Supporting Information

Synthesis of *N*-methyl secondary amides via diboronic acid anhydride-catalyzed dehydrative condensation of carboxylic acids with aqueous methylamine

Hinata Iwasawa,[a] Naoya Takahashi,[b] and Naoyuki Shimada[a]*

[a] Laboratory of Organic Chemistry for Molecular Transformations, Department of Chemistry and the Institute of Natural Sciences, Nihon University, Tokyo 156-8550, Japan

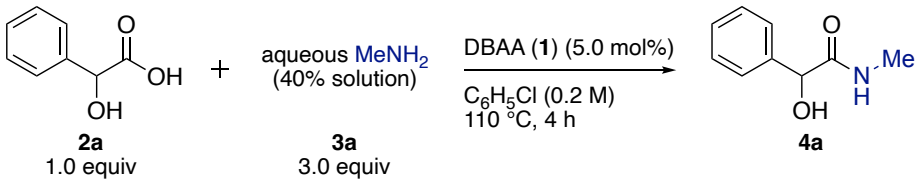
[b] Laboratory of Organic Chemistry for Drug Development and Medical Research Laboratories, Department of Pharmaceutical Sciences, Kitasato University, Tokyo 108-8641, Japan

Table of Contents

1. Supplementary Information S2
2. ^{1}H and ^{13}C NMR spectra S4

1. Supplementary Information

SI-Table 1. Optimization of solvent for the diboronic acid anhydride-catalyzed amidation of α-hydroxycarboxylic acid.

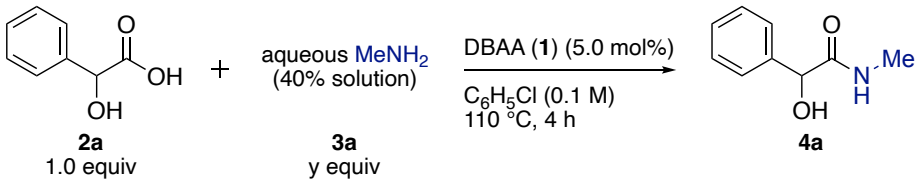


2a 1.0 equiv | **3a** 3.0 equiv | **4a**

Entry	Solvent	NMR yield[a]
1	toluene	62%
2	ethylbenzene	23%
3	mesitylene	23%
4	*m*-xylene	18%
5	*o*-xylene	58%
6	DMF	n.d.
7	**C_6H_5Cl**	**70%**
8	$C_6H_5CF_3$	10%

[a] Determined by ^{1}H NMR of a crude reaction mixture of products using 1,1,2,2- tetrachloroethane as an internal standard.

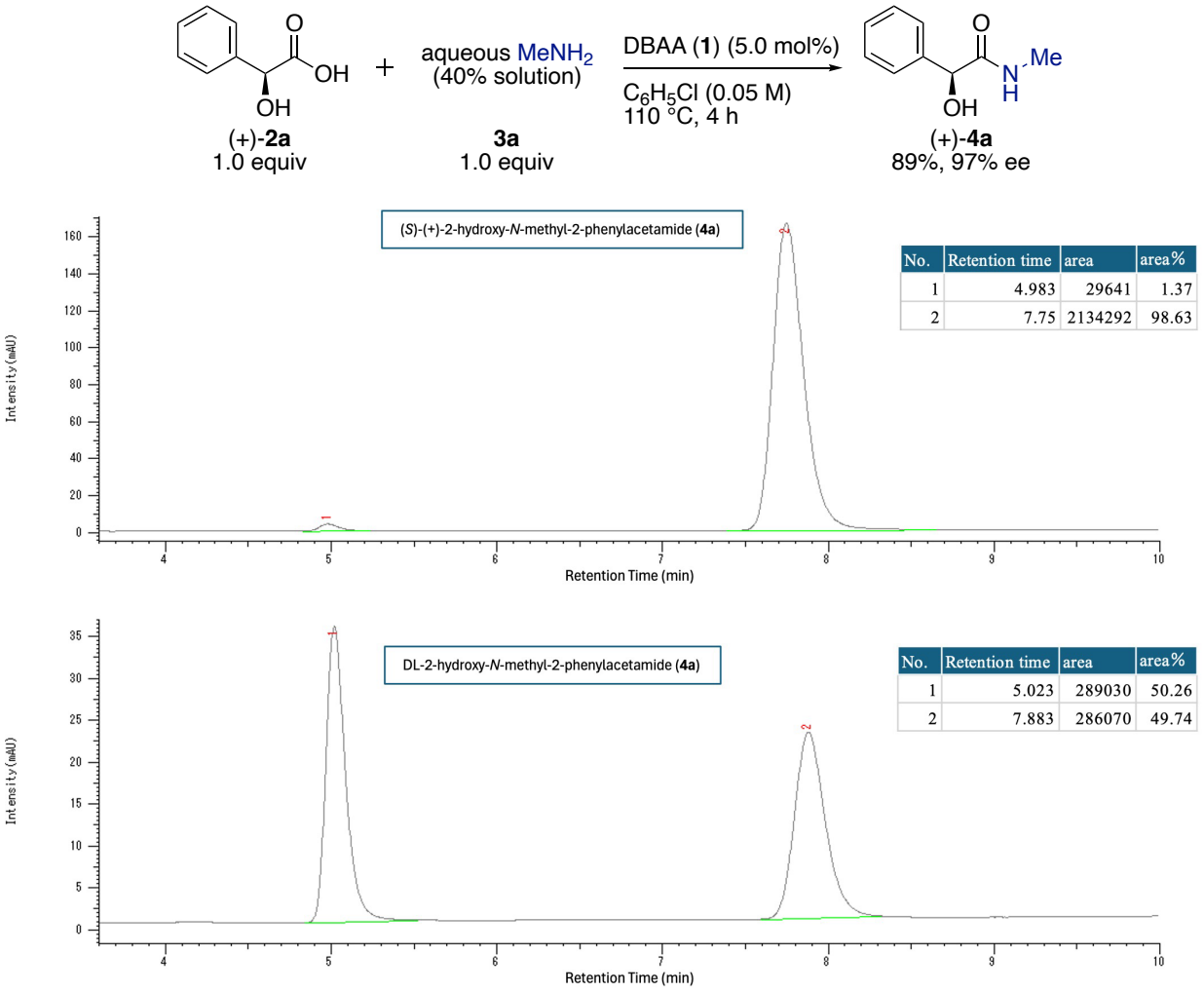
SI-Table 2. Optimization of molar equivalent of methyl amine (3a) for the diboronic acid anhydride-catalyzed amidation of α-hydroxycarboxylic acid.



2a 1.0 equiv | **3a** y equiv | **4a**

Entry	Equivalent of **3a**	NMR yield[a]
1	**2**	**92%**
2	1	88%
3	5	7%

[a] Determined by ^{1}H NMR of a crude reaction mixture of products using 1,1,2,2- tetrachloroethane as an internal standard.

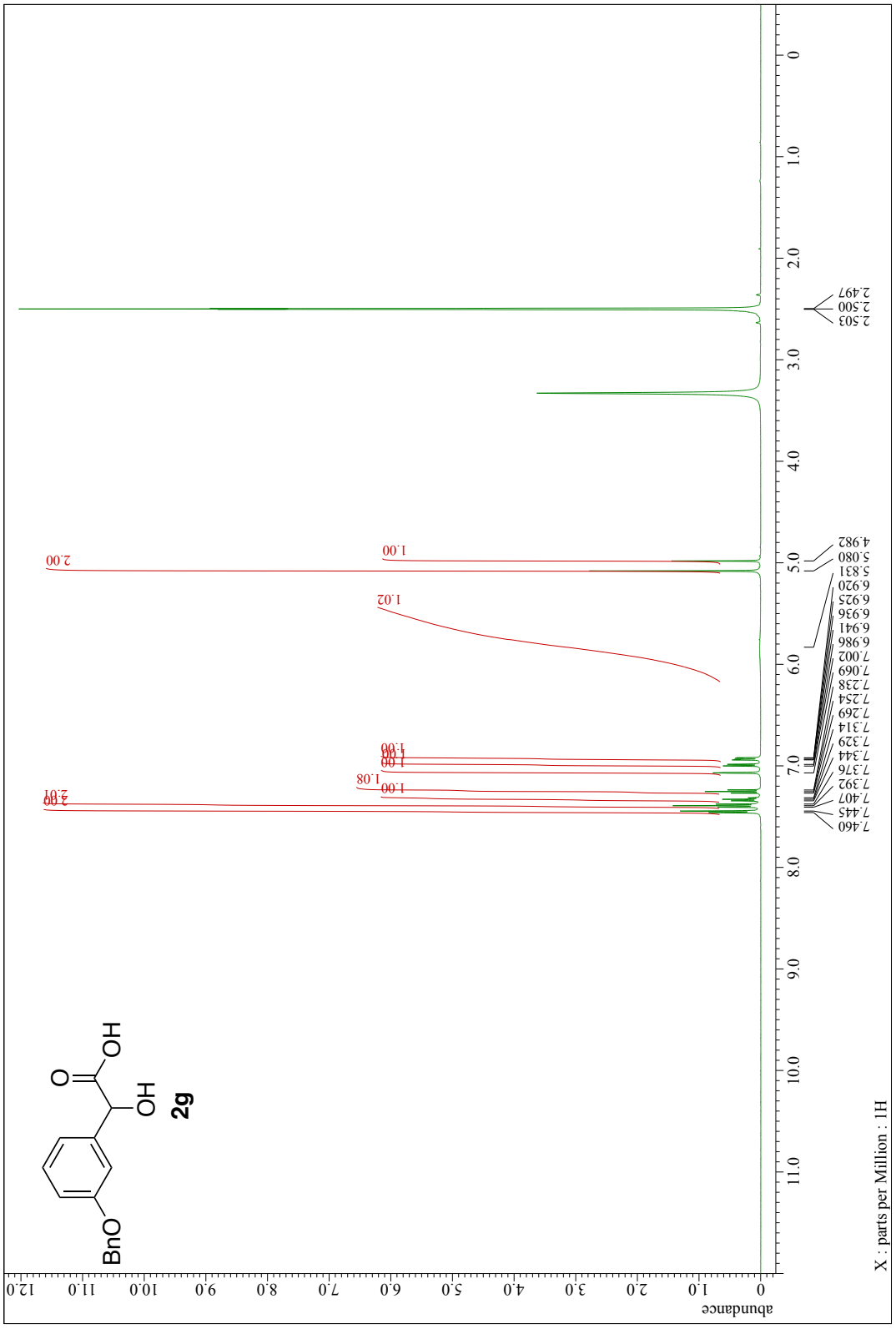


SI-Figure 1. Charts of chiral HPLC analysis of amide (+)-4a derived from (+)-mandelic acid ((+)-(2a)) (Scheme 2F).

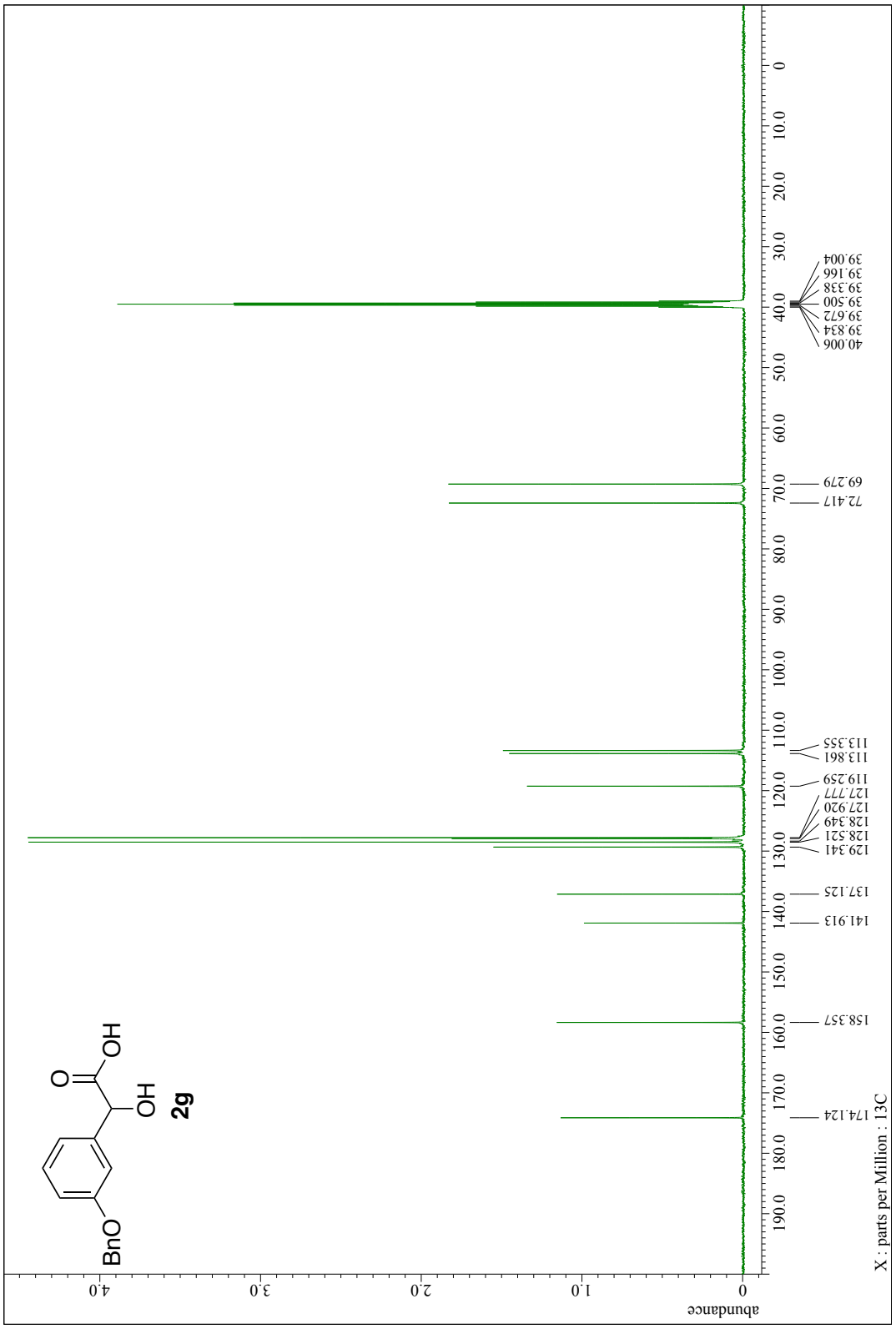
The enantiomeric excess (ee) was determined by chiral HPLC analysis [CHIRALPAK® IH-3 (ϕ 4.6 mm × 250 mm), hexane/IPA = 50:50, 210 nm, flow rate 1.2 mL/min, t_R = 5.0 min (minor), 7.9 min (major)]. The racemic sample was prepared by DBAA (**1**)-catalyzed amidation of (±)-mandelic acid (**2a**) with aqueous methylamine (**3a**) (40% solution).

2. ^{1}H and ^{13}C NMR spectra

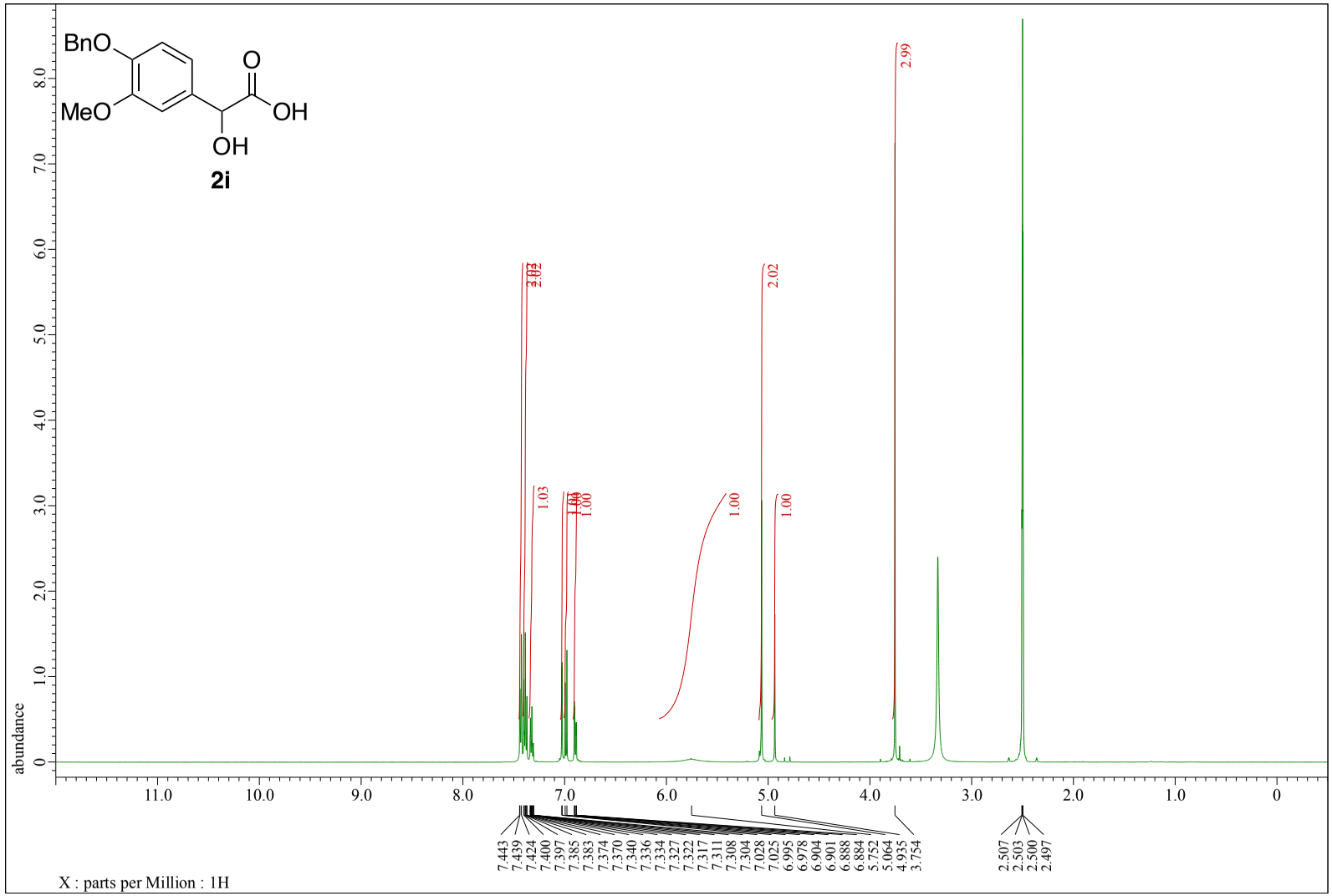
^{1}H NMR spectrum of 2g (500 MHz, DMSO-*d6*)



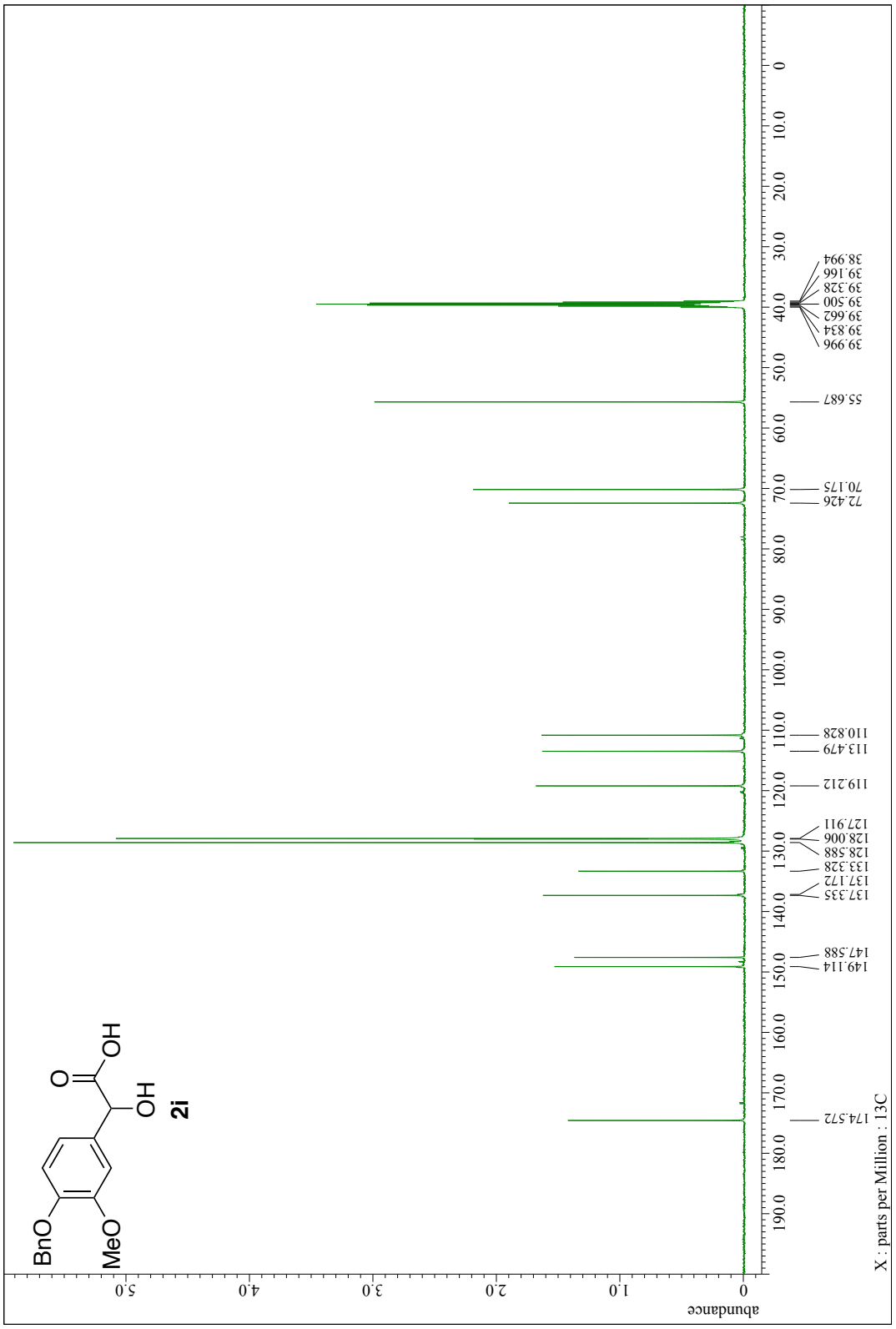
^{13}C NMR spectrum of 2g (126 MHz, DMSO-*d6*)



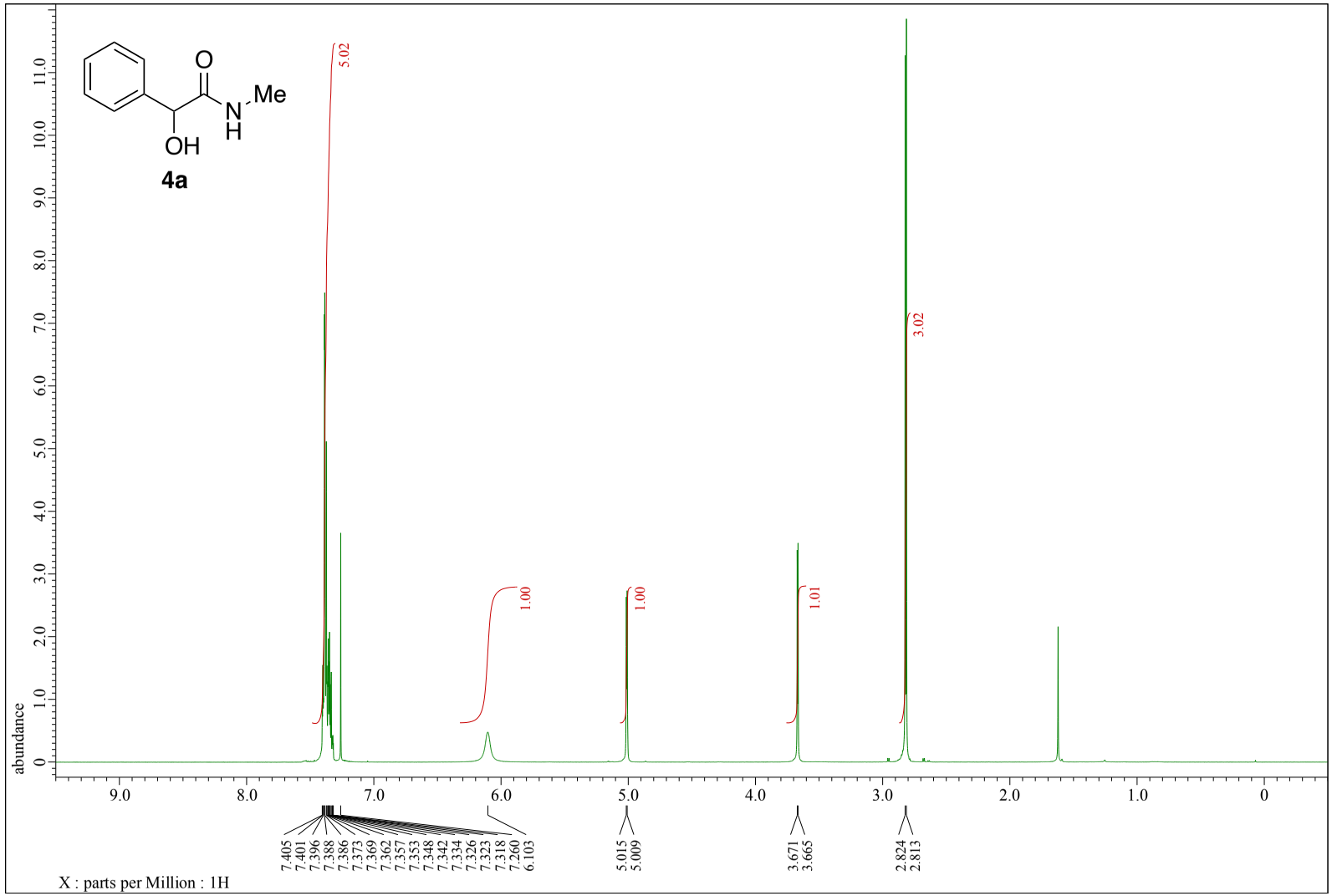
^{1}H NMR spectrum of 2i (500 MHz, DMSO-*d6*)



