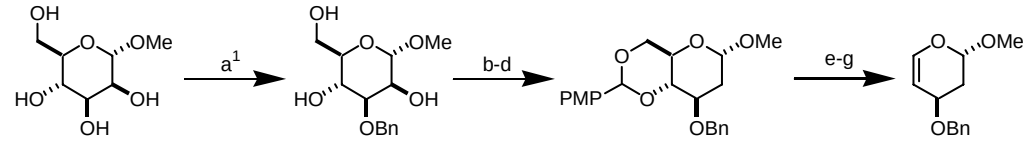
Stereoselective Epoxidation of 4-Deoxypentenosides: A Polarized-π Model
Supporting Information

Synthesis of 4-Deoxypentenosides

4-Deoxypentenosides (4-DPs) **1-4** were synthesized from their corresponding methyl glycosides as described in Ref. 2 (*Org. Lett.* **2002**, *4*, 2281; *J. Org. Chem.*, **2004**, *69*, 3391). The synthesis and complete characterization of 2-amino-2,4-dideoxy-4-pentenosides **5-10** will be described elsewhere. 2,4-Dideoxy-4-pentenoside **11** was synthesized according to Scheme S1.

Scheme S1



methyl α-D-mannoside **S-1** **S-2** **11**

Reagents and conditions: (a) Bu_2SnO, toluene, reflux; then $Bu_4N^+I^-$, BnBr (57%);[1] (b) *p*-$MeOC_6H_4CH(OMe)_2$, CSA, THF, 85 °C (67%); (c) NaH, CS_2, MeI, THF, 0 °C; (d) Bu_3SnH, AIBN, toluene, reflux (65% over 2 steps); (e) 8:1:1 AcOH:THF:H_2O, 45 °C (87%); (f) NaOCl, TEMPO (5 mol%), satd aq. $NaHCO_3$, CH_2Cl_2, 0 °C; (g) DMF dineopentyl acetal, toluene, 130 °C (60% over 2 steps).

2,4-Dideoxy-4-pentenoside **11:** $[\alpha]_D^{20}$ = +249 (*c* = 1.0 in $CHCl_3$); ^{1}H NMR (C_6D_6): δ 7.10–7.37 (m, 5H), 6.31 (d, 1H), 4.87–4.93 (m, 2H), 4.40 (d, 1H), 4.30 (d, 1H), 3.91 (q, 1H), 3.29 (s, 3H), 2.10 (ddd, 1H), 1.90 (ddd, 1H); ^{13}C NMR (C_6D_6): δ 141.6, 139.0, 138.9, 102.2, 99.2, 69.9, 67.4, 55.8, 34.0.

Epoxidation of 4-DPs

A typical epoxidation reaction was performed as follows: A solution of 4-deoxypentenoside **2** (43 mg, 0.133 mmol) in CH_2Cl_2 (0.2 mL) was stirred at –55 °C and treated with a freshly prepared solution of DMDO (2.7 mL, 0.1 M in acetone). The resulting mixture was stirred at –55 °C under argon for 2 days, then warmed to 0 °C over a period of 4 hours. The mixture was concentrated to an oil to yield the desired epoxypyranoside as a 10:1 α:β mixture (45 mg, 99%).

Epoxide stereochemistry was confirmed by S_N2 ring opening at C5 using $LiAlH_4$, $LiAlD_4$, or LiSEt as the nucleophile (Nu). Reaction conditions are as follows:

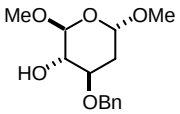
$LiAlD_4$ or $LiAlH_4$ addition: A solution of $LiAlH_4$ or $LiAlD_4$ (36.5 mg, 0.869 mmol) in Et_2O (3 mL) was stirred at rt under argon atmosphere, then treated with a solution of the epoxide in Et_2O (4 mL, 0.043 M solution). The mixture was stirred for 15 min at rt, cooled to 0 °C, diluted with 1 M HCl (3 mL) and extracted with Et_2O (20 mL), then dried over Na_2SO_4 and concentrated. Silica gel chromatography using a 20:80 to 50:50 EtOAc–

[1] For a similar reaction, see: Yu, H. N.; Furukawa, J.-I.; Ikeda, T.; Wong, C.-H. *Org. Lett.* **2004**, *6*, 723.

hexanes gradient containing 0.1% of Et_3N yielded the corresponding C5 adduct, which was characterized by ^1H NMR coupling constant analysis.

LiSEt addition: A solution of EtSH (0.1 mL, 1.35 mmol) in dry THF (1 mL) at 0 °C was treated with *n*-BuLi (20 μL, 2.6 M in hexanes) under an argon atmosphere. The resulting mixture was treated with the crude epoxide (45 mg, 0.133 mmol) in 0.5 mL of THF at 0 °C and stirred for 2 hours. The reaction was quenched with satd. aq. $NaHCO_3$, extracted with EtOAc, dried over Na_2SO_4 and concentrated. Silica gel chromatography using a hexanes–EtOAc gradient yielded the corresponding C5 thioacetal, which was characterized by ^1H NMR coupling constant analysis.

In the case of 2,4-dideoxy-4-pentenoside **11**, the corresponding epoxide was unstable upon isolation at r.t and was therefore trapped by addition of MeOH (1.5 mL) at –55 °C, then warmed to 0 °C over a period of 5 hours (cf Figure 3 in text). The reaction was concentrated to dryness, producing 1,5-bisacetal **12** in quantitative yield.



12

2-Deoxypentoside, 1,5-bisacetal **12**: ^1H NMR (300 MHz, C_6D_6): δ 7.31–7.07 (m, 10 H, Ar-H), 4.66 (d, 1 H, *J* 12.3 Hz, C*H*Ph), 4.55-4.48 (m, 3 H, H-1, H-5, C*H*Ph), 3.92 (ddd, 1 H, $J_{2eq,3}$ 5.1 Hz, $J_{2ax,3}$ 9.3 Hz, $J_{3,4}$ 9.0 Hz, H-3), 3.68 (ddd, 1 H, $J_{3,4}$ 9.0 Hz, $J_{4,5}$ 8.4 Hz, $J_{4,OH}$ 2.4 Hz, H-4), 3.27 (s, 3 H, OCH_3), 3.03 (s, 3 H, OCH_3), 2.31 (d, 1 H, *J* 2.4 Hz, O*H*), 2.05 (ddd, 1 H, 1.5 Hz, 5.1 Hz 13.2 Hz H-2eq), 1.58 (ddd, 1 H, 3.9 Hz, 9.3 Hz, 13.2 Hz, H-2ax).

Table S1. Selected NMR coupling constants (in Hz, C_6D_6) of 4-DPs **1**,**2** and **5-10**:

compd	*J*(1,2)	*J*(2,3)
1 (α-*Glc*-4-DP)[a]	2.4	6.0
2 (β-*Glc*-4-DP)	7.2	6.3
5 (α-*GlcNPhth*-4-DP)	2.7	9.9
6 (β-*GlcNPhth*-4-DP)	9.0	9.3
7 (α-*GlcN*$_3$-4-DP)	2.1	6.6
8 (β-*GlcN*$_3$-4-DP)	8.1	7.5
9 (α-*GlcNBn*$_2$-4-DP)	2.7	9.0
10 (β-*GlcNBn*$_2$-4DP)	6.6	6.3

Table S2. Selected NMR coupling constants (in Hz, C_6D_6) of C5 adducts derived from 4-DPs **1-8** and **10**, following DMDO epoxidation and S_N2 ring opening:

initial 4-DP	config of C5 adduct	*J*(1,2)	*J*(2,3)	*J*(3,4)	*J*(4,5)
1 (α-*Glc*-4-DP)[a]	α-L-*Ara*	3.3	9.6	3.3	*e*
2 (β-*Glc*-4-DP) [a]	β-D-*Xyl*	6.3	8.1	7.5	9.3
3 (α-*Man*-4-DP)[a]	α-D-*Lyx*	2.1	*e*	9.6	9.6
4 (β-*Man*-4-DP)[b]	β-D-*Lyx*	3.3	3.0	7.8	*e*
5 (α-*GlcNPhth*-4-DP)[c]	α-L-*Alt*	3.6	11.1	3.0	2.1
6 (β-*GlcNPhth*-4-DP)[c]	β-D-*Glc*	8.7	8.4	10.5	9.9
7 (α-*GlcN*$_3$-4-DP)[c]	α-L-*Alt*	1.5	6.0	*e*	6.9
8 (β-*GlcN*$_3$-4-DP)[c]	β-D-*Glc*	8.1	*e*	*e*	9.6
10 (β-*GlcNBn*$_2$-4DP)[c]	β-D-*Glc*	6.0	7.8	*e*	9.3
11 (α-2-deoxy-*Glc*-4-DP)[d]	α-D-*Glc*	1.5,3.9	5.1,9.3	9.0	8.4

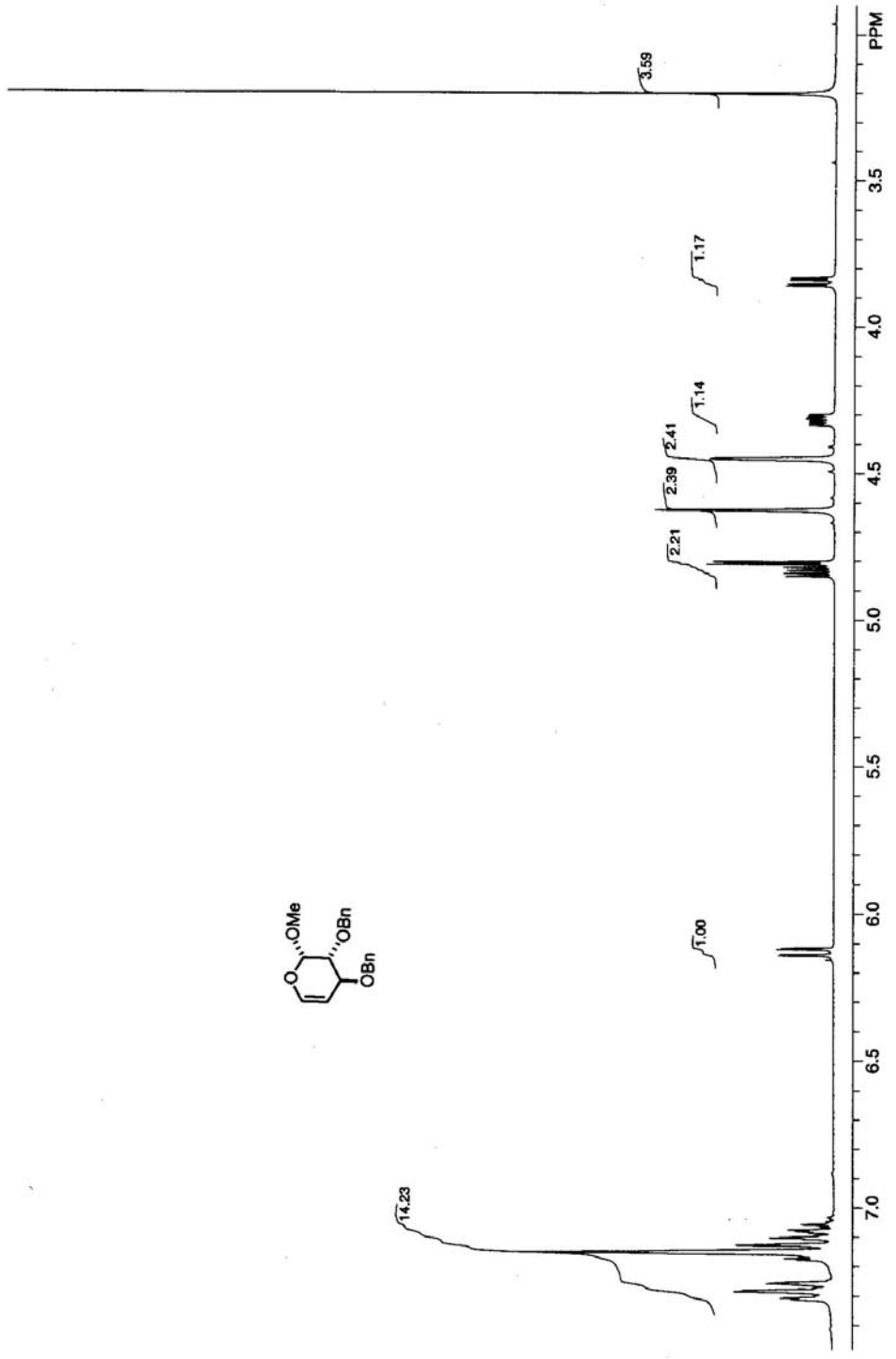
[a] Nu=$LiAlD_4$ [b] Nu=$LiAlH_4$; [c] Nu=LiSEt; [d] Nu=MeOH; [e] Peaks buried by other signals

DFT and PPFMO calculations

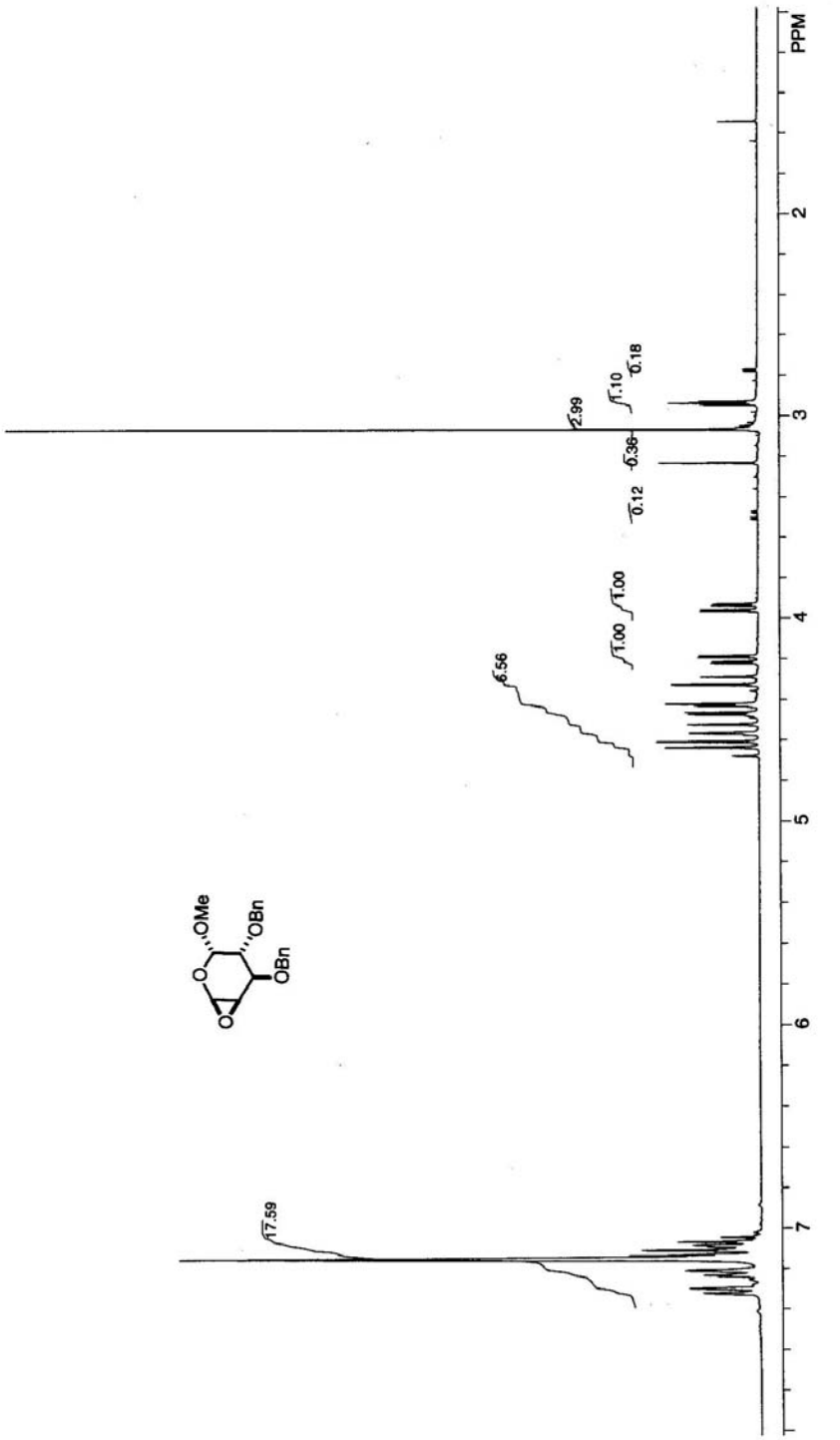
Calculations were performed using the Gaussian®03W Software Package Version 6, Revision-B.03. Initial structures were constructed using GaussView and were optimized employing the 6-31G(d,p) basis set. DFT calculations were based on Becke's three–parameter hybrid functional in conjunction with the nonlocal correlation functional by Lee, Yang, and Parr (B3LYP; Becke, A. D. *J. Chem. Phys*. **1993**, *98*, 5648; Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B*, **1988**, *37*, 785).

