Iron-Catalyzed Oxidative Homo-Coupling of Aryl Grignard Reagents

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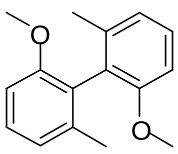
Supporting Data

General. All anaerobic and/or moisture sensitive manipulations were carried out with standard Schlenk techniques under predried nitrogen or with glovebox techniques under prepurified argon. Tetrahydrofuran and diethyl ether were distilled from sodium benzophenone ketyl under nitrogen prior to use. The Grignard reagents **1a**-**1f** were prepared in dry diethyl ether from the corresponding commercially available aryl bromides by the standard method. 2-Methyl-1-naphthylmagnesium bromide (**1h**) was prepared in benzene/Et_2O according to the literature procedure.[1] 2-Methoxy-6-methylbromobenzene, which is the precursor of the Grignard reagent **1g**, was prepared according to the literature method.[2] Methoxymethyl phenyl ether (**4**)[3] and 5,5-dimethyl-2-phenyl-2-oxazoline (**6**)[4] were prepared according to the literature methods. Melting points were uncorrected. NMR spectra were recorded on a JEOL JNM LA500 spectrometer (^1H, 500 MHz; ^{13}C, 125 MHz). ^1H and ^{13}C chemical shifts are reported in ppm downfield of internal tetramethylsilane.

General procedure for the iron-catalyzed homo-coupling. To a refluxing solution of $FeCl_3$ (0.0026 mmol) and 1,2-dichloroethane (0.62 mmol) in diethyl ether (4 mL) was added a Grignard reagent (0.52 mmol) and the reaction mixture was refluxed for 1 h. The reaction was quenched by addition of aqueous HCl (1 N). The organic layer was separated and the aqueous layer was extracted by ether. The combined organic layers were dried over anhydrous magnesium sulfate. All volatiles were removed under reduced pressure and the residue was chromatographed on silica gel. Spectroscopic and analytical data of the new biaryls are as follows;

2,2 -dimethoxy-6,6 -dimethyl-1,1 -biphenyl (3g). White solid. Mp 84-85 ßC. ^1H NMR ($CDCl_3$): δ 7.23 (m, 2H), 6.90 (d, J = 7.1 Hz, 2H), 6.82 (d, J = 8.2 Hz, 2H), 3.69 (s, 6H), 1.94 (s, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 156.96, 138.18, 127.86, 126.23, 122.20, 108.35, 55.77, 19.55. Anal. Calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49;. Found: C, 79.61; H, 7.64.



Procedure for directed ortho-metallation followed by homocoupling reaction

Synthesis of 5. To a solution of methoxymethyl phenyl ether (**4)** (200 mg, 1.45 mmol) in Et_2O (2.0 mL) was added *n*-BuLi (1.54 M in hexane, 1.04 mL, 1.60 mmol) at room temperature and the resulting solution was stirred for 3. The mixture was added to a solution of anhydrous $MgBr_2$, which was freshly prepared by treatment of Mg (53.0 mg, 2.18 mmol) with 1,2-dibromoethane (175 µL, 2.03 mmol) in Et_2O (2.0 mL), and the resulting yellow solution was stirred at room temperature for 0.5 h. To this was added a solution of $FeCl_3$ (12 mg, 0.074 mmol) and 1,2-dichloroethane (172 µL, 2.18 mmol) in

Et_2O (2.0 mL), and the reaction mixture was refluxed for 15 h before it was quenched with water. The organic layer was separated and the aqueous layer was extracted with Et_2O. The combined organic layers were dried over anhydrous K_2CO_3. All volatiles were removed under reduced pressure and the residue was chromatographed on silica gel (Hexane/EtOAc = 9/1) to give 2,2 -bis(methoxymethoxy)biphenyl (**5**)[5] (220 mg, 71%).

Synthesis of 7. To a solution of 2-phenyl-4,4-dimethyl-2-oxazoline (**6**) (200 mg, 1.14 mmol) in Et_2O (2.0 mL) was added *s*-BuLi (1.01 M in hexane/cyclohexane, 1.24 mL, 1.25 mmol) at —78ßC and the resulting solution was stirred at that temperature for 1.5 h. The mixture was allowed to warm to 0 ßC and the solution was stirred at 0ßC for 1.5 h. This was added to a solution of anhydrous $MgBr_2$, which was freshly prepared by treatment of Mg (42 mg, 1.71 mmol) with 1,2-dibromoethane (138 µL, 1.60 mmol) in Et_2O (2.0 mL), and the resulting yellow solution was stirred at room temperature for 0.5 h. To this was added a solution of $FeCl_3$ (9.0 mg, 0.055 mmol) and 1,2-dichloroethane (135 µL, 1.71 mmol) in Et_2O (2.0 mL), and the reaction mixture was refluxed for 15 h before it was quenched with water. The organic layer was separated and the aqueous layer was extracted by ether. The combined organic layers were dried over anhydrous Na_2SO_4. All volatiles were removed under reduced pressure and the residue was purified with preparative TLC on silica gel (hexane/Et_2O = 1/1) to give 2,2 -bis(4,4-dimethyl-2-oxazolin-2-yl)biphenyl (**7**)[6] (124 mg, 63%).

NMR Spectra. NMR spectra for known (**3a**,[7] **3b**,[7] **3c**,[8] **3d**,[7] **3e**,[9] **3f**,[7] **3h,**[10] **5**,[5] and **7**[6]) and new (**3g**) biaryls are given in pp S3-S13.

References

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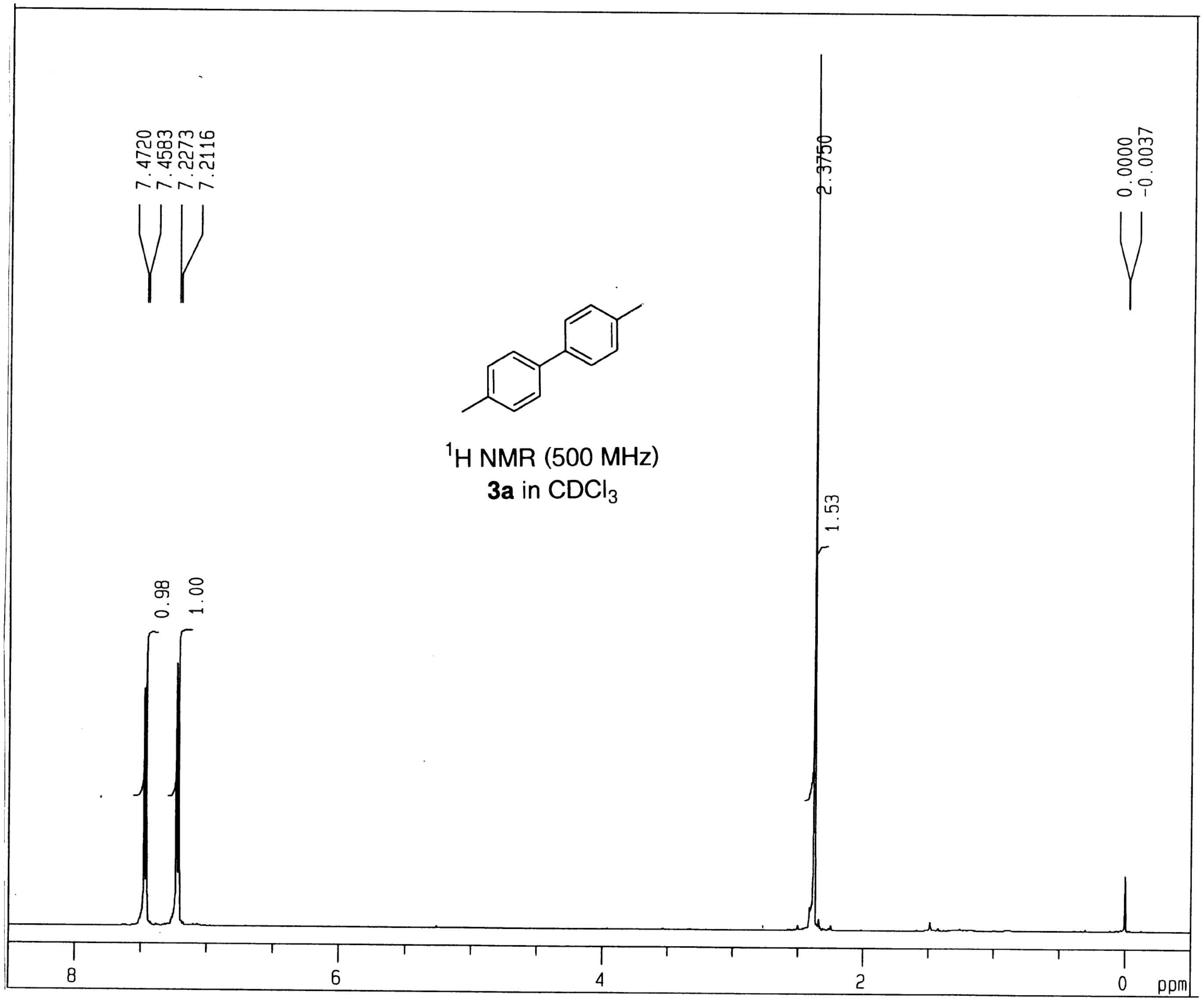
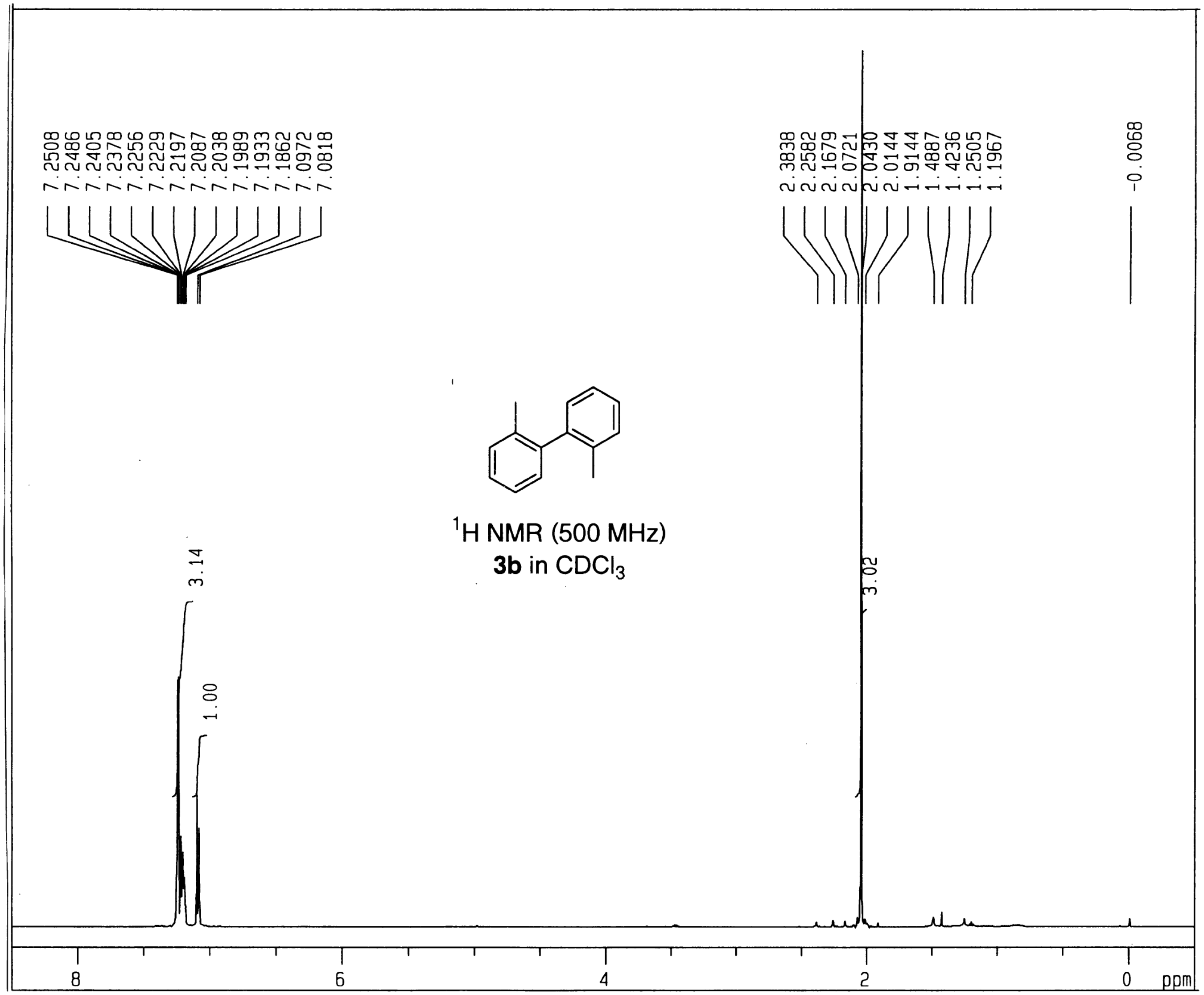