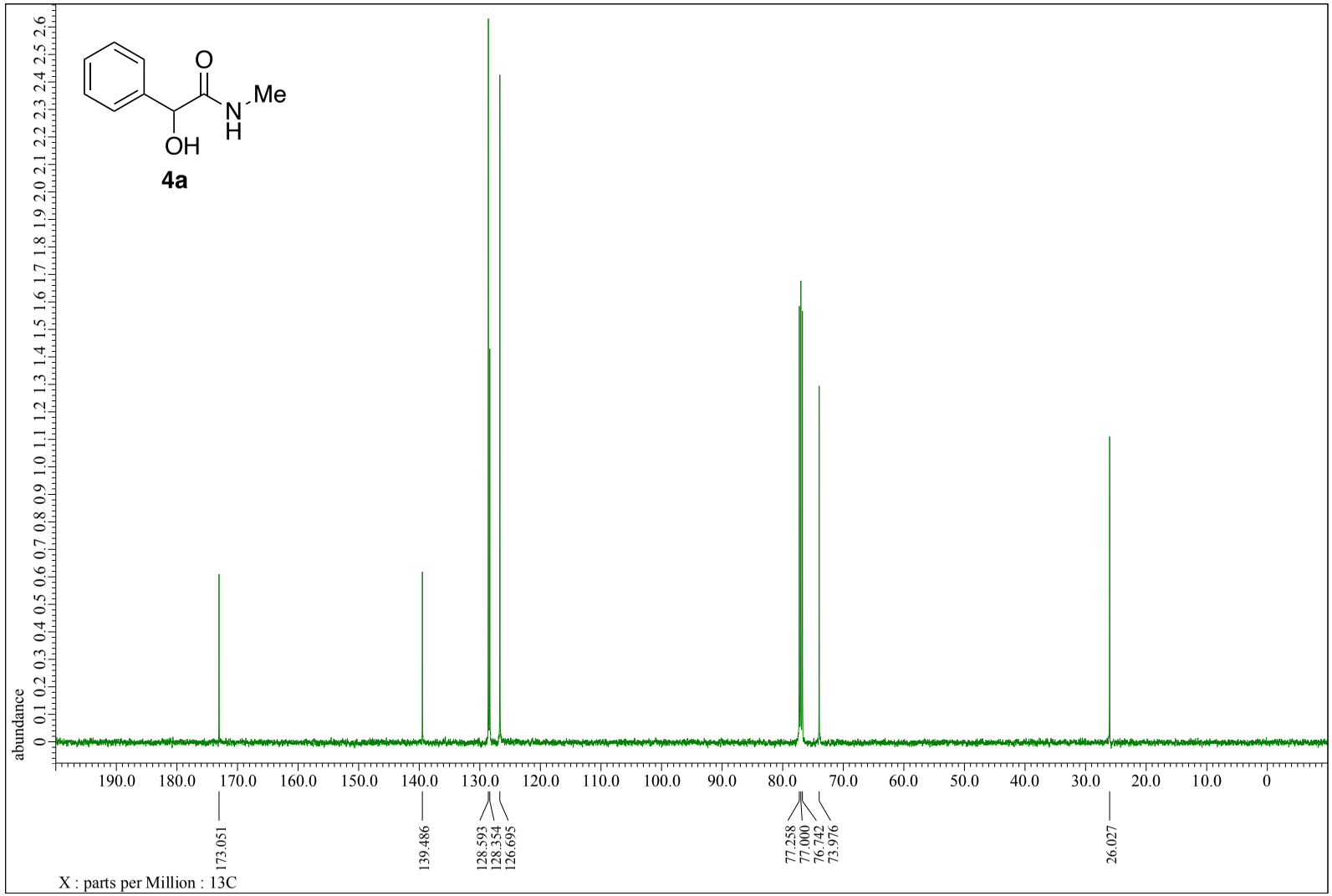
^{13}C NMR spectrum of 2i (126 MHz, DMSO-*d6*)



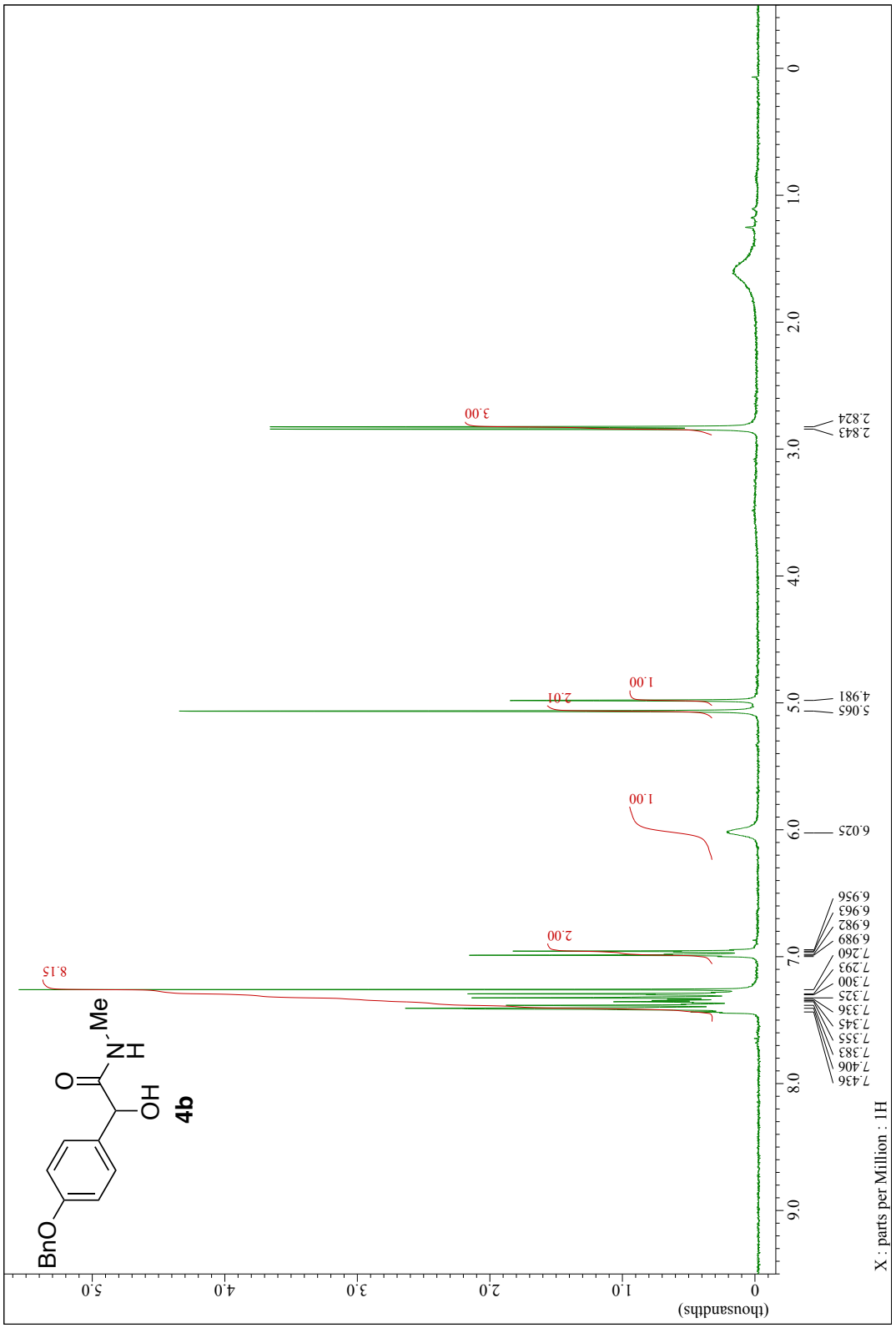
^{1}H NMR spectrum of 4a (500 MHz, $CDCl_3$)



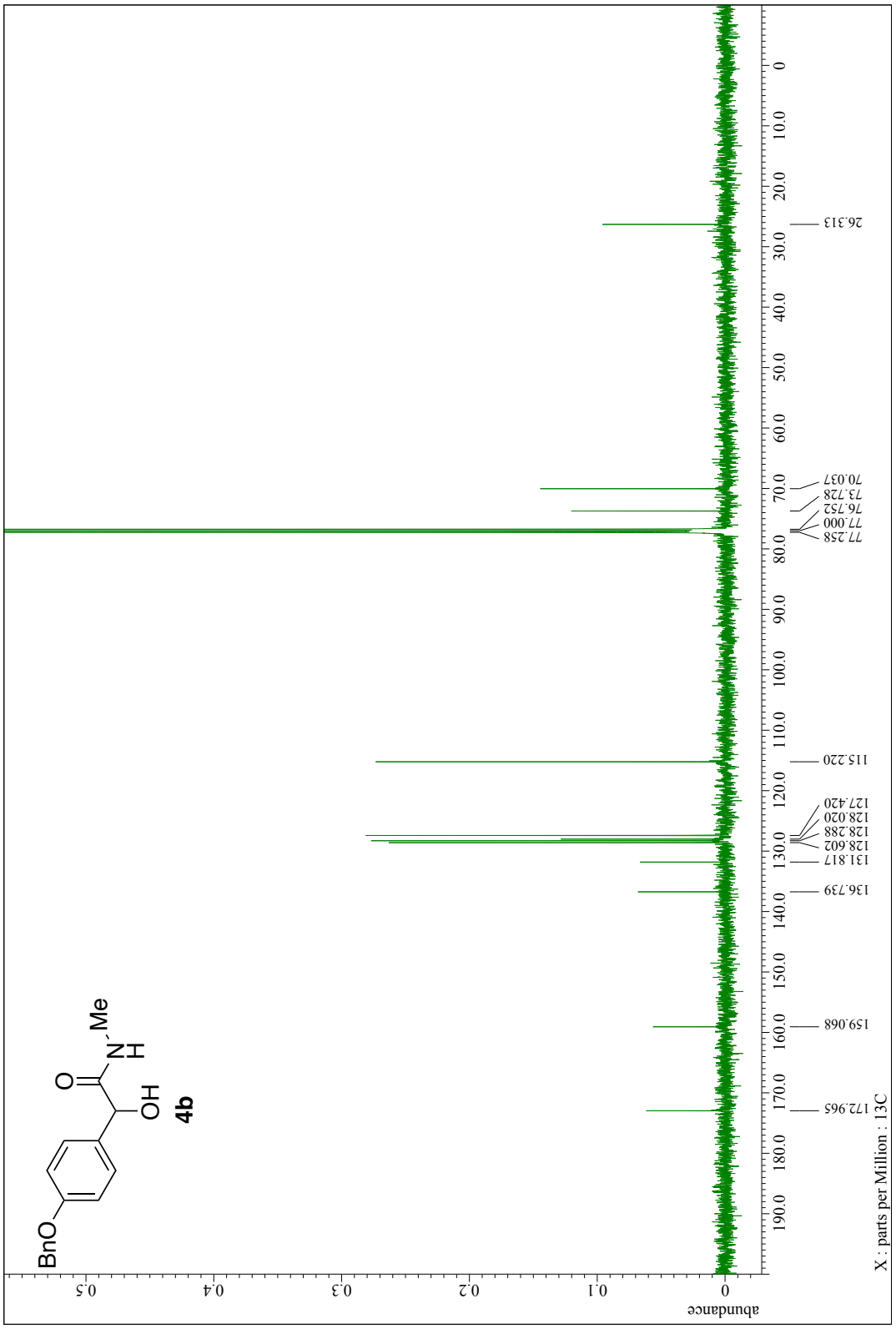
^{13}C NMR spectrum of 4a (126 MHz, $CDCl_3$)



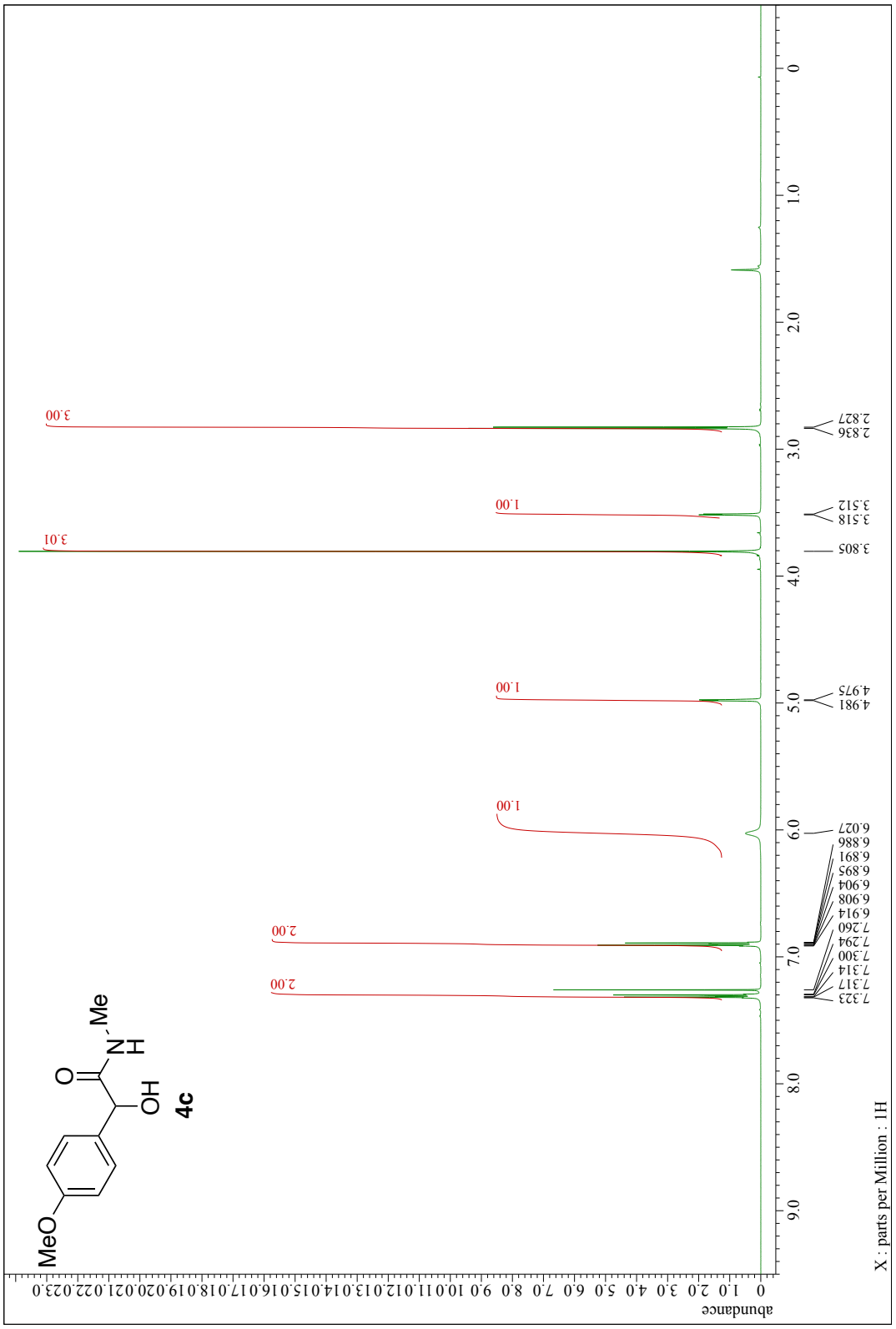
^{1}H NMR spectrum of 4b (500 MHz, $CDCl_3$)



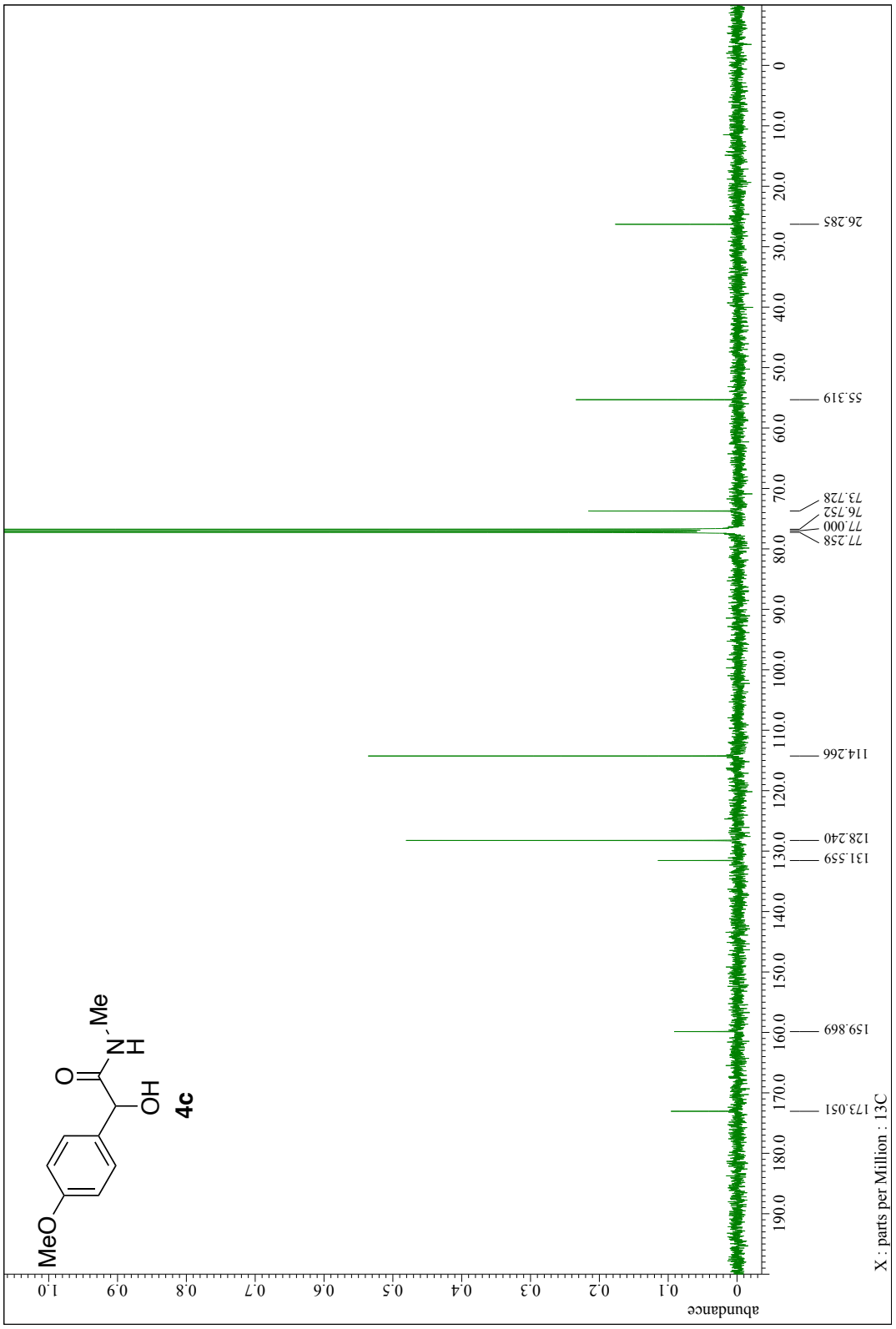
^{13}C NMR spectrum of 4b (126 MHz, $CDCl_3$)



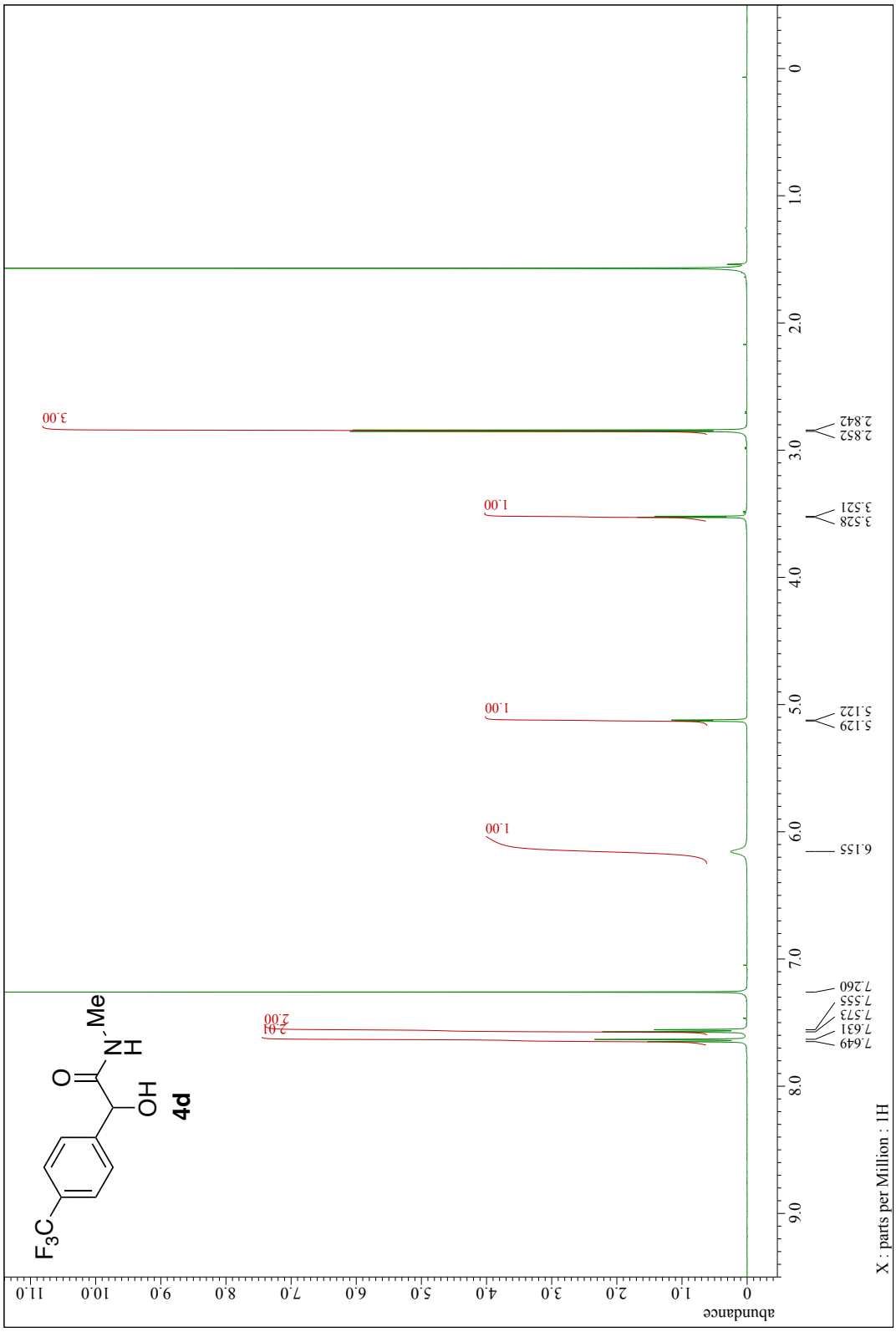
^{1}H NMR spectrum of 4c (500 MHz, $CDCl_3$)



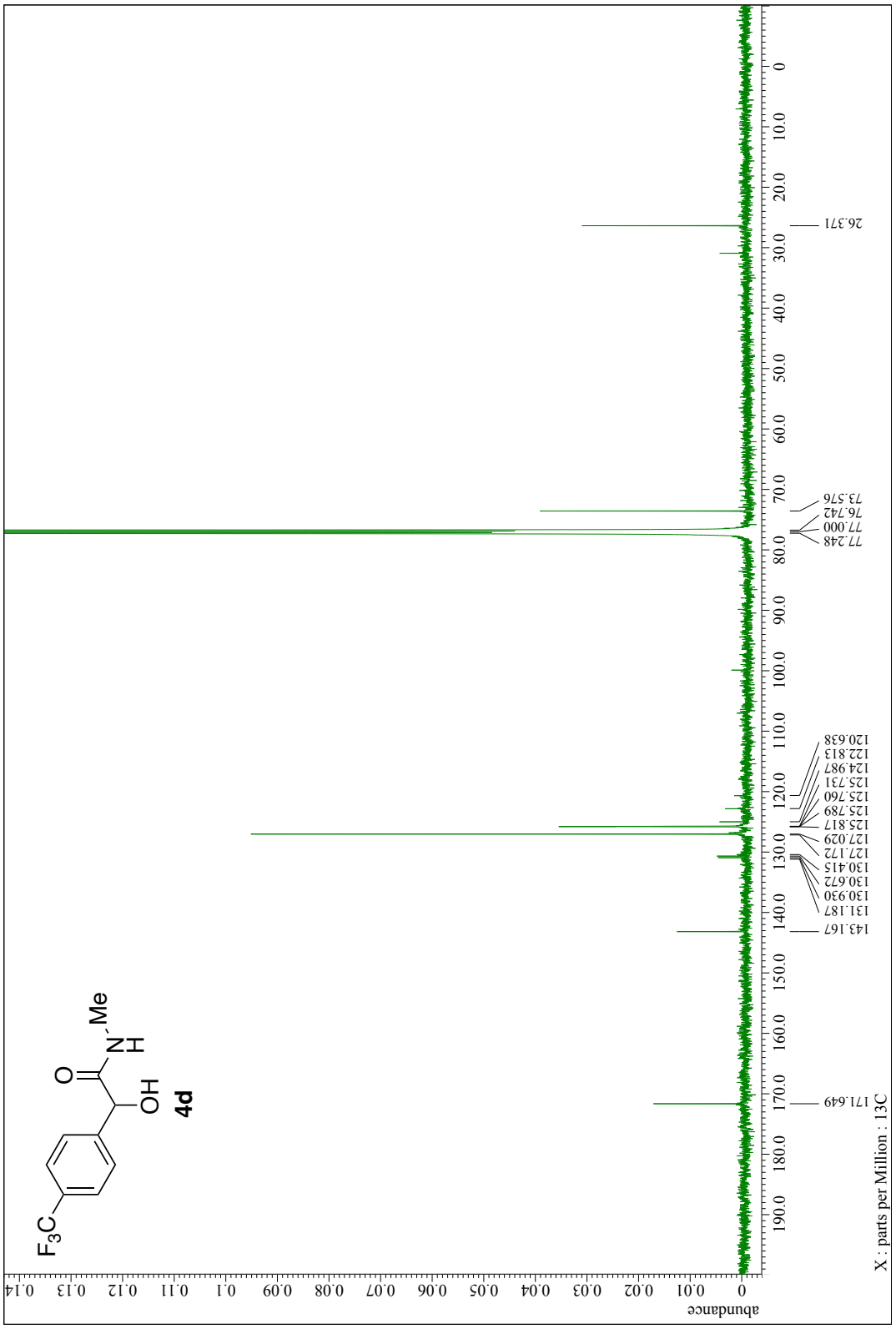
^{13}C NMR spectrum of 4c (126 MHz, $CDCl_3$)