PPFMO calculations were carried out at the B3LYP/STO-3G level of theory using the DFT-optimized geometries. Four *s*-functions (denoted *Bq* in output files) were positioned above and below the lobes of the $2p_y$ orbitals centered at C4 and C5, at a distance of 1.3 Å from the carbon nuclei. The *s*-functions are essentially reduced to a single Gaussian function scaled to a level of 1.0. The values of the exponent of the *s* orbital and its contract coefficient were chosen to be 0.1 and 1.0 respectively, based on reference 9(a). The resulting *s* and $2p_y$ coefficients were extracted from the highest occupied π-orbital to determine the polarization in charge density at C4 and C5.

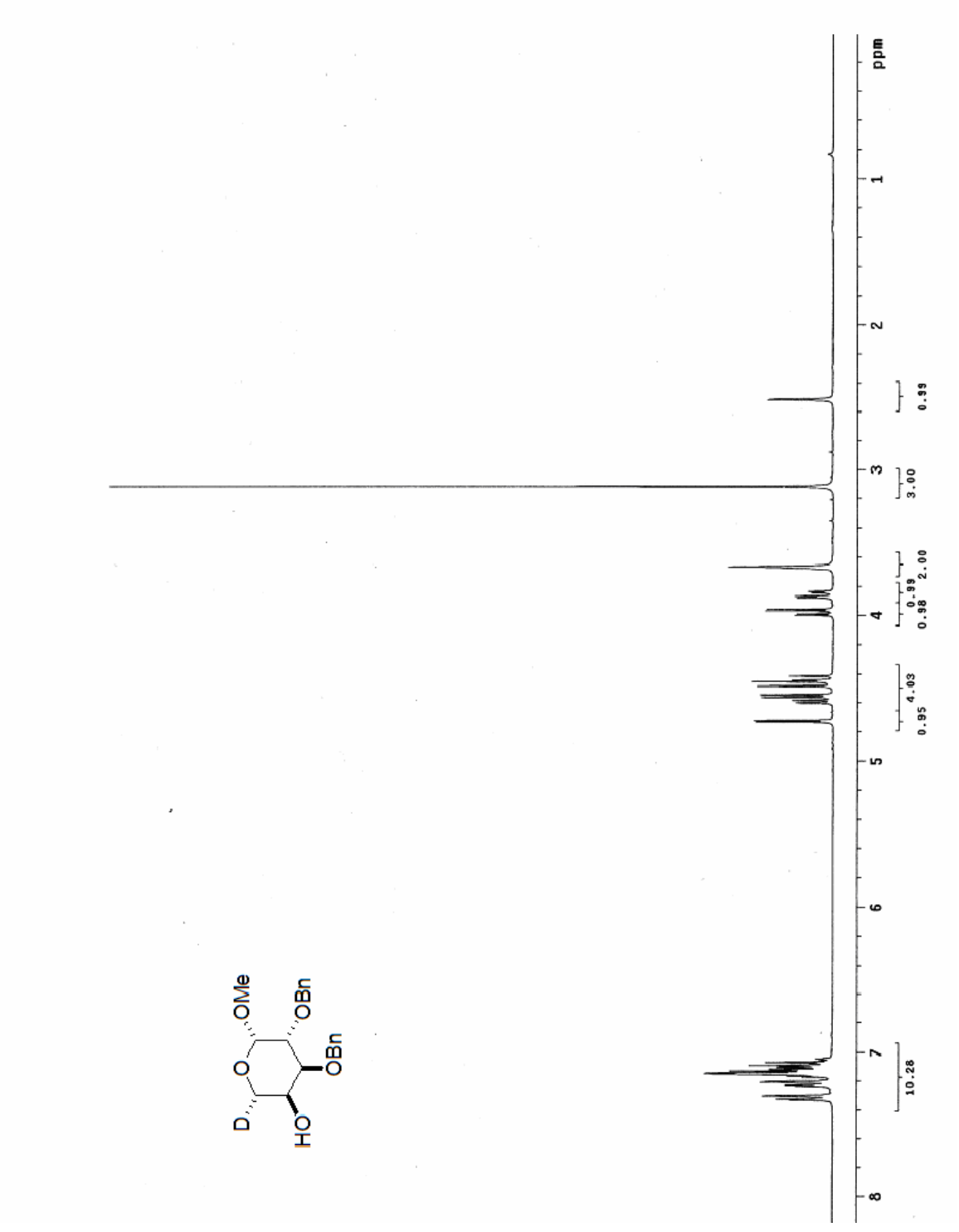
^{1}H NMR (300 MHz, C_6D_6) of **1**:



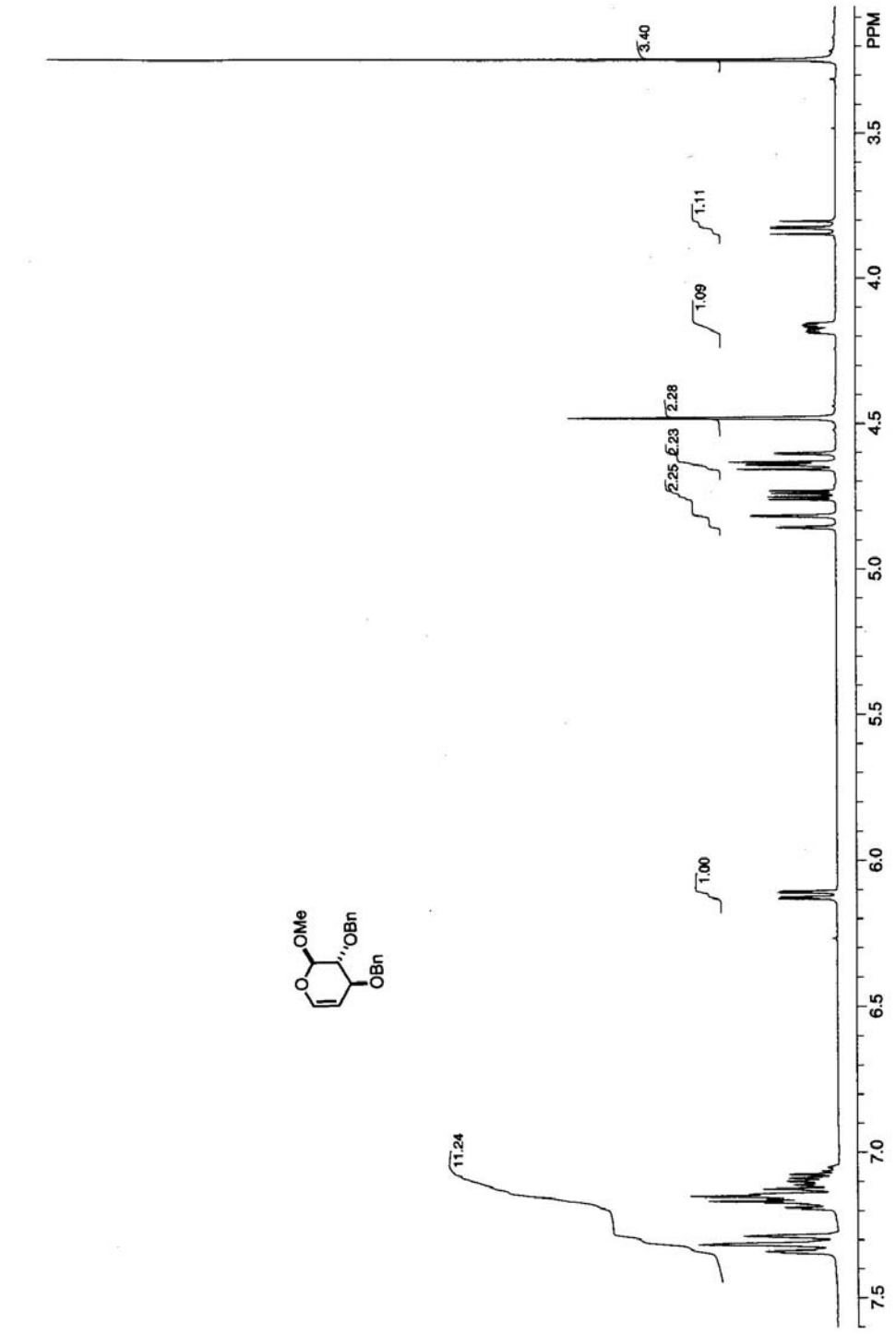
^{1}H NMR (300 MHz, C_6D_6) of 4β-epoxide of **1** (10:1 β/α):



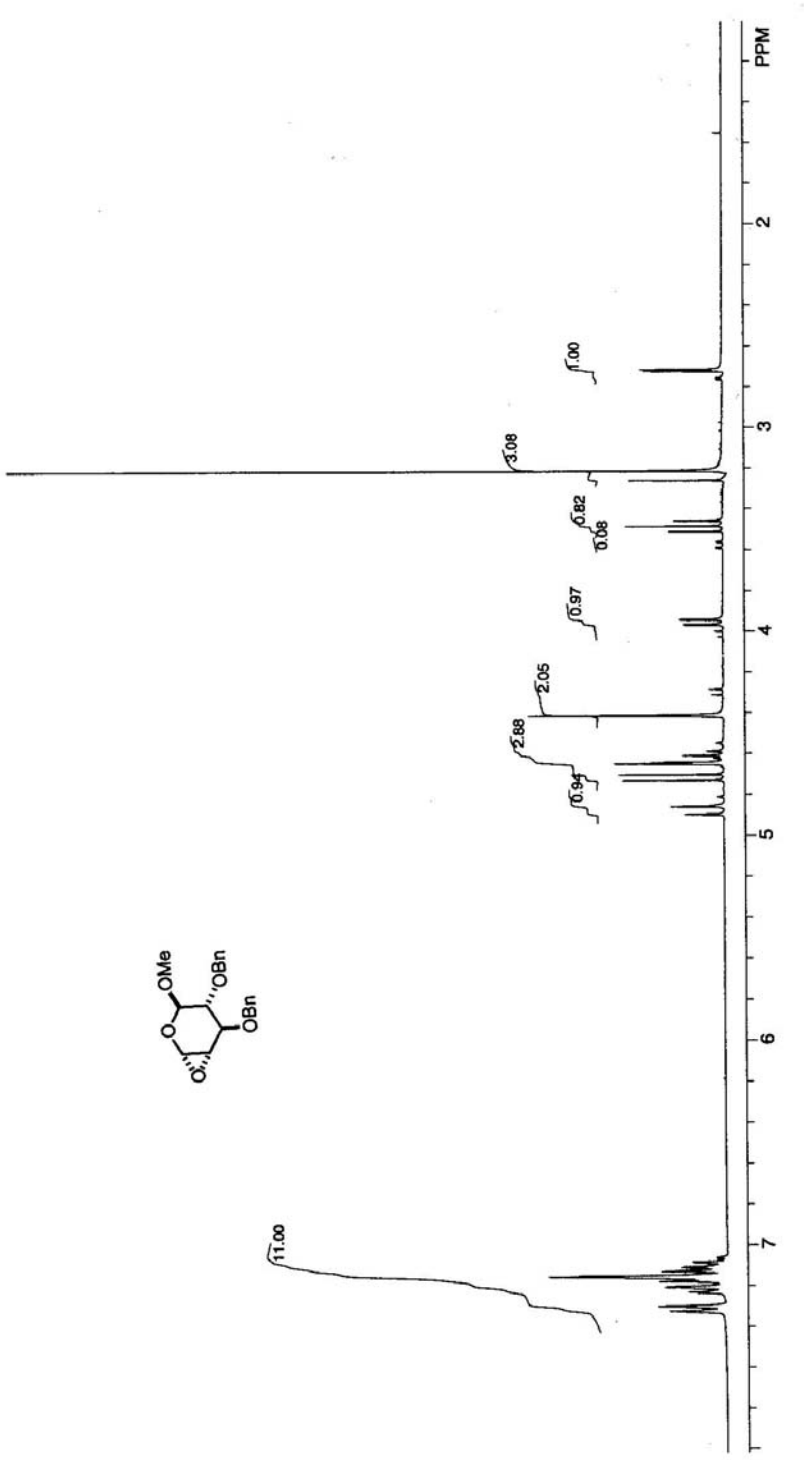
^{1}H NMR (300 MHz, C_6D_6) of 5*S*-*d*-L-arabinoside derived from **1**:



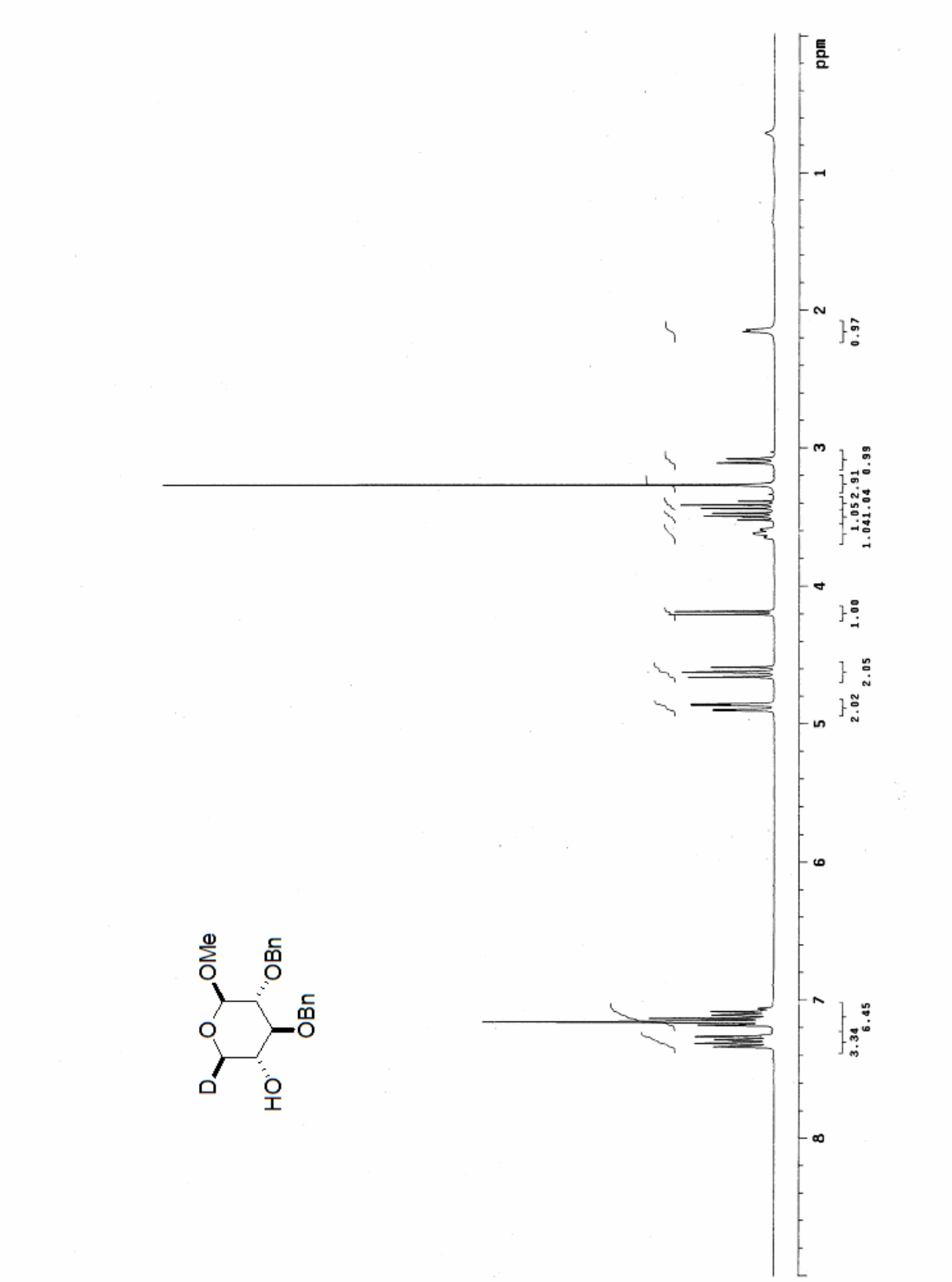
^{1}H NMR (300 MHz, C_6D_6) of **2**:



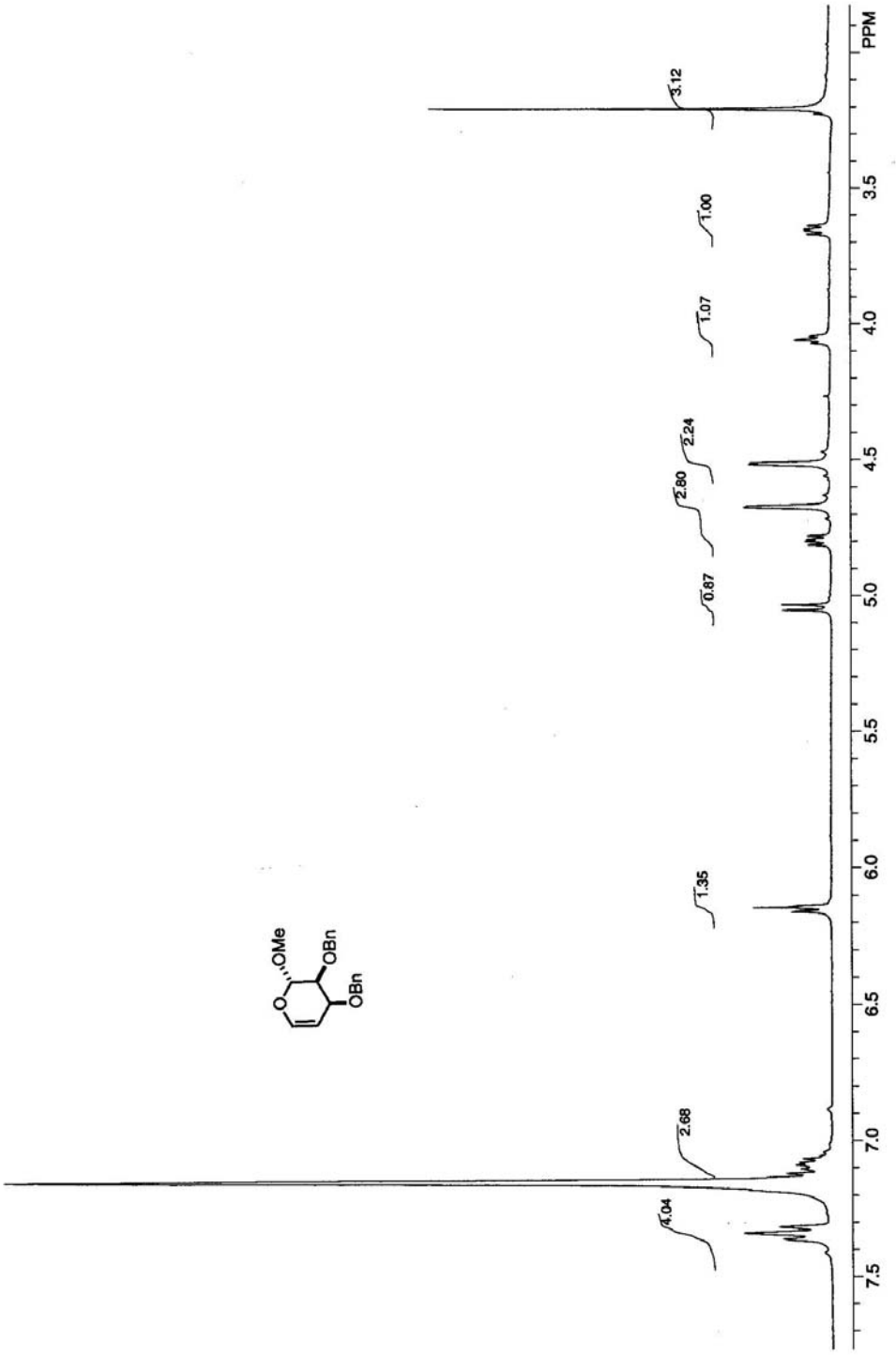
^{1}H NMR (300 MHz, C_6D_6) of 4α-epoxide of **2** (1:10 β/α):



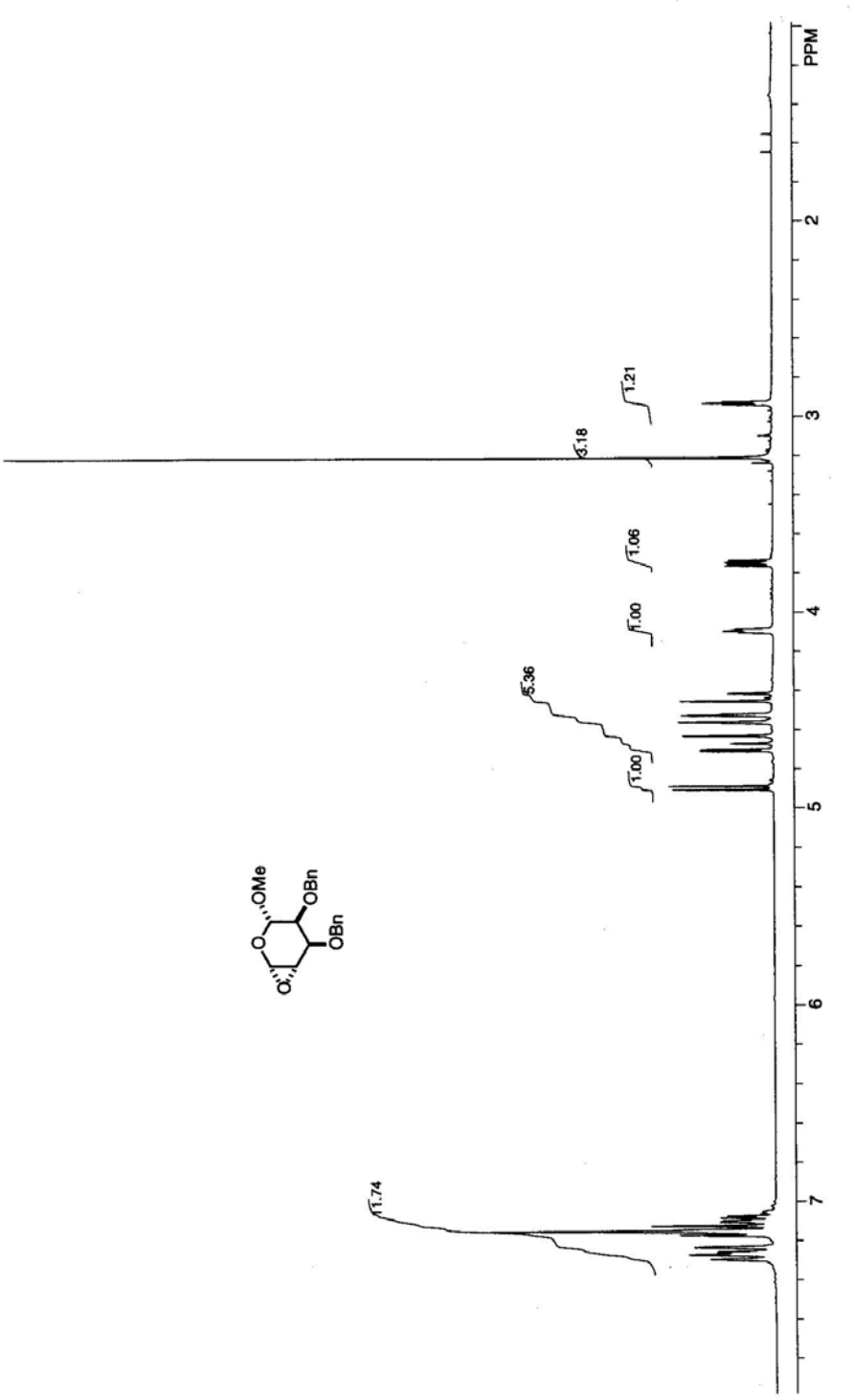
^{1}H NMR (300 MHz, C_6D_6) of 5*R*-*d*-D-xyloside derived from **2**



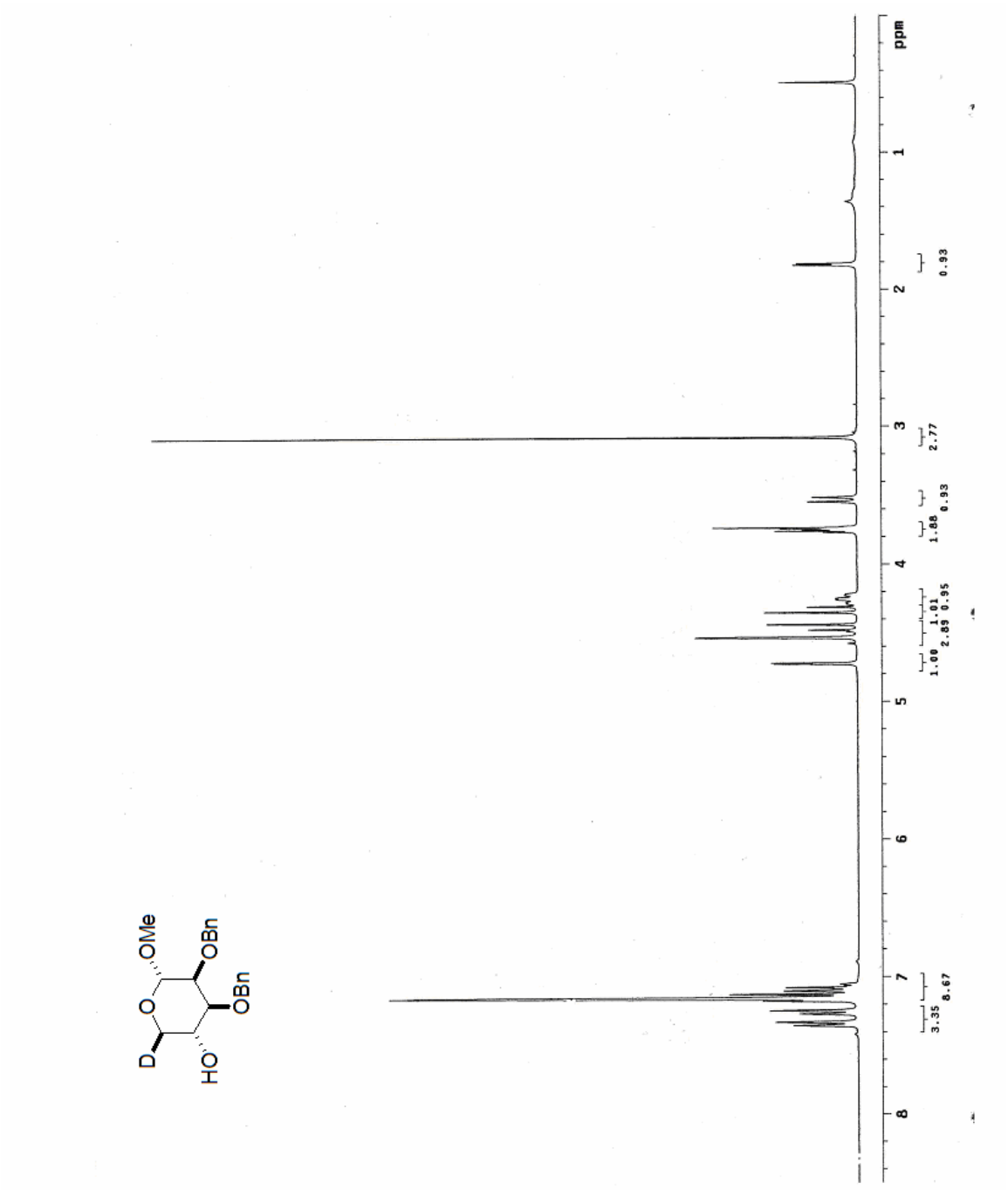
^{1}H NMR (300 MHz, C_6D_6) of **3**:



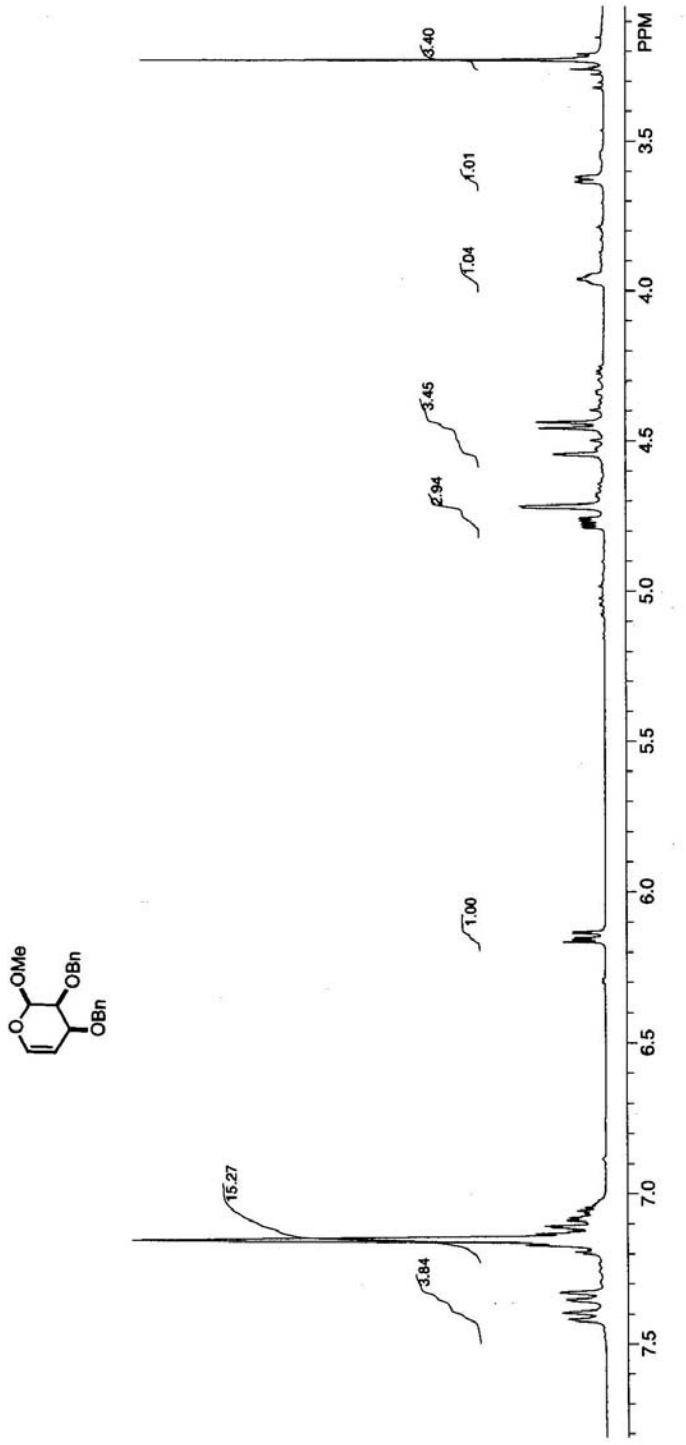
^{1}H NMR (300 MHz, C_6D_6) of 4α-epoxide of **3** (<1:20 β/α):



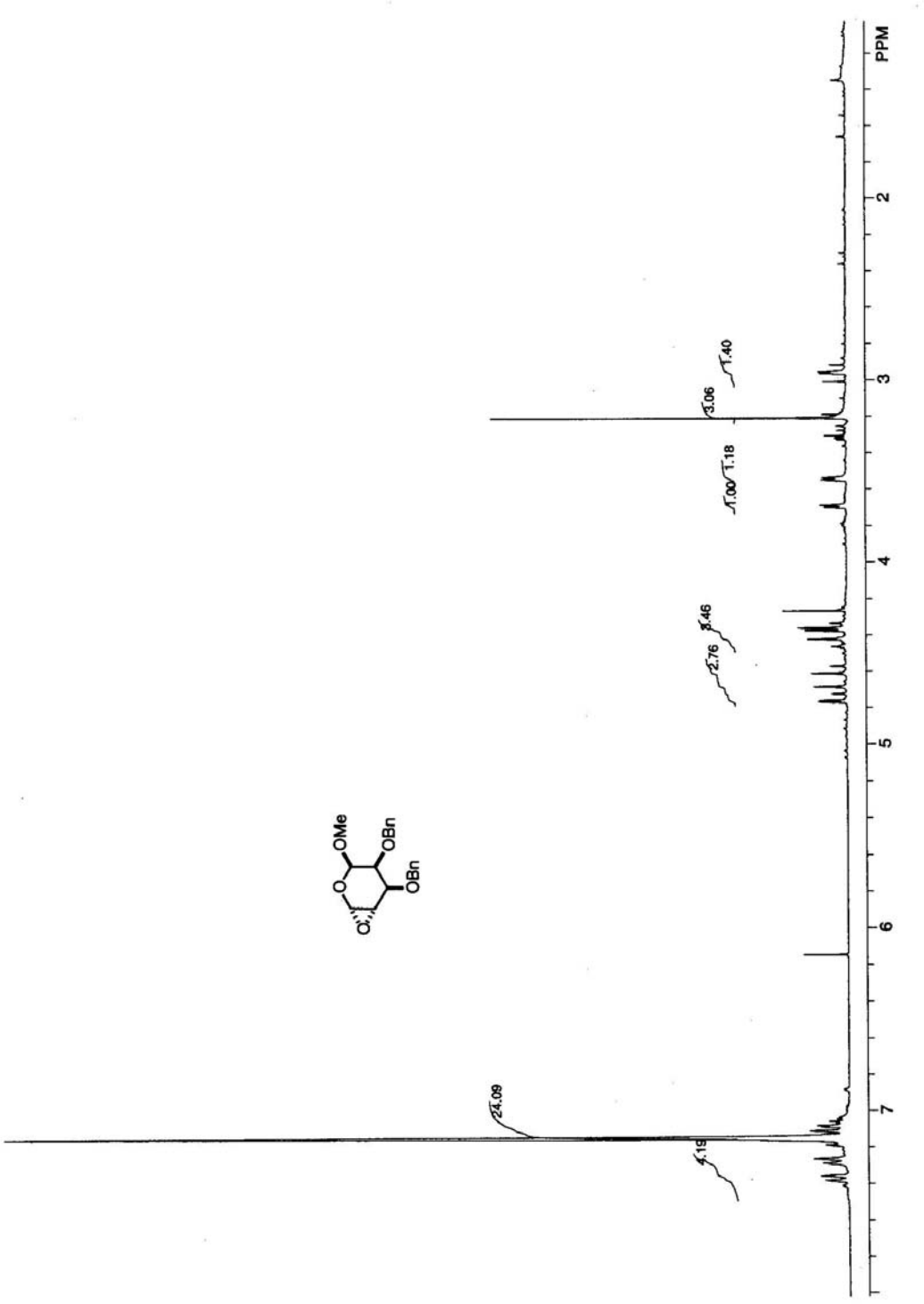
^{1}H NMR (300 MHz, C_6D_6) of 5*R*-*d*-D-lyxopyranoside derived from **3**:



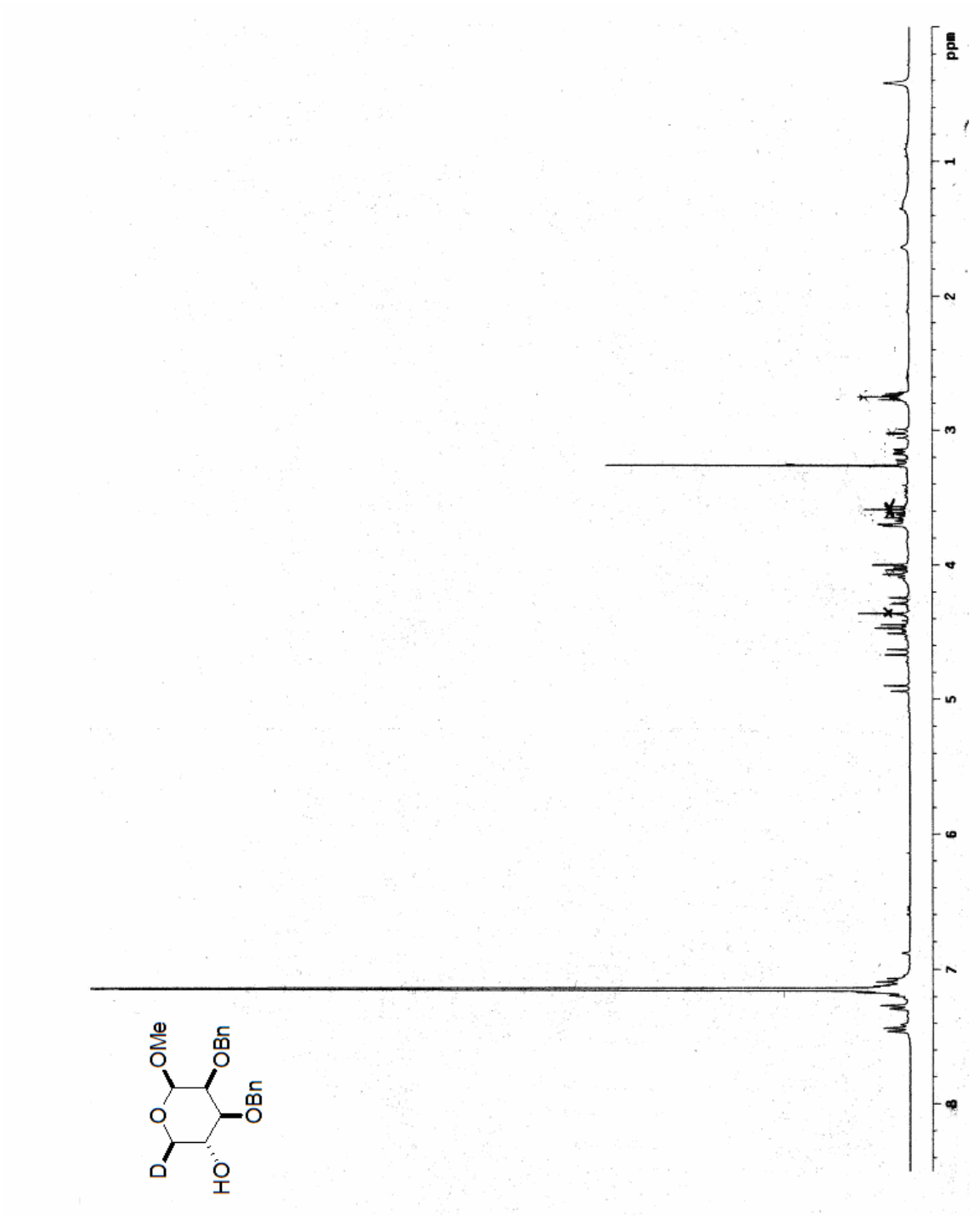
^{1}H NMR (300 MHz, C_6D_6) of **4**:



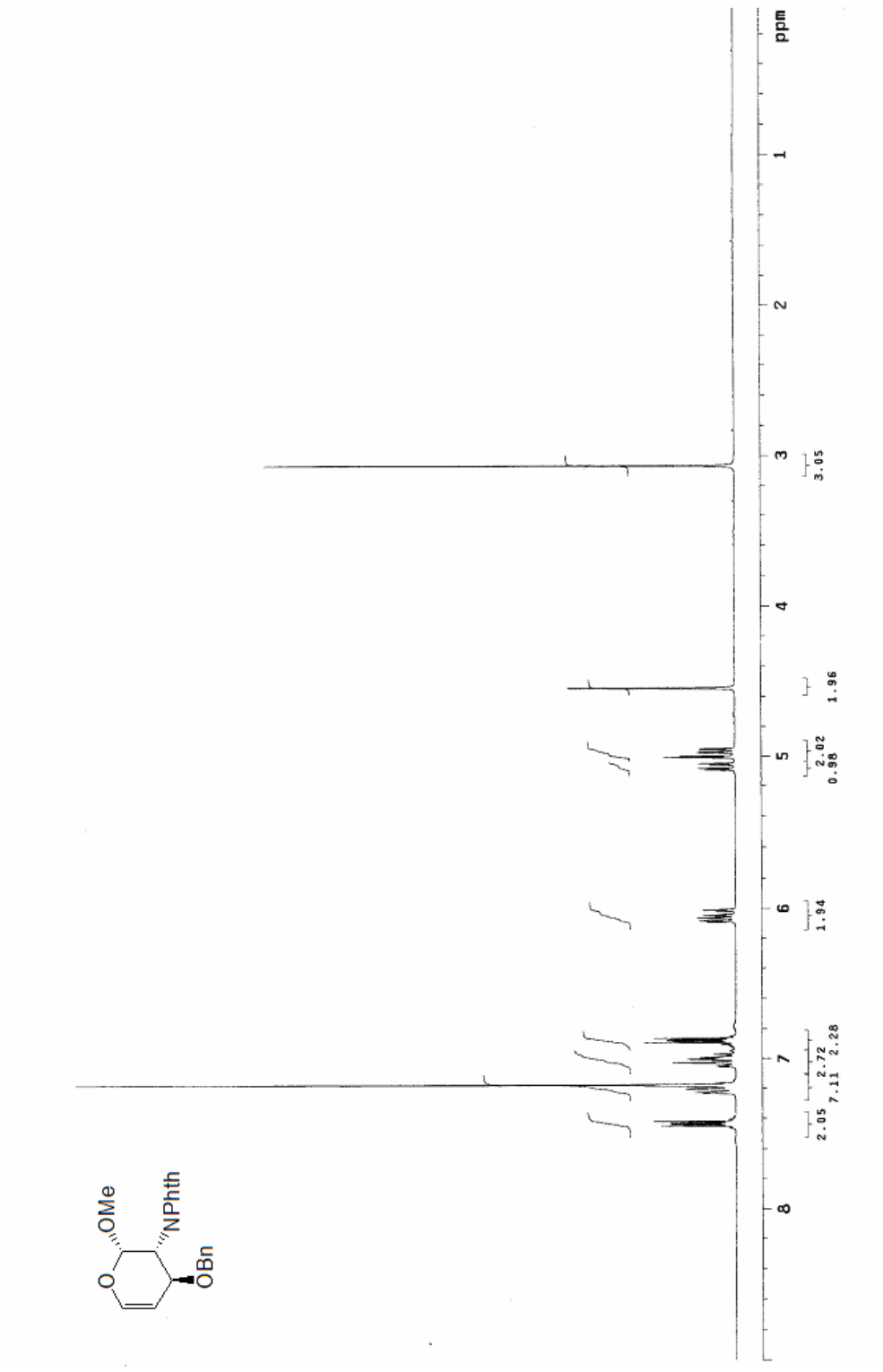
^{1}H NMR (300 MHz, C_6D_6) of 4α-epoxide of **4** (1:15 β/α):



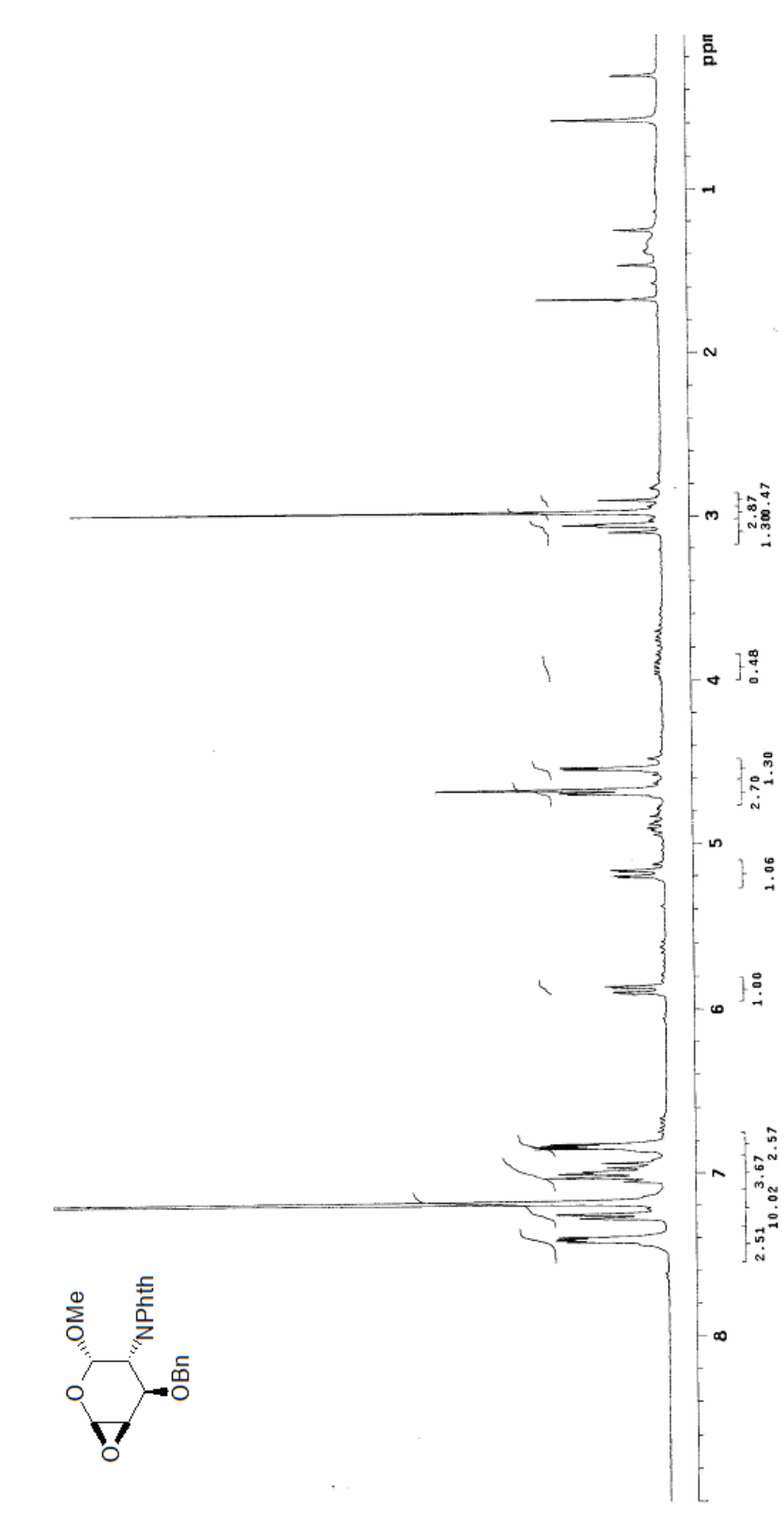
^{1}H NMR (300 MHz, C_6D_6) of 5*R*-*d*-D-lyxopyranoside derived from **4**:



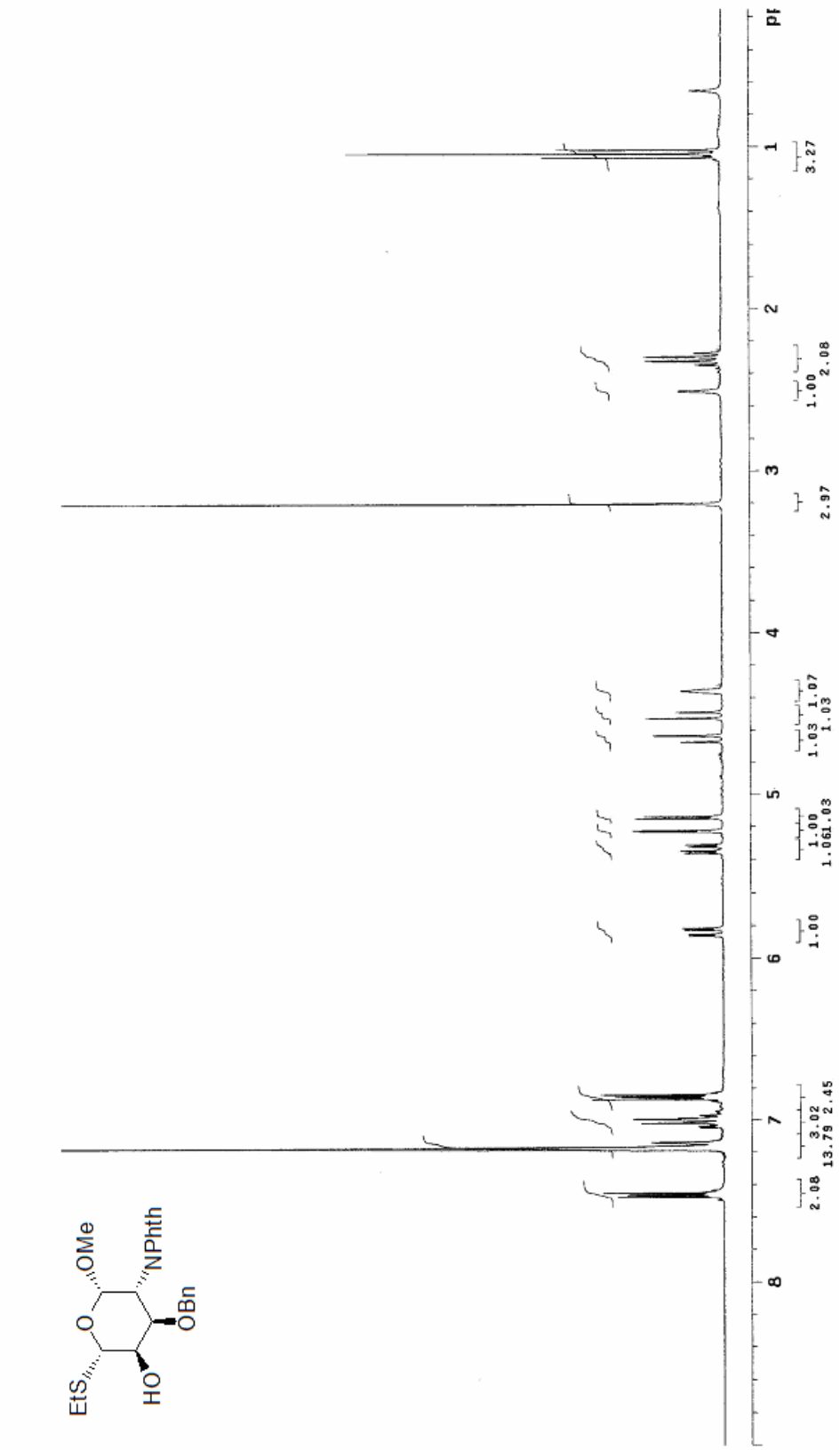
^{1}H NMR (300 MHz, C_6D_6) of **5**:



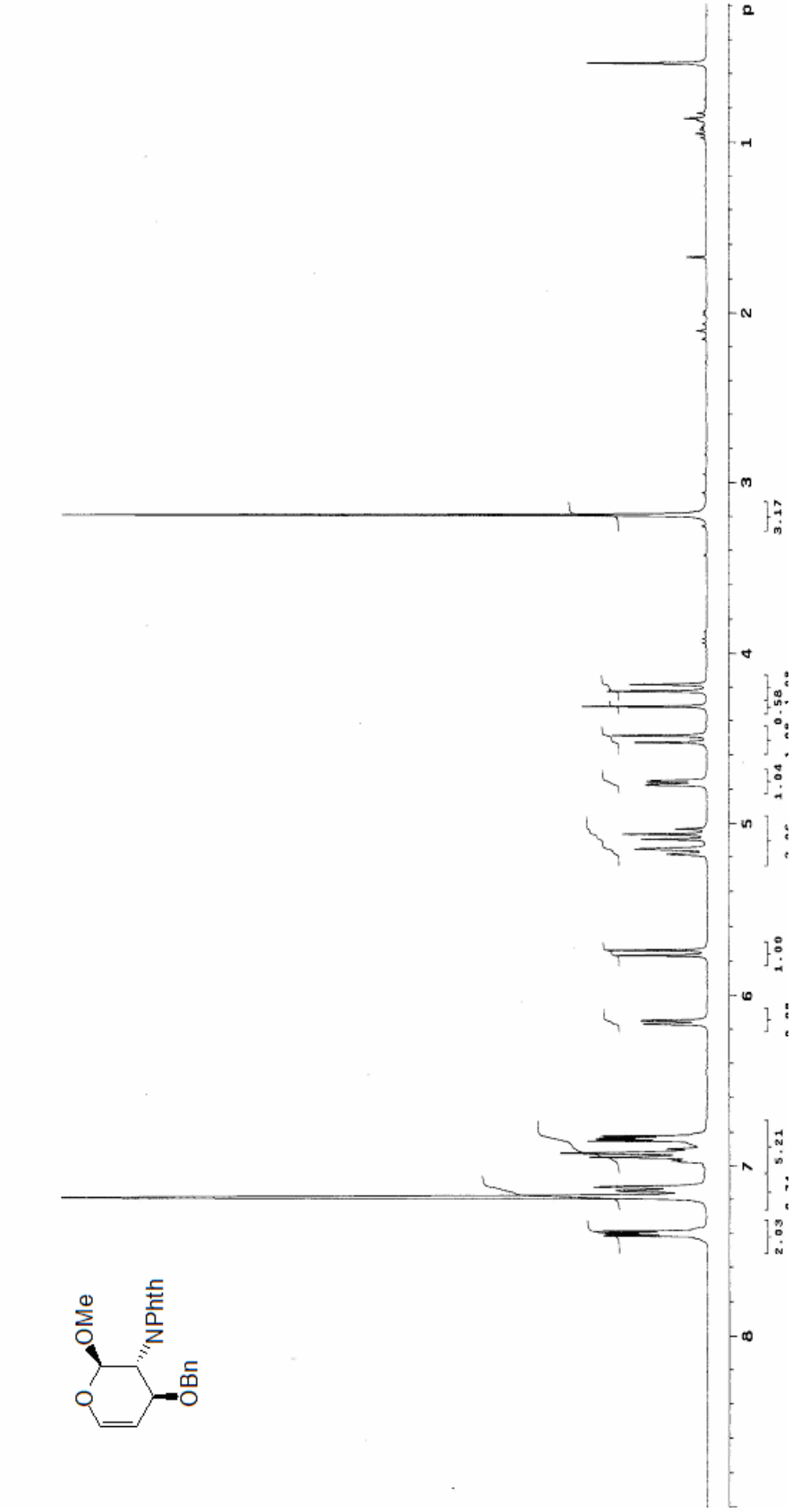
^{1}H NMR (300 MHz, C_6D_6) of 4β-epoxide of **5** (10:1 β/α):



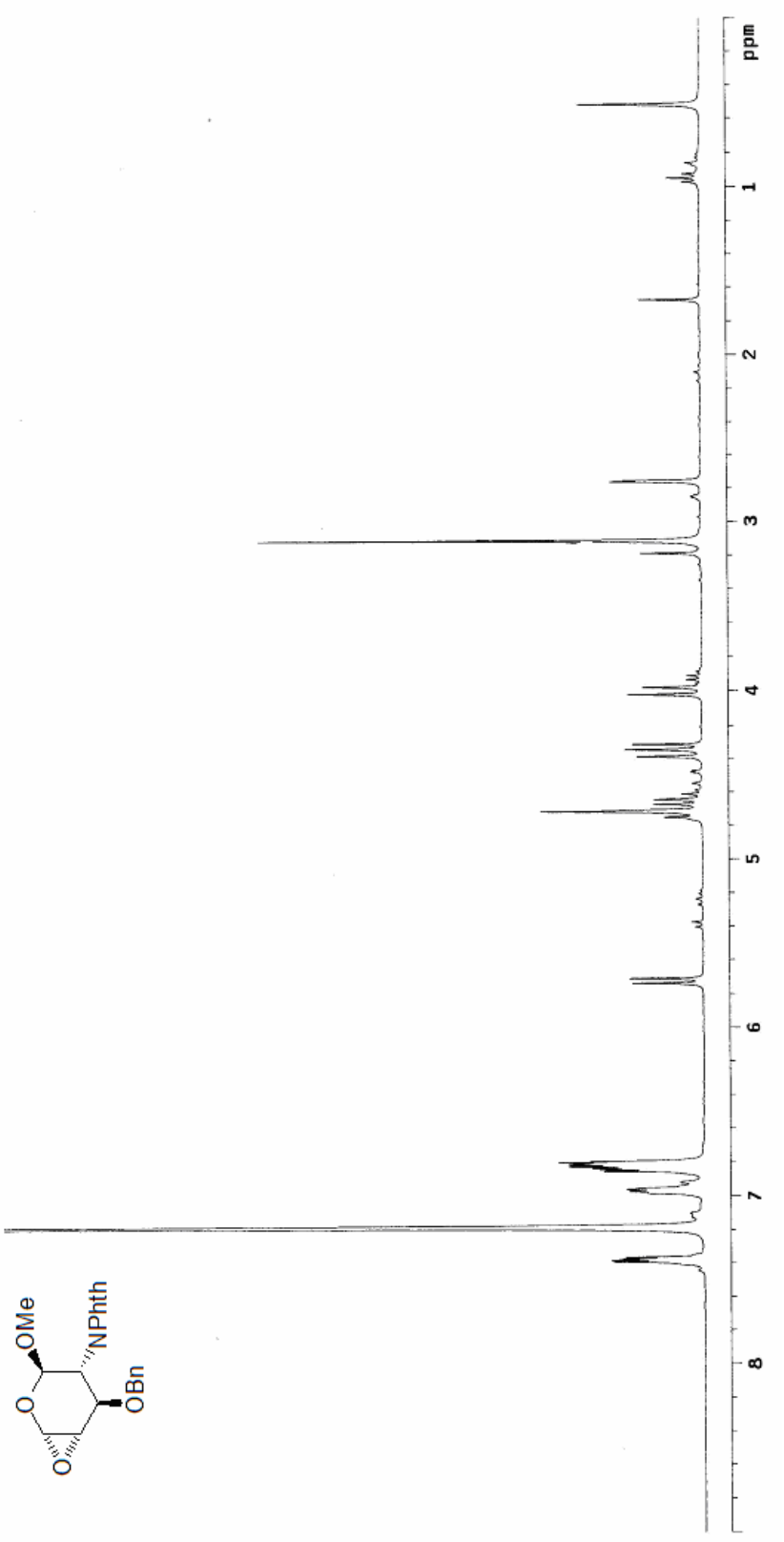
^{1}H NMR (300 MHz, C_6D_6) of 5*S*-(L-*altro*) ethylthioacetal derived from **5**:



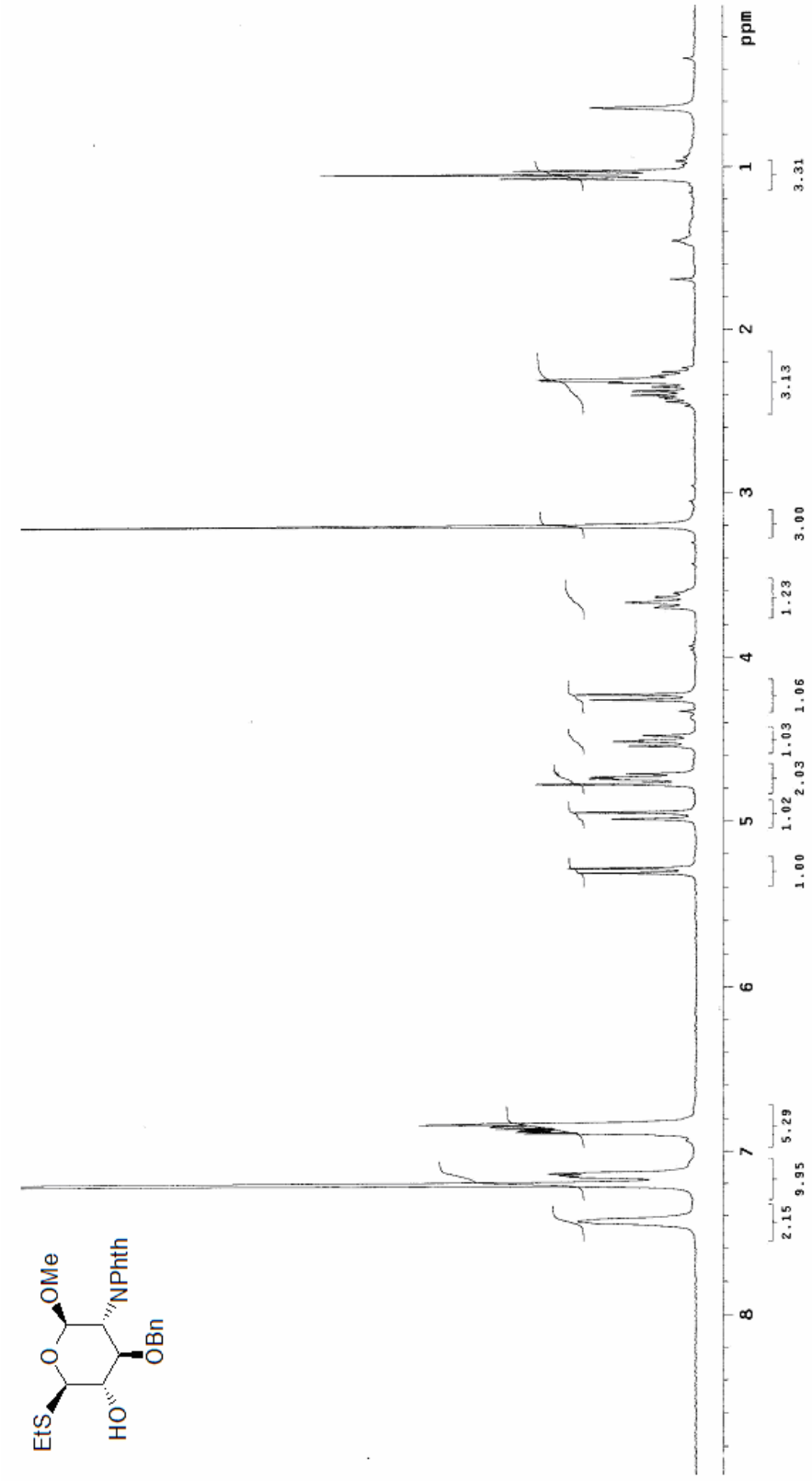
^{1}H NMR (300 MHz, C_6D_6) of **6**:



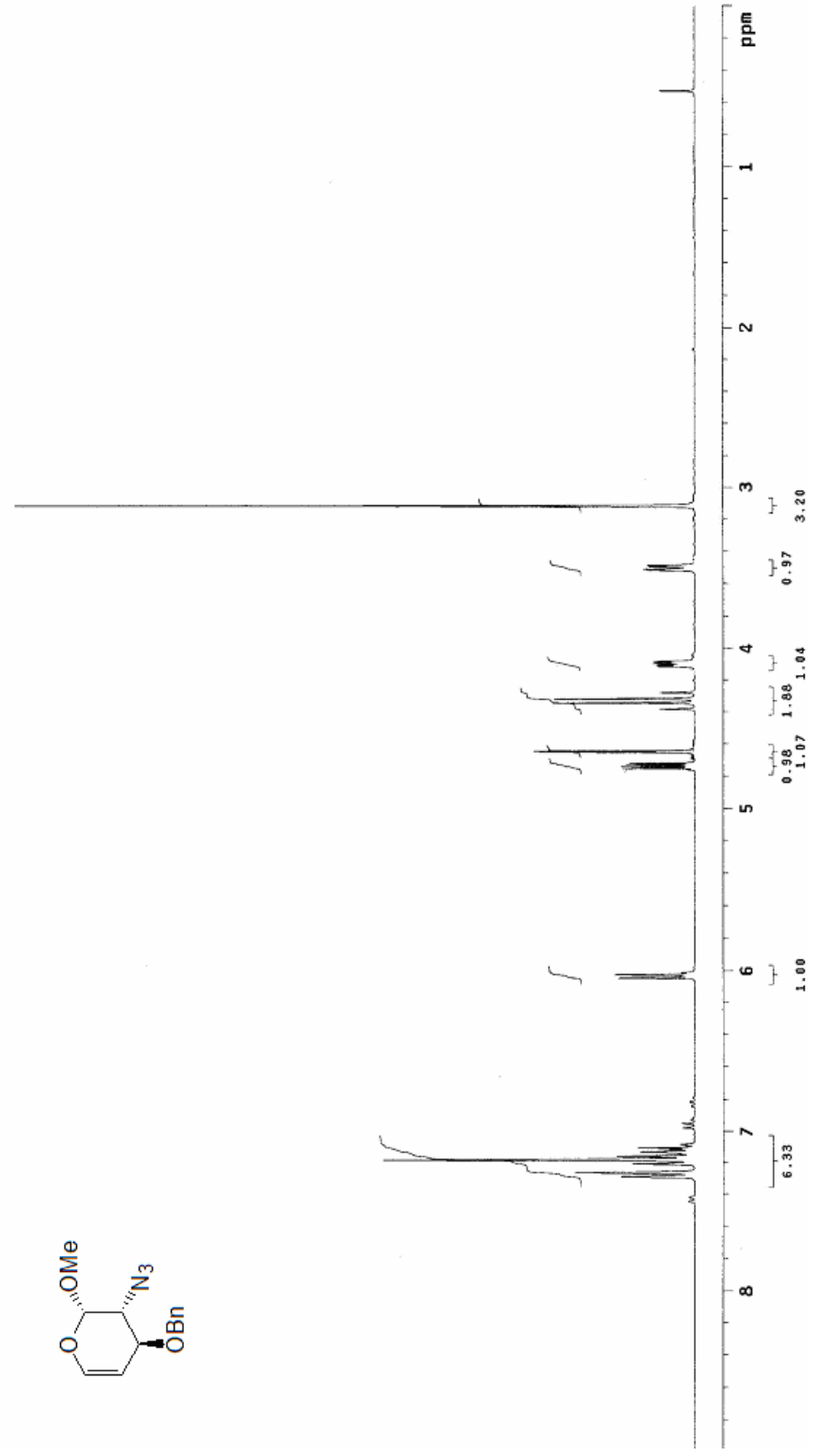
^{1}H NMR (300 MHz, C_6D_6) of 4α-epoxide of **6** (1:10 β/α):



