

Versatile use of ytterbium(III) triflate and acid washed molecular sieves in the activation of glycosyltrifluoroacetimidate donors. Assemblage of a biologically relevant tetrasaccharide sequence related to Globo-H

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S1-S8 Experimental procedures and analytical data

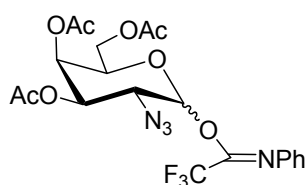
S9-S32 ^1H and ^{13}C Spectra of **2**, **4-6**, **8-14** in CDCl_3 and of **15** in D_2O

General - ^1H and ^{13}C NMR spectra were recorded in CDCl_3 (internal standard CHCl_3 at δ 7.26) or D_2O . Assignment of proton chemical shifts were based on decoupling experiments. Analytical thin layer chromatography (TLC) were performed on aluminium plates precoated with Silica Gel 60 F₂₅₄ as the adsorbent. Column chromatography was performed on Kieselgel 60 (63-200 mesh). Mass spectra were recorded in a reflection positive mode on a MALDI-TOF spectrometer. Acid washed molecular sieves and Ytterbium(III) triflate were dried by overnight heating at 200°C under vacuum before their use in glycosidations.

Preparation of 5Å acid washed molecular sieves

Commercial 5Å molecular sieves (UOP Type 5Å, 1/8" rods, purchased from Fluka) were treated three times with a saturated aqueous solution of ammonium chloride for 20 minutes. The sieves were then repeatedly washed with distilled water until neutralization of the washing liquid. The sieves were left to dry at room temperature and then were heated at 200°C under vacuum for 5 hours. The latter procedure was repeated until no further generation of moisture was observed from the sieves upon this treatment.

Synthesis of donor 4

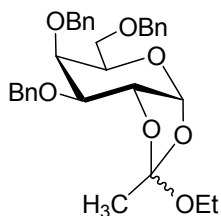


2-azido-3,4,6-tri-*O*-acetylglucopyranose¹ (417 mg, 1.3 mmol) was dissolved in anhydrous dichloromethane (3 mL). To this solution *N*-phenyl trifluoroacetimidoyl chloride² (250 μL , 2 mmol) and sodium hydride (60% suspension in oil, 69 mg, 1.7 mmol) were added at 0°C. After three hours the mixture was concentrated under vacuum and the residue chromatographed on a silica gel column eluted with petroleum ether/ethyl acetate 4:1 (with a few drops of triethylamine) to afford the imidate **4** (496 mg, 76% yield) as an oil.

- 1 Hernandez R.; Leon E. I.; Pilar M.; Riesco-Fagundo C.; Suarez E. *J. Org. Chem.* **2004**, 69, 8437 and references therein.
- 2 Tamura K.; Mizukami H.; Maeda K.; Watanabe H.; Uneyama K. *J. Org. Chem.* **1993**, 58, 32

4 (β : α ca. 2.5:1) ^1H NMR (200 MHz, CDCl_3) : δ 7.40–6.80 (aromatics), 6.46 (1H, bs, H-1 α), 5.60 (1H, bs, H-1 β), 5.53 (1H, bd, H-4 α), 5.42-5.32 (overlapped signals, H-4 β and H-3 α), 4.88 (1H, dd, $J_{2,3} = 9.8$ Hz, $J_{3,4} = 3.2$ Hz, H-3 β), 4.63 (1H, bt, $J_{5,6a} = J_{5,6b} = 6.8$ Hz, H-5 α), 4.30-4.18 (6-CH₂ α and β), 4.05-3.60 (overlapped signals, H-5 β , H-2 α and β), 2.17, 2.07, and 2.00 (3x 3H, 3x s, 3x -COCH₃ β), 2.16, 2.08, and 2.06 (3x 3H, 3x s, 3x -COCH₃ α). ^{13}C NMR and DEPT (50 MHz, CDCl_3): δ (β -anomer) 170.1, 169.8, and 169.5 (COCH₃), 142.8 (aromatic C), 128.7, 124.6, and 119.0 (aromatic CH), 95.5 (C-1), 71.7, 71.0, and 66.0 (C-3, C-4 and C-5), 60.8 (C-6), 59.8 (C-2), 20.4 (COCH₃). Signals of the α -anomer 93.5 (C-1), 69.0, 68.5, and 66.8 (C-3, C-4 and C-5), 61.1 (C-6), 56.8 (C-2). C₂₀H₂₁F₃N₄O₈: calcd C 47.81, H 4.21, N 11.15; found C 47.90, H 4.32, N 10.95.

Synthesis of 7³



Triethylsilane (1.6 mL, 10 mmol) was added to a solution of commercially available penta-*O*-acetyl- β -galactose (3.00 g, 7.7 mmol) and iodine (2.540 g, 10.0 mmol) in anhydrous dichloromethane (15 mL). The mixture was refluxed for 20-30 minutes (the quantitative obtention of the UV visible glycosyl iodide can be monitored by TLC analysis), and then cooled to 0°C. Lutidine (3.0 mL, 31.0 mmol), ethanol (2.2 mL, 46.2 mmol), and TBAB (845 mg, 2.6 mmol) were sequentially added at 0°C

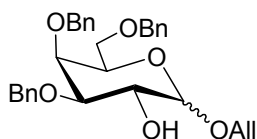
and the mixture was allowed to warm to room temperature. After stirring overnight, the mixture was concentrated under vacuum and the crude product suspended in anhydrous toluene (12.5 mL). After the addition of KOH (10.3 g, 0.183 mol), the mixture was heated up to reflux and benzyl bromide (10.0 mL, 77.4 mmol) was added. After two hours the organic phase was washed with water until neutrality and the collected aqueous phases extracted with dichloromethane. The collected organic phases were then dried and concentrated under vacuum. The residue was purified by a silica gel chromatography (eluent petroleum ether/ethyl acetate 9:1 with a few drops of triethyl amine) to yield orthoester **7** as an oil (2.246 g, 56 % overall yield from peracetylated galactose).

7 (4:1 mixture of diastereoisomers) ^1H NMR of the major diastereoisomer (300 MHz, CDCl_3): δ 7.40-7.15 (aromatic protons), 5.74 (1H, d, $J_{1,2} = 4.8$ Hz, H-1), 4.96-4.40 (7H, m, 3x benzyl CH_2 and H-2), 4.15-4.05 (3H, m, H-3, H-4, and H-5), 3.74-3.55 (4H, m, 6- CH_2 and $-\text{OCH}_2\text{CH}_3$), 1.64 (3H, s, orthoester CH_3), 1.24 (3H, t, $J_{\text{vic}} = 6.9$ Hz, $-\text{OCH}_2\text{CH}_3$).

^{13}C NMR of the major diastereoisomer (50 MHz, CDCl_3): δ 138.1, 137.9, and 137.7 (aromatic C), 128.3-127.5 (aromatic CH), 121.6 (quaternary C orthoester), 97.6 (C-1), 57.7 ($-\text{OCH}_2\text{CH}_3$), 24.7 (orthoester CH_3), 15.1 ($-\text{OCH}_2\text{CH}_3$). Other signals at 80.2, 79.4, 74.4, 73.4, 73.0, 72.8, 71.3, 67.9.

3 Adinolfi M.; Iadonisi A.; Ravidà A.; Schiattarella M. *Tetrahedron Lett.* **2003**, 44, 7863

Synthesis of 8

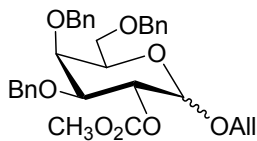


Acetyl chloride (530 μL , 6.75 mmol) was added to a solution of compound **7** (1.312 g, 2.5 mmol) in allyl alcohol (11 mL). The mixture was heated at 70°C for two hours and then concentrated under vacuum. The residue was purified on a short silica gel column (petroleum ether/ethyl acetate 9:1) to afford **8** (1.09 g, 88% yield) as a white solid.

8 (α : β ca 3.5) ^1H NMR of the major anomer (300 MHz, CDCl_3): δ 7.40-7.20 (aromatic protons), 6.00-5.84 (1H, m, $\text{CH}_2-\text{CH}=\text{CH}_2$), 5.26 (1H, bd, $J_{\text{trans}} = 17.1$ Hz, $\text{CH}_2-\text{CH}=\text{CH}_{\text{trans}}$), 5.17 (1H, bd, $J_{\text{cis}} = 12.0$ Hz, $\text{CH}_2-\text{CH}=\text{CH}_{\text{cis}}$), 4.98 (1H, d, $J_{1,2} = 3.9$ Hz, H-1), 4.90-4.39 (6H, 3xAB, 3x benzyl CH_2), 4.24-4.20 (3H, overlapped signals, H-2 and $\text{CH}_2-\text{CH}=\text{CH}_2$), 3.98 (1H, bd, $J_{3,4} = 2.4$ Hz, H-4), 3.94 (1H, bt, $J_{5,6a} = J_{5,6b} = 6.6$ Hz, H-5), 3.71 (1H, dd, $J_{2,3} = 9.6$ Hz, H-3), 3.65-3.50 (2H, m, 6- CH_2). Significant signals of the β anomer at δ 4.27 (1H, d, $J_{1,2} = 7.8$ Hz, H-1), 3.42 (1H, bd, $J_{2,3} = 9.6$ Hz, $J_{3,4} = 2.4$ Hz, H-3).

^{13}C NMR major anomer (50 MHz, CDCl_3) δ 138.3, 138.1, 137.7 (aromatic C), 133.6 ($-\text{CH}_2-\text{CH}=\text{CH}_2$), 128.2-127.4 (aromatic CH), 117.6 ($-\text{CH}_2-\text{CH}=\text{CH}_2$), 97.6 (C-1). Other signals at δ 79.5, 74.5, 73.9, 73.3, 72.3, 69.5, 68.8, 68.7, 68.3. Significant signals of the β anomer at δ 133.8 ($-\text{CH}_2-\text{CH}=\text{CH}_2$), 101.9 (C-1). $\text{C}_{30}\text{H}_{34}\text{O}_6$: calcd C 73.45, H 6.99; found C 73.21, H 6.81.

Synthesis of 9



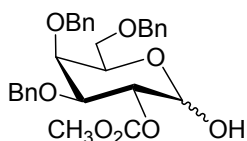
TMEDA (290 μL , 1.9 mmol) and methylchloroformate (200 μL , 2.6 mmol) were sequentially added at 0°C to a solution of **8** (672 mg, 1.4 mmol) in anhydrous dichloromethane (8 mL). After 30' the mixture was diluted with dichloromethane and washed with water and the aqueous phase extracted with dichloromethane. The collected organic phases were concentrated to yield pure **9** (765 mg, quantitative yield) as an oil.