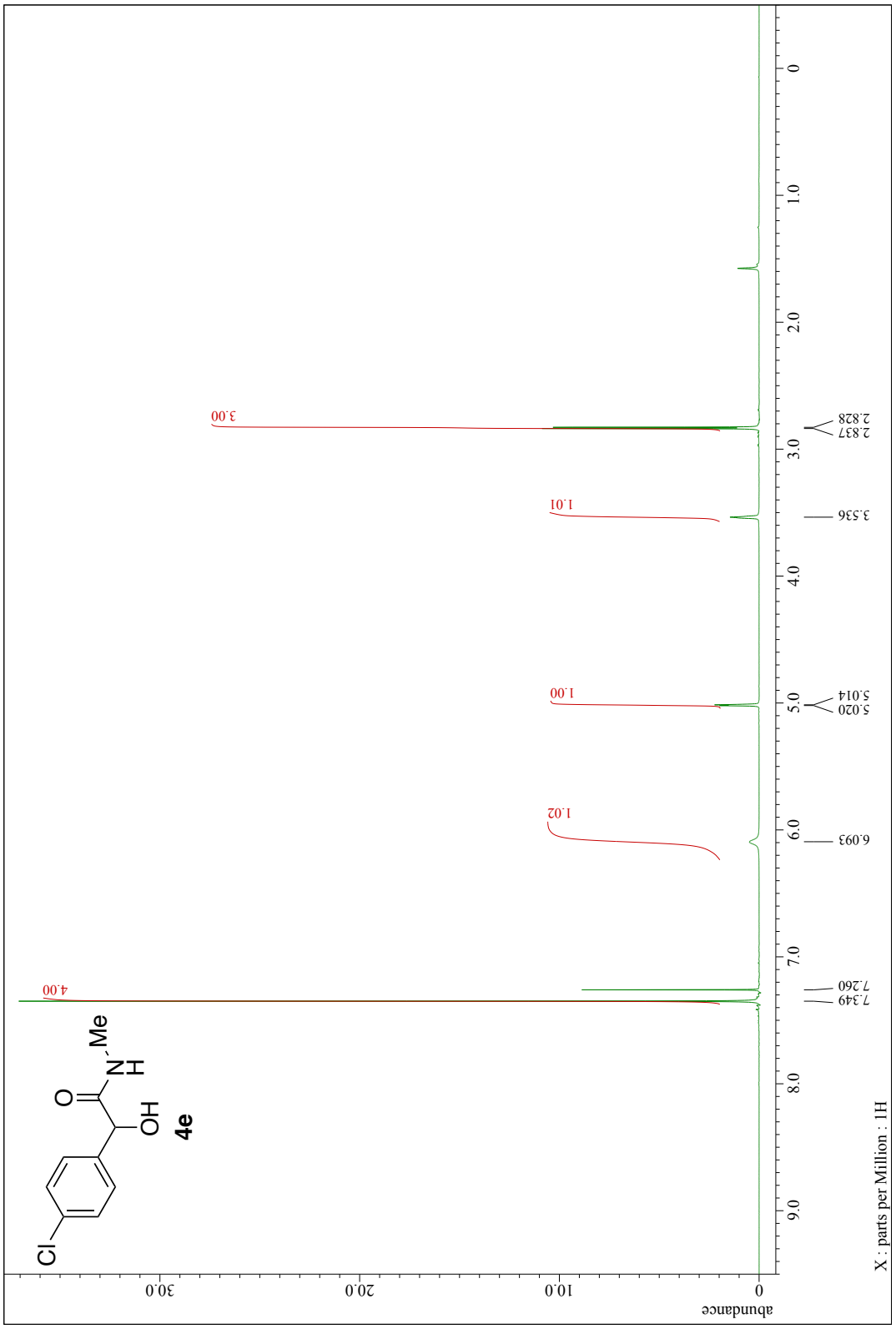
^{1}H NMR spectrum of 4d (500 MHz, $CDCl_3$)



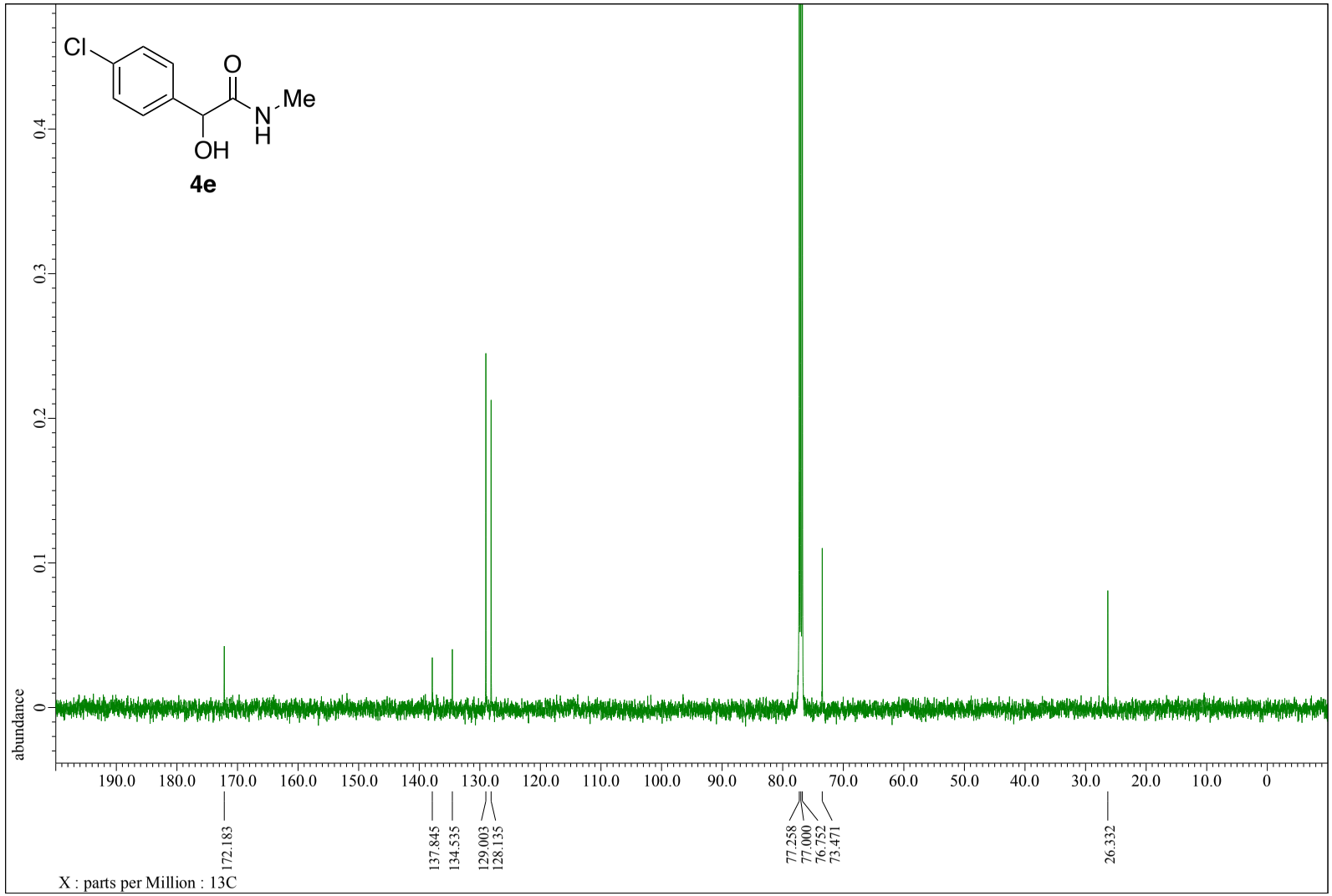
^{13}C NMR spectrum of 4d (126 MHz, $CDCl_3$)



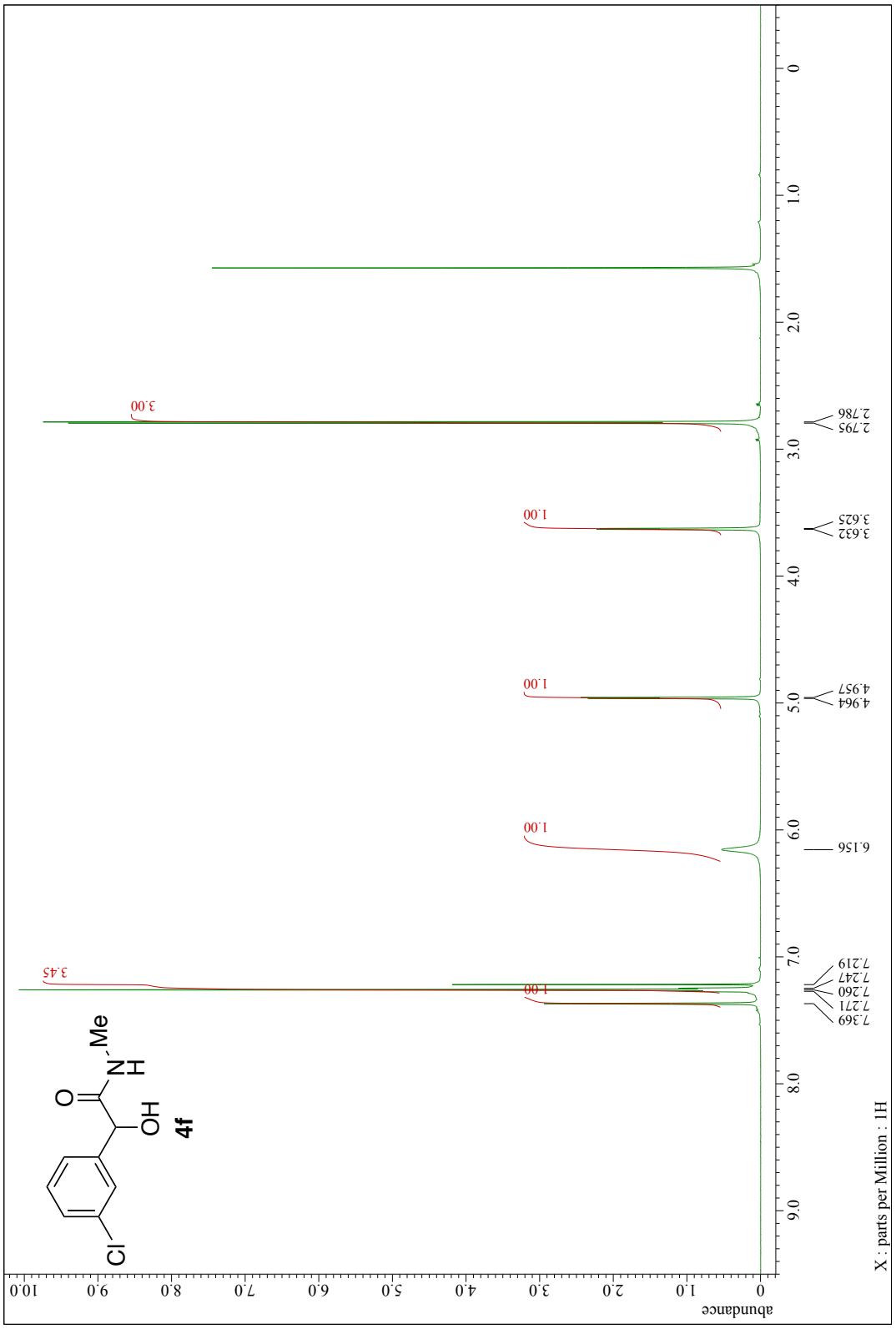
^{1}H NMR spectrum of 4e (500 MHz, $CDCl_3$)



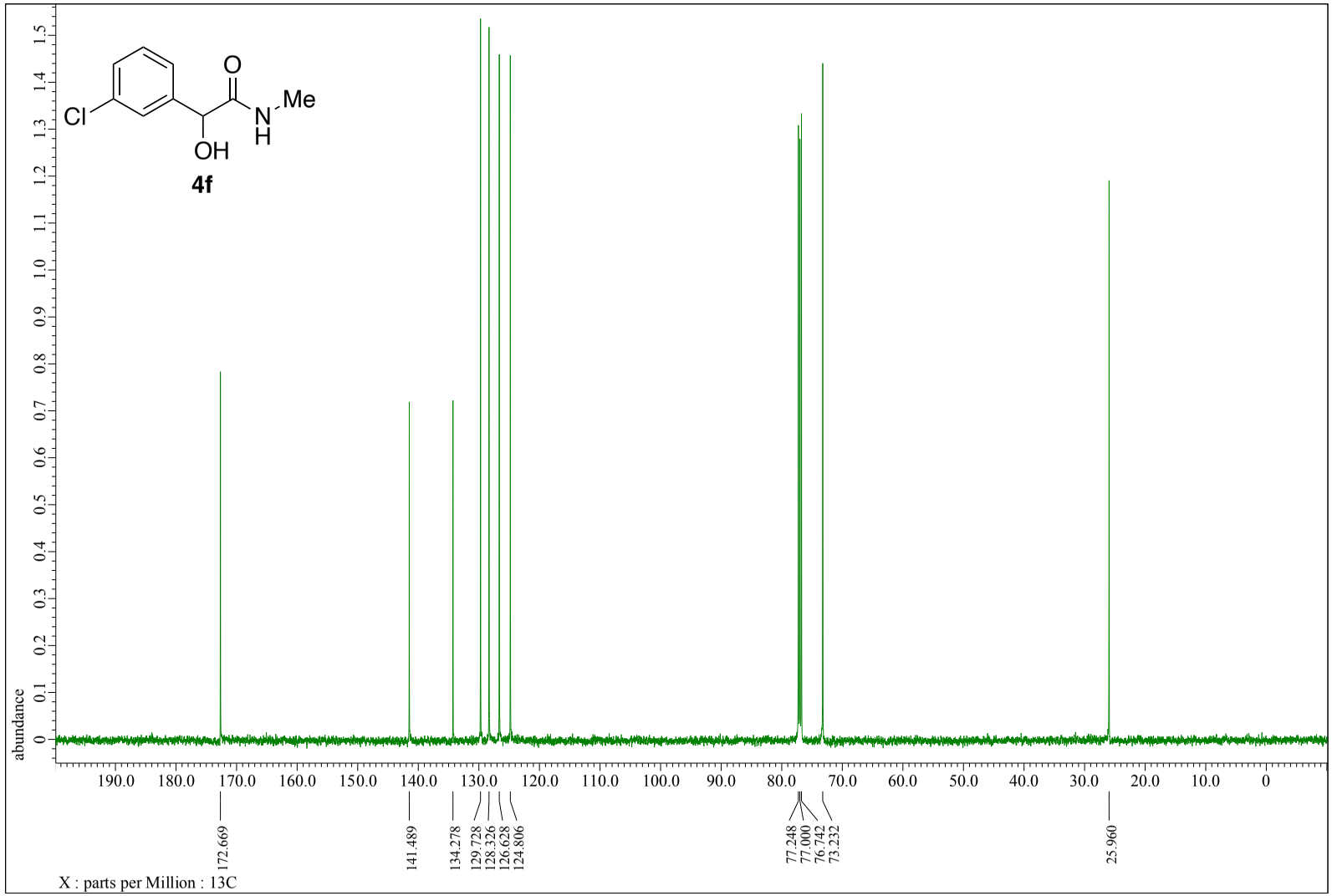
^{13}C NMR spectrum of 4e (126 MHz, $CDCl_3$)



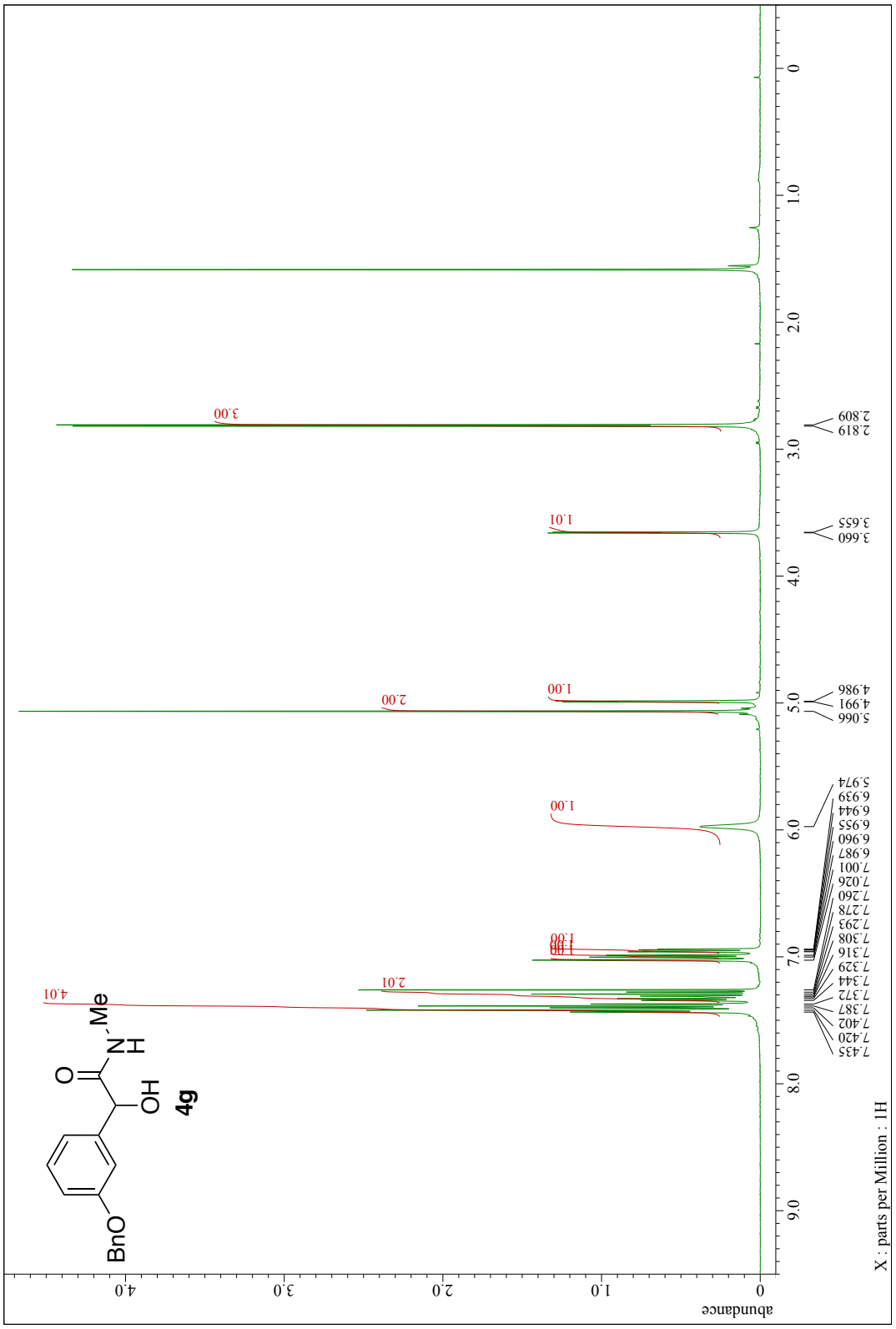
^{1}H NMR spectrum of 4f (500 MHz, $CDCl_3$)



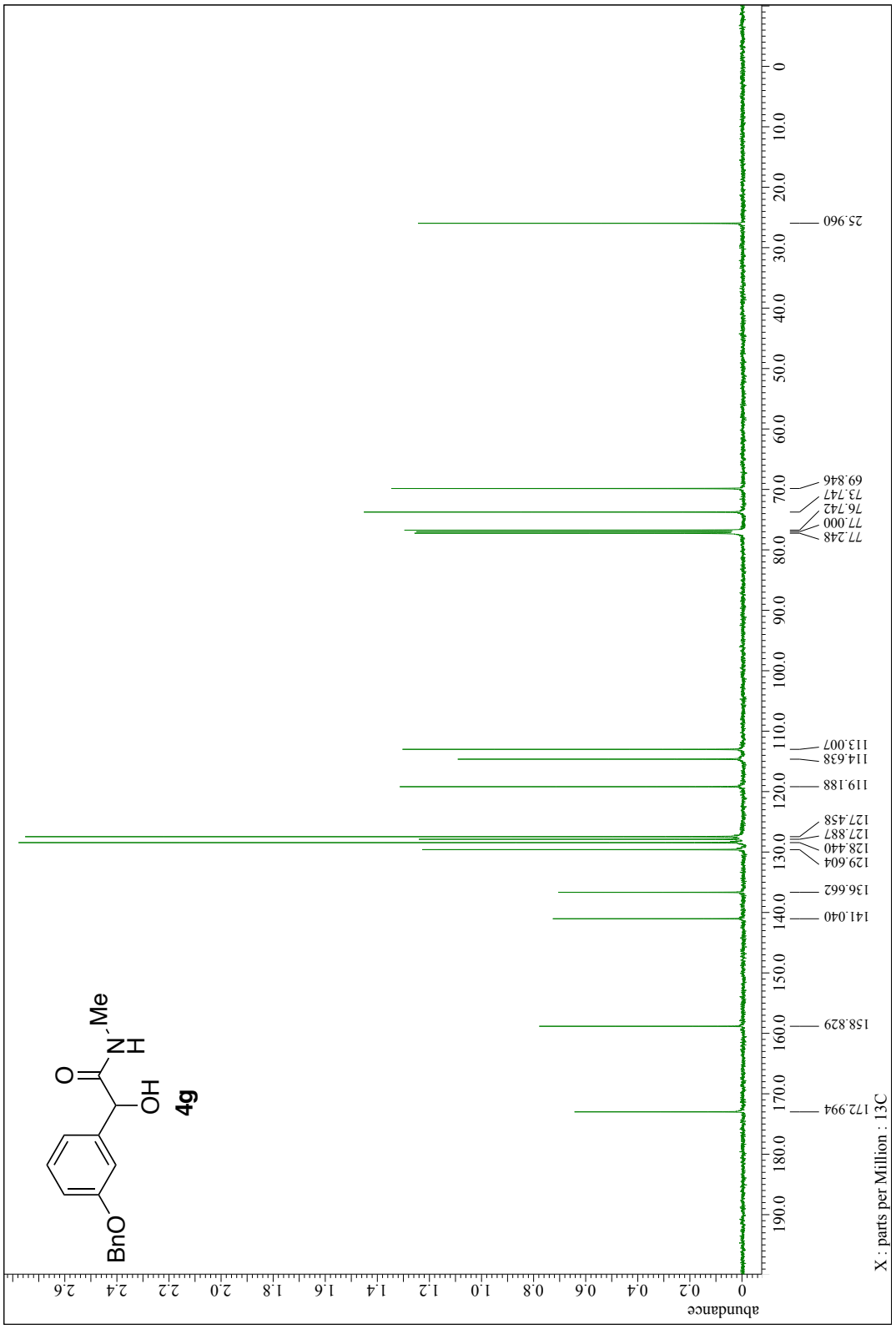
^{13}C NMR spectrum of 4f (126 MHz, $CDCl_3$)



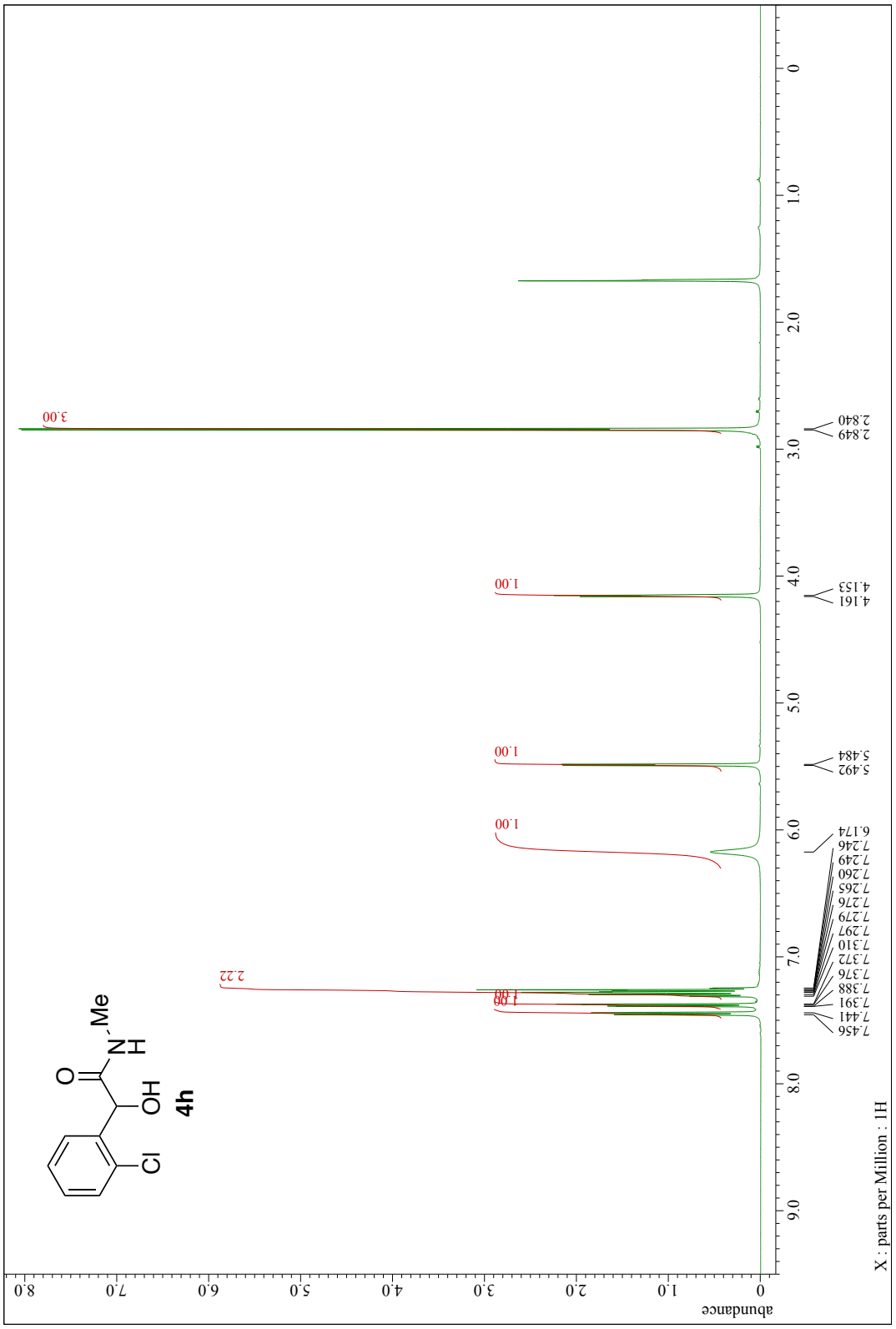
^{1}H NMR spectrum of 4g (500 MHz, $CDCl_3$)