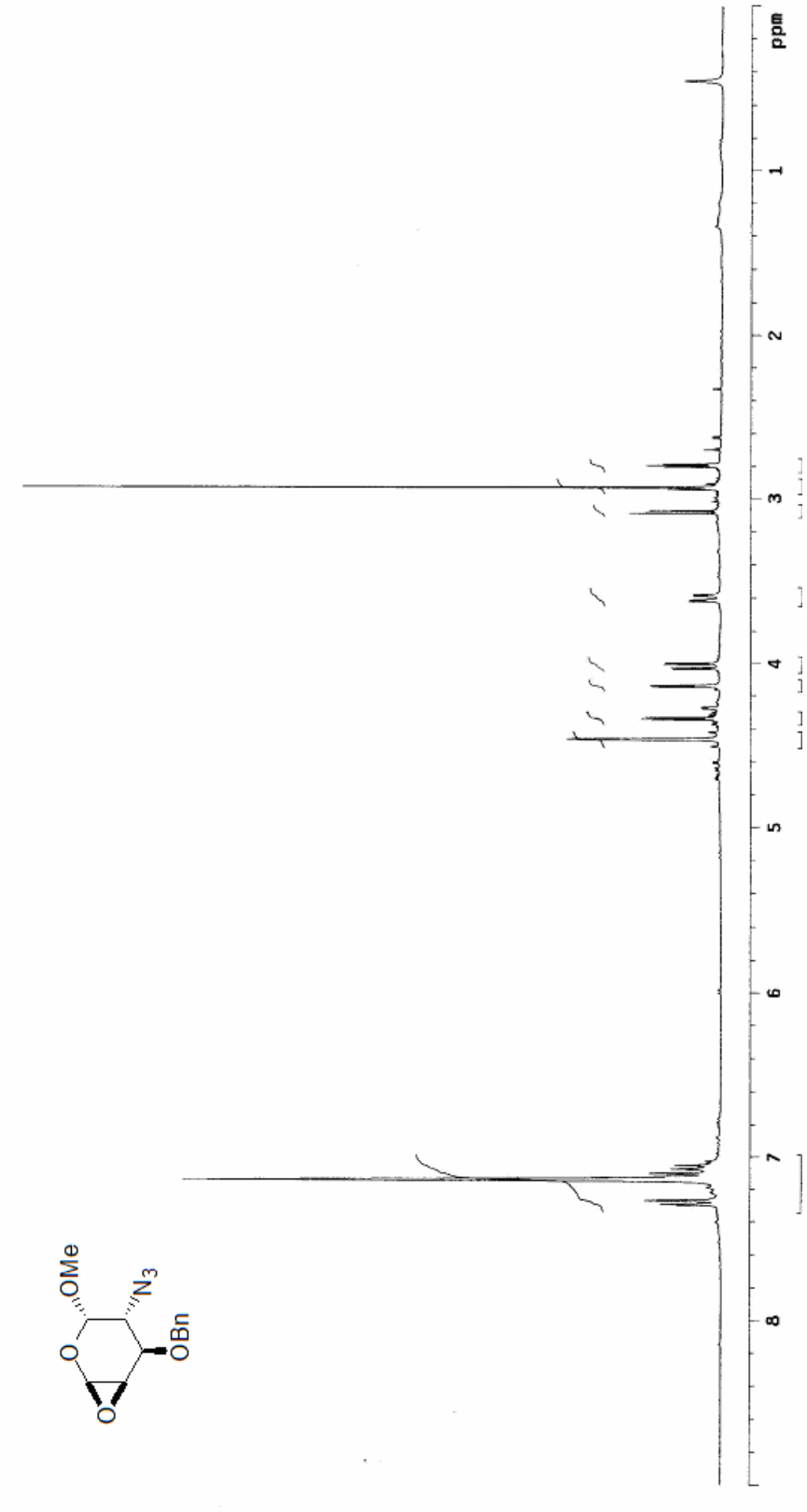
^{1}H NMR (300 MHz, C_6D_6) of 5*S*-(D-*gluco*) ethylthioacetal derived from **6**:



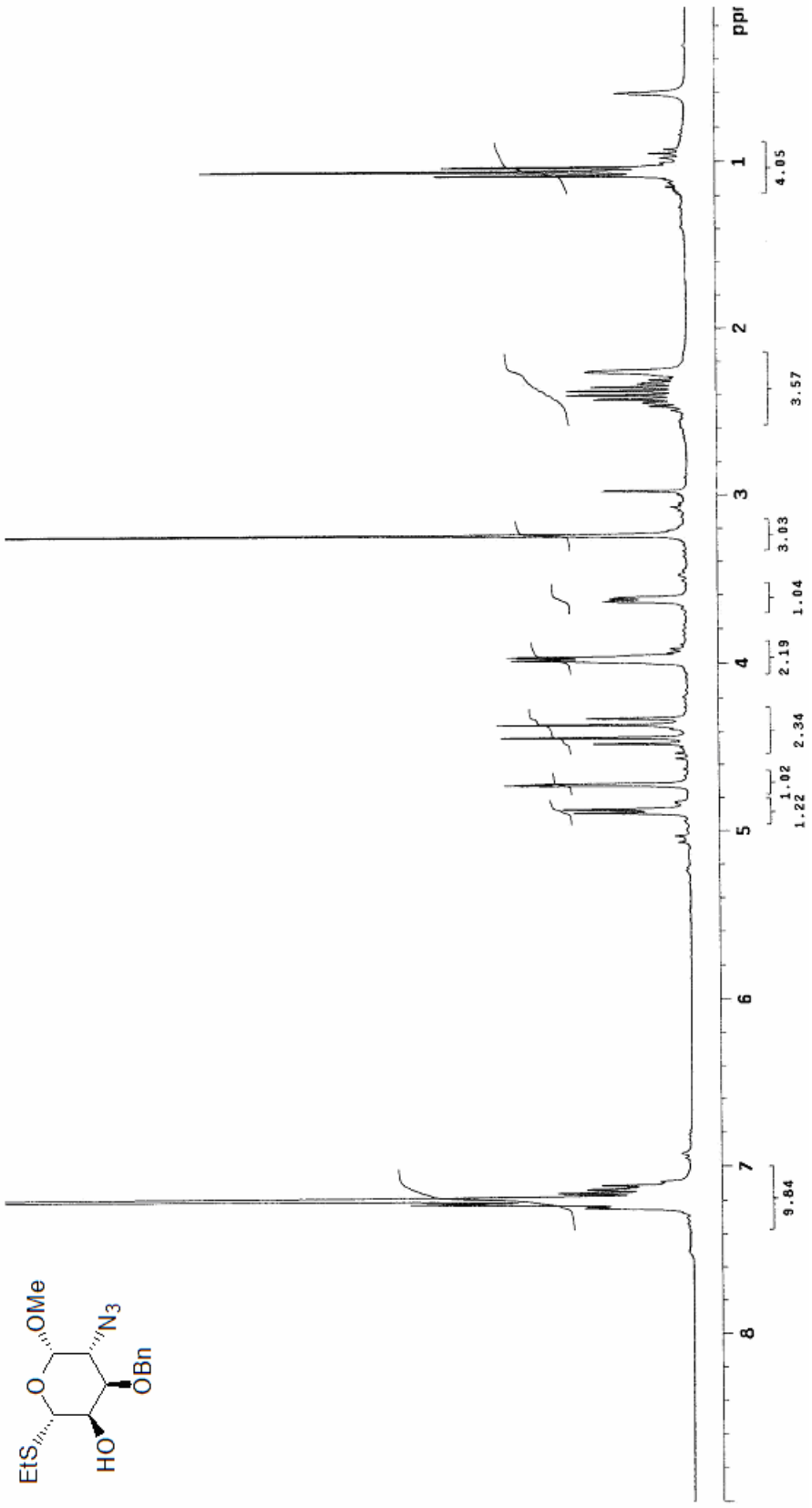
^{1}H NMR (300 MHz, C_6D_6) of **7**:



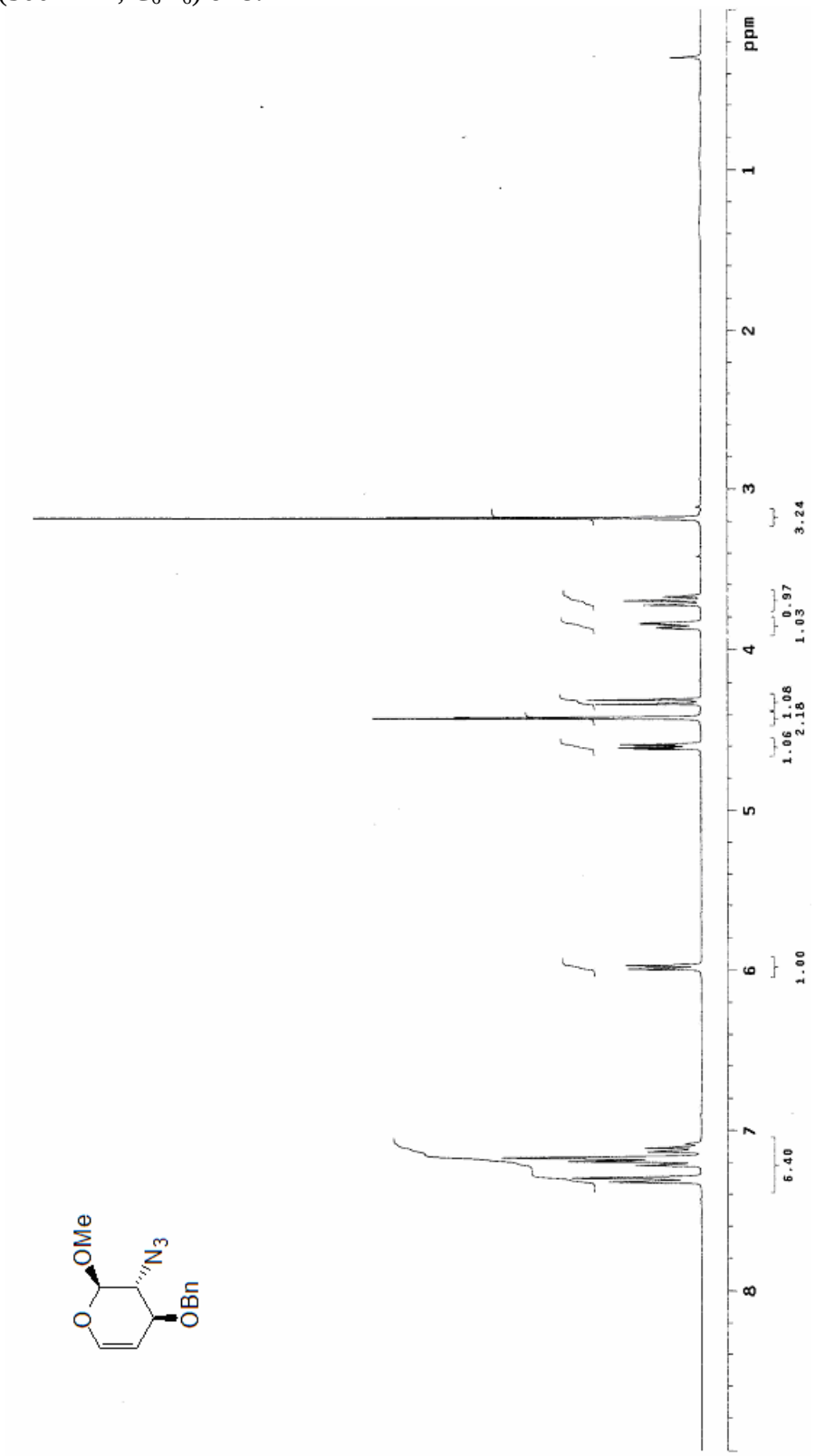
^{1}H NMR (300 MHz, C_6D_6) of 4β-epoxide of **7** (>20:1 β/α):



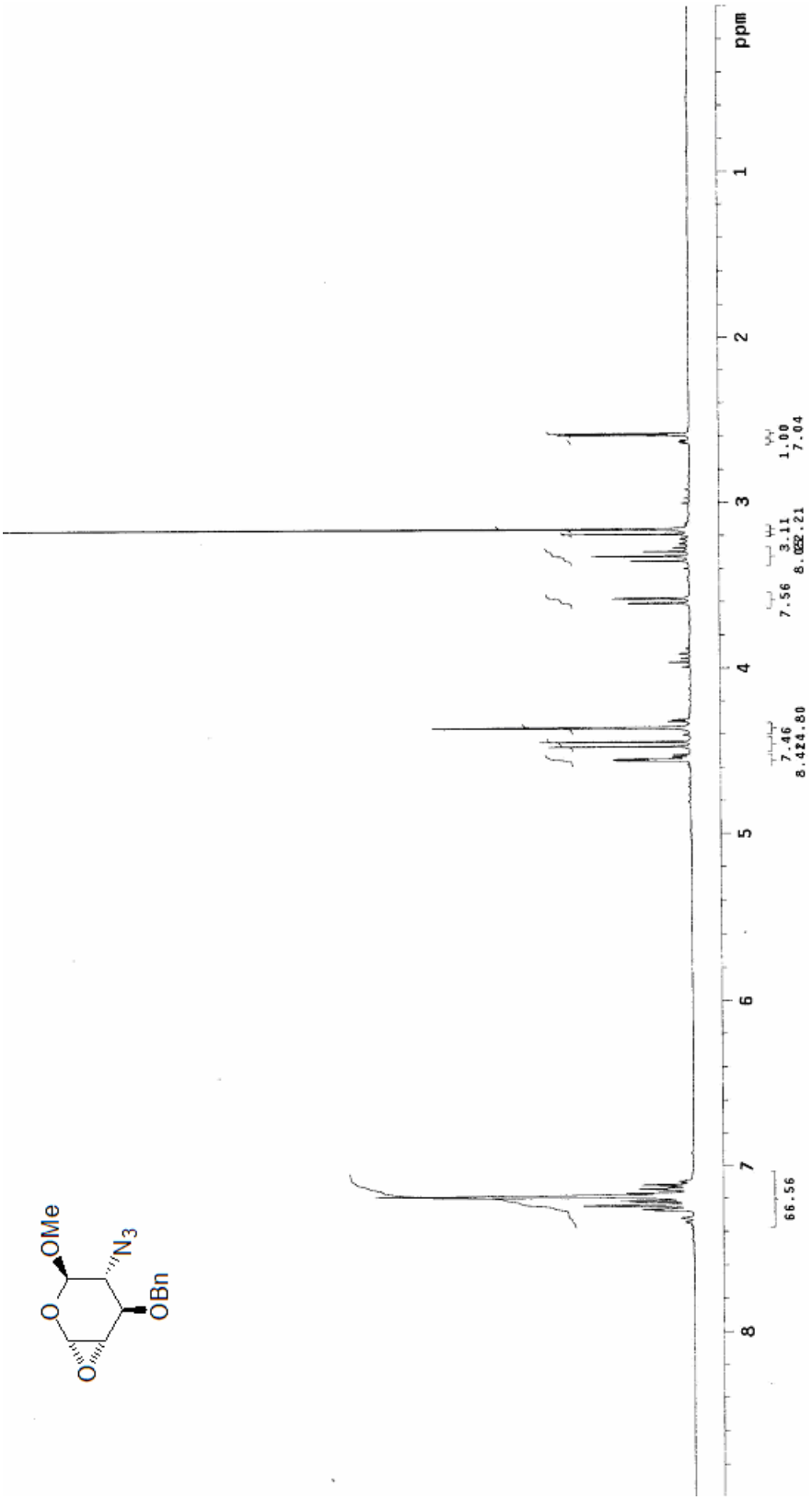
^{1}H NMR (300 MHz, C_6D_6) of 5*S*-(L-*altro*) ethylthioacetal derived from **7**:



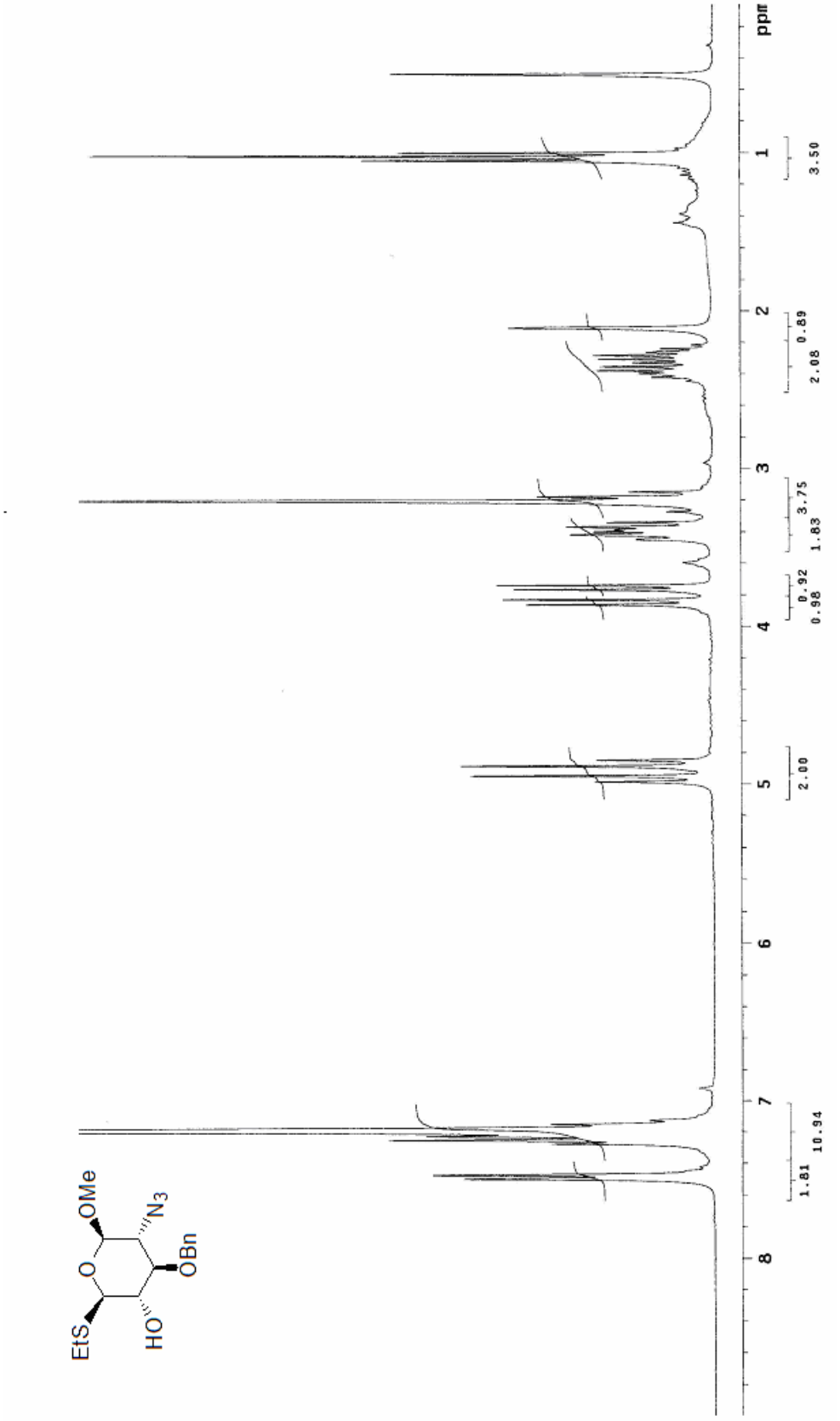
^{1}H NMR (300 MHz, C_6D_6) of **8:**



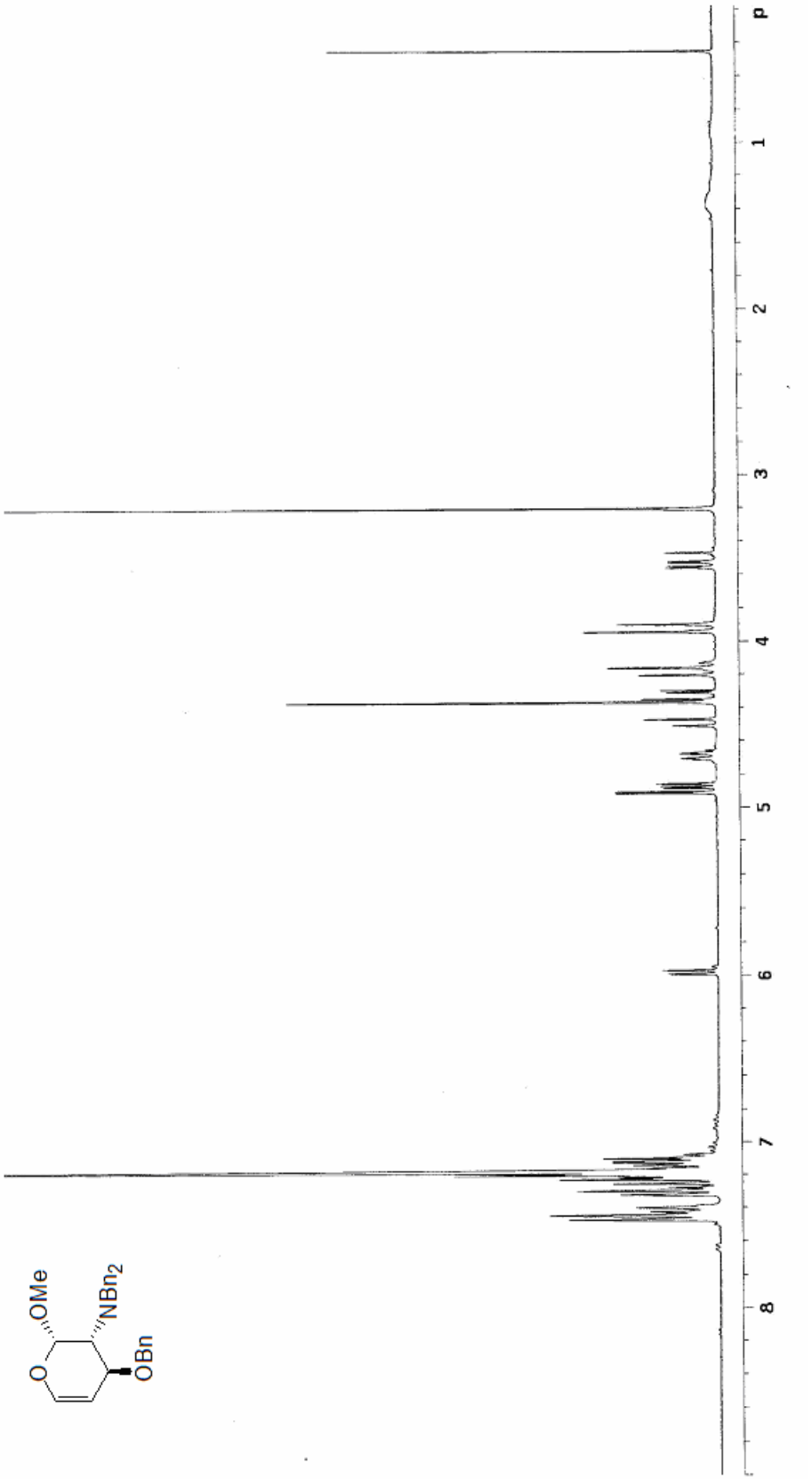
^{1}H NMR (300 MHz, C_6D_6) of 4α-epoxide of **8** (1:10 β/α):



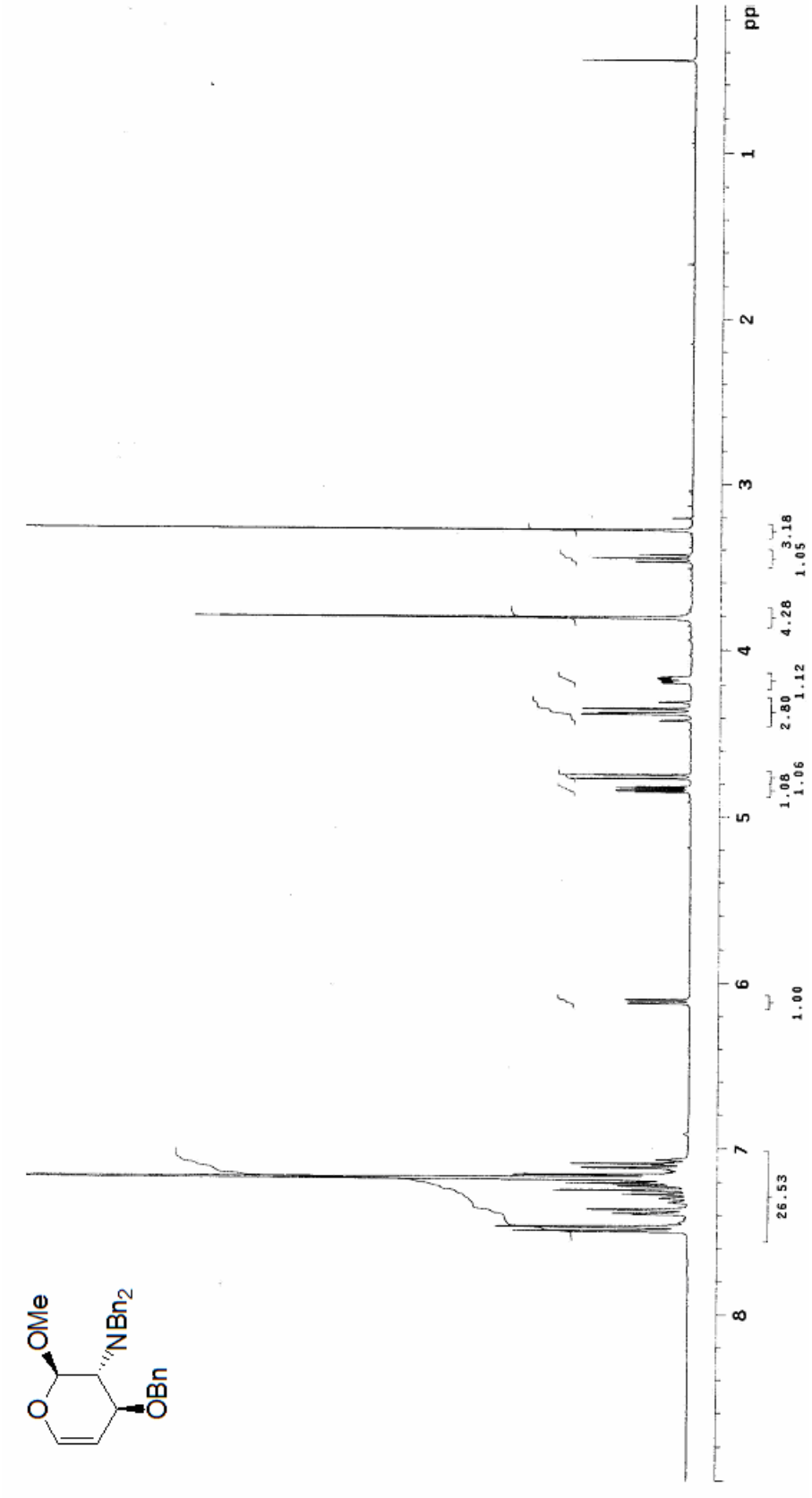
^{1}H NMR (300 MHz, C_6D_6) of 5*S*-(D-*gluco*) ethylthioacetal derived from **8**:



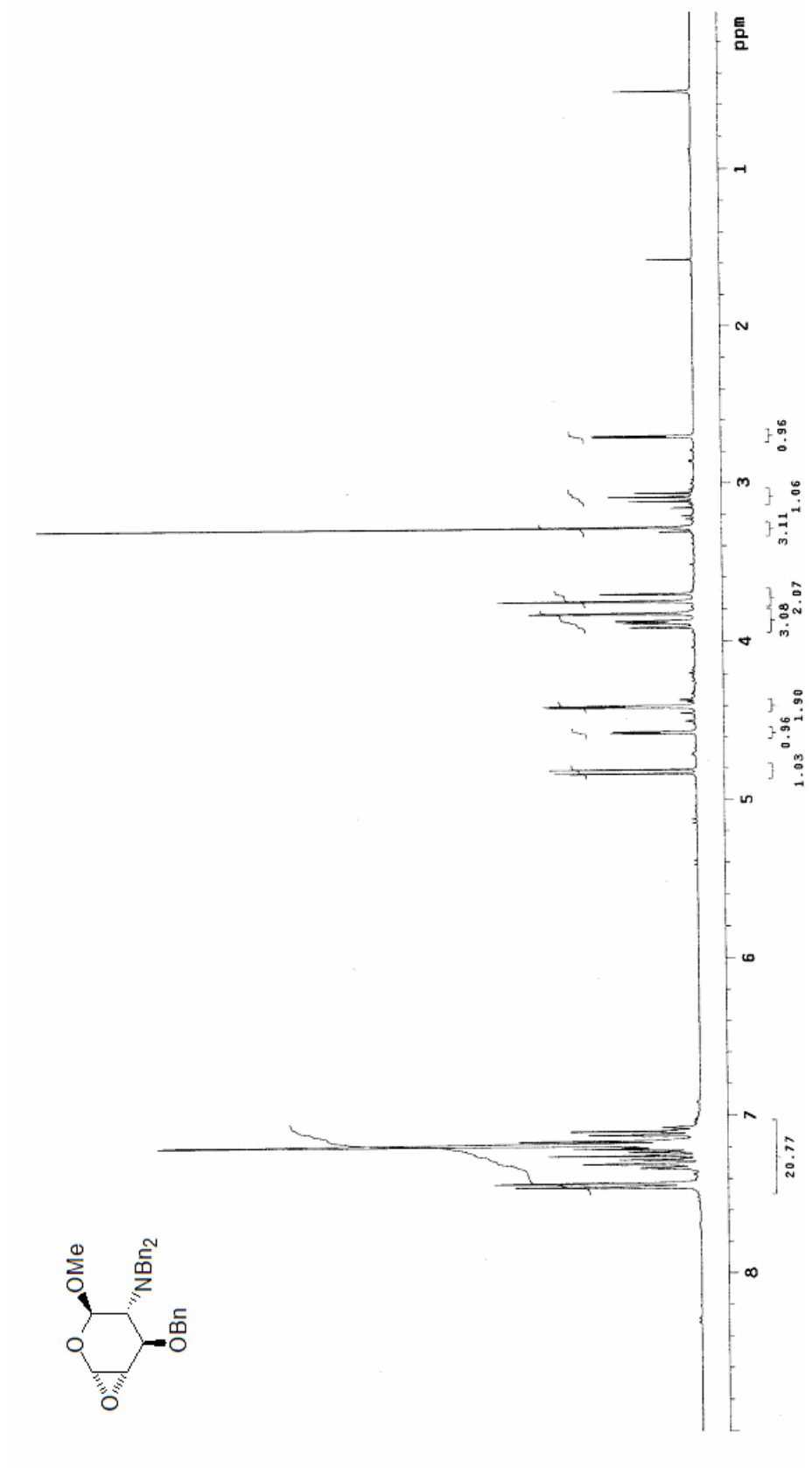
^{1}H NMR (300 MHz, C_6D_6) of **9:**



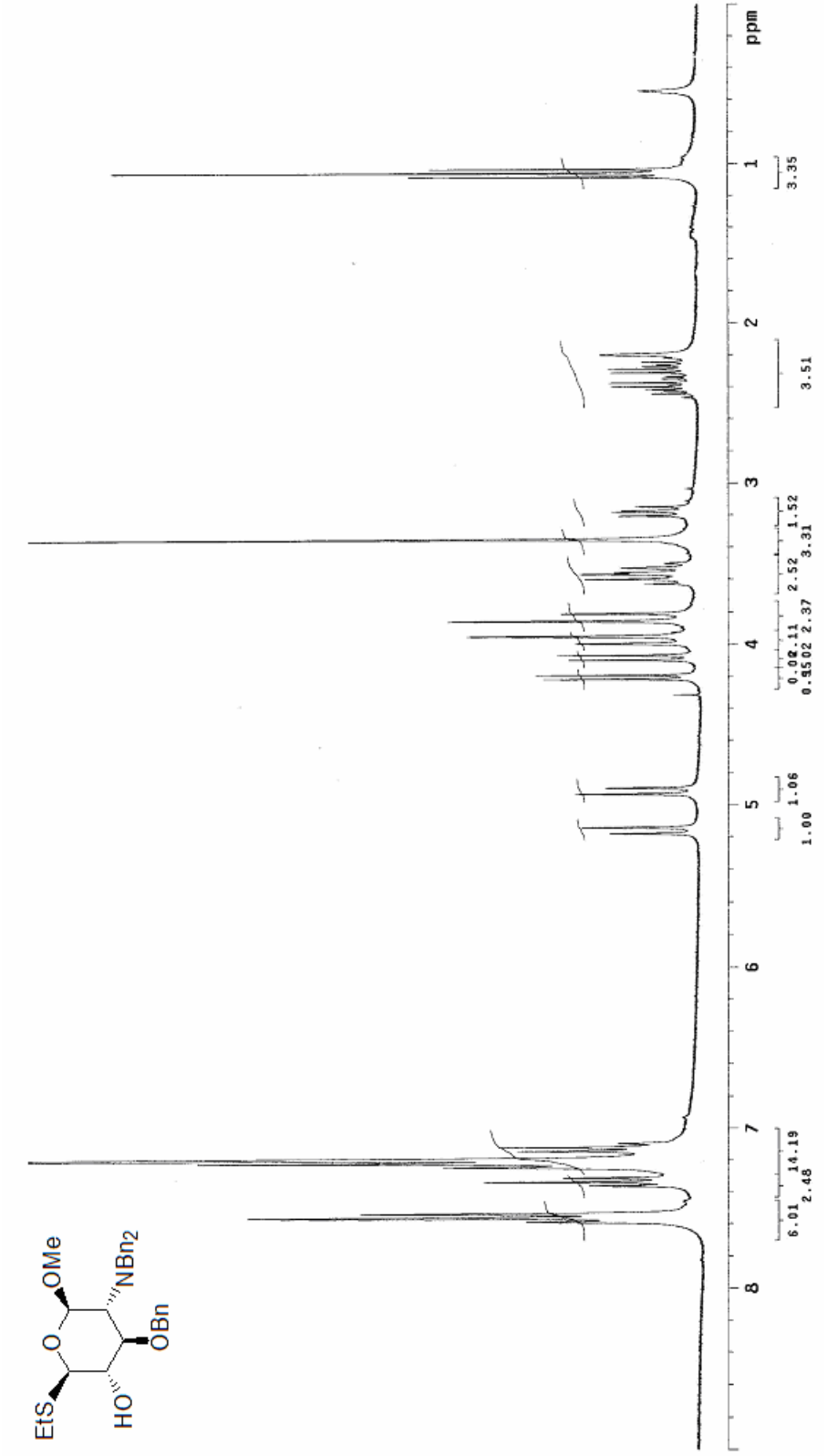
^{1}H NMR (300 MHz, C_6D_6) of **10:**



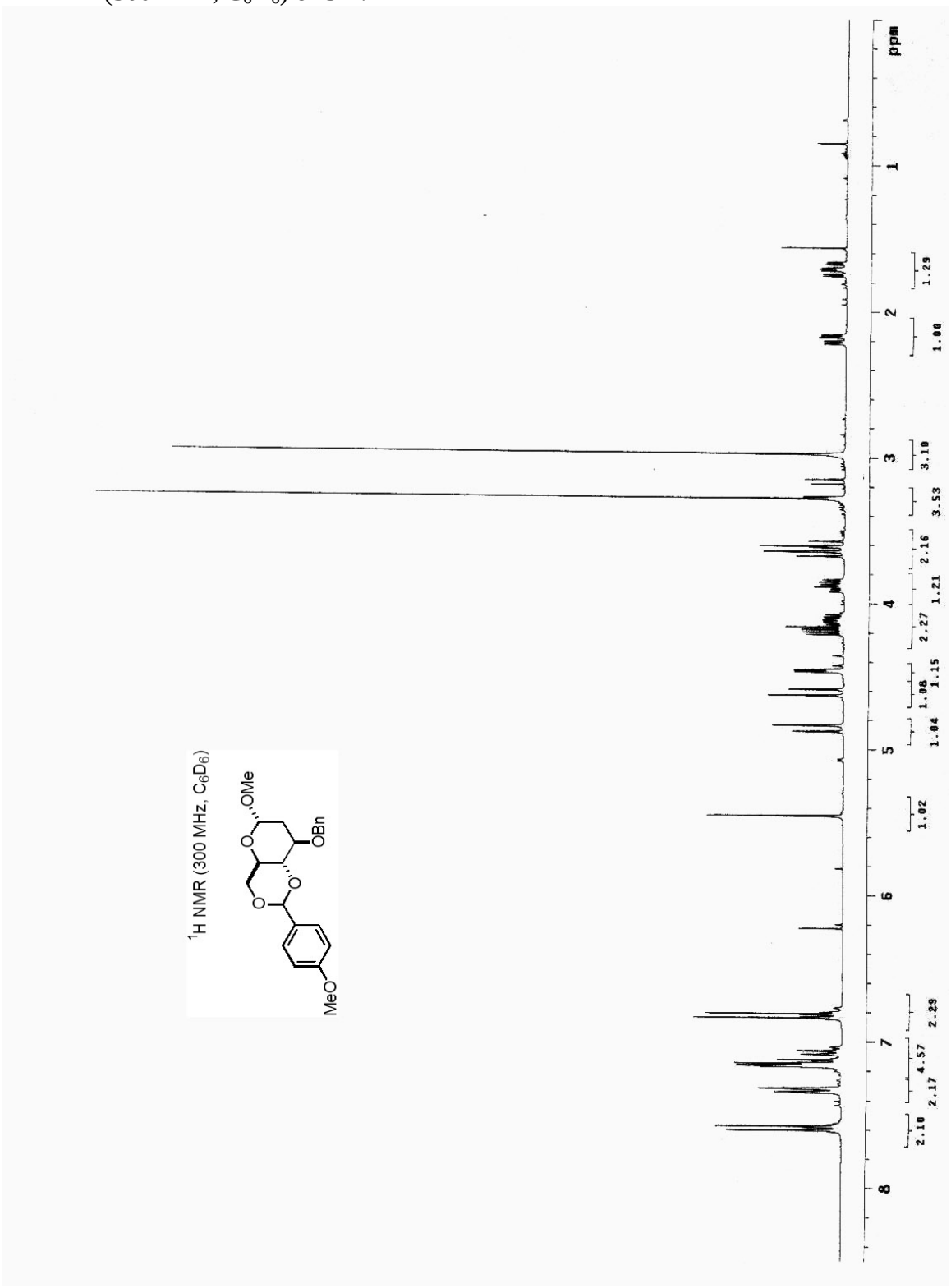
^{1}H NMR (300 MHz, C_6D_6) of 4α-epoxide of **10** (<1:20 β/α):



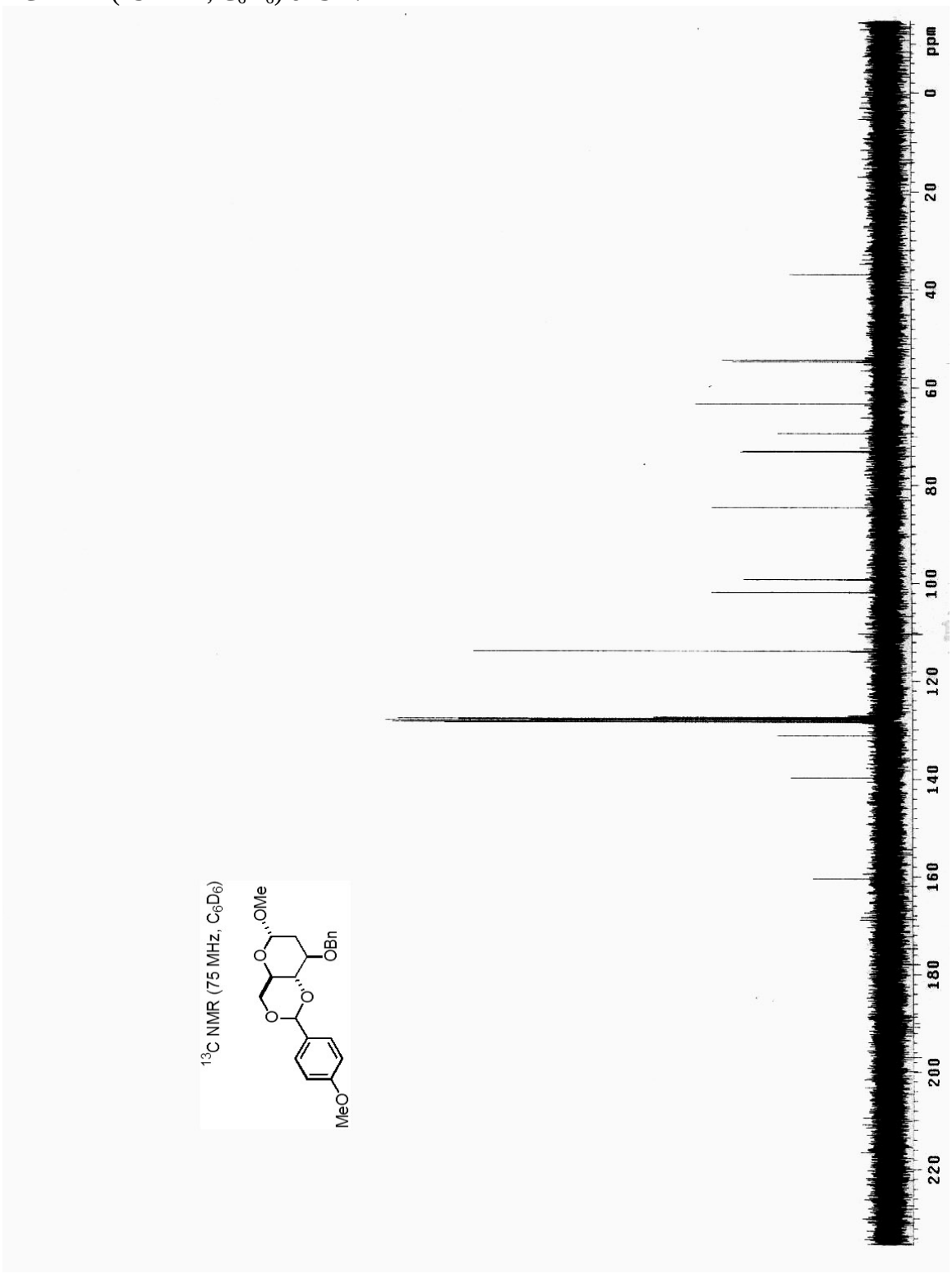
^{1}H NMR (300 MHz, C_6D_6) of 5*S*-(D-*gluco*) ethylthioacetal derived from **10**:



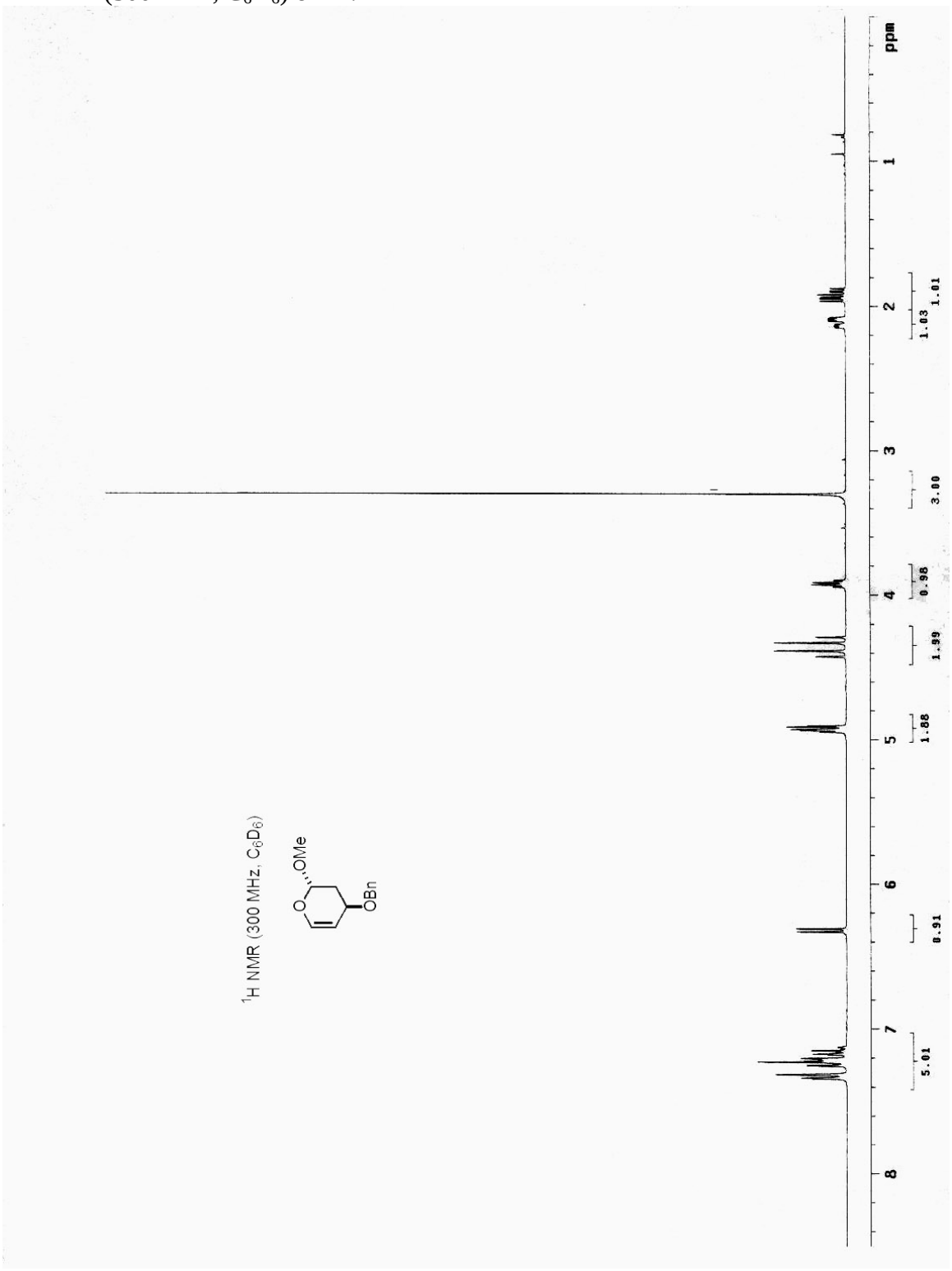
^{1}H NMR (300 MHz, C_6D_6) of **S-2**:



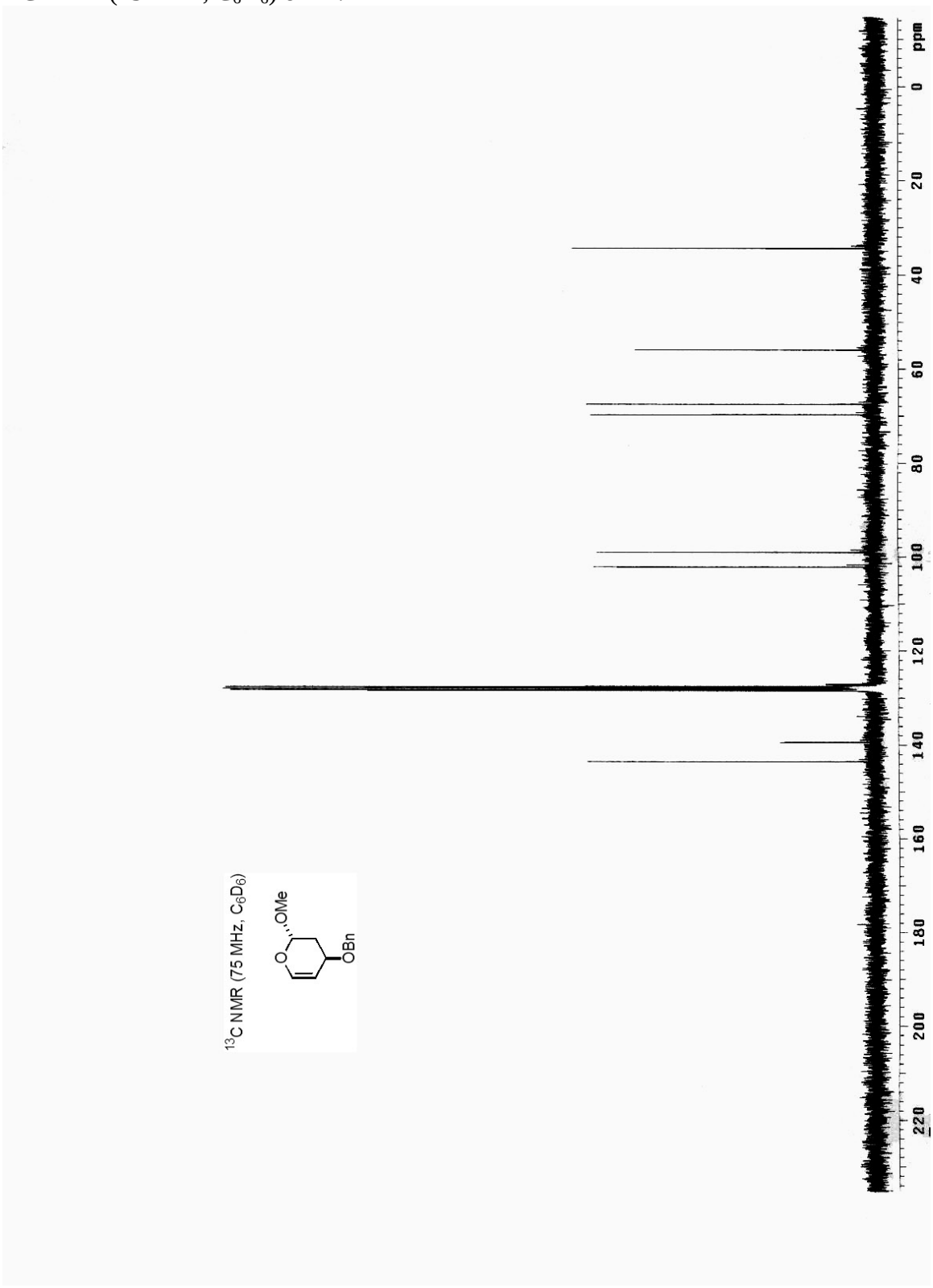
^{13}C NMR (75 MHz, C_6D_6) of **S-2**:



^{1}H NMR (300 MHz, C_6D_6) of **11**:



^{13}C NMR (75 MHz, C_6D_6) of **11**:



^{1}H NMR (300 MHz, C_6D_6) of **12**: