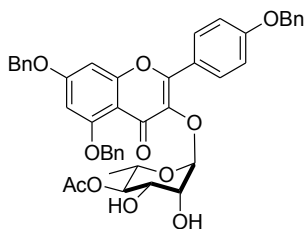
5,7-dihydroxy-2-(4-hydroxyphenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-methyltetrahydro-2*H*-pyran-2-yl)oxy)-4*H*-chromen-4-one (1a)³⁻⁶



Yield: 80%; Pale yellow solid, mp: 140-142 °C; $R_f = 0.71$ (5:1 (v/v) Et₂O/MeOH); $[\alpha]_D^{25} = -96$ ($c = 1.3$, MeOH); IR (thin film, cm⁻¹) 3259 (broad), 2924, 2855, 1653, 1607, 1442, 1360, 1251, 1207, 1172, 1057, 996; ¹H NMR (CD₃OD, 600 MHz) δ 7.72 (d, $J = 8.4$ Hz, 2H), 6.89 (d, $J = 9.0$ Hz, 2H), 6.30 (d, $J = 2.4$ Hz, 1H), 6.13 (d, $J = 1.8$ Hz, 1H), 5.33 (d, $J = 1.8$ Hz, 1H), 4.18 (dd, $J =$

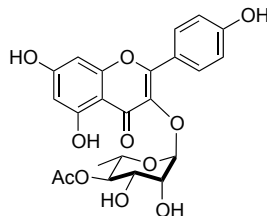
3.0, 1.8 Hz, 1H), 3.67 (dd, $J = 9.0, 2.4$ Hz, 1H), 3.30-3.27 (m, 4H), 0.88 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 179.5, 163.2, 161.6, 159.1, 158.7, 136.1, 131.9, 122.7, 116.6, 105.5, 103.5, 100.4, 95.2, 73.2, 72.2 (2C), 71.9, 17.6; HRMS (ESI) calcd. for $[\text{C}_{21}\text{H}_{20}\text{O}_{10}+\text{Na}]^+$: 455.0954, Found: 455.0949.

(2*S*,3*R*,4*S*,5*R*,6*S*)-6-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-4,5-dihydroxy-2-methyltetrahydro-2*H*-pyran-3-yl acetate (B)



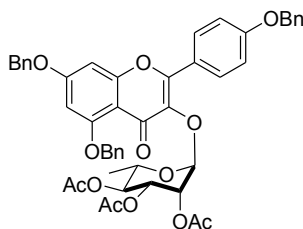
Pale yellow solid, mp: 90.5-92.5 °C; $R_f = 0.67$ (10:1 (v/v) $\text{Et}_2\text{O}/\text{MeOH}$); $[\alpha]_D^{25} = -116$ ($c = 0.8$, CHCl_3); IR (thin film, cm^{-1}) 3424 (broad), 3066, 3035, 2928, 1741, 1605, 1574, 1509, 1498, 1486, 1454, 1375, 1354, 1299, 1251, 1199, 1177, 1144, 1102, 1049, 1004, 955; ^1H NMR (acetone- d_6 , 600 MHz) δ 7.82 (d, $J = 9.0$ Hz, 2H), 7.53 (d, $J = 7.8$ Hz, 2H), 7.46-7.27 (m, 13H), 7.09 (d, $J = 9.0$ Hz, 2H), 6.55 (d, $J = 2.4$ Hz, 1H), 6.45 (d, $J = 2.4$ Hz, 1H), 5.51 (d, $J = 1.8$ Hz, 1H), 5.27 (s, 2H), 5.15 (s, 2H), 5.07 (s, 2H), 4.78 (dd, $J = 9.6, 9.0$ Hz, 1H), 4.51 (ddd, $J = 3.6, 3.6, 2.4$ Hz, 1H), 3.93 (ddd, $J = 8.4, 7.8, 3.0$ Hz, 1H), 3.45 (d, $J = 4.2$ Hz, 1H), 3.40 (dq, $J = 9.6, 6.6$ Hz, 1H), 2.91 (d, $J = 7.8$ Hz, 1H), 2.05 (s, 3H), 0.81 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (acetone- d_6 , 150 MHz) δ 173.5, 171.2, 163.0, 160.5, 159.8, 158.9, 154.6, 137.8, 136.4, 136.3, 135.6, 130.5, 128.8, 128.7, 128.6, 128.4, 128.2, 127.8, 127.6, 127.3, 126.8, 123.3, 114.7, 109.9, 101.4, 98.4, 94.0, 74.7, 70.8, 70.7, 70.5, 70.2, 69.9, 67.8, 21.0, 17.1; HRMS (ESI) calcd. for $[\text{C}_{44}\text{H}_{40}\text{O}_{11}+\text{H}]^+$: 745.2649, Found: 745.2642.

(2*S*,3*R*,4*S*,5*R*,6*S*)-6-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-4,5-dihydroxy-2-methyltetrahydro-2*H*-pyran-3-yl acetate (1b)⁵



Yield: 87%; Yellow solid, mp: 150-152 °C; R_f = 0.18 (1:3 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -145$ ($c = 1.3$, MeOH); IR (thin film, cm^{-1}) 3317 (broad), 2927, 1721, 1651, 1607, 1500, 1446, 1359, 1253, 1207, 1172, 1141, 1085, 1047, 1004, 970, 952; ^1H NMR (acetone- d_6 , 600 MHz) δ 7.84 (d, $J = 9.0$ Hz, 2H), 7.05 (d, $J = 9.0$ Hz, 2H), 6.47 (d, $J = 1.8$ Hz, 1H), 6.28 (d, $J = 1.8$ Hz, 1H), 5.53 (d, $J = 1.2$ Hz, 1H), 4.82 (dd, $J = 9.6, 9.6$ Hz, 1H), 4.23 (dd, $J = 3.6, 1.8$ Hz, 1H), 3.85 (dd, $J = 9.6, 3.6$ Hz, 1H), 3.40 (dq, $J = 9.6, 6.0$ Hz, 1H), 2.87 (brs, 1H), 1.97 (s, 3H), 0.78 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (acetone- d_6 , 150 MHz) δ 179.3, 170.9, 165.1, 163.1, 161.1, 158.7, 158.2, 135.7, 131.8, 122.5, 116.4, 105.9, 102.4, 99.6, 94.7, 74.6, 71.5, 69.8, 69.1, 21.0, 17.6; HRMS (ESI) calcd. for $[\text{C}_{23}\text{H}_{22}\text{O}_{11} + \text{Na}]^+$: 497.1060, Found: 497.1054.

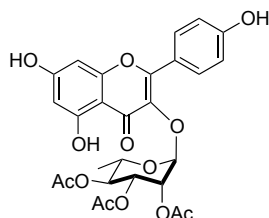
(2*S*,3*R*,4*R*,5*S*,6*S*)-2-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3,4,5-triyl triacetate (C)



White solid, mp: 90-92 °C; R_f = 0.58 (1:1 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -175$ ($c = 1.3$, CHCl_3); IR (thin film, cm^{-1}) 3035, 2982, 2938, 1746, 1632, 1605, 1574, 1509, 1498, 1486, 1453, 1432, 1368, 1298, 1247, 1217, 1174, 1136, 1101, 1044, 1019, 968; ^1H NMR (CDCl_3 , 600 MHz) δ 7.86 (d, $J = 9.0$ Hz, 2H), 7.56 (d, $J = 7.2$ Hz, 2H), 7.46-7.27 (m, 13H), 7.14 (d, $J = 9.0$ Hz, 2H), 6.56 (d, $J = 2.4$ Hz, 1H), 6.45 (d, $J = 2.4$ Hz, 1H), 5.73 (d, $J = 1.8$ Hz, 1H), 5.72 (dd, $J = 3.6, 1.8$ Hz, 1H), 5.32 (dd, $J = 10.2, 3.0$ Hz, 1H), 5.26 (s, 2H), 5.15 (s, 2H), 5.08 (s, 2H), 4.92 (dd, $J = 10.2,$

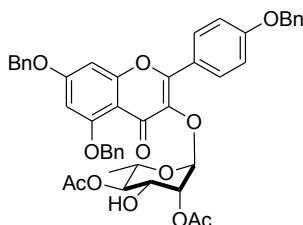
9.6 Hz, 1H), 3.37 (dq, $J = 10.2, 6.6$ Hz, 1H), 2.11 (s, 3H), 1.99 (s, 3H), 1.96 (s, 3H), 0.85 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 172.9, 169.9, 169.8, 169.5, 162.9, 160.6, 159.9, 158.8, 154.2, 136.5, 136.4, 136.3, 135.6, 130.4, 128.8, 128.7, 128.6, 128.4, 128.2, 127.7, 127.5, 127.4, 126.6, 123.1, 114.9, 110.1, 98.4, 97.9, 94.0, 70.8, 70.7, 70.5, 70.2, 69.3, 69.1, 68.1, 20.9, 20.8, 20.7, 17.1; HRMS (ESI) calcd. for $[\text{C}_{48}\text{H}_{44}\text{O}_{13}+\text{Na}]^+$: 851.2679, Found: 851.2678.

(2*S*,3*R*,4*R*,5*S*,6*S*)-2-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-6-methyltetrahydro-2*H*-pyran-3,4,5-triyl triacetate (1c**)⁷**



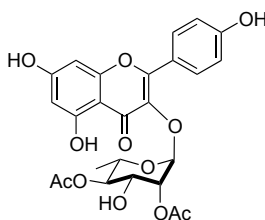
Yield: 86%; Yellow solid, mp: 152-154 °C; $R_f = 0.42$ (1:2 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -128$ ($c = 1.4$, CHCl_3); IR (thin film, cm^{-1}) 3372 (broad), 2982, 1749, 1654, 1609, 1504, 1364, 1207, 1174, 1085, 1043, 971; ^1H NMR (CDCl_3 , 600 MHz) δ 12.5 (s, 1H), 7.77 (d, $J = 9.0$ Hz, 2H), 6.98 (d, $J = 8.4$ Hz, 2H), 6.35 (d, $J = 1.8$ Hz, 1H), 6.25 (d, $J = 2.4$ Hz, 1H), 5.62 (dd, $J = 3.6, 1.8$ Hz, 1H), 5.55 (d, $J = 1.8$ Hz, 1H), 5.32 (dd, $J = 10.2, 3.6$ Hz, 1H), 4.97 (dd, $J = 10.2, 9.6$ Hz, 1H), 3.54 (dq, $J = 10.2, 6.0$ Hz, 1H), 2.13 (s, 3H), 2.02 (s, 3H), 2.01 (s, 3H), 0.94 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 177.9, 170.8, 170.3, 170.1, 162.5, 162.1, 158.6, 157.4, 156.9, 134.1, 130.7, 122.1, 115.7, 105.7, 99.3, 98.2, 94.1, 70.4, 69.4, 69.2, 68.4, 20.9, 20.8, 20.7, 17.1; HRMS (ESI) calcd. for $[\text{C}_{27}\text{H}_{26}\text{O}_{13}+\text{Na}]^+$: 581.1271, Found: 581.1266.

(2*S*,3*R*,4*R*,5*R*,6*S*)-2-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-4-hydroxy-6-methyltetrahydro-2*H*-pyran-3,5-diyl diacetate (D)



White solid, mp: 99.5-101.5 °C; $R_f = 0.58$ (1:2 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -115$ ($c = 1.1$, CHCl₃); IR (thin film, cm⁻¹) 3430 (broad), 3032, 2927, 1741, 1628, 1604, 1575, 1509, 1499, 1486, 1453, 1433, 1373, 1299, 1225, 1196, 1174, 1136, 1099, 1047, 1017, 963; ¹H NMR (CDCl₃, 600 MHz) δ 7.81 (d, $J = 9.0$ Hz, 2H), 7.56 (d, $J = 7.2$ Hz, 2H), 7.46-7.27 (m, 13H), 7.11 (d, $J = 9.0$ Hz, 2H), 6.55 (d, $J = 2.4$ Hz, 1H), 6.45 (d, $J = 2.4$ Hz, 1H), 5.58 (d, $J = 1.2$ Hz, 1H), 5.57 (dd, $J = 3.6, 1.8$ Hz, 1H), 5.26 (s, 2H), 5.16 (s, 2H), 5.07 (s, 2H), 4.76 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.11 (ddd, $J = 9.6, 6.6, 3.0$ Hz, 1H), 3.50 (dq, $J = 10.2, 6.6$ Hz, 1H), 2.28 (d, $J = 6.6$ Hz, 1H), 2.12 (s, 3H), 2.06 (s, 3H), 0.89 (d, $J = 6.0$ Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz) δ 173.0, 171.2, 170.5, 162.9, 160.6, 159.9, 158.8, 154.3, 136.9, 136.3, 135.6, 130.3, 128.8, 128.7, 128.6, 128.4, 128.2, 127.7, 127.6, 127.3, 126.7, 123.1, 114.9, 110.0, 98.4, 98.3, 94.0, 74.1, 72.1, 70.8, 70.5, 70.2, 68.8, 67.9, 21.0, 20.9, 17.1; HRMS (ESI) calcd. for [C₄₆H₄₂O₁₂+Na]⁺: 809.2574, Found: 809.2567.

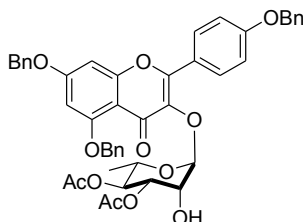
(2*S*,3*R*,4*R*,5*R*,6*S*)-2-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-4-hydroxy-6-methyltetrahydro-2*H*-pyran-3,5-diyl diacetate (1d)⁸



Yield: 88%; Yellow solid, mp: 127-129 °C; $R_f = 0.24$ (1:2 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -93$ ($c = 0.96$, MeOH); IR (thin film, cm⁻¹) 3311 (broad), 2925, 1721, 1653, 1608, 1502, 1445, 1362, 1205, 1171, 1144, 1129, 1085, 1047, 1007, 970; ¹H NMR (acetone-d₆, 600 MHz) δ 7.85 (d, $J = 9.0$ Hz, 2H), 7.06 (d, $J = 8.4$ Hz, 2H), 6.48 (d, $J = 1.8$ Hz, 1H), 6.28 (d, $J = 1.8$ Hz, 1H), 5.60 (s,

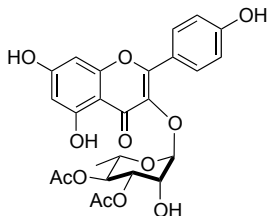
1H), 5.47 (dd, $J = 3.6, 1.8$ Hz, 1H), 4.76 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.04 (dd, $J = 9.6, 3.6$ Hz, 1H), 3.38 (dq, $J = 10.2, 6.0$ Hz, 1H), 2.06 (s, 3H), 1.99 (s, 3H), 0.81 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (acetone- d_6 , 150 MHz) δ 179.0, 170.8, 170.3, 165.2, 163.0, 161.2, 158.8, 158.1, 134.8, 131.8, 122.3, 116.5, 105.8, 99.7, 99.3, 94.7, 74.4, 72.4, 69.2, 68.0, 21.0, 20.9, 17.7; HRMS (ESI) calcd. for $[\text{C}_{25}\text{H}_{24}\text{O}_{12}+\text{Na}]^+$: 539.1166, Found: 539.1159.

(2*S*,3*S*,4*S*,5*R*,6*S*)-6-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-5-hydroxy-2-methyltetrahydro-2*H*-pyran-3,4-diyl diacetate (E**)**



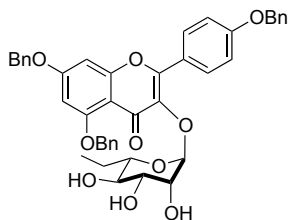
White solid, mp: 93-95 °C; $R_f = 0.59$ (2:3 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -151$ ($c = 1.3$, CHCl_3); IR (thin film, cm^{-1}) 3394 (broad), 3064, 2924, 1741, 1604, 1509, 1453, 1432, 1369, 1353, 1296, 1249, 1222, 1172, 1100, 1043, 1004, 958; ^1H NMR (CDCl_3 , 600 MHz) δ 7.86 (d, $J = 8.4$ Hz, 2H), 7.55 (d, $J = 7.8$ Hz, 2H), 7.46-7.27 (m, 13H), 7.12 (d, $J = 9.0$ Hz, 2H), 6.56 (d, $J = 2.4$ Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 5.53 (d, $J = 2.4$ Hz, 1H), 5.31 (dd, $J = 9.0, 3.0$ Hz, 1H), 5.26 (s, 2H), 5.15 (s, 2H), 5.08 (s, 2H), 4.98 (dd, $J = 9.6, 9.0$ Hz, 1H), 4.57 (dd, $J = 6.6, 3.6$ Hz, 1H), 3.46 (dq, $J = 9.6, 6.6$ Hz, 1H), 2.87 (brs, 1H), 2.07 (s, 3H), 1.99 (s, 3H), 0.82 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 173.3, 169.9, 169.8, 163.0, 160.5, 159.9, 158.9, 154.5, 137.6, 136.4, 136.3, 135.6, 130.5, 128.8, 128.7, 128.6, 128.4, 128.2, 127.7, 127.6, 127.3, 126.7, 123.2, 114.8, 109.9, 101.9, 98.3, 94.0, 74.7, 71.2, 70.8, 70.5, 70.1, 69.5, 67.9, 20.9, 20.8, 17.2; HRMS (ESI) calcd. for $[\text{C}_{46}\text{H}_{42}\text{O}_{12}+\text{Na}]^+$: 809.2574, Found: 809.2569.

(2*S*,3*S*,4*S*,5*R*,6*S*)-6-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-5-hydroxy-2-methyltetrahydro-2*H*-pyran-3,4-diyl diacetate - SL0101 (1)^{5, 8}



Yield: 91%; Yellow solid, mp: 147-149 °C; $R_f = 0.26$ (1:2 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -163$ ($c = 1.6$, MeOH); IR (thin film, cm^{-1}) 3211 (broad), 2980, 2930, 1722, 1650, 1607, 1502, 1444, 1361, 1206, 1171, 1045, 1005, 970; ^1H NMR (acetone- d_6 , 600 MHz) δ 7.86 (d, $J = 9.0$ Hz, 2H), 7.05 (d, $J = 9.0$ Hz, 2H), 6.48 (d, $J = 1.8$ Hz, 1H), 6.28 (d, $J = 1.8$ Hz, 1H), 5.56 (d, $J = 1.8$ Hz, 1H), 5.17 (dd, $J = 10.2, 3.0$ Hz, 1H), 5.07 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.42 (dd, $J = 3.0, 1.8$ Hz, 1H), 3.49 (dq, $J = 9.6, 6.0$ Hz, 1H), 2.02 (s, 3H), 1.96 (s, 3H), 0.82 (d, $J = 6.0$ Hz, 3H); ^{13}C NMR (acetone- d_6 , 150 MHz) δ 179.2, 170.7, 170.4, 165.1, 163.0, 161.1, 158.7, 158.2, 135.5, 131.8, 122.4, 116.5, 105.8, 102.2, 99.7, 99.6, 94.7, 72.3, 71.2, 69.3, 69.2, 21.0, 20.8, 17.6; HRMS (ESI) calcd. for $[\text{C}_{25}\text{H}_{24}\text{O}_{12} + \text{Na}]^+$: 539.1166, Found: 539.1161.

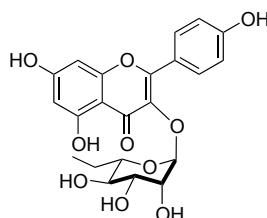
5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-6-ethyl-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)oxy)-4*H*-chromen-4-one (F)



White solid, mp: 96.4-99.0 °C; $R_f = 0.38$ (20:1 EtOAc/MeOH); $[\alpha]_D^{25} = -97.0$ ($c = 0.54$, CHCl_3); IR (thin film, cm^{-1}) 3407 (broad), 2923, 2869, 1605, 1509, 1455, 1376, 1296, 1256, 1178, 1080, 946, 736; ^1H NMR (CD_3OD , 600 MHz) δ 7.85 (d, $J = 9.0$ Hz, 2H), 7.53 (d, $J = 7.2$ Hz, 2H), 7.44-7.26 (m, 13H), 7.11 (d, $J = 9.0$ Hz, 2H), 6.65 (d, $J = 1.8$ Hz, 1H), 6.50 (d, $J = 2.4$ Hz, 1H), 5.56 (d, $J = 1.2$ Hz, 1H), 5.18 (s, 2H), 5.14 (d, $J = 12.0$ Hz, 1H), 5.12 (d, $J = 12.0$ Hz, 1H), 5.10 (d, $J = 12.0$ Hz, 1H), 5.07 (d, $J = 12.0$ Hz, 1H), 4.29 (dd, $J = 3.6, 1.8$ Hz, 1H), 3.75 (dd, $J = 9.6,$

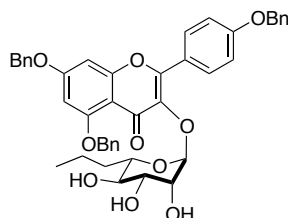
3.6 Hz, 1H), 3.40 (dd, $J = 9.6, 9.6$ Hz, 1H), 3.05 (ddd, $J = 9.0, 9.0, 2.4$ Hz, 1H), 1.53-1.46 (m, 1H), 1.21-1.13 (m, 1H), 0.48 (dd, $J = 7.8, 7.2$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 175.3, 164.8, 162.2, 160.8, 160.1, 155.8, 138.4, 138.2, 138.0, 137.5, 131.8, 129.62, 129.57, 129.5, 129.2, 129.0, 128.84, 128.75, 128.6, 128.1, 124.3, 116.0, 110.5, 102.6, 99.3, 95.2, 76.6, 72.4, 71.8, 71.7, 71.6, 71.4, 71.1, 25.2, 9.7; HRMS (ESI) calcd. for $[\text{C}_{43}\text{H}_{40}\text{O}_{10}+\text{Na}]^+$: 739.2514, Found: 739.2519.

3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-6-ethyl-3,4,5-trihydroxytetrahydro-2*H*-pyran-2-yl)oxy)-5,7-dihydroxy-2-(4-hydroxyphenyl)-4*H*-chromen-4-one (2)



Yield: 54%; Pale yellow solid, mp: 149.6-151.1 °C; $R_f = 0.26$ (20:1 (v/v) EtOAc/MeOH); $[\alpha]_D^{25} = -119.1$ ($c = 1.0$, MeOH); IR (thin film, cm^{-1}) 3342 (broad), 2931, 1655, 1608, 1507, 1456, 1361, 1284, 1208, 1176, 1085, 970; ^1H NMR (CDCl_3 , 400 MHz) δ 7.82 (d, $J = 8.8$ Hz, 2H), 6.94 (d, $J = 8.8$ Hz, 2H), 6.38 (d, $J = 2.4$ Hz, 1H), 6.20 (d, $J = 1.6$ Hz, 1H), 5.57 (d, $J = 1.2$ Hz, 1H), 4.22 (dd, $J = 3.2, 1.6$ Hz, 1H), 3.73 (dd, $J = 9.6, 3.2$ Hz, 1H), 3.39 (dd, $J = 9.6, 9.6$ Hz, 1H), 3.13 (ddd, $J = 9.2, 9.2, 2.4$ Hz, 1H), 1.61-1.51 (m, 1H), 1.25-1.14 (m, 1H), 0.54 (dd, $J = 7.6, 7.2$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 179.6, 165.9, 163.2, 161.7, 158.6, 158.5, 135.9, 132.0, 122.7, 116.6, 105.9, 102.9, 99.8, 94.7, 76.7, 72.3, 71.8, 71.4, 25.2, 9.7; HRMS (ESI) calcd. for $[\text{C}_{22}\text{H}_{22}\text{O}_{10}+\text{H}]^+$: 447.1286, Found: 447.1289.