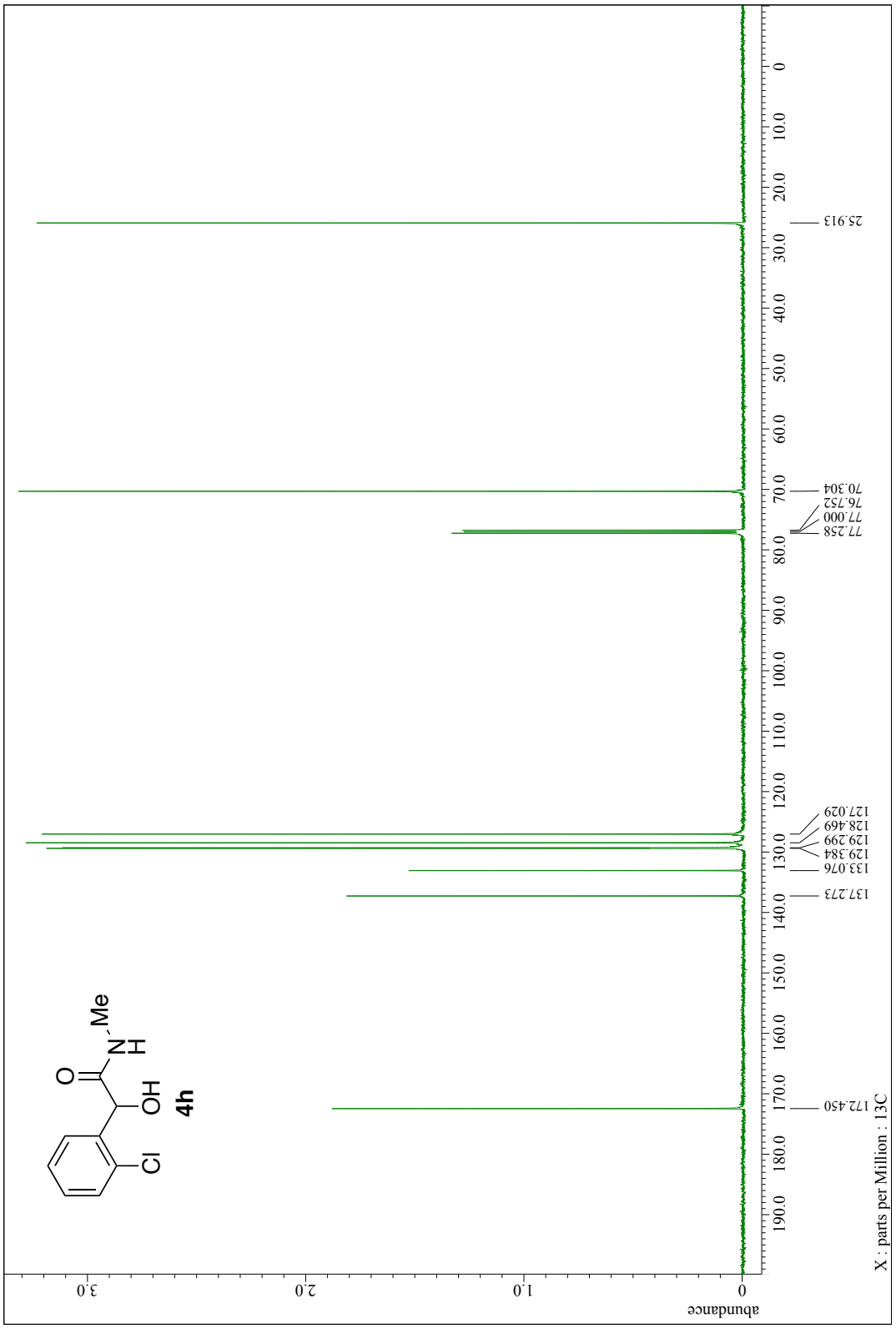
^{13}C NMR spectrum of 4g (126 MHz, $CDCl_3$)



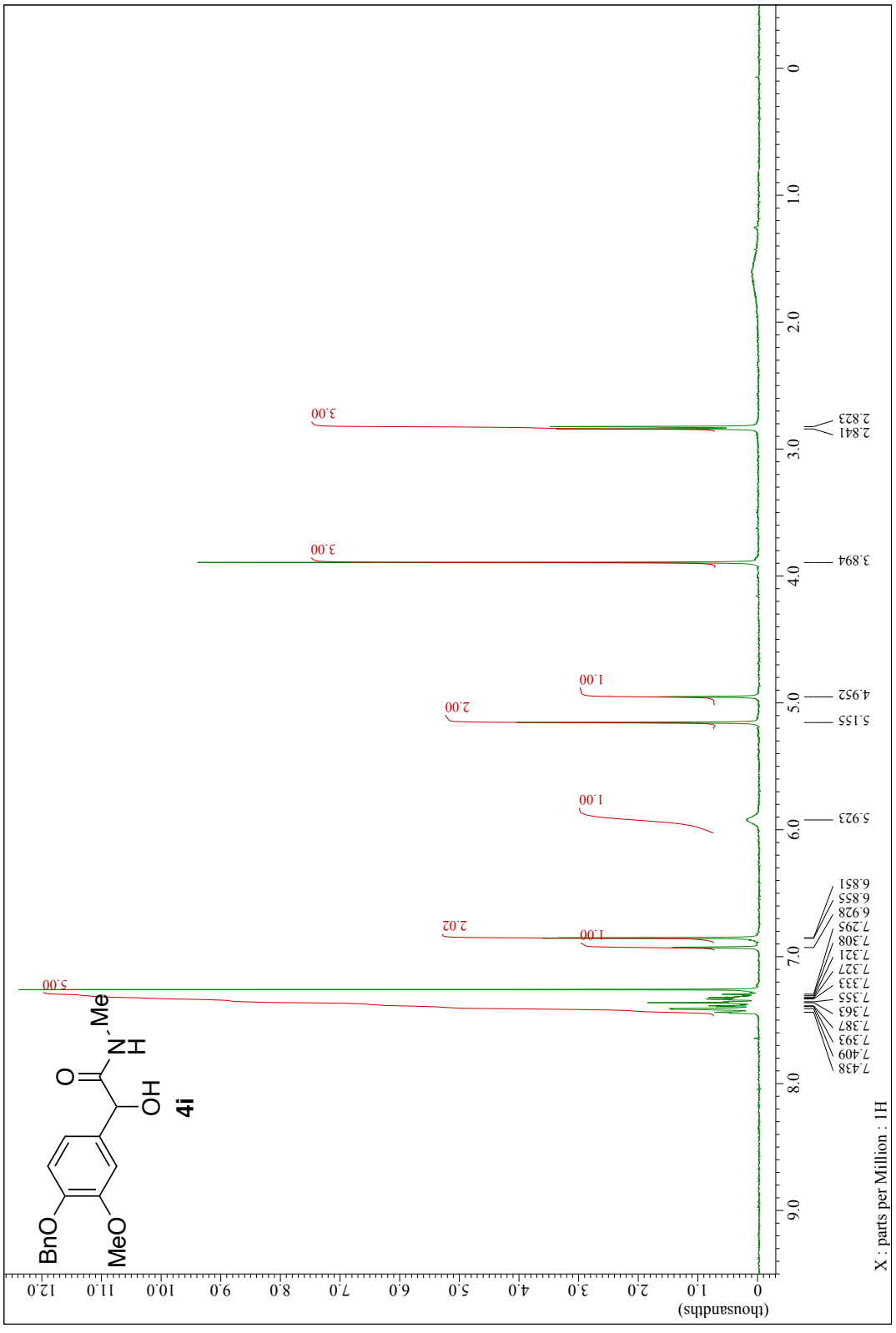
^{1}H NMR spectrum of 4h (500 MHz, $CDCl_3$)



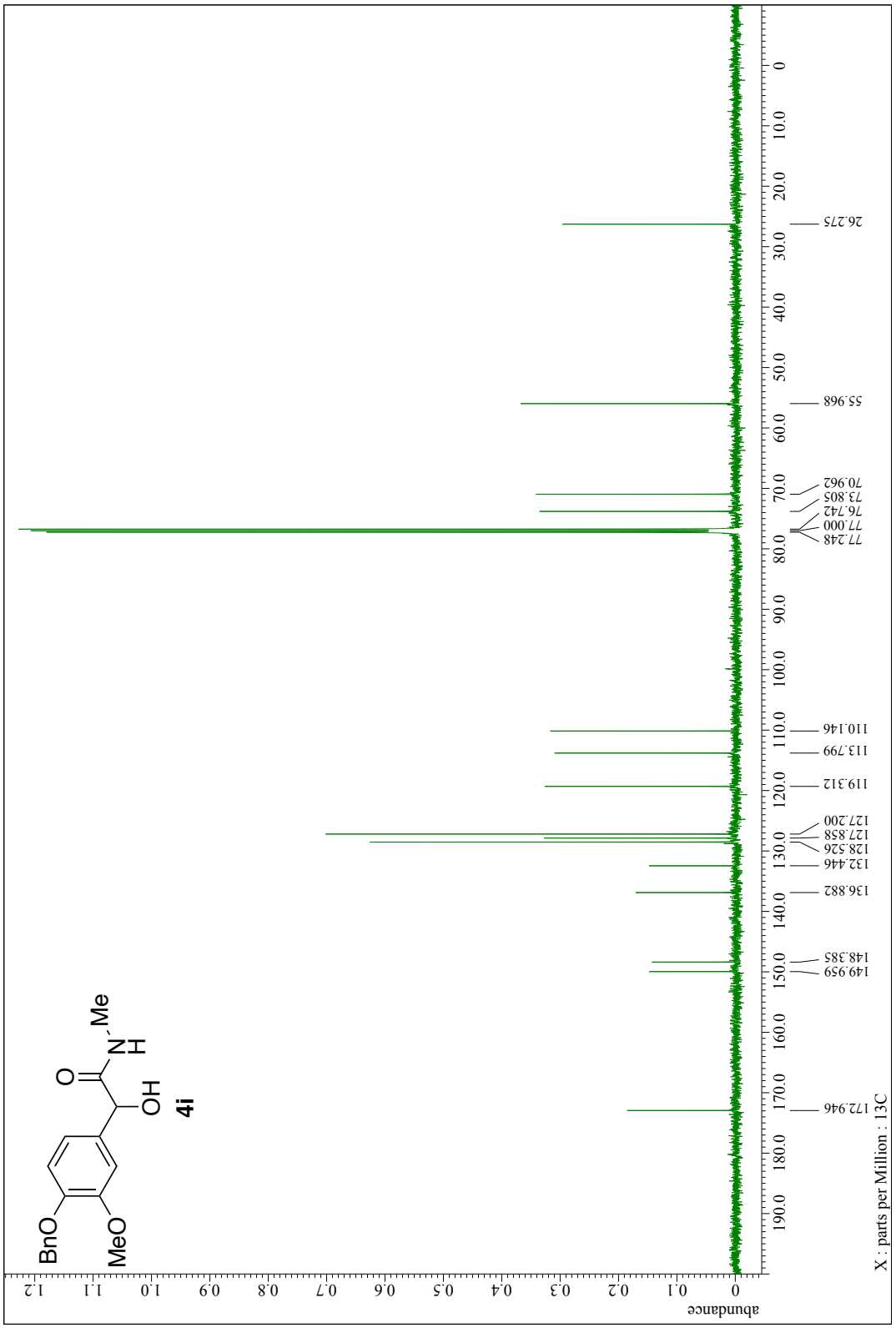
^{13}C NMR spectrum of 4h (126 MHz, $CDCl_3$)



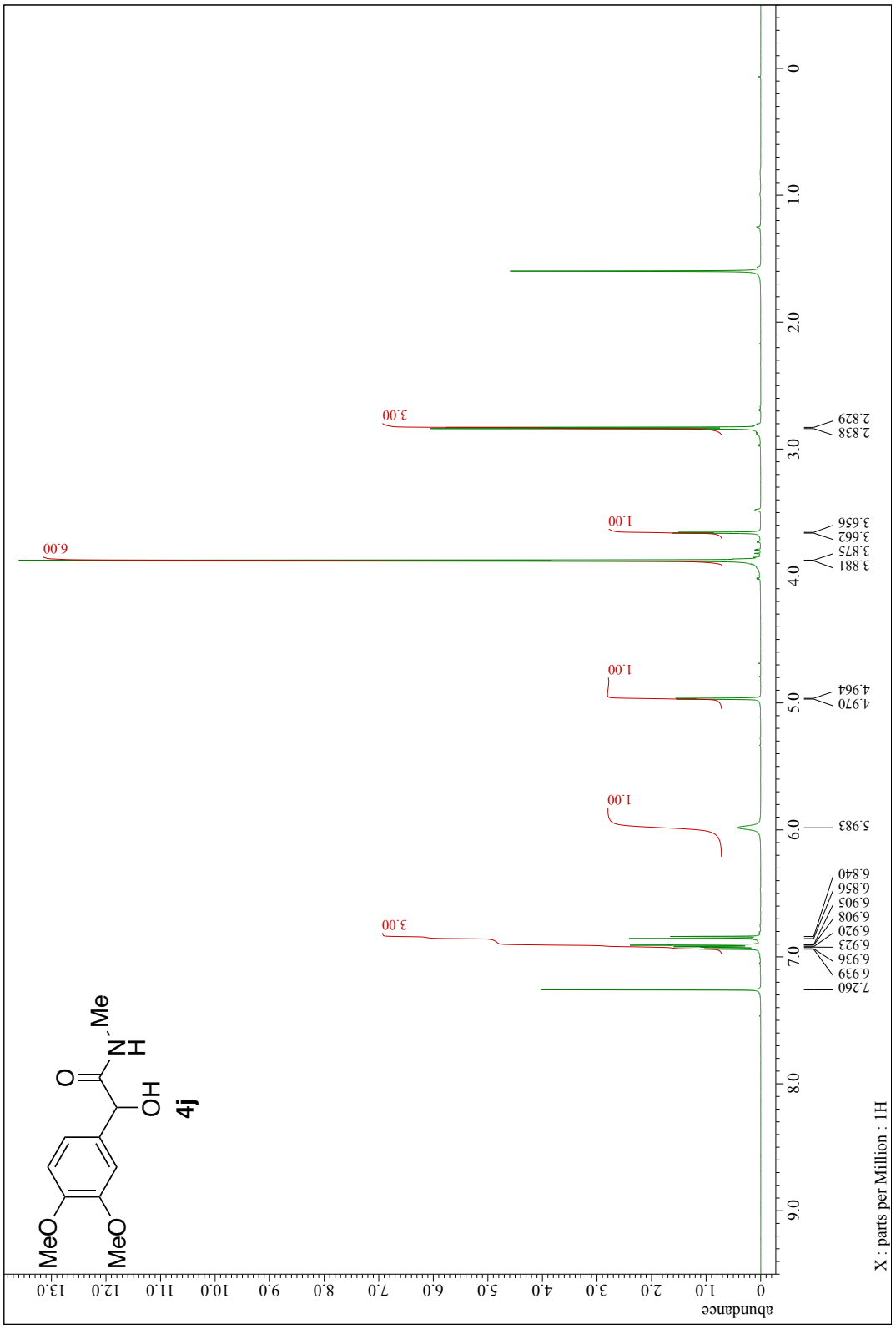
^{1}H NMR spectrum of 4i (500 MHz, $CDCl_3$)



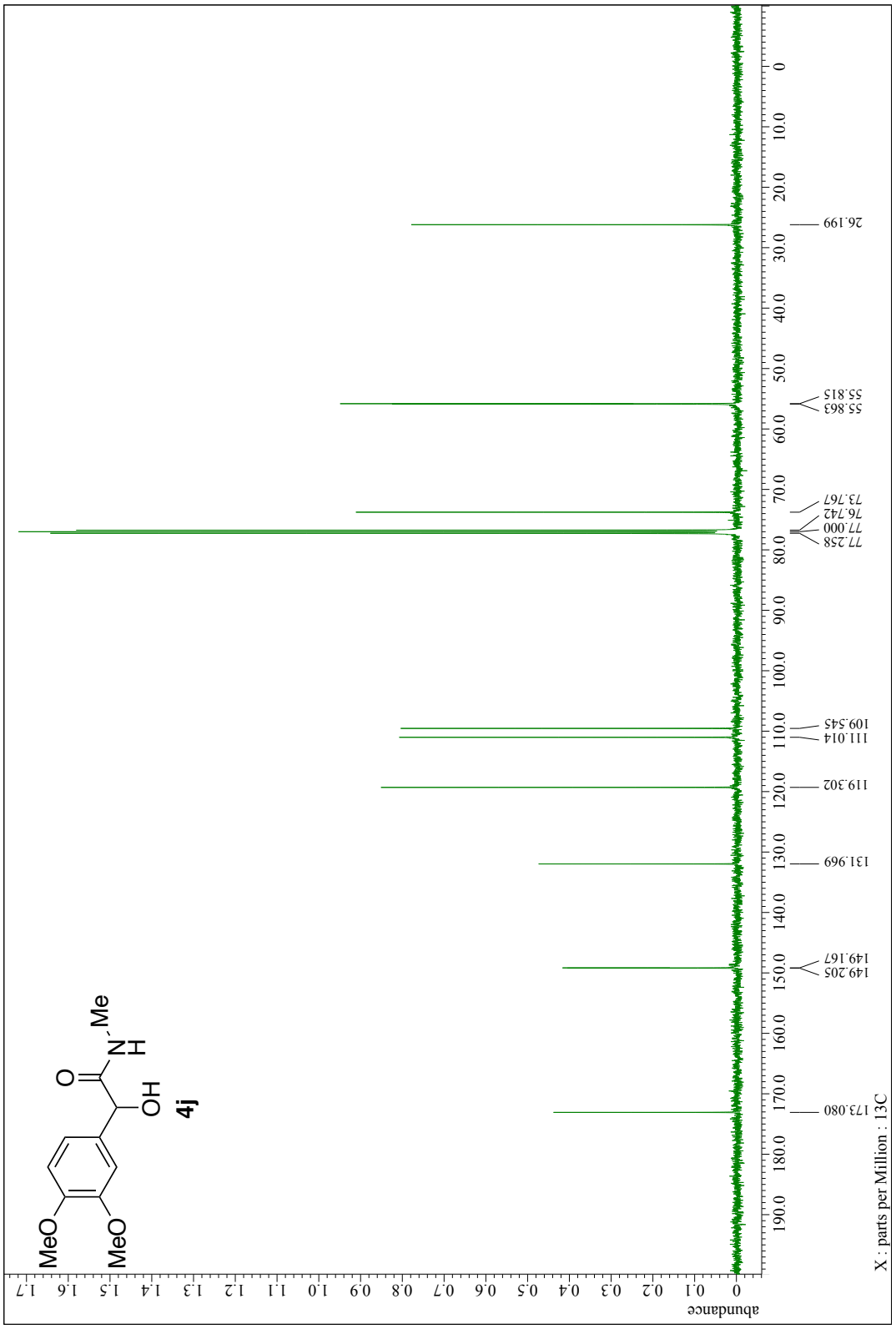
^{13}C NMR spectrum of 4i (126 MHz, $CDCl_3$)



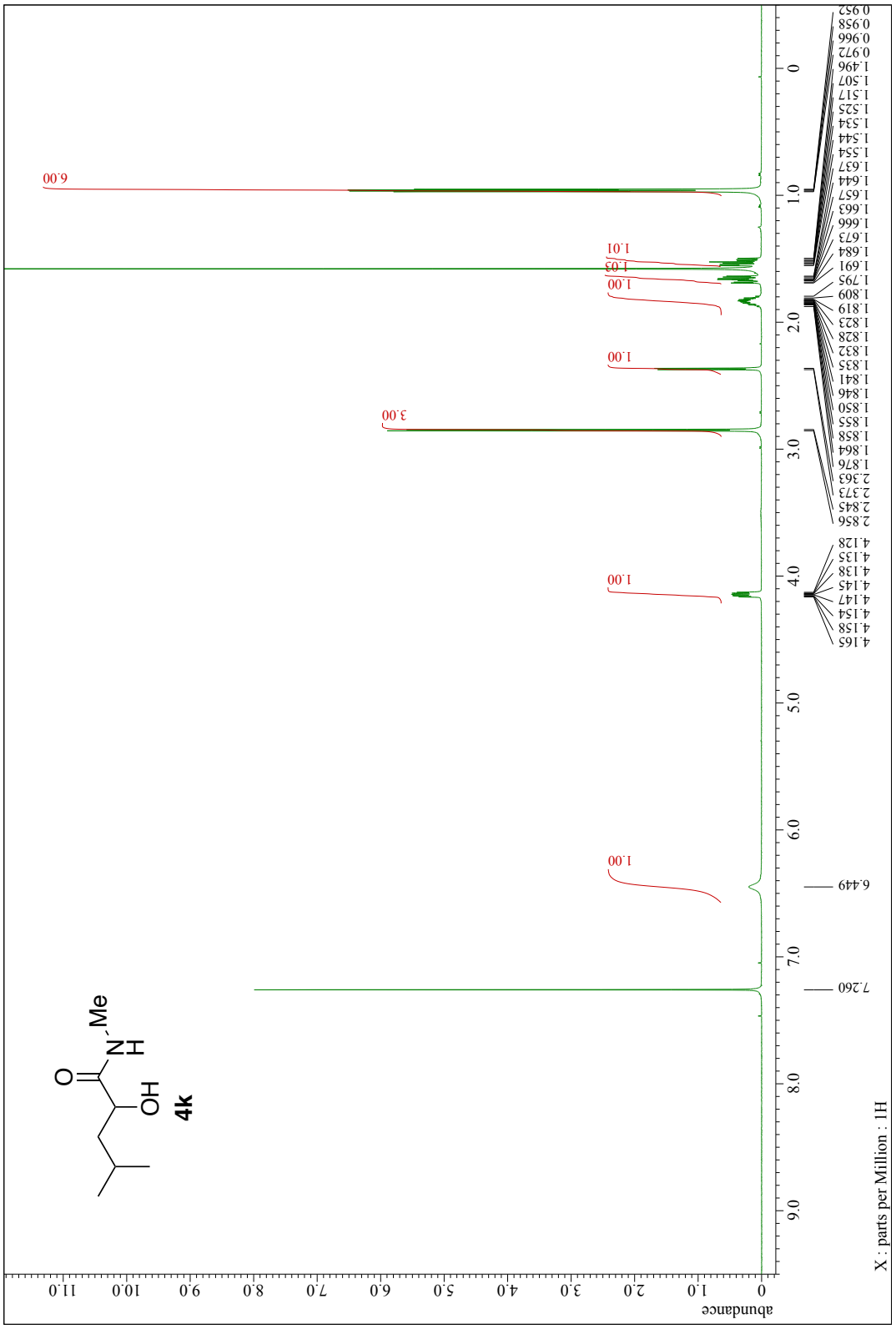
^{1}H NMR spectrum of 4j (500 MHz, $CDCl_3$)



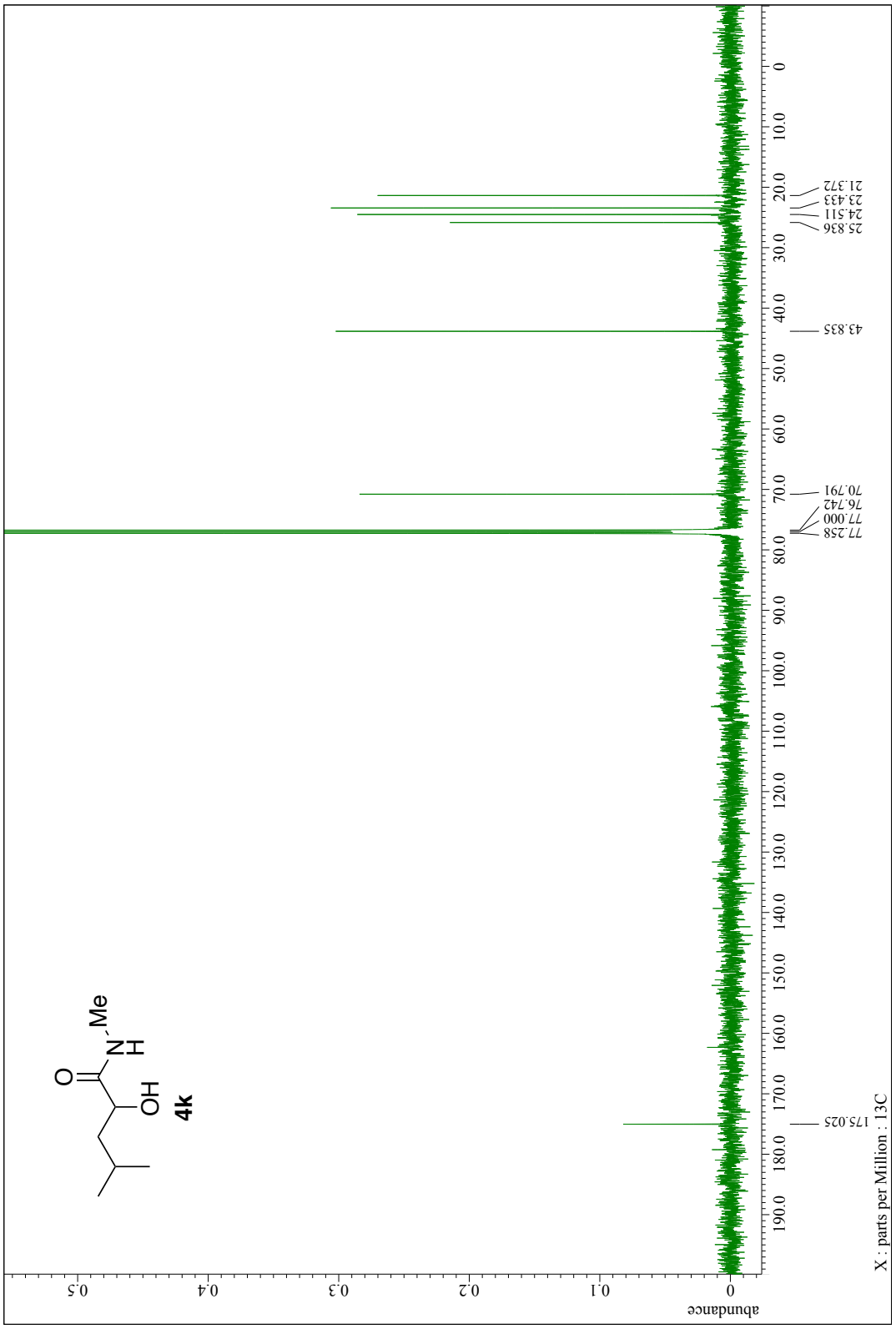
^{13}C NMR spectrum of 4j (126 MHz, $CDCl_3$)



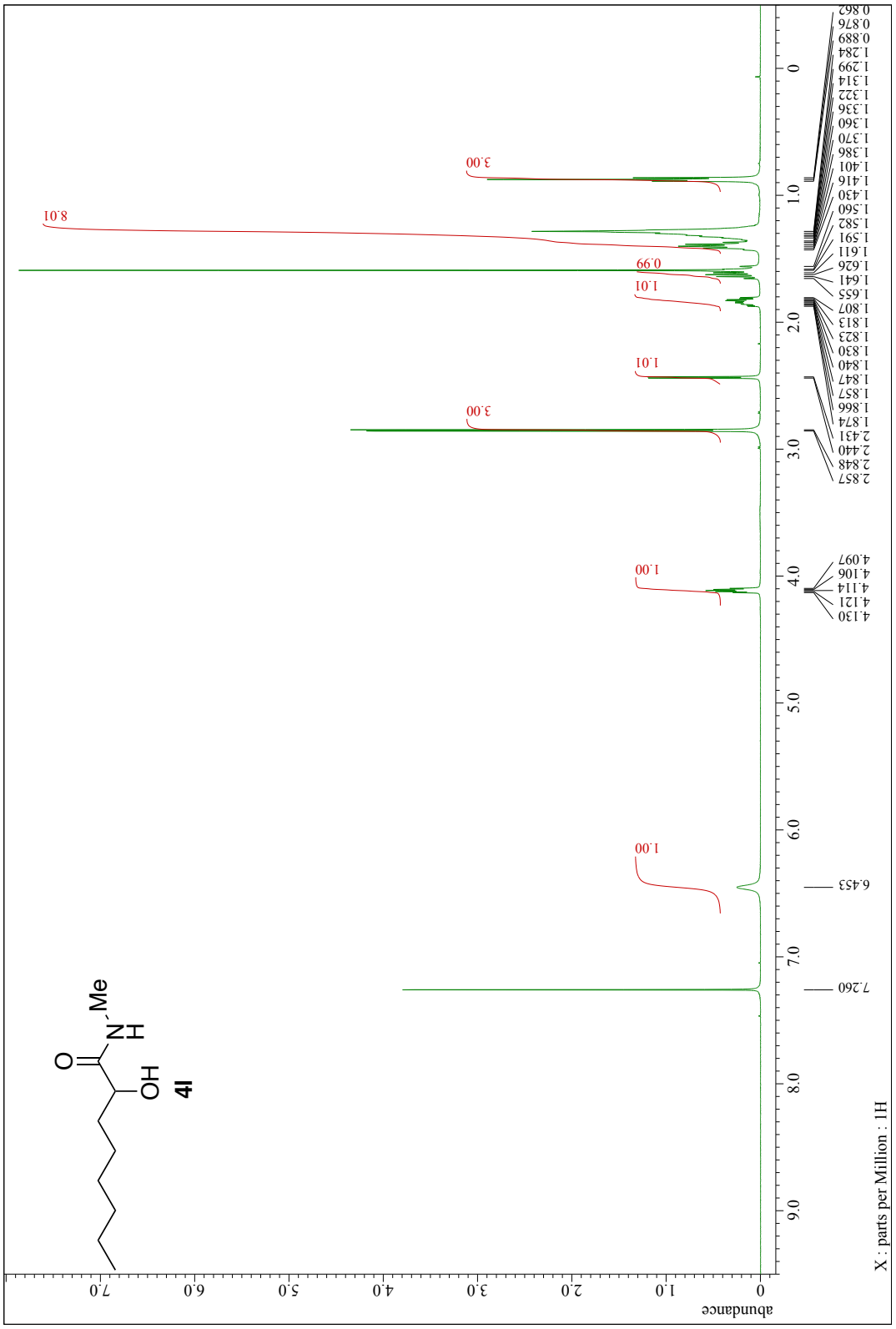
^{1}H NMR spectrum of 4k (500 MHz, $CDCl_3$)



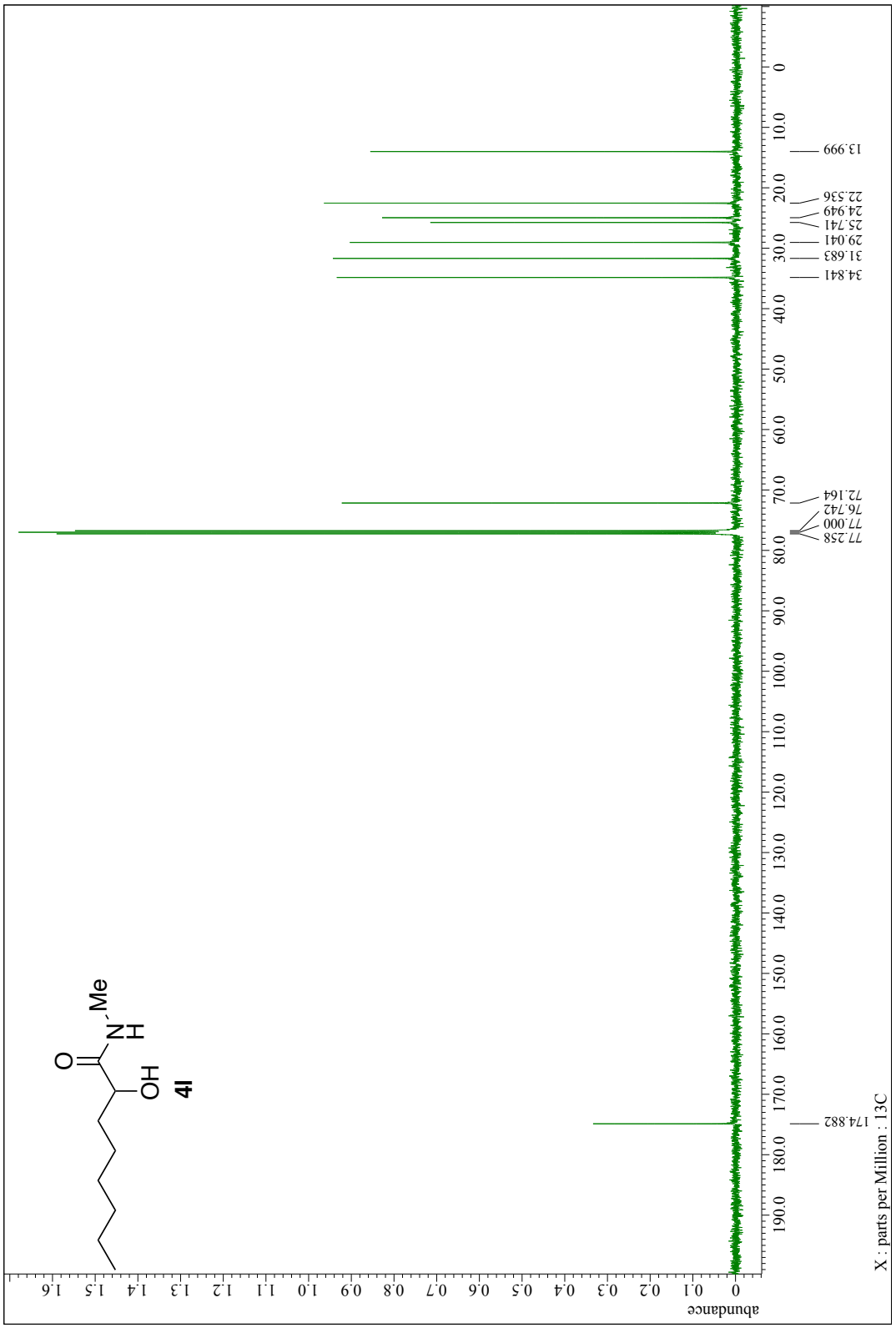
^{13}C NMR spectrum of 4k (126 MHz, $CDCl_3$)



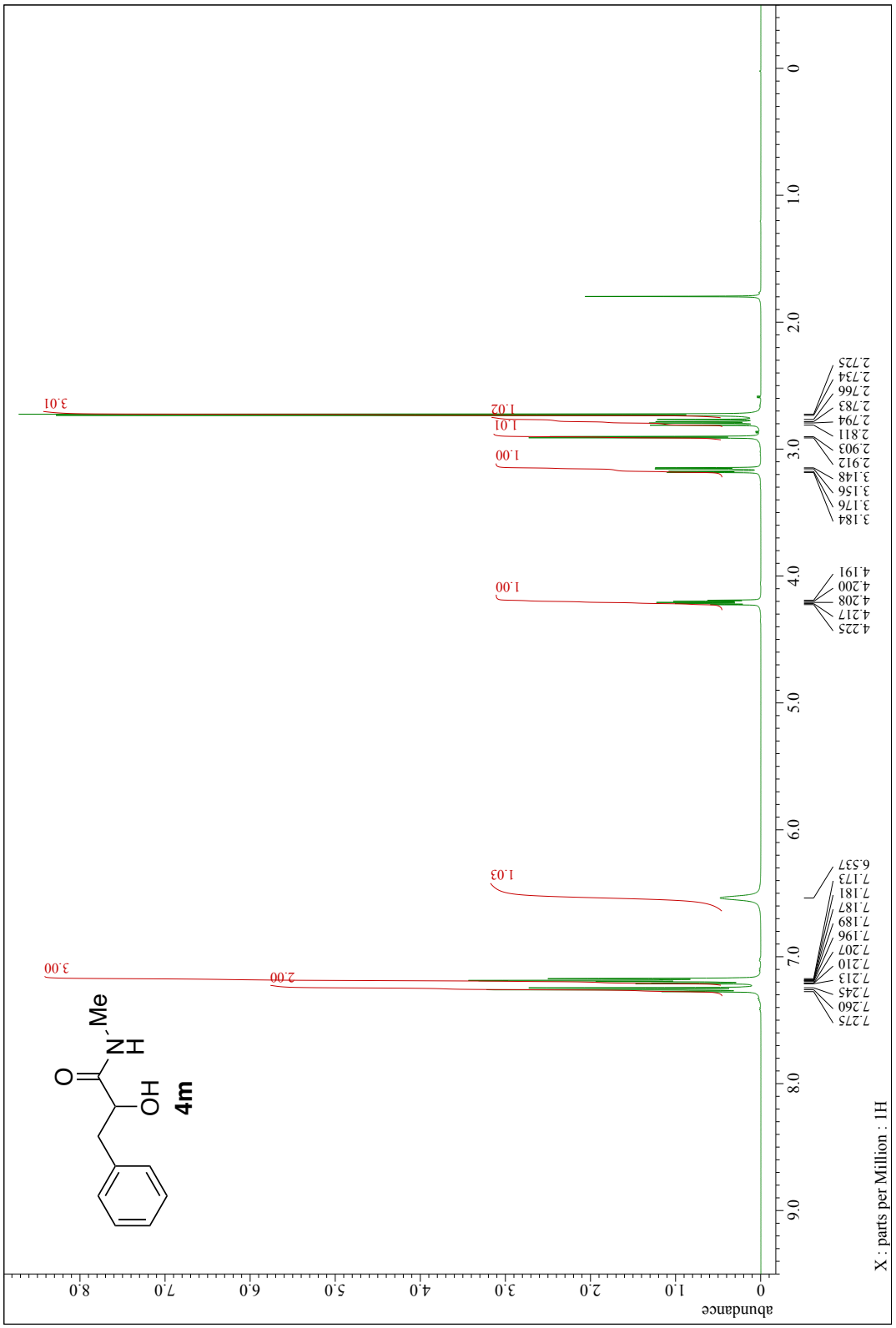
^{1}H NMR spectrum of 4l (500 MHz, $CDCl_3$)



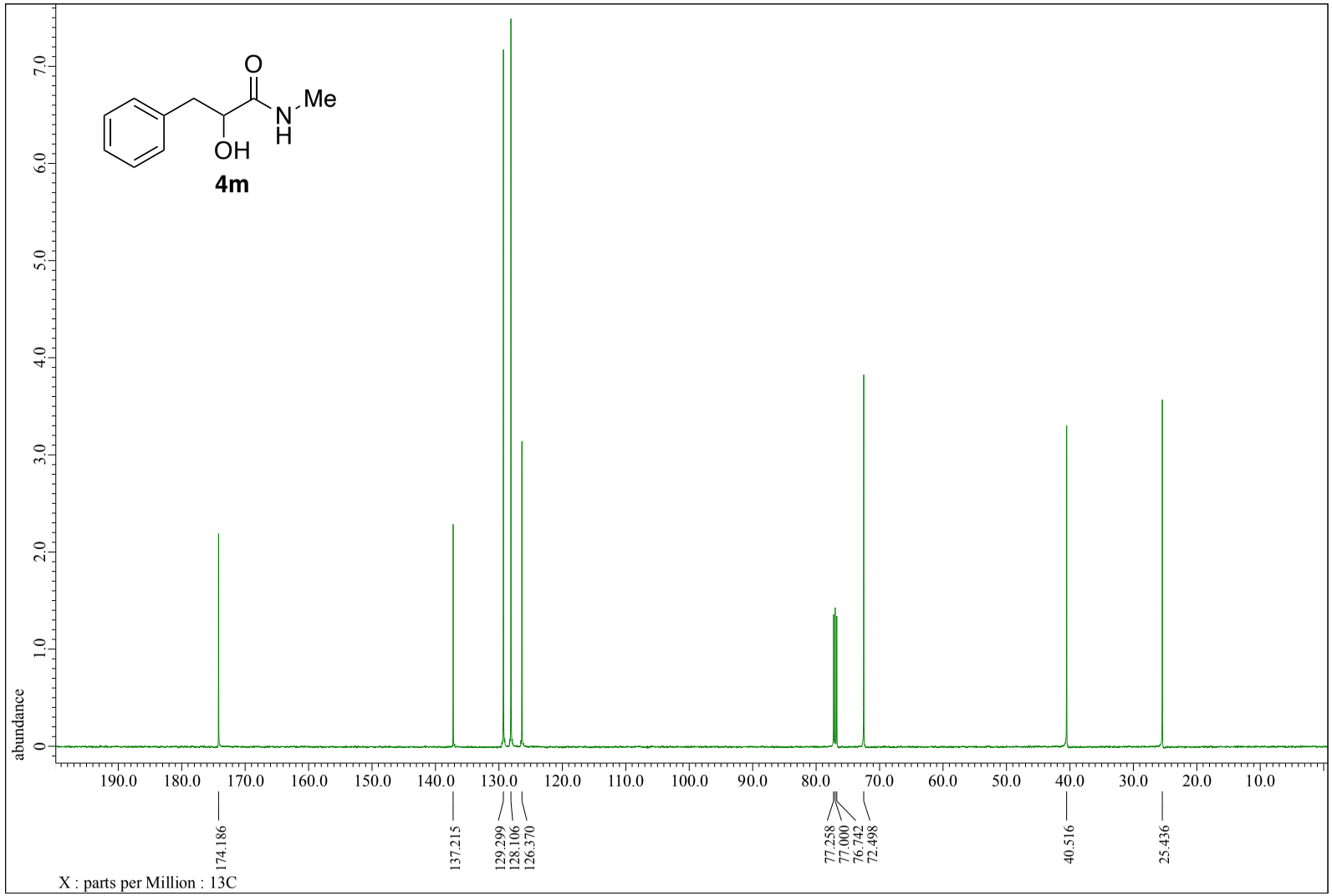
^{13}C NMR spectrum of 4l (126 MHz, $CDCl_3$)



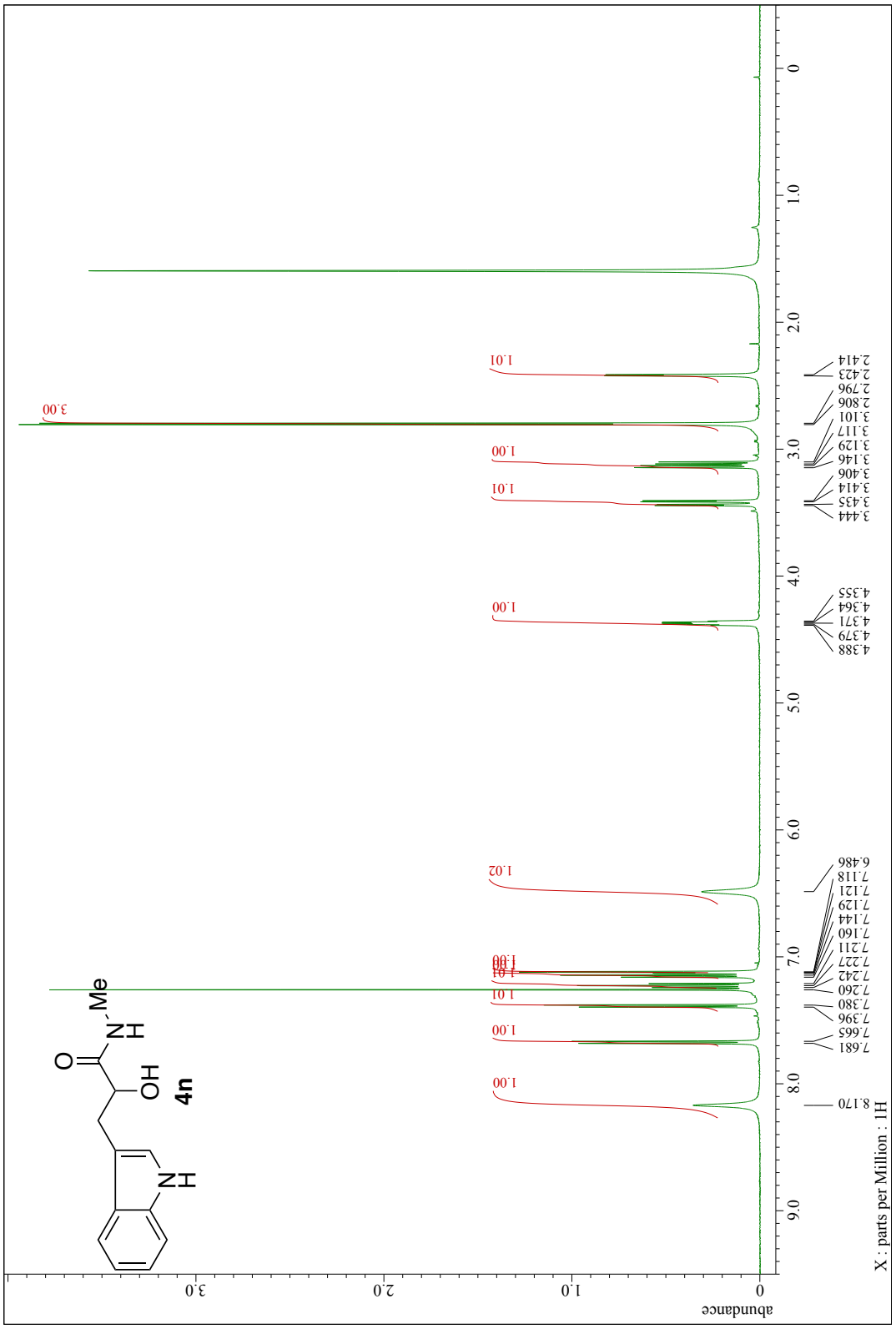
^{1}H NMR spectrum of 4m (500 MHz, $CDCl_3$)



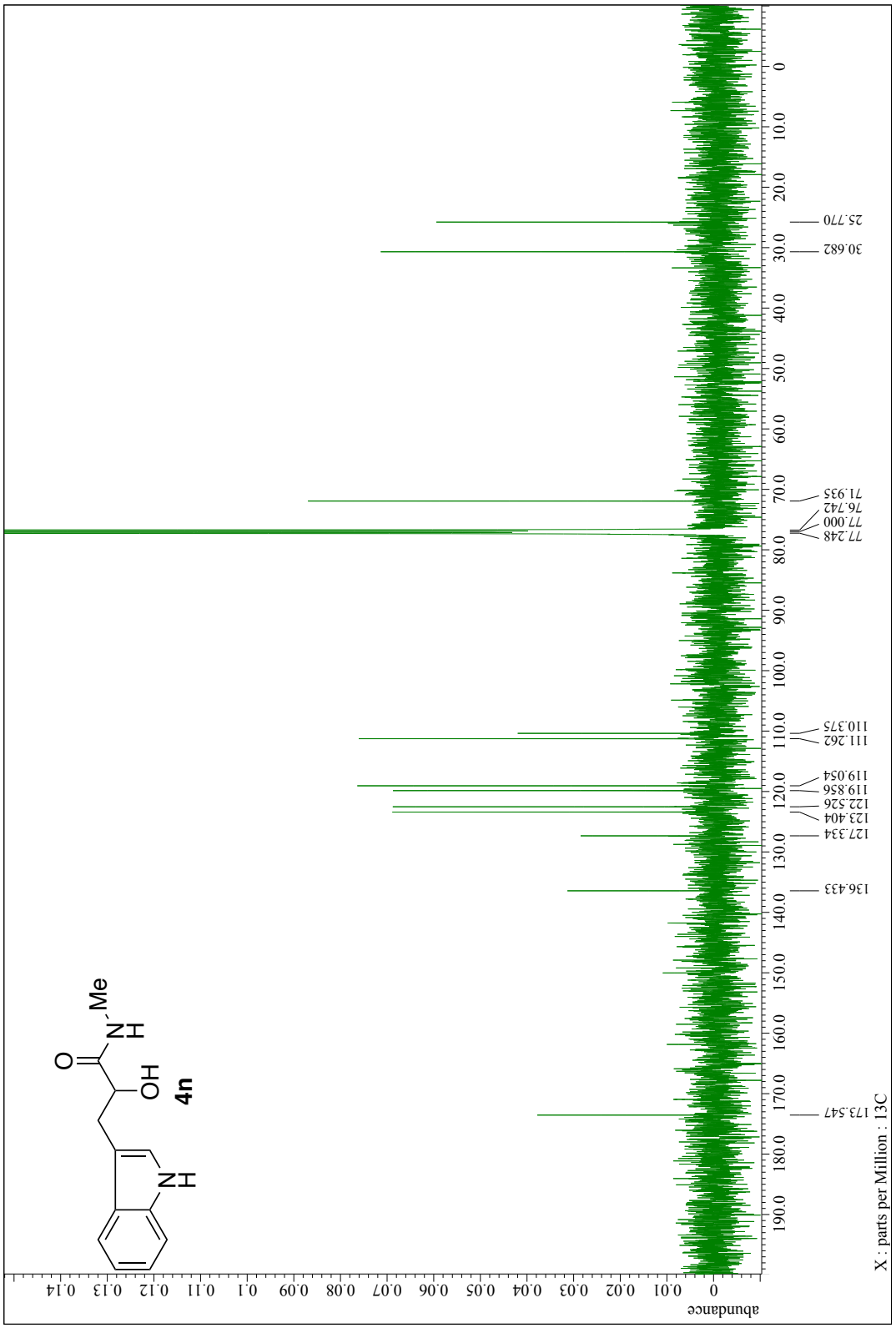
^{13}C NMR spectrum of 4m (126 MHz, $CDCl_3$)



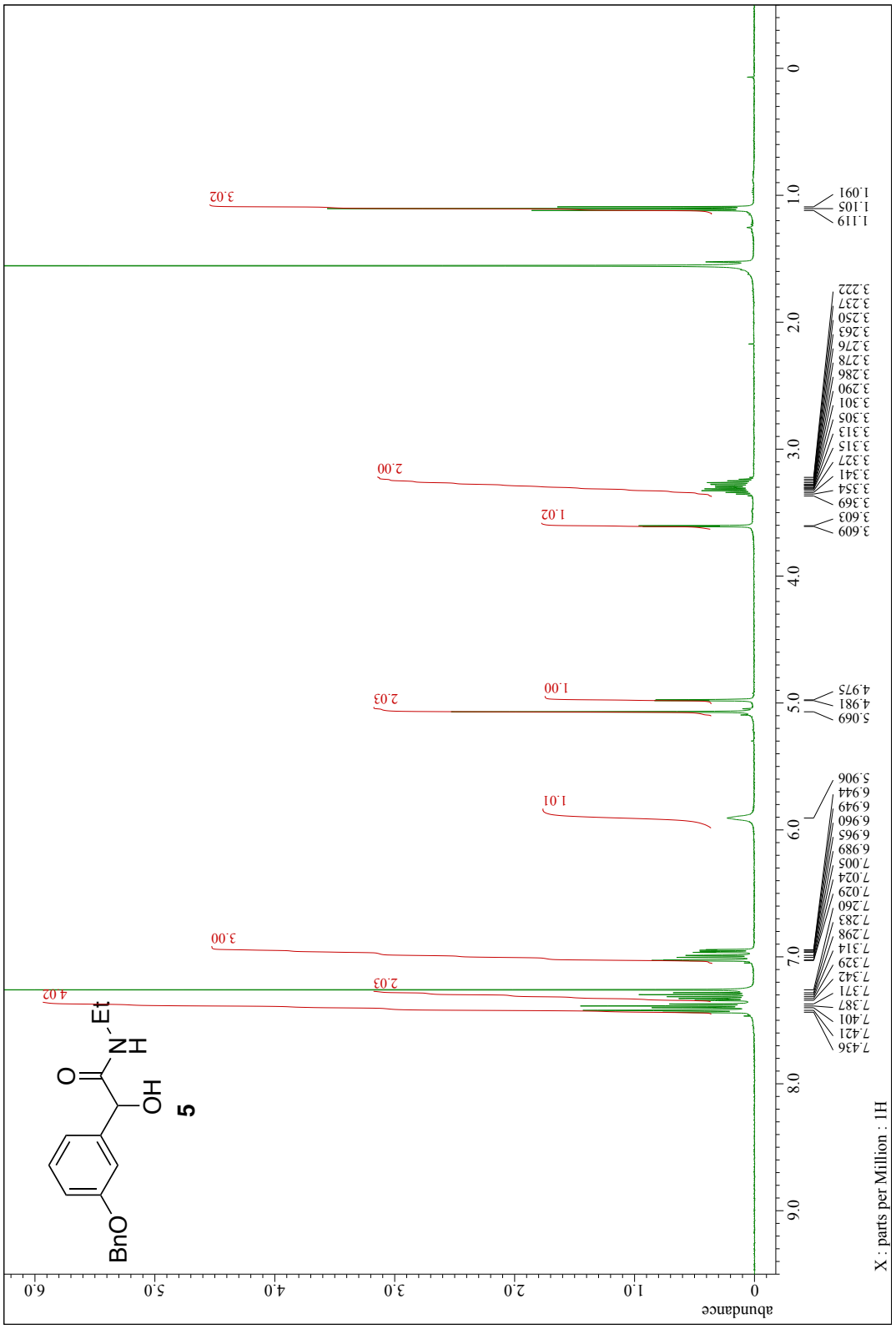
^{1}H NMR spectrum of 4n (500 MHz, $CDCl_3$)



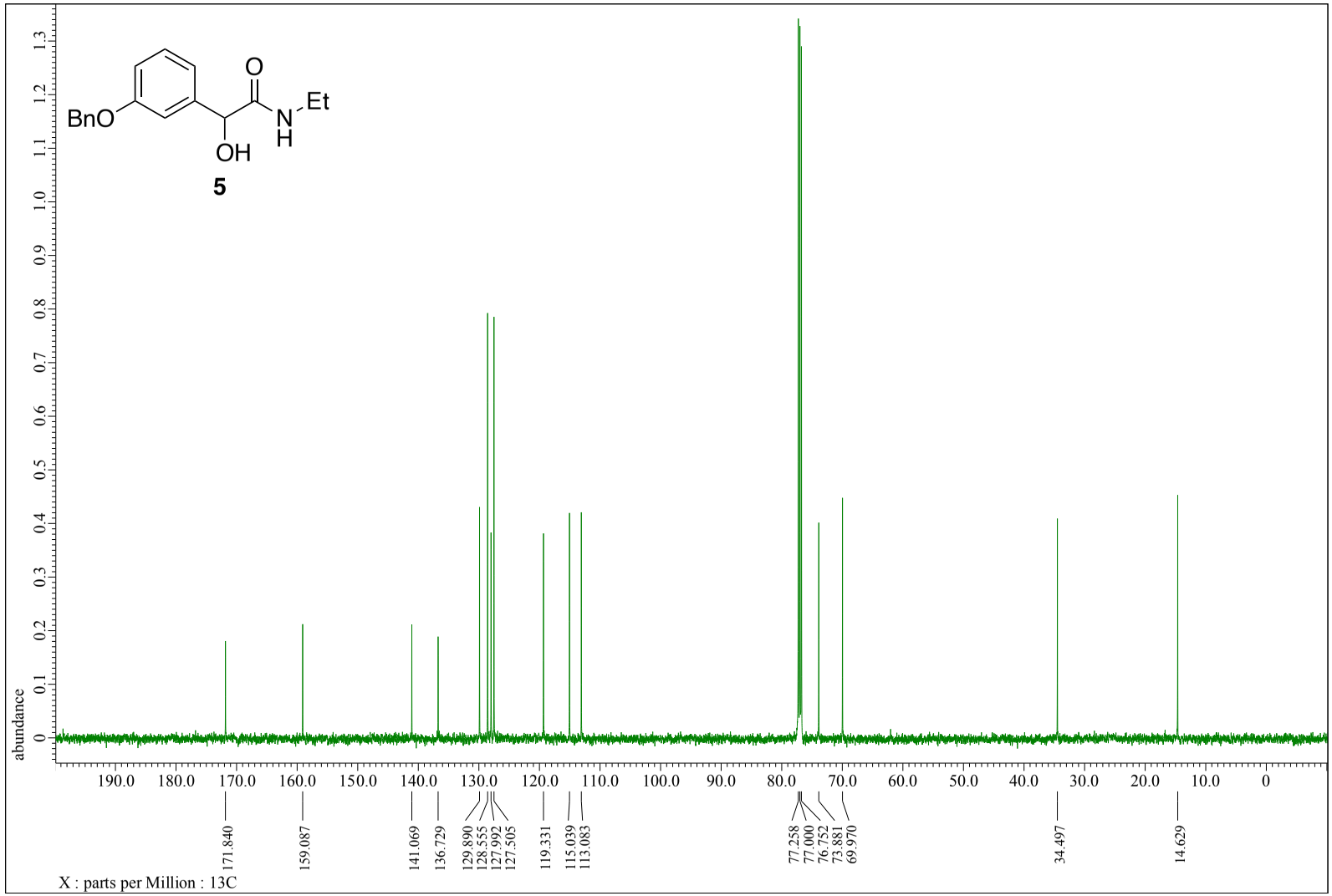
^{13}C NMR spectrum of 4n (126 MHz, $CDCl_3$)



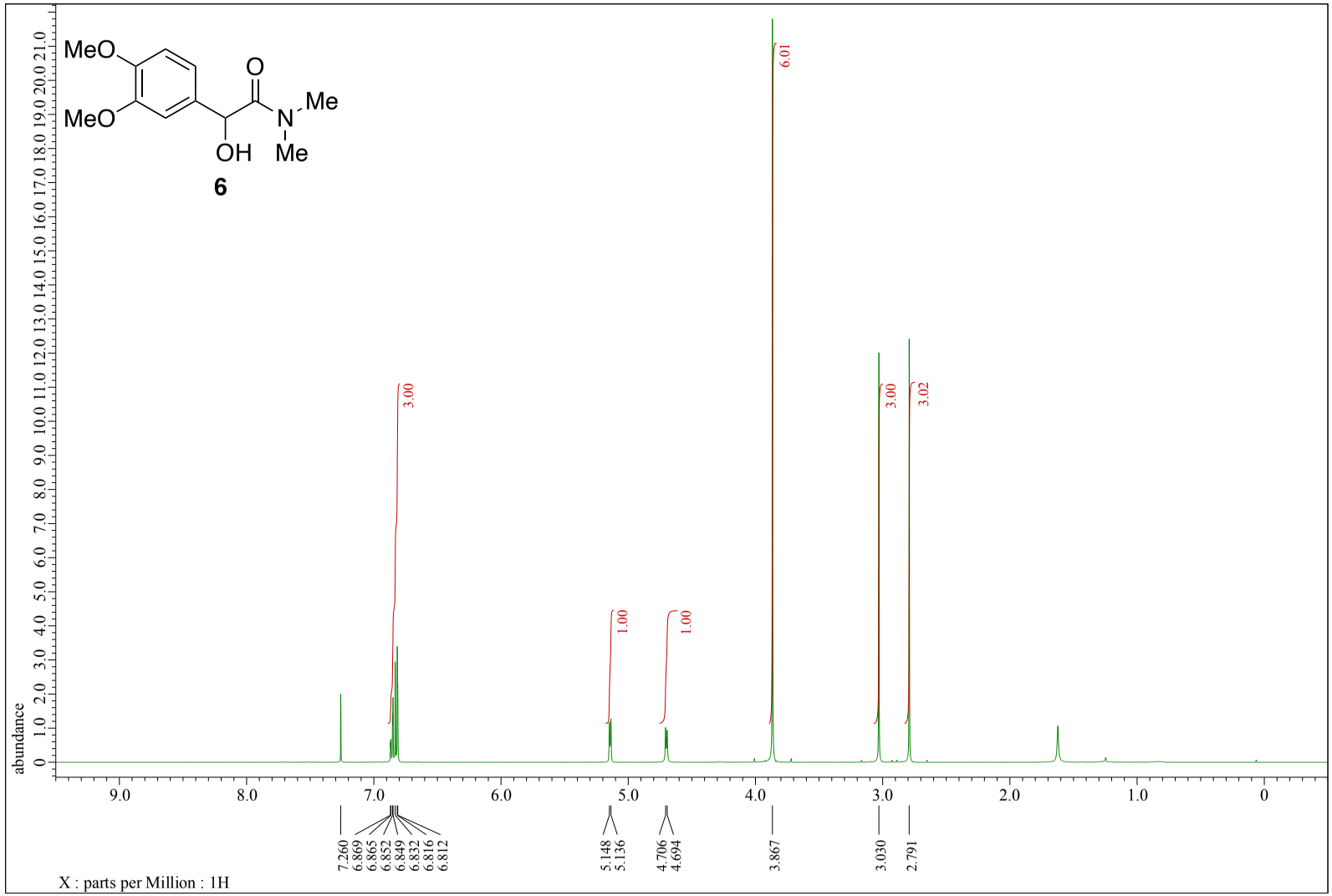
^{1}H NMR spectrum of 5 (500 MHz, $CDCl_3$)



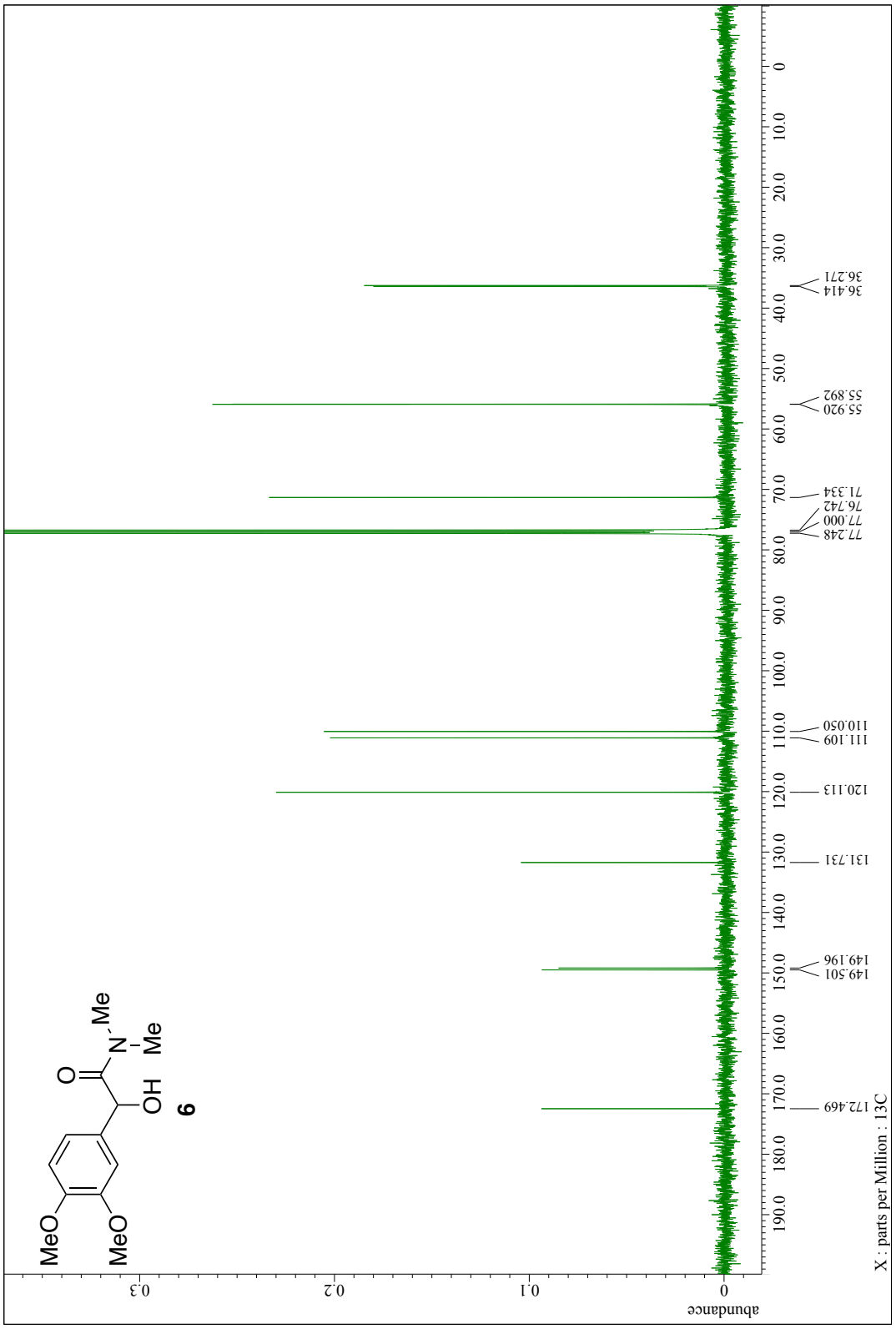
^{13}C NMR spectrum of 5 (126 MHz, $CDCl_3$)



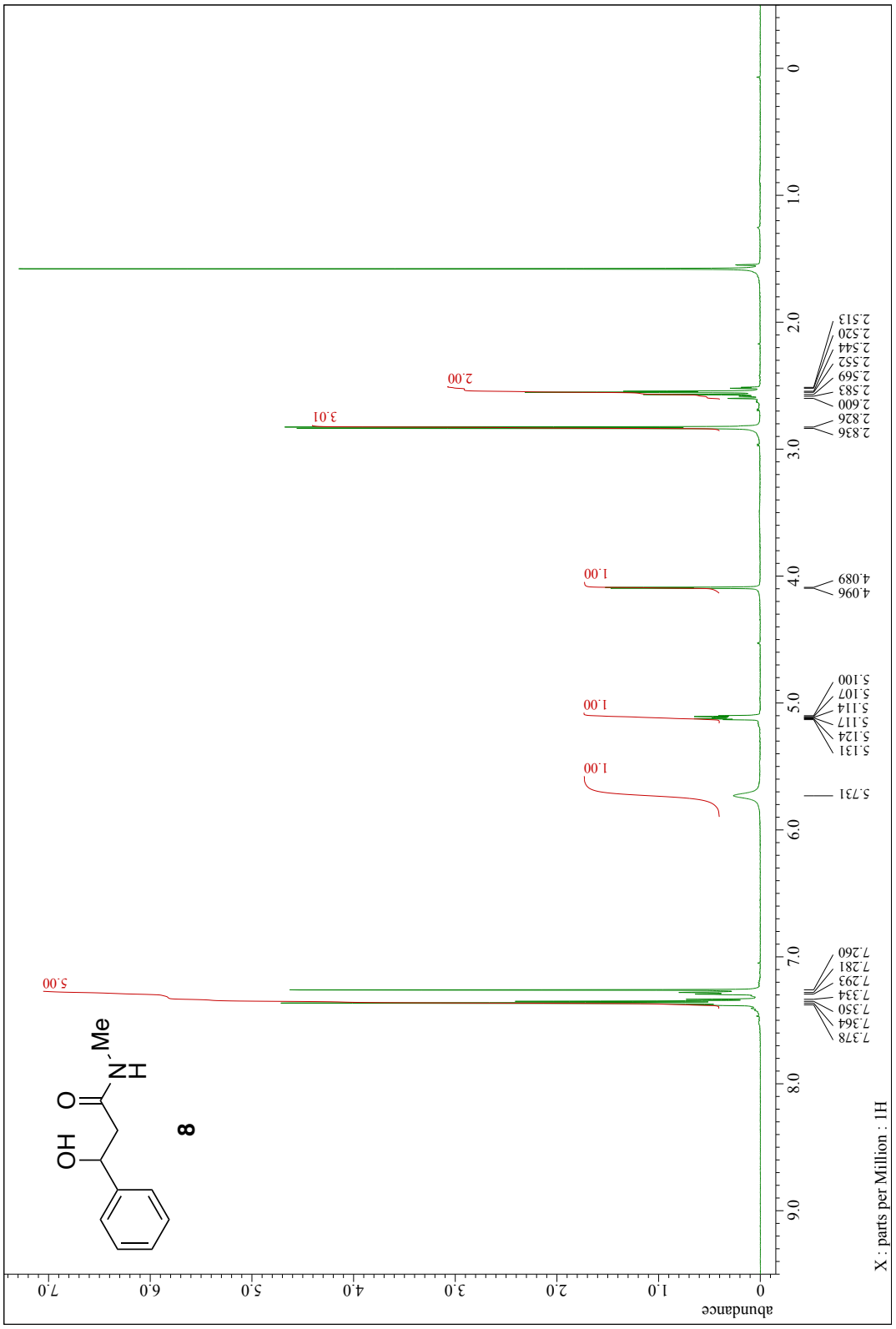
^{1}H NMR spectrum of 6 (500 MHz, $CDCl_3$)



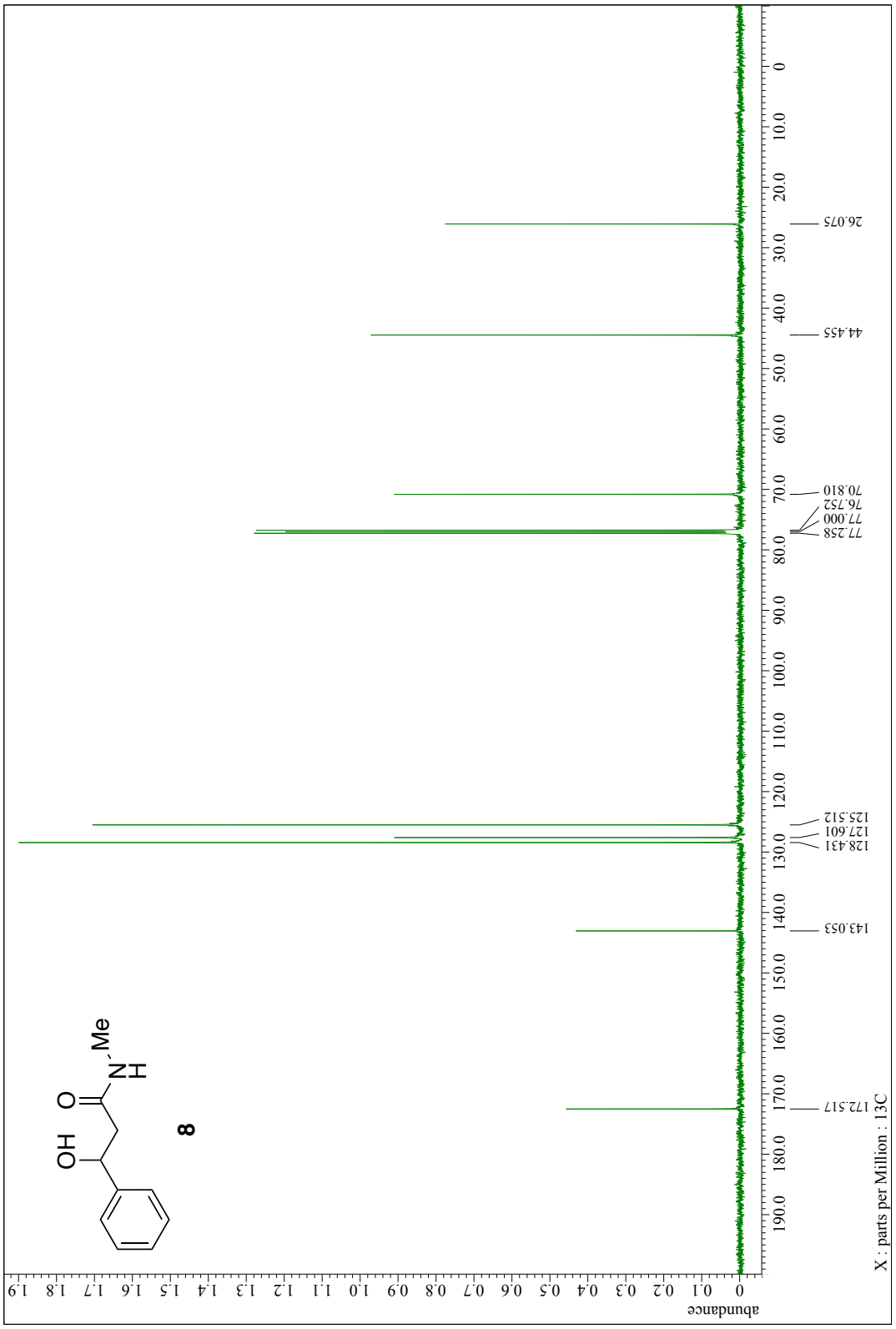
^{13}C NMR spectrum of 6 (126 MHz, $CDCl_3$)



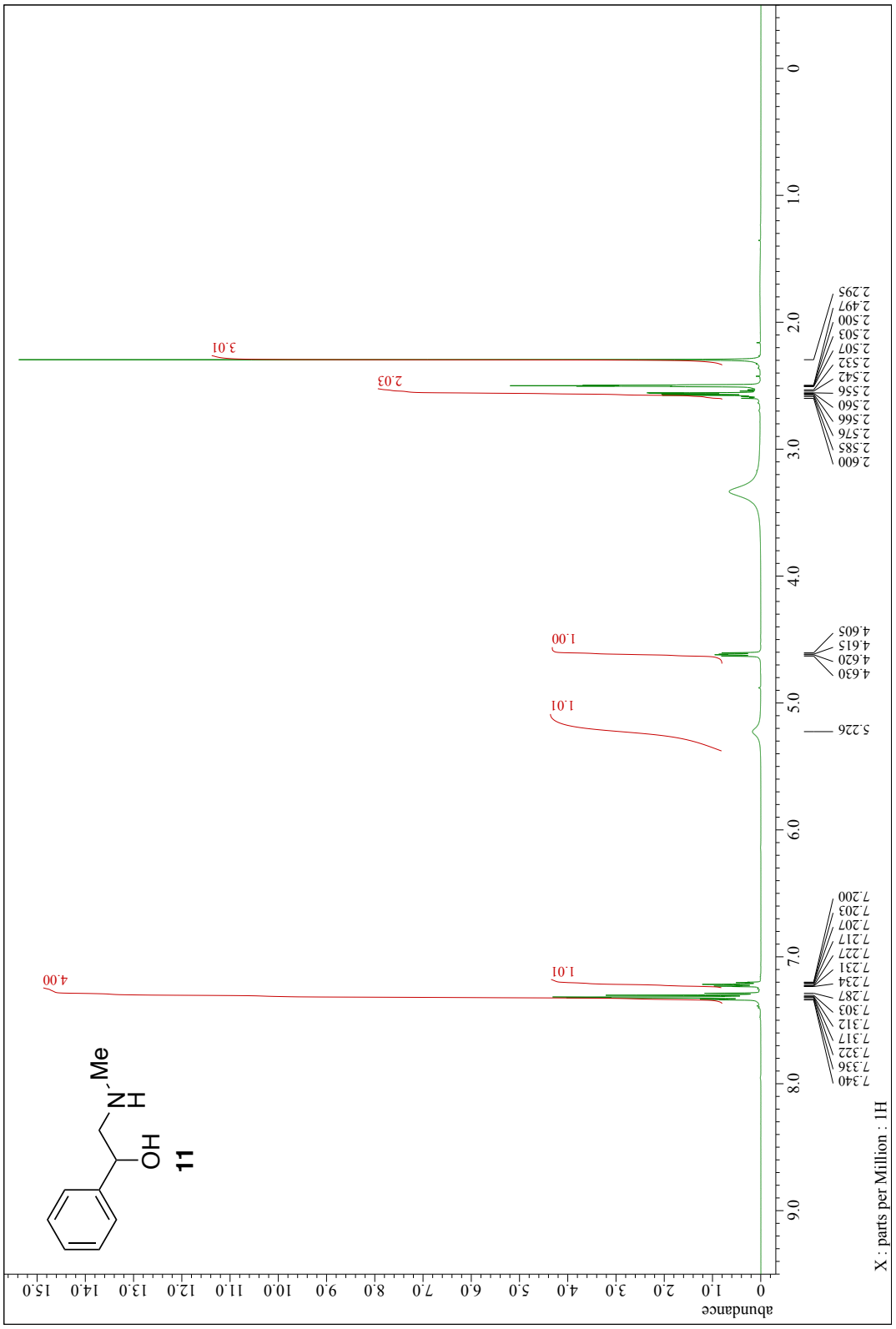
^{1}H NMR spectrum of 8 (500 MHz, $CDCl_3$)



