Supplementary information

Aluminium triflate catalysed *O*-glycosidation: temperature-switched selective Ferrier rearrangement or direct addition with alcohols

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General

Chemical methods

All reactions were performed under an atmosphere of either nitrogen or argon. Reagents were used as received from commercial sources without further purification. Unless otherwise stated, dry solvents were used in oven dried, flamed out glass apparatus. Room temperature refers to *ca.* 20-23 ºC.

Chromatography

Qualitative thin layer chromatography (TLC) was conducted on "Merck GF254 precoated silica plates" (0.25 mm layer). The chromatograms were eluted using an appropriate solvent system as indicated for column chromatography. Compounds were visualised by their fluorescence under UV light (254 nm), as well as by spraying the plate with anisaldehyde spray followed by heating with a heat gun or over a Bunsen burner. "Flash chromatography" refers to column chromatography under nitrogen pressure using "Merck Kieselgel 60 (230-400 mesh), with eluents mixed in a volume per volume ratio.

Spectroscopic data

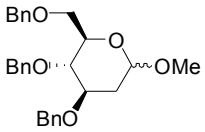
NMR spectra were recorded by means of a Varian Gemini 2000, 300 MHz and a Bruker Ultrashield 400 MHz spectrometer in $CDCl_3$ unless otherwise indicated. *J* values are given in Hz. Fractional numbers of protons given in the ^{1}H NMR data, below, reflect the relative ratio of the isomers. Mass spectrometry was performed on Thermo Double Focussing Sector high resolution mass spectrometer. Ionisation techniques include EIMS and CIMS. A Tensor 27 spectrophotometer was used to record IR spectra using an ATR fitting. The data are listed with the characteristic peaks indicated in wavenumber (cm^{-1}). Melting points were determined using a Gallencamp oil immersion apparatus and are uncorrected.

General experimental procedure

To a solution of the specific glycal in DCE or DCM (2 mL), were added a glycosyl acceptor alcohol (1.5 eq) and 5 mol% $Al(OTf)_3$ and the resulting mixture was stirred at the temperature indicated (0 °C, room temperature or heated at 60 °C) until TLC analysis showed completion of the reaction. Thereafter, the reaction was quenched by addition of a saturated aqueous $NaHCO_3$ solution (0.5 mL). The reaction mixture was extracted twice with DCM (5 mL) and the organic layer washed with H_2O (2 mL). The organic layer was dried over anhydrous $MgSO_4$ and the solvent removed *in vacuo*. The crude product was purified by column chromatography on silica gel using a mixture of ethyl acetate and hexane as eluent.

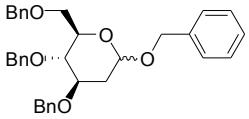
Fractional numbers of protons given in the ^{1}H NMR data below, where presented, reflect the relative ratio of the isomers. There was generally quite substantial overlap of signals.

***O*-Glycoside 2a**[1]



This compound has been previously prepared.[1]

***O*-Glycoside 2b**[2]

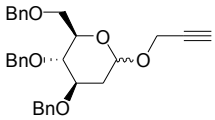


This product has been previously reported[2] but no data are presented.

Glycosidation of 3,4,6-tri-*O*-benzyl-D-glucal (200 mg, 0.48 mmol) with benzyl alcohol (78 mg, 0.72 mmol, 1.5 eq.) at 60 °C for 1 hour afforded glucoside **2b** as an inseparable α/β (3:2) mixture in a combined yield of 174 mg (69%) as a light yellow oil.

Found C, 77.9; H, 6.7%. $C_{34}H_{36}O_5$ requires C, 77.8; H, 6.9%; R_f = 0.43 (7:1, Hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40-7.05 (m, 20H), 4.97 (s, 0.7H), 4.89 (d, 0.3H, *J* 8.0), 4.85 (s, 0.3H), 4.81 (d, 0.7H, *J* 8.0), 4.65-4.30 (m, 8H), 4.09-3.85 (m, 1H), 3.80-3.49 (m, 3H), 2.25 (dd, 0.7H, *J* 16.0, 4.0), 2.12 (d, 0.3H, *J* 12.0), 1.67 (t, 0.7H, *J* 12.0), 1.58 (t, 0.3H, *J* 10.0); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.6, 138.5, 138.4, 138.1, 137.9, 137.6, 128.8, 128.5, 128.3, 128.2, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 126.9, 97.6, 96.7, 78.2, 77.7, 77.3, 75.4, 75.0, 73.4, 73.0, 71.8, 71.5, 71.4, 71.3, 70.9, 70.5, 69.8, 68.8, 35.4, 35.0; IR ν_{max} 1698, 1492, 1454, 1070, 1011, 732, 694 cm^{-1}; HR-CIMS calc for $C_{27}H_{30}O_5$ 434.2093 $[M\text{-}C_7H_6]^+$, found 434.2063.

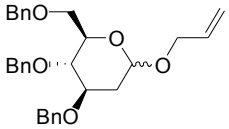
_O_-Glycoside 2c



Glycosidation of 3,4,6-tri-*O*-benzyl-D-glucal (200 mg, 0.48 mmol) with propargyl alcohol (40 mg, 0.72 mmol, 1.5 eq.) at 60 °C for 1 hour afforded glucoside **2c** as an inseparable α/β (7:3) mixture in a combined yield of 167 mg (74%) as a light yellow oil.

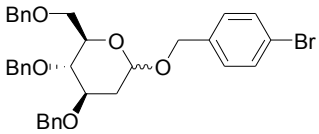
R_f = 0.39 (7:1, Hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.06 (m, 15H), 5.05 (s, 0.7H), 4.95 (s, 0.3H), 4.80 (t, 1H, *J* 10.2), 4.61-4.35 (m, 6H), 4.18 (s, 0.6H, OCH_2), 4.09 (1.4H, OCH_2), 3.95-3.86 (m, 1H), 3.69 (d, 1H, *J* 10.8), 3.62-3.49 (m, 2H), 2.33 (s, 0.3H), 2.31 (s, 0.7H), 2.26-2.19 (m, 1H), 1.71-1.56 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.4, 138.3, 138.0), 137.5, 128.4, 128.0, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 96.6, 96.1, 80.2, 79.2, 78.0, 77.9, 77.4, 74.9, 74.3, 74.1, 73.4, 71.7, 71.1, 70.8, 68.8, 68.6, 57.2, 53.9, 35.3, 35.0; IR ν_{max}/cm^{-1} 2860, 1501, 1456, 1301, 1070, 736, 698; MS: No useful peaks were identified from the CIMS spectrum.

_O_-Glycoside 2d[3]



This compound has been previously prepared.[3]

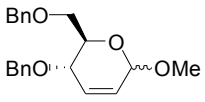
_O_-Glucoside 2e



Glycosidation of 3,4,6-tri-*O*-benzyl-D-glucal (200 mg, 0.48 mmol) with *p*-bromobenzyl alcohol (134 mg, 0.72 mmol, 1.5 eq.) at 60 °C for 1 hour afforded glucoside **2e** as an inseparable α/β (4:1) mixture in a combined yield of 194 mg (67%) as a light yellow oil.

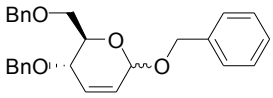
Found C, 67.7; H, 5.7%. $C_{34}H_{35}BrO_5$ requires C, 67.7; H, 5.9%; R_f = 0.53 (4:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38-7.08 (m, 19H), 4.95 (s,1H), 4.74 (d, 1H, *J* 10.5), 4.61-4.40 (m, 6H), 4.31 (d, 1H, *J* 12.0), 3.94-3.85 (m,1H), 3.69 (d, 2H, *J* 9.0), 3.58-3.50 (m,2H), 2.20 (dd, 1H, *J* 13.1, 4.3), 1.67 (dd, 1H, *J* 16.6, 7.9); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.3, 138.0, 137.6, 136.6, 131.5, 131.4, 129.5, 129.2, 128.5, 128.4, 128.0, 127.9, 127.8, 127.8, 127.7, 127.7, 127.6, 127.5, 126.9, 121.6, 121.3, 96.7, 78.2, 77.6, 75.0, 73.5, 71.0, 70.9, 68.9, 68.1, 35.3; IR ν_{max}/cm^{-1} 3088, 3030, 2864, 1493, 1362, 1096, 803, 734, 696; MS: No useful peaks were identified from the CIMS spectrum apart from those arising from the bromobenzyl fragment.

_O_-Glucoside 3a



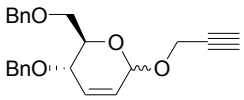
This compound has been previously prepared.[4]

_O_-Glucoside 3b



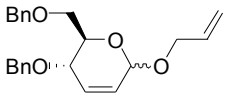
This compound has been previously prepared.[4]

_O_-Glucoside 3c



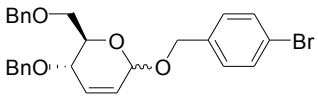
This compound has been previously prepared.[5]

_O_-Glucoside 3d



This compound has been previously prepared.[4]

_O_-Glucoside 3e

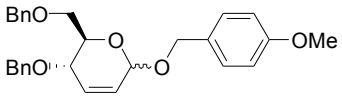


Glycosidation of 3,4,6-tri-*O*-benzyl-D-glucal (200 mg, 0.48 mmol) with *p*-bromobenzyl alcohol (134 mg, 0.72 mmol, 1.5 eq.) at 0 °C for 7 hours afforded **3e** as an inseparable α/β (4:1) mixture in a combined yield of 150 mg (63%) as a light yellow oil.

Found C, 65.7; H, 5.9%. $C_{27}H_{27}BrO_4$ requires C, 65.5; H, 5.5%; R_f = 0.49 (5:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38-7.09 (m, 14H), 6.00 (d, 1H, *J* 10.2), 5.69 (dt, 1H, *J* 10.3, 2.3), 5.10 (d, 0.2H, *J* 1.2), 5.01 (d, 0.8H, *J* 2.1), 4.73-4.33 (m, 6H), 4.09 (dt, 1H, *J* 9.3, 1.5), 3.91-3.89 (m,1H), 3.60-3.58 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.0, 137.9, 137.1, 131.4, 130.9, 129.6, 128.3, 127.9, 127.8, 127.7, 127.6, 126.2, 121.4,

94.0, 73.3, 71.0, 70.2, 69.3, 69.2, 68.6; IR ν_{max}/cm^{-1} 3063, 2865, 1453, 1362, 1096, 803, 734, 696; MS: No useful peaks were identified from the CIMS spectrum.

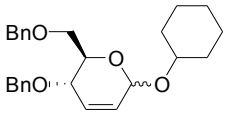
_O_-Glucoside 3f



Glycosidation of 3,4,6-tri-*O*-benzyl-D-glucal (200 mg, 0.48 mmol) with *p*-methoxybenzyl alcohol (90 μL, 0.72 mmol, 1.5 eq.) at 0 °C for 7 hours afforded **3f** as an inseparable α/β (9:1) mixture in a combined yield of 146 mg (76%) as a light yellow oil.

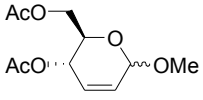
Found C, 75.3; H, 7.1%. $C_{28}H_{30}O_5$ requires C, 75.3; H, 6.8%; R_f = 0.46 (5:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26-7.11 (m,12H), 6.78-6.76 (m,2H), 5.98 (d, 1H, *J* 10.2), 5.68 (d, 1H, *J* 10.2), 5.10 (s, 0.1H), 5.02 (s, 0.9H), 4.68-4.33 (m,6H), 4.10 (d, 1H, *J* 9.3), 3.93 (m, 1H), 3.72-3.56 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.1, 138.1, 138.0, 130.6, 130.0, 129.7, 129.8, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 126.6, 113.7, 93.6, 73.3, 70.9, 70.3, 69.6, 69.2, 68.8, 55.2; IR ν_{max}/cm^{-1} 3031, 2865, 1513, 1247, 1027, 820, 733, 697; MS: No useful peaks were identified from the CIMS spectrum

_O_-Glucoside 3g



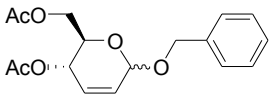
This compound has been previously prepared.[4]

_O_-Glucoside 5a[6]



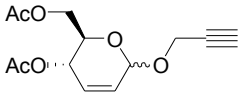
This compound has been previously prepared.[6]

_O_-Glucoside 5b[4]



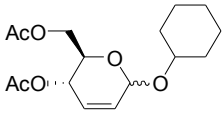
This compound has been previously prepared.[4]

_O_-Glucoside 5c[7]



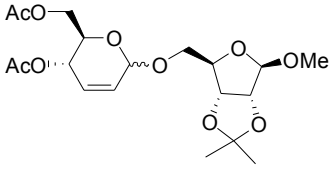
This compound has been previously prepared.[7]

_O_-Glucoside 5d[4]



This compound has been previously prepared.[4]

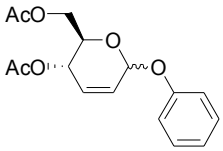
Disaccharide 5e



Glycosidation of 3,4,6-tri-*O*-acetyl-D-glucal (200 mg, 0.735 mmol) with methyl 2,3-*O*-isopropylidine-β-D-ribofuranoside (224 mg, 1.1 mmol, 1.5 eq.) for 1 hour at room temperature afforded glycoside **5e** as an inseparable α/β (9:1) mixture in a combined yield of 208 mg (68%) as a clear oil.

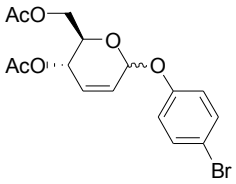
Found C, 55.0; H, 7.2%. $C_{19}H_{28}O_{10}$ requires C, 54.8; H, 6.8%; R_f = 0.31 (3:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.87-5.71 (m, 2H), 5.21 (dd, 1H, *J* 9.9, 1.2), 5.07 (s, 0.1H), 4.95 (s, 0.9H), 4.9 (s, 1H), 4.61 (d, 1H, *J* 5.7), 4.48 (d, 1H, *J* 5.7), 4.29-4.26 (m, 1H), 4.19-4.07 (m, 2H), 4.02-3.97 (m, 1H), 3.71-3.68 (m, 1H), 3.46-3.43 (m, 1H), 3.21 (s, 3H), 2.00-1.98 (m, 6H), 1.38 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 170.8, 170.2, 129.3, 127.4, 112.3, 109.3, 95.0, 85.1, 85.0, 82.0, 69.6, 67.0, 65.0, 62.7, 54.8, 26.4, 24.9, 20.9, 20.7; IR ν_{max}/cm^{-1} 2987, 2939, 2836, 1741, 1371, 1224, 1015, 869,736; HR-CIMS calc for $C_{18}H_{25}O_{10}$ 401.1448 $[M\text{-}CH_3]^+$, found 401.1363.

_O_-Glucoside 5f[8]



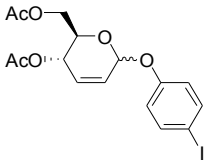
This compound has been previously reported.[8]

_O_-Glucoside 5g[8]



This compound has been previously reported.[8]

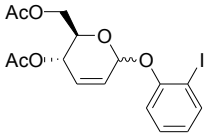
_O_-Glucoside 5h



Glycosidation of 3,4,6-tri-*O*-acetyl-D-glucal (200 mg, 0.735 mmol) with 4-iodophenol (194 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69mg) in DCM (2.0 mL) at –20 ºC for 3 hours afforded glycoside **5h** as an inseparable α/β (9:1) mixture in a combined yield of 257 mg (81%) as a cream solid.

Found C, 44.6; H, 4.3%. $C_{16}H_{17}IO_6$ requires C, 44.5; H, 4.0%; Mp 56-58 ºC; R_f = 0.55 (3:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.55 (d, 2H, *J* 9.0), 6.85 (d, 2H, *J* 8.7), 6.01(d, 1H, *J* 10.2), 5.94 (dt, 1H, *J* 10.3, 2.3), 5.62 (s, 1H), 5.34 (dd, 1H, *J* 9.5, 1.4), 4.27-4.12 (m, 2H), 4.09 (dd, 1H, *J* 11.6, 1.6), 2.07 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.6, 170.2, 156.8, 138.2, 130.3, 126.6, 119.3, 92.8, 85.0, 67.8, 64.8, 62.5, 20.9, 20.6; IR ν_{max}/cm^{-1} 2952 , 2360, 1735, 1483, 1368, 1219, 978, 816; HR-CIMS calc for $C_{14}H_{14}IO_6$ 372.9937 $[M\text{-}C_2H_3O_2]^+$, found 327.9980.

_O_-Glucoside 5i

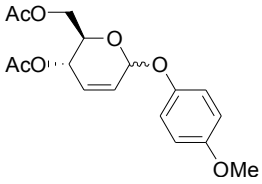


Glycosidation of 3,4,6-tri-*O*-acetyl-D-glucal (200 mg, 0.735 mmol) with 2-iodophenol (194 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69 mg) in DCM (2.0 mL) at –20 ºC for 7 hours afforded glycoside **5i** as an inseparable α/β (9:1) mixture in a combined yield of 241 mg (76%) as a cream solid.

Found C, 44.8; H, 3.9%. $C_{16}H_{17}IO_6$ requires C, 44.5; H, 4.0%; Mp 47-49 ºC; R_f = 0.59 (3:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 7.71 (dd, 1H, *J* 8.1, 1.5), 7.23 (ddd, 1H, *J* 8.4, 7.5, 1.5), 7.14 (dd, 1H, *J* 8.2, 1.6), 6.74 (ddd, 1H, *J* 9.0, 7.2 1.5), 6.02-5.89 (unresolved fine ABX system, 2H), 5.58 (d, 1H, *J* 1.8), 5.33 (dd, 1H, *J* 9.3, 1.2), 4.27-4.19 (m, 2H), 4.10 (d, 1H, *J* 9.9), 2.05 (s, 3H), 1.95 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.7, 170.2, 156.2, 139.3, 130.5, 129.5, 126.6, 124.6, 117.4, 94.4, 88.5, 68.0, 64.9, 62.5, 21.0, 20.7; IR ν_{max}/cm^{-1}

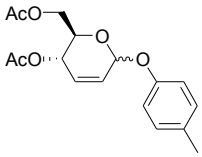
2931, 2360, 1739, 1438, 1367, 1225, 1042, 958, 750; HR-CIMS calc for $C_{14}H_{14}IO_4$ 372.9937 $[M\text{-}C_2H_3O_2]^+$, found 372.9983.

_O_-Glucoside 5j[9]



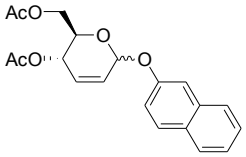
This compound has been previously prepared.[9]

_O_-Glucoside 5k[10]



This compound has been previously prepared.[10]

_O_-Glucoside 5l



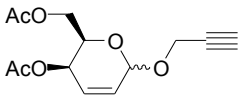
Glycosidation of 3,4,6-tri-*O*-acetyl-D-glucal (200 mg, 0.735 mmol) with 2-naphthol (127 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69 mg) in DCM (2.0 mL) at –20 ºC for 7 hours afforded glycoside **5l** as an inseparable α/β (9:1) mixture in a combined yield of 178 mg (68%) as a cream solid.

This compound has been previously reported,[11] but the structure apparently incorrectly assigned. We are able to obtain both the *O*- and *C*-glycosides, depending on the reaction conditions and we report the analytical data for the *O*-glycoside here. The reported data[11] concur with the *C*-glycoside in our hands, not the *O*-glycoside. (See main text discussing

Scheme 3, relating to *C*-glycoside formation. We also obtained a single crystal X-ray structure of the *C*-glycoside.[12] For this compound, H-1 resonates as a doublet of doublets at 6.29 ppm (*J* 4.2 and 2.7 Hz) while in the *O*-glycoside H-1 resonates as a fine doublet at 5.79 ppm with *J* 1.5 Hz.)