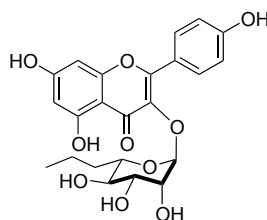
5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-propyltetrahydro-2*H*-pyran-2-yloxy)-4*H*-chromen-4-one (G)



White solid, mp: 100.3-101.5 °C; $R_f = 0.11$ (2:1 (v/v) EtOAc/Hexane); $[\alpha]_D^{25} = -102.8$ ($c = 2.15$, MeOH); IR (thin film, cm^{-1}) 3417 (broad), 2956, 1604, 1508, 1453, 1352, 1299, 1252, 1176,

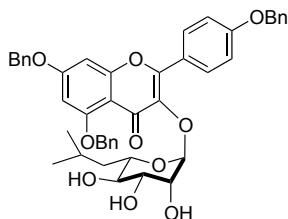
1142, 1101, 1012, 947, 736; ^1H NMR (CD_3OD , 600 MHz) δ 7.85 (d, $J = 9.0$ Hz, 2H), 7.68 (d, $J = 8.4$ Hz, 2H), 7.43-7.24 (m, 13H), 7.09 (d, $J = 9.0$ Hz, 2H), 6.61 (d, $J = 2.4$ Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 5.61 (d, $J = 1.8$ Hz, 1H), 5.16 (d, $J = 12.6$ Hz, 1H), 5.14 (d, $J = 11.4$ Hz, 1H), 5.12 (d, $J = 12.0$ Hz, 1H), 5.09 (d, $J = 11.4$ Hz, 1H), 5.07 (d, $J = 11.4$ Hz, 1H), 5.05 (d, $J = 11.4$ Hz, 1H), 4.28 (dd, $J = 3.6, 1.8$ Hz, 1H), 3.75 (dd, $J = 9.6, 3.6$ Hz, 1H), 3.38 (dd, $J = 9.6, 9.6$ Hz, 1H), 3.11 (ddd, $J = 9.6, 9.0, 3.0$ Hz, 1H), 1.49-1.43 (m, 1H), 1.19-1.10 (m, 1H), 1.09-1.02 (m, 1H), 0.79-0.69 (m, 1H), 0.60 (dd, $J = 7.8, 7.2$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 175.3, 164.7, 162.2, 160.8, 160.1, 155.5, 138.3, 138.2, 138.0, 137.5, 131.7, 129.6, 129.5, 129.2, 129.0, 128.9, 128.7, 128.6, 128.1, 124.2, 116.0, 110.5, 102.3, 99.3, 95.1, 75.7, 72.3, 71.8, 71.7, 71.6, 71.5, 71.1, 34.8, 19.4, 14.6; HRMS (ESI) calcd. for $[\text{C}_{44}\text{H}_{42}\text{O}_{10}+\text{H}]^+$: 731.2851, Found: 731.2856.

5,7-dihydroxy-2-(4-hydroxyphenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-propyl-tetrahydro-2*H*-pyran-2-yl)oxy)-4*H*-chromen-4-one (3)



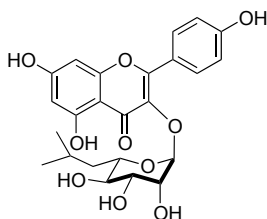
Yield: 66%; Pale yellow solid, mp: 165.3-166.2 °C; $R_f = 0.14$ (3:1 (v/v) EtOAc/Hexane); $[\alpha]_D^{25} = -119.2$ ($c = 0.74$, MeOH); IR (thin film, cm^{-1}) 3313 (broad), 2959, 1655, 1607, 1507, 1449, 1361, 1277, 1208, 1177, 1087, 970; ^1H NMR (CD_3OD , 600 MHz) δ 7.83 (d, $J = 8.4$ Hz, 2H), 6.94 (d, $J = 8.4$ Hz, 2H), 6.37 (d, $J = 1.8$ Hz, 1H), 6.21 (d, $J = 2.4$ Hz, 1H), 5.62 (d, $J = 1.8$ Hz, 1H), 4.20 (dd, $J = 3.6, 1.8$ Hz, 1H), 3.73 (dd, $J = 9.6, 3.0$ Hz, 1H), 3.37 (dd, $J = 9.6, 9.6$ Hz, 1H), 3.20 (ddd, $J = 9.6, 9.0, 2.4$ Hz, 1H), 1.54-1.48 (m, 1H), 1.21-1.08 (m, 2H), 0.87-0.80 (m, 1H), 0.68 (dd, $J = 7.2, 7.2$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 179.8, 166.0, 163.4, 161.8, 158.6 (2C), 135.9, 132.1, 122.8, 116.8, 106.0, 102.8, 100.0, 94.8, 75.9, 72.4, 71.9, 71.8, 34.9, 19.6, 14.6; HRMS (ESI) calcd. for $[\text{C}_{23}\text{H}_{24}\text{O}_{10}+\text{Na}]^+$: 483.1262, Found: 483.1264.

5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-3-((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-propyltetrahydro-2*H*-pyran-2-yloxy)-4*H*-chromen-4-one (H)



White solid, mp: 83.7-86.0 °C; $R_f = 0.40$ (5:1 (v/v) EtOAc/Hexane); $[\alpha]_D^{25} = -90.1$ ($c = 0.93$, CHCl₃); IR (thin film, cm⁻¹) 3421 (broad), 2927, 2859, 1734, 1610, 1510, 1455, 1350, 1304, 1254, 1177, 1140, 1107, 1010, 948; ¹H NMR (CDCl₃, 400 MHz) δ 7.91 (d, $J = 8.8$ Hz, 2H), 7.50 (d, $J = 8.0$ Hz, 2H), 7.43-7.28 (m, 13H), 7.06 (d, $J = 9.6$ Hz, 2H), 6.55 (d, $J = 2.4$ Hz, 1H), 6.41 (d, $J = 1.6$ Hz, 1H), 5.85 (d, $J = 0.8$ Hz, 1H), 5.27 (s, 2H), 5.09 (s, 2H), 5.05 (s, 2H), 4.52 (m, 1H), 3.92 (m, 1H), 3.69 (brs, 1H), 3.45 (dd, $J = 9.6, 8.8$ Hz, 1H), 3.39 (brs, 1H), 3.27 (dd, $J = 8.8, 8.0$ Hz, 1H), 2.66 (brs, 1H), 1.42-1.18 (m, 3H), 0.64 (d, $J = 6.0$ Hz, 3H), 0.42 (d, $J = 6.4$ Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz) δ 174.1, 163.2, 160.9, 159.8, 158.9, 153.8, 137.5, 136.5, 136.4, 135.7, 130.7, 129.0, 128.9, 128.7, 128.4, 128.0, 127.9, 127.8, 127.0, 123.2, 115.0, 109.8, 100.4, 98.4, 93.9, 73.0, 72.1, 71.7, 70.9, 70.7, 70.4, 70.3, 41.3, 24.8, 23.8, 22.1; HRMS (ESI) calcd. for [C₄₅H₄₄O₁₀+H]⁺: 745.3007, Found: 745.3013.

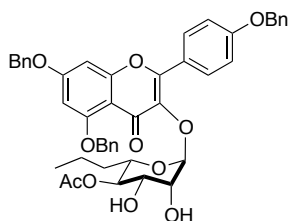
5,7-dihydroxy-2-(4-hydroxyphenyl)-3-(((2*S*,3*R*,4*R*,5*R*,6*S*)-3,4,5-trihydroxy-6-isobutyltetrahydro-2*H*-pyran-2-yl)oxy)-4*H*-chromen-4-one (4)



Yield: 58%; Pale yellow solid, mp: 149.5-151.8 °C; $R_f = 0.28$ (20:1 (v/v) EtOAc/MeOH); $[\alpha]_D^{25} = -79.2$ ($c = 0.25$, MeOH); IR (thin film, cm⁻¹) 3259 (broad), 2959, 2858, 1717, 1650, 1613, 1513, 1453, 1368, 1273, 1207, 1172, 1072, 996; ¹H NMR (CD₃OD, 400 MHz) δ 7.86 (d, $J = 8.4$ Hz, 2H), 6.93 (d, $J = 8.8$ Hz, 2H), 6.37 (d, $J = 1.6$ Hz, 1H), 6.19 (d, $J = 1.6$ Hz, 1H), 5.82 (d, $J = 0.8$ Hz, 1H), 4.16 (dd, $J = 3.2, 1.6$ Hz, 1H), 3.73 (dd, $J = 9.6, 3.2$ Hz, 1H), 3.34-3.31 (m, 1H),

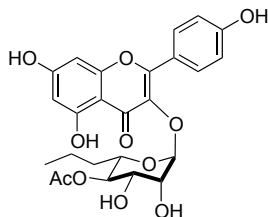
3.24 (ddd, $J = 9.6, 9.6, 1.2$ Hz, 1H), 1.45-1.40 (m, 1H), 1.38-1.26 (m, 1H), 1.21-1.13 (m, 1H), 0.67 (d, $J = 6.4$ Hz, 3H), 0.52 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR (CD_3OD , 100 MHz) δ 179.6, 165.9, 163.2, 161.8, 158.4, 157.7, 135.4, 131.9 (2C), 122.5, 116.6 (2C), 105.8, 101.8, 99.8, 94.6, 74.6, 72.0 (2C), 71.5, 42.3, 25.9, 24.2, 22.4; HRMS (ESI) calcd. for $[\text{C}_{24}\text{H}_{26}\text{O}_{10}+\text{H}]^+$: 475.1599, Found: 475.1605.

(2*S*,3*R*,4*S*,5*R*,6*S*)-6-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-4,5-dihydroxy-2-propyltetrahydro-2*H*-pyran-3-yl acetate (I)



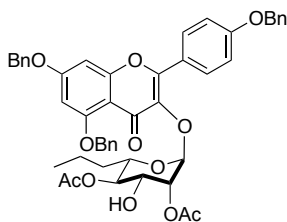
Pale liquid; $R_f = 0.25$ (1:1 (v/v) $\text{Et}_2\text{O}/\text{Hexane}$); $[\alpha]_D^{25} = -92.9$ ($c = 0.36$, CHCl_3); IR (thin film, cm^{-1}) 3423 (broad), 3035, 2928, 1738, 1609, 1508, 1363, 1254, 1176, 1107, 1045, 1014, 947, 830, 736, 696; ^1H NMR (CDCl_3 , 600 MHz) δ 7.88 (d, $J = 9.0$ Hz, 2H), 7.54 (d, $J = 7.2$ Hz, 2H), 7.47-7.29 (m, 13H), 7.10 (d, $J = 9.0$ Hz, 2H), 6.57 (d, $J = 2.4$ Hz, 1H), 6.46 (d, $J = 2.4$ Hz, 1H), 5.65 (d, $J = 1.8$ Hz, 1H), 5.27 (s, 2H), 5.16 (s, 2H), 5.09 (d, $J = 11.4$ Hz, 1H), 5.07 (d, $J = 12.0$ Hz, 1H), 4.81 (dd, $J = 9.0, 8.6$ Hz, 1H), 4.41 (dd, $J = 3.0, 2.4$ Hz, 1H), 3.96 (dd, $J = 9.0, 3.6$ Hz, 1H), 3.35 (ddd, $J = 9.0, 8.4, 3.6$ Hz, 1H), 2.07 (s, 3H), 1.59 (brs, 2H), 1.25-1.15 (m, 1H), 1.10-1.04 (m, 1H), 0.89-0.85 (m, 1H), 0.79-0.72 (m, 1H), 0.65 (dd, $J = 7.2, 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 173.7, 171.5, 163.2, 160.8, 160.1, 159.1, 154.2, 137.7, 136.6, 136.5, 135.8, 130.7, 129.0, 128.9, 128.85, 128.7, 128.4, 128.0, 127.8, 127.6, 126.9, 123.5, 115.0, 110.1, 100.8, 98.6, 94.2, 73.6, 71.7, 71.1, 70.8, 70.7, 70.4, 70.3, 33.8, 21.3, 18.1, 14.3; HRMS (ESI) calcd. for $[\text{C}_{46}\text{H}_{44}\text{O}_{11}+\text{H}]^+$: 773.2956, Found: 773.2955.

(2*S*,3*R*,4*S*,5*R*,6*S*)-6-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl) oxy)-4,5-dihydroxy-2-propyltetrahydro-2*H*-pyran-3-yl acetate (5)



Yield: 56%; Yellow gummy solid; $R_f = 0.25$ (100% EtOAc); $[\alpha]_D^{25} = -70.0$ ($c = 0.16$, MeOH); IR (thin film, cm^{-1}) 3293 (broad), 2937, 1724, 1654, 1604, 1505, 1448, 1364, 1258, 1210, 1175, 1088, 1048, 970, 829; $^1\text{H NMR}$ (CD_3OD , 600 MHz) δ 7.79 (d, $J = 9.0$ Hz, 2H), 6.94 (d, $J = 9.0$ Hz, 2H), 6.38 (d, $J = 2.4$ Hz, 1H), 6.20 (d, $J = 1.8$ Hz, 1H), 5.72 (d, $J = 1.8$ Hz, 1H), 4.84 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.53 (brs, 1H), 4.18 (dd, $J = 3.6, 1.8$ Hz, 1H), 3.85 (dd, $J = 10.2, 3.6$ Hz, 1H), 3.16 (ddd, $J = 9.6, 7.8, 2.4$ Hz, 1H), 2.00 (s, 3H), 1.35-1.27 (m, 1H), 1.45-1.08 (m, 1H), 0.89-0.81 (m, 2H), 0.64 (dd, $J = 7.2, 6.6$ Hz, 3H); $^{13}\text{C NMR}$ (CD_3OD , 150 MHz) δ 179.5, 172.4, 165.9, 163.3, 161.8, 158.7, 158.5, 135.2, 132.0, 122.6, 116.6, 105.9, 101.8, 99.9, 94.7, 73.6, 73.1, 71.6, 70.2, 34.8, 21.0, 19.2, 14.4; HRMS (ESI) calcd. for $[\text{C}_{25}\text{H}_{26}\text{O}_{11} + \text{Na}]^+$: 525.1367, Found: 525.1369.

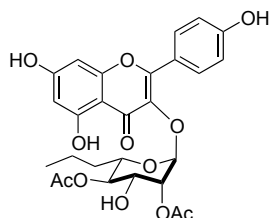
(2*S*,3*R*,4*R*,5*R*,6*S*)-2-(5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yloxy)-4-hydroxy-6-propyltetrahydro-2*H*-pyran-3,5-diyl diacetate (J)



White solid, mp: 98.6-100.1 °C; $R_f = 0.53$ (1:1 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -80.3$ ($c = 0.75$, CHCl_3); IR (thin film, cm^{-1}) 3462 (broad), 3033, 2922, 1743, 1628, 1604, 1573, 1509, 1453, 1486, 1435, 1372, 1298, 1249, 1227, 1176, 1139, 1100, 1046, 1023, 957, 835, 733; $^1\text{H NMR}$ (CDCl_3 , 600 MHz) δ 7.86 (d, $J = 9.0$ Hz, 2H), 7.56 (d, $J = 7.2$ Hz, 2H), 7.46-7.28 (m, 13H), 7.12 (d, $J = 9.0$ Hz, 2H), 6.56 (d, $J = 2.4$ Hz, 1H), 6.44 (d, $J = 2.4$ Hz, 1H), 5.81 (d, $J = 1.8$ Hz, 1H),

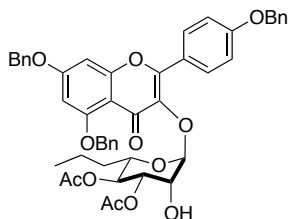
5.56 (dd, $J = 3.6, 1.8$ Hz, 1H), 5.27 (d, $J = 13.2$ Hz, 1H), 5.25 (d, $J = 12.6$ Hz, 1H), 5.16 (s, 2H), 5.08 (d, $J = 12.0$ Hz, 1H), 5.06 (d, $J = 11.4$ Hz, 1H), 4.81 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.13 (ddd, $J = 9.6, 7.2, 3.6$ Hz, 1H), 3.38 (ddd, $J = 10.2, 6.0, 4.8$ Hz, 1H), 2.28 (d, $J = 7.2$ Hz, 1H), 2.12 (s, 3H), 2.06 (s, 3H), 1.27-1.15 (m, 3H), 0.95-0.85 (m, 1H), 0.69 (d, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 173.2, 171.4, 170.6, 163.0, 160.8, 160.0, 159.0, 153.8, 136.7, 136.6, 135.8, 130.6, 128.9 (2C), 128.8, 128.6, 128.4, 127.9, 127.8, 127.5, 126.8, 123.3, 115.1, 110.1, 98.6, 97.7, 94.1, 73.0, 72.1, 71.5, 71.0, 70.7, 70.4, 69.0, 33.6, 21.2, 21.1, 18.1, 14.2; HRMS (ESI) calcd. for $[\text{C}_{48}\text{H}_{46}\text{O}_{12}+\text{Na}]^+$: 837.2882, Found: 837.2886.

(2*S*,3*R*,4*R*,5*R*,6*S*)-2-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl) oxy)-4-hydroxy-6-propyltetrahydro-2*H*-pyran-3,5-diyl diacetate (6)



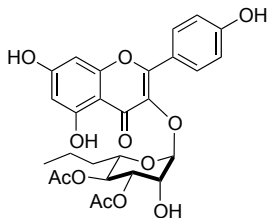
Yield: 91%; Yellow solid, mp: 151.7-152.8 °C; $R_f = 0.13$ (1:1 (v/v) hexane/EtOAc); $[\alpha]_{\text{D}}^{25} = -67.4$ ($c = 0.89$, MeOH); IR (thin film, cm^{-1}) 3383 (broad), 2960, 1724, 1655, 1609, 1509, 1451, 1368, 1244, 1207, 1144, 1086, 1046, 1006, 970, 953, 840; ^1H NMR (CD_3OD , 600 MHz) δ 7.81 (d, $J = 9.0$ Hz, 2H), 6.97 (d, $J = 9.0$ Hz, 2H), 6.39 (d, $J = 2.4$ Hz, 1H), 6.21 (d, $J = 2.4$ Hz, 1H), 5.75 (d, $J = 1.8$ Hz, 1H), 5.42 (dd, $J = 3.6, 1.8$ Hz, 1H), 4.81 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.05 (dd, $J = 10.2, 3.6$ Hz, 1H), 3.23 (ddd, $J = 9.6, 7.8, 3.0$ Hz, 1H), 2.11 (s, 3H), 2.02 (s, 3H), 1.16-1.11 (m, 3H), 0.91-0.86 (m, 1H), 0.67 (dd, $J = 7.2, 6.6$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 179.4, 172.3, 172.0, 166.1, 163.4, 162.1, 158.8, 158.6, 134.7, 132.1, 122.5, 116.8, 105.9, 100.1, 98.9, 94.9, 73.5, 73.2, 73.1, 68.6, 34.8, 21.0, 20.9, 19.3, 14.4; HRMS (ESI) calcd. for $[\text{C}_{27}\text{H}_{28}\text{O}_{12}+\text{Na}]^+$: 567.1473, Found: 567.1476.

(2*S*,3*S*,4*S*,5*R*,6*S*)-6-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-5-hydroxy-2-propyltetrahydro-2*H*-pyran-3,4-diyl diacetate (K)



White solid, mp: 86.4-88.1 °C; $R_f = 0.45$ (1:1 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -150.0$ ($c = 1.1$, CHCl₃); IR (thin film, cm⁻¹) 3391 (broad), 2959, 1744, 1604, 1509, 1454, 1433, 1369, 1297, 1249, 1226, 1176, 1100, 1046, 1008, 953; ¹H NMR (CDCl₃, 600 MHz) δ 7.89 (d, $J = 9.0$ Hz, 2H), 7.55 (d, $J = 7.2$ Hz, 2H), 7.46-7.28 (m, 13H), 7.13 (d, $J = 8.4$ Hz, 2H), 6.57 (d, $J = 2.4$ Hz, 1H), 6.46 (d, $J = 1.8$ Hz, 1H), 5.53 (d, $J = 2.4$ Hz, 1H), 5.34 (dd, $J = 9.0, 3.6$ Hz, 1H), 5.27 (s, 2H), 5.15 (s, 2H), 5.09 (d, $J = 11.4$ Hz, 1H), 5.07 (d, $J = 11.4$ Hz, 1H), 5.04 (dd, $J = 9.6, 9.0$ Hz, 1H), 4.54 (dd, $J = 3.0, 2.4$ Hz, 1H), 3.32 (ddd, $J = 9.6, 8.4, 3.6$ Hz, 1H), 2.08 (s, 3H), 1.98 (s, 3H), 1.26-1.05 (m, 3H), 0.79-0.71 (m, 1H), 0.65 (dd, $J = 7.2, 6.6$ Hz, 3H); ¹³C NMR (CDCl₃, 150 MHz) δ 173.5, 170.1, 170.0, 163.1, 160.8, 160.0, 159.1, 154.1, 137.5, 136.6, 136.5, 135.8, 130.8, 129.0, 128.9, 128.8, 128.6, 128.4, 127.9, 127.8, 127.6, 126.9, 123.4, 115.0, 110.1, 100.5, 98.5, 94.1, 71.7, 71.6, 71.0, 70.7, 70.4, 70.3, 69.5, 33.9, 21.2, 21.0, 17.9, 14.2; HRMS (ESI) calcd. For [C₄₈H₄₆O₁₂+Na]⁺: 837.2882, Found: 837.2886.

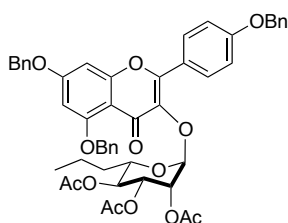
(2*S*,3*S*,4*S*,5*R*,6*S*)-6-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-5-hydroxy-2-propyltetrahydro-2*H*-pyran-3,4-diyl diacetate (7)



Yield: 71%; Yellow solid, mp: 148.9-150.0 °C; $R_f = 0.26$ (1:1 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -175.3$ ($c = 1.2$, MeOH); IR (thin film, cm⁻¹) 3376 (broad), 2966, 1725, 1654, 1607, 1508, 1447, 1365, 1261, 1211, 1176, 1048, 1005, 970, 841; ¹H NMR (CD₃OD, 600 MHz) δ 7.83 (d, $J = 9.0$ Hz, 2H), 6.97 (d, $J = 9.0$ Hz, 2H), 6.40 (d, $J = 2.4$ Hz, 1H), 6.21 (d, $J = 1.8$ Hz, 1H), 5.82 (d, $J =$

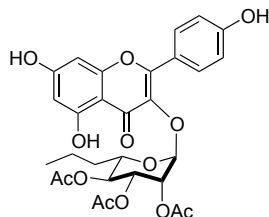
1.8 Hz, 1H), 5.19 (dd, $J = 10.2, 3.6$ Hz, 1H), 5.04 (dd, $J = 10.2, 9.6$ Hz, 1H), 4.33 (dd, $J = 3.0, 1.8$ Hz, 1H), 3.19 (ddd, $J = 10.2, 9.6, 1.8$ Hz, 1H), 2.07 (s, 3H), 1.96 (s, 3H), 1.19-1.11 (m, 3H), 0.90-0.85 (m, 1H), 0.66 (dd, $J = 7.2, 6.6$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 179.5, 172.2, 171.8, 166.1, 163.4, 162.0, 158.8, 158.7, 135.0, 132.2, 122.6, 116.9, 106.0, 101.3, 100.1, 94.9, 73.2, 73.1, 70.7, 69.4, 34.8, 21.0, 20.8, 19.3, 14.4; HRMS (ESI) calcd. for $[\text{C}_{27}\text{H}_{28}\text{O}_{12}+\text{Na}]^+$: 567.1473, Found: 567.1476.