9 (α : β ca 3.5:1) ^1H NMR of the major anomer (200 MHz, CDCl_3): δ 7.45-7.20 (aromatic protons), 6.05-5.80 (1H, m, $-\text{CH}_2-\text{CH}=\text{CH}_2$), 5.40-5.16 (4H, overlapped signals, H-1, H-2, and $-\text{CH}_2-\text{CH}=\text{CH}_2$), 5.04-4.40 (6H, 3x AB, 3x benzyl CH_2), 4.28-3.96 (5H,

overlapped signals, H-3, H-4, H-5, and $-\underline{\text{CH}}_2-\text{CH}=\text{CH}_2$), 3.81 (3H, $-\text{OCH}_3$), 3.70-3.55 (2H, m, 6- CH_2). Significant signals of the β anomer at δ 4.45 (1H, d, $J_{1,2} = 7.8$ Hz, H-1), 3.82 (3H, $-\text{OCH}_3$).

^{13}C NMR major anomer (50 MHz, CDCl_3) δ 155.2 ($-\text{CO}_2\text{CH}_3$), 138.4, 138.2, 137.9 (aromatic C), 133.7 ($-\text{CH}_2-\underline{\text{CH}}=\text{CH}_2$), 128.3-127.3 (aromatic CH), 117.4 ($-\text{CH}_2-\text{CH}=\underline{\text{CH}}_2$), 95.4 (C-1), 54.7 (OCH_3). Other signals at 74.6, 74.5, 73.3, 72.9, 69.4, 68.7, 68.3. Significant signals of the β anomer at δ 155.0 ($-\text{CO}_2\text{CH}_3$), 116.9 ($-\text{CH}_2-\text{CH}=\underline{\text{CH}}_2$), 100.0 (C-1). $\text{C}_{32}\text{H}_{36}\text{O}_8$: calcd C 70.06, H 6.61; found C 70.19, H 6.52.

Synthesis of 10

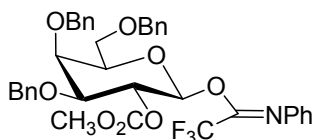


PdCl_2 (51 mg, 0.28 mmol) was added to a solution of **9** (759 mg, 1.4 mmol) in non anhydrous methanol (10 mL). After stirring for 5 hours at room temperature the mixture was concentrated and the residue filtrated on a short silica gel plug (eluent dichloromethane/methanol 95:5) to remove the palladium byproducts. The filtrated was concentrated to yield crude **10** (715 mg) in a satisfying purity to be directly used in the following step.

10 ($\alpha:\beta$ ca 1.5:1) ^1H NMR of the major anomer (200 MHz, CDCl_3): δ 7.45-7.20 (aromatic protons), 5.51 (1H, t, $J_{1,2} = J_{1,\text{OH}} = 3.4$ Hz, H-1), 5.21 (1H, t, $J_{2,3} = 9.6$ Hz, H-2), 4.96-4.38 (6H, 3xAB, 3x benzyl CH_2), 4.17 (1H, bt, $J_{5,6a} = J_{5,6b} = 6.0$ Hz, H-5), 3.99 (1H, dd, $J_{3,4} = 2.8$ Hz, H-3), 3.93 (1H, bd, H-4), 3.78 (3H, s, $-\text{OCH}_3$), 3.65-3.40 (2H, m, 6- CH_2), 2.55 (1H, bd, 1-OH). Significant signals of the β anomer at δ 5.01 (1H, dd, $J_{1,2} = 7.8$ Hz, $J_{2,3} = 9.8$ Hz, H-2), 4.68 (1H, d, $J_{1,2} = 7.8$ Hz, H-1), 3.81 (3H, $-\text{OCH}_3$).

^{13}C NMR major anomer (50 MHz, CDCl_3) δ 155.1 ($-\text{CO}_2\text{CH}_3$), 138.1, 138.1, 137.3 (aromatic C), 128.2-127.3 (aromatic CH), 90.4 (C-1), 54.5 (OCH_3). Other signals at 76.3, 74.6, 74.4, 73.2, 72.8, 69.0. Significant signals of the β anomer at δ 155.7 ($-\text{CO}_2\text{CH}_3$), 95.4 (C-1), 54.9 ($-\text{OCH}_3$).

Synthesis of donor 5

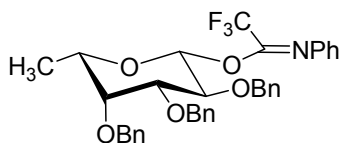


Crude compound **10** (715 mg, 1.4 mmol) was dissolved in anhydrous dichloromethane (7 mL). DIPEA (890 μL , 5.0 mmol) and *N*-phenyltrifluoroacetimidoyl chloride² (560 μL , 4.2 mmol) were added at 0°C . The mixture was stirred for 36 hours at room temperature and then concentrated. The residue was chromatographed on a silica gel column eluted with petroleum ether/ethyl acetate 95:5 (with a few drops of TEA) to yield **5** (658 mg, 73% yield from **8**) as an oil.

5: $[\alpha]_D + 53.6$ (c 0.9 in CH_2Cl_2). ^1H NMR (300 MHz, CDCl_3) δ 7.50-6.80 (aromatic protons), 5.77 (1H, bs, H-1), 5.48 (1H, bt, $J_{1,2} = J_{2,3} = 9.6$ Hz, H-2), 5.04-4.46 (6H, 3x AB, 3x benzyl CH_2), 4.05 (1H, bd, $J_{3,4} = 2.4$ Hz, H-4), 3.88 (3H, s, OCH_3), 3.60-3.85 (4H, overlapped signals, H-3, H-5 and 6- CH_2).

^{13}C NMR (50 MHz, CDCl_3) δ 154.7 (OCO_2CH_3), 143.2, 138.0, 137.6, and 137.4 (aromatic C), 128.6-127.4, 124.2, and 119.2 (aromatic CH), 95.1 (C-1), 55.1 (OCH_3). Other signals at 79.8, 74.6, 74.5, 73.4, 72.4, 67.8. MALDI-TOF MS for $\text{C}_{37}\text{H}_{36}\text{F}_3\text{NO}_8$ (m/z): M_r (calcd) 679.24, M_r (found) 701.94 ($M+\text{Na}$)⁺. $\text{C}_{37}\text{H}_{36}\text{F}_3\text{NO}_8$: calcd C 65.38, H 5.34; found C 65.43, H 5.39.

Synthesis of donor 6

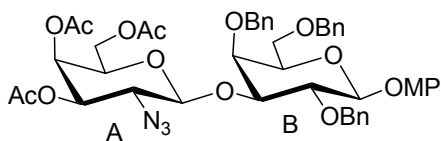


Donor **6** was prepared from the commercially available hemiacetal (purchased from CMS Chemicals) with the same procedure adopted for donor **4**. In this case the chromatographical purification was conducted on neutral alumina (eluent petroleum ether/ethyl acetate 95:5 with a few drops of TEA) to yield **6** (99%) as a white solid.⁴

⁴ Adinolfi M.; Iadonisi A.; Ravidà A.; Schiattarella M. *Synlett* **2004**, 257

6: $[\alpha]_D -92.4$ (c 0.7 in CH_2Cl_2). ^1H NMR (500 MHz, CDCl_3) δ 7.40-6.75 (aromatic protons), 5.58 (1H, bs, H-1), 5.04-4.64 (6H, 3xAB, 3x- benzyl CH_2), 4.04 (1H, bq, $J_{5,6} = 6.8$ Hz, H-5), 3.70-3.50 (3H, H-2, H-3, and H-5), 1.17 (3H, d, 6- CH_3). ^{13}C NMR (50 MHz, CDCl_3) δ 143.5, 138.1, 138.1, and 138.0 (aromatic C), 128.5-127.5, 124.0, and 119.2 (aromatic CH), 97.4 (C-1), 16.5 (C-6). Other signals at 82.3, 77.9, 75.8, 75.4, 74.7, 73.0 and 71.5. $\text{C}_{35}\text{H}_{34}\text{F}_3\text{NO}_5$: calcd C 69.41, H 5.66; found C 69.29, H 5.38.

Synthesis of disaccharide 11



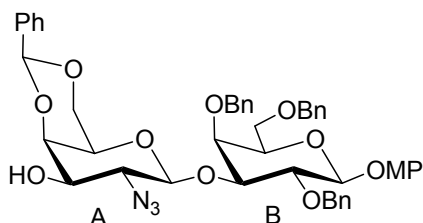
Donor **4** (246 mg, 0.49 mmol) and acceptor **3**⁵ (194 mg, 0.35 mmol) were coevaporated three times with anhydrous toluene and kept for an hour under vacuum. After the addition of freshly activated 4Å AW 300 MS (ca 400 mg in pellets), the mixture was dissolved under argon in anhydrous acetonitrile (1.8 mL) at 0°C. After 15 minutes a solution of $\text{Yb}(\text{OTf})_3$ (21.7 mg, 0.035 mmol) in acetonitrile (1.1 mL) was added. The mixture was allowed to warm to room temperature and left overnight under stirring to ensure complete glycosidation. The reaction was quenched with a few drops of pyridine and the mixture filtered on a short plug of silica gel eluted with 9:1 dichloromethane/methanol (with a few drops of pyridine). The residue was then chromatographed on a silica gel column eluted with petroleum ether/ethyl acetate (from 8:2 to 7:3) to yield pure disaccharide **11** (211 mg, 70%).

⁵ Bazin, H. G.; Du, Y.; Polat, T.; Linhardt, R. J. *J. Org. Chem.* **1999**, 64, 7254

11: $[\alpha]_D -32.6$ (c 0.5 in CH_2Cl_2). ^1H NMR (400 MHz, CDCl_3): δ 7.40–6.80 (aromatic protons), 5.33 (1H, bd, $J_{3,4} = 3.4$ Hz, H-4A), 5.11-4.36 (6H, 3x AB, 3x benzyl CH_2), 4.86 (2H, 2xd, $J_{1,2} = 7.6$ Hz, $J_{1,2} = 8.0$ Hz, H-1 A and B), 4.76 (1H, dd, $J_{2,3} = 11.0$ Hz, H-3 A), 4.22-4.06 (3H, overlapped signals, 6- CH_2 A and H-2 B), 3.98-3.90 (2H, overlapped signals, H-3 and H-4 B), 3.78 (3H, s, - OCH_3), 3.74-3.56 (5H, overlapped signals, H-5 A and B, 6- CH_2 B and H-2 B), 2.16, 2.07, 2.00 (3x3H, 3xs, 3x - COCH_3).