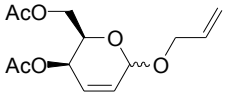
Mp 72-74 ºC; R_f = 0.58 (3:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$) δ_H δ 7.73-7.69 (m, 3H), 7.46 (d, 1H, *J* 2.4), 7.39 (ddd, 1H, *J* 9.3, 7.2, 1.2), 7.30 (ddd, 1H, *J* 9.3, 6.9, 1.2), 7.18 (dd, 1H, *J* 9.9, 3.9), 6.00 (unresolved fine ABXY system, 2H), 5.79 (d, 1H, *J* 1.5), 5.37 (d, 1H, *J* 9.6), 4.32-4.20 (m, 2H), 4.06 (d, 1H, *J* 10.5), 2.05 (s, 3H), 1.83 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.8, 170.3, 154.7, 134.4, 130.1, 129.7, 129.3, 127.6, 127.1, 127.0, 126.4, 124.3, 119.1, 111.2, 92.9, 67.9, 65.0, 62.6, 20.9, 20.6; IR ν_{max}/cm^{-1} 3296, 1631, 1602, 1513, 1468, 1218, 843; HR-CIMS calc for $C_{18}H_{17}O_4$ 297.1127 $[M-C_2H_3O_2]^+$, found 297.1098.

_O_-Glucoside 7a[7]



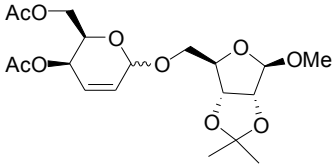
This compound has been previously prepared.[7]

_O_-Glucoside 7b[7]



This compound has been previously prepared.[7]

Disaccharide 7c



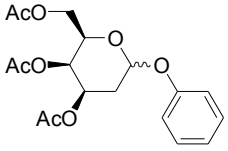
Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with methyl 2,3-*O*-isopropylidine-β-D-ribofuranoside (224 mg, 1.1 mmol, 1.5 eq.) for 3 hours at room temperature afforded **7c** as an inseparable α/β (9:1) mixture a combined yield of 193 mg (63%).

Found C, 54.7; H, 6.8%. $C_{19}H_{28}O_{10}$ requires C, 54.8; H, 6.8%; R_f = 0.33 (2:1, hexane/EtOAc); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.08 (dd, 1H, *J* 10.0, 5.1), 6.00 (dd, 1H, *J* 10.0, 2.6), 5.12 (s, 0.1H), 5.04 (s, 0.9H), 4.98-4.96 (m, 1H), 4.92 (s, 1H), 4.63 (d, 1H, *J* 6.0), 4.54 (d, 1H, *J* 3.9), 4.39-4.18 (m, 1H), 4.19 (d, 2H, *J* 6.0), 3.77 (dd, 1H, *J* 10.0, 5.6), 3.49 (t, 1H, *J* 9.6), 2.05 (s, 3H), 2.04 (s, 3H), 1.44 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): 170.6, 170.3, 130.2, 125.2, 112.3, 109.3, 94.5, 85.1, 84.9, 82.0, 69.2, 66.9, 63.9, 62.6, 54.9, 26.4, 24.9, 20.8, 20.7; IR ν_{max}/cm^{-1} 2941, 2834, 2364, 1742, 1371, 1224, 1036, 869, 733; HR-CIMS $C_{18}H_{25}O_{10}$ 401.1448 $[M\text{-}CH_3]^+$, found 401.1358.

5.3.6 *O*-glycosylation of tri-*O*-acetyl-D-galactal with phenolic nucleophiles

Tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) was stirred in DCM (2 mL) with the phenol (1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (5 mol%, 17 mg) at 0 ºC. After completion of the reaction as traced by TLC, the reaction was quenched at 0 ºC by adding concentrated sodium bicarbonate (2 mL) solution and the mixture extracted with CH_2Cl_2 (3×5 mL). The combined organic phases were dried over anhydrous magnesium sulfate. The volatile component was removed under vacuum leaving the crude product that was subjected to column chromatography on flash silica for purification, and a solution of hexane and ethyl acetate (Hexane: EtOAc, 3:1) was used as eluent.

_O_-Galactoside 8a[13]



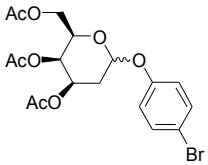
This compound has been previously prepared but no data are given.[13]

Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with phenol (83 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69 mg) in DCM (2.0 mL) at 0 ºC for 4

hours afforded glycoside **8a** as an inseparable α/β (>19:1) mixture in a combined yield of 183 mg (68%) as a cream solid.

Found C, 59.1; H, 5.8%. $C_{18}H_{22}O_8$ requires C, 59.0; H, 6.1%; Mp 120-122 ºC; R_f = 0.41 (3:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.21 (t, 2H, *J* 7.4), 6.66-6.92 (m, 3H), 5.67 (br s, 1H), 5.43 (dd, 1H, *J* 9.2, 2.6), 5.33 (br s, 1H), 4.19 (t, 1H, *J* 6.4), 4.02-3.98 (m, 2H), 2.18 (br t, 1H, *J* 12.6), 2.09 (s, 3H), 2.03 (dd, 1H, *J* 9.6 and 5.2), 1.95 (s, 3H), 1.84 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.3, 170.2, 170.0, 156.2, 129.4, 122.3, 116.4, 95.7, 67.4, 66.4, 65.9, 62.0, 30.1, 20.8, 20.6, 20.5; IR ν_{max}/cm^{-1} 2962, 1740, 1490, 1226, 1016, 798; HR-CIMS calc for $C_{18}H_{23}O_8$ 367.1393 $[M+H]^+$, found 367.1374, calc for $C_{16}H_{20}O_6$ $[M-C_2H_3O_2]^+$ 307.1182, found 307.1129.

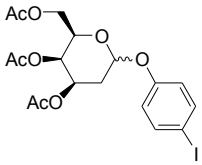
_O_-Galactoside 8b



Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with 4-bromophenol (152 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69 mg) in DCM (2.0 mL) at 0 ºC for 6 hours afforded glycoside **8b** as an inseparable α/β (18:1) mixture in a combined yield of 249 mg (76%) as a cream solid.

Found C, 48.2; H, 5.0%. $C_{18}H_{21}BrO_8$ requires C, 48.6; H, 4.8%; R_f = 0.44 (3:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.35 (d, 2H, *J* 8.4), 6.92 (d, 2H, *J* 8.4), 5.66 (br s, 1H), 5.43 (d, 1H, *J* 12.0), 5.35 (br s, 1H), 4.17 (t, 1H, *J* 6.4), 4.04-4.00 (m, 2H), 2.22 (br t, 1H, *J* 12.4), 2.12 (s, 3H), 2.06 (dd, 1H, *J* 12.8, 5.2), 1.98 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.3, 170.1, 170.0, 155.3, 132.3, 118.2, 114.7, 95.9, 67.6, 66.3, 65.8, 62.0, 30.0, 20.8, 20.6, 20.5; IR ν_{max}/cm^{-1} 2960, 1743, 1487, 1367, 1221, 1198, 1115, 1018, 823; HR-CIMS calc for $C_{18}H_{21}BrO_8$ 444.0420, 446.0399 $[M]^+$, found 444.0418, 446.0292, calc for $C_{16}H_{18}BrO_6$ $[M-C_2H_3O_2]^+$ 385.0287, 387.0266, found 385.0284, 387, 0269.

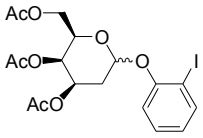
_O_-Galactoside 8c



Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with 4-iodophenol (194 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69 mg) in DCM (2.0 mL) at 0 ºC for 6 hours afforded glycoside **8c** as an inseparable α/β (11:1) mixture in a combined yield of 264 mg (73%) as a cream solid.

Found C, 43.7; H, 4.1%. $C_{18}H_{21}IO_8$ requires C, 43.9; H, 4.3%; Mp 62-64 ºC; R_f = 0.45 (3:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.52 (d, 2H, *J* 7.6), 6.80 (d, 2H, *J* 8.0), 5.66 (br s, 1H), 5.42 (d, 1H, *J* 12.4), 5.34 (s, 1H), 4.16 (t, 1H, *J* 6.4), 4.06-3.96 (m, 2H), 2.21 (br t, 1H, *J* 12.0), 2.11 (s, 3H), 2.05 (dd, 1H, *J* 9.8, 5.0), 1.98 (s, 3H), 1.89 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.2, 170.1, 169.9, 156.0, 138.2, 118.7, 95.8, 84.9, 67.6, 66.2, 65.7, 61.9, 30.0, 20.8, 20.6, 20.5; IR ν_{max}/cm^{-1} 2955, 1744, 1483, 1369, 1221, 1114, 1021, 820, 731; HR-CIMS calc for $C_{16}H_{18}IO_6$ $[M-C_2H_3O_2]^+$ 433.0148, found 433.0251.

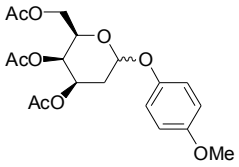
_O_-Galactoside 8d



Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with 2-iodophenol (194 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69 mg) in DCM (2.0 mL) at 0 ºC for 7 hours afforded glycoside **8d** as an inseparable α/β (>19:1) mixture in a combined yield of 239 mg (66%) as a cream solid.

Found C, 43.9; H, 4.4%. $C_{18}H_{21}IO_8$ requires C, 43.9; H, 4.3%; Mp 80-82 ºC; R_f = 0.44 (3:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.70 (d, 1H, *J* 8.0), 7.20 (t, 1H, *J* 7.6), 7.03 (d, 1H, *J* 8.4), 6.71 (t, 1H, *J* 7.6), 5.70 (br s, 1H), 5.55-5.50 (m, 1H), 5.37 (br s, 1H), 4.18 (t, 1H, *J* 6.6), 3.99 (d, 2H, *J* 6.6), 2.24-2.14 (m, 2H), 2.08 (s, 3H), 1.95 (s, 3H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.2, 170.0, 169.8, 154.8, 139.3, 129.2, 124.1, 115.3, 96.4, 87.5, 68.0, 66.3, 65.9, 61.9, 30.0, 20.7, 20.6, 20.5; IR ν_{max}/cm^{-1} 2963, 1730, 1472, 1224, 1197, 1018, 799; HR-CIMS calc for $C_{16}H_{18}IO_6$ $[M-C_2H_3O_2]^+$ 433.0148, found 433.0060.

_O_-Galactoside 8e[14]

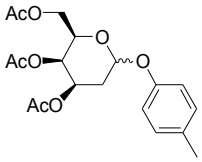


This compound has been previously reported[14] but no analytical data were given.

Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with 4-methoxyphenol (109 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69mg) in DCM (2.0 mL) at 0 ºC for 4 hours afforded glycoside **8e** as an inseparable α/β (>19:1) mixture in a combined yield of 186 mg (64%) as a cream solid.

Found C, 57.9; H, 6.3%. $C_{19}H_{24}O_9$ requires C, 57.6; H, 6.1%; Mp 60-62 ºC; R_f = 0.40 (3:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 6.96 (d, 2H, *J* 9.2), 6.78 (d, 2H, *J* 8.8), 5.59 (d, 1H, *J* 2.8), 5.48-5.43 (m, 1H), 5.36 (d, 1H, *J* 2.8), 4.26 (t, 1H, *J* 6.6), 4.07-4.03 (m, 2H), 3.73 (s, 3H), 2.20 (td, 1H, *J* 9.5, 2.7), 2.12 (s, 3H), 2.06 (dd, 1H, *J* 9.6, 5.2), 1.98 (s, 3H), 1.91 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.4, 170.2, 170.0, 154.9, 150.2, 117.7, 114.4, 96.5, 67.3, 66.4, 66.0, 62.1, 55.5, 30.2, 20.8, 20.7, 20.6; IR ν_{max}/cm^{-1} 2944, 1730, 1497, 1245, 1204, 1011, 975; HR-CIMS calc for $C_{19}H_{24}O_9$ $[M\text{-}C_2H_3O_2]^+$ 337,1287, found 337.1315.

_O_-Galactoside 8f[14]



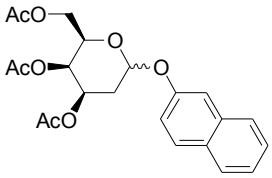
This compound has been previously reported[14] but no analytical data were given.

Glycosidation of 3,4,6-tri-*O*-acetyl-D-galactal (200 mg, 0.735 mmol) with *p*-cresol (95 mg, 1.2 equivalents, 0.882 mmol) and $Al(OTf)_3$ (20 mol%, 69mg) in DCM (2.0 mL) at 0 ºC for 4 hours afforded glycoside **8f** as an inseparable α/β (>19:1) mixture in a combined yield of 198 mg (71%) as a light yellow oil.

Found C, 59.8; H, 6.2%. $C_{19}H_{24}O_8$ requires C, 60.0; H, 6.4%; R_f = 0.46 (3:1, hexane/EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.05 (d, 2H, *J* 8.0), 6.92 (d, 2H, *J* 7.6), 5.65 (s, 1H), 5.46 (m, 1H), 5.36 (s, 1H), 4.24 (t, 1H, *J* 6.6), 4.08-4.01 (m, 2H), 2.26 (s, 3H), 2.19 (d, 1H, *J* 12.4),

2.12 (s, 3H), 2.06 (dd, 1H, *J* 9.4, 4.6), 1.99 (s, 3H), 1.90 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.3, 170.2, 170.0, 154.1, 131.6, 129.8, 116.4, 96.0, 67.3, 66.4, 66.0, 62.0, 30.2, 20.8, 20.6, 20.5, 20.4; IR ν_{max}/cm^{-1} 2961, 1742, 1509, 1220, 1037, 1018, 785; HR-CIMS calc for $C_{17}H_{21}O_6$ $[M\text{-}C_2H_3O_2]^+$ 321.1338, found 321.1271.

_O_-Galactoside 8g[15]

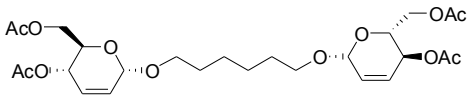


This compound has been previously reported.[15]

Synthesis of symmetrical bolaform type compounds

Tri-*O*-acetyl-D-glucal (400 mg, 1.470 mmol) was stirred in DCM (5 mL) with the diol (0.5 equivalents, 0.735 mmol) and $Al(OTf)_3$ (5 mol%, 17 mg) at room temperature. After completion of the reaction as traced by TLC, the reaction was quenched by adding concentrated sodium bicarbonate (4 mL) solution and the mixture extracted with CH_2Cl_2 (3×5 mL). The combined organic phases were dried over anhydrous magnesium sulfate. The volatile component was removed under vacuum leaving the crude product that was subjected to column chromatography on flash silica for purification, using neat ethyl acetate as eluent.

Glucoside bolaform 9[16]



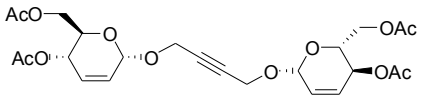
2 h reaction time. Yellow oil, 331 mg, 61%.

This compound has been previously reported[16] and the data are in good agreement with those presented here.

Found C, 57.6; H, 7.3. $C_{26}H_{38}O_{12}$ requires C, 57.6; H, 7.1%; R_f = 0.71 (Ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 5.90-5.73 (m, 4H), 5.25 (d, 2H, *J* 9.6), 4.96 (s, 2H), 4.24-3.95

(m, 6H), 3.75-3.66 (m, 2H), 3.49-3.40 (m, 2H), 2.03 (d, 12H, *J* 3.9), 1.61-1.44 (m, 4H), 1.38-1.25 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.6, 170.2, 128.9, 127.8, 94.3, 68.7, 66.8, 65.2, 62.9, 29.6, 26.0, 20.9, 20.7; IR ν_{max}/cm^{-1} 2935, 1738, 1370, 1222, 974, 772; MS: No useful peaks were identified from the CIMS spectrum. However, a carbohydrate-derived fragment was observed at HR-CIMS calc for $C_{10}H_{13}O_5$ 213.0763, found 213.0793.

Glucoside bolaform 10



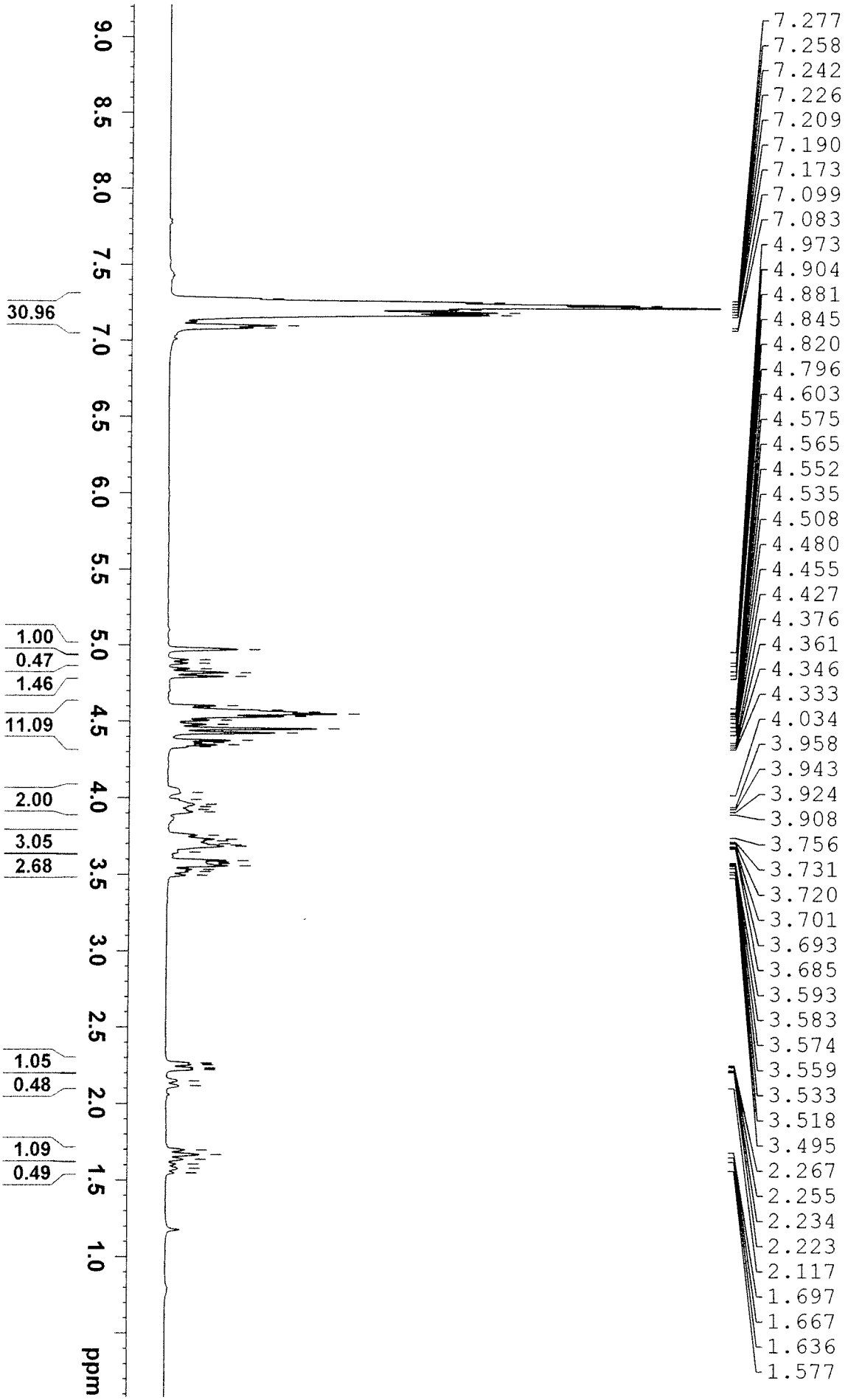
2 h reaction time, cream solid, 444 mg, 87%.