(2*S*,3*R*,4*R*,5*S*,6*S*)-2-((5,7-bis(benzyloxy)-2-(4-(benzyloxy)phenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-6-propyltetrahydro-2*H*-pyran-3,4,5-triyl triacetate (L)



White solid, mp: 89.8-91.1 °C; $R_f = 0.26$ (2:1 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -130.1$ ($c = 1.61$, CHCl_3); IR (thin film, cm^{-1}) 3033, 2962, 1751, 1632, 1605, 1573, 1509, 1454, 1434, 1369, 1249, 1220, 1174, 1140, 1101, 1048, 1023, 962; ^1H NMR (CDCl_3 , 600 MHz) δ 7.92 (d, $J = 8.4$ Hz, 2H), 7.55 (d, $J = 7.2$ Hz, 2H), 7.46-7.28 (m, 13H), 7.15 (d, $J = 8.4$ Hz, 2H), 6.57 (d, $J = 2.4$ Hz, 1H), 6.45 (d, $J = 2.4$ Hz, 1H), 5.98 (d, $J = 1.8$ Hz, 1H), 5.07 (dd, $J = 3.0, 1.8$ Hz, 1H), 5.35 (dd, $J = 10.2, 3.6$ Hz, 1H), 5.26 (s, 2H), 5.15 (s, 2H), 5.09 (d, $J = 11.4$ Hz, 1H), 5.07 (d, $J = 11.4$ Hz, 1H), 4.97 (dd, $J = 10.2, 9.6$ Hz, 1H), 3.24 (ddd, $J = 10.2, 8.4, 2.4$ Hz, 1H), 2.11 (s, 3H), 2.00 (s, 3H), 1.95 (s, 3H), 1.26-1.12 (m, 3H), 0.86-0.82 (m, 1H), 0.67 (dd, $J = 7.2, 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 150 MHz) δ 173.1, 170.1, 170.0, 169.8, 163.0, 160.8, 160.0, 158.9, 136.6, 136.5, 136.3, 135.8, 130.6, 128.9, 128.8, 128.7, 128.6, 128.4, 127.9, 127.8, 127.6, 126.8, 123.2, 115.1, 110.1, 98.5, 97.3, 94.1, 71.6, 71.0, 70.7, 70.3, 69.6, 69.4, 69.3, 33.6, 21.0, 20.9, 18.0, 14.1; HRMS (ESI) calcd. for $[\text{C}_{50}\text{H}_{48}\text{O}_{13}+\text{Na}]^+$: 879.2987, Found: 879.2994.

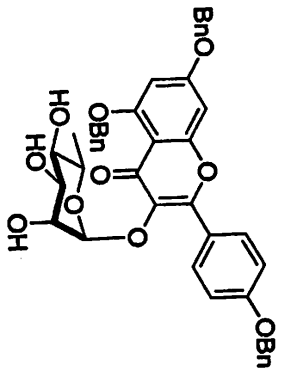
(2*S*,3*R*,4*R*,5*S*,6*S*)-2-((5,7-dihydroxy-2-(4-hydroxyphenyl)-4-oxo-4*H*-chromen-3-yl)oxy)-6-propyltetrahydro-2*H*-pyran-3,4,5-triyl triacetate (8)



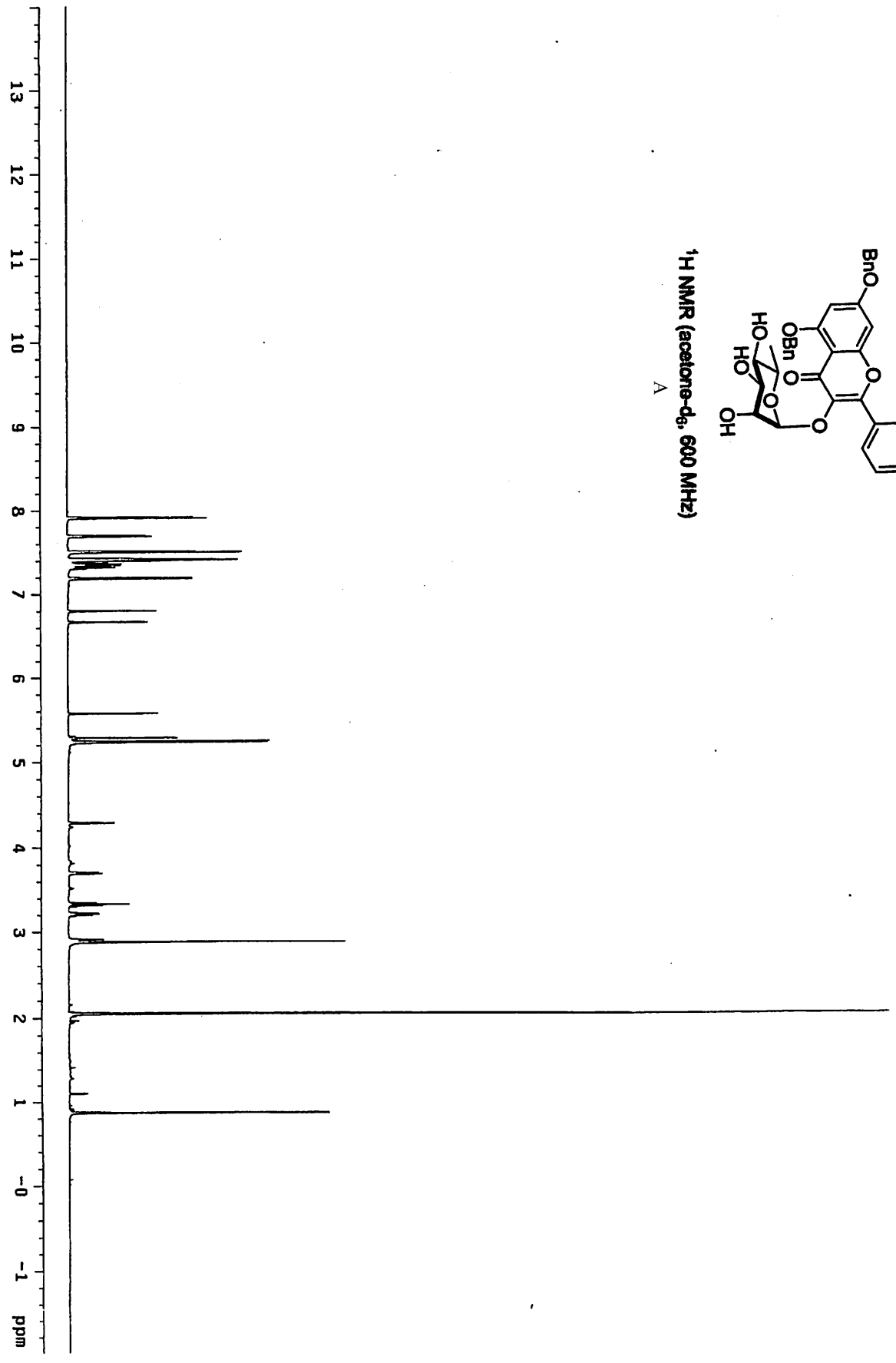
Yield: 71%; Yellow solid, mp: 133.2-134.3 °C; $R_f = 0.42$ (1:1 (v/v) hexane/EtOAc); $[\alpha]_D^{25} = -148.5$ ($c = 0.92$, MeOH); IR (thin film, cm^{-1}) 3394 (broad), 2961, 1753, 1724, 1656, 1607, 1500, 1366, 1211, 1174, 1086, 1048, 970, 841; ^1H NMR (CD_3OD , 600 MHz) δ 7.85 (d, $J = 9.0$ Hz, 2H), 6.98 (d, $J = 9.0$ Hz, 2H), 6.40 (d, $J = 2.4$ Hz, 1H), 6.22 (d, $J = 1.8$ Hz, 1H), 5.88 (d, $J = 1.8$ Hz, 1H), 5.58 (d, $J = 3.6, 1.8$ Hz, 1H), 5.29 (dd, $J = 10.2, 3.6$ Hz, 1H), 4.92 (dd, $J = 10.2, 9.6$ Hz, 1H), 3.23 (ddd, $J = 10.2, 5.4, 5.4$ Hz, 1H), 2.12 (s, 3H), 1.98 (s, 3H), 1.96 (s, 3H), 1.18-1.11 (m, 3H), 0.95-0.85 (m, 1H), 0.67 (dd, $J = 7.2, 7.2$ Hz, 3H); ^{13}C NMR (CD_3OD , 150 MHz) δ 179.3, 171.8, 171.7, 171.6, 166.2, 163.4, 162.1, 158.7, 158.6, 134.4, 132.1, 122.4, 116.9, 105.9, 100.1, 98.6, 94.9, 73.1, 70.8, 70.3, 70.2, 34.6, 20.8, 20.7, 19.1, 14.3; HRMS (ESI) calcd. for $[\text{C}_{29}\text{H}_{30}\text{O}_{13}+\text{Na}]^+$: 609.1579, Found: 609.1582.

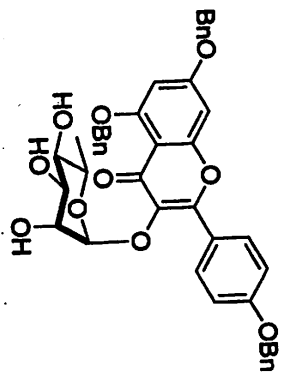
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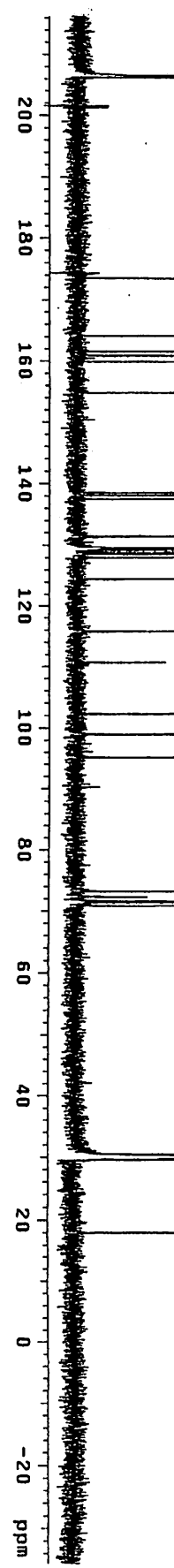
¹H NMR (acetone-d₆, 600 MHz) Δ

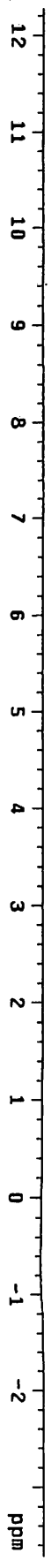
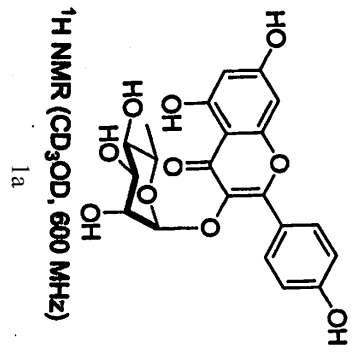


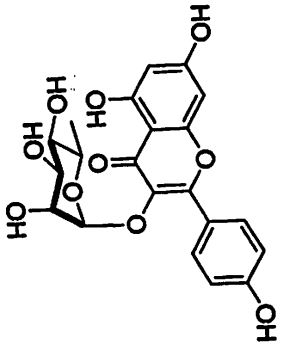


¹³C NMR (acetone-d₆, 150 MHz)

A

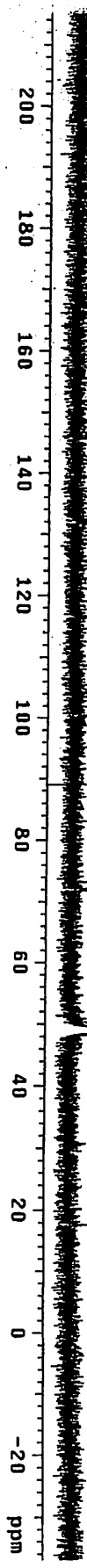


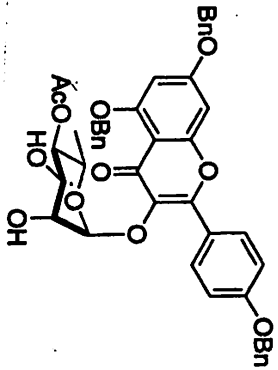




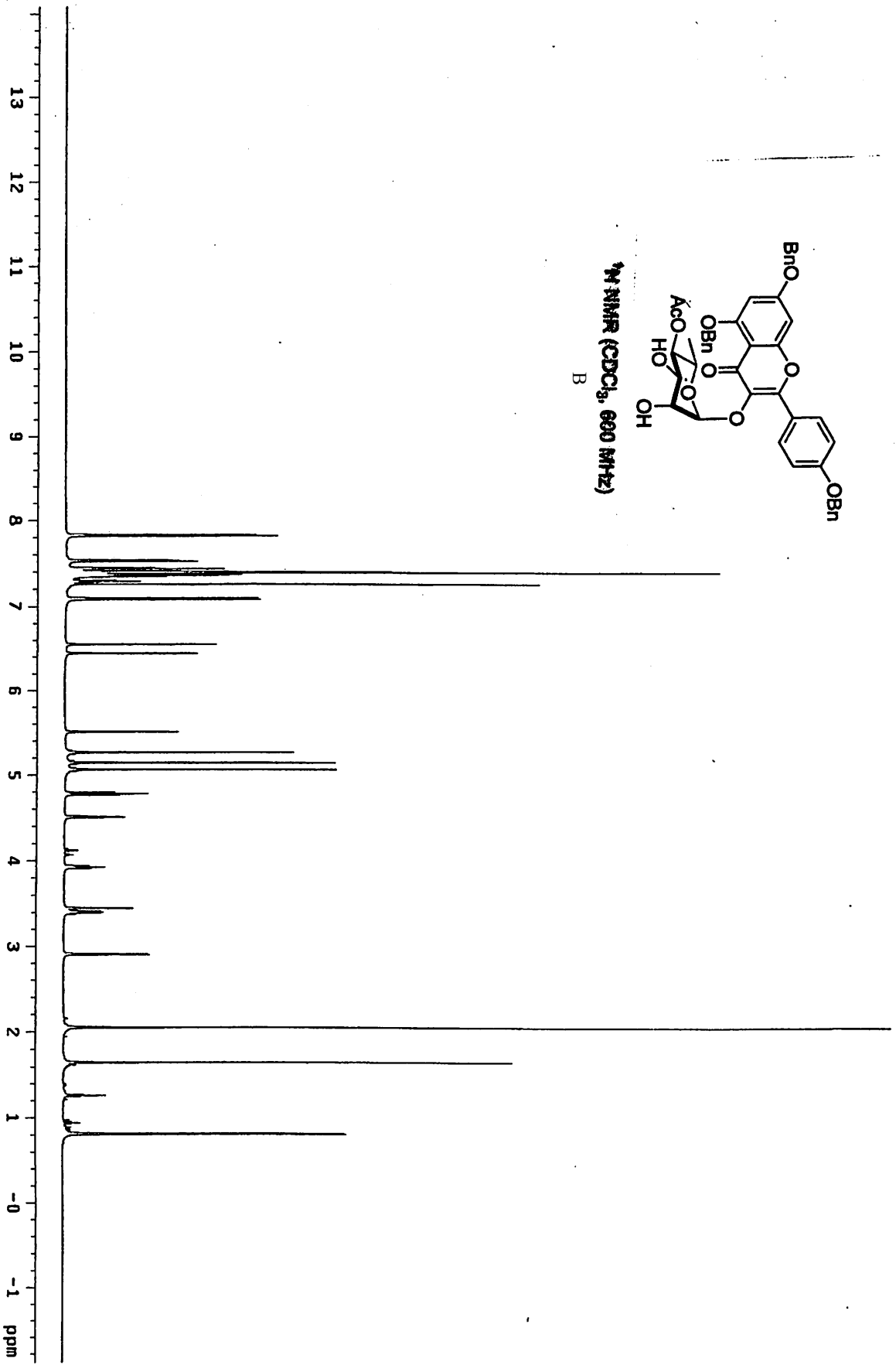
¹³C NMR (CD₃OD, 150 MHz)

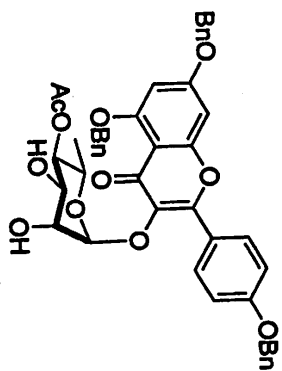
1a





¹H NMR (CDCl₃, 600 MHz)
B

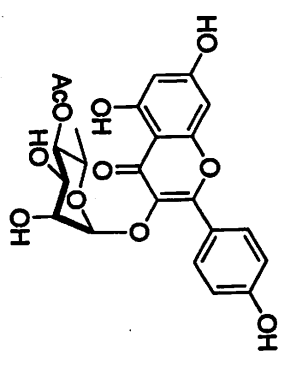




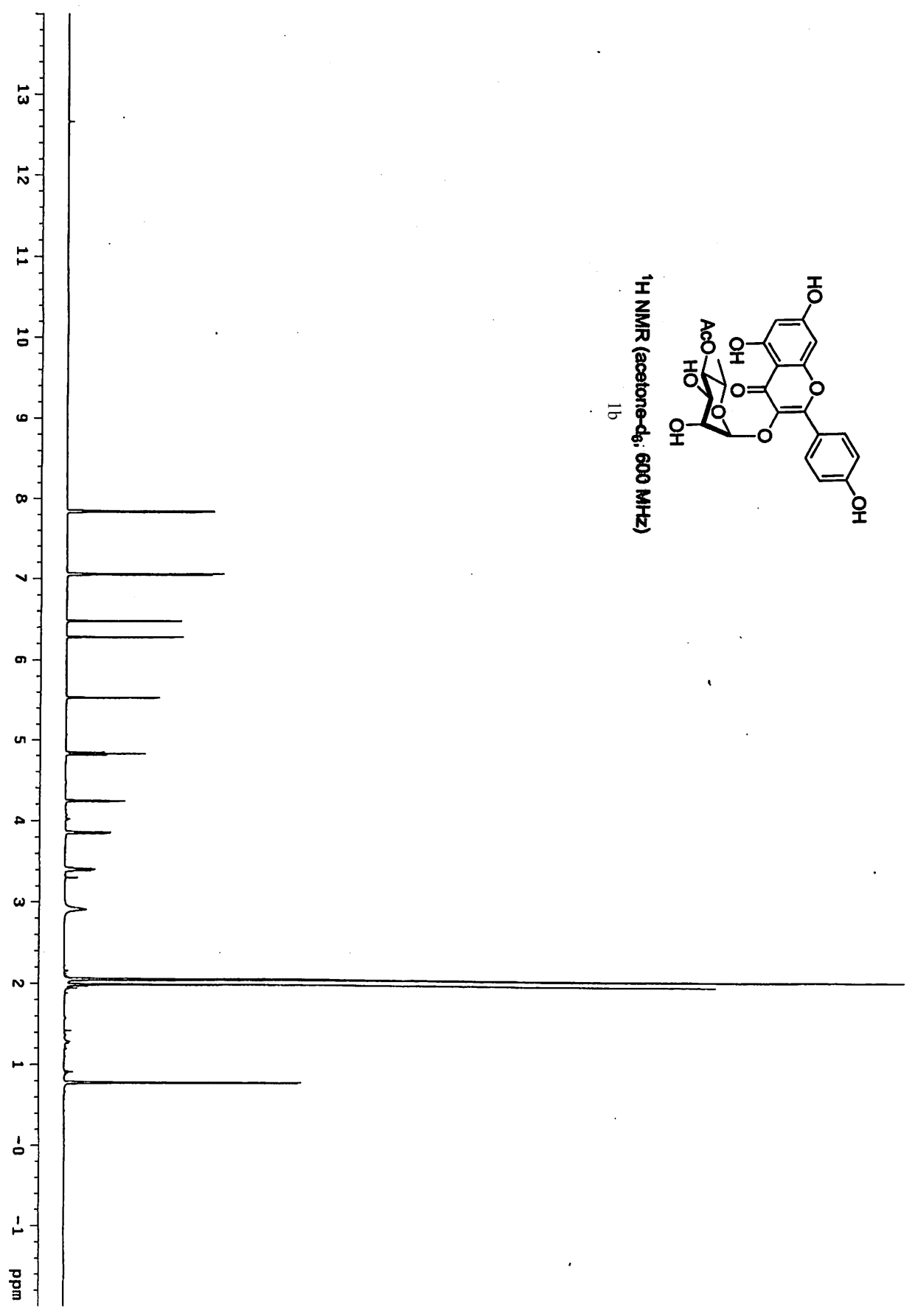
¹³C NMR (CDCl₃, 150 MHz)

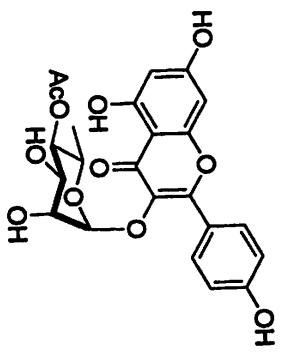
B





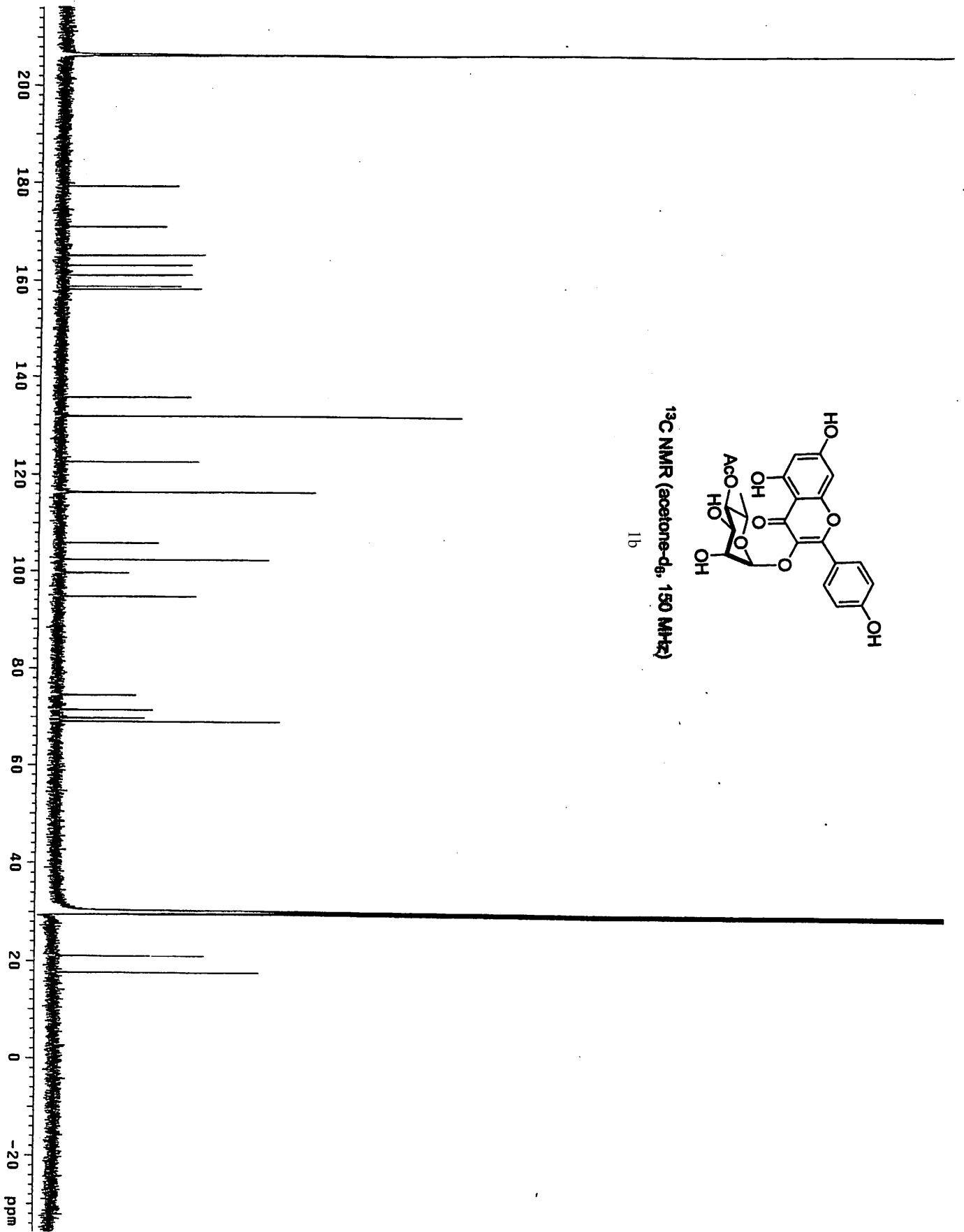
¹H NMR (acetone-d₆; 600 MHz)
1b

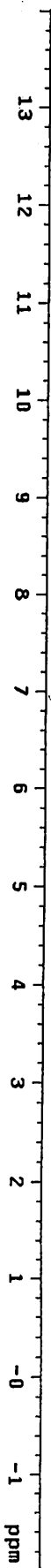
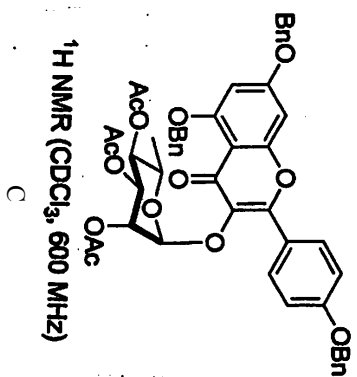