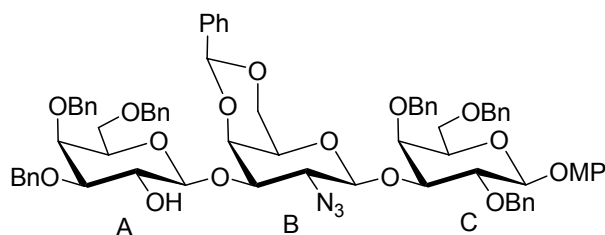
^{13}C NMR (50 MHz, CDCl_3): δ 171.2, 170.2, and 169.4 (COCH_3), 155.3 and 151.5 (oxygenated aromatic C), 138.5, 138.5, and 137.8 (non oxygenated aromatic C), 128.5-127.8 (aromatic CH), 118.5 and 114.5 (aromatic CH methoxyphenol), 103.1 and 102.7 (C-1), 55.6 (OCH_3), 20.6 (COCH_3). Other signals at 80.4, 79.2, 75.7, 75.3, 74.8, 73.7, 73.6, 70.9, 70.6, 68.8, 66.4, 61.4, 61.1. $\text{C}_{46}\text{H}_{51}\text{N}_3\text{O}_{14}$: calcd C 63.51, H 5.91; found C 63.23, H 5.68.

Synthesis of 12



Disaccharide **11** (199 mg, 0.23 mmol) was dissolved in MeOH (9.8 mL). Ammonium hydroxide (32% aqueous solution, 1.1 mL) was then added and the mixture was left under stirring at room temperature. After 3 hours the mixture was concentrated under vacuum and the residue

Synthesis of 14



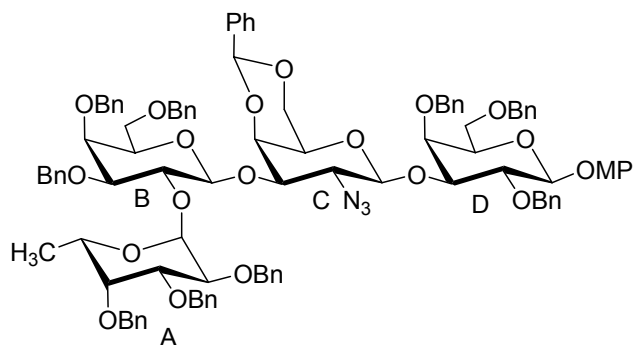
Trisaccharide **13** (119 mg, 0.090 mmol) was dissolved with a saturated solution of K_2CO_3 in MeOH (12 mL, prepared suspending 5 mg of K_2CO_3 per mL of MeOH). The solution was stirred at 40 °C for 8 hours and then diluted with dichloromethane. The organic phase was washed with water and the residue

purified through a short silica gel chromatography (9:1 dichloromethane/methanol) to afford acceptor **14** (107 mg, 89%).

14: $[\alpha]_D -14.1$ (c 0.5 in CH_2Cl_2). 1H NMR (400 MHz, $CDCl_3$): δ 7.50–6.80 (aromatic protons), 5.49 (1H, s, benzylidene non aromatic CH), 5.10–4.54 (12H, 6x AB, 6x benzyl CH_2), 4.93 (1H, d, $J_{1,2} = 7.6$ Hz, H-1 C), 4.84 (2x 1H, 2x d, $J_{1,2} = 7.6$ Hz, H-1 A and C), 4.30–4.20 (2H, H-6a and H-4 B), 4.15–4.05 (3H, H-2 A and C, H-4 C), 3.94–3.80 (4H, H-3 A and C, H-4 A, H-6b B), 3.76 (3H, s, $-OCH_3$), 3.70–3.45 (H-3 B, H-5 A and C, 6- CH_2 A and C), 3.24 (1H, s, H-5 A).

^{13}C NMR (50 MHz, $CDCl_3$): δ 155.0 and 151.6 (oxygenated aromatic C), 138.6, 138.5, 138.5, 137.8, 137.7, 137.7, and 135.9 (non oxygenated aromatic C), 128.9–126.3 (aromatic CH of benzyl and benzylidene), 118.4 and 114.4 (aromatic CH of methoxyphenol), 105.1, 103.0, 103.0 and 101.0 (C-1 and non aromatic benzylidene CH), 55.5 (OCH_3). Other signals at 81.8, 81.1, 79.0, 77.9, 75.7, 75.2, 75.1, 74.7, 74.6, 74.0, 73.9, 73.4, 73.0, 71.4, 69.1, 68.0. $C_{74}H_{77}N_3O_{16}$: calcd C 70.29, H 6.14; found C 70.39, H 6.01.

Synthesis of 2



Trisaccharide **14** (69 mg, 0.055 mmol) and the fucosyl donor **6** (99 mg, 0.16 mmol) were coevaporated three times in anhydrous toluene. After adding 4Å AW 300 MS, the mixture was dissolved under argon in 4:1 dichloromethane/diethyl ether (1.5 mL) and immediately cooled to -30 °C. After stirring for 15 minutes, a solution of ytterbium triflate (3.4 mg, 5.5 μ mol) in dioxane (300 μ L) was added

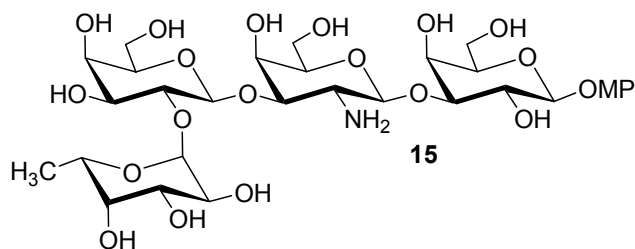
dropwise. After three hours at -30 °C the mixture was allowed to warm to room temperature to ensure the consumption of residual amounts of the donor and the reaction was then quenched with pyridine. The mixture was filtered on a short plug of silica gel washed with 9:1 dichloromethane/methanol (with drops of pyridine). The residue was then purified on a silica gel column eluted with toluene/ethyl acetate (from 5:1 to 3:1) to yield tetrasaccharide **2** (61 mg, 66%) as the only detectable anomer.

2: $[\alpha]_D -38.6$ (c 0.5 in CH_2Cl_2). 1H NMR and COSY (400 MHz, $CDCl_3$): δ 7.50–6.80 (aromatic protons), 5.61 (1H, d, $J_{1,2} = 3.2$ Hz, H-1 A), 5.18–4.40 (18 H, 9x AB, 9x benzyl CH_2), 5.54 (1H, s, benzylidene non aromatic CH), 4.89 (1H, d, $J_{1,2} = 7.6$ Hz, H-1 D), 4.78 (1H, d, $J_{1,2} = 8.0$ Hz, H-1 C), 4.75 (1H, d, $J_{1,2} = 7.6$ Hz, H-1 B), 4.34 (1H, bq, $J_{5,6} = 6.8$ Hz, H-5 A), 4.28–4.15 (5H, H-6a C, H-2 B and D, H-4 B and C), 4.10–3.90 (4H, H-2 A, H-3 B

and D, H-4 D), 3.79 (3H, s, -OCH₃), 3.80-3.50 (H-3 and H-4 A, H-3C, H-5 B and D, 6-CH₂ B and D), 3.26 (1H, s, H-5 C), 0.69 (3H, d, 6-CH₃ A).

¹³C NMR (50 MHz, CDCl₃): δ 155.2 and 151.6 (oxygenated aromatic C), 139.0, 139.0, 138.9, 138.6, 138.4, 138.3, 138.2, 138.0, 137.9, and 137.9 (non oxygenated aromatic C), 128.5-126.3 (aromatic CH of benzyl and benzylidene), 118.5 and 114.4 (aromatic CH of methoxyphenol), 103.6, 103.3, 102.9, 101.2, and 97.8 (C-1 and non aromatic CH of benzylidene), 55.6 (OCH₃), 16.1 (6-CH₃ A). Other signals at 84.0, 81.2, 79.9, 79.1, 78.4, 76.2, 75.5, 75.4, 75.3, 74.9, 74.5, 74.0, 73.5, 73.0, 72.8, 72.6, 72.4, 71.4, 69.1, 68.9, 66.7, 66.4. MALDI-TOF MS for C₁₀₁H₁₀₅N₃O₂₀ (m/z): M_r (calcd) 1679.72, M_r (found) 1702.40 (M+Na)⁺. C₁₀₁H₁₀₅N₃O₂₀: calcd C 72.17, H 6.30; found C 71.90, H 6.45.