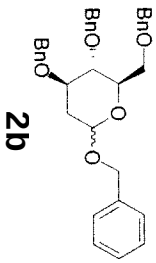
Found C, 56.2; H, 6.2%. $C_{24}H_{30}O_{12}$ requires C, 56.5; H, 5.9%; Mp: 90-92 ºC; R_f = 0.67 (Ethyl acetate); ^{1}H NMR (300 MHz, $CDCl_3$): δ_H 5.83 (d, 2H, *J* 10.4), 5.77 (dt, 2H, *J* 10.2, 2.4), 5.29-5.22 (m, 2H), 5.14 (s, 2H), 4.36-3.96 (m, 10H), 2.03 (d, 12H, *J* 4.5); ^{13}C NMR (75 MHz, $CDCl_3$): δ_C 170.6, 170.1, 129.6, 127.1, 92.5, 81.9, 67.0, 65.0, 62.6, 55.1, 20.8, 20.6; IR ν_{max}/cm^{-1} 2923, 1727, 1374, 1230, 1187, 1031, 957; MS: No useful peaks were identified from the CIMS spectrum. However, a carbohydrate-derived fragment was observed at HR-CIMS calc for $C_{10}H_{13}O_5$ 213.0763, found 213.0750.

References

1. M. S. Kumar and H. B. Mereyala, WO2004/058786, Council for Scientific and Industrial Research, 2004.
2. K. C. Nicolaou, J. Pastor, S. Barluenga and N. Winssinger, *Chem. Commun*., 1998, **18**, 1947.
3. W. J. Morris and M. D. Shair, Org. Lett., 2009, **11**, 9; K. Pachamuthu, Y.D. Vankar, *J. Org. Chem.*, 2001, **66**, 7511.
4. Z. Guisheng, L. Qingfeng, S. Lei and W. Jiuxia, *Tetrahedron,* 2008, **64**, 339.
5. M. –C. José and R. –C. Juliana, *J. Org. Chem*, 1999, **64**, 8302.
6. K. Karsten, G. Dietmar, K. Oliver and V. R. Teunis, *J. Carbohydr. Chem.*, 2003, **22**, 377.
7. B. Rengarajan and R. K. Srinivasa, *Tetrahedron*, 2009, **65**, 8139.
8. S. Y. Jhillu, V. Basi, R. Subba and S. Shyam, *J. Chem. Soc*., *Perkin Trans. 1*, 2002, 2390.

9. K. De, J. Legros, B. Crousse and D. Bonnet-Delpon, *Tetrahedron*, 2008, **64**, 10497.
10. S. B. Boga and K. K. Balasubramanian, *ARKIVOC*, 2004, **(viii)**, 87.
11. B. K. Gorityala, S. Cai, R. Lorpitthaya, J. Ma, K. K. Pasunooti and X. –W. Liu, *Tetrahedron Lett*., 2009, **50**, 676.
12. D.B.G. Williams, S. Simelane, H.H. Kinfe, B. Owaga, CCDC 834632
13. S. Hotha and A. Tripathi, *Tetrahedron Lett*., 2005, **46**, 4555.
14. C. Booma and K. K. Balasubramanian, *Tetrahedron Lett*., 1995, **36**, 5807.
15. S. N. Lam and J. Gervay-Hague, *Org. Lett*., 2003, **5**, 4219.
16. E. Wieczorek and J. Thiem, *J. Carbohydr. Chem*., 1998, **17**, 785.





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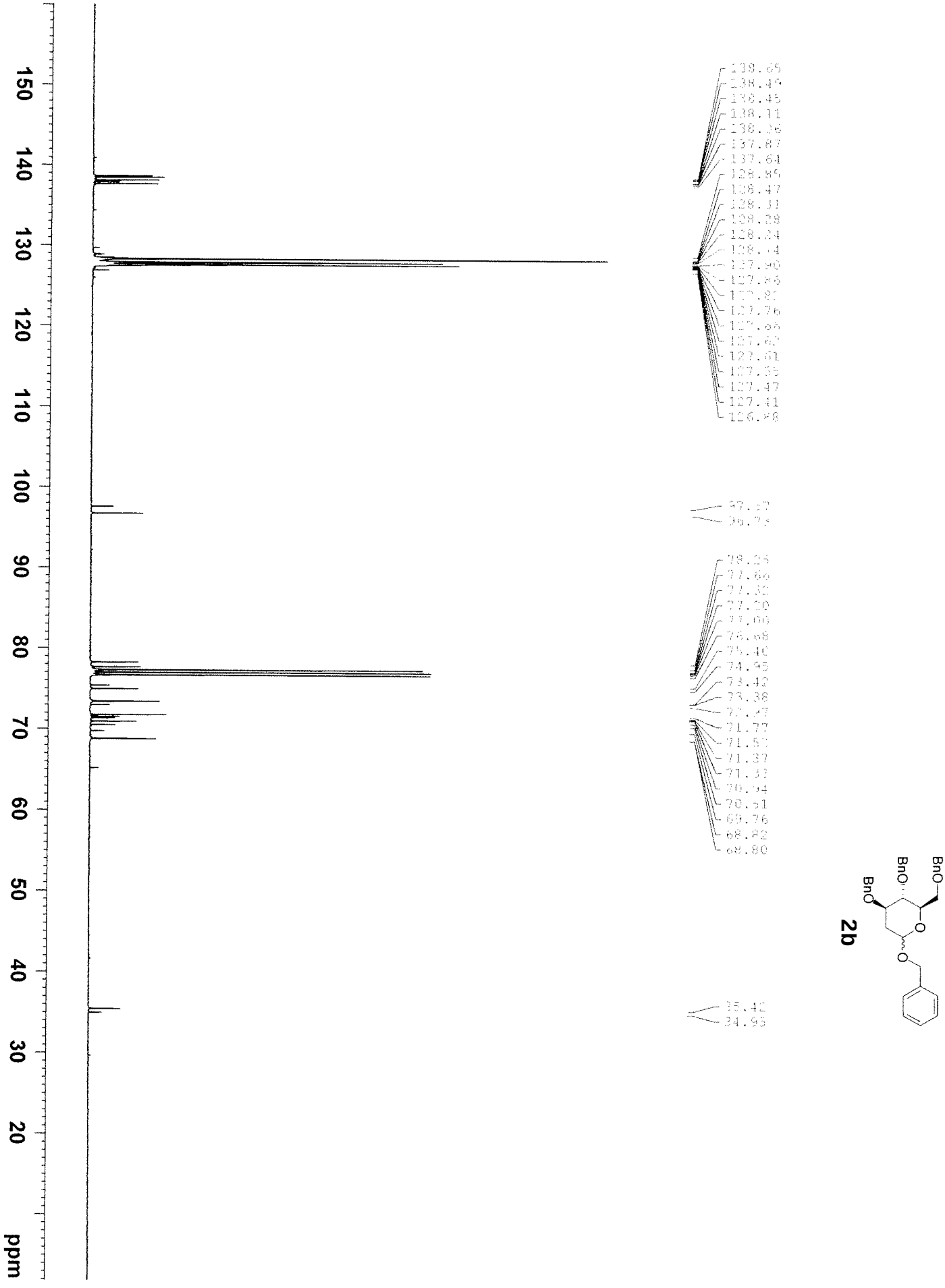

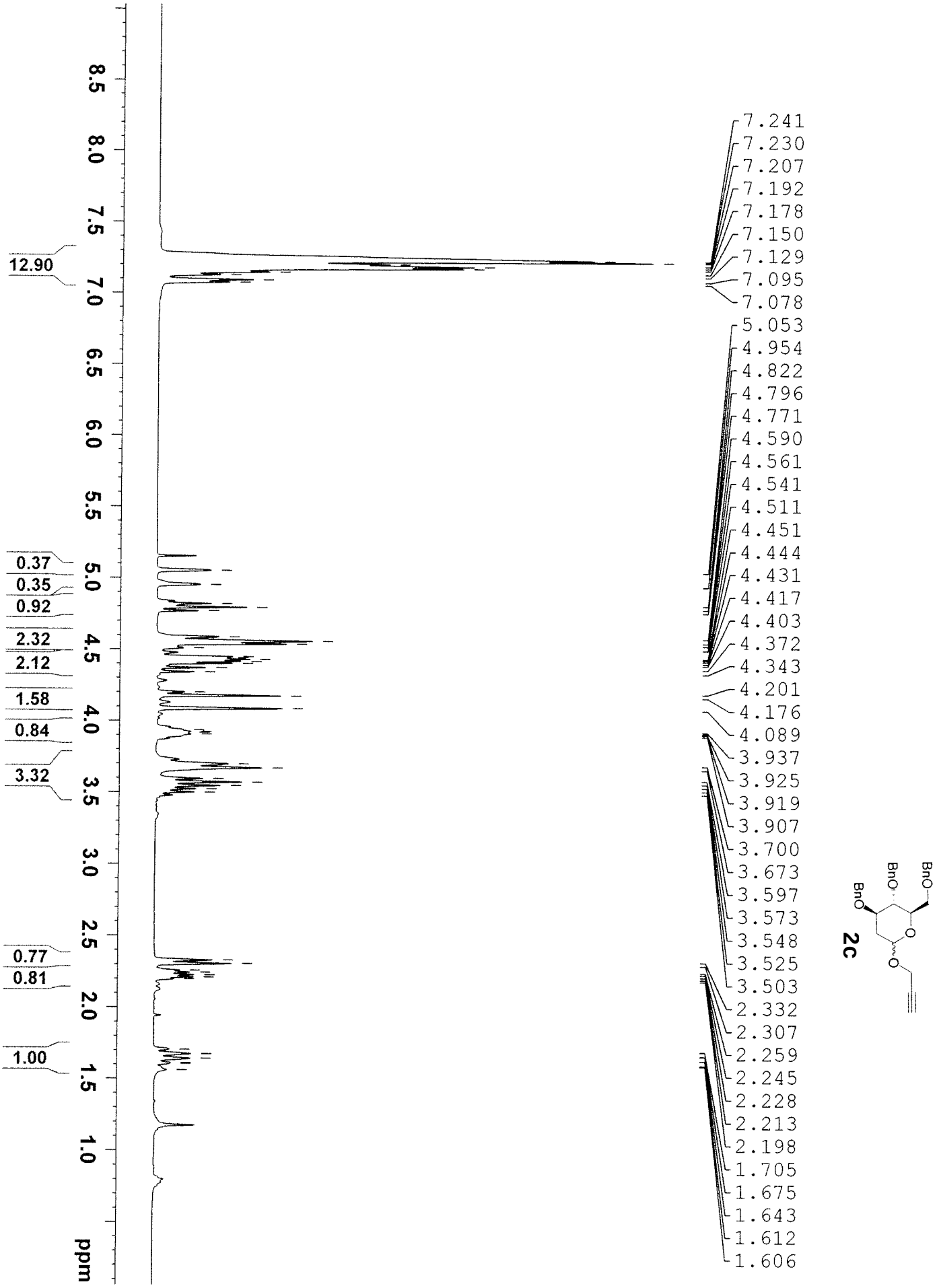

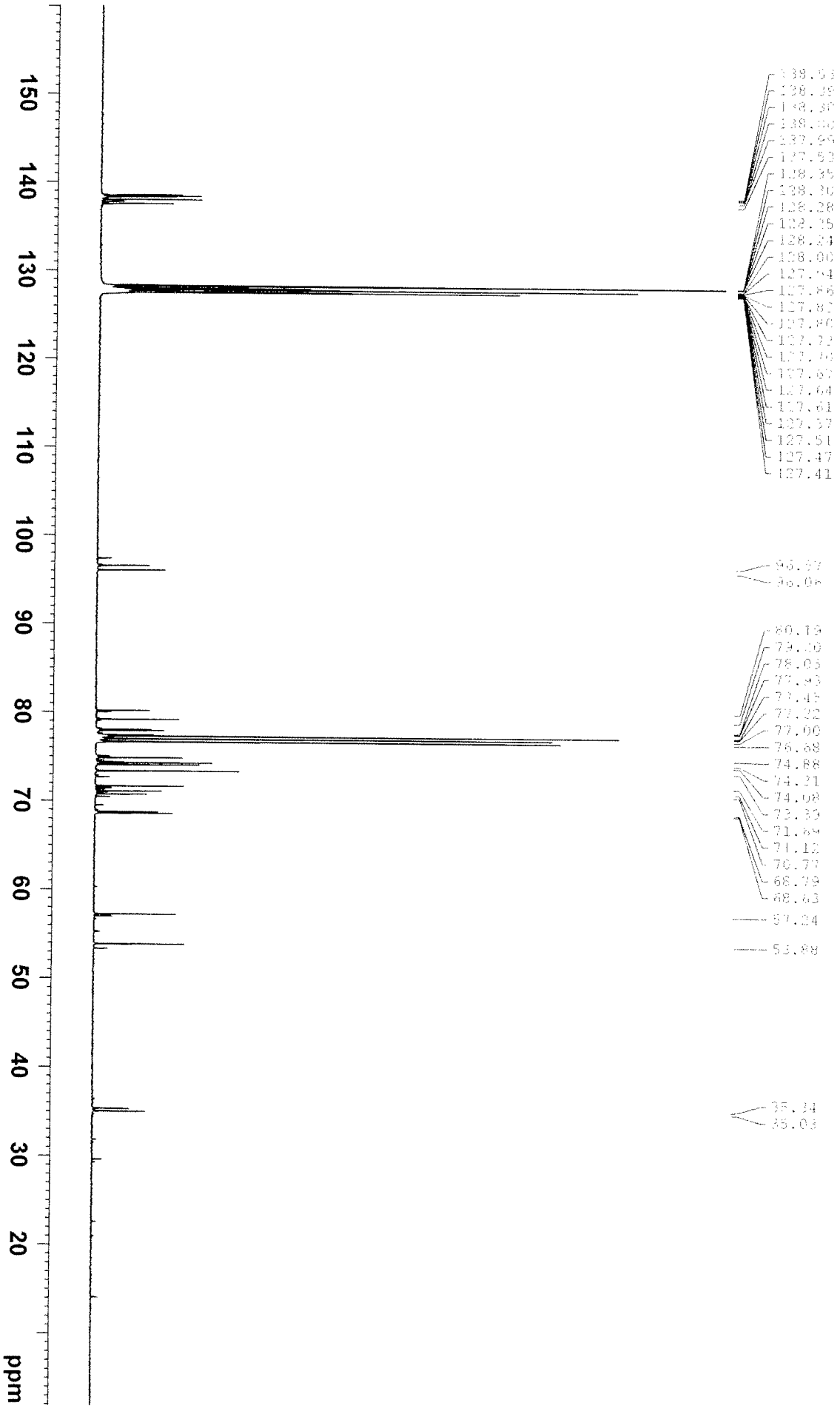

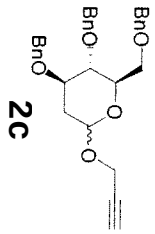

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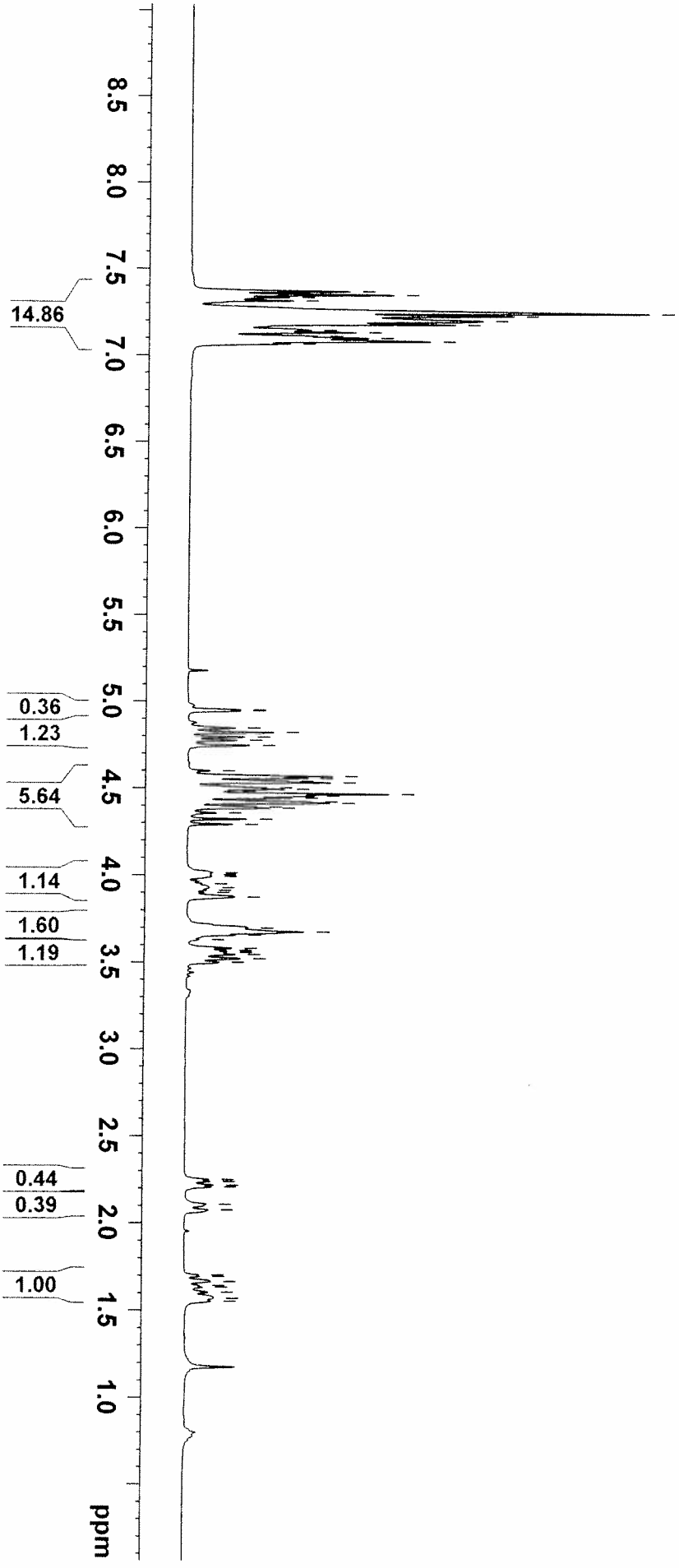