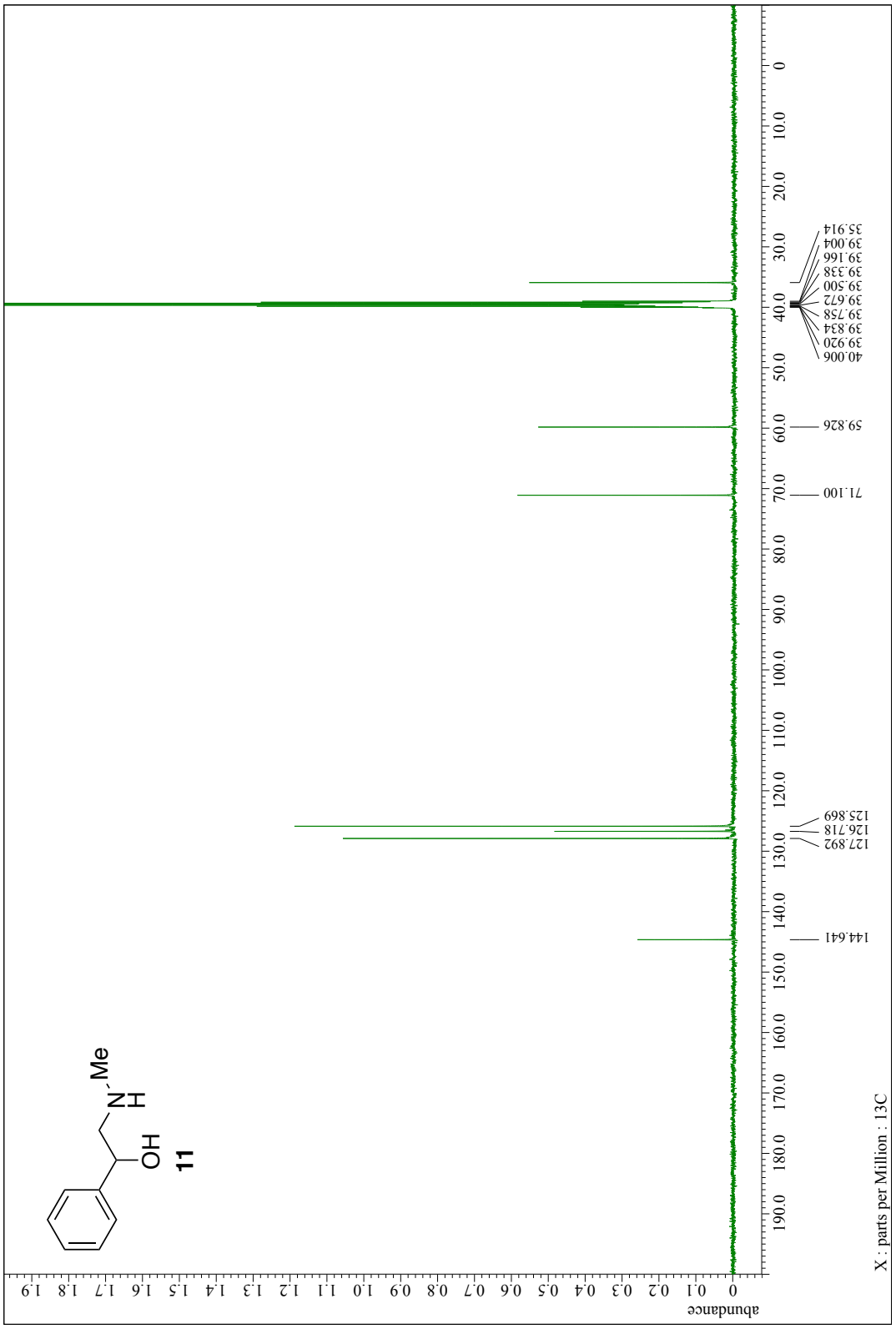
^{13}C NMR spectrum of 8 (126 MHz, $CDCl_3$)



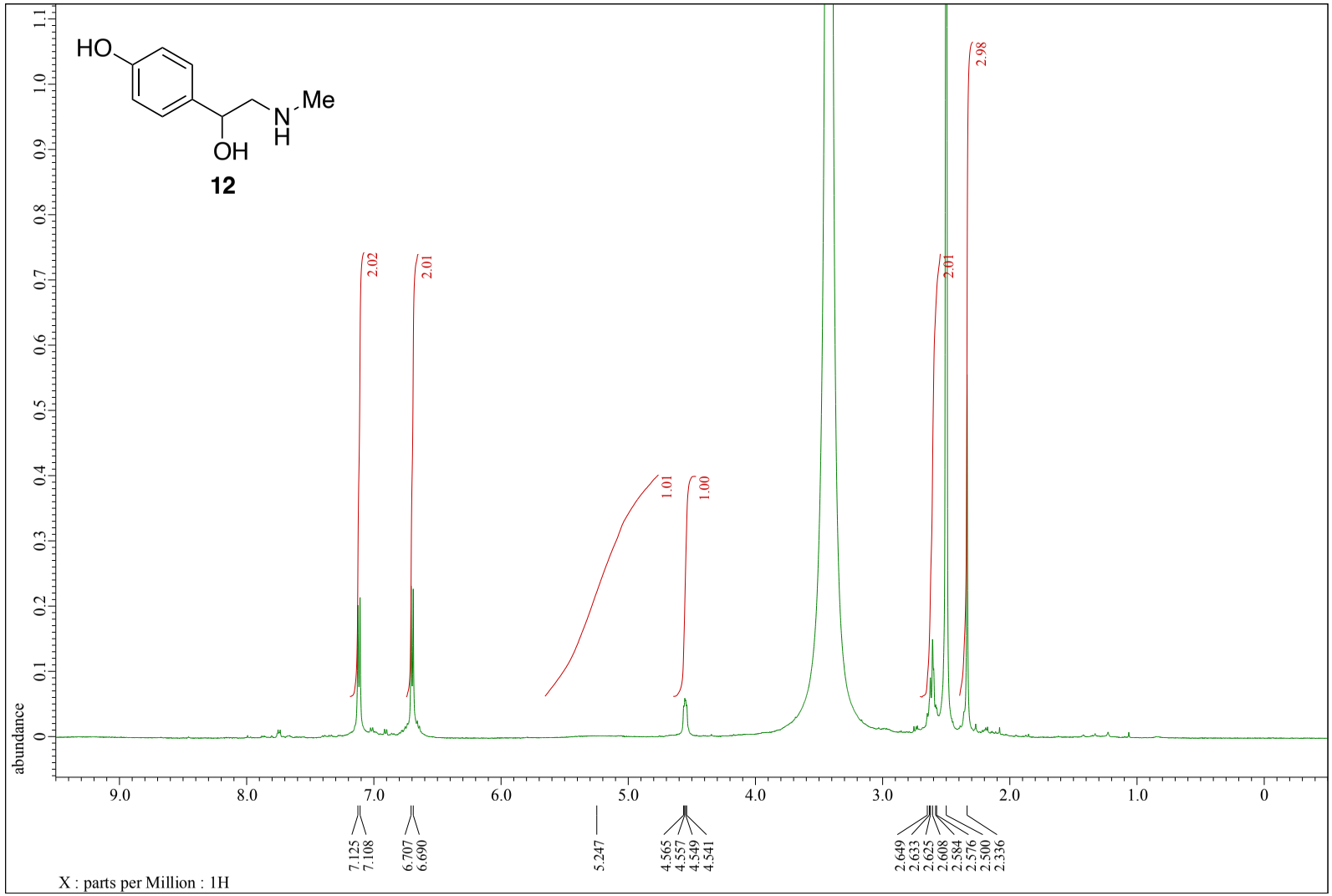
^{1}H NMR spectrum of 11 (500 MHz, DMSO-*d6*)



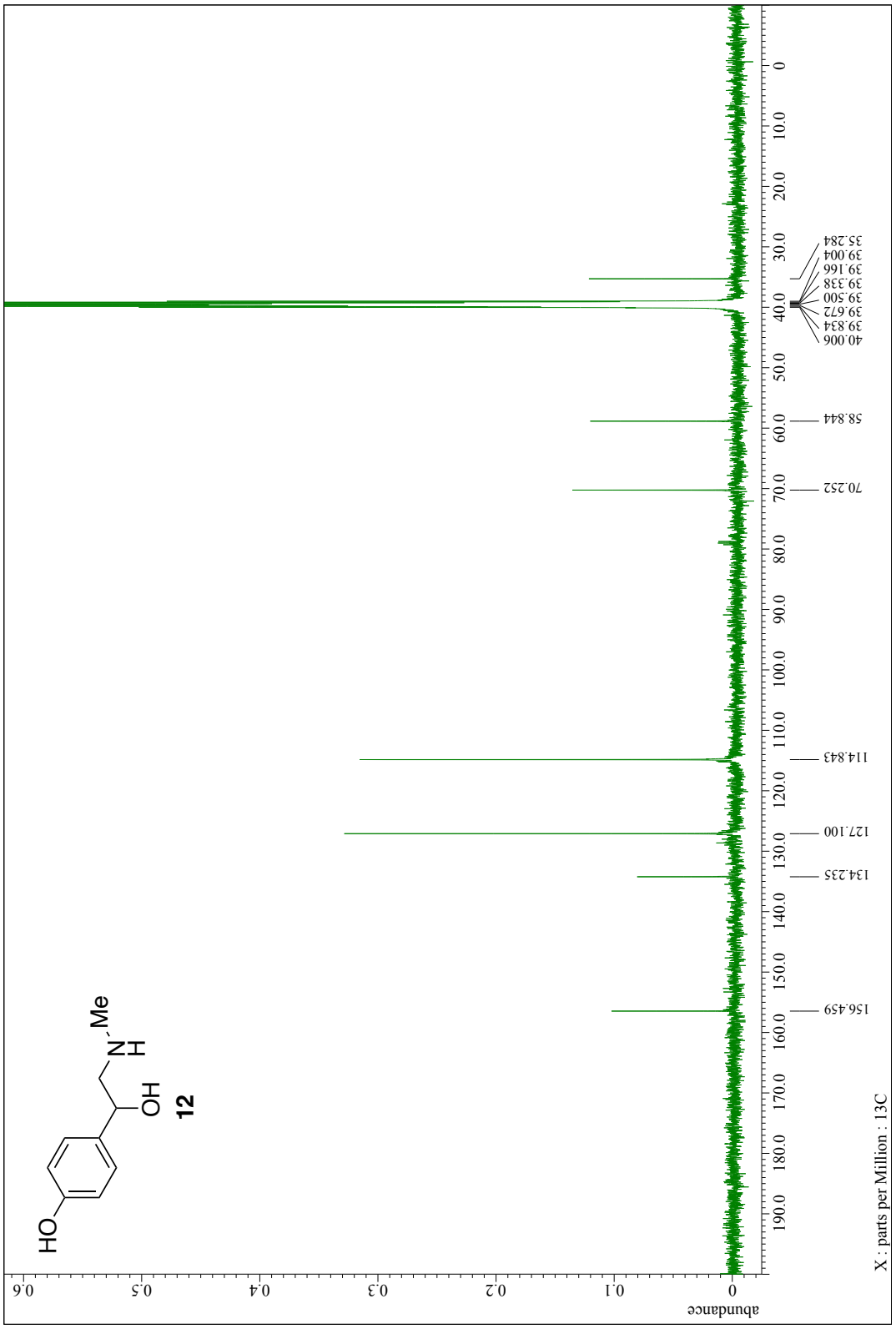
^{13}C NMR spectrum of 11 (126 MHz, DMSO-*d6*)



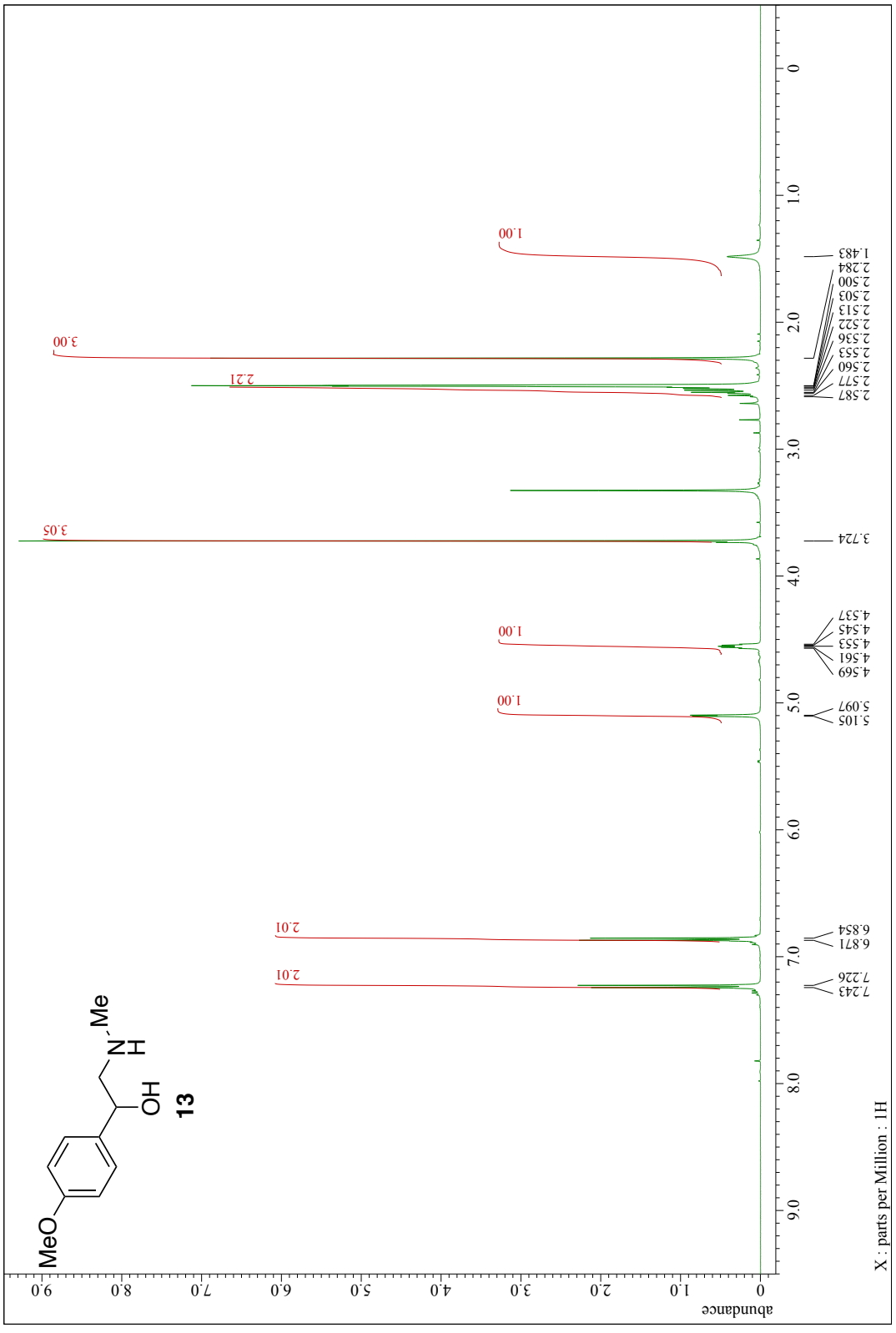
^{1}H NMR spectrum of 12 (500 MHz, DMSO-*d6*)



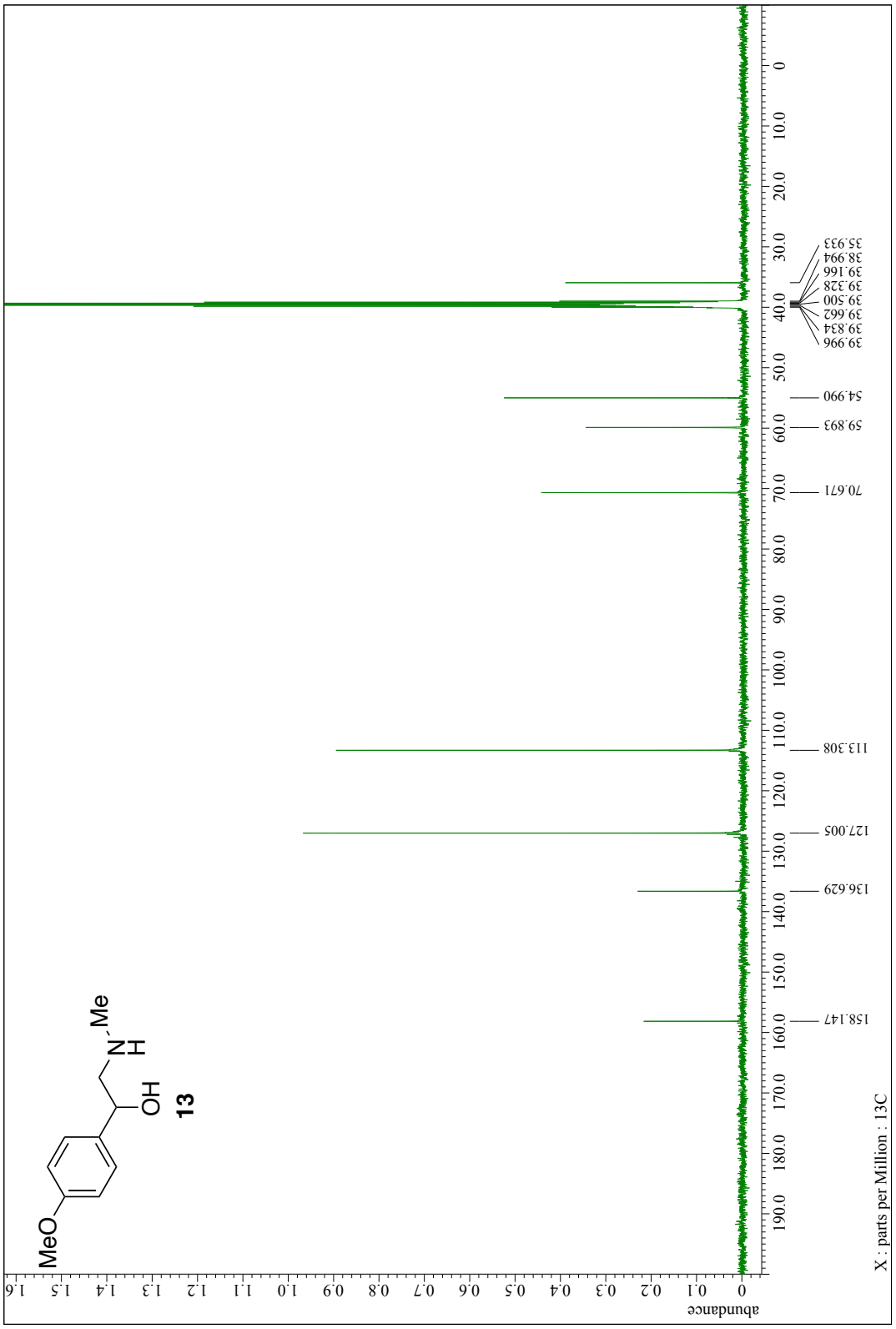
^{13}C NMR spectrum of 12 (126 MHz, DMSO-*d6*)



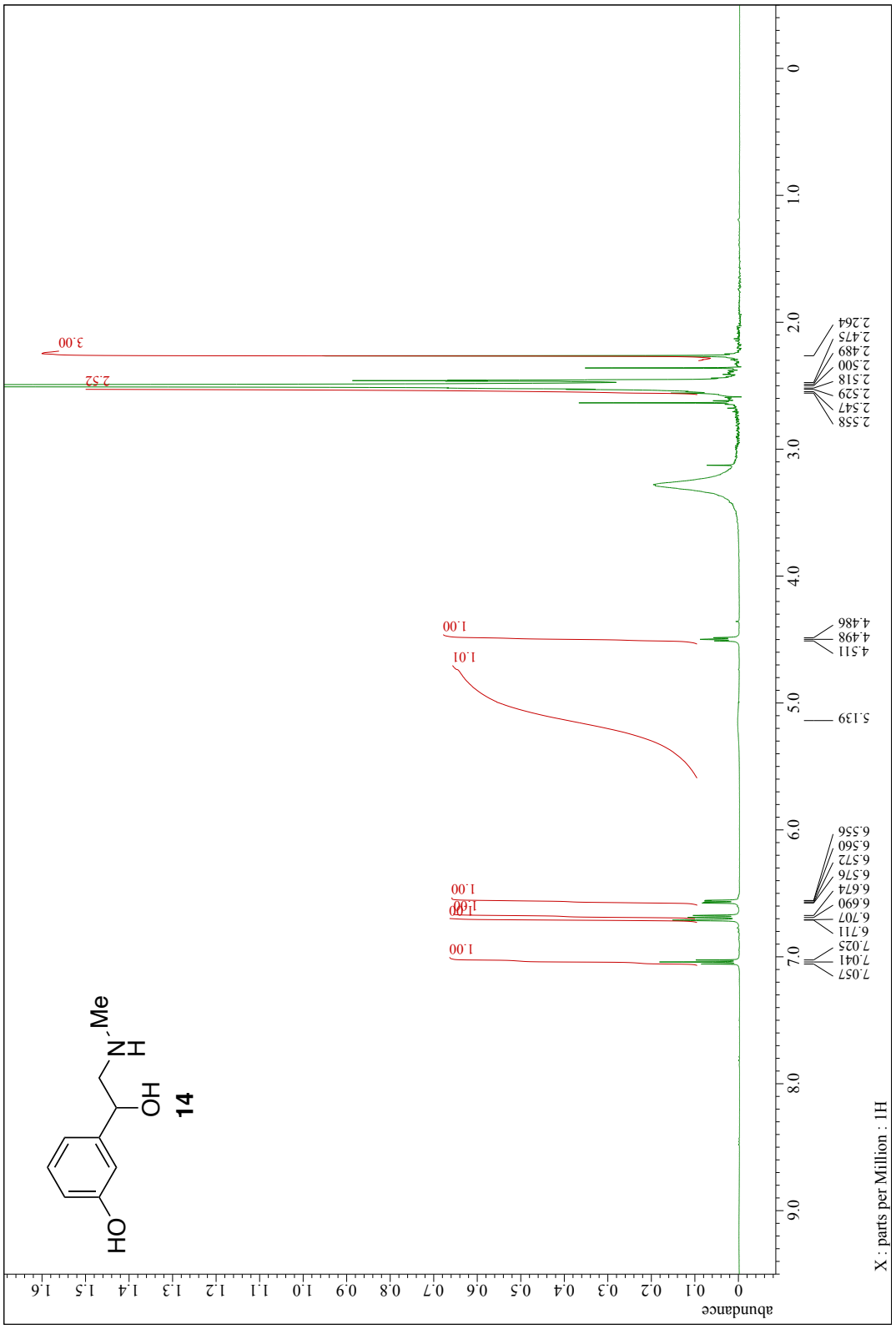
^{1}H NMR spectrum of 13 (500 MHz, DMSO-*d6*)



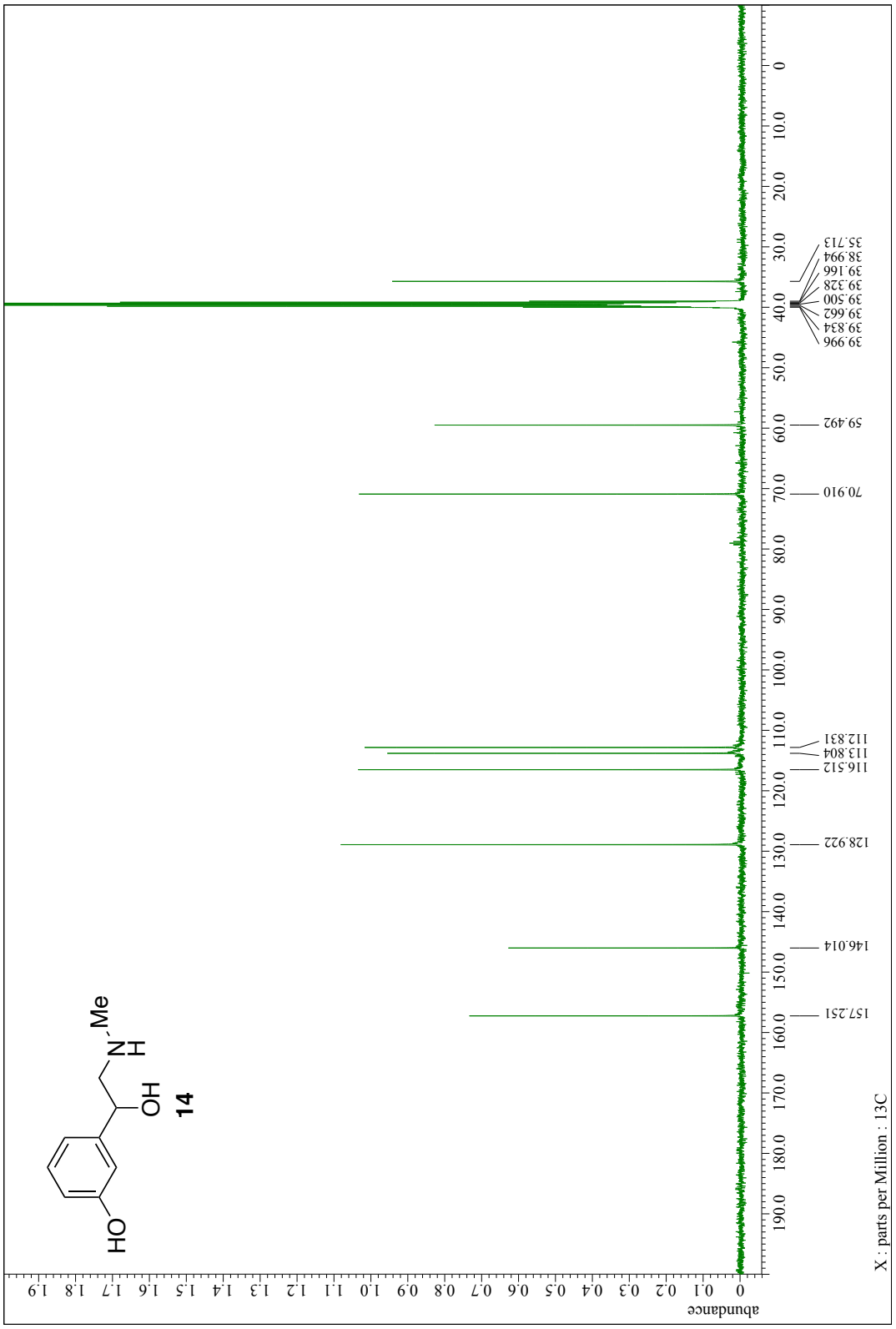
^{13}C NMR spectrum of 13 (126 MHz, DMSO-*d6*)