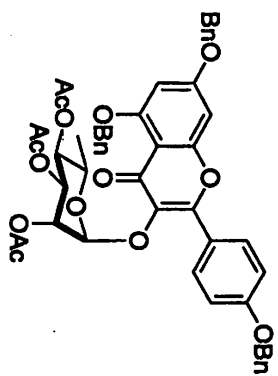


¹³C NMR (acetone-d₆, 150 MHz)

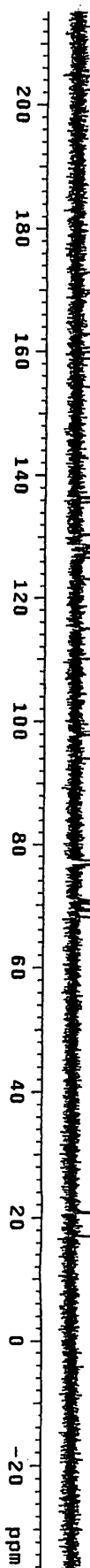
1b

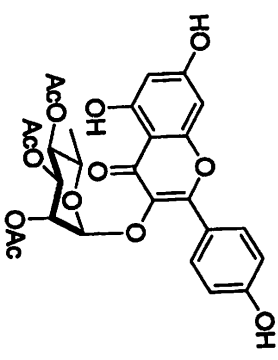




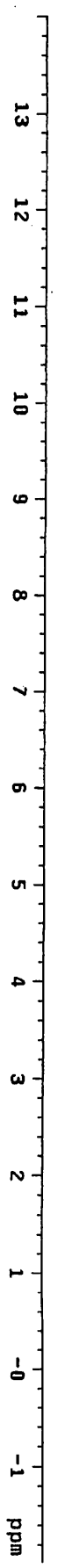


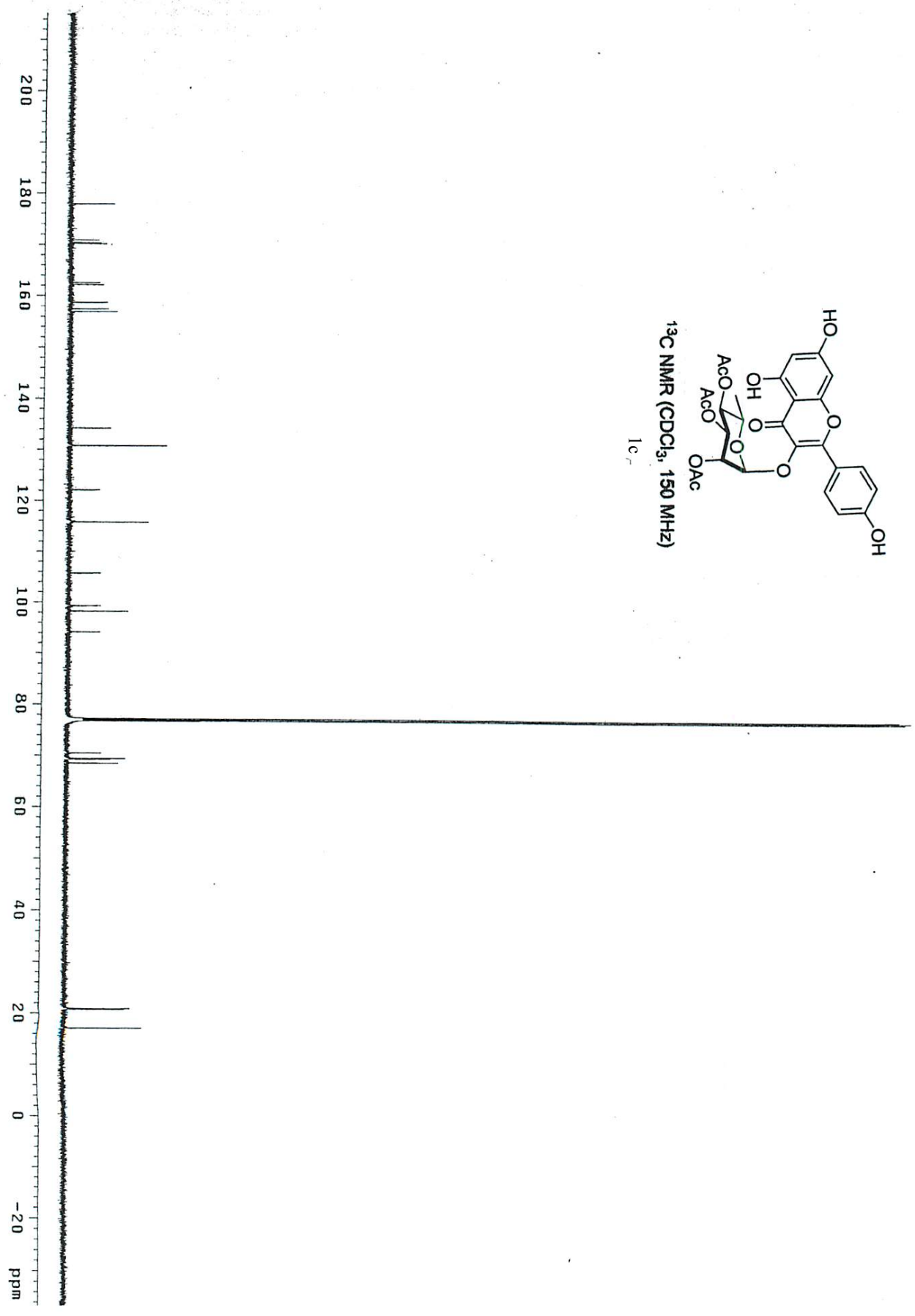
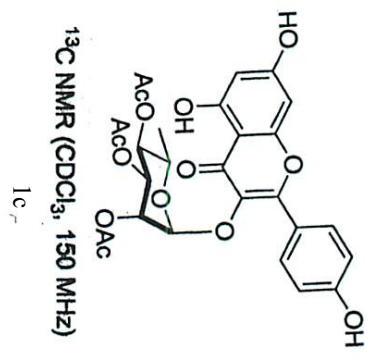
¹³C NMR (CDCl₃, 150 MHz)

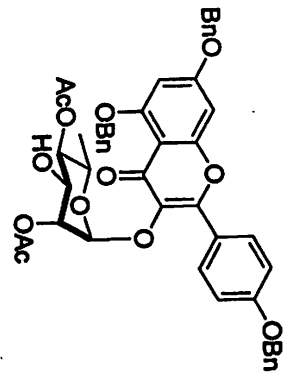




¹H NMR (CDCl₃, 600 MHz)
1c

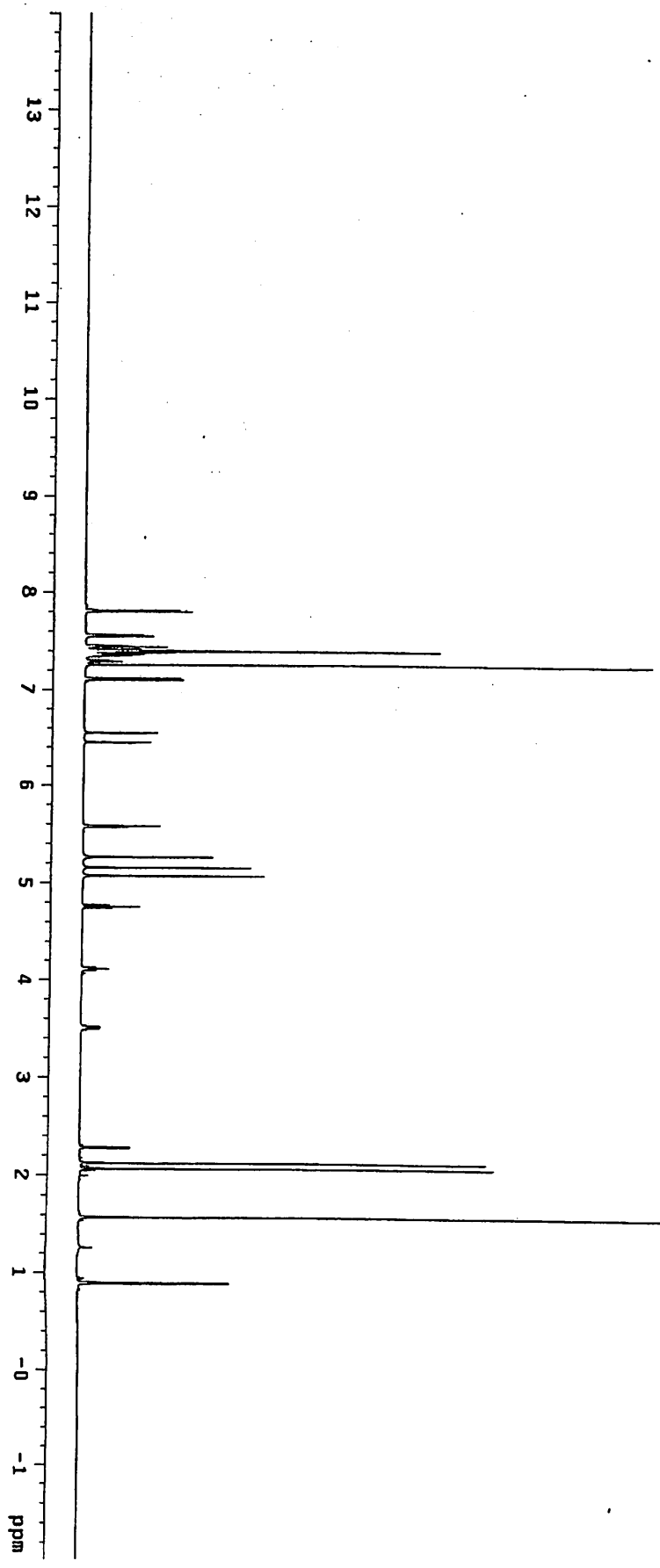


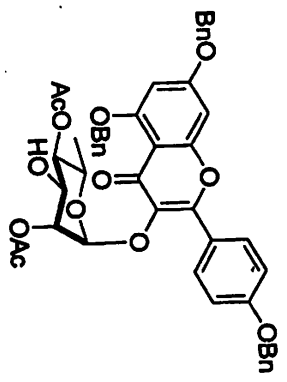




¹H NMR (CDCl₃, 600 MHz)

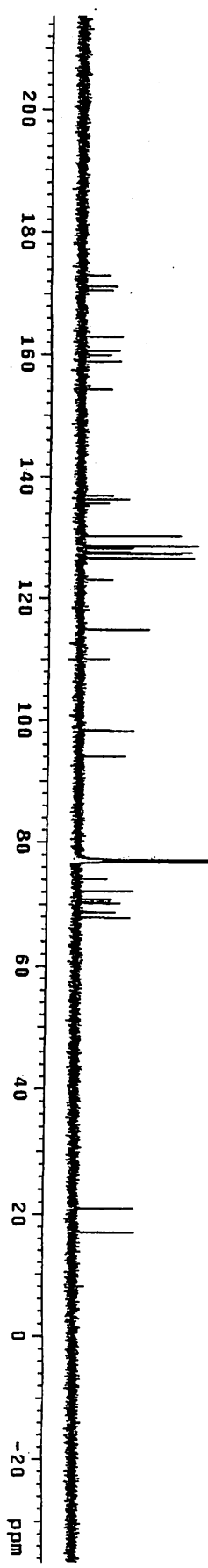
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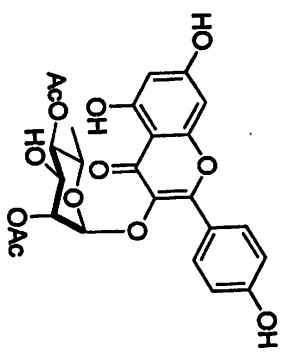




¹³C NMR (CDCl₃, 150 MHz)

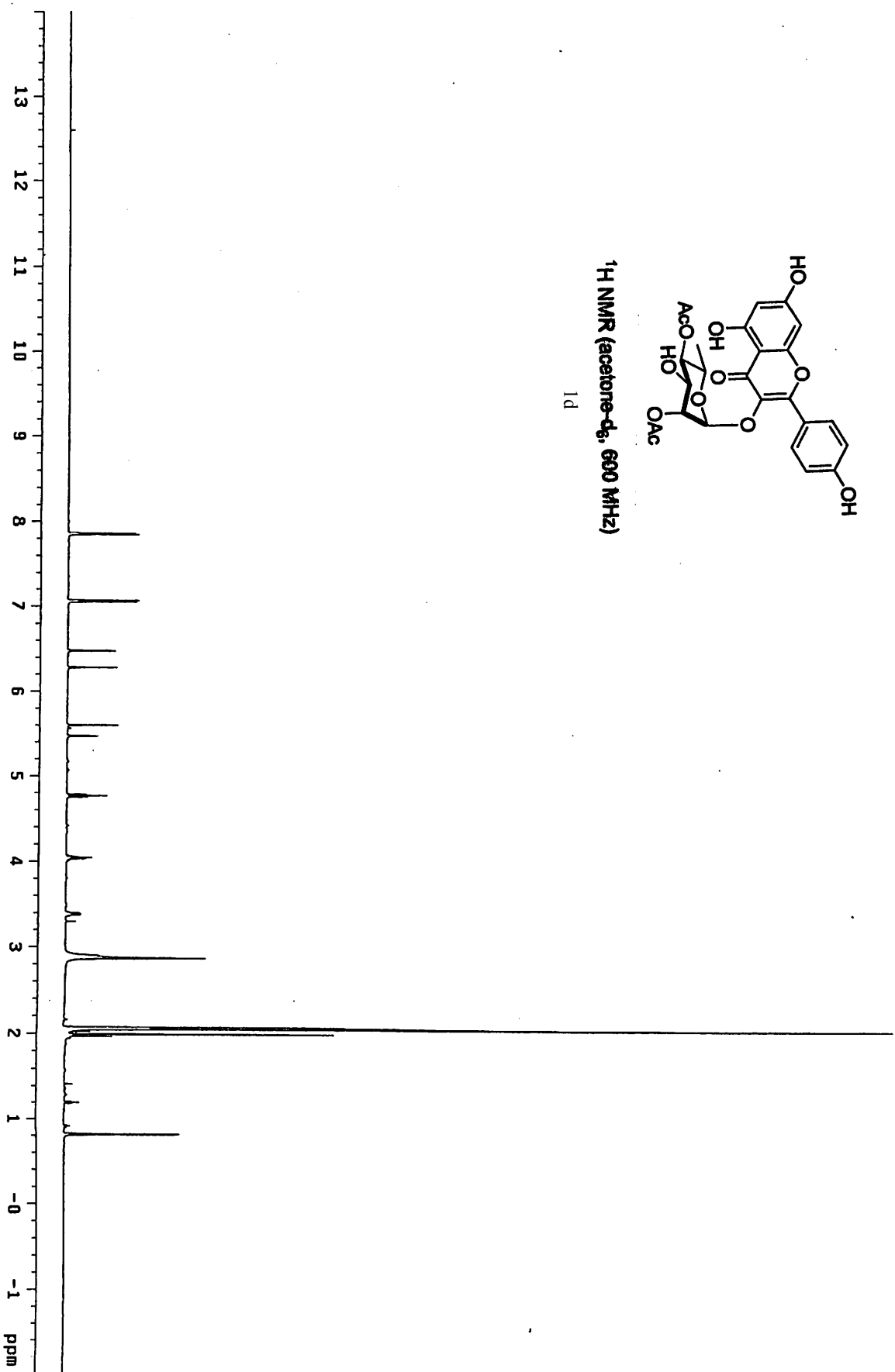
D

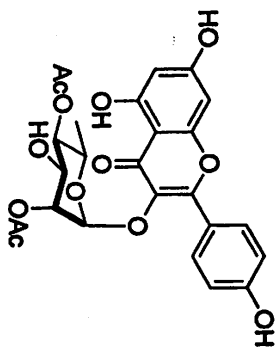




¹H NMR (acetone-d₆, 600 MHz)

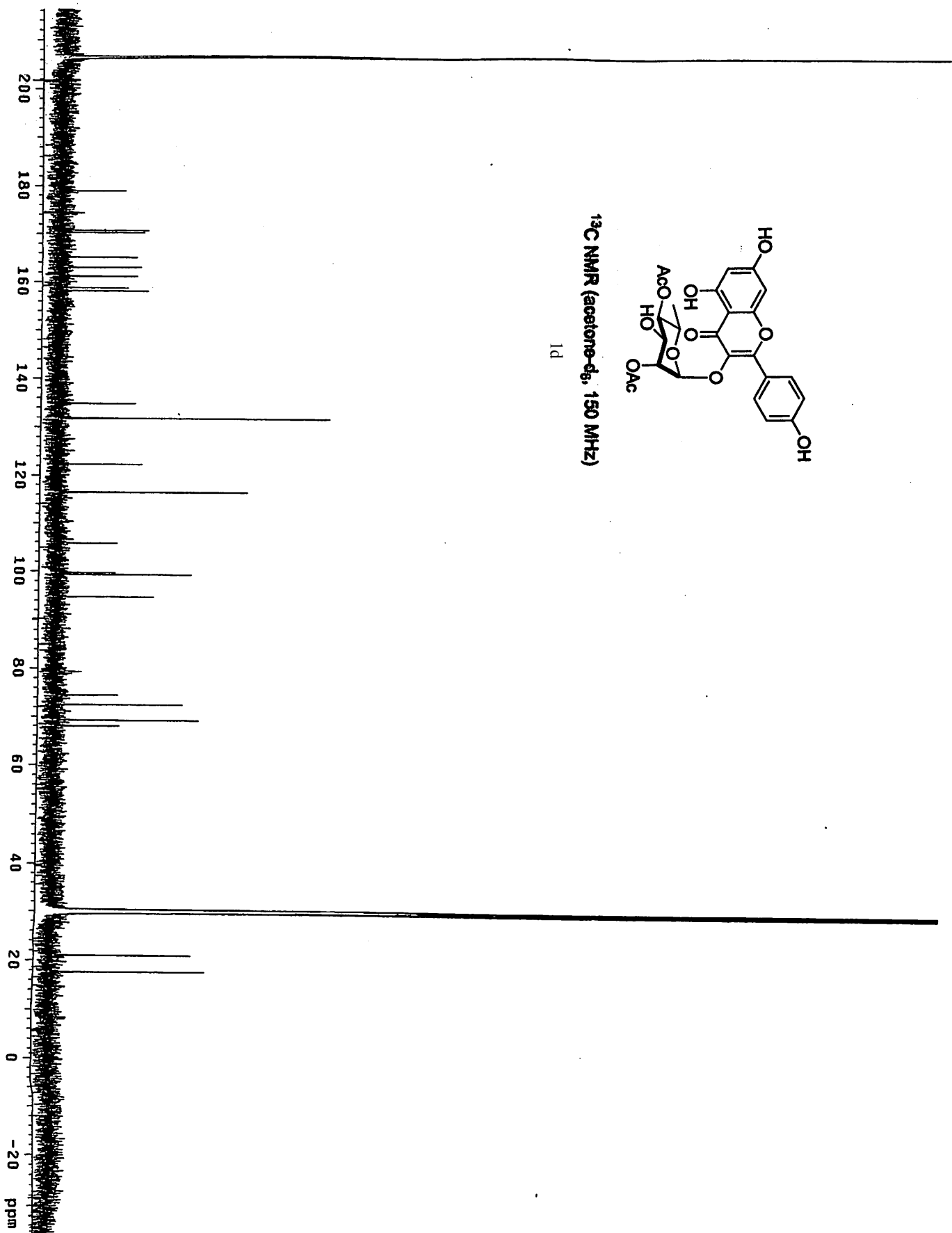
1d

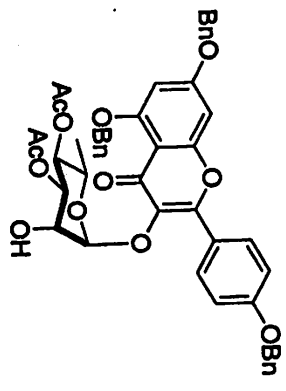




¹³C NMR (acetone-d₆, 150 MHz)

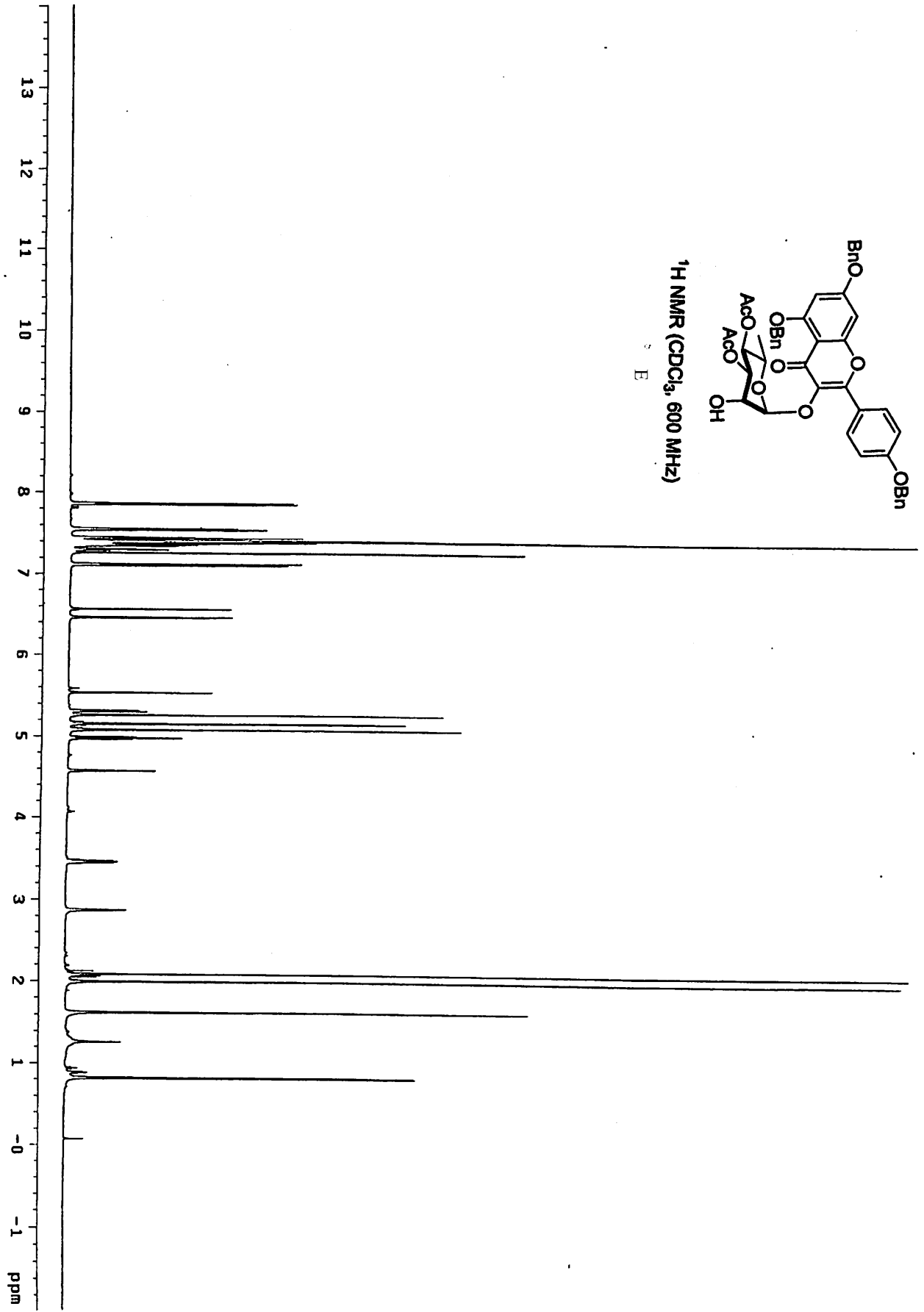
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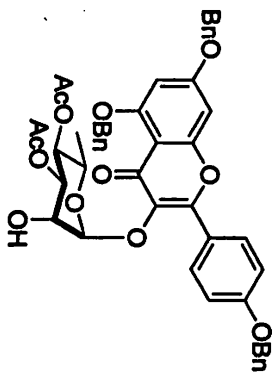