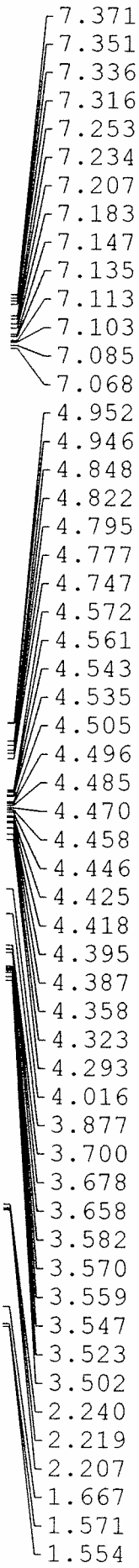

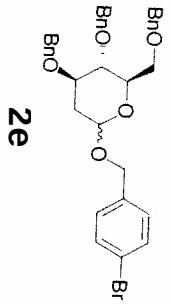

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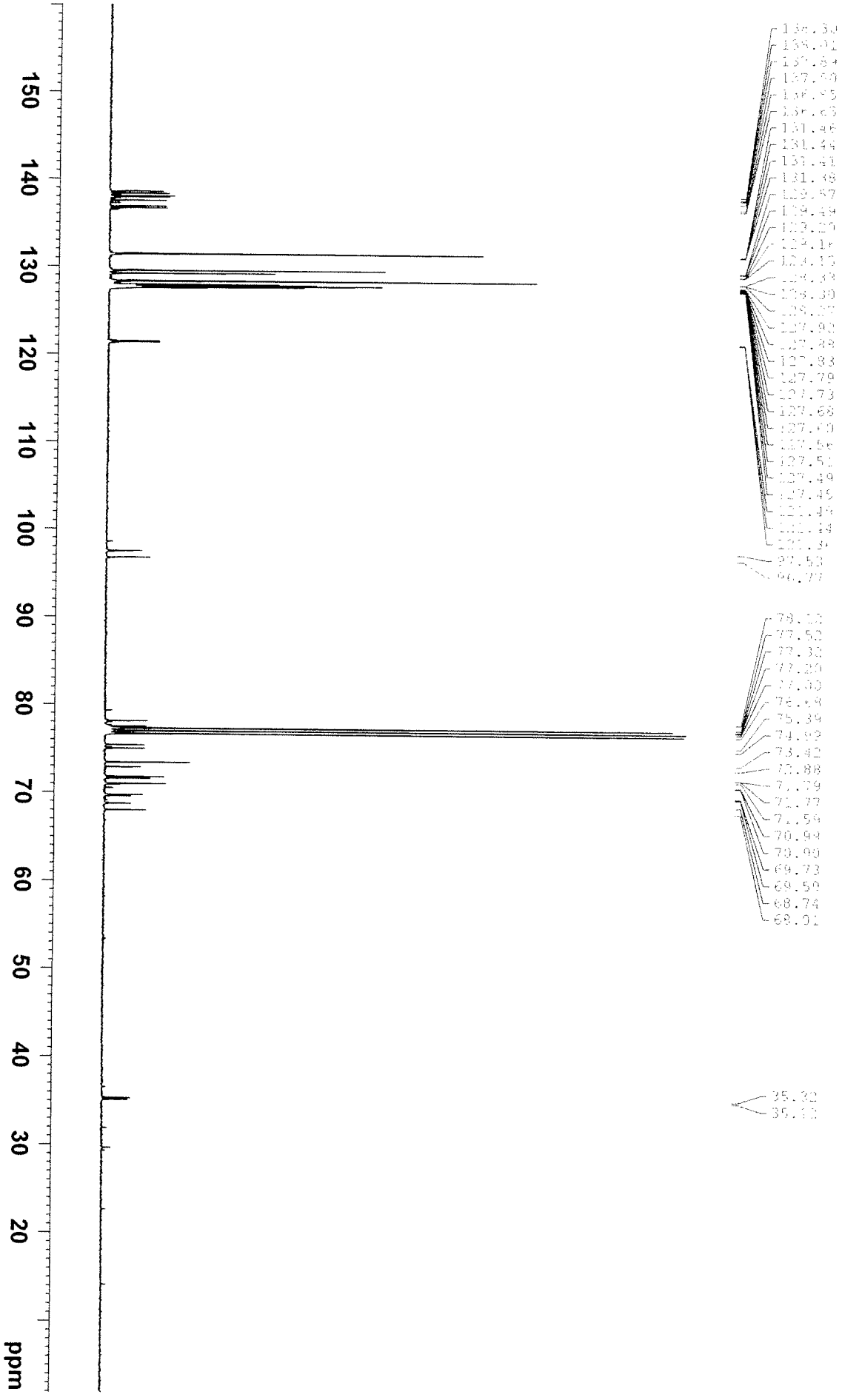

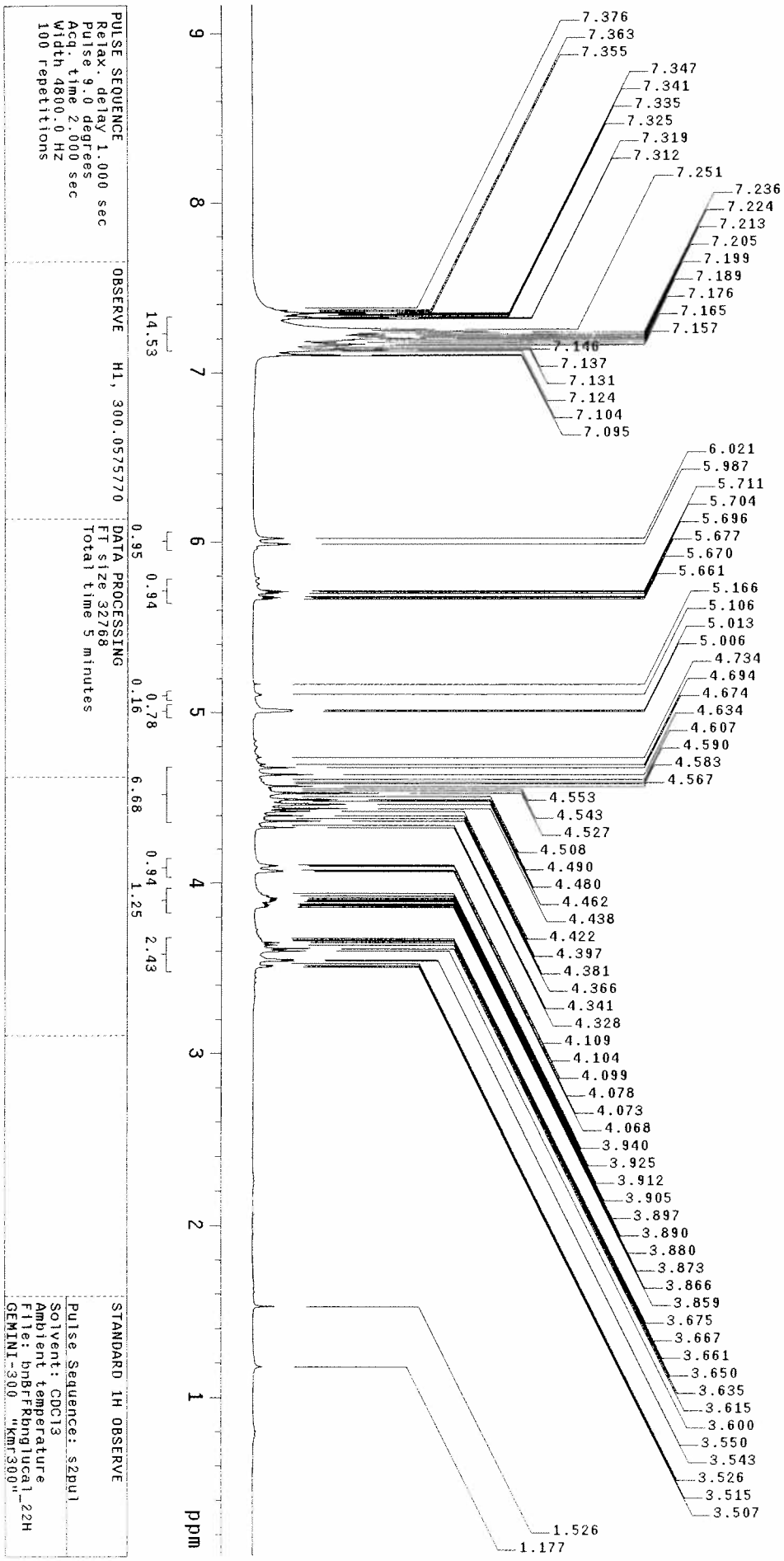

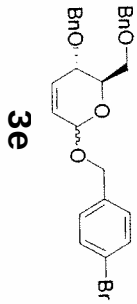

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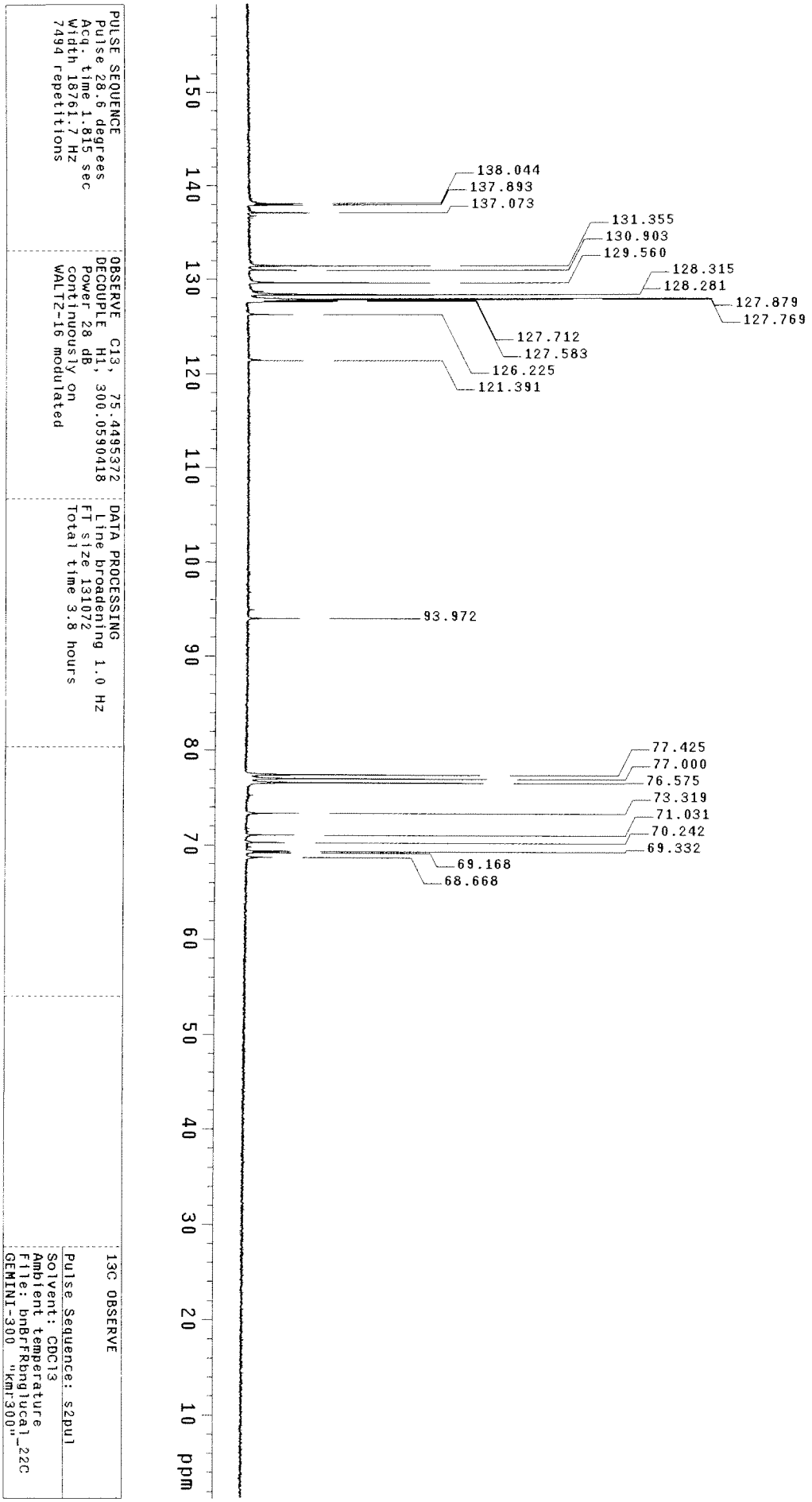

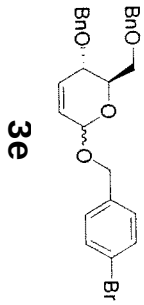

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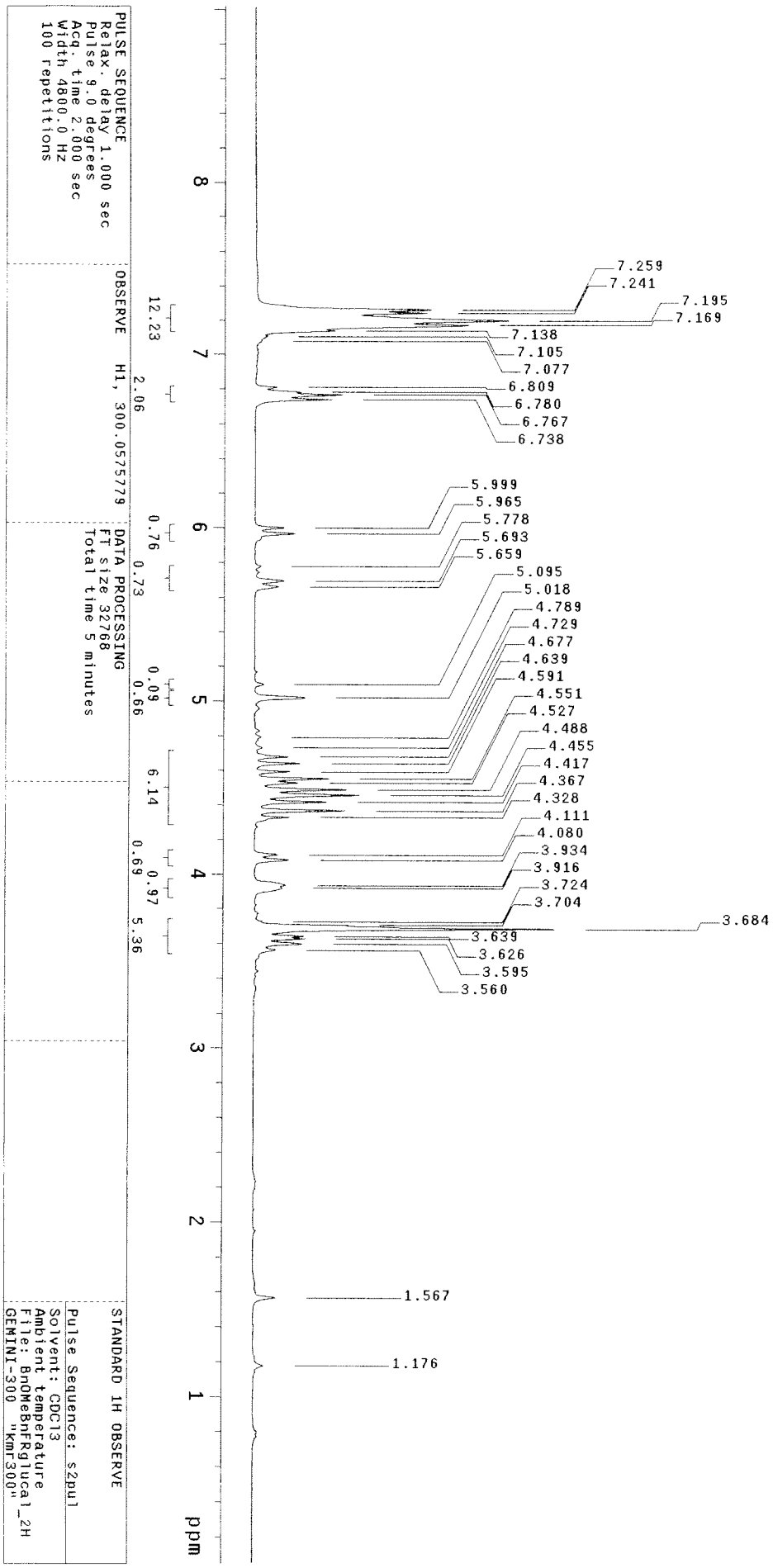

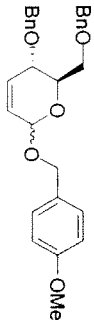

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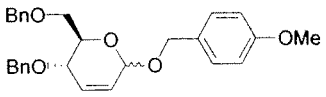

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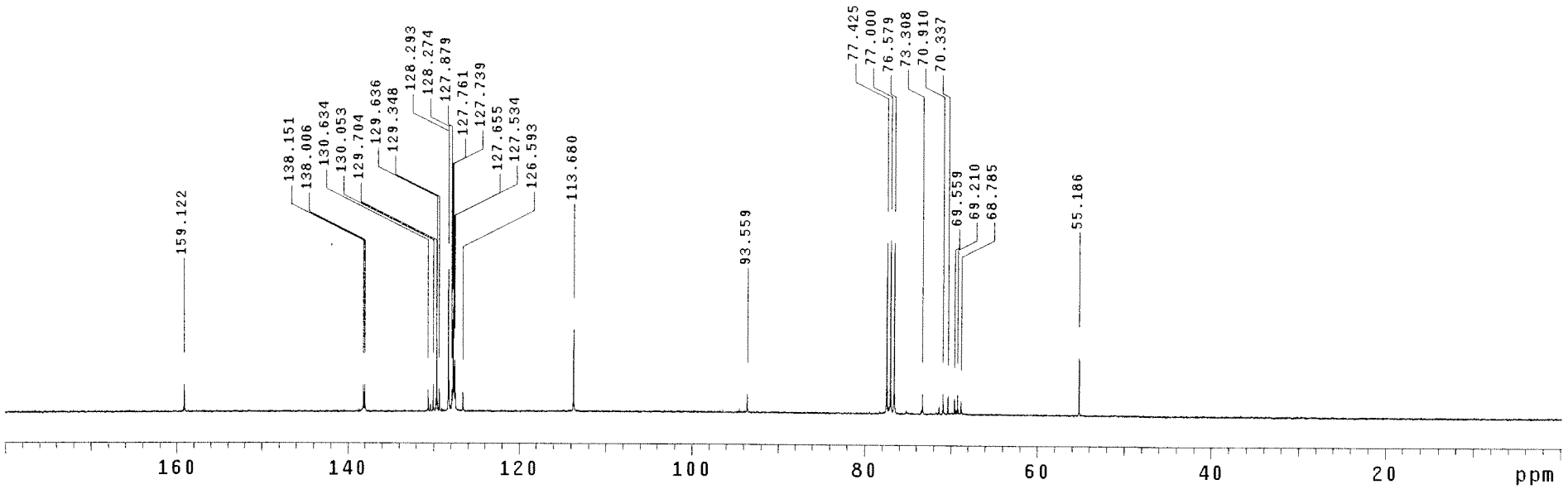

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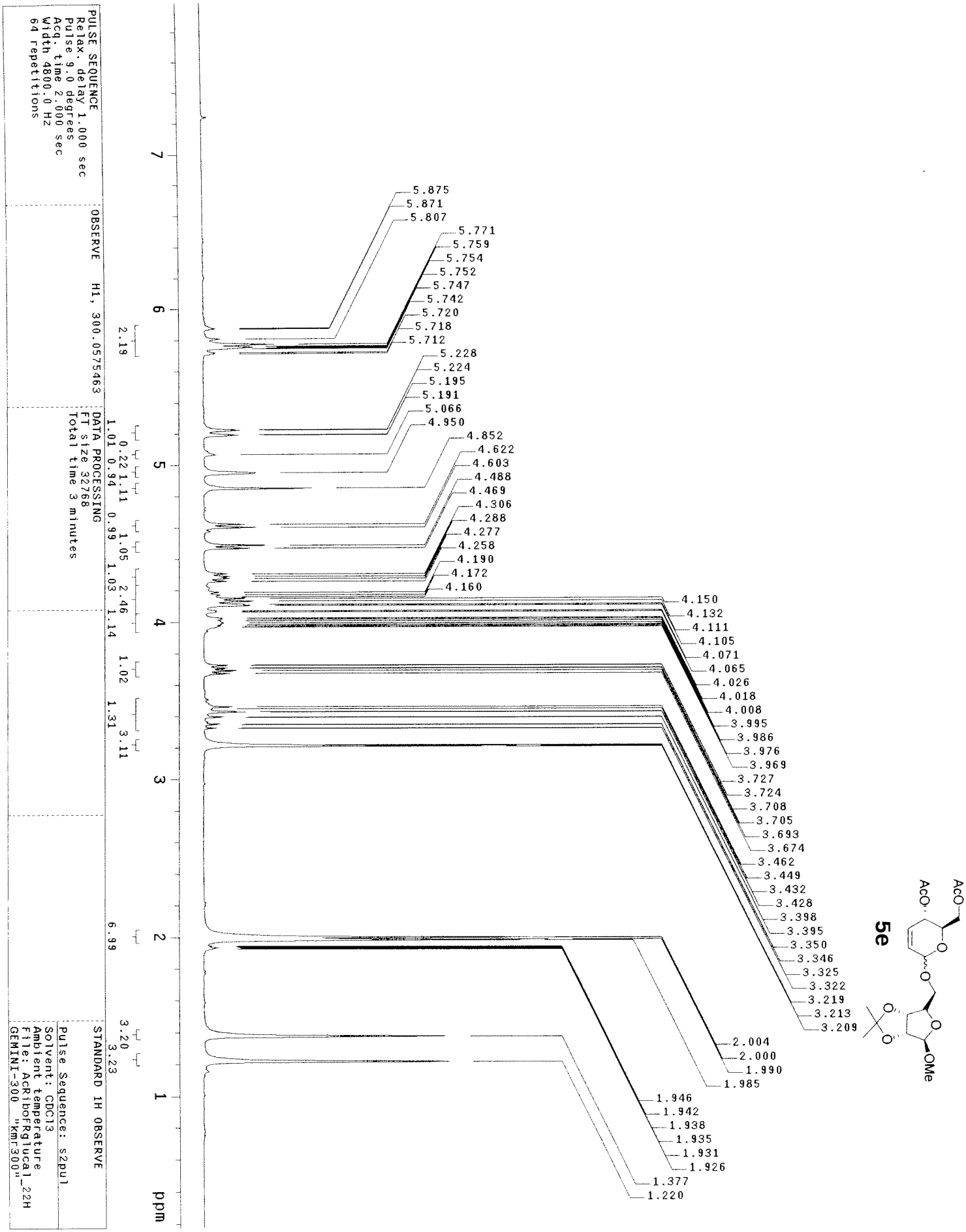