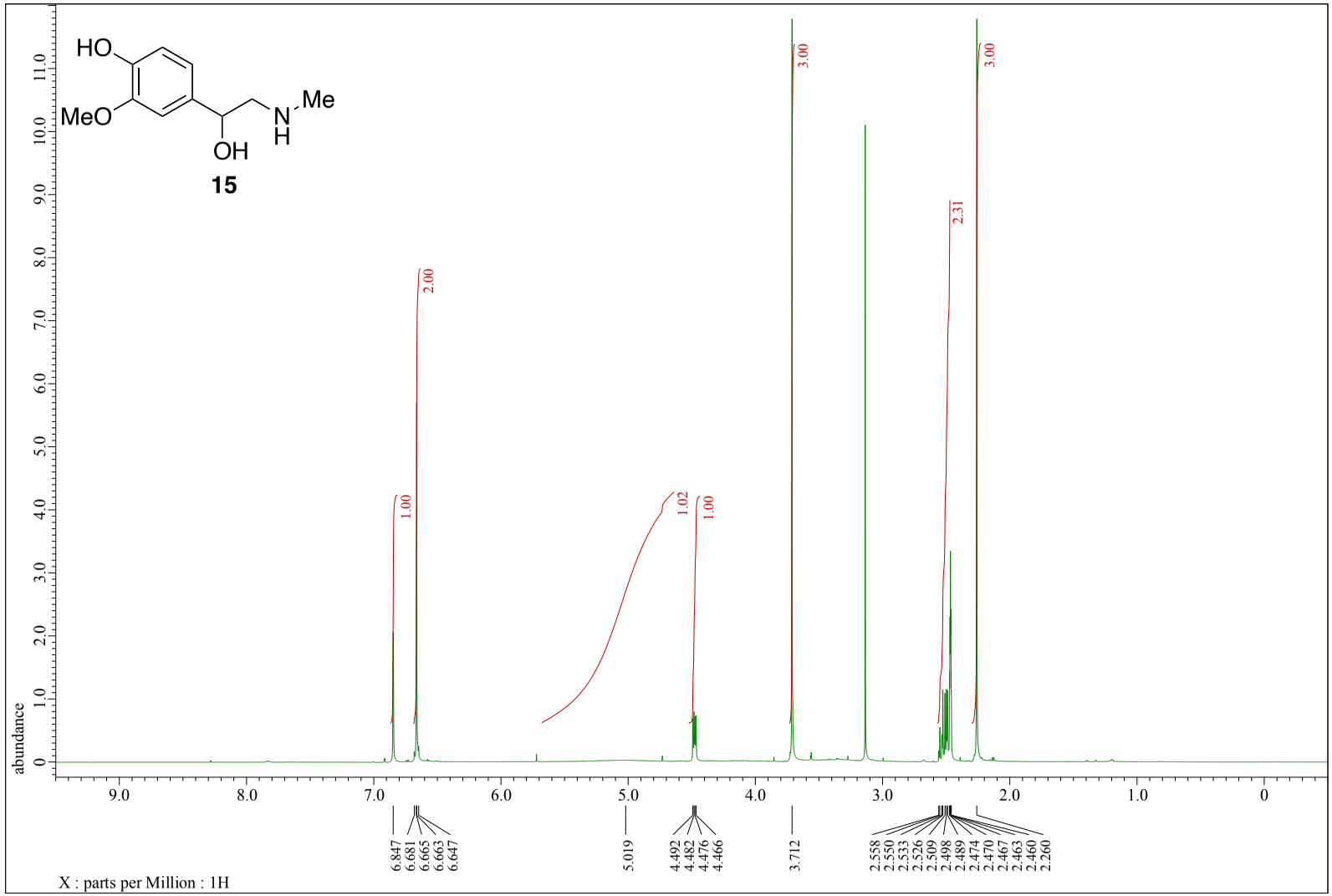
^{1}H NMR spectrum of 14 (500 MHz, DMSO-*d6*)



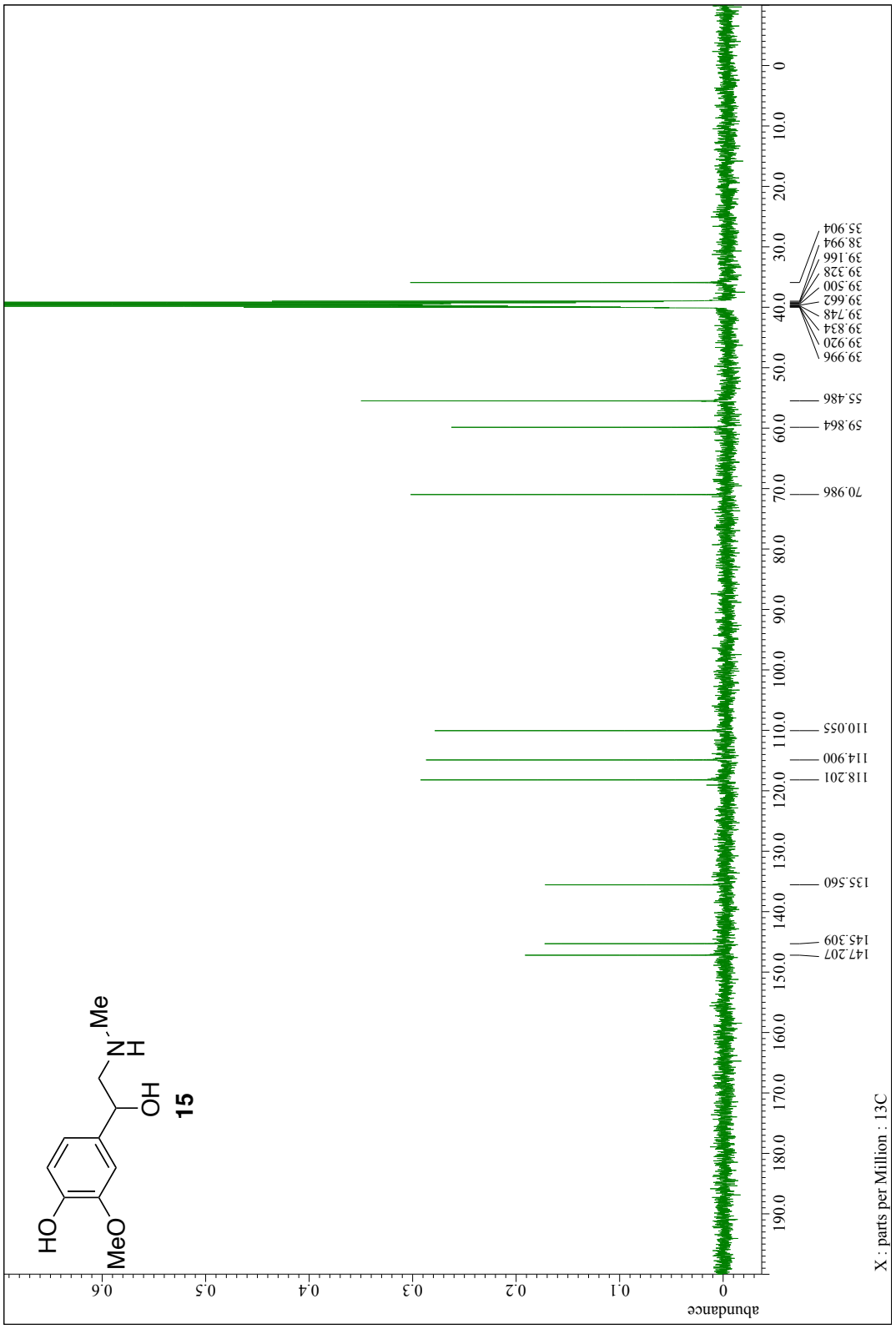
^{13}C NMR spectrum of 14 (126 MHz, DMSO-*d6*)



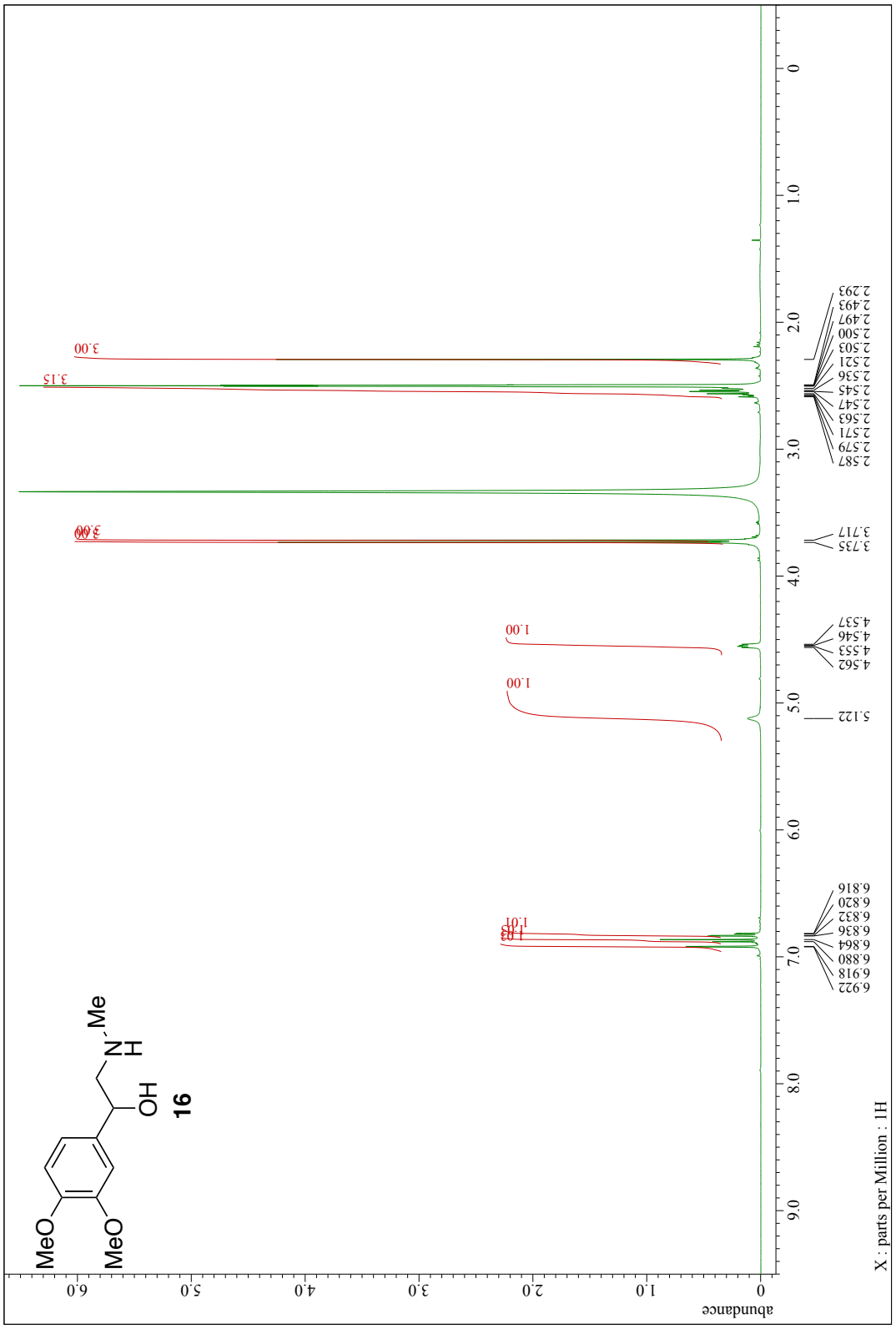
^{1}H NMR spectrum of 15 (500 MHz, DMSO-*d6*)



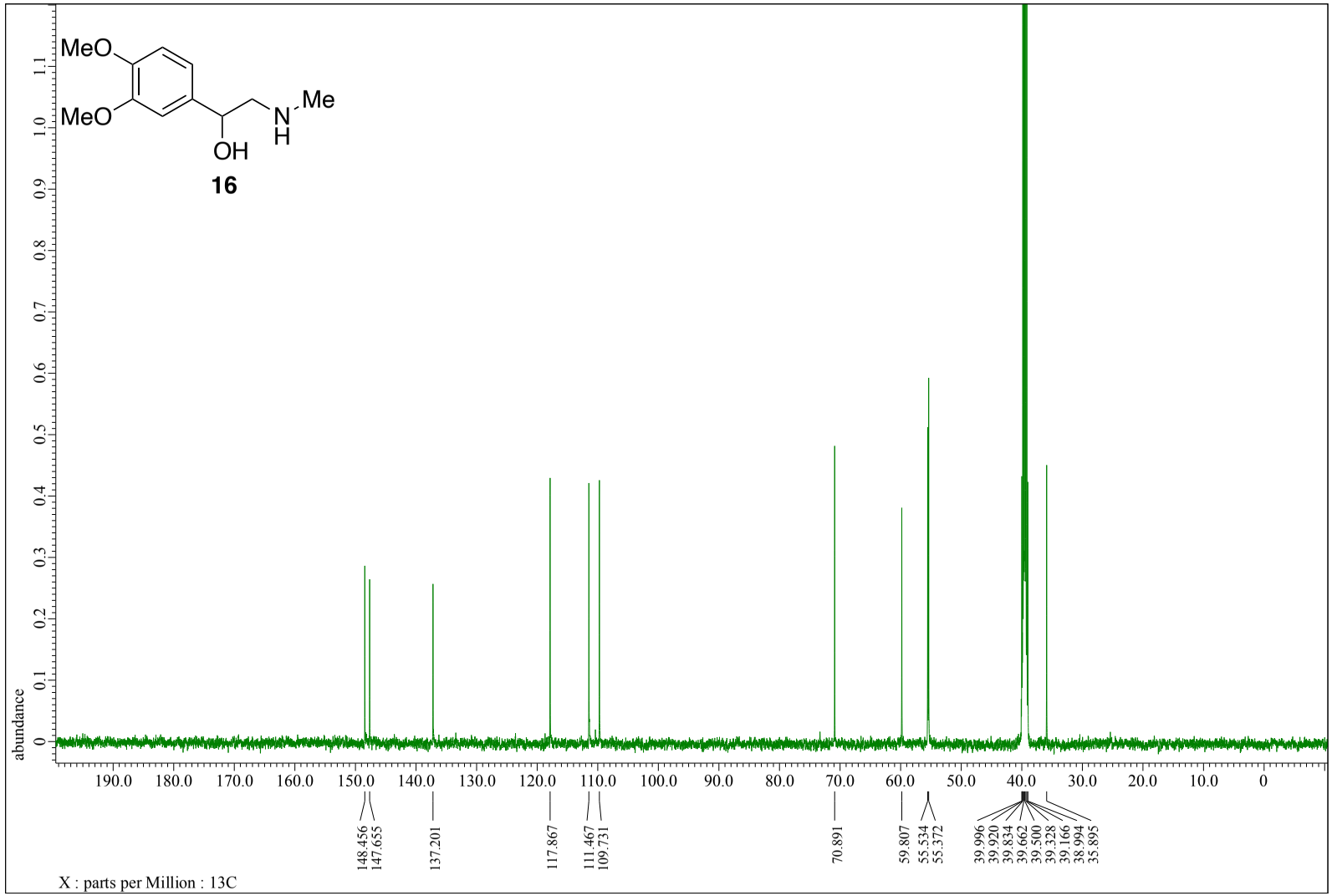
^{13}C NMR spectrum of 15 (126 MHz, DMSO-*d6*)



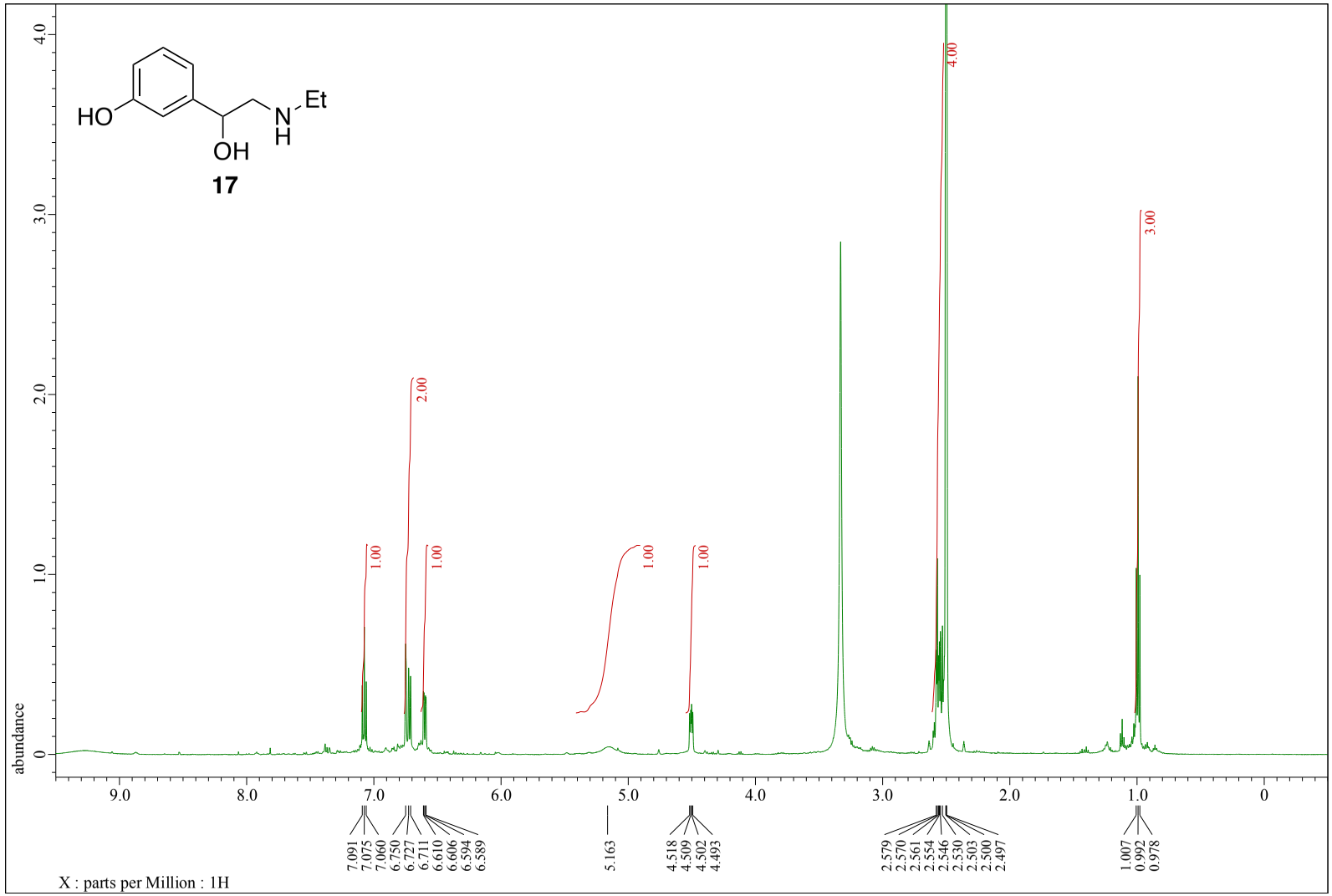
^{1}H NMR spectrum of 16 (500 MHz, DMSO-*d6*)



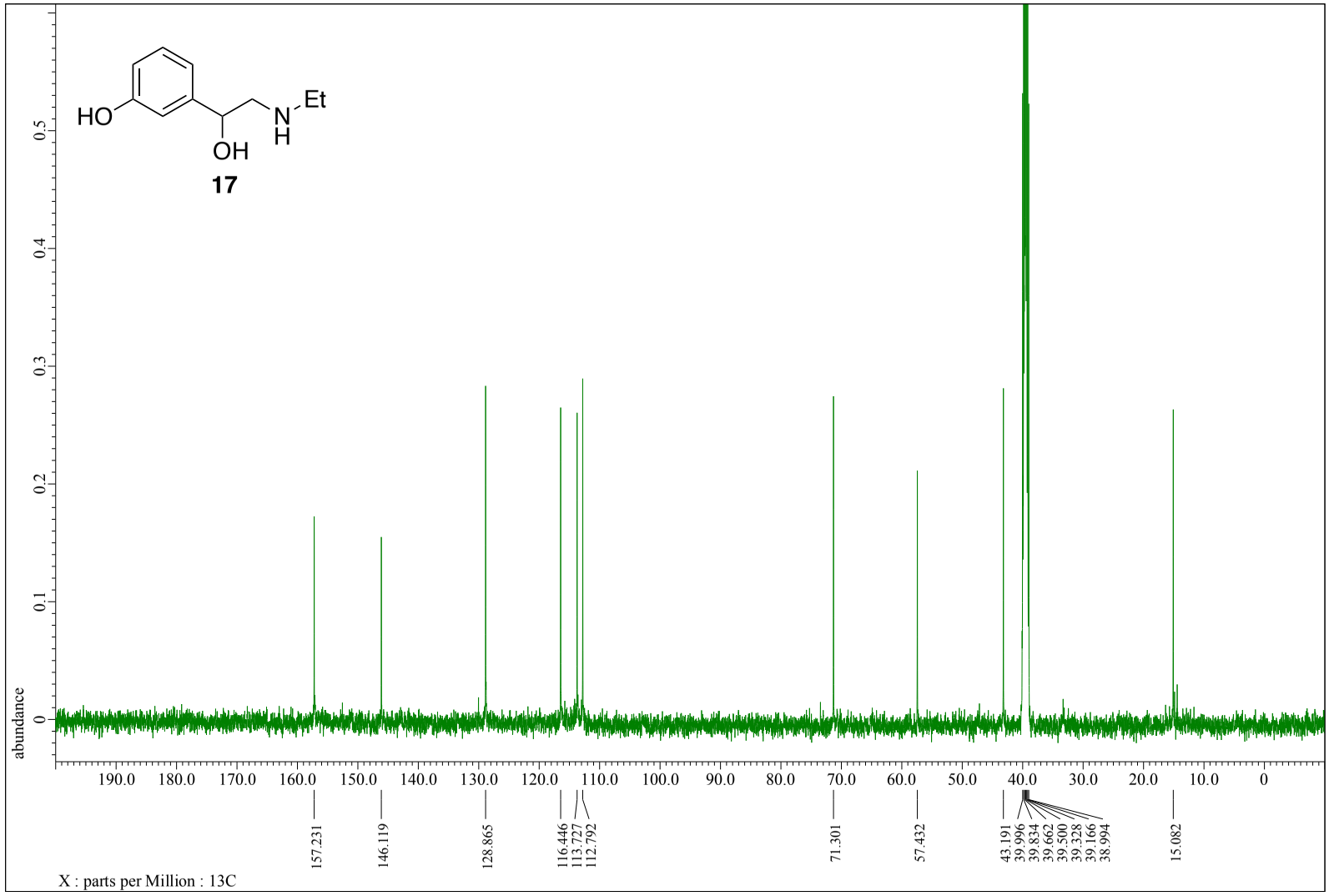
^{13}C NMR spectrum of 16 (126 MHz, DMSO-*d6*)



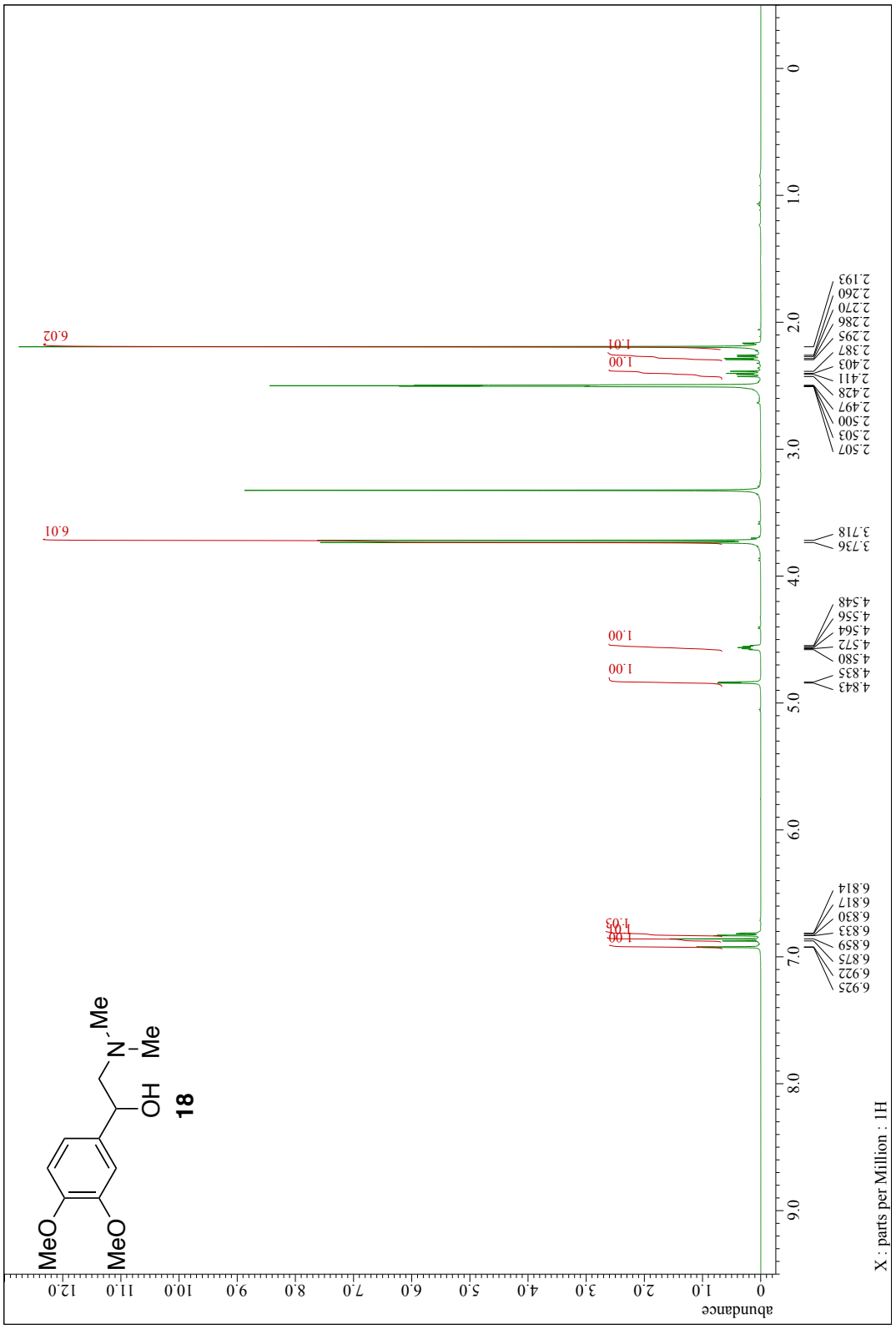
^{1}H NMR spectrum of 17 (500 MHz, DMSO-*d6*)



^{13}C NMR spectrum of 17 (126 MHz, DMSO-*d6*)



^{1}H NMR spectrum of 18 (500 MHz, DMSO-*d6*)



^{13}C NMR spectrum of 18 (126 MHz, DMSO-*d6*)