¹H NMR (CDCl₃, 600 MHz)

5 E

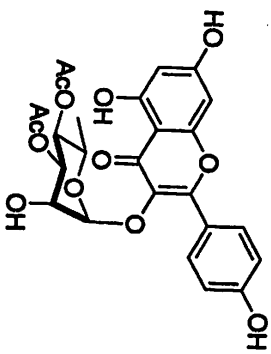




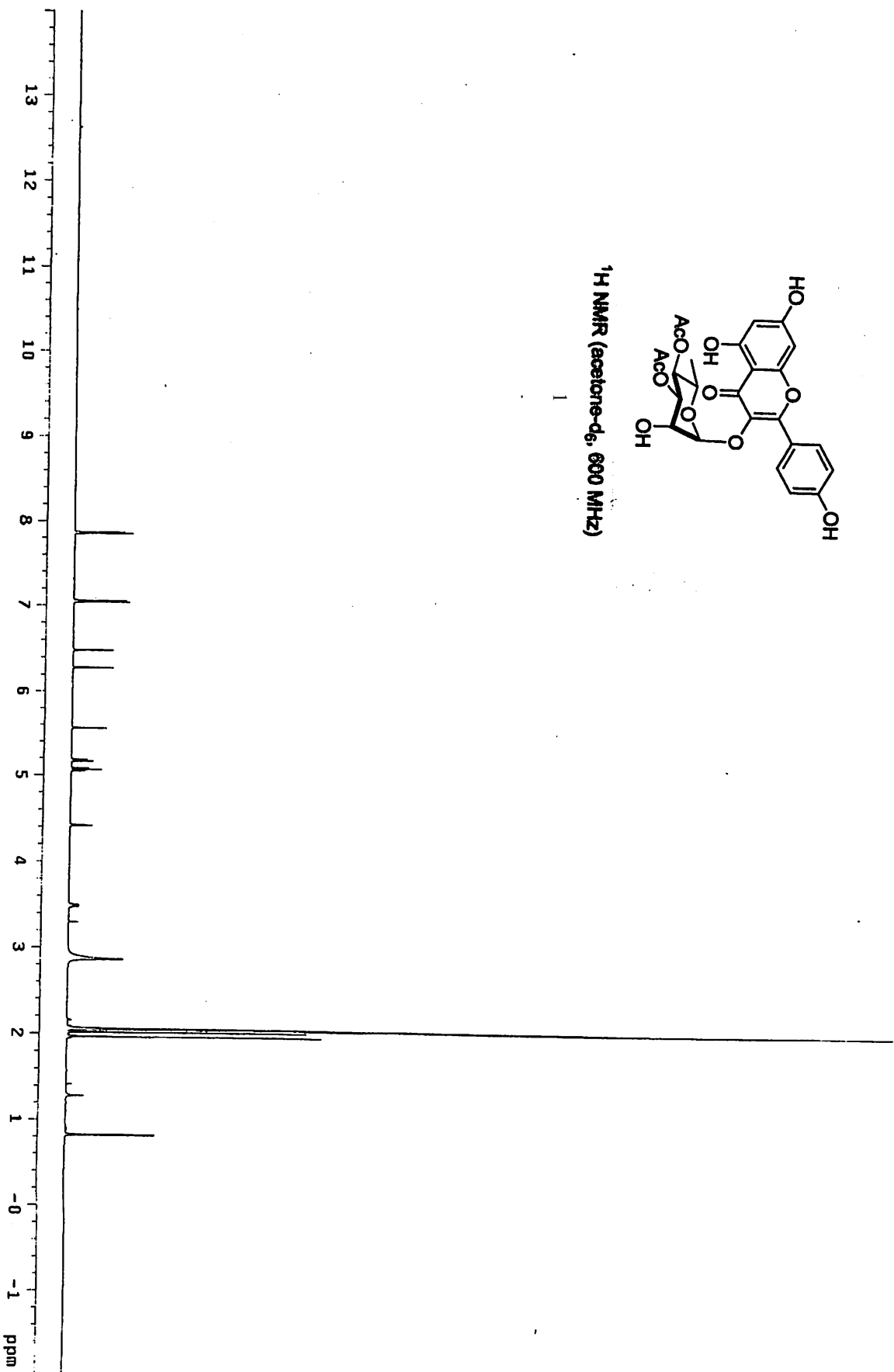
^{13}C NMR (CDCl₃, 150 MHz)

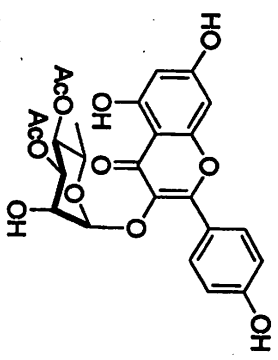
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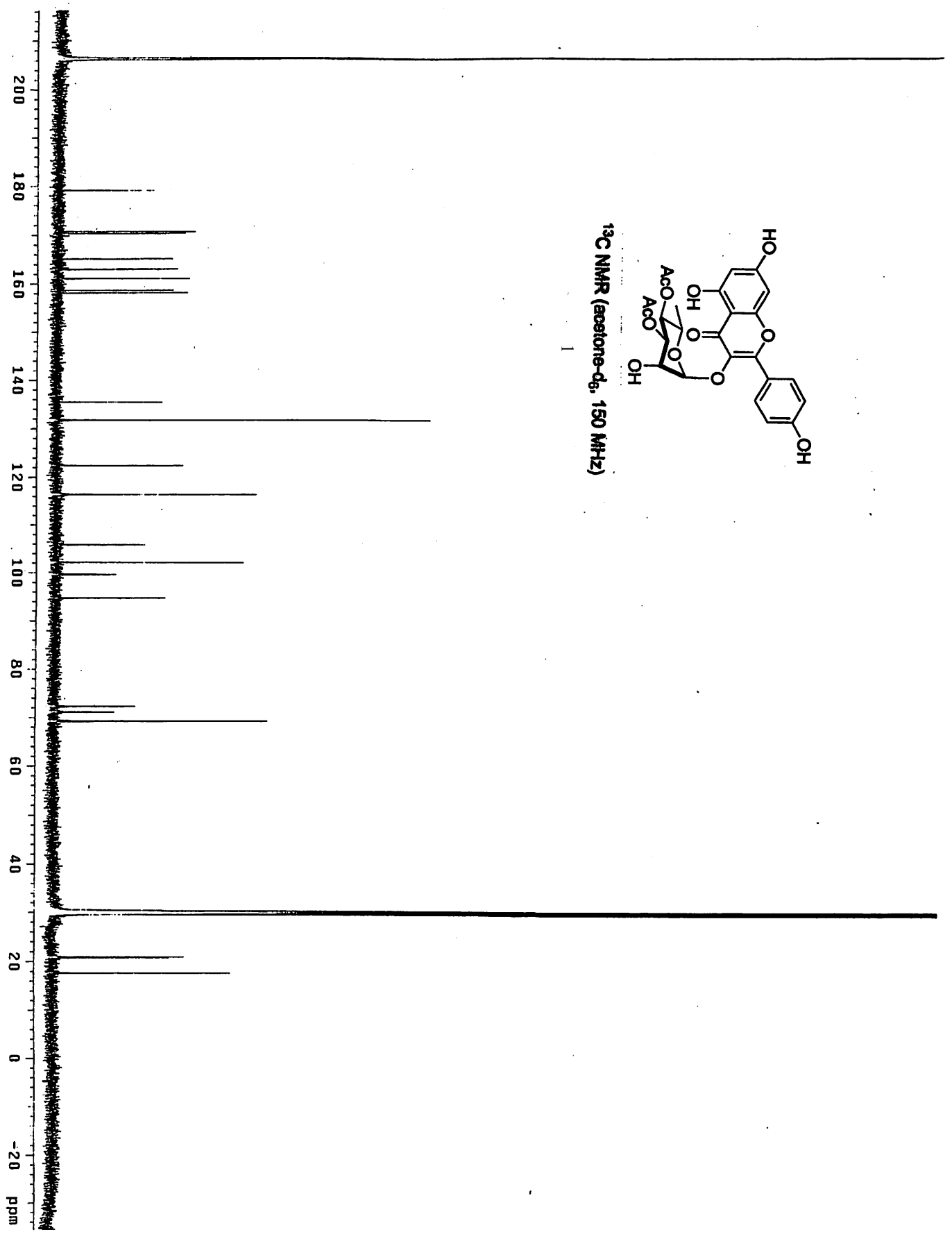


¹H NMR (acetone-d₆, 600 MHz)

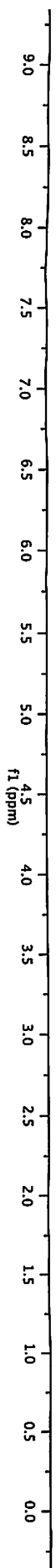
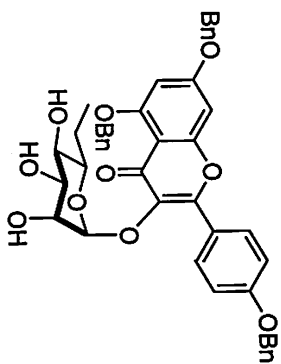


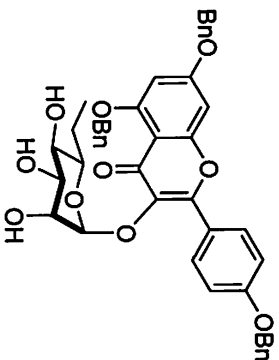


¹³C NMR (acetone-d₆, 150 MHz)

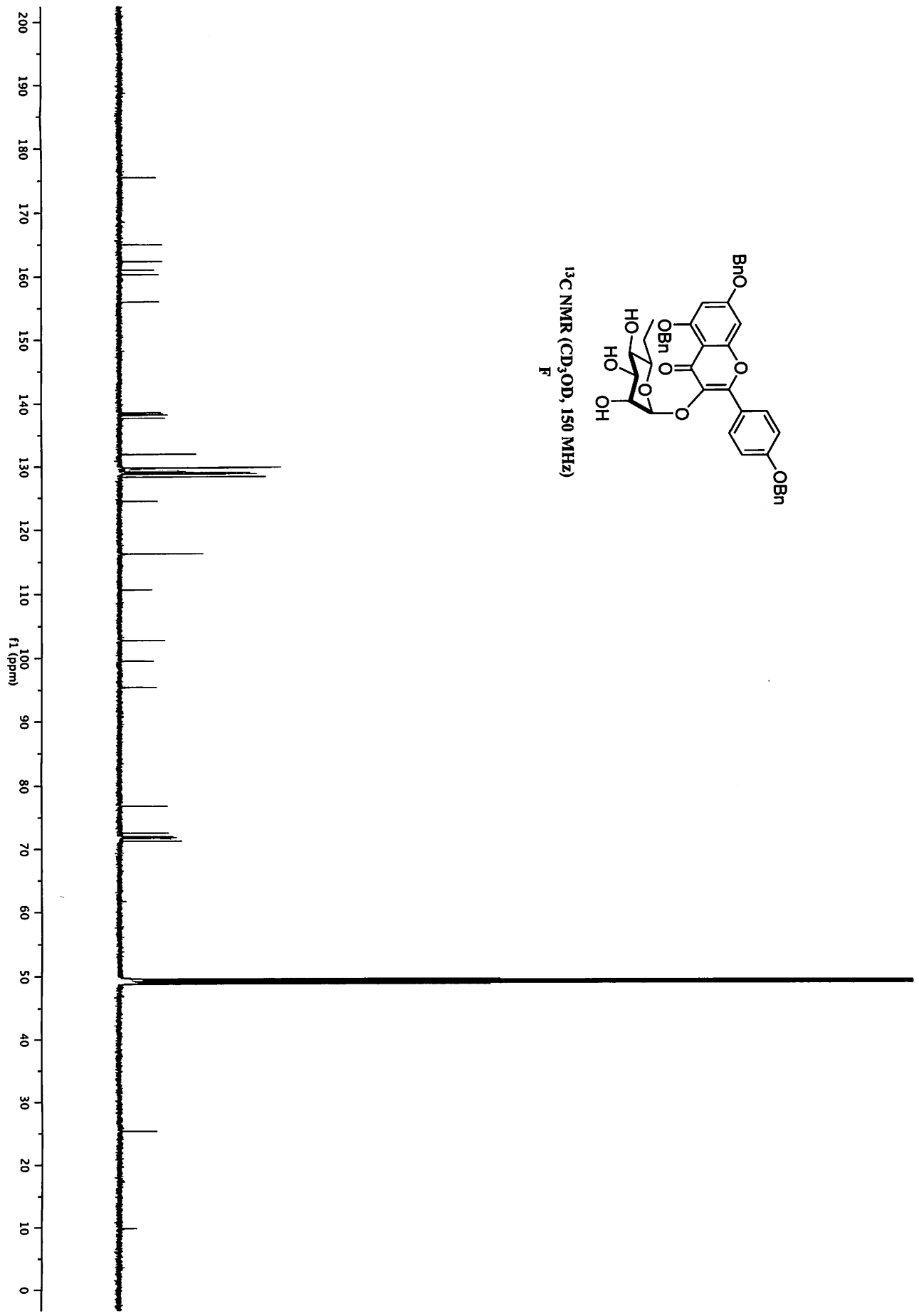


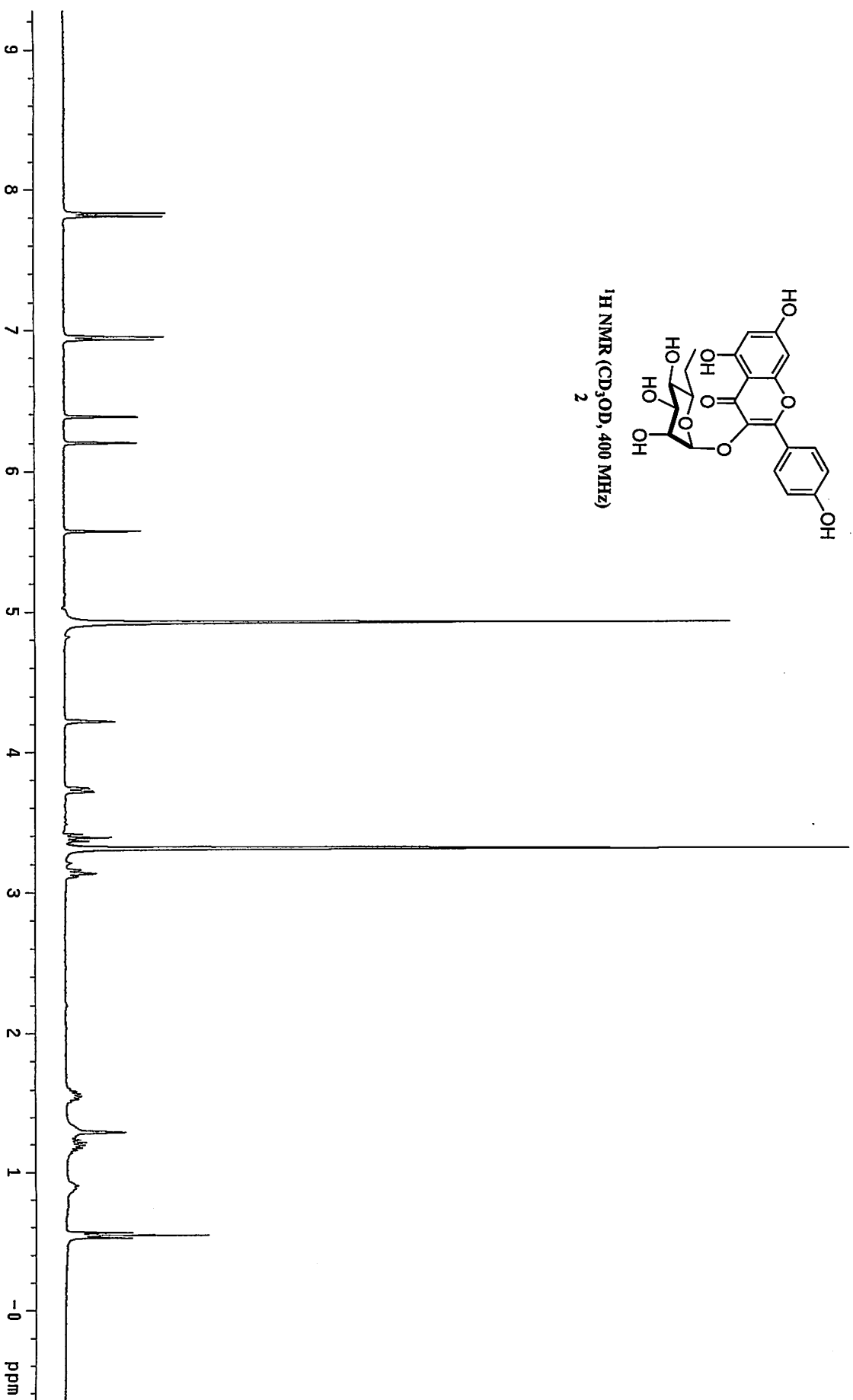
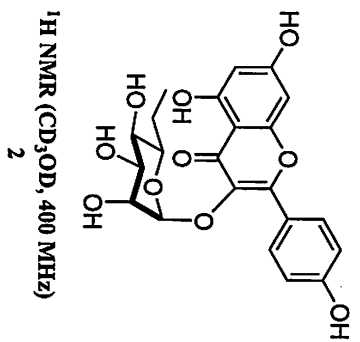
¹H NMR (CD₃OD, 600 MHz)

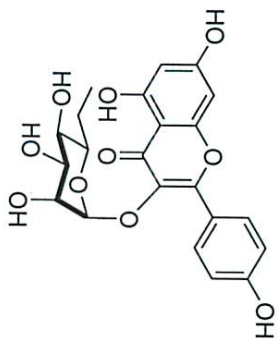




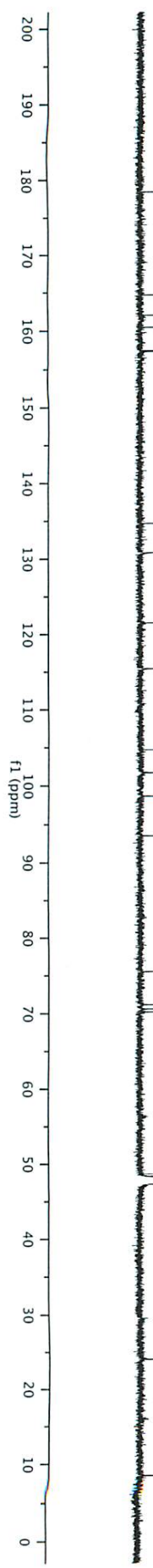
¹³C NMR (CD₃OD, 150 MHz)
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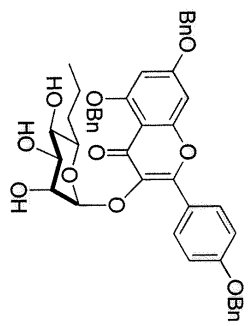






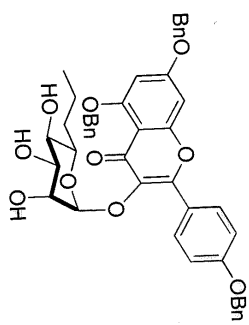
¹³C NMR (CD₃OD, 150 MHz)
2



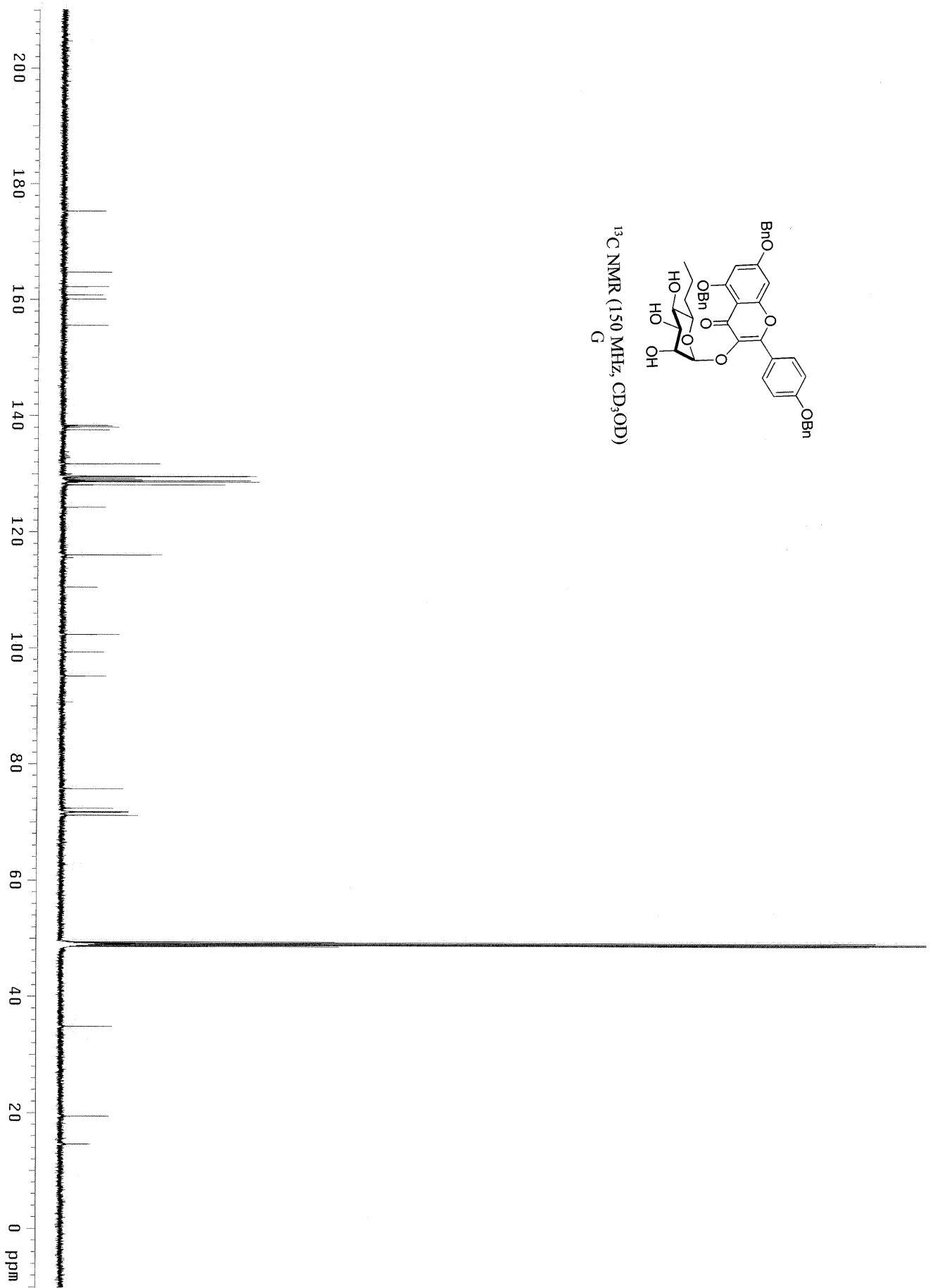


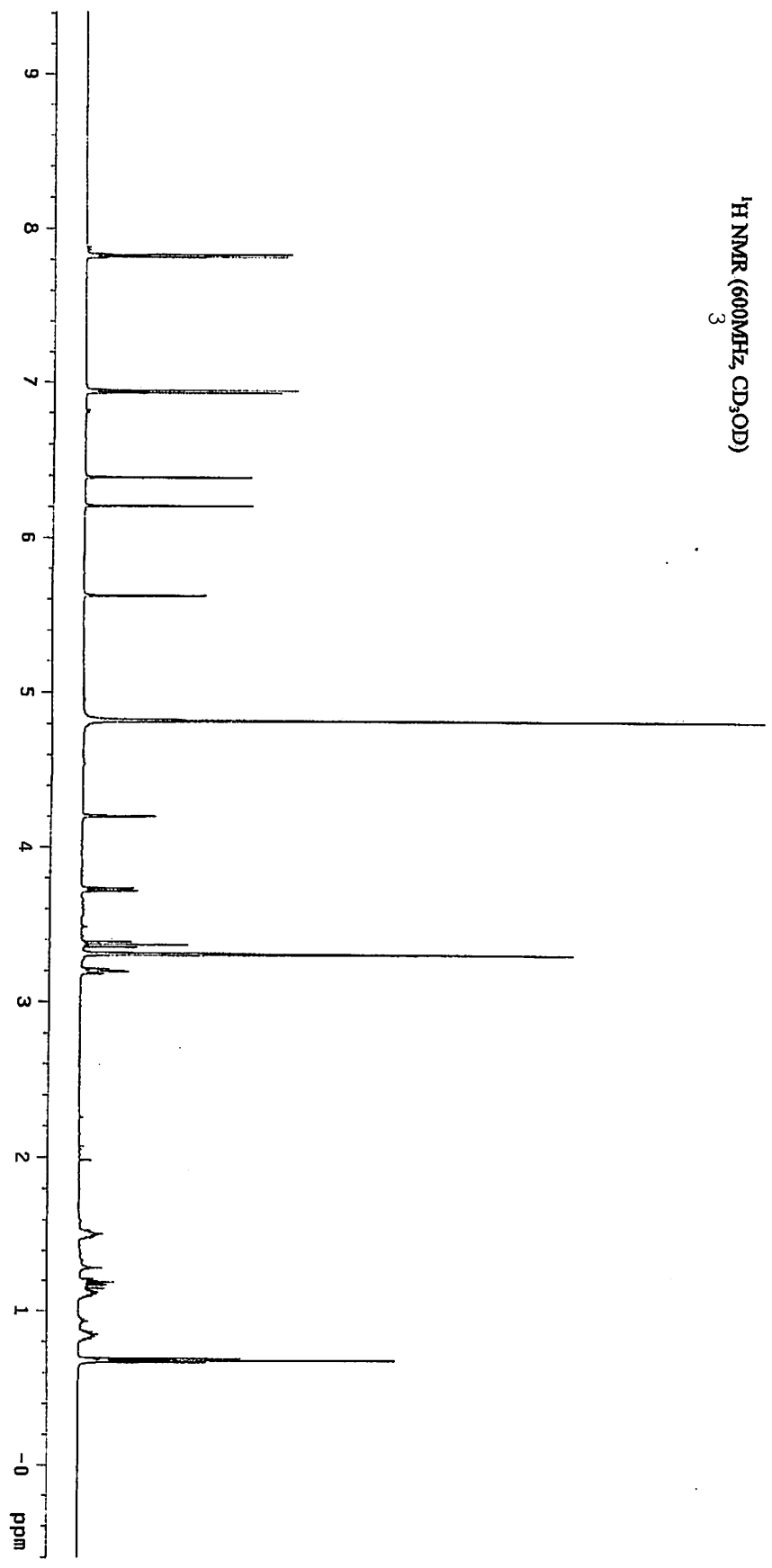
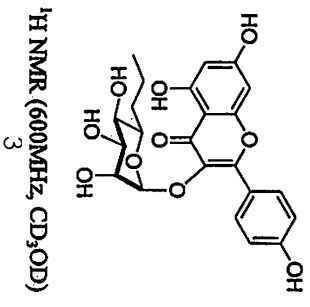
¹H NMR (600MHz, CD₃OD)
G

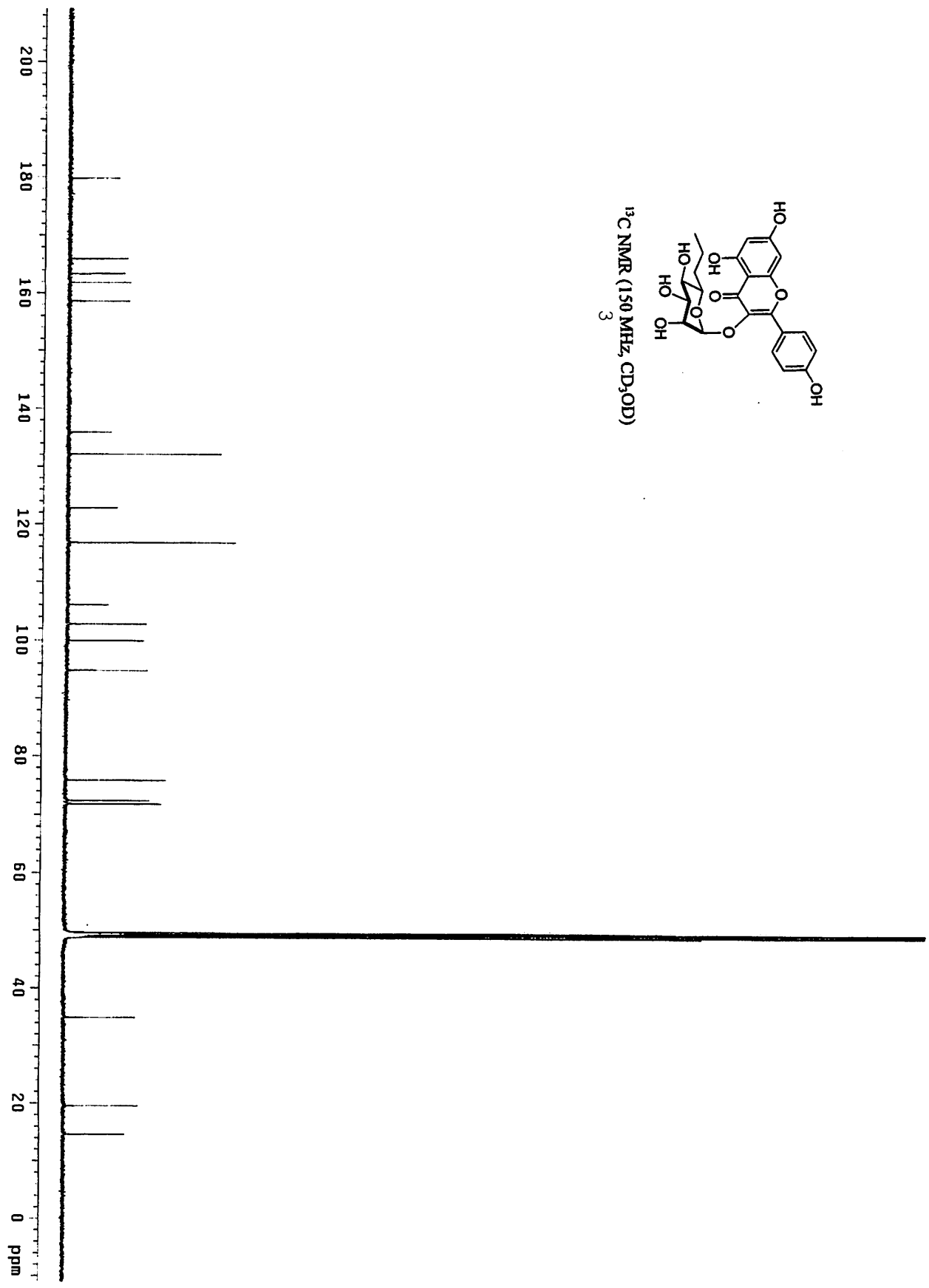
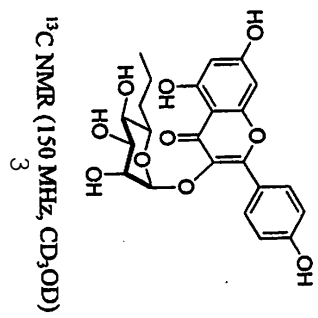


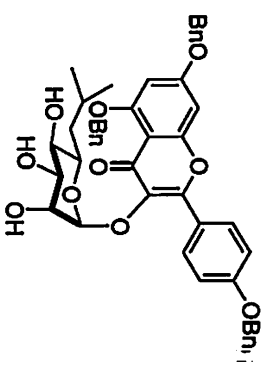


^{13}C NMR (150 MHz, CD_3OD)
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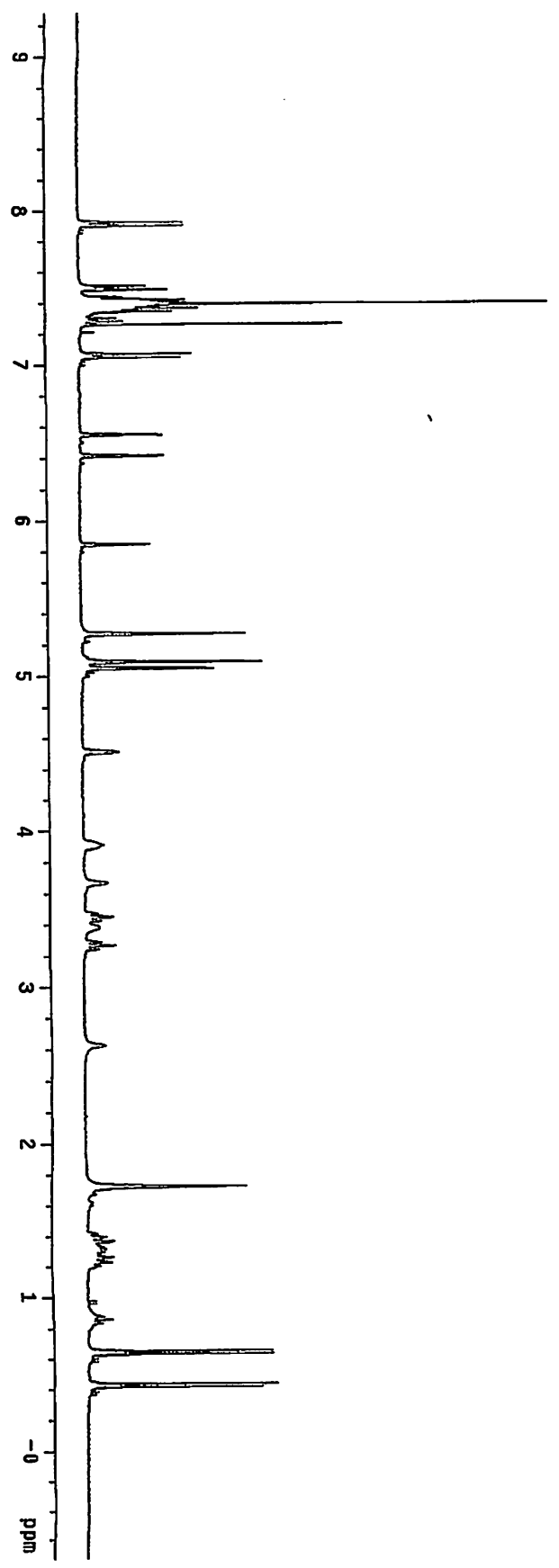


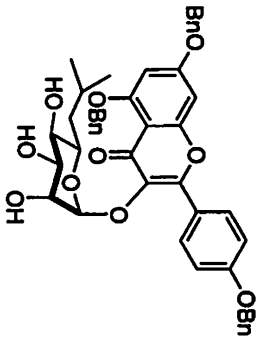




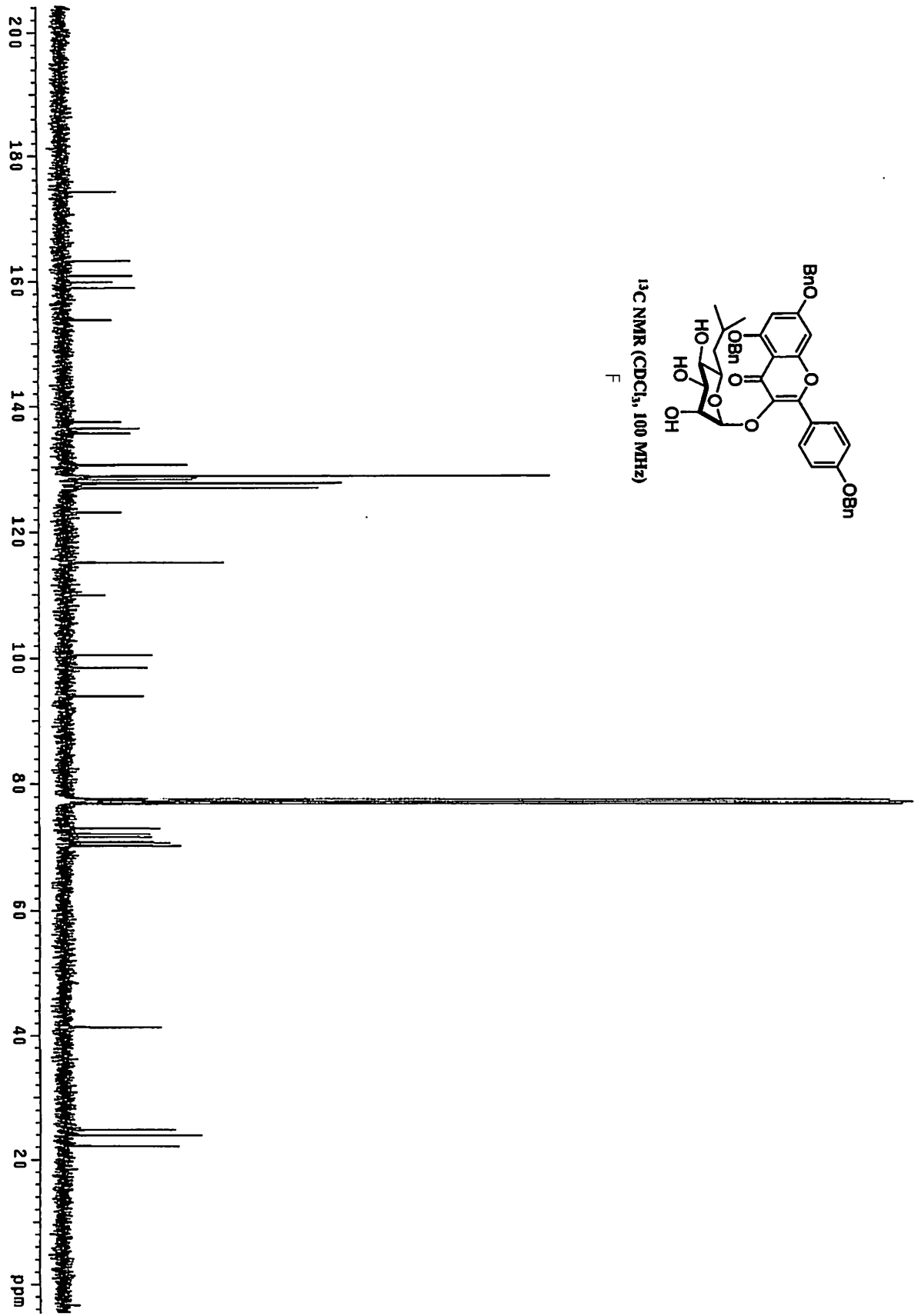


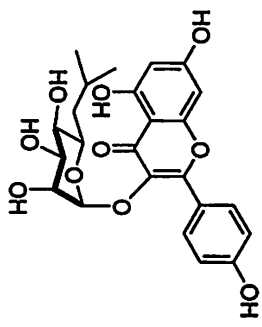
¹H NMR (CDCl₃, 400 MHz)
F





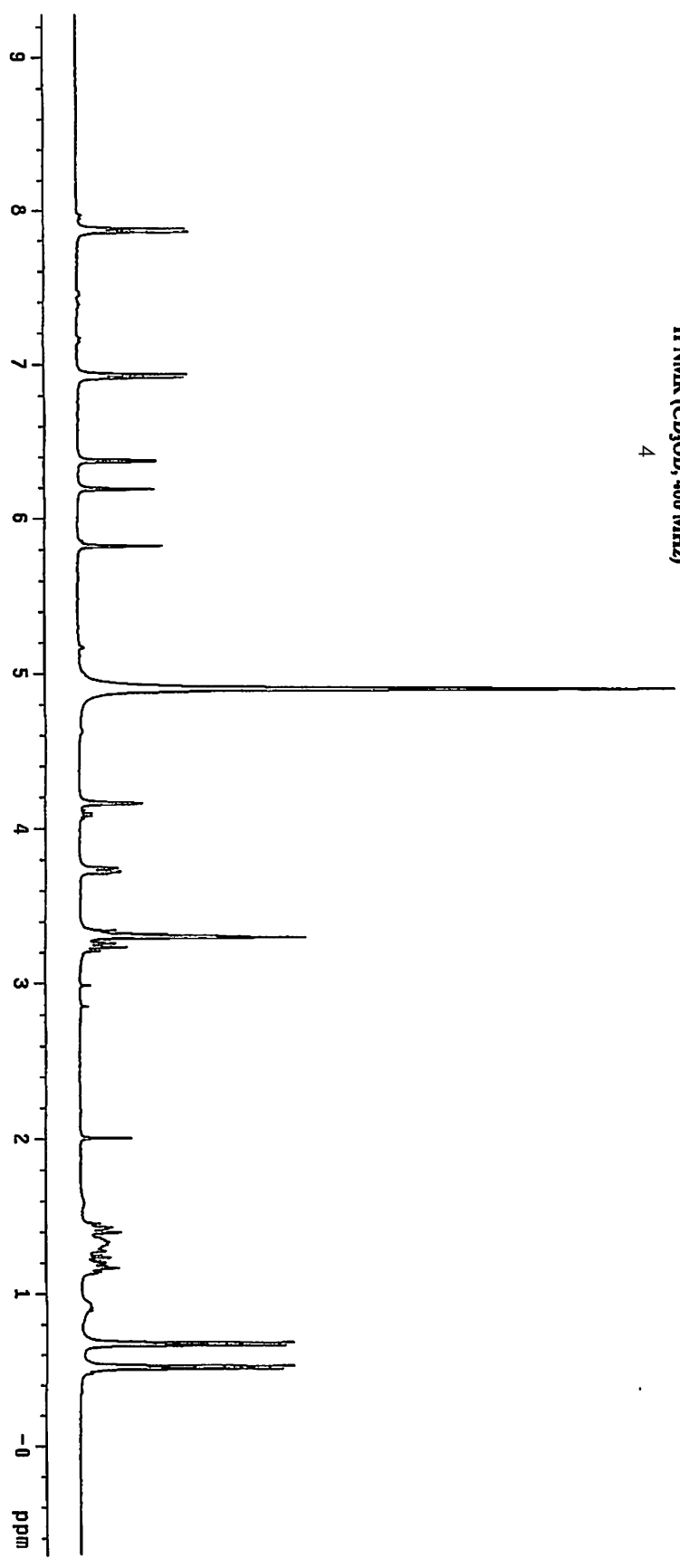
¹³C NMR (CDCl₃, 100 MHz)
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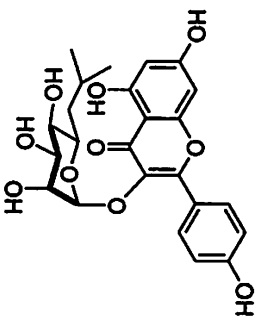




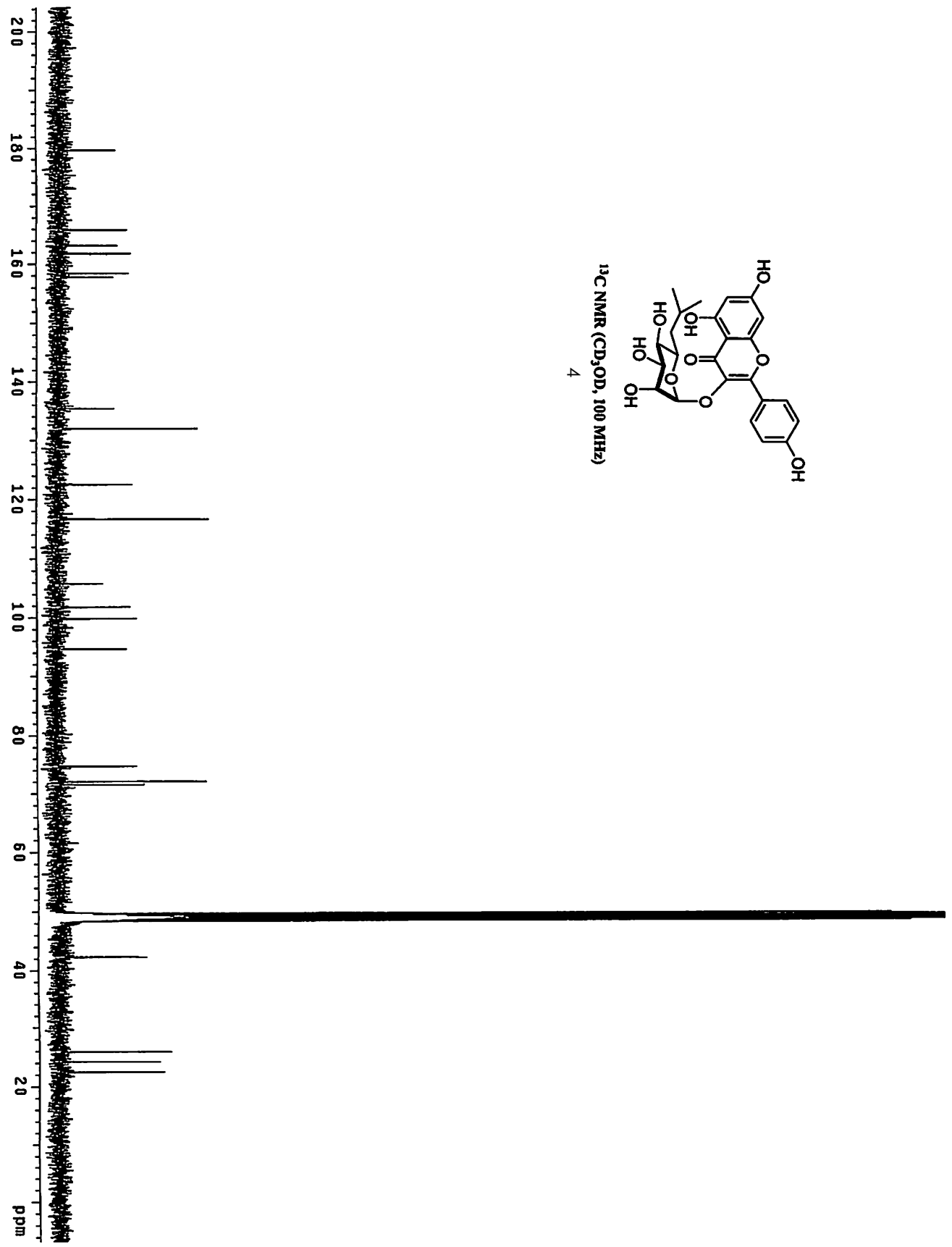
¹H NMR (CD₃OD, 400 MHz)

