Reaction of carbohydrates with Vilsmeier reagent: A tandem selective chloro *O*-formylation of sugars

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Supporting Information

Experimental section

General methods:

All reagents for chemical synthesis were obtained from Sigma–Aldrich. All the solvents used in reactions were distilled and dried before use. All reactions were monitored by TLC on 0.25 mm silica gel 60 F254 plates (E. Merck) using ceric sulfate solution for detection of the spots. Silica gel 60–120 mesh was used for column chromatography. All NMR spectra were recorded on Bruker DPX 200 and DPX 500 instrument using $CDCl_3$ as the solvent with TMS as internal standard. Chemical shift is expressed in δ (ppm) and coupling constants in Hertz. Mass spectra were recorded on ESI-esquire 3000 Bruker Daltonics instrument.

General procedure for chloro-*O*-formylation:

A stirred, cooled DMF solution of the complex $POCl_3$/DMF (prepared from 1.52 g $POCl_3$, in 5 mL anhydrous DMF, 0 °C) was added dropwise to cold solution of sugar (0.2 g, 1.0 mmol in 10 mL DMF) under inert atmosphere. The mixture was then agitated at 60 °C the reaction monitored by the TLC and after the completion of the reaction (reaction time given in table-2) the contents treated with saturated $NaHCO_3$ solution (30 mL), followed by extraction with solvent ether (4x30 mL), desolventisation of organic solvent the crude product was purified by column chromatography over silica gel to afford corresponding chloro-O-formylated sugar derivatives.

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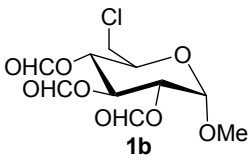
Methyl 6-chloro-2,3,4-tri-*O*-formyl-α-D-glucopyronoside (1b).

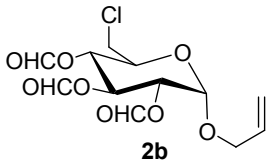


1b

Anal. calc. for $C_{10}H_{13}ClO_8$: C, 40.49; H, 4.42; Cl, 11.95. Found: C, 40.52; H, 4.49; Cl, 11.99. MS (%) M^+ at m/z 297; $[\alpha]_D^{26}$ +60.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz $CDCl_3$): δ 3.47 (s, 3H, OCH_3), 3.59 (dd, 1H, *J*= 12.2, 6.1 Hz, H-6^a), 3.69 (dd, 1H, *J*= 12.2, 2.4 Hz, H-6^b), 4.10 (ddd, 1H, *J*= 9.6, 6.1, 2.4 Hz, H-5), 5.03-5.05 (m, 1H, H-2), 5.08 (d, 1H, *J*= 3.4 Hz, H-1), 5.23 (t, 1H, *J*= 9.6 Hz, H-3/H-4), 5.69 (t, 1H, *J*= 9.5 Hz, H-3/H-4), 8.05 (s, 2H, 2xCHO), 8.08

(s, 1H, CHO). ^{13}C NMR ($CDCl_3$): δ 43.6, 56.1, 68.9, 69.2, 69.6, 71.5, 96.7, 159.9, 160.7, 160.9.

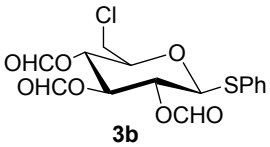
Allyl 6-chloro-2,3,4-tri-*O*-formyl-α-D-glucopyronoside (2b).



2b

Anal. calc. for $C_{10}H_{13}ClO_8$: C, 40.49; H, 4.42; Cl, 11.95. Found: C, 40.52; H, 4.49; Cl, 11.99. MS (%) M^+ at *m/z* 297; $[\alpha]_D^{26}$ +116.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.56 (dd, 1H, *J*=12.2, 6.1 Hz, H-6^a), 3.63 (dd, 1H, *J*= 12.2, 2.5 Hz, H-6^b), 4.04 (dd, 1H, *J*= 12.8, 6.3 Hz, -OC*H*$_2$), 4.11 (ddd, 1H, *J*= 9.3, 6.3, 2.5 Hz, H-5), 4.22 (dd, 1H, *J*= 12.8, 5.3 Hz, -OC*H*$_2$), 5.00-5.03 (m, 1H, H-2), 5.18-5.24 (m, 3H, =CH_2 & H-1), 5.32 (t, 1H, *J*= 9.6 Hz, H-3/H-4), 5.68 (t, 1H, *J*= 10.0 Hz, H-3/H-4), 5.82-5.90 (m, 1H, =CH), 8.02, 8.03, 8.04 (s, 1H each, 3xCHO). ^{13}C NMR ($CDCl_3$): δ 43.6, 56.1, 68.9, 69.2, 69.6, 71.5, 96.7, 159.9, 160.7, 160.9.

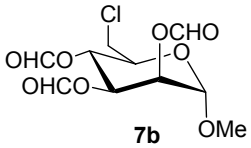
Phenyl 6-chloro-2,3,4-tri-*O*-formyl-β-D-thio-glucopyronoside (3b) .



3b

Anal. calc. for $C_{15}H_{15}ClO_7S$: C, 48.07; H, 4.03; Cl, 9.46; S, 8.56. Found: C, 48.04; H, 4.09; Cl, 9.53; S, 8.62. MS (%) M^+ at *m/z* 475; $[\alpha]_D^{26}$ +7.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 3.55-3.57 (dd, 1H, *J*= 12.3, 6.1 Hz, H-6^a), 3.60-3.65 (dd, 1H, *J*= 12.3, 2.4 Hz, H-6^b), 3.74-3.78 (ddd, 1H, *J*= 9.3, 6.1, 2.4 Hz, *H*-5), 4.71 (d, 1H, *J*= 10.05 Hz, H-1), 5.02 (t, 1H, *J*= 9.64 Hz, H-2), 5.12 (t, 1H, *J*= 10.7 Hz, H-3/H-4), 5.39 (t, 1H, *J*= 9.3 Hz, H-3/H-4), 7.24-7.28 (m, 3H, 3xAr-H), 7.48 (d, 2H, *J*= 5.4 Hz, 2xAr-H), 7.93, 7.96, 7.99 (s, 1H each, 3xCHO). ^{13}C NMR ($CDCl_3$): δ 41.8, 67.6, 68.0, 71.4, 84.3, 127.7, 128.0, 129.7, 132.5, 157.8, 157.9, 158.4.

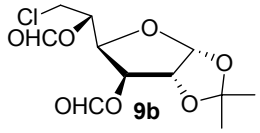
Methyl 6-chloro-2,3,4-tri-*O*-formyl-α-D-manopyronoside (7b).



7b

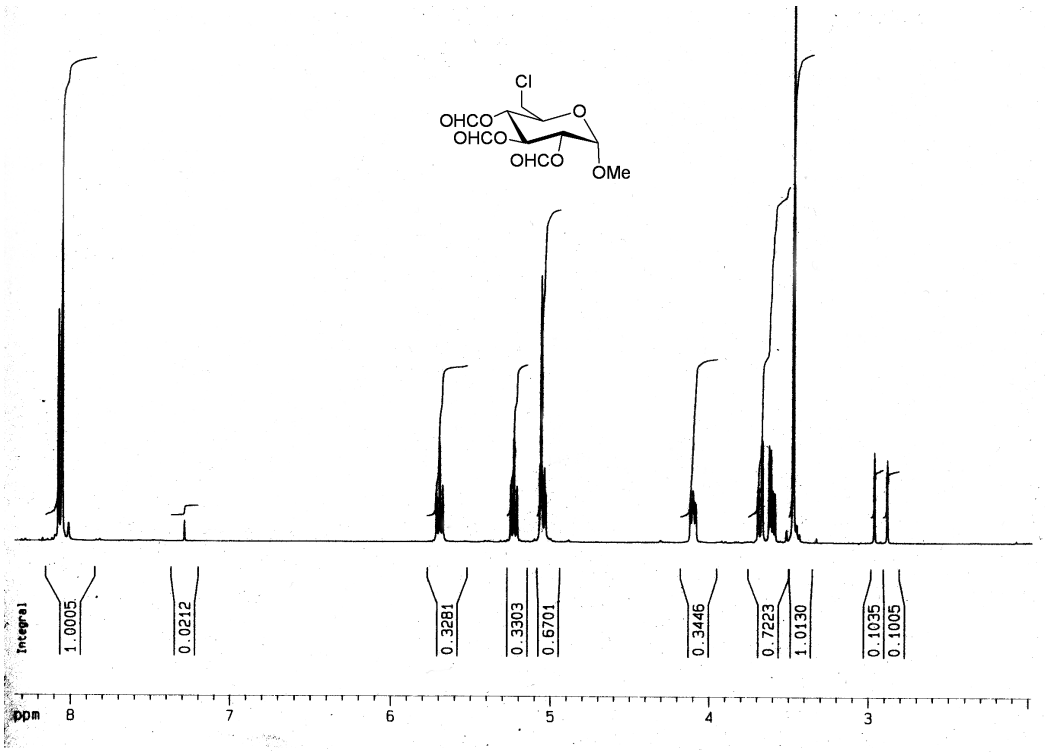
Anal. cal. for $C_{10}H_{13}ClO_8$: C, 40.55; H, 4.42; Cl, 11.95. Found: C, 40.59; H, 4.46; Cl, 12.02. MS (%) M^+ at *m/z* 296; $[\alpha]_D^{26}$ +54.8 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 3.46 (s, 3H, OCH_3), 3.59 (dd, 1H, *J*= 12.2, 2.6 Hz, H-6^a), 3.69 (dd, 1H, *J*= 12,2, 2.6 Hz, H-6^b), 4.06 (ddd, 1H, *J* = 9.3, 6.2, 2.6 Hz, H-5), 4.79 (d, 1H, *J*= 1.4 Hz, H-1), 5.43-5.57 (m, 3H, H-2,H-3,H-4), 7.96, 8.08, 8.12 (s, 1H each, 3xCHO). ^{13}C NMR ($CDCl_3$): δ 43.2, 55.7, 66.7, 68.3, 68.8, 69.7, 98.2, 159.4, 159.5, 160.9.

6-Chloro-3,5-di-*O*-formyl-1,2-*O*-isopropylidene-α-D-glucofuranose (9b).



9b

Anal. cal. for for $C_{11}H_{15}ClO_7$: C 44.83, H 5.13, Cl 12.03: found C 44.86, H 5.17, Cl 12.08. MS (%) M^+ at *m/z* 295; $[\alpha]_D^{26}$ -4.0 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 1.33 & 1.54 (s, 3H each, 2xCH_3), 3.77-3.99 (m, 2H, CH_2Cl), 4.53 (d, 1H, *J*= 3.5 Hz, H-2), 4.59(d, 1H, *J*= 2.7 Hz, H-4) 5.31-5.38 (m, 1H, H-5), 5.42 (d, 1H, *J*= 2.7 Hz, H-3), 5.93 (d, 1H, *J*= 3.5 Hz, H-1), 8.0 (s, 2H, 2xCHO). ^{13}C NMR ($CDCl_3$): δ 26.7, 27.1, 44.4, 66.6, 68.6, 74.8, 83.4, 105.4, 113.4, 159.6, 159.6.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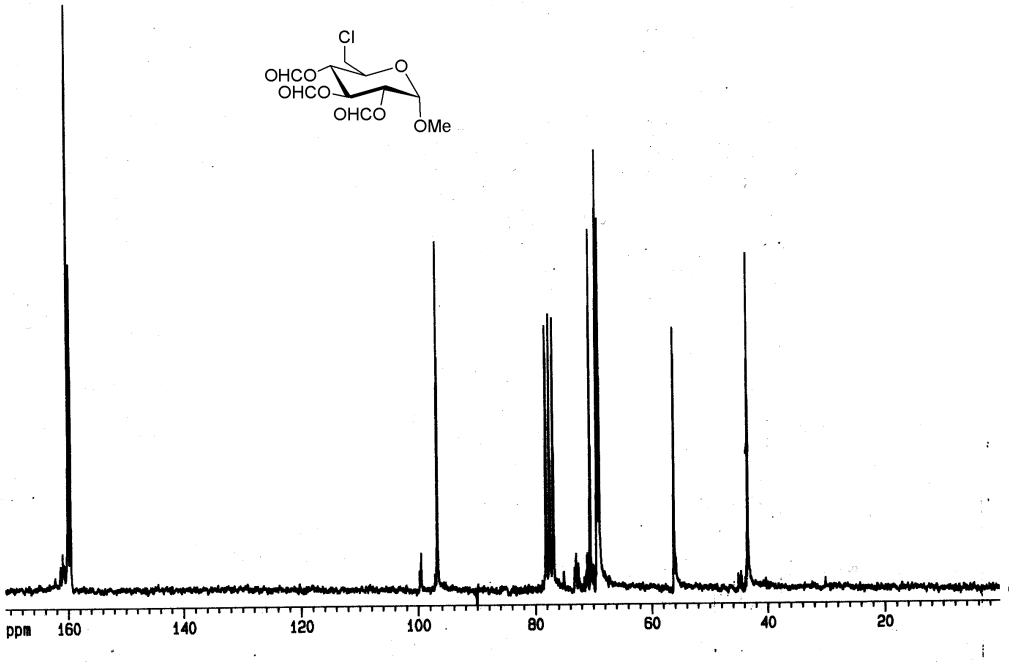
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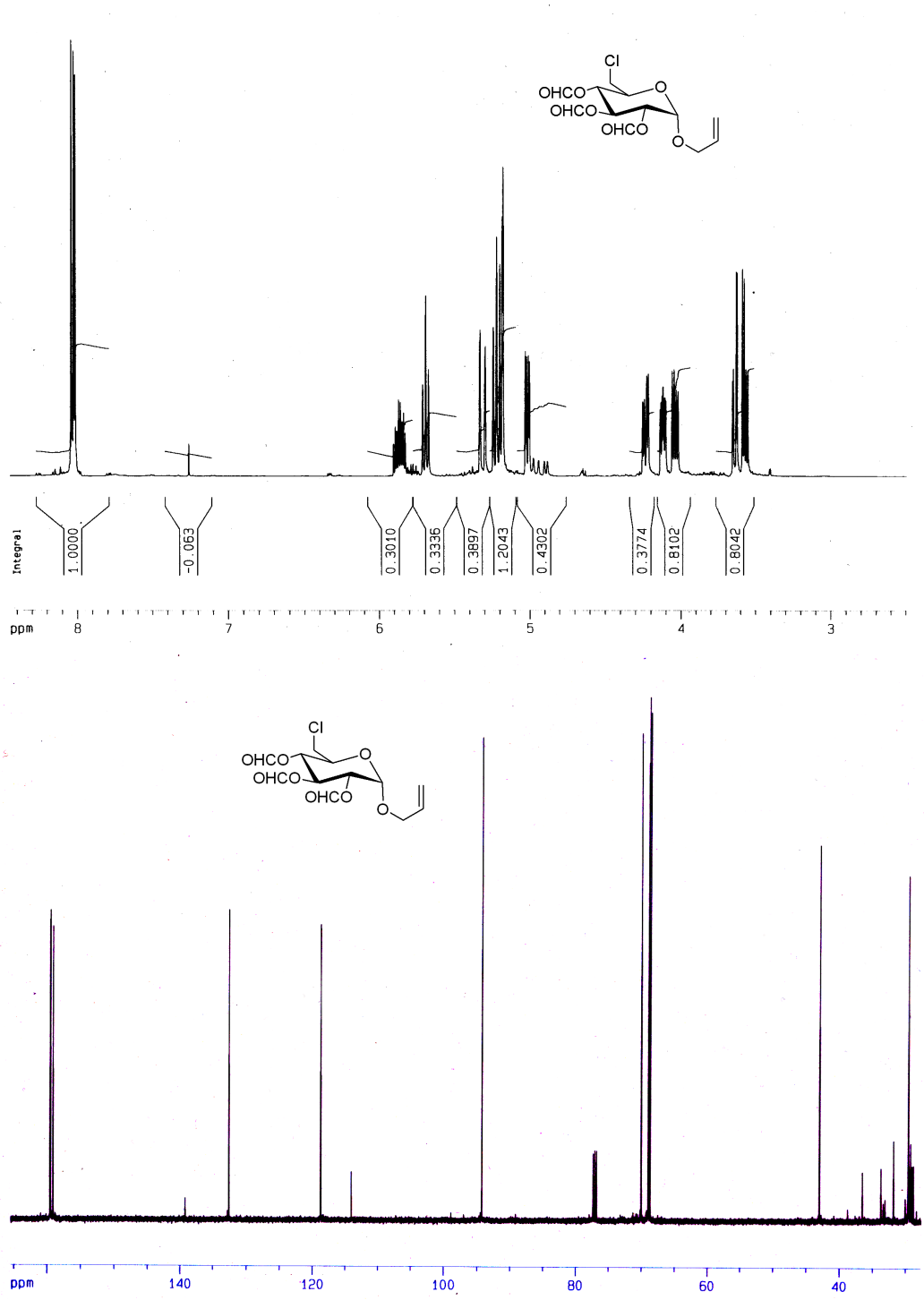
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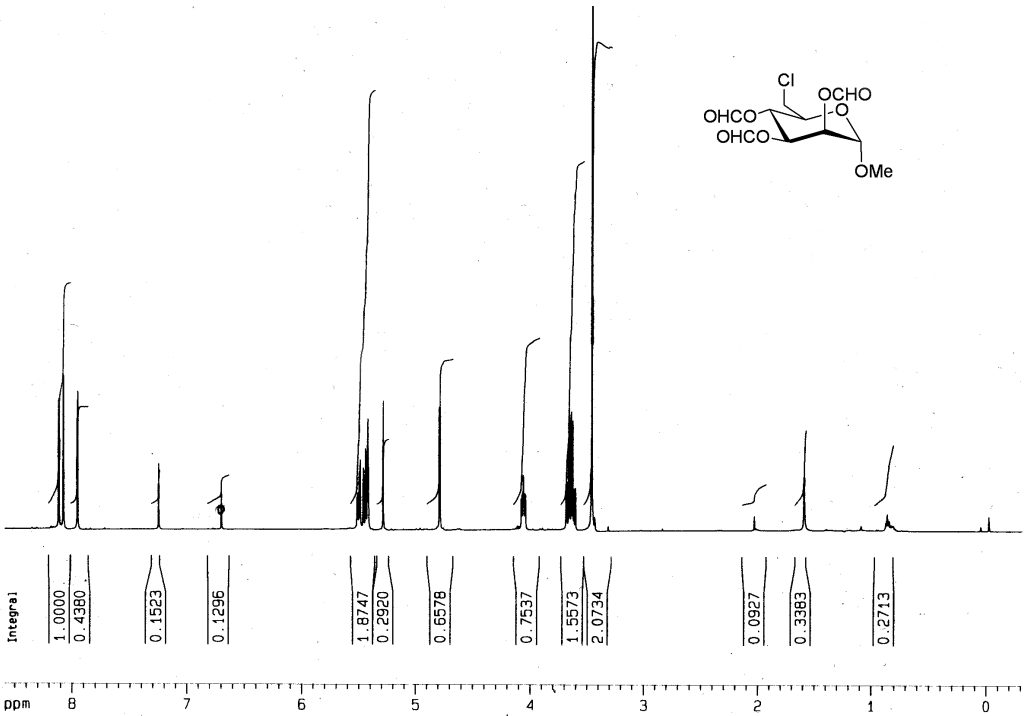
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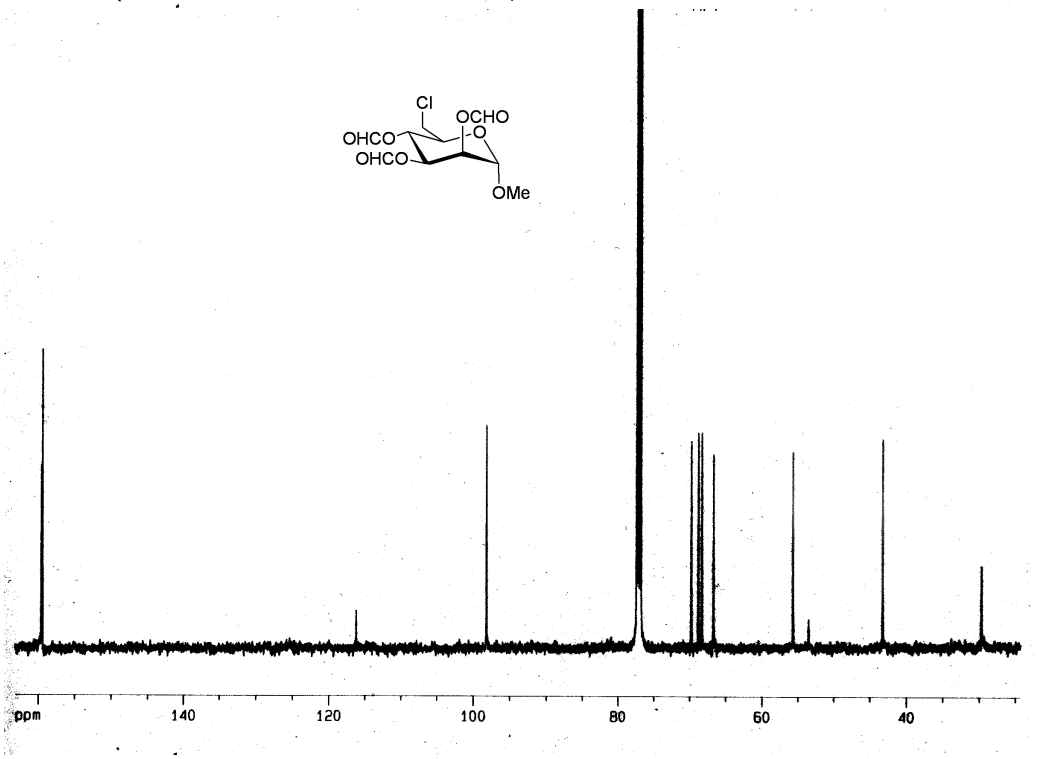
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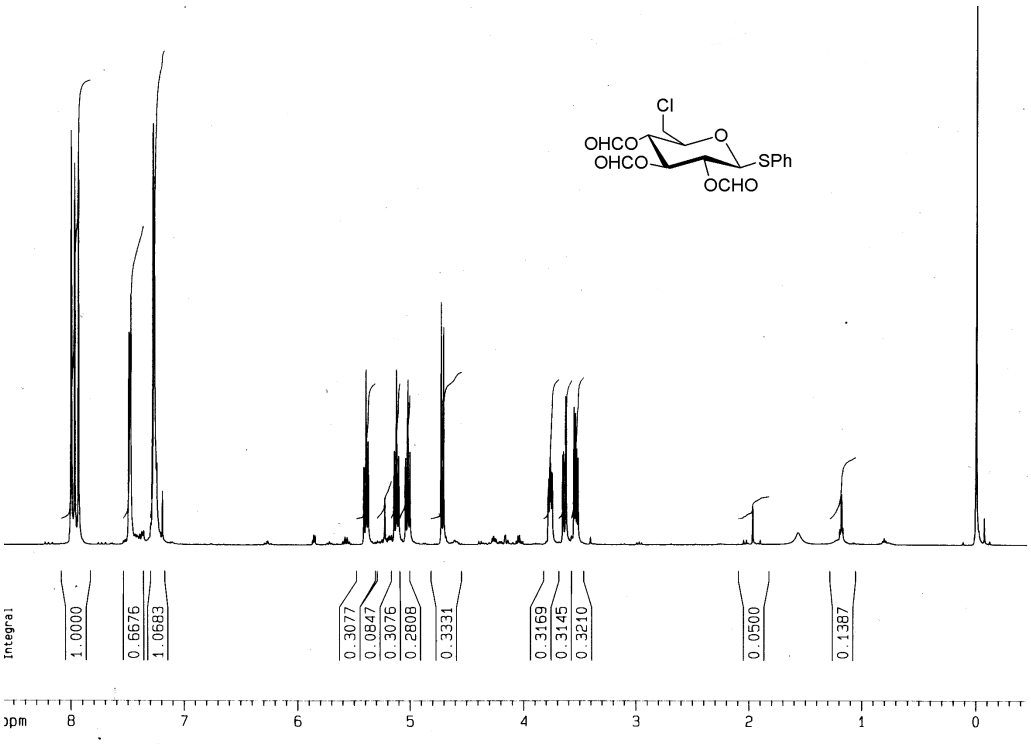
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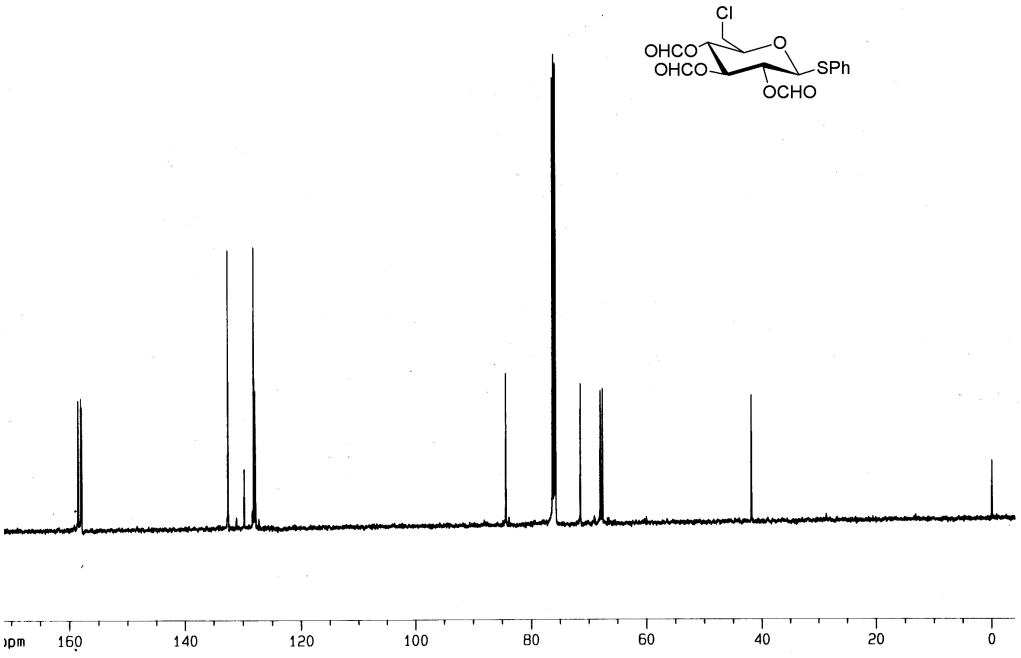
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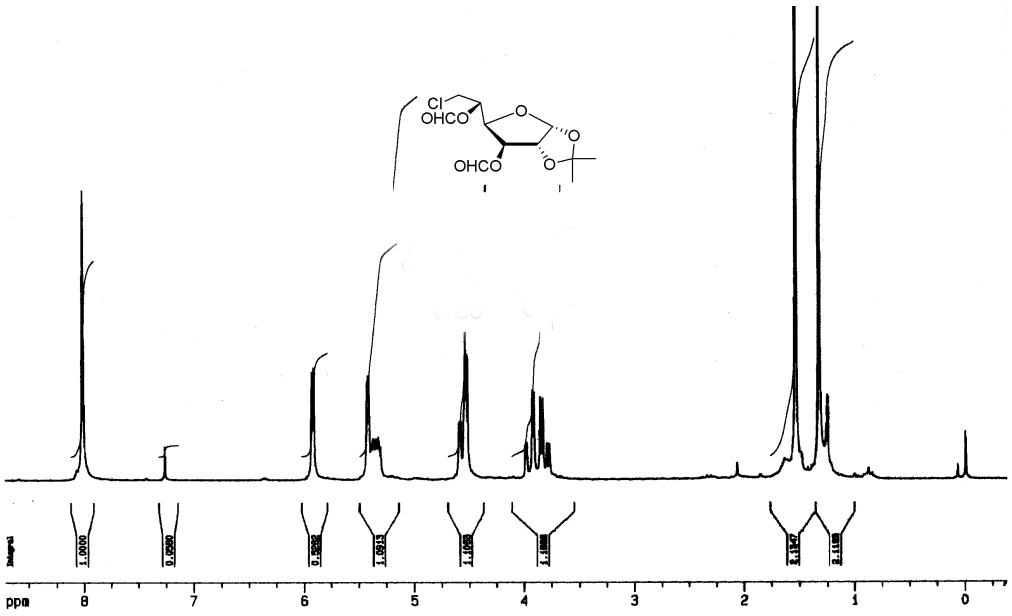
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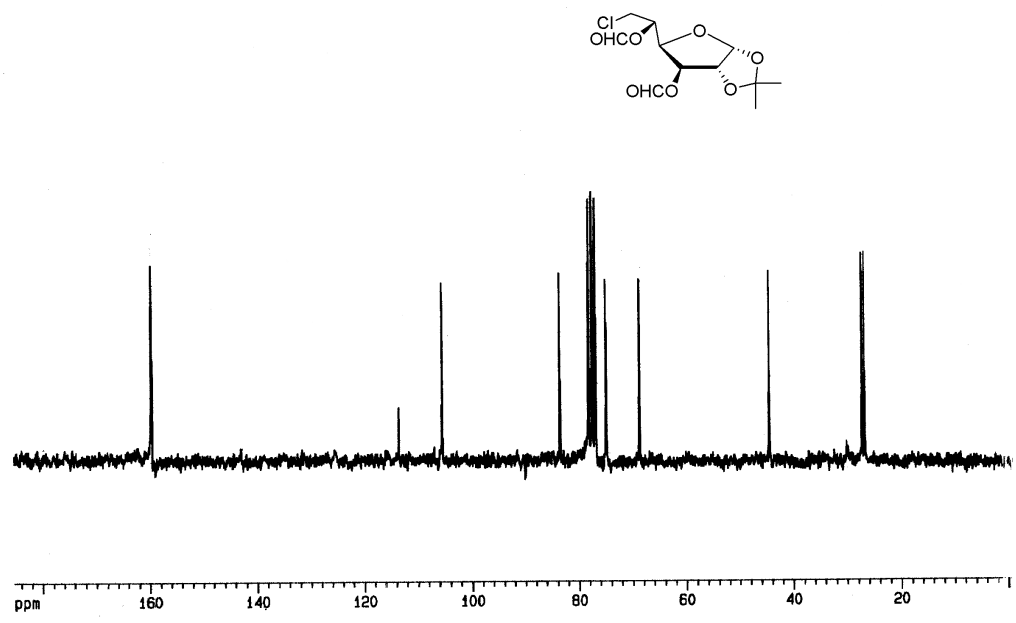
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