Synthesis of **15**

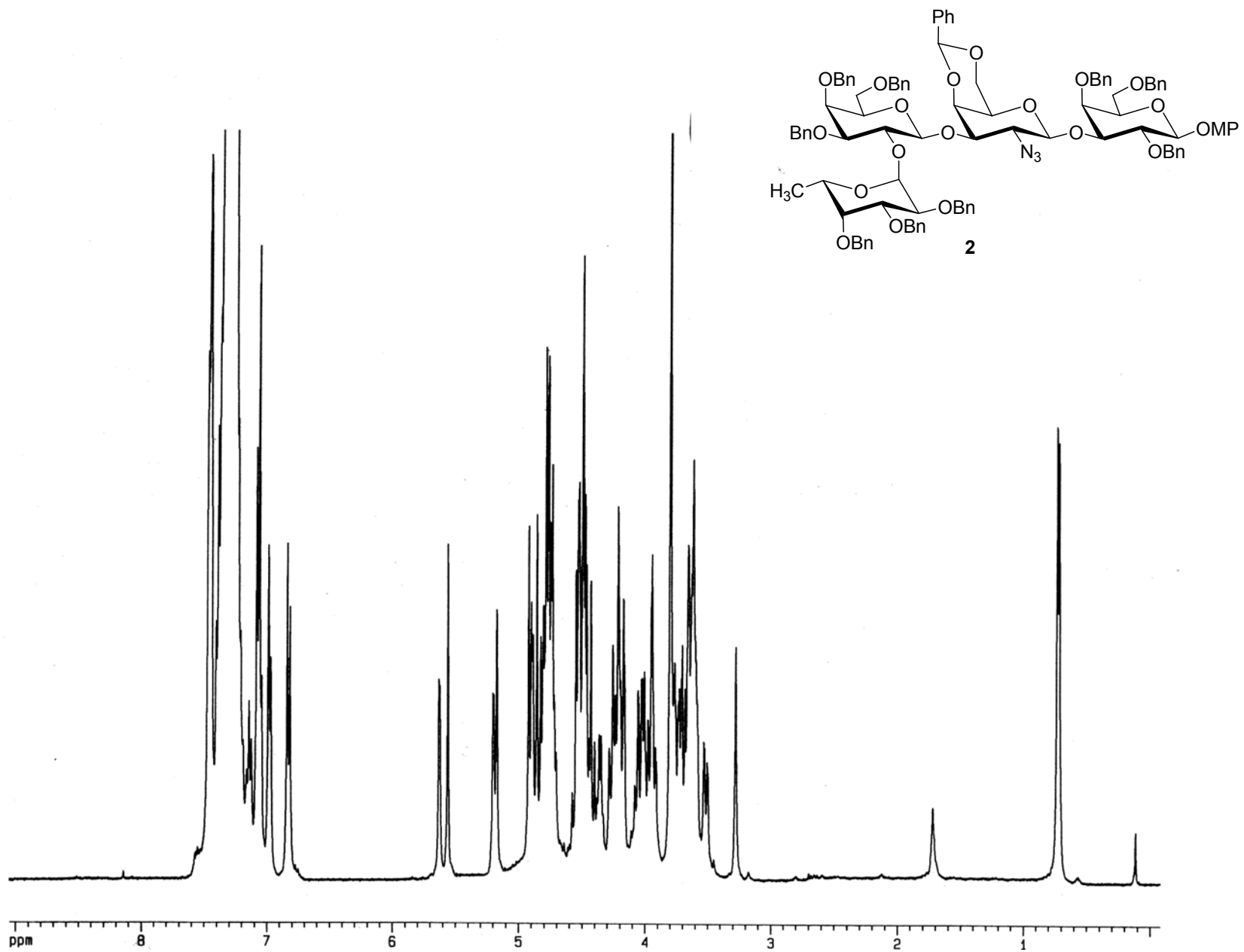


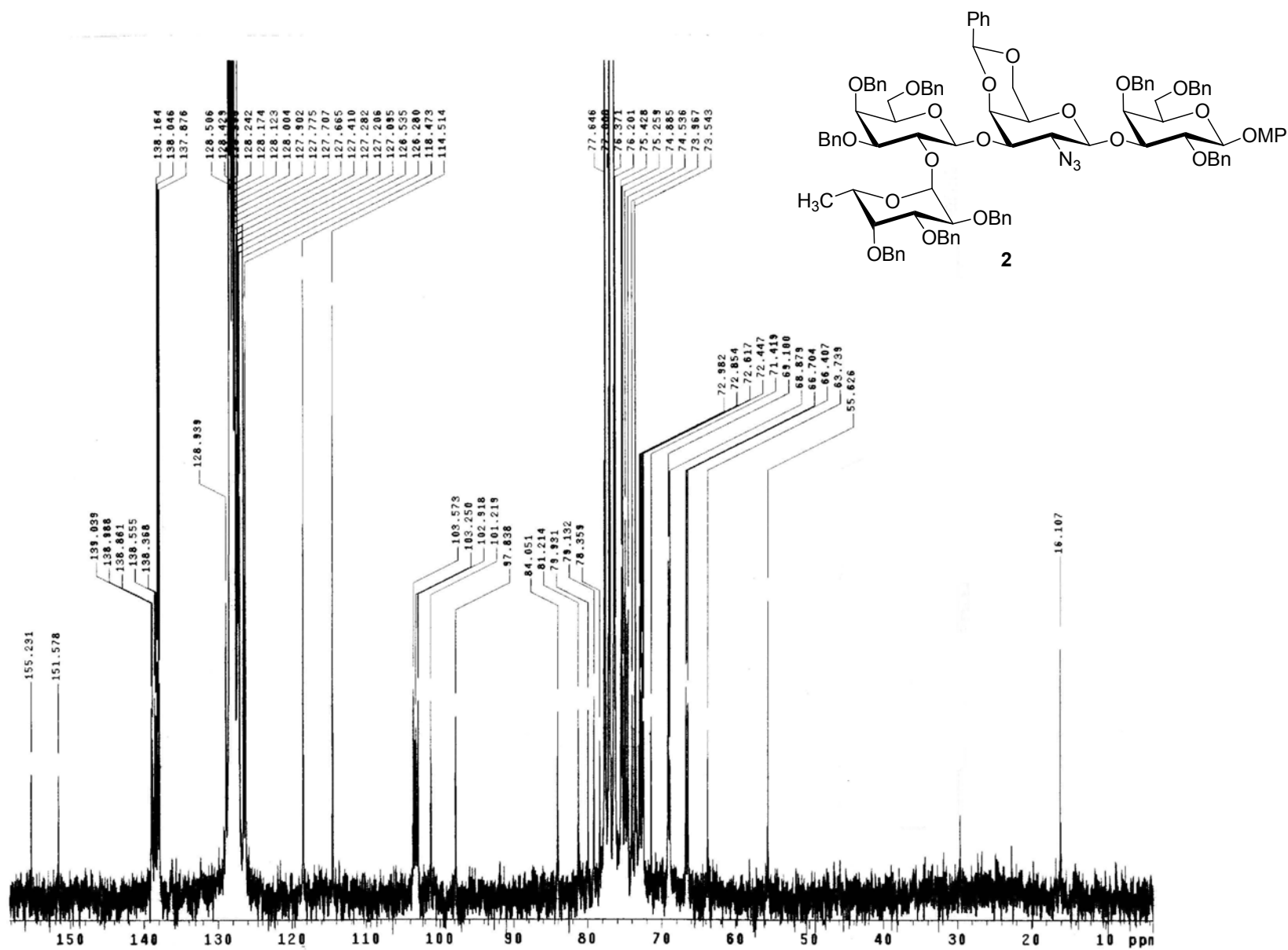
Pd(OH)₂/C (68 mg) was added to a solution of tetrasaccharide **14** (44 mg, 0.026 mmol) in 3:3:1 DCM/MeOH/H₂O (15 mL) and the mixture was hydrogenolized for 72 h at room temperature. The mixture was then filtered on a Celite pad that was washed with 18:13.5:3 MeOH/H₂O/DCM. The

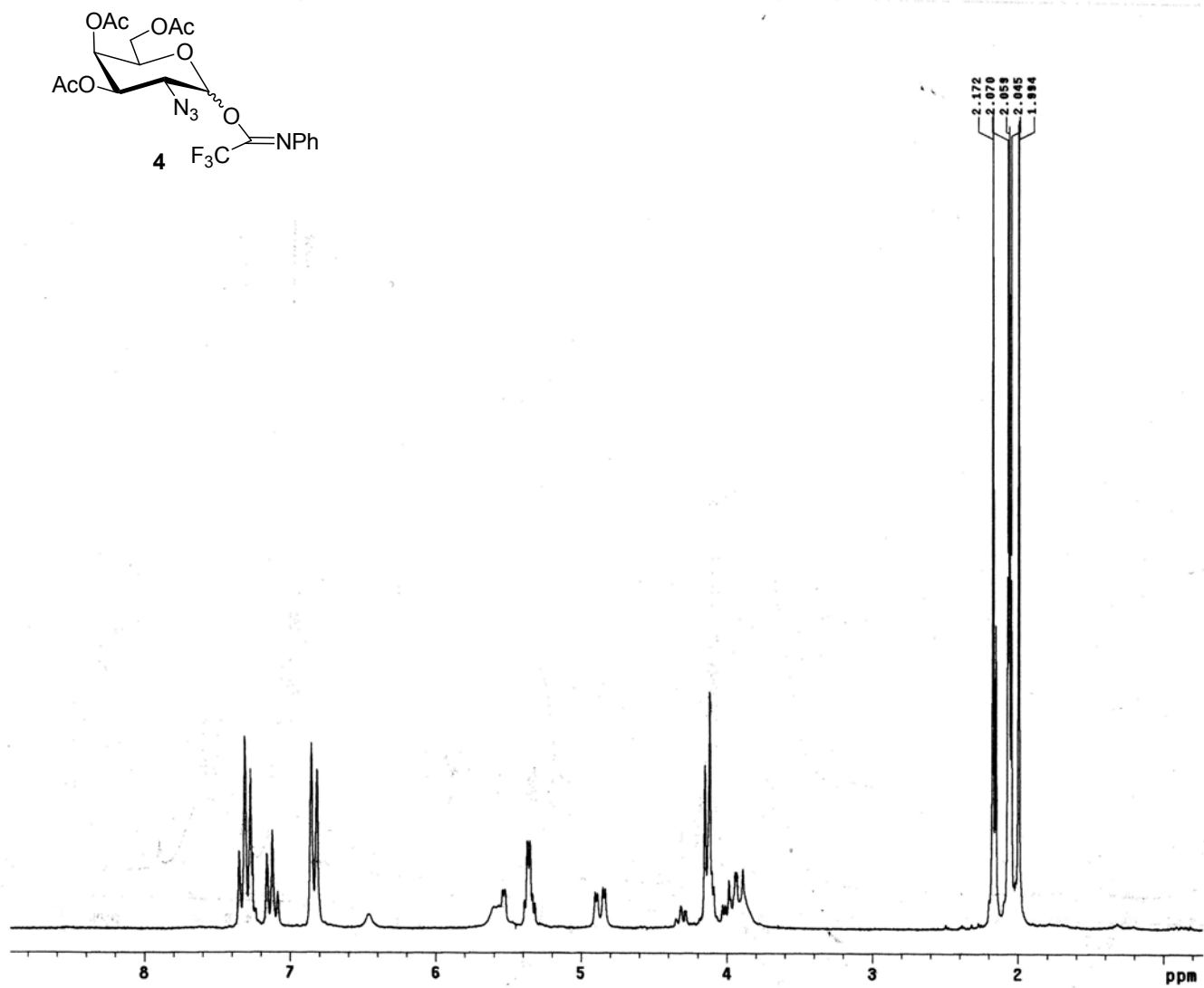
residue from the evaporation of the filtrate was treated with water and the soln was lyophilized to give **15** (18 mg, 90%).

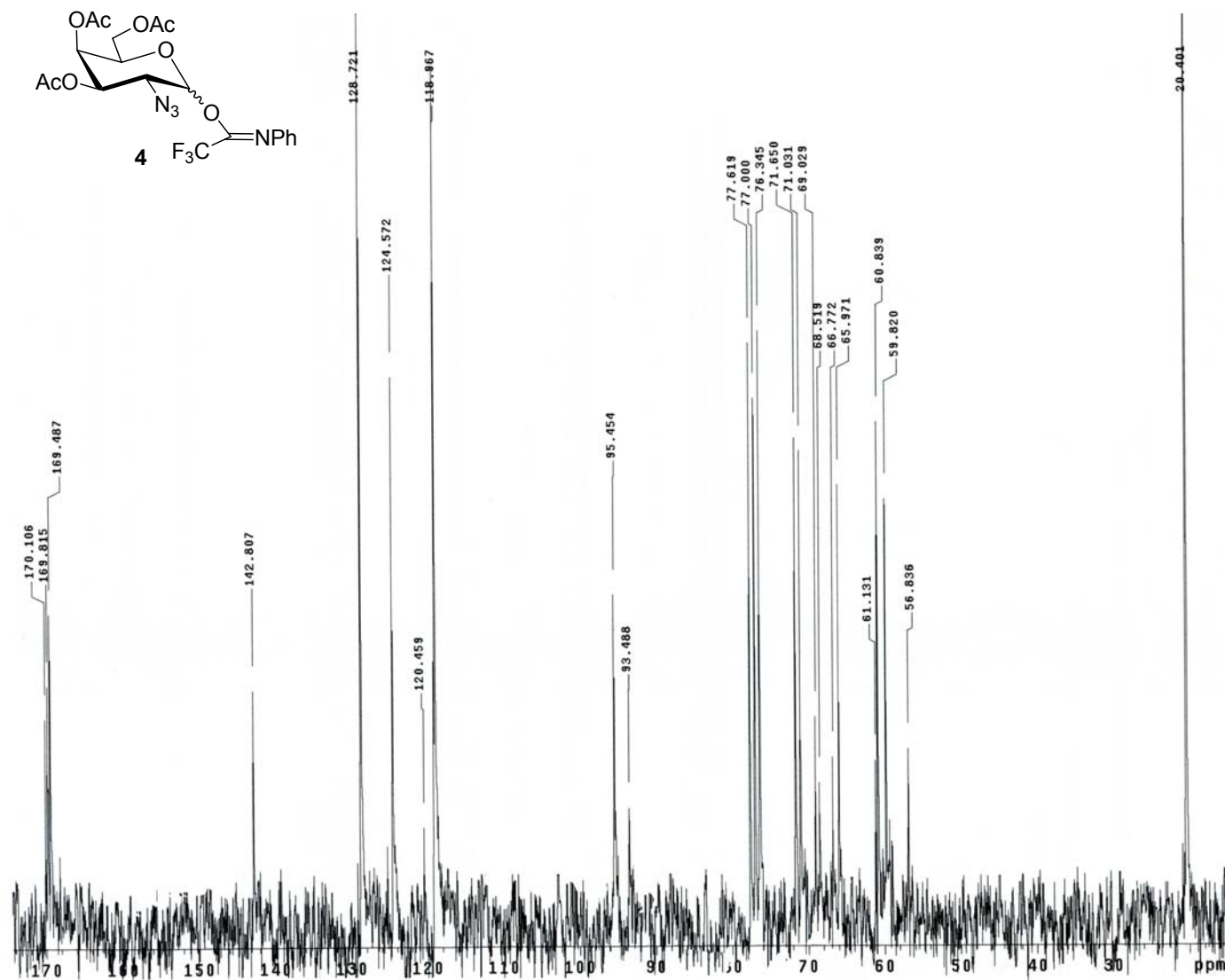
[α]_D - 27.9 (c 0.5 in MeOH). ¹H NMR (500 MHz, D₂O): δ 6.98̄-6.83 (aromatic protons), 5.14 (1H, d, J_{1,2} = 3.5 Hz), 4.90 (1H, d, J_{1,2} = 8.0 Hz), 4.88 (1H, d, J_{1,2} = 8.0 Hz), 4.69 (1H, d, J_{1,2} = 7.5 Hz), 4.24 (1H, bd, J_{3,4} = 3.0 Hz), 4.19 (1H, bq, J_{5,6} = 6.5 Hz), 4.14 (1H, bd, J_{3,4} = 3.0 Hz), 3.90-3.50 (overlapped signals), 3.70 (1H, s, -OCH₃), 3.43 (1H, t, J_{1,2} = J_{2,3} = 8.0 Hz), 1.16 (3H, d, J_{5,6} = 6.5 Hz).

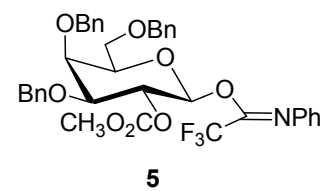
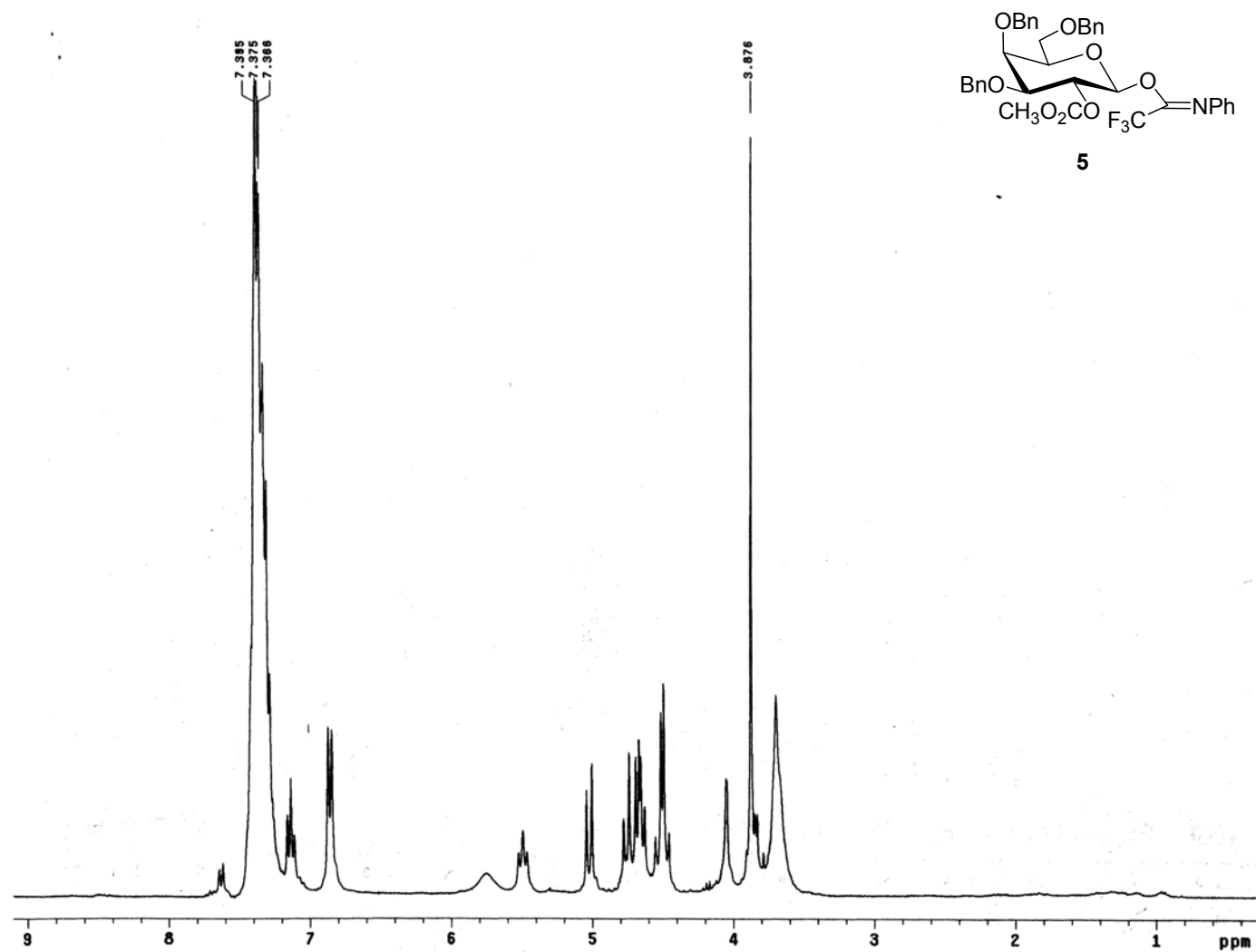
¹³C NMR (125 MHz, D₂O): δ 154.9 e 151.1 (oxygenated aromatic C), 118.4 and 115.2 (aromatic CH of methoxyphenol), 103.2, 101.7, 100.6, 100.2 (4x C-1), 56.0 (OCH₃), 52.8 (C-2 C), 15.9 (6-CH₃ A). Other signals at 81.7, 80.0, 78.2, 75.2, 75.0, 72.0, 71.8, 70.0, 69.6, 69.2, 68.7, 68.6, 68.5, 67.7, 61.0, 60.9. MALDI-TOF MS for C₃₀H₄₇NO₂₁ (m/z): M_r (calcd) 757.26, M_r (found) 780.21 (M+Na)⁺

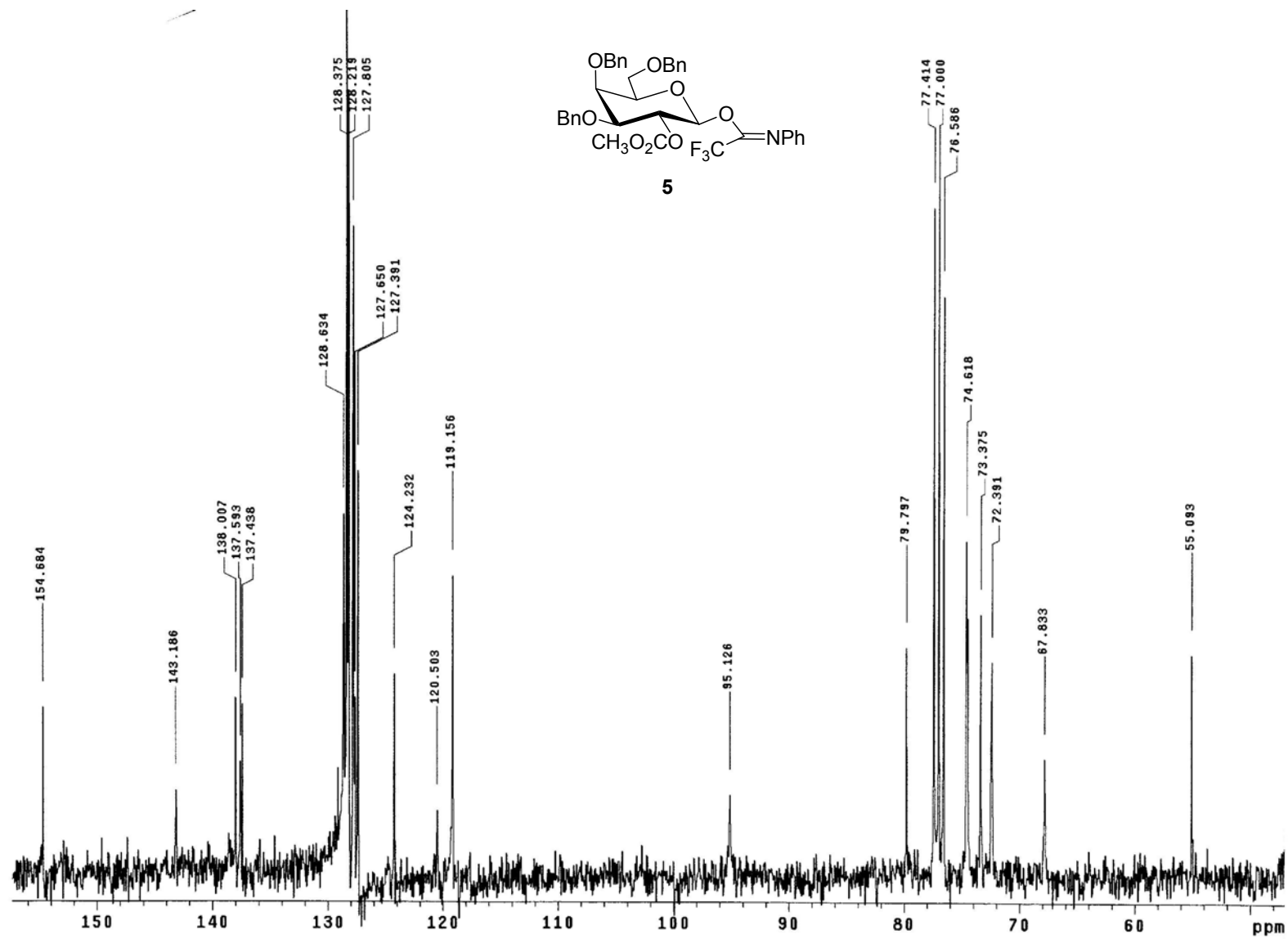


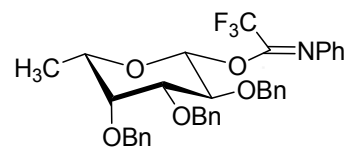




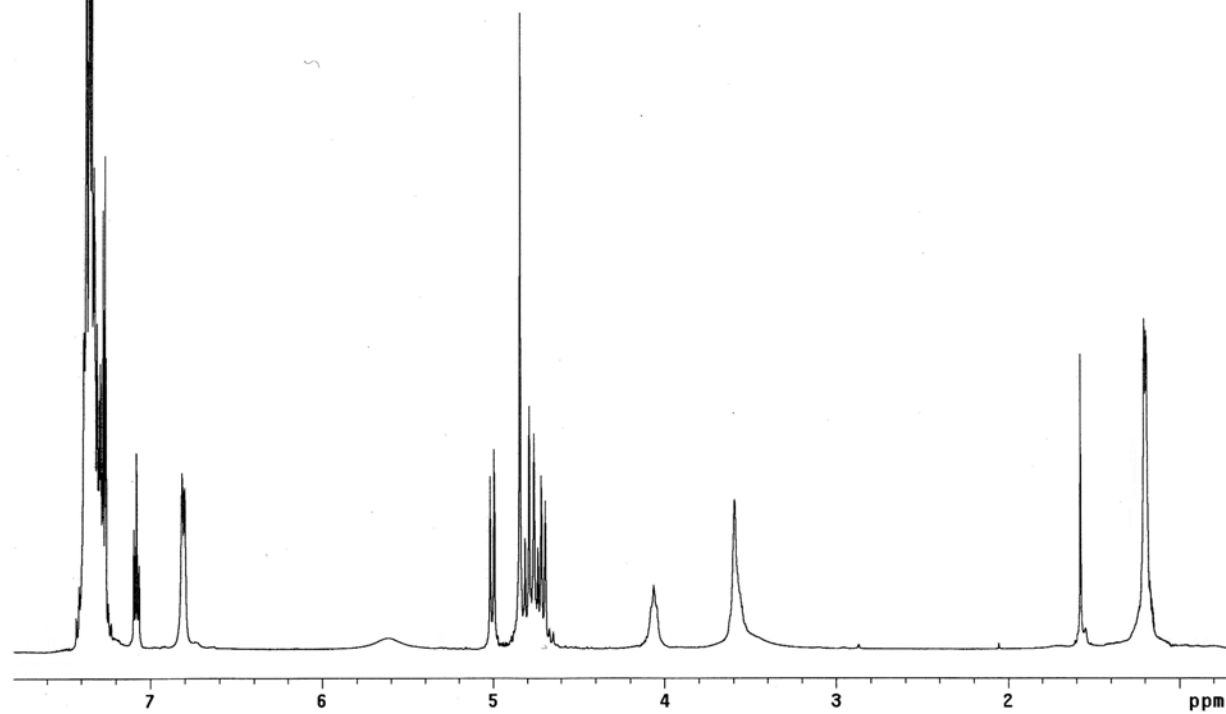


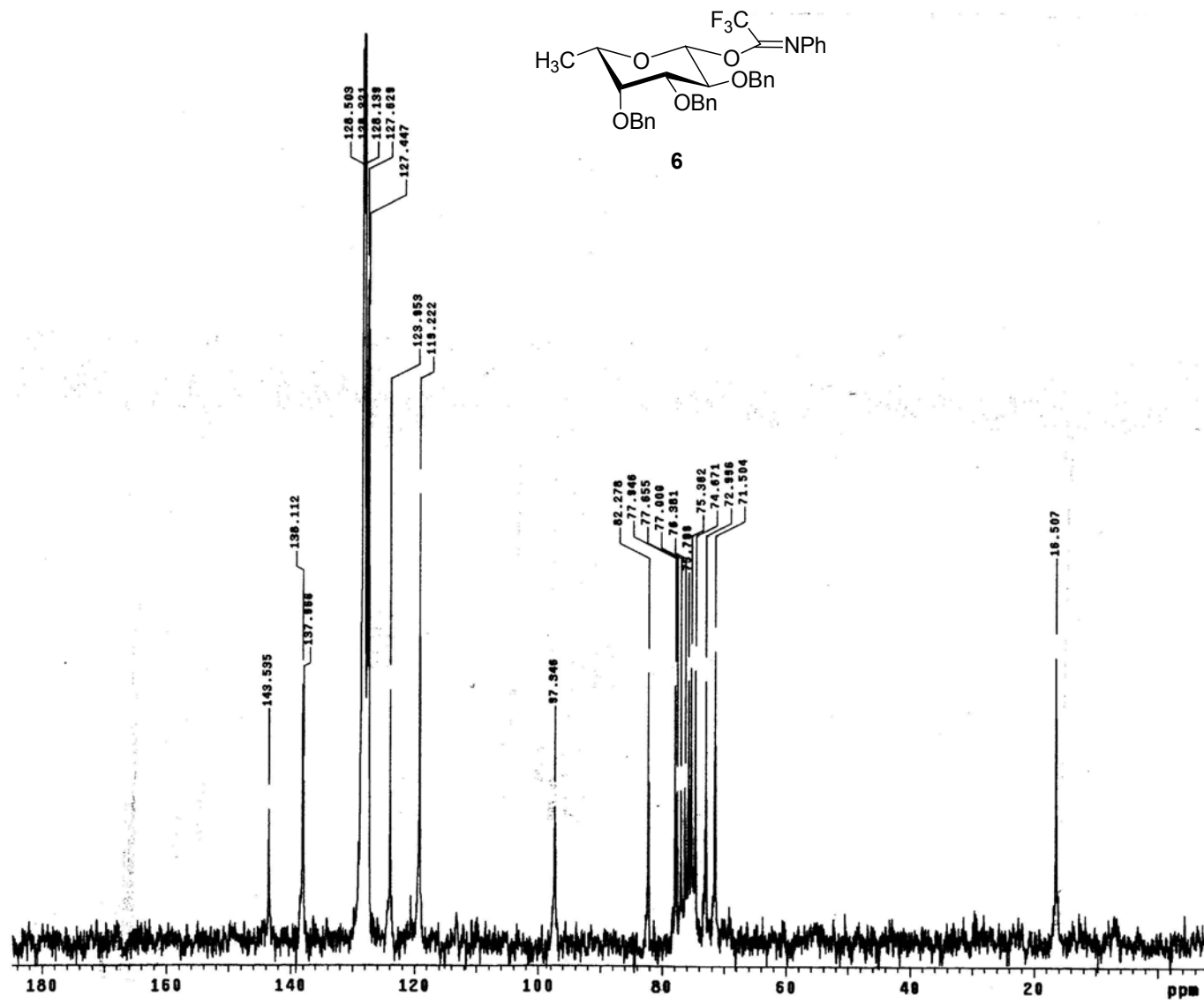


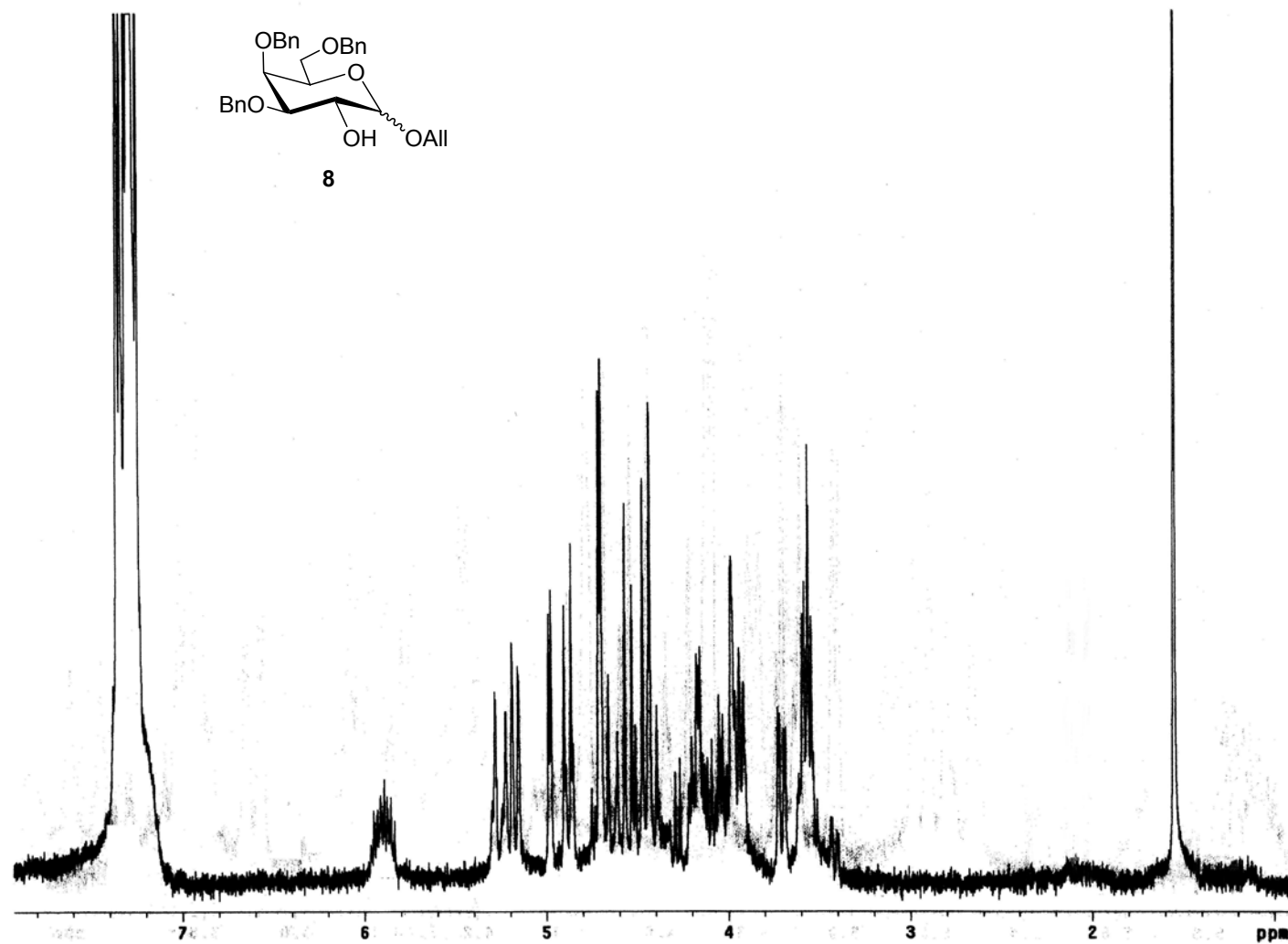


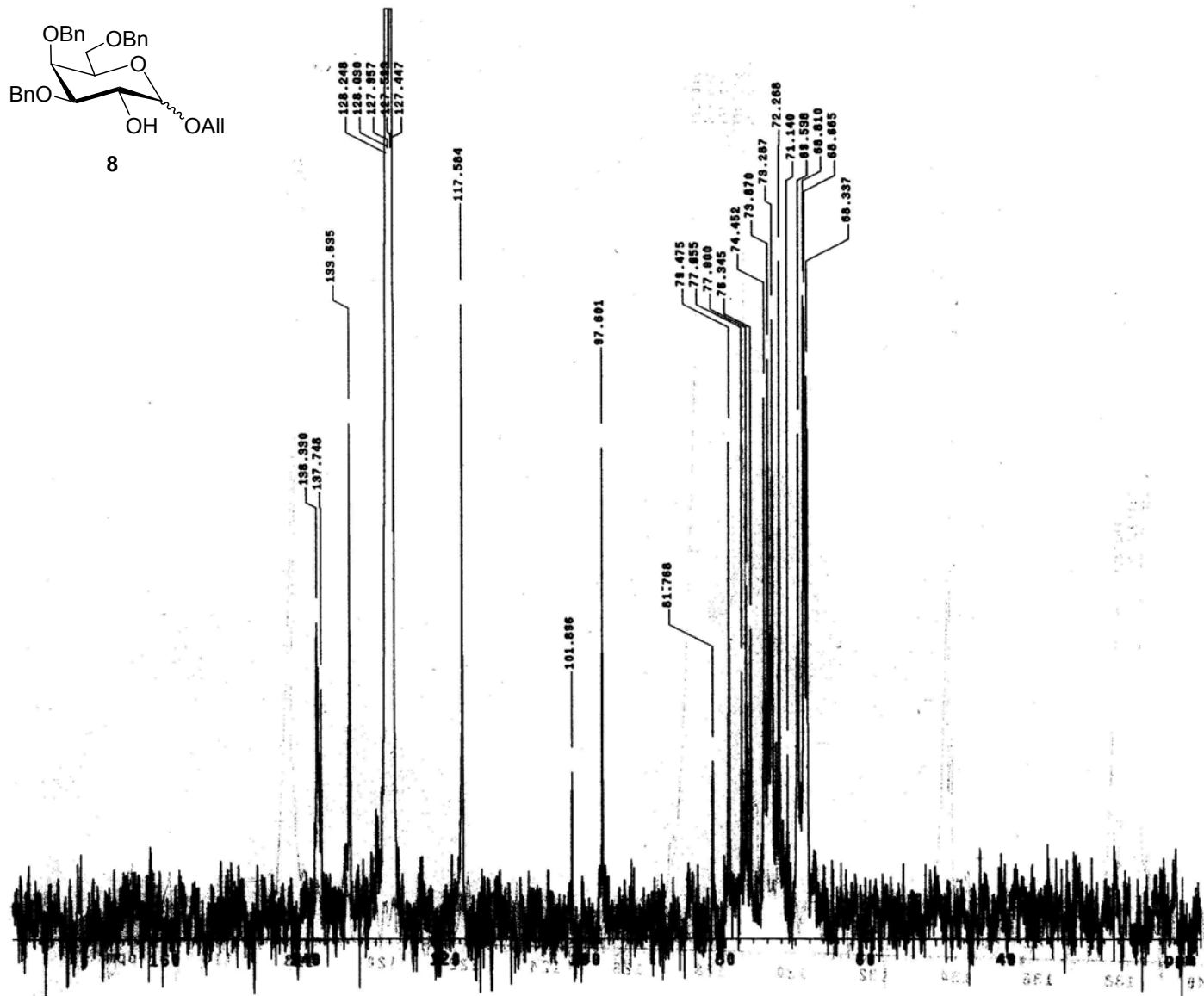
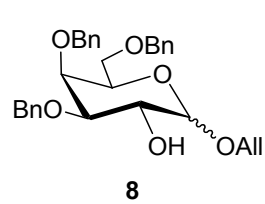


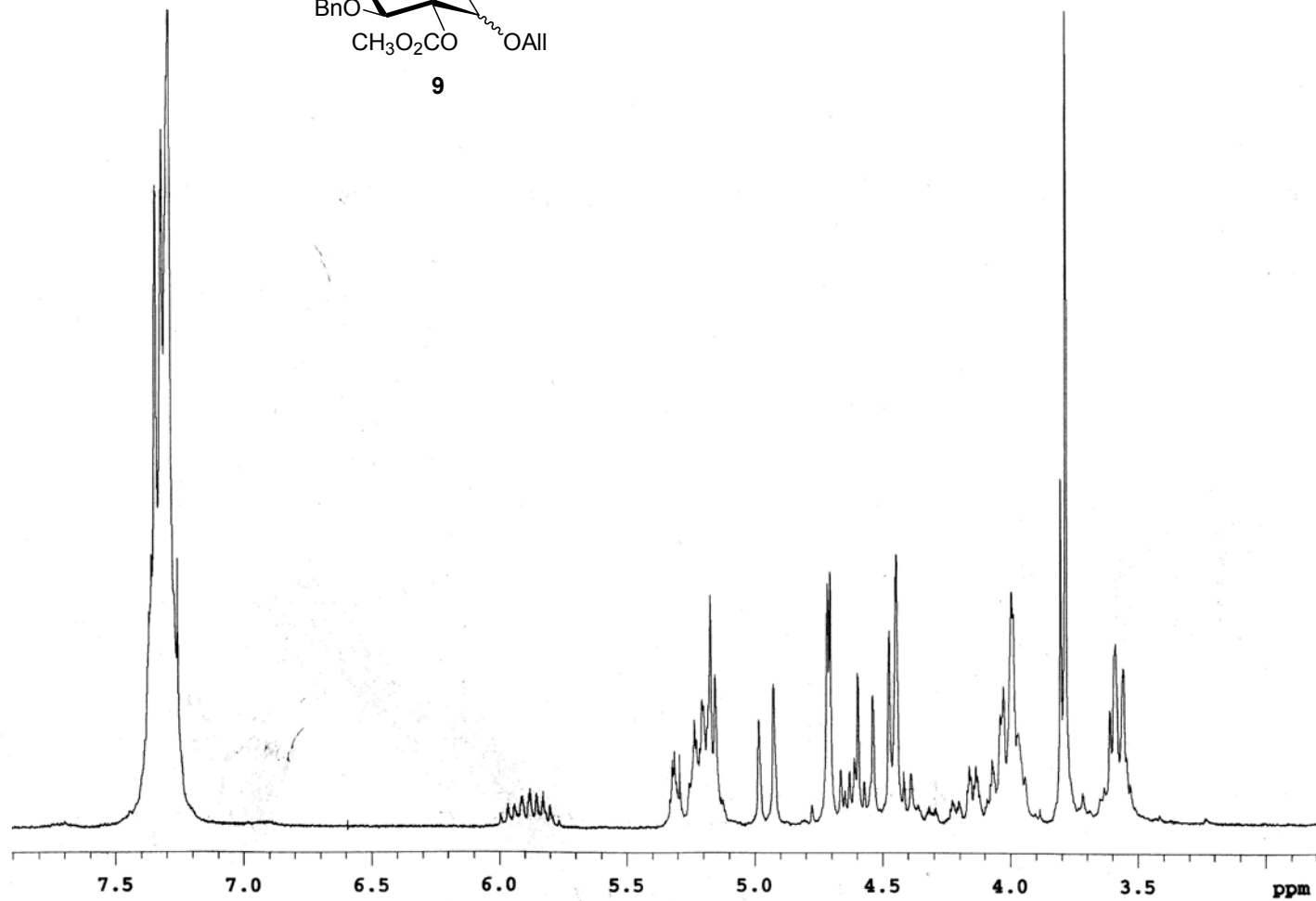
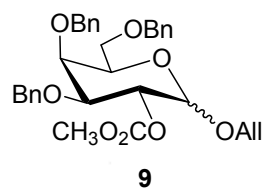
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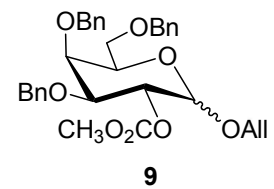
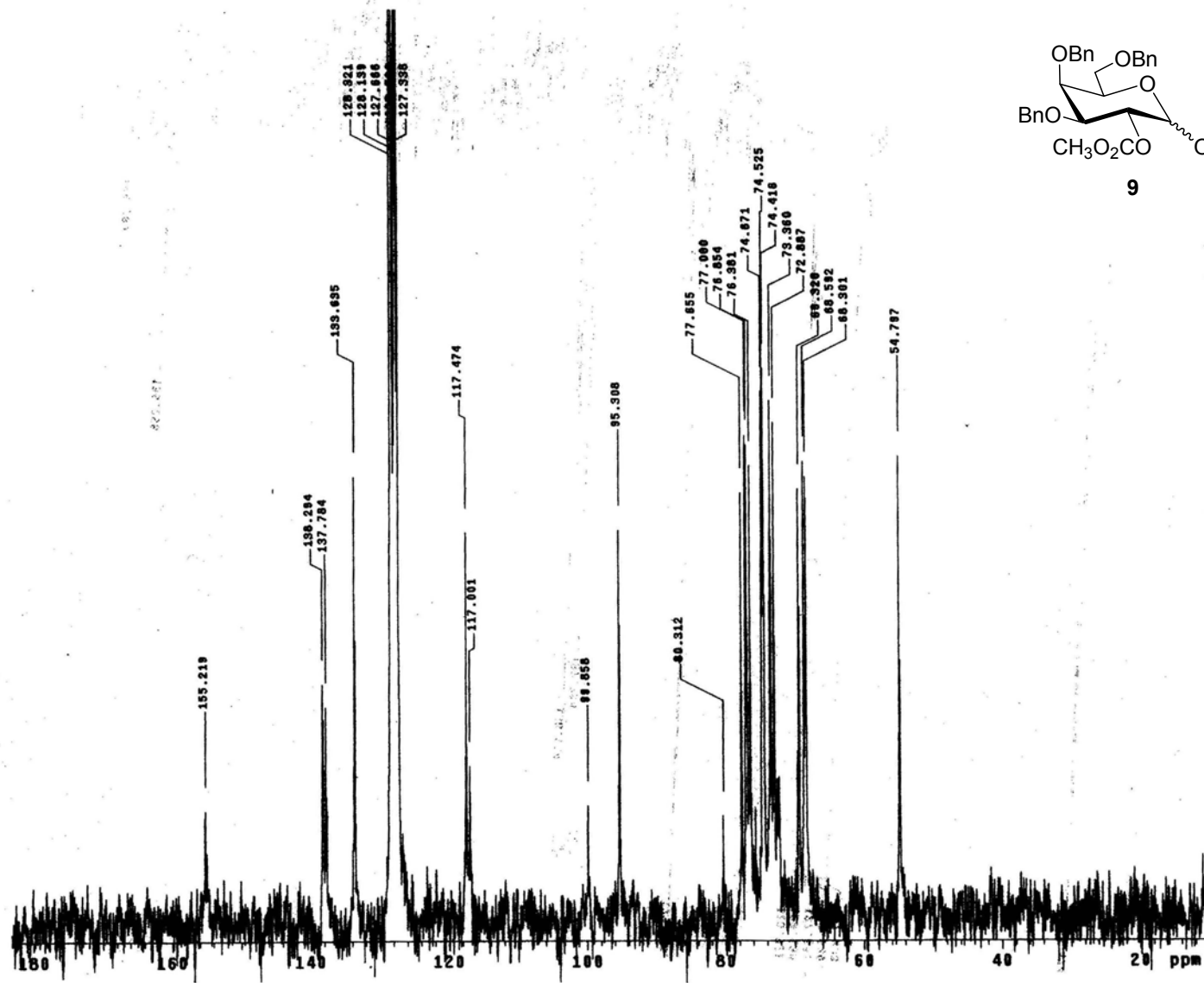


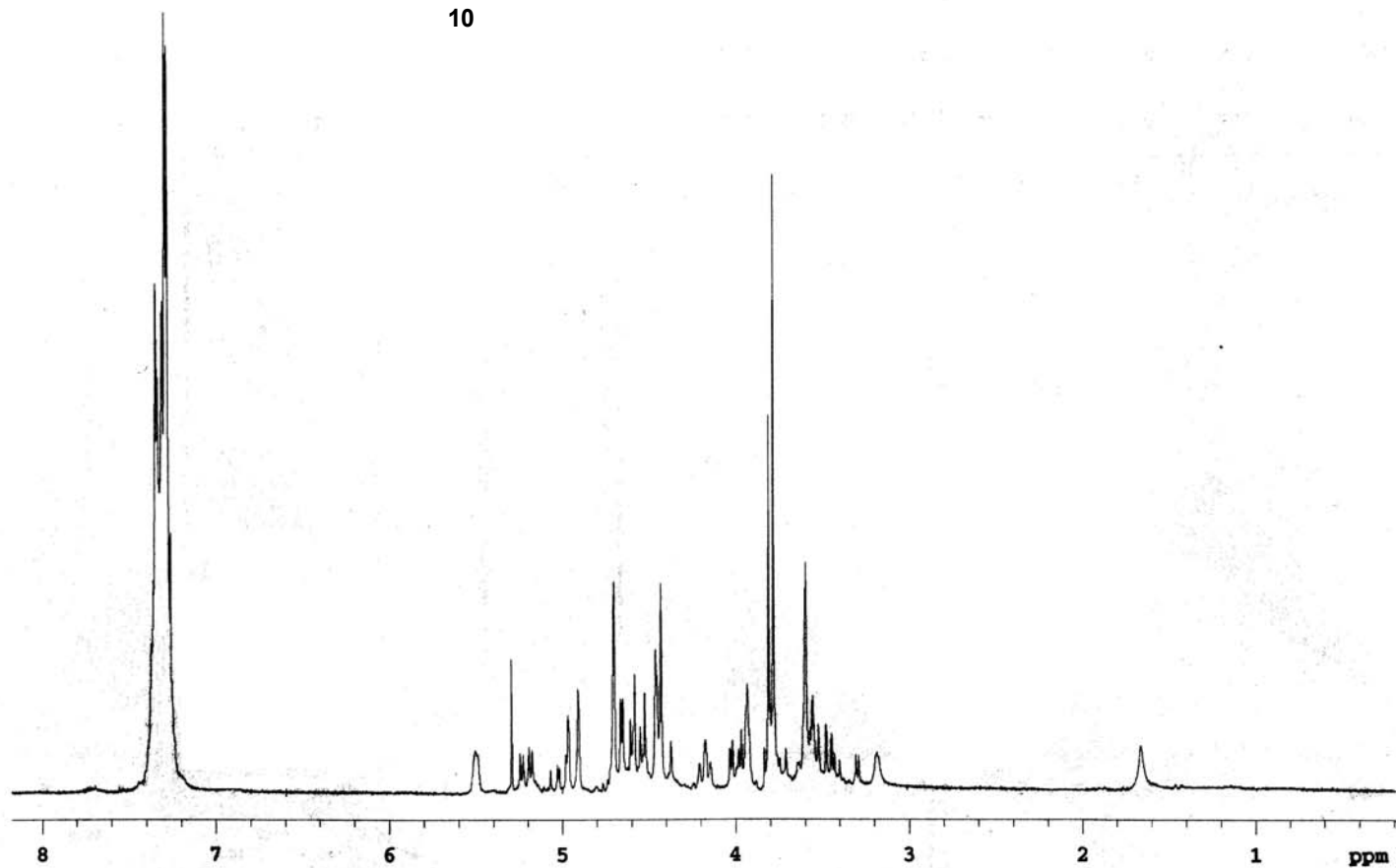
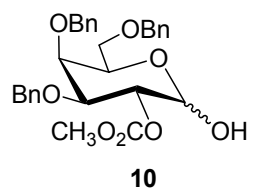


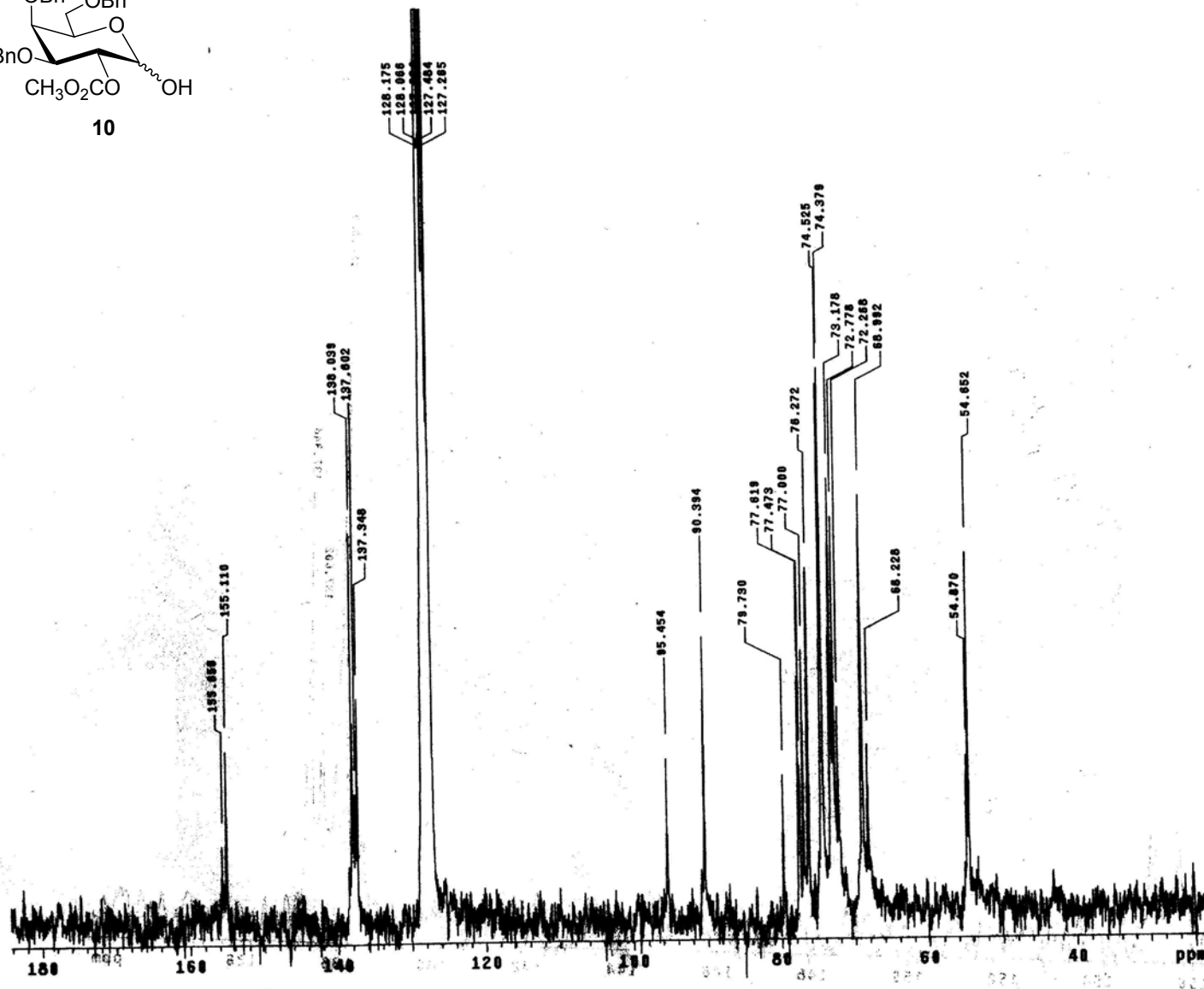
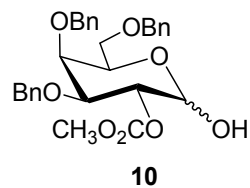




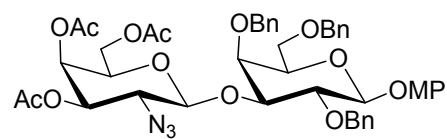












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