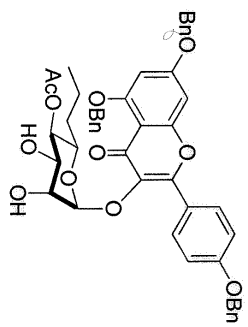
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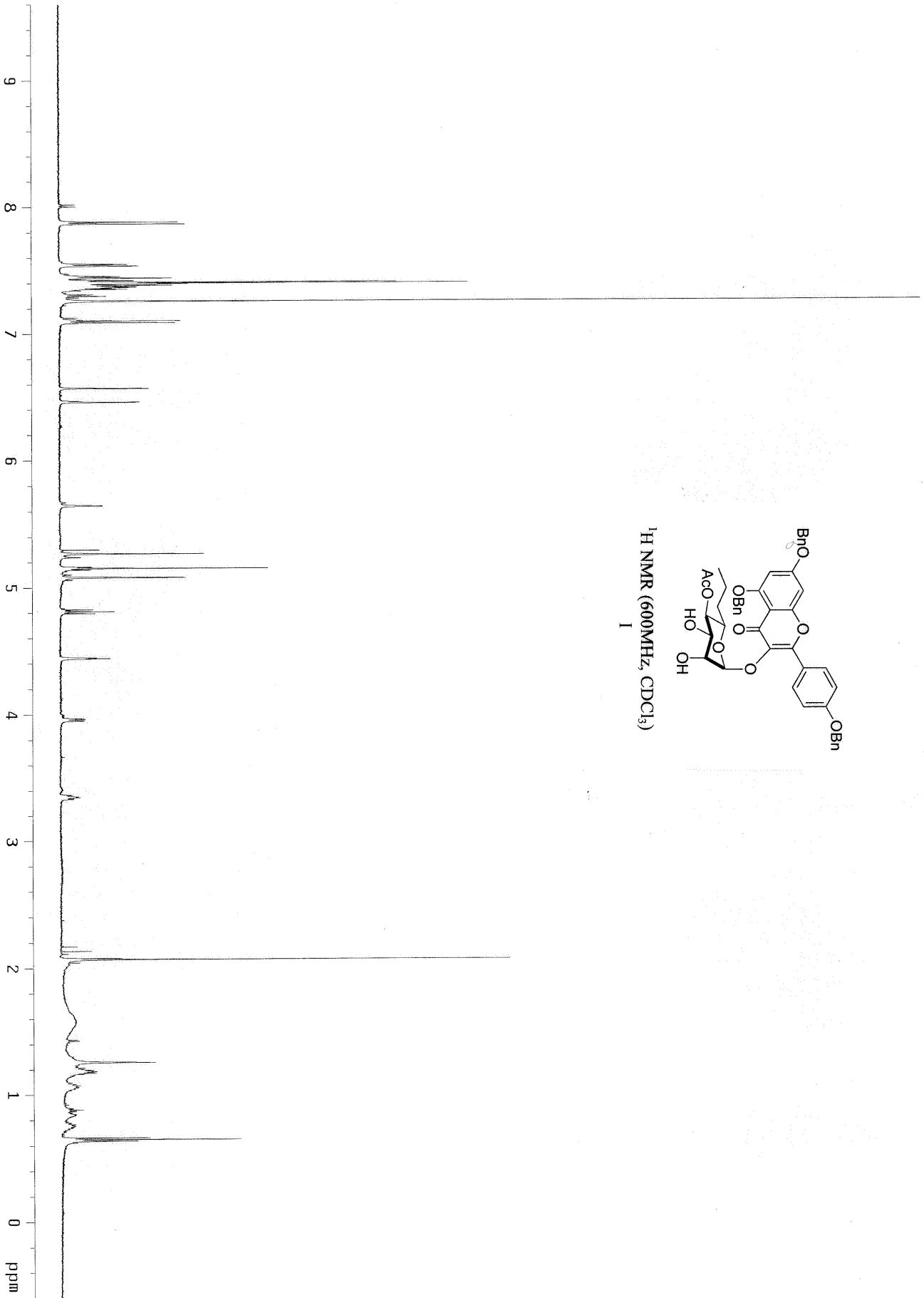


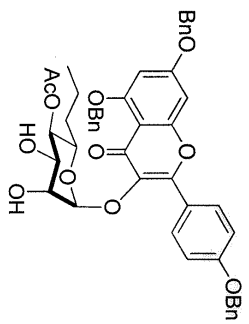
¹³C NMR (CD₃OD, 100 MHz)
4



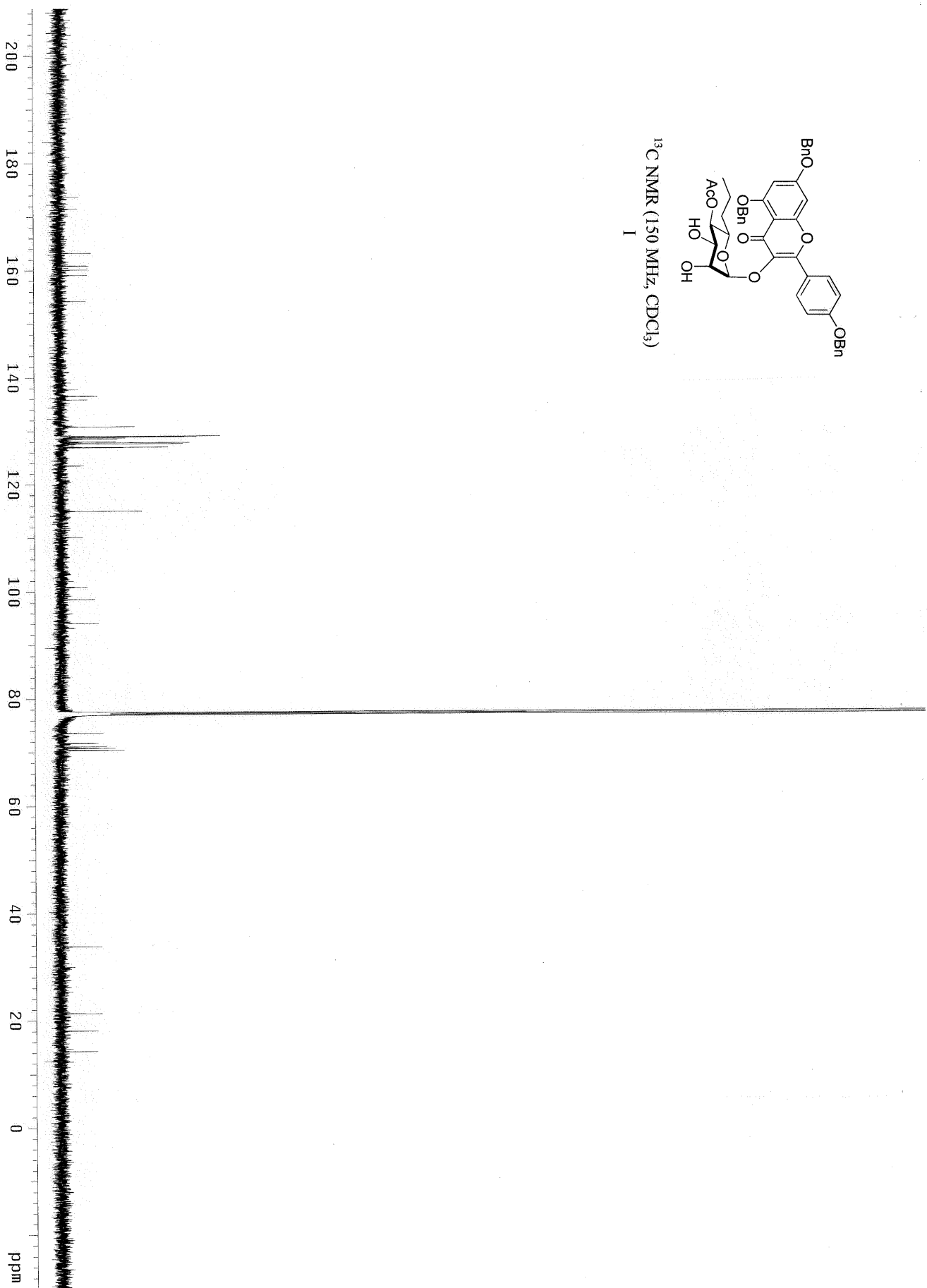


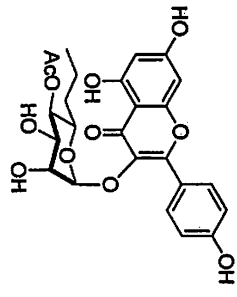
¹H NMR (600MHz, CDCl₃)
1



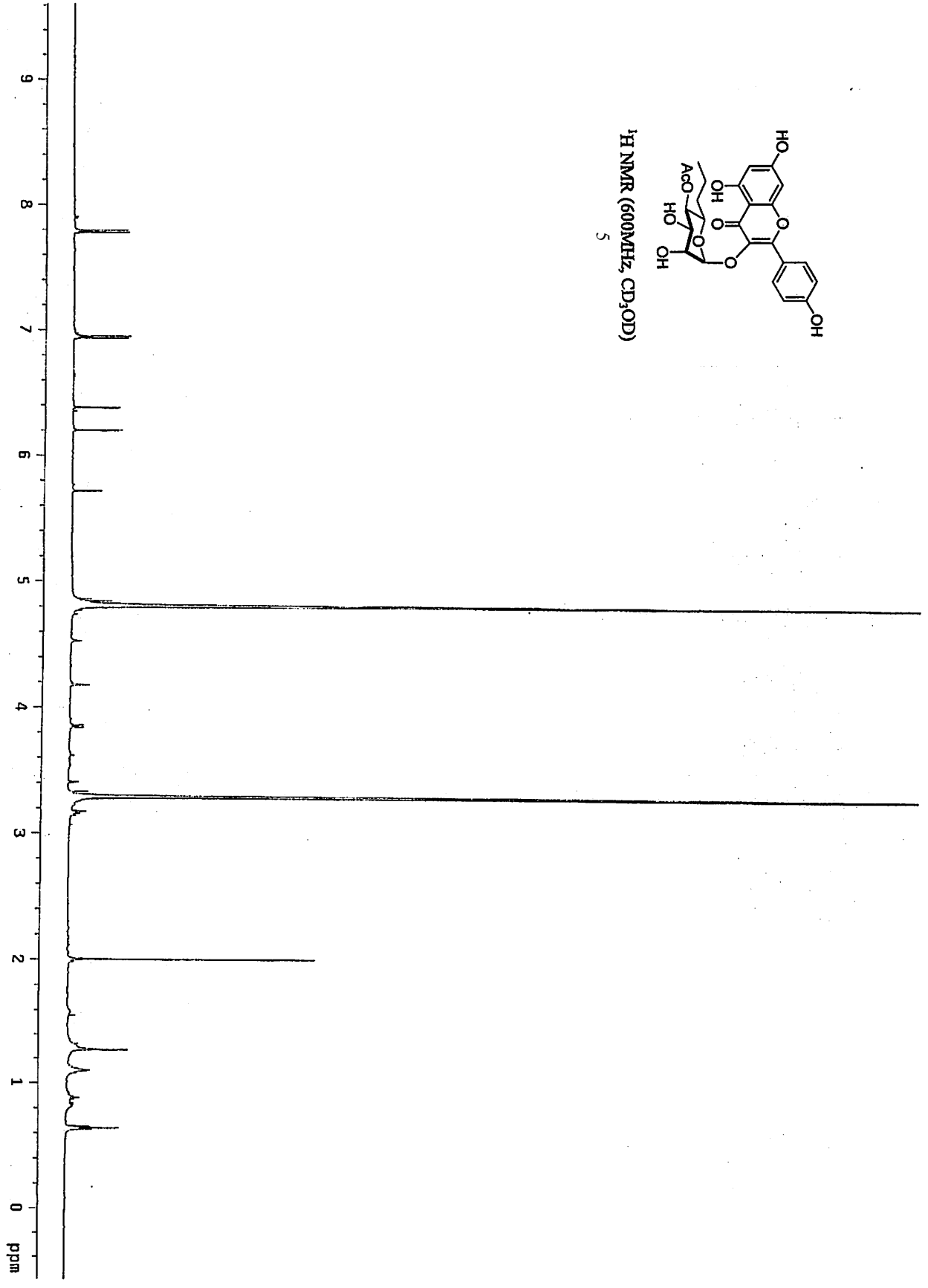


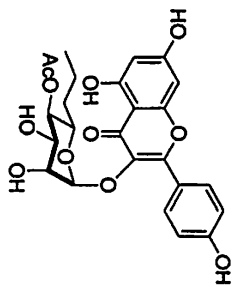
^{13}C NMR (150 MHz, CDCl_3)
I



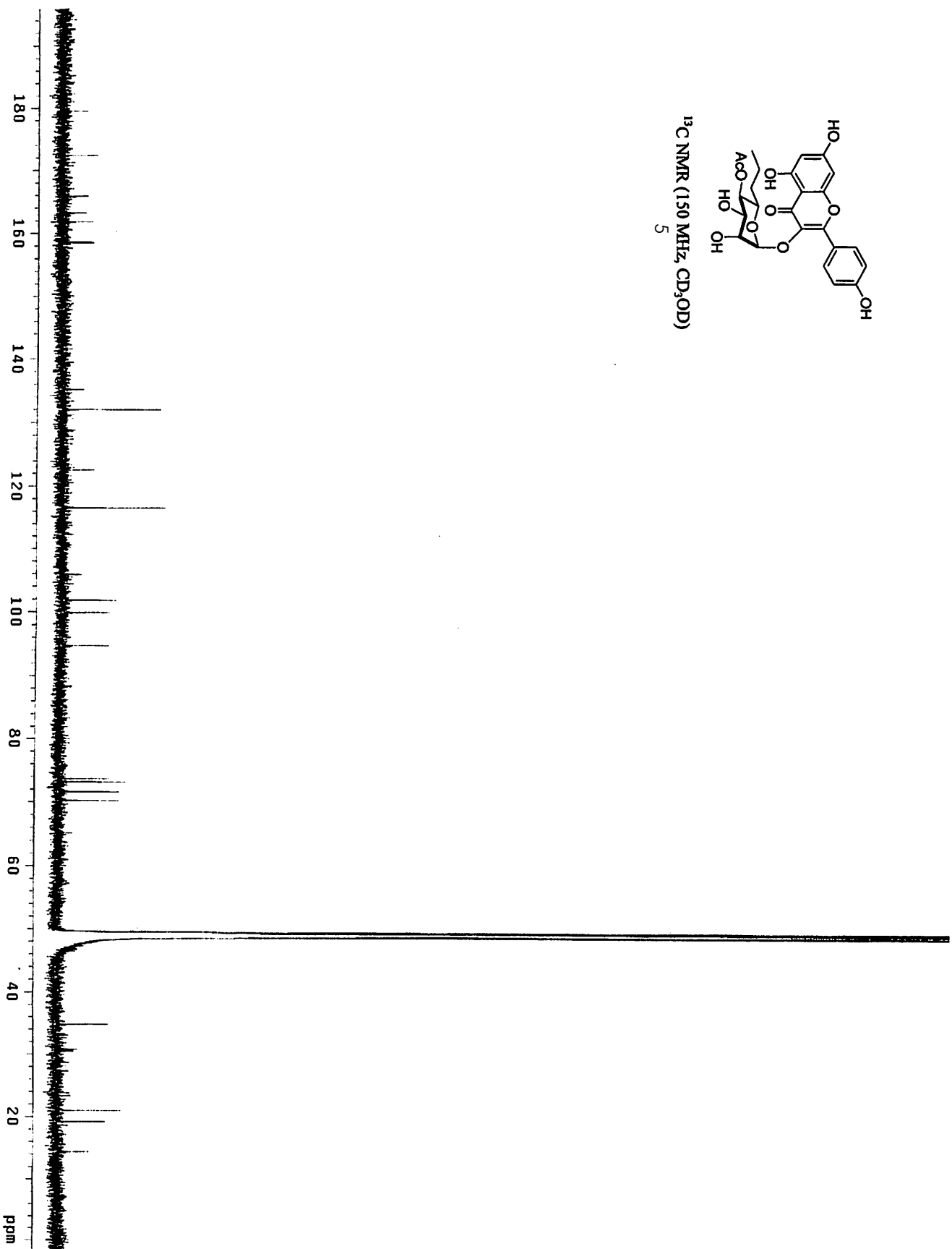


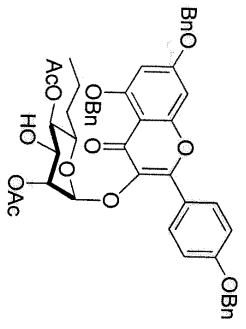
¹H NMR (600MHz, CD₃OD)
5



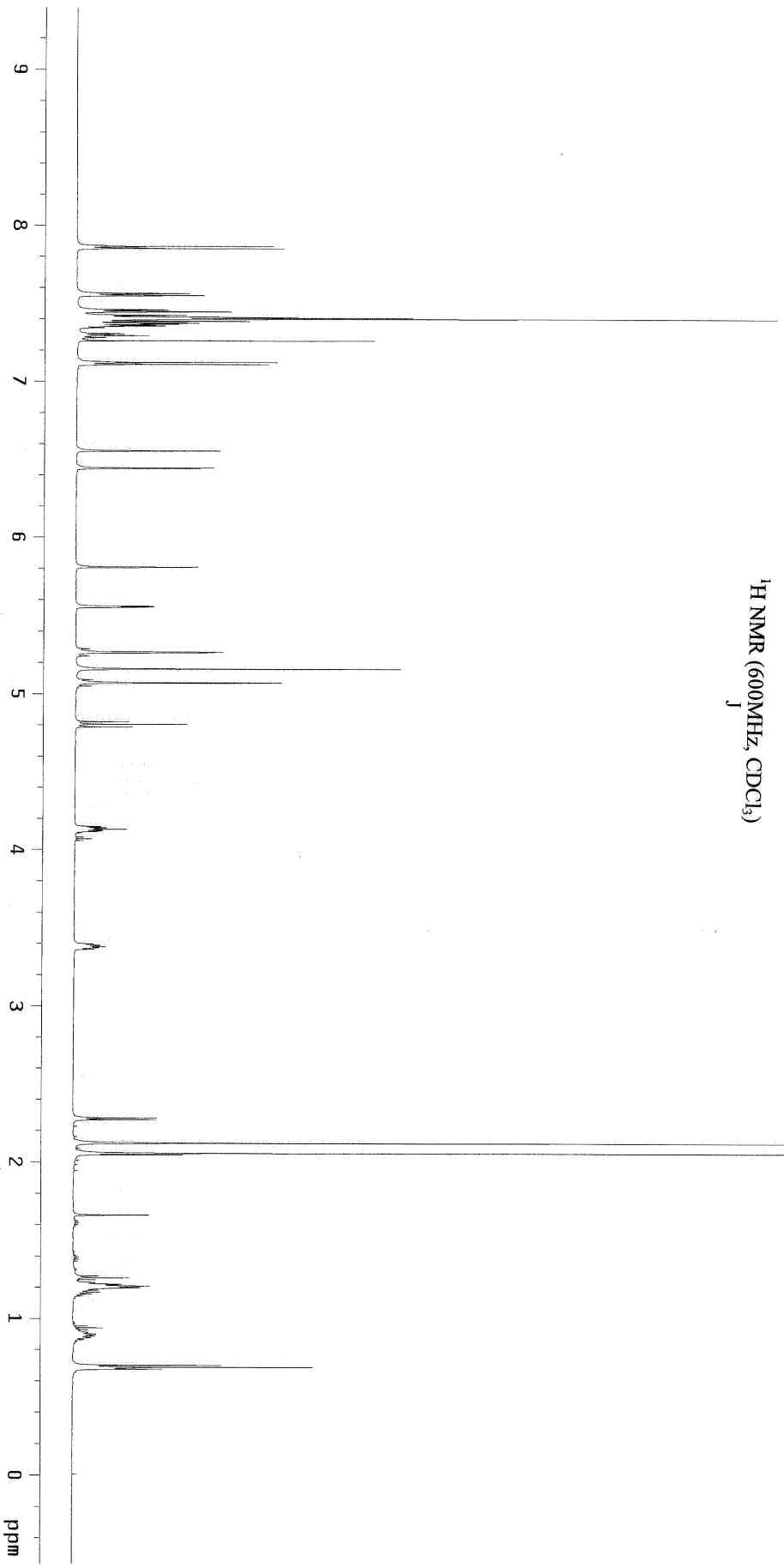


¹³C NMR (150 MHz, CD₃OD)
5

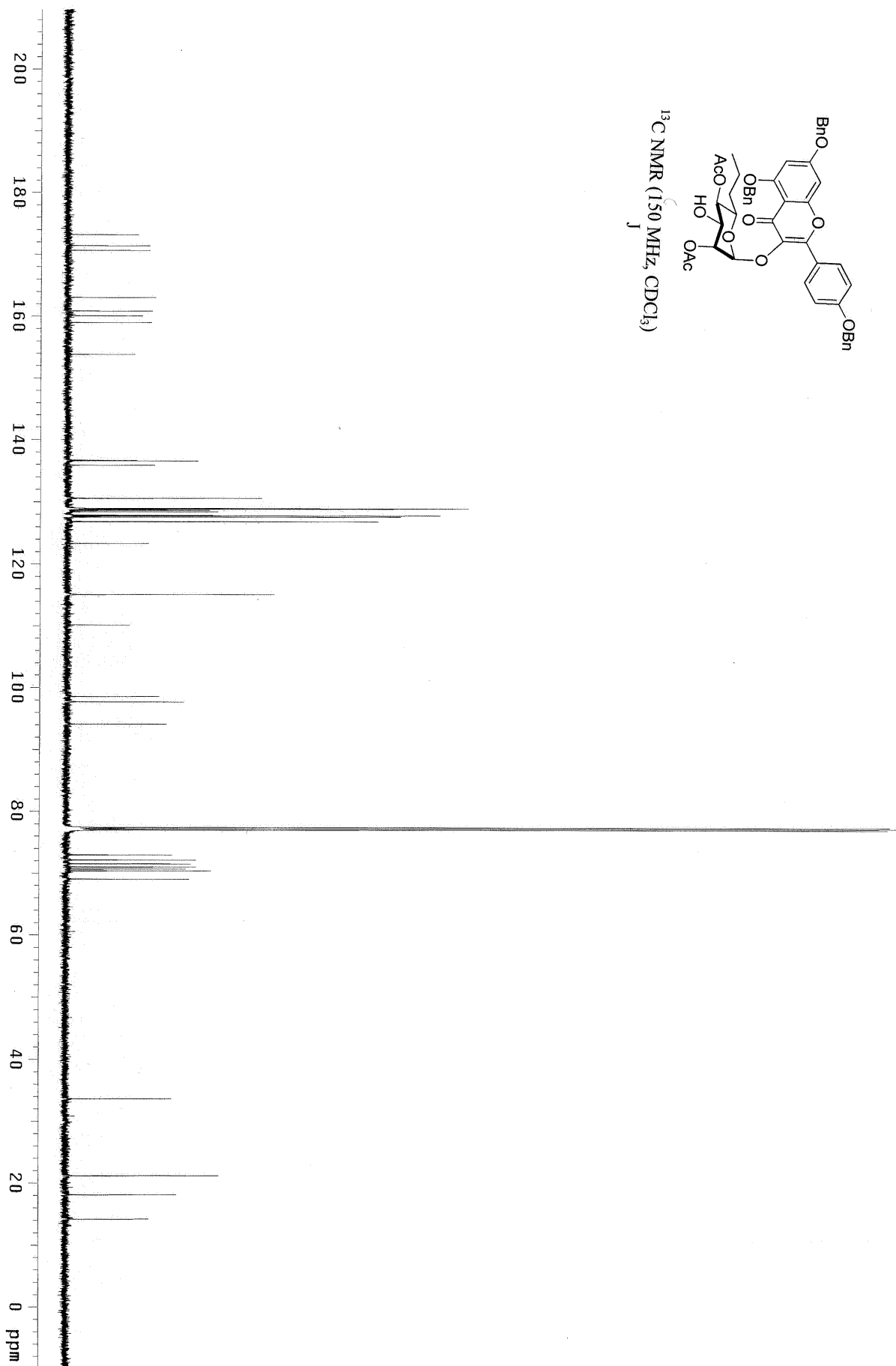
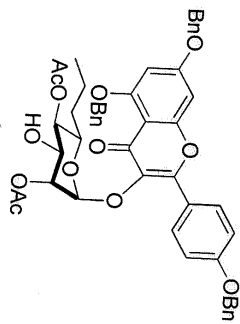


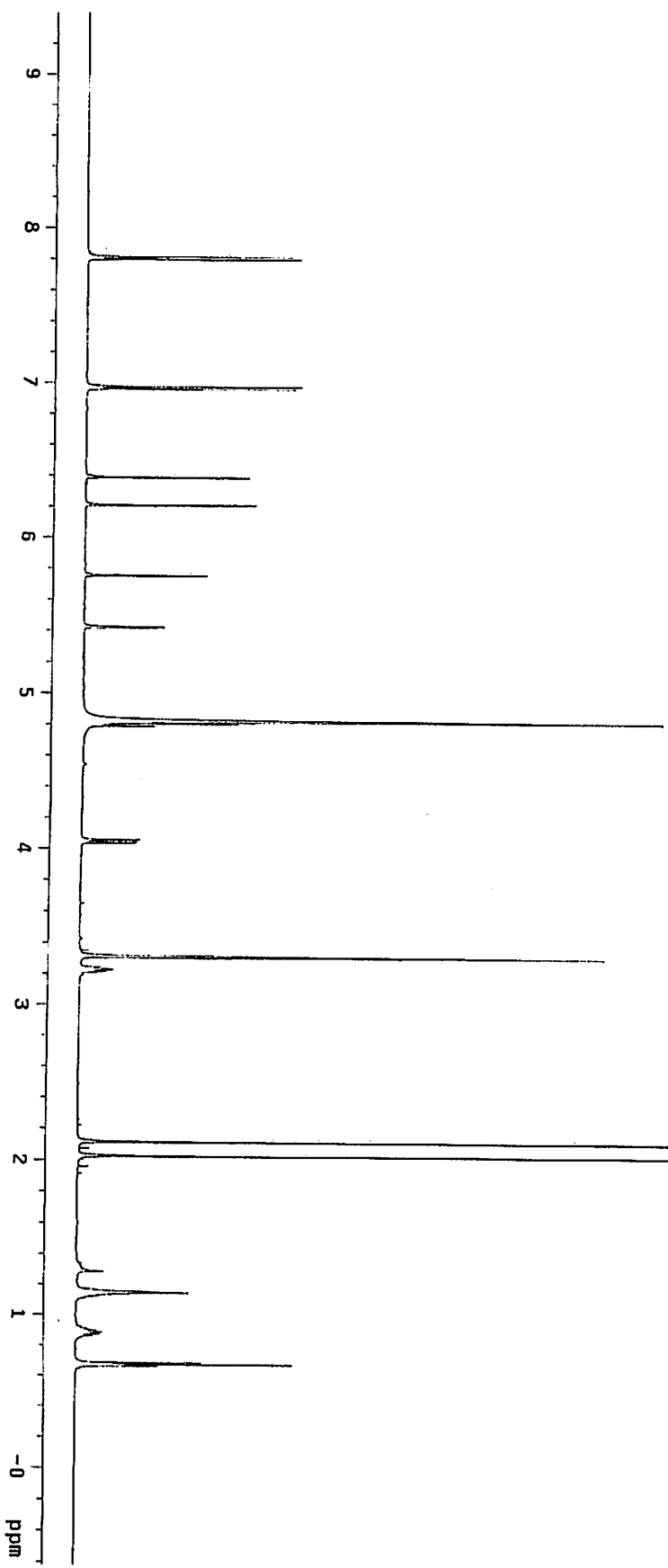
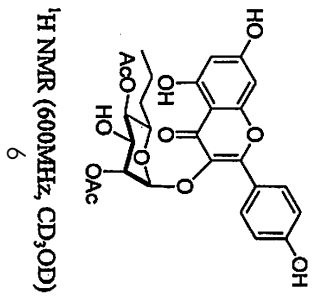


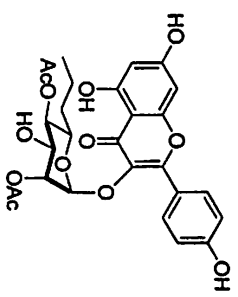
¹H NMR (600MHz, CDCl₃)



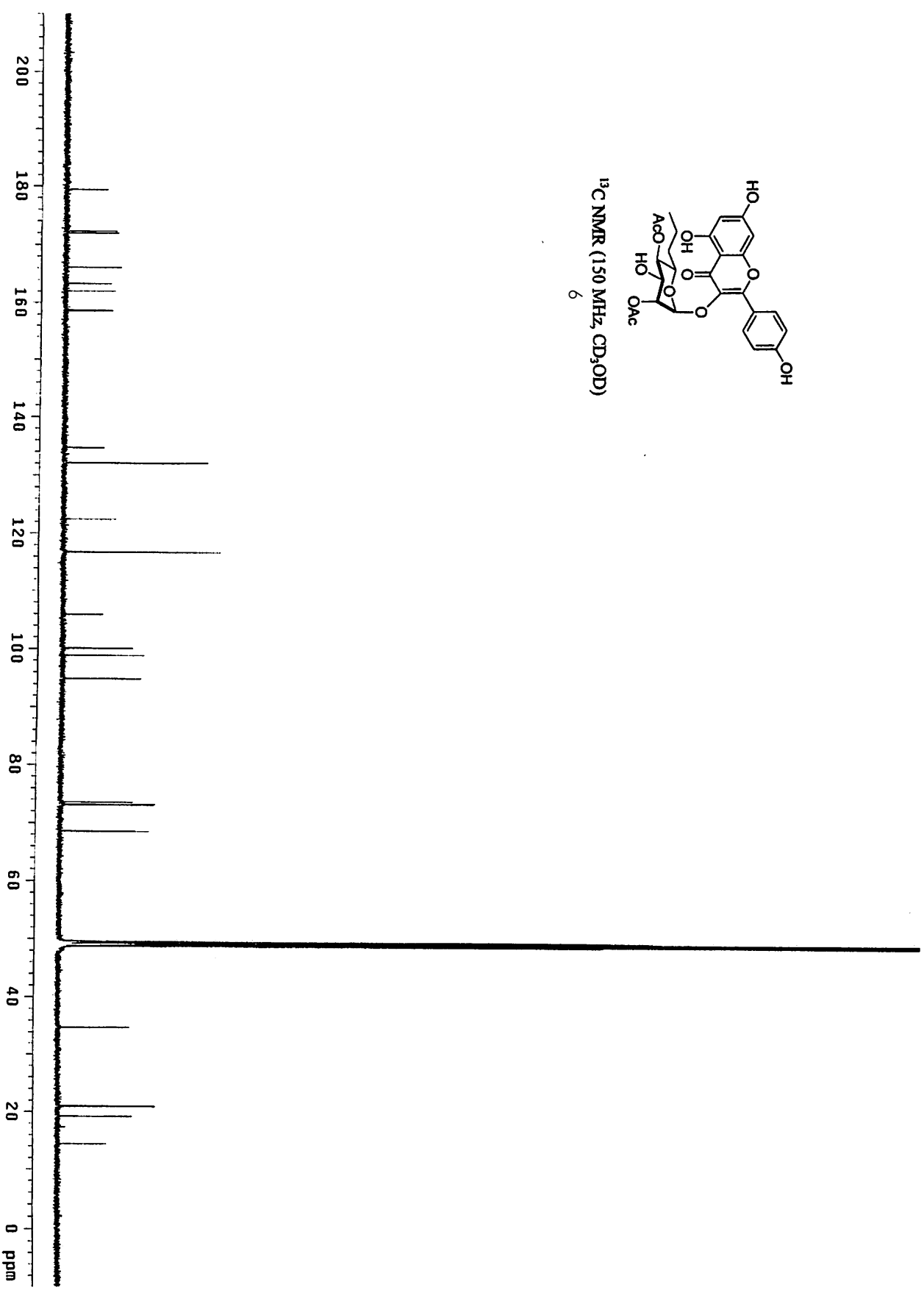
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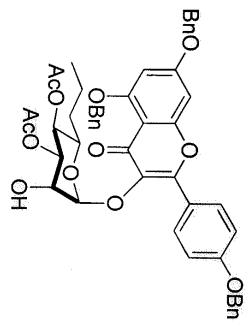




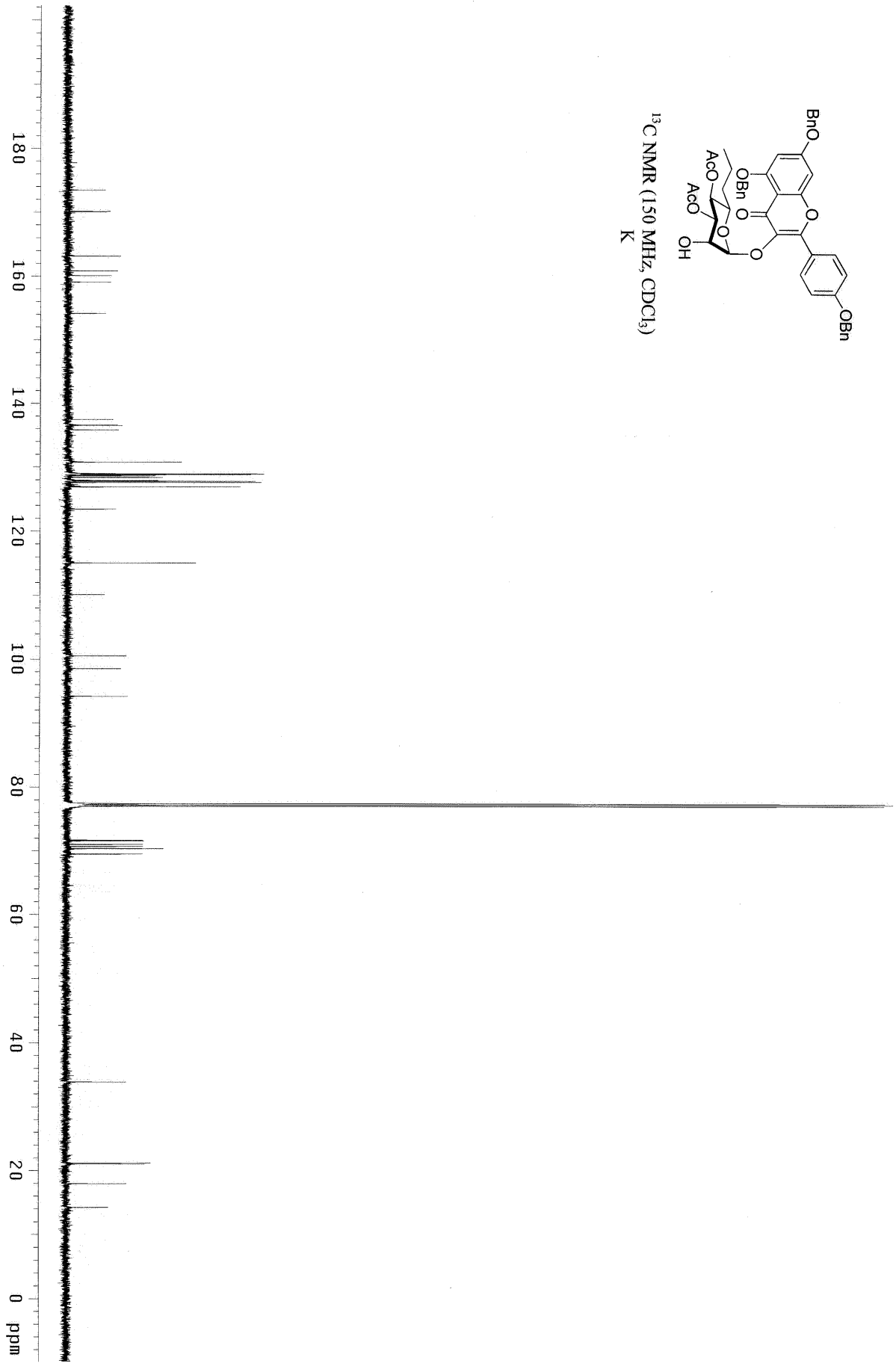


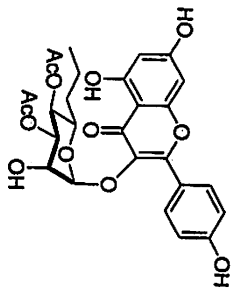
¹³C NMR (150 MHz, CD₃OD)
6



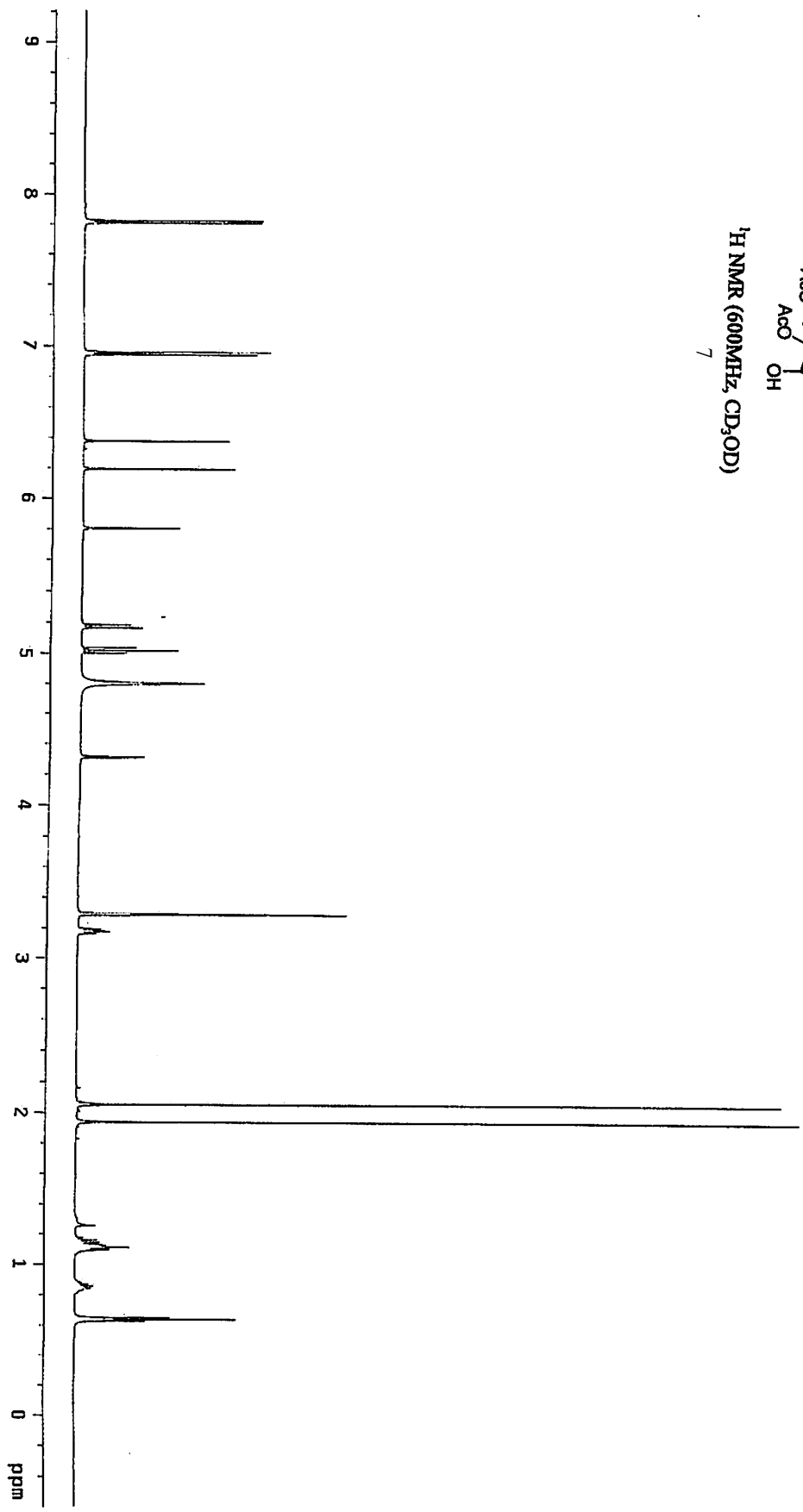


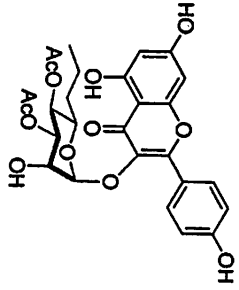
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K



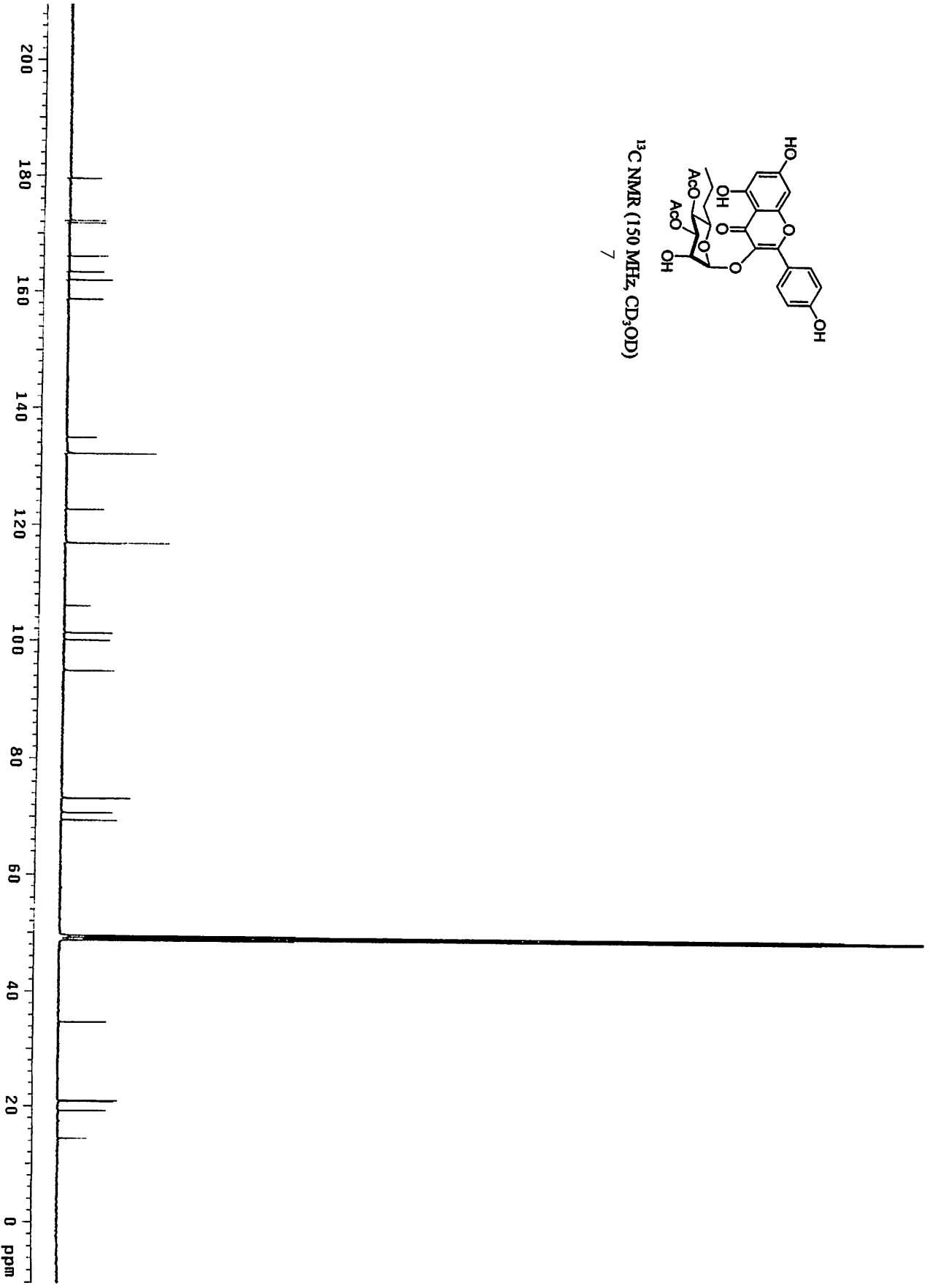


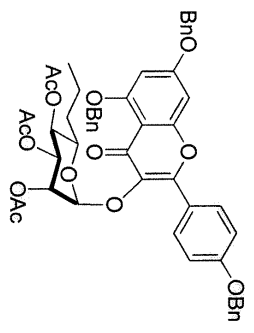
¹H NMR (600MHz, CD₃OD)
7



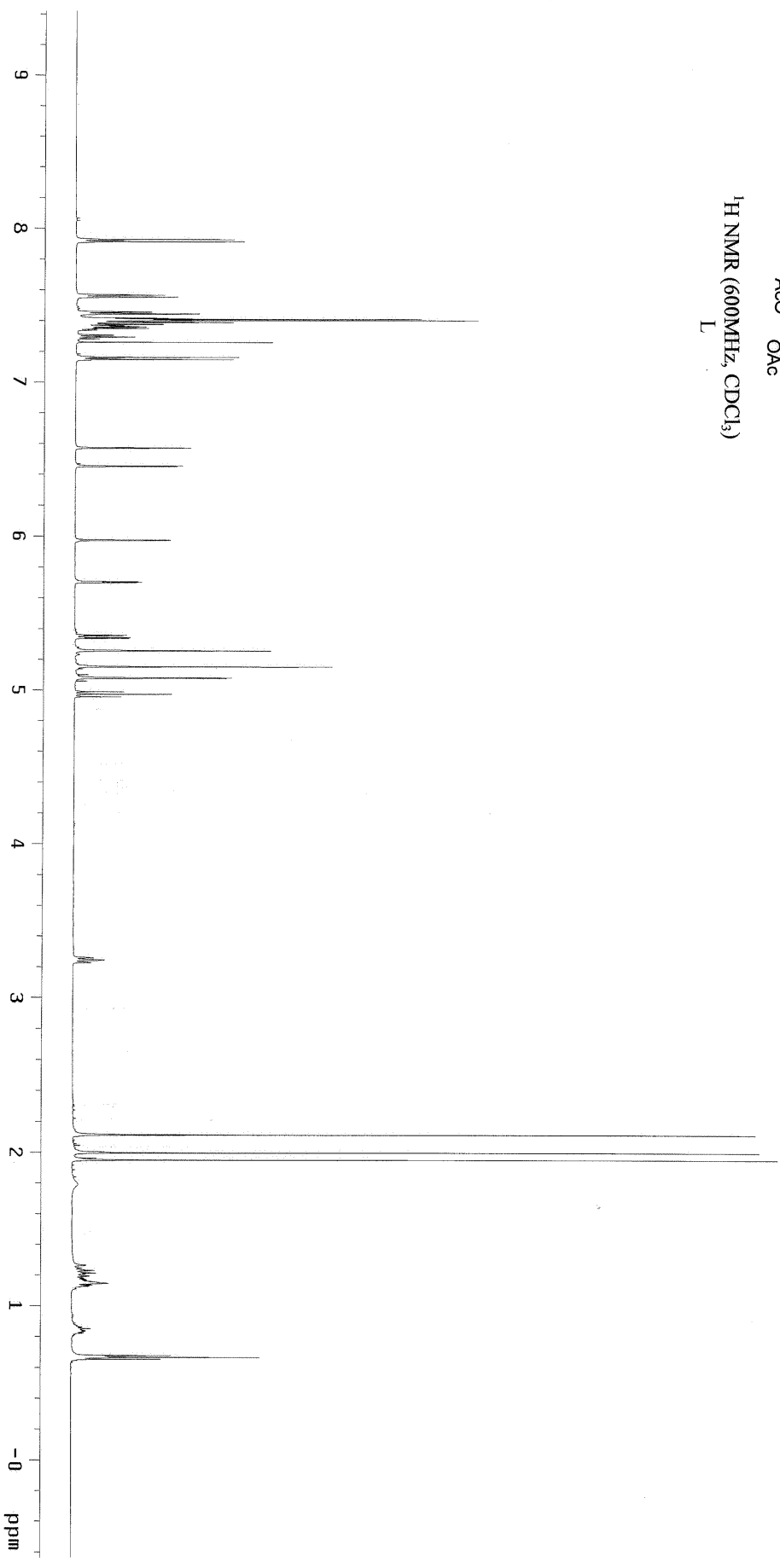


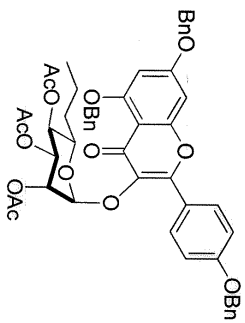
¹³C NMR (150 MHz, CD₃OD)
7





¹H NMR (600MHz, CDCl₃)
L





¹³C NMR (150 MHz, CDCl₃)
L