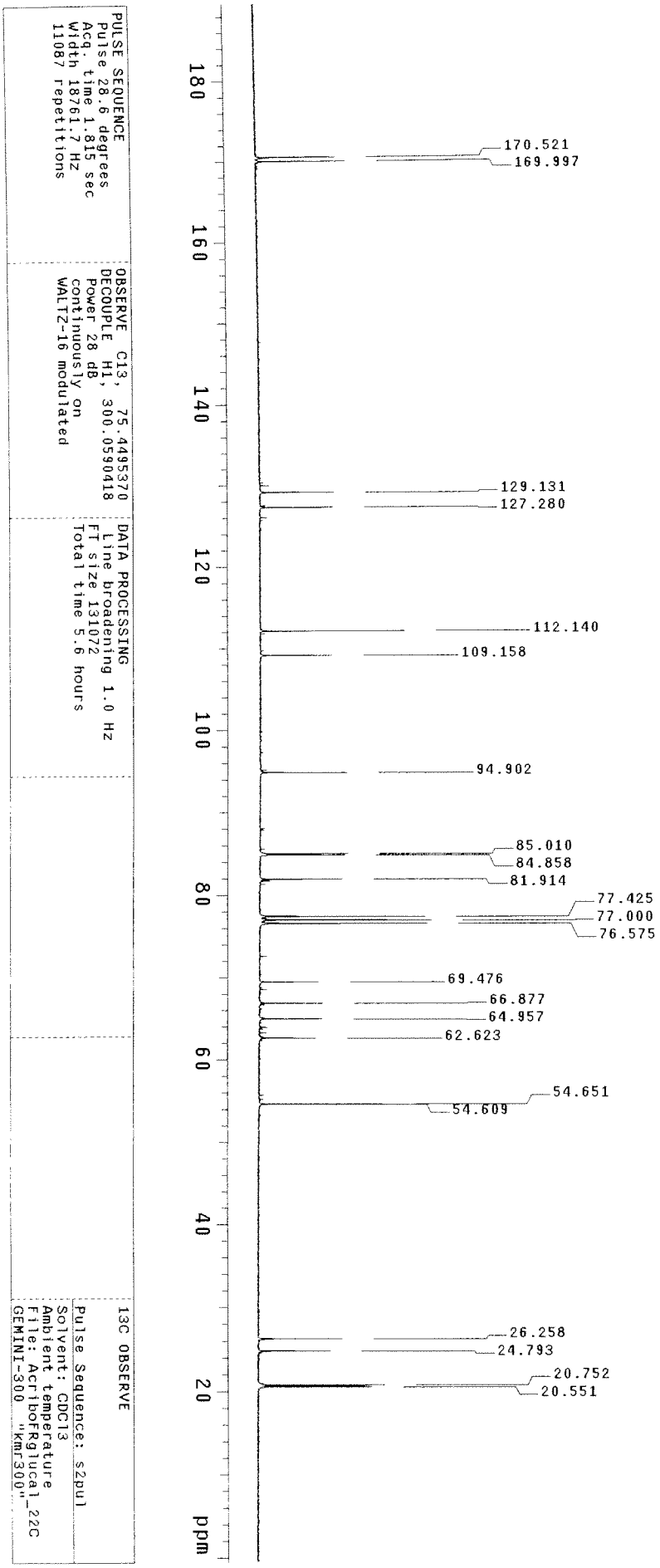

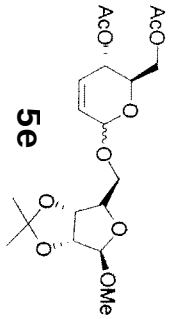

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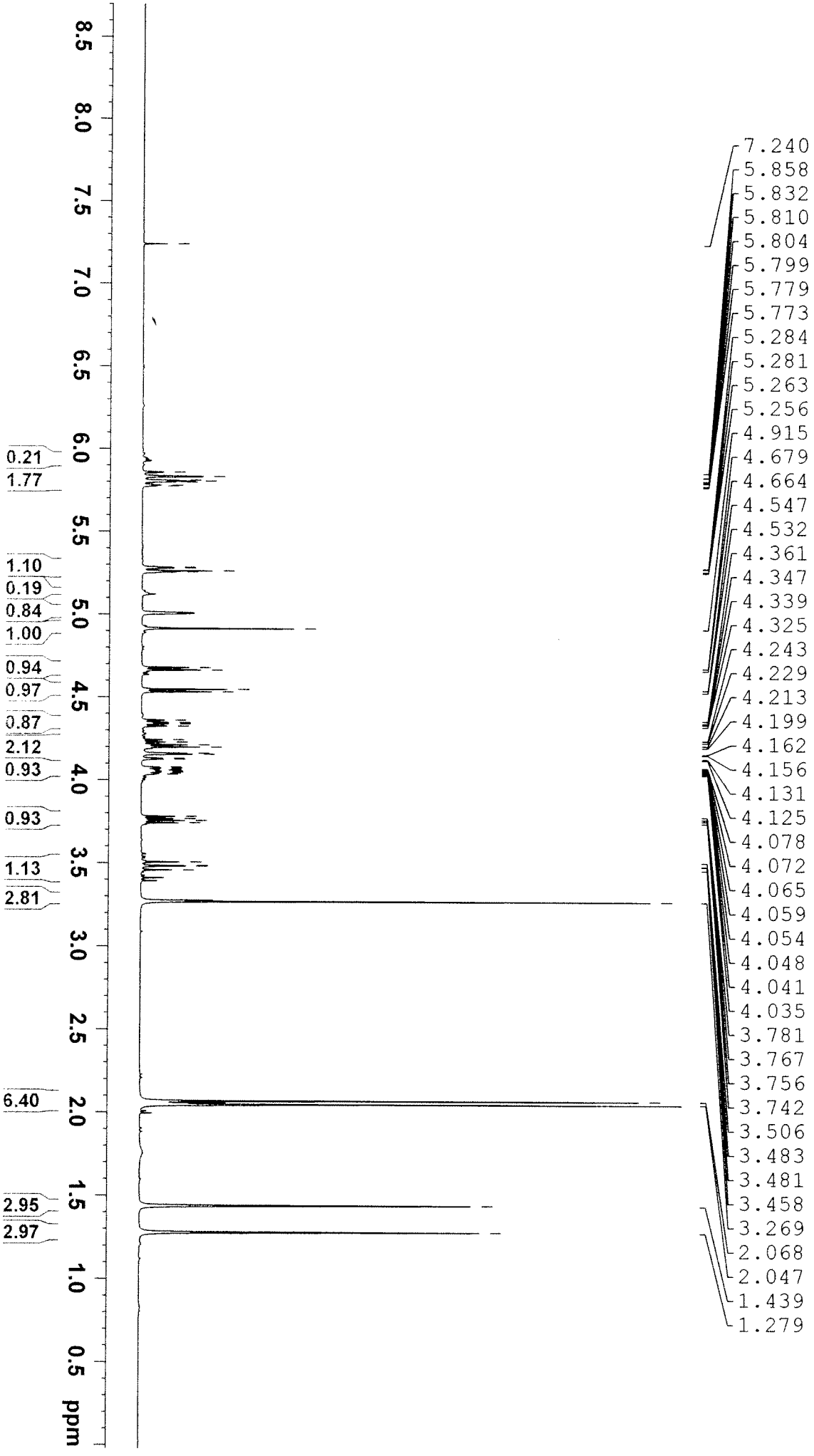

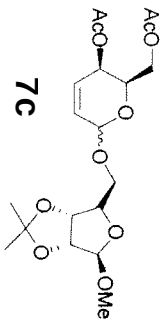

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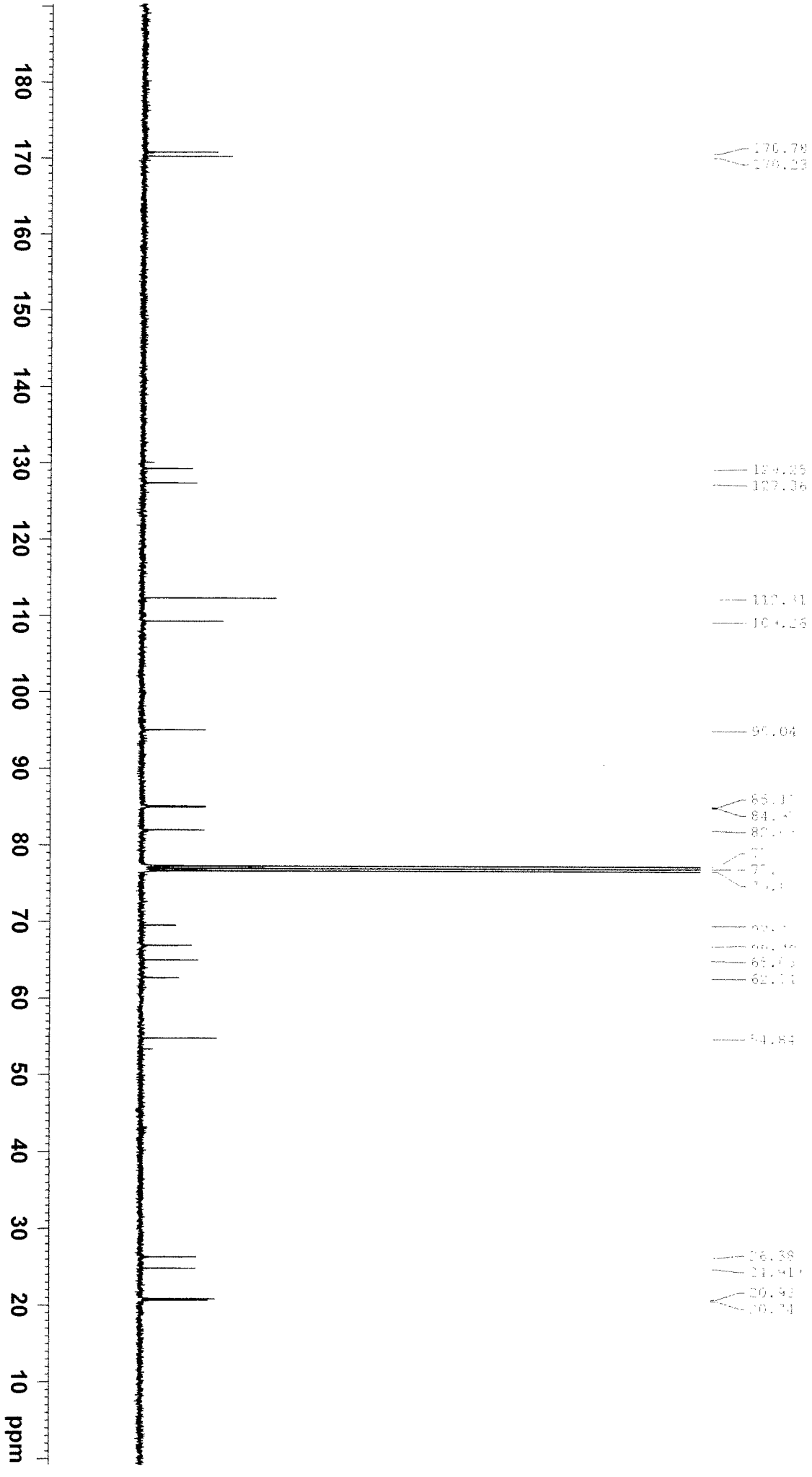

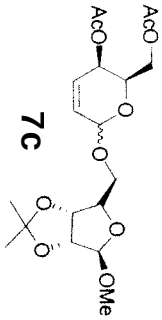

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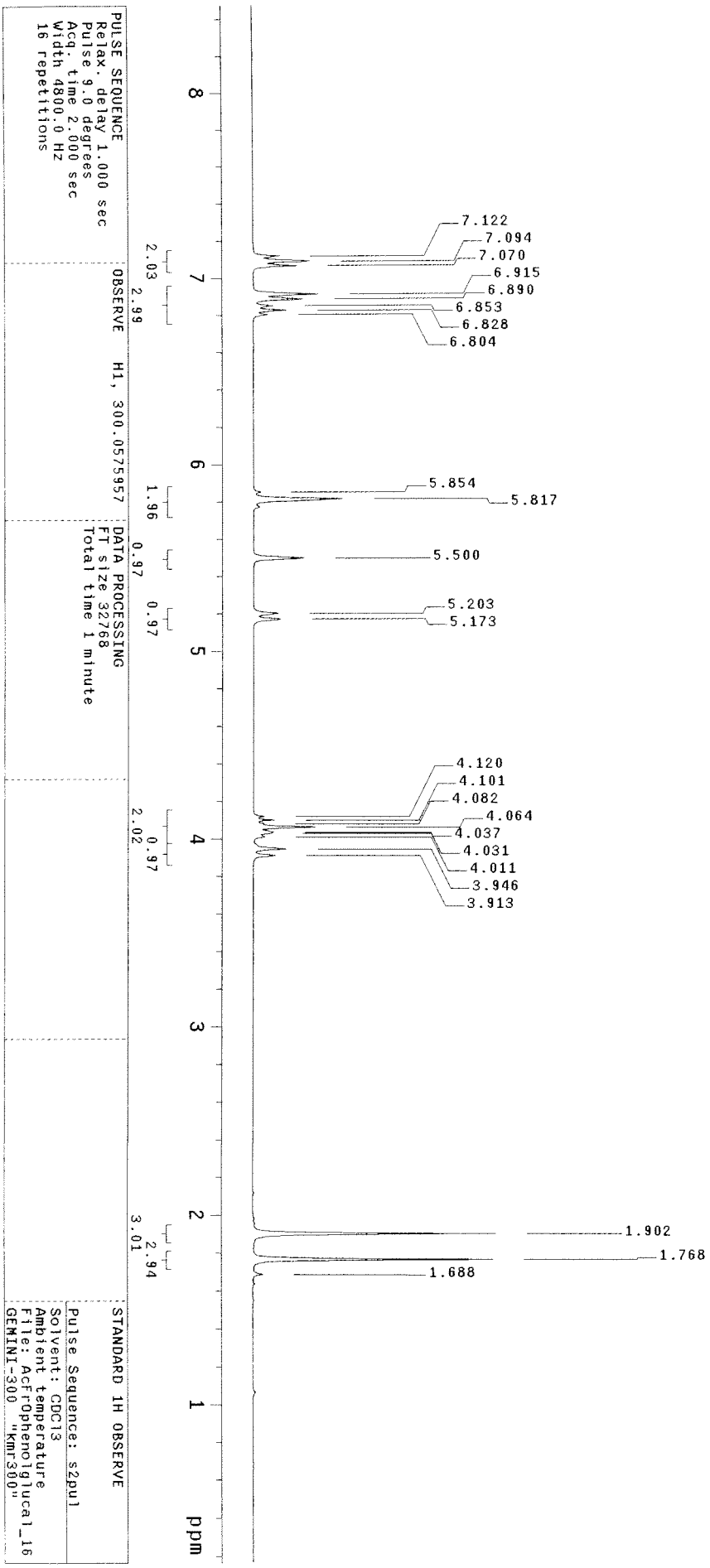

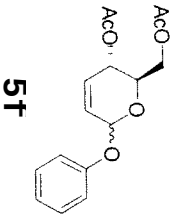

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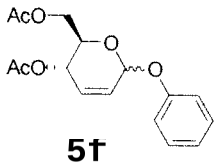

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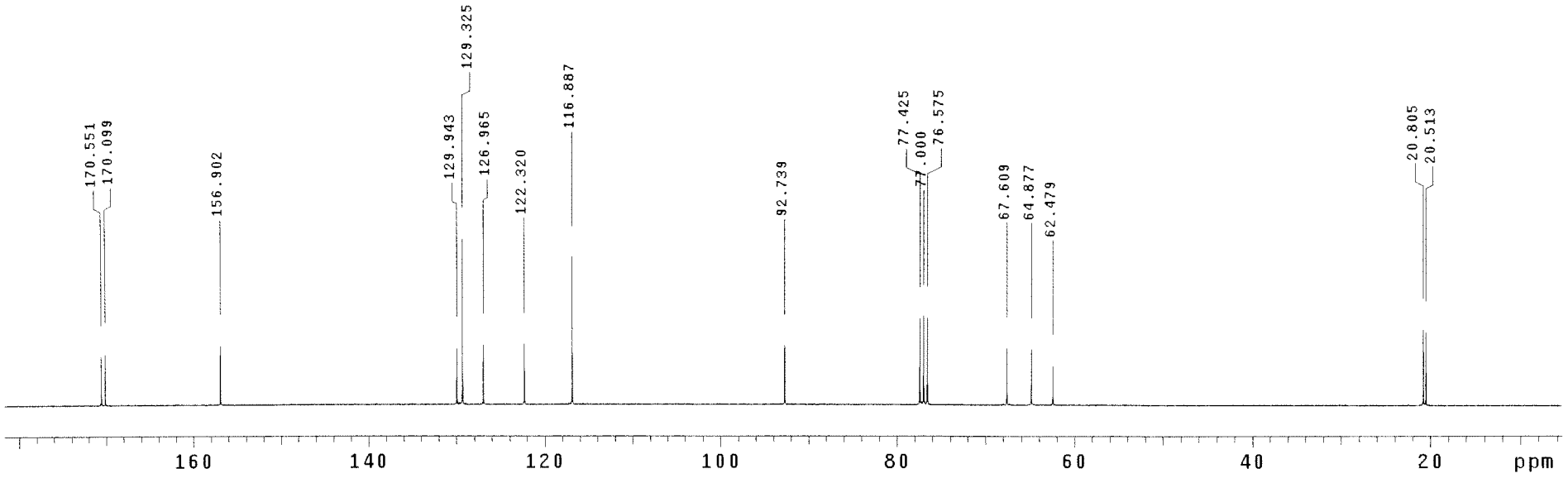

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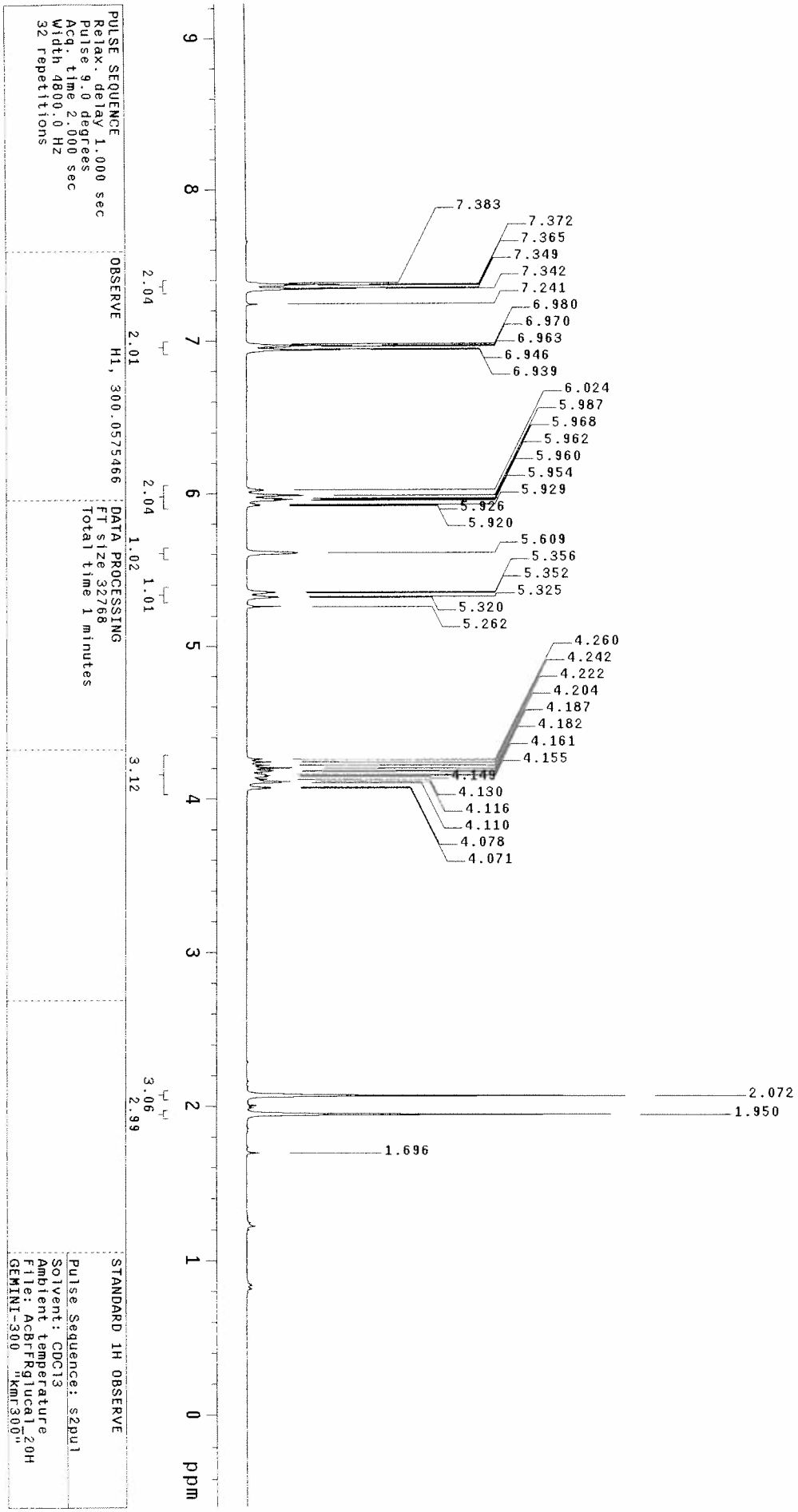

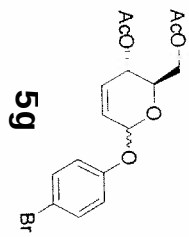

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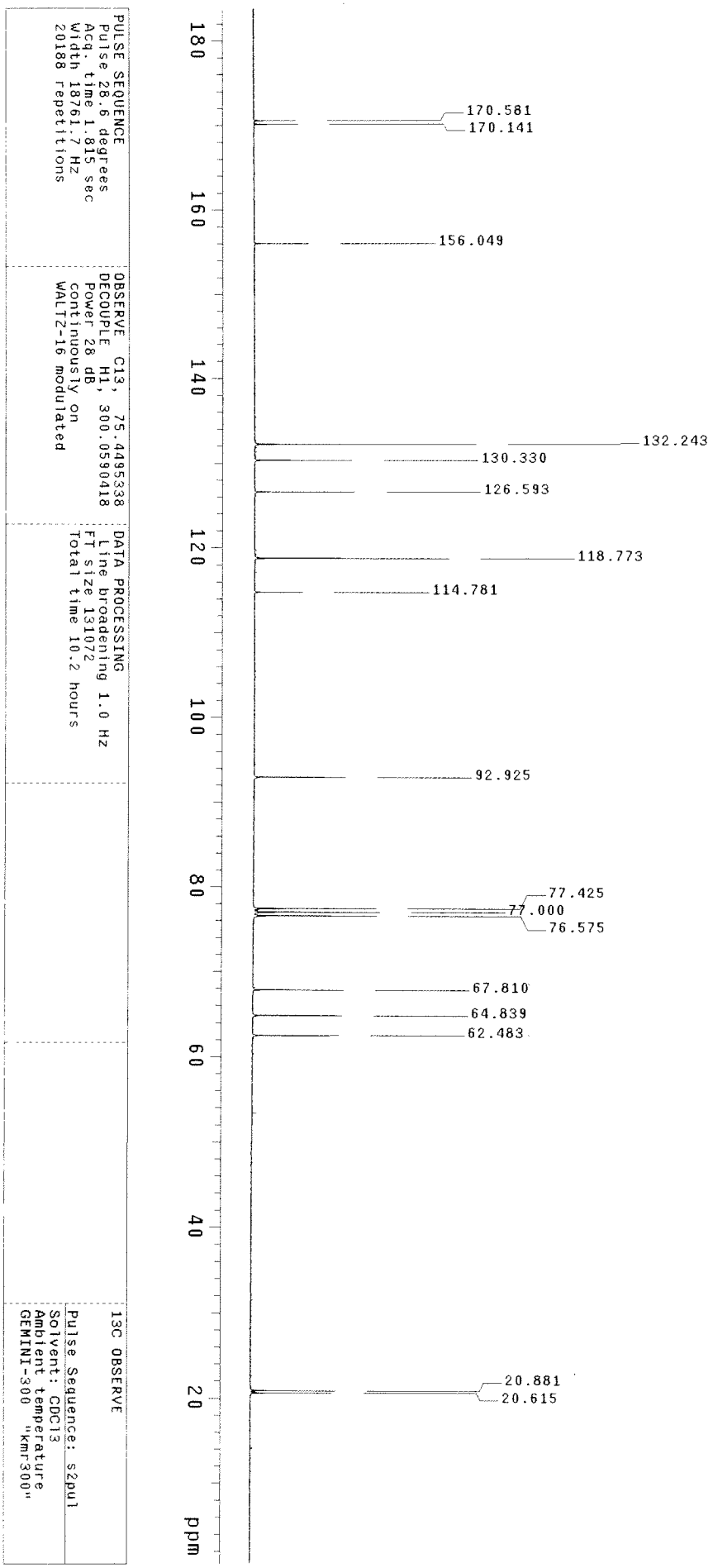

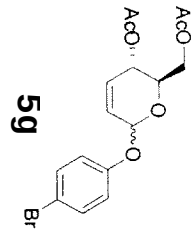

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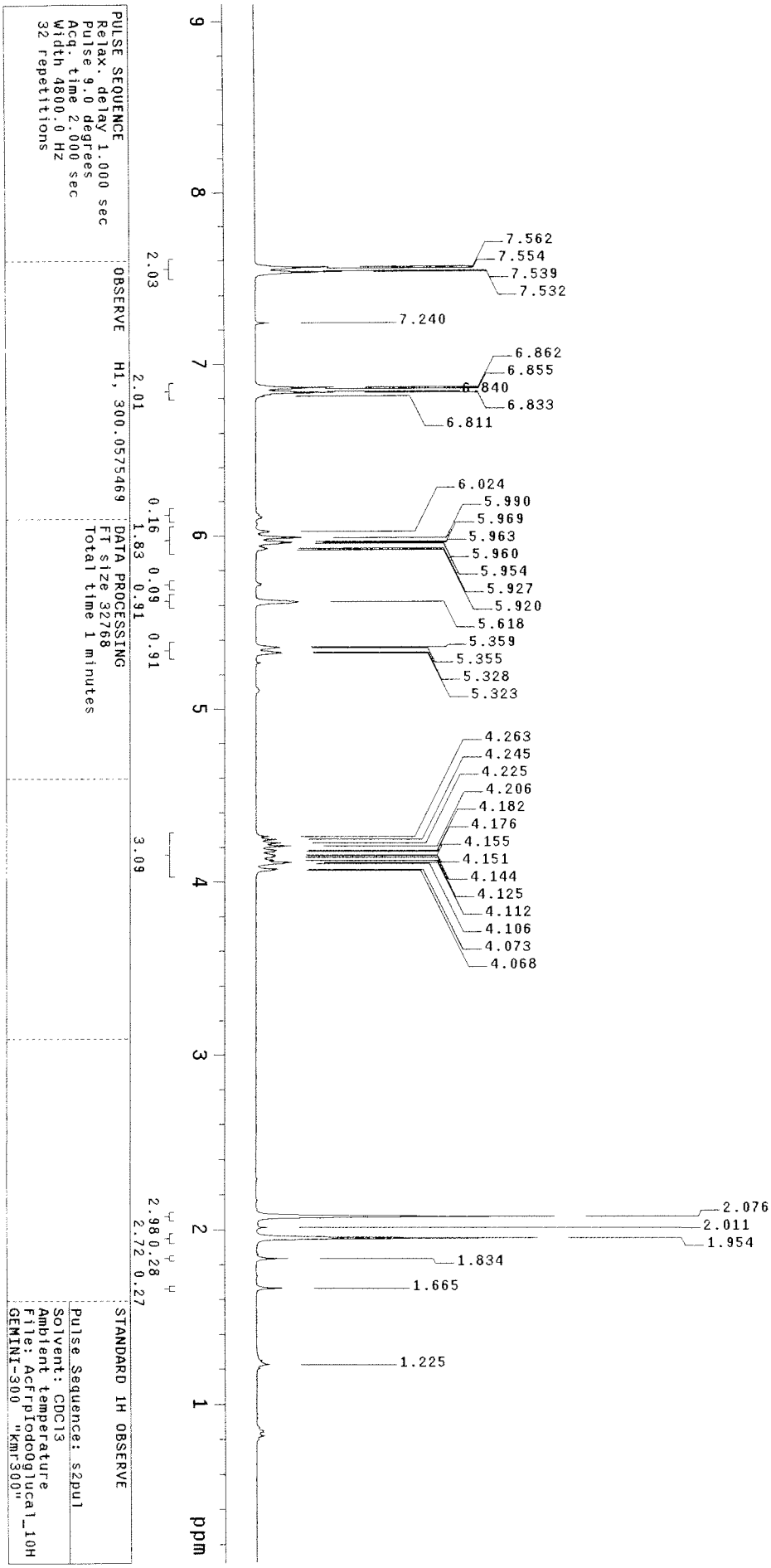

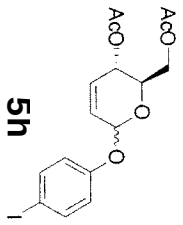

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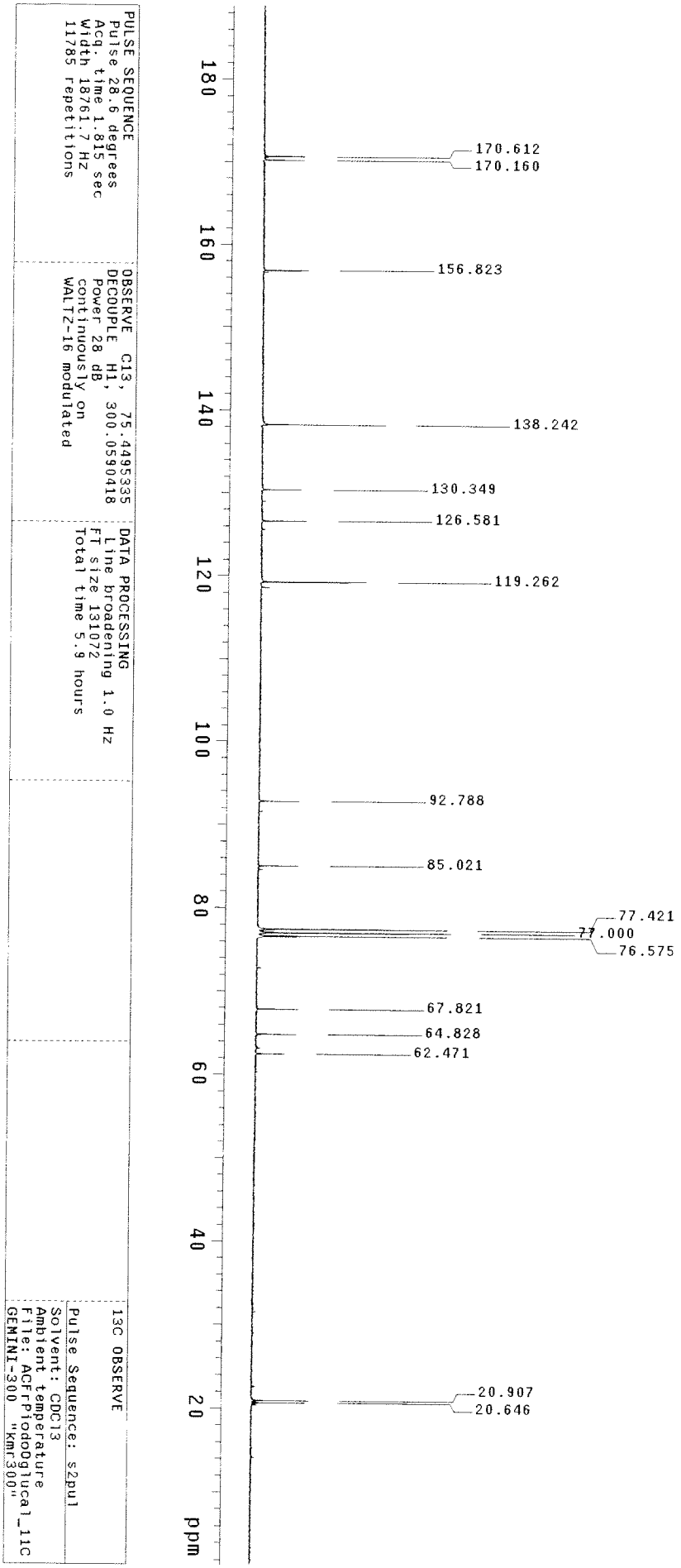

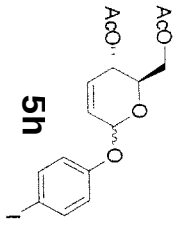

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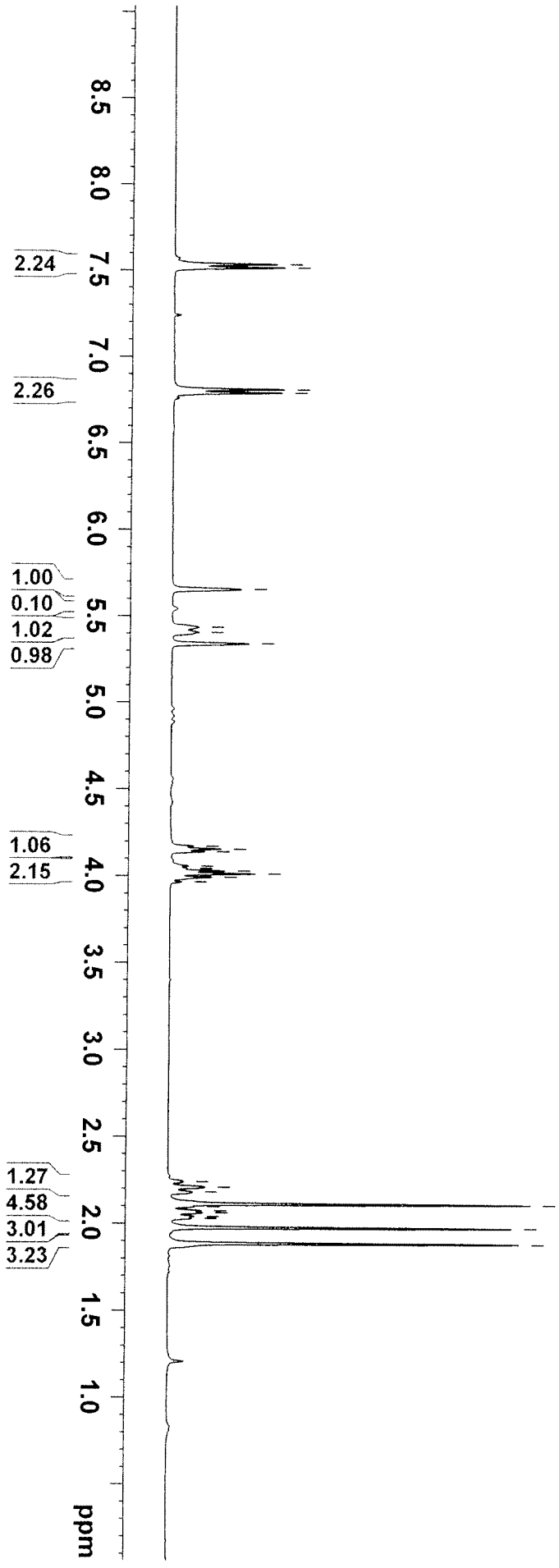

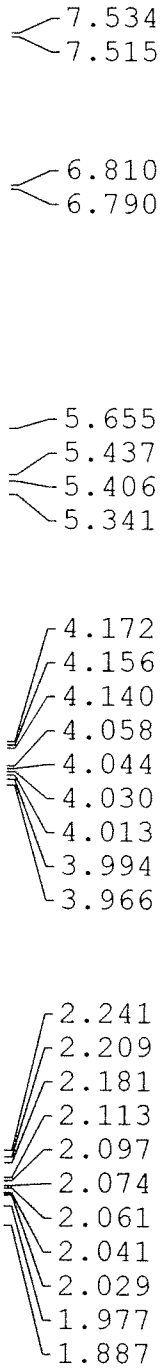

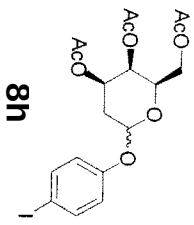

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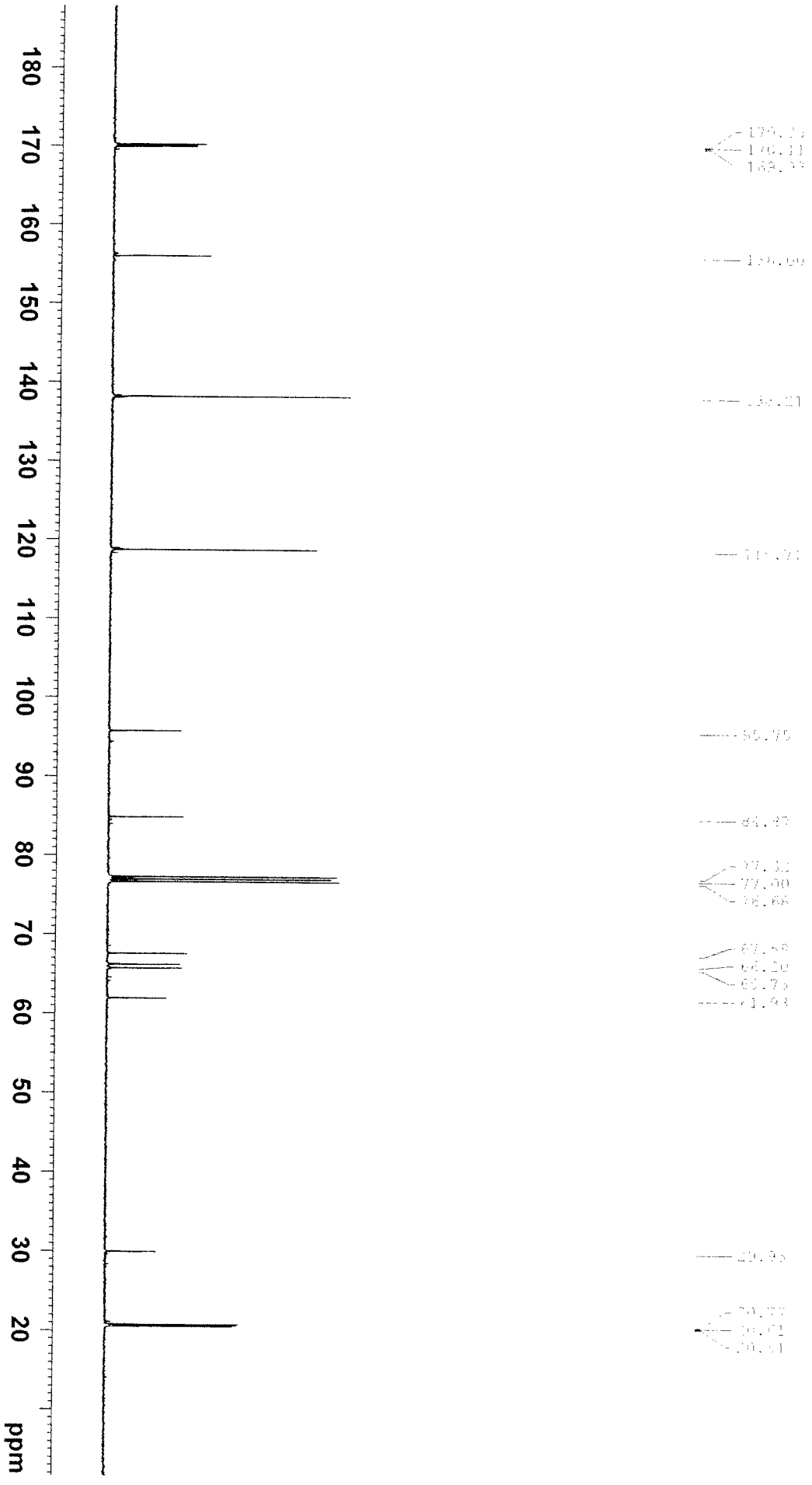

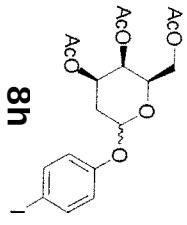

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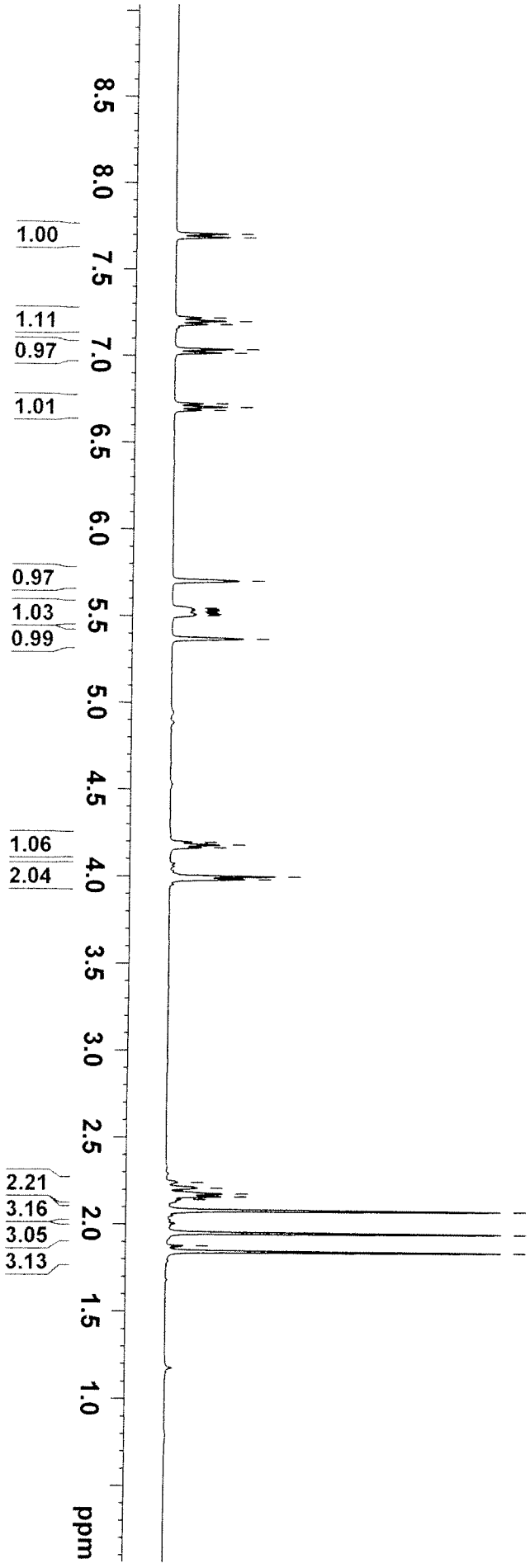

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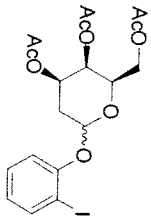

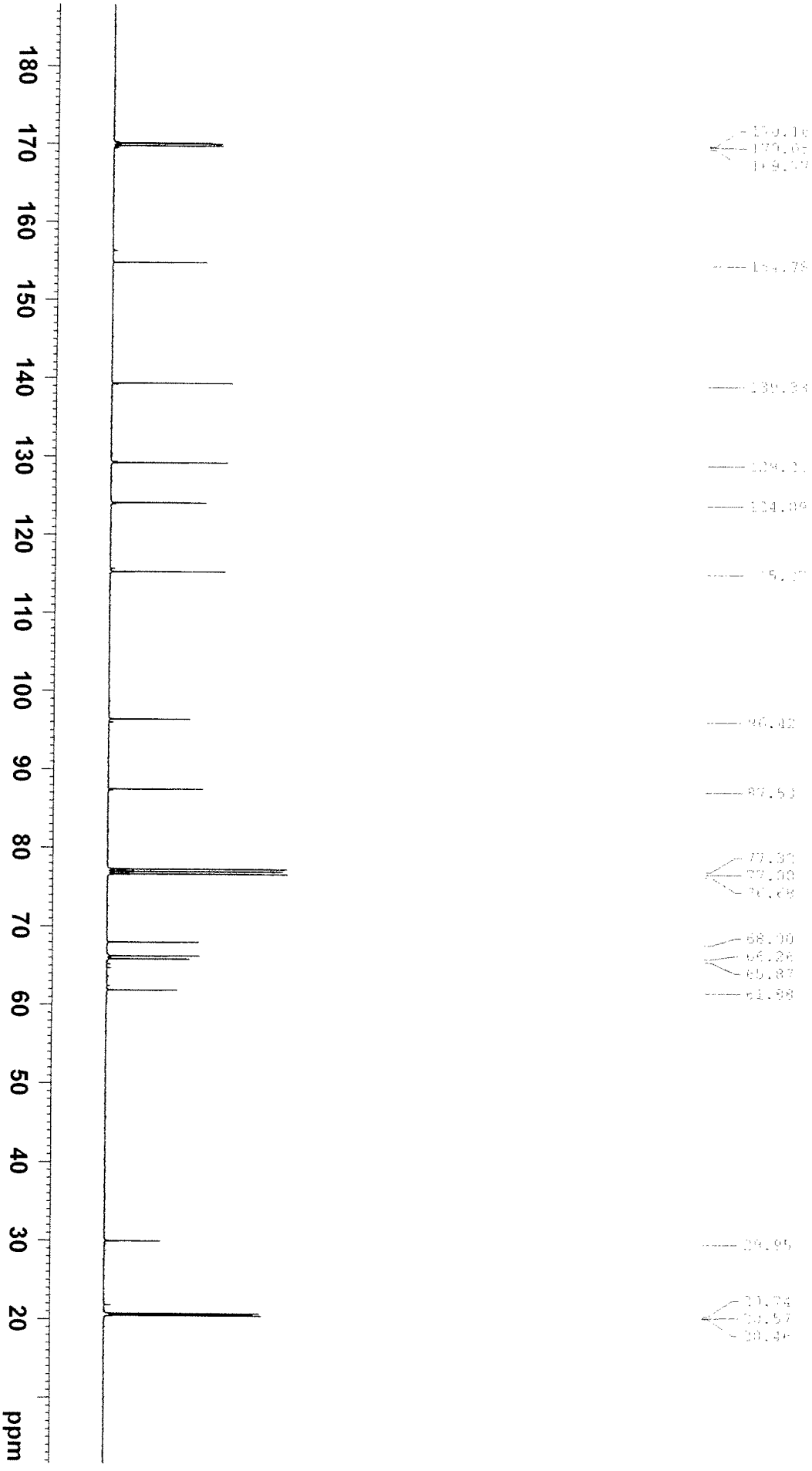

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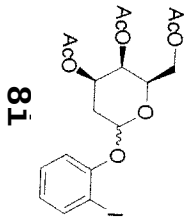

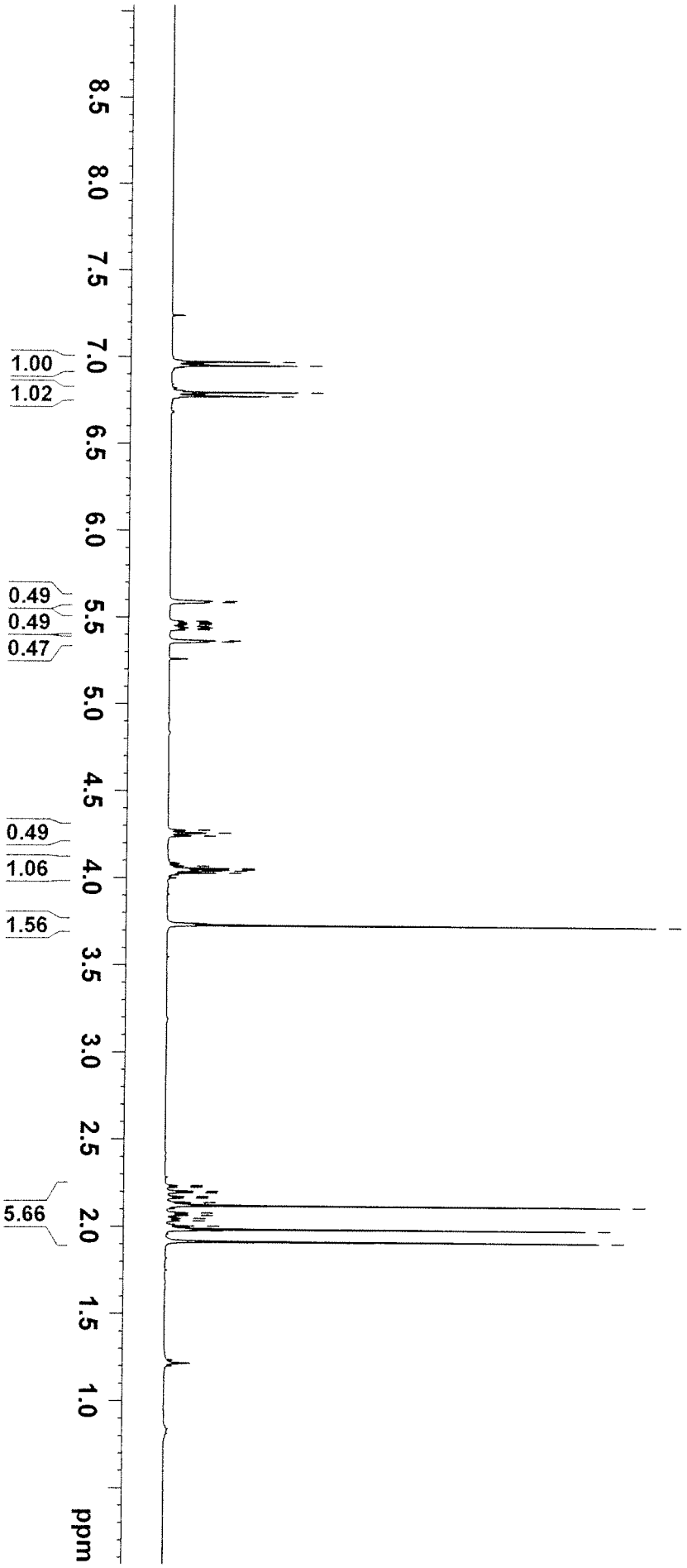

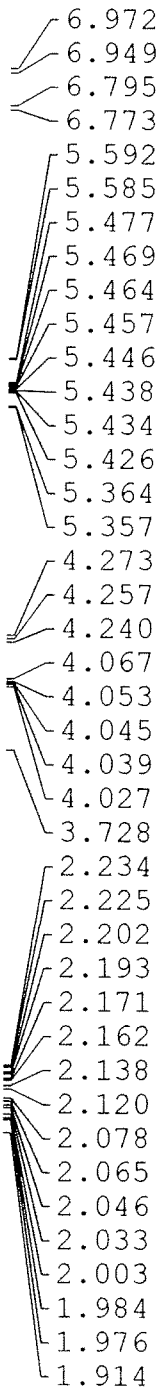

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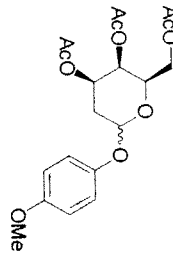

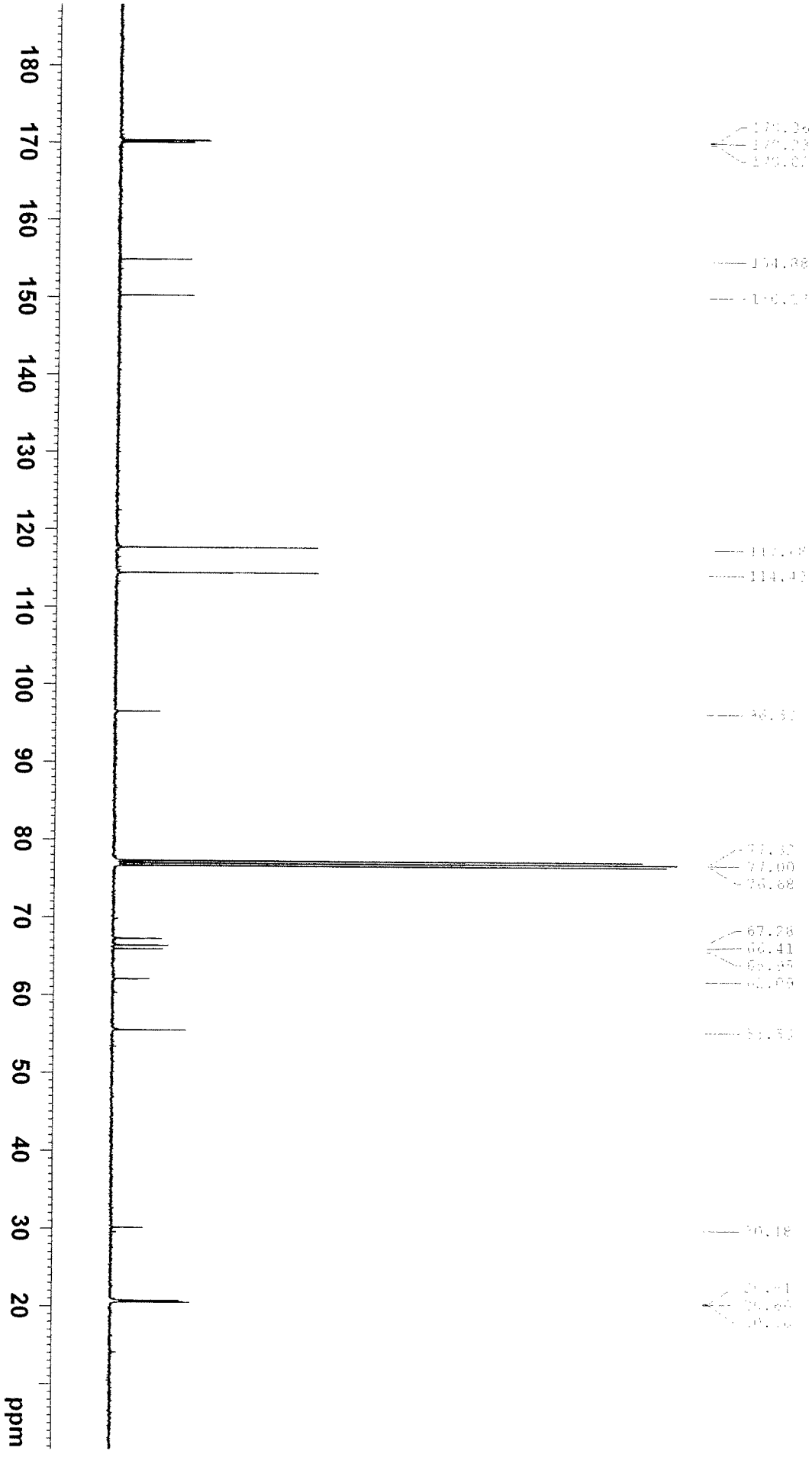

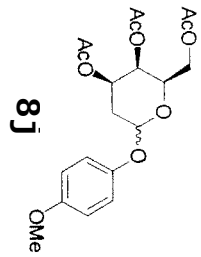

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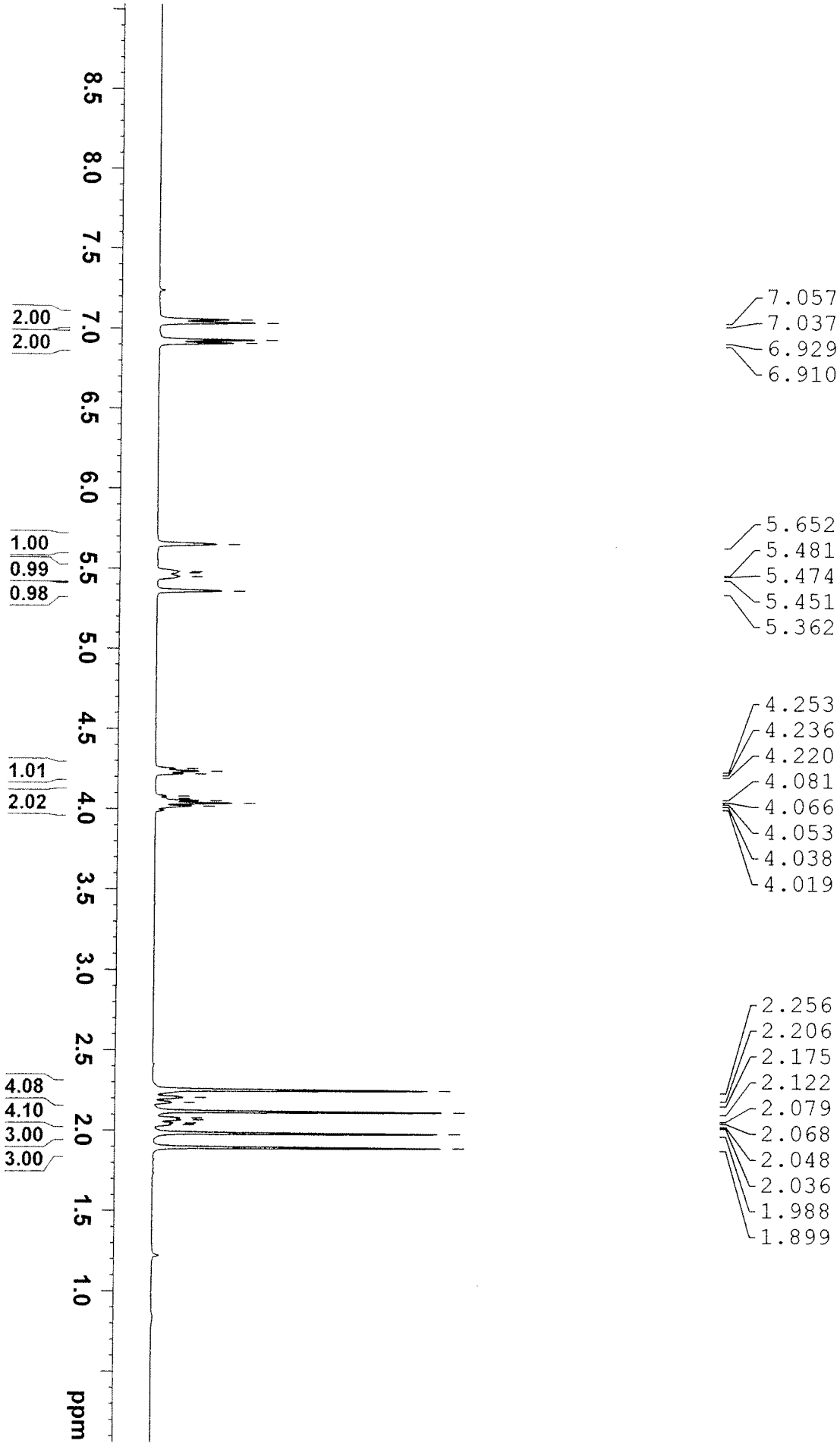

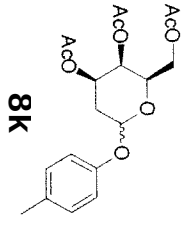

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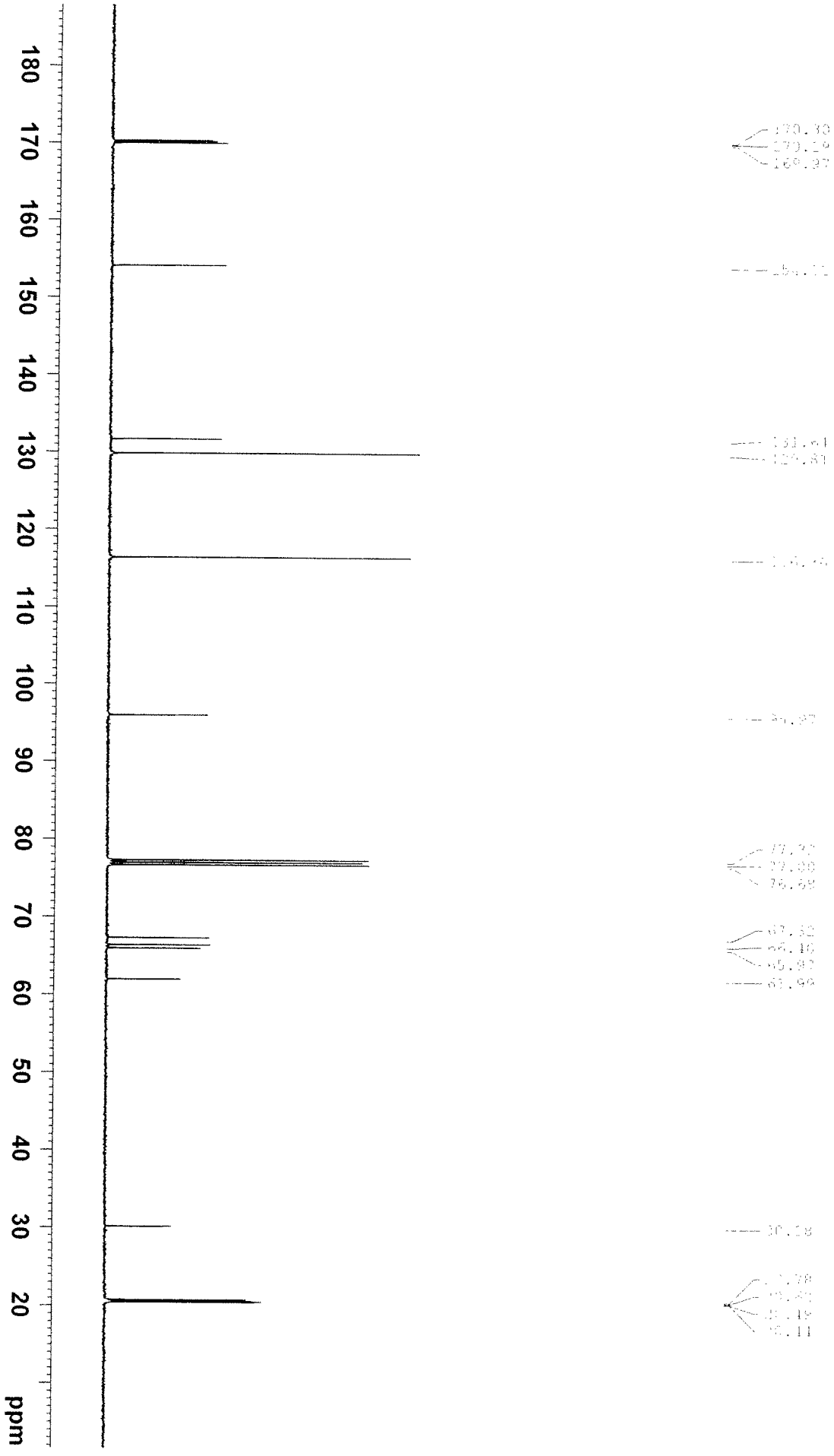

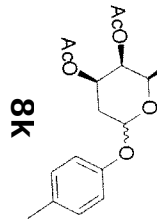

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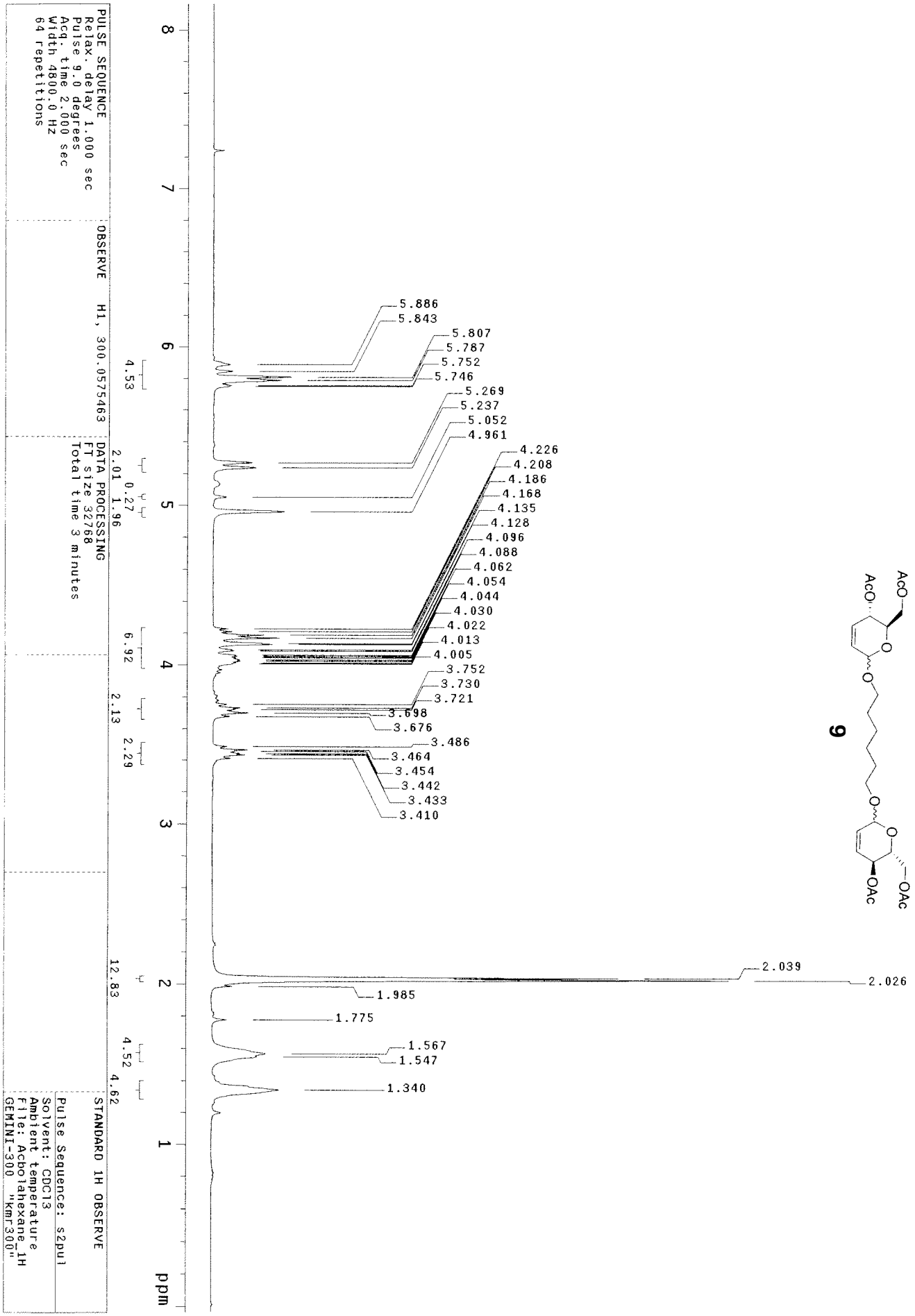

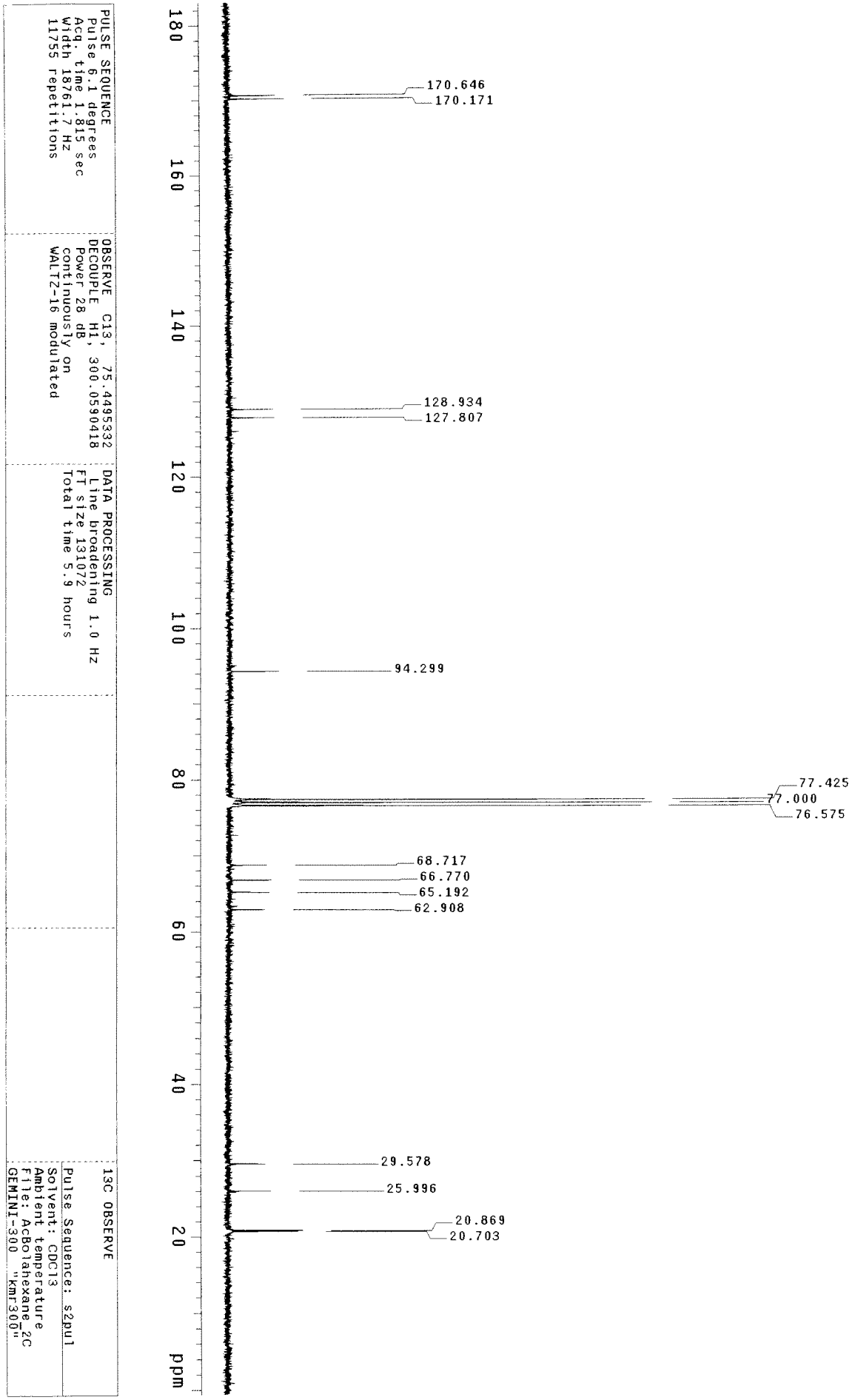

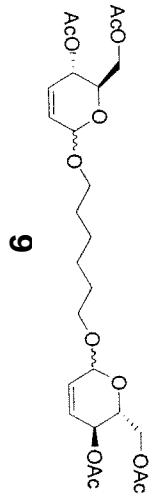

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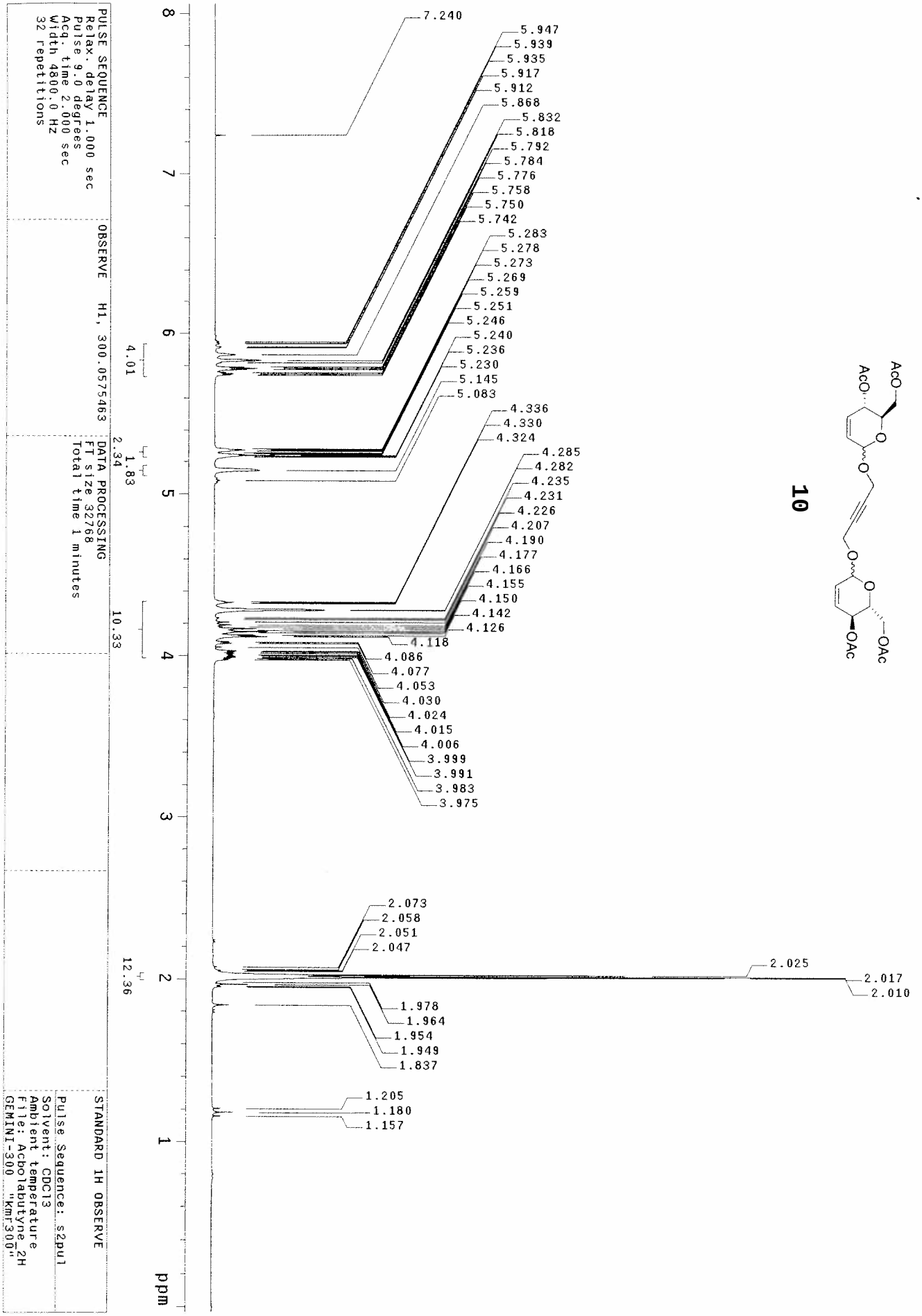

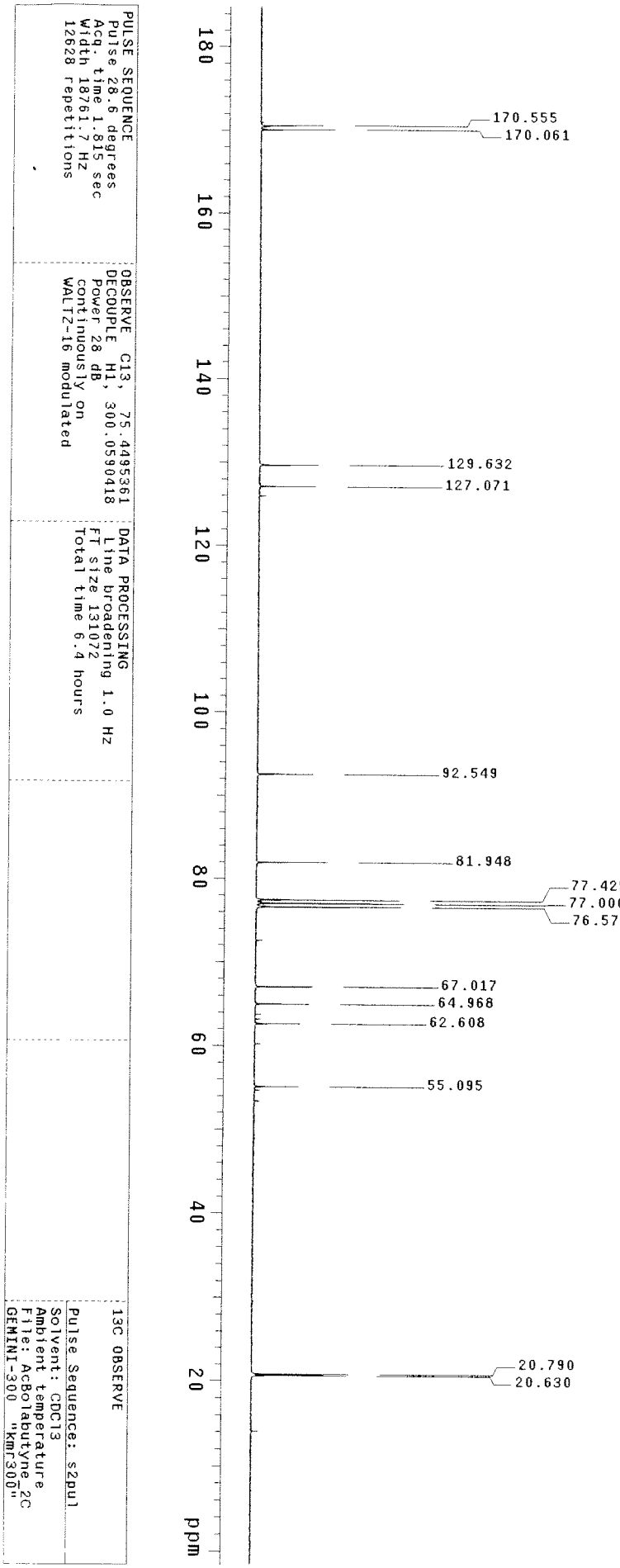

10