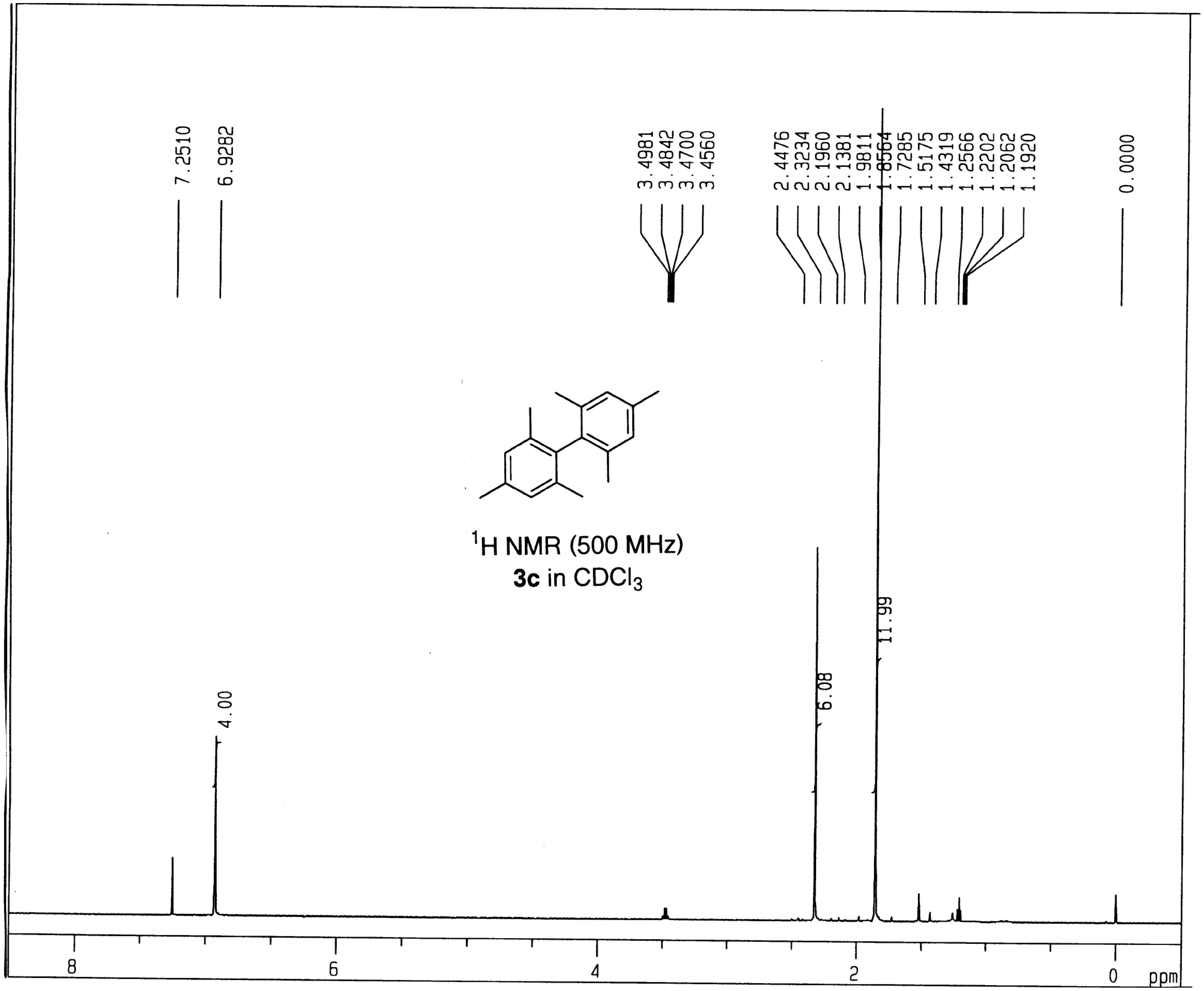
^{1}H NMR (500 MHz)

3a in $CDCl_3$

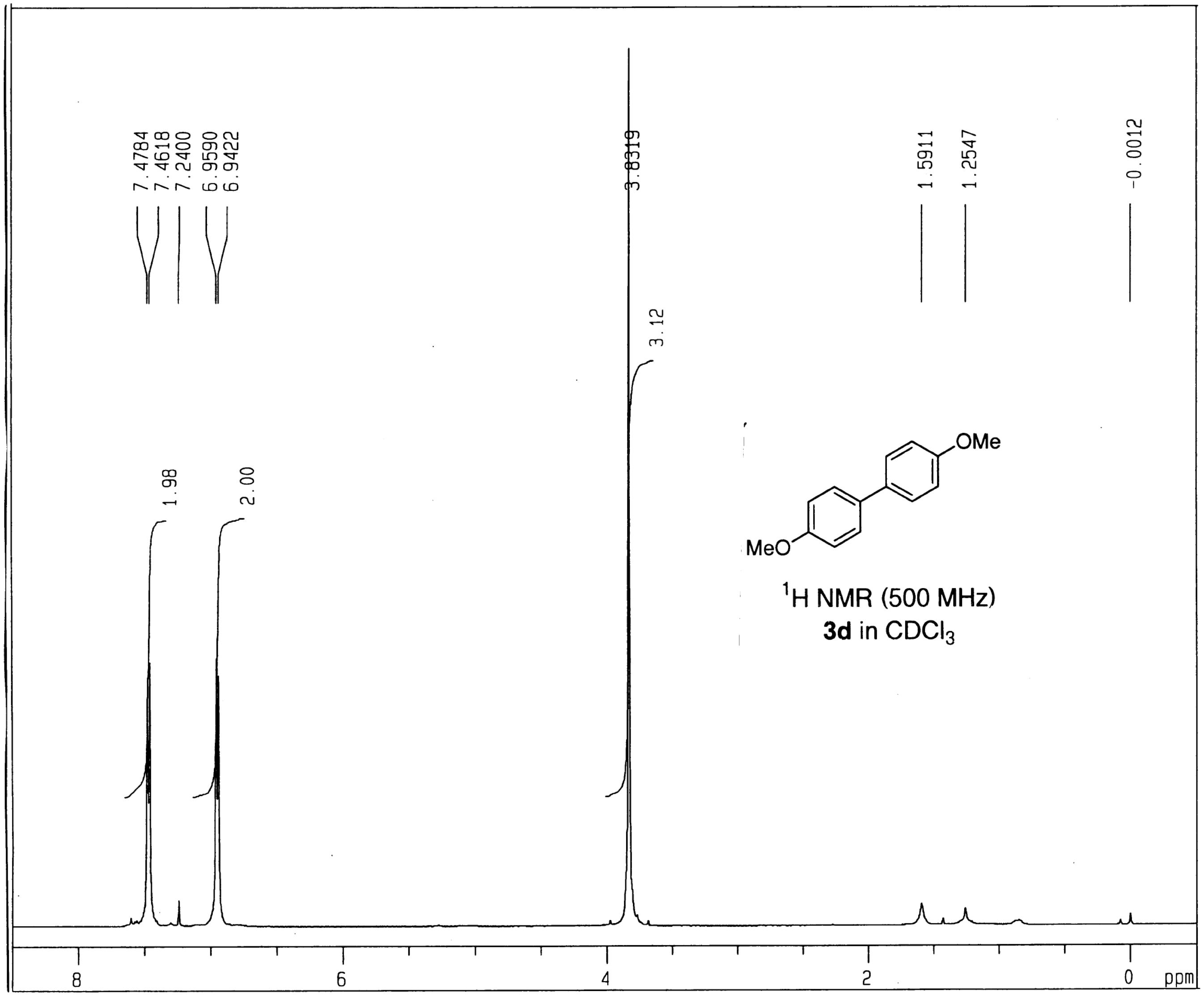


^{1}H NMR (500 MHz)

3b in $CDCl_3$



^{1}H NMR (500 MHz)
3c in $CDCl_3$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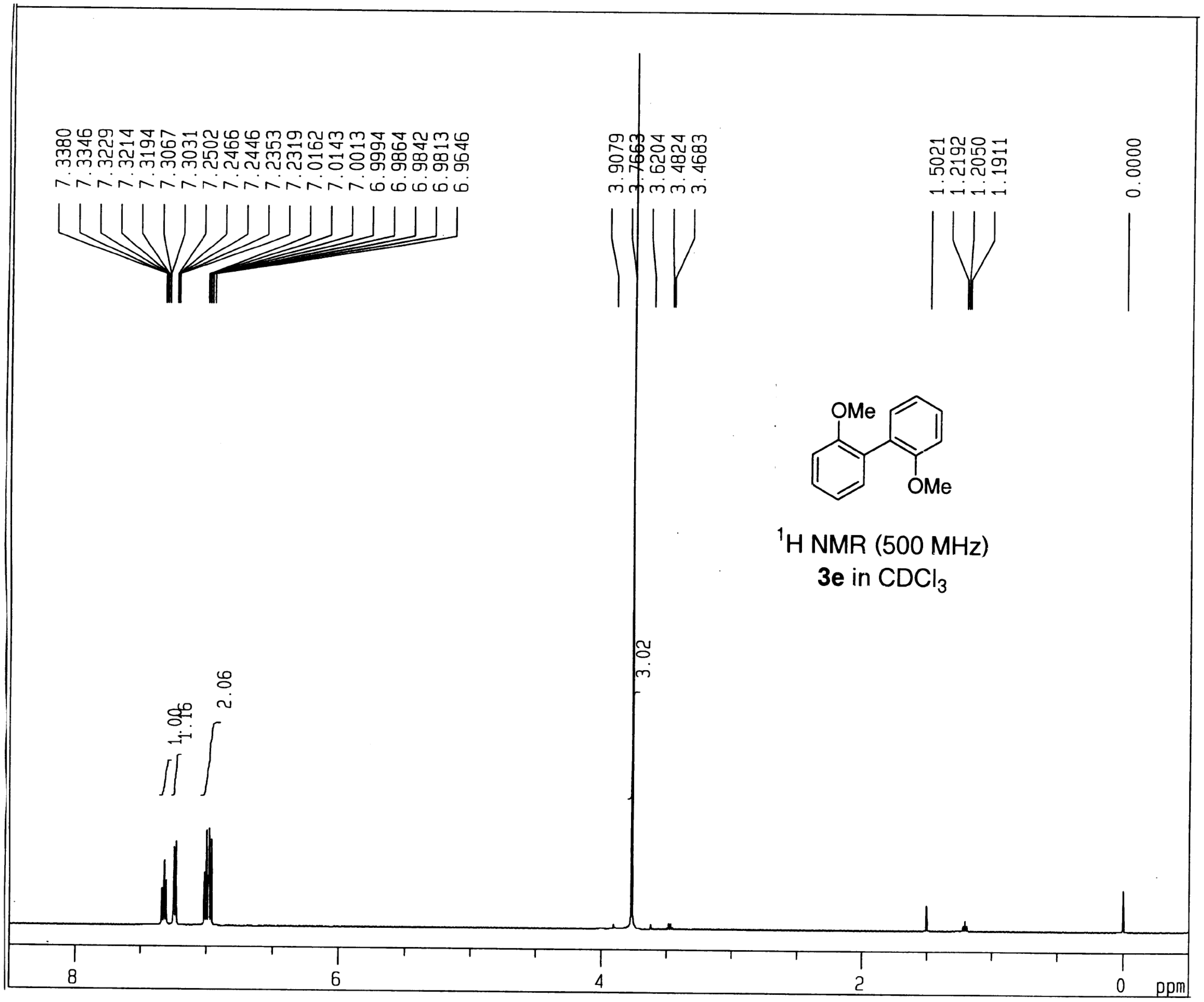
7.2400
6.9590
6.9422
3.8319
1.5911
1.2547
-0.0012
1.98
2.00
3.12
MeO
OMe
^{1}H NMR (500 MHz)
3d in $CDCl_3$
8
6
4
2
0
ppm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7.3214
7.3194
7.3067
7.3031
7.2502
7.2466
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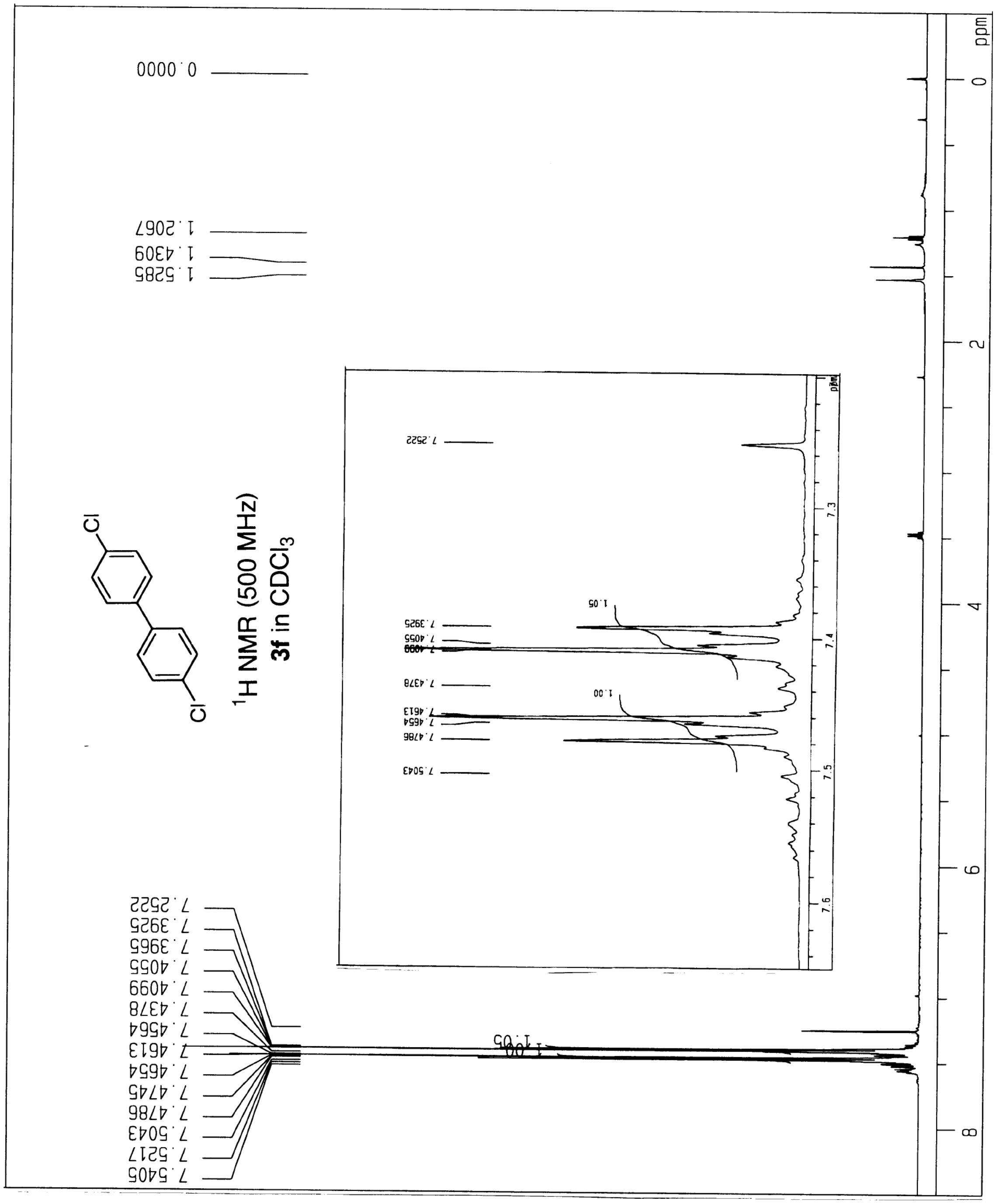
7.2353
7.2319
7.0162
7.0143
7.0013
6.9994
6.9864
6.9842
6.9813
6.9646
3.9079
3.7663
3.6204
3.4824
3.4683
1.5021
1.2192
1.2050
1.1911
0.0000
OMe
OMe
^{1}H NMR (500 MHz)
3e in $CDCl_3$
1.00
1.16
2.06
3.02
8
6
4
2
0
ppm


Cl
Cl
^{1}H NMR (500 MHz)
3f in CDCl$_3$
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1.5285
7.2522
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7.3965
7.4055
7.4099
7.4378
7.4564
7.4613
7.4654
7.4745
7.4786
7.5043
7.5217
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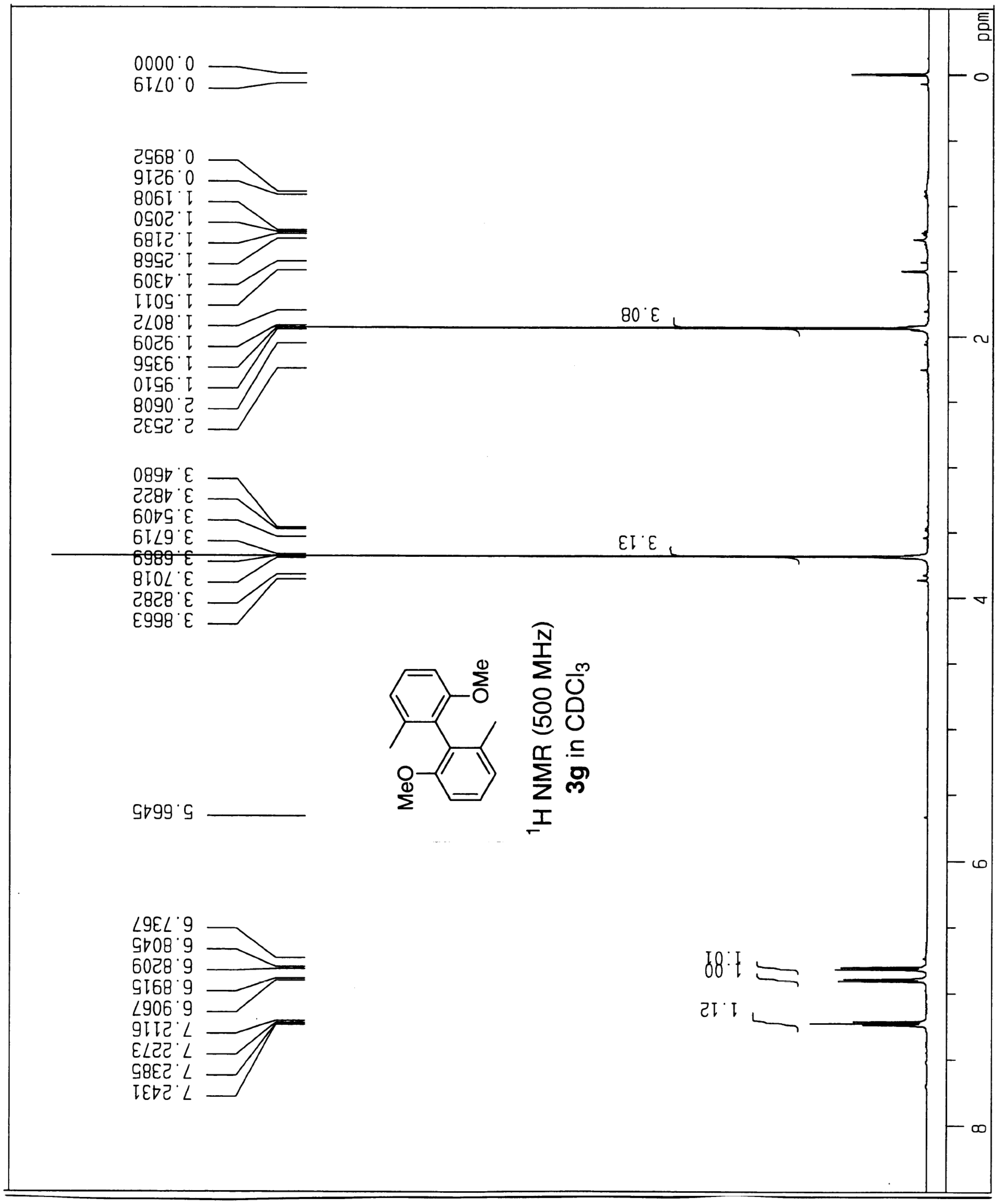
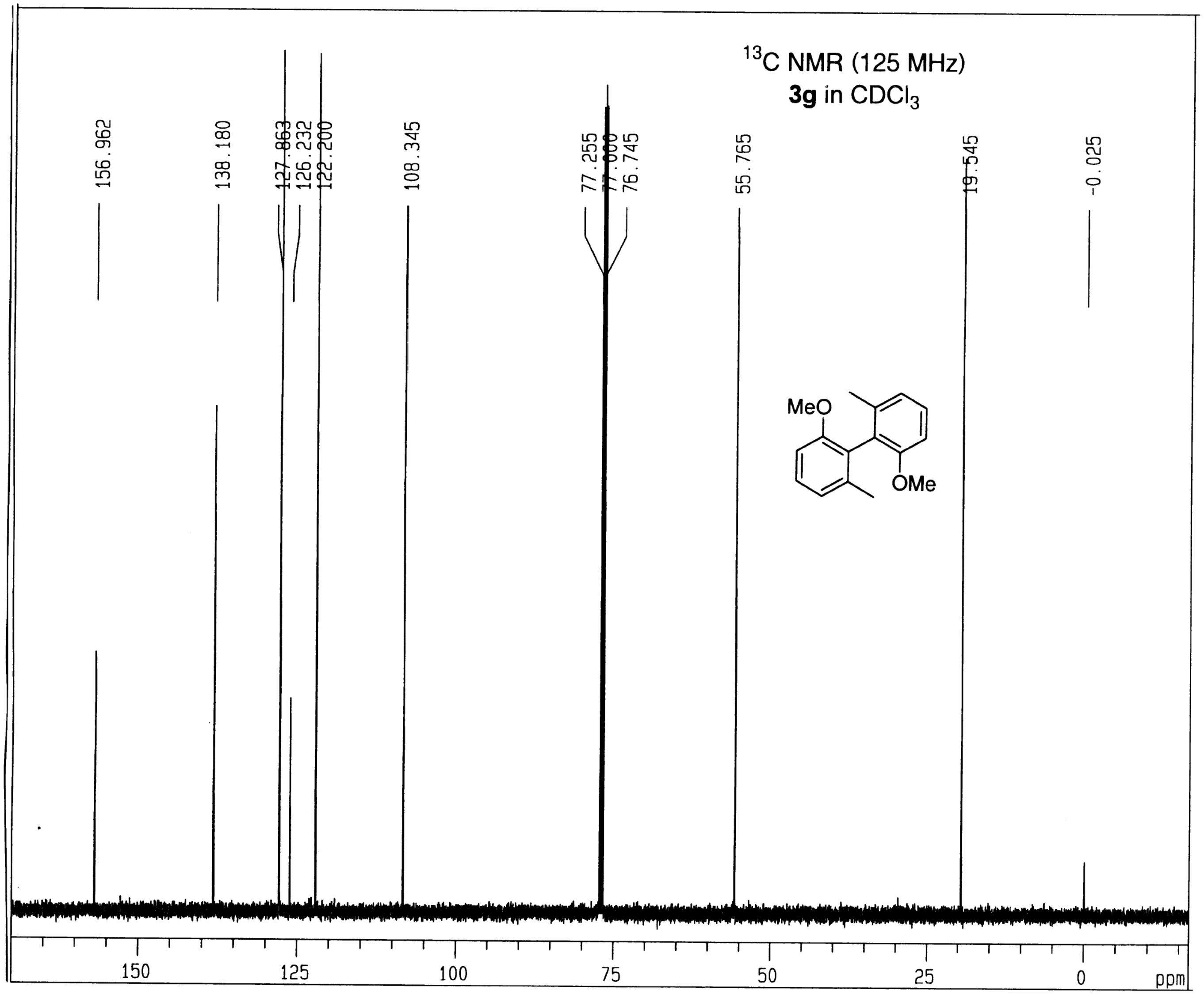
1.05
1.00
ppm
0
2
4
6
8
7.3
7.4
7.5
7.6

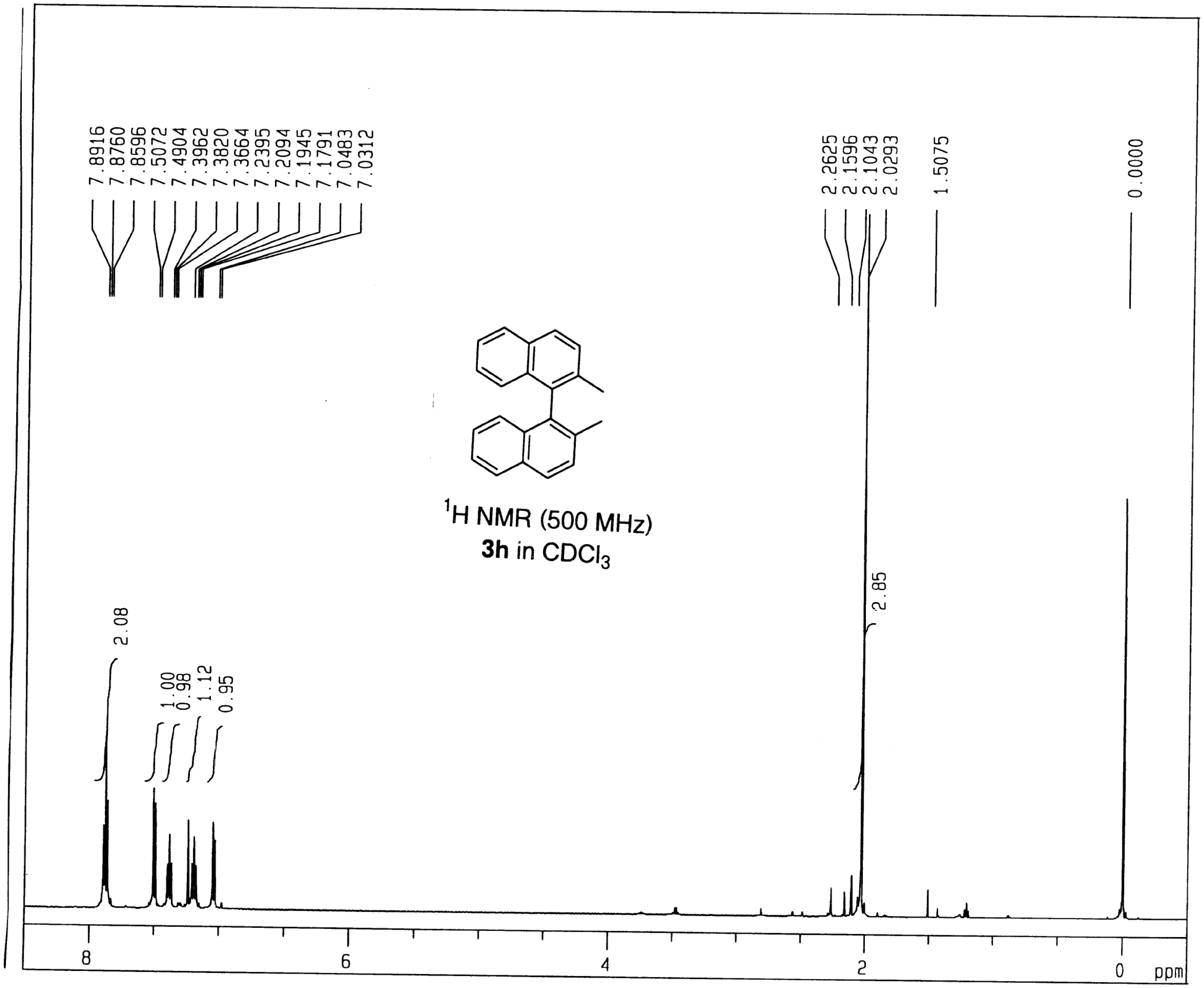


^{1}H NMR (500 MHz)

3g in $CDCl_3$

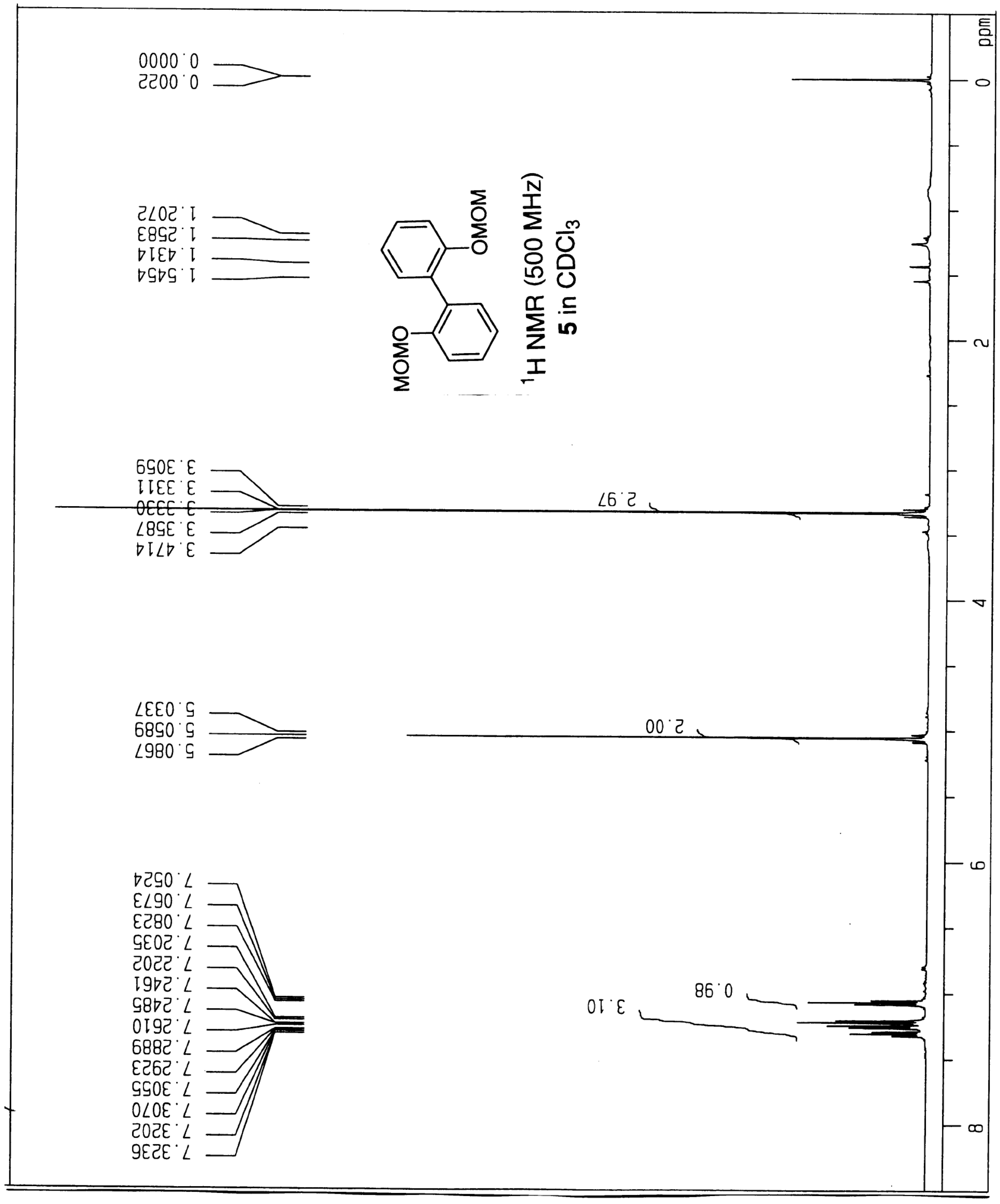


^{13}C NMR (125 MHz)
3g in $CDCl_3$



^{1}H NMR (500 MHz)

3h in $CDCl_3$


MOMO
OMOM
^{1}H NMR (500 MHz)
5 in CDCl$_3$
0.0000
0.0022
1.2072
1.2583
1.4314
1.5454
3.3059
3.3311
3.3330
3.3587
3.4714
5.0337
5.0589
5.0867
7.0524
7.0673
7.0823
7.2035
7.2202
7.2461
7.2485
7.2610
7.2889
7.2923
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7.3070
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2.97
2.00
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3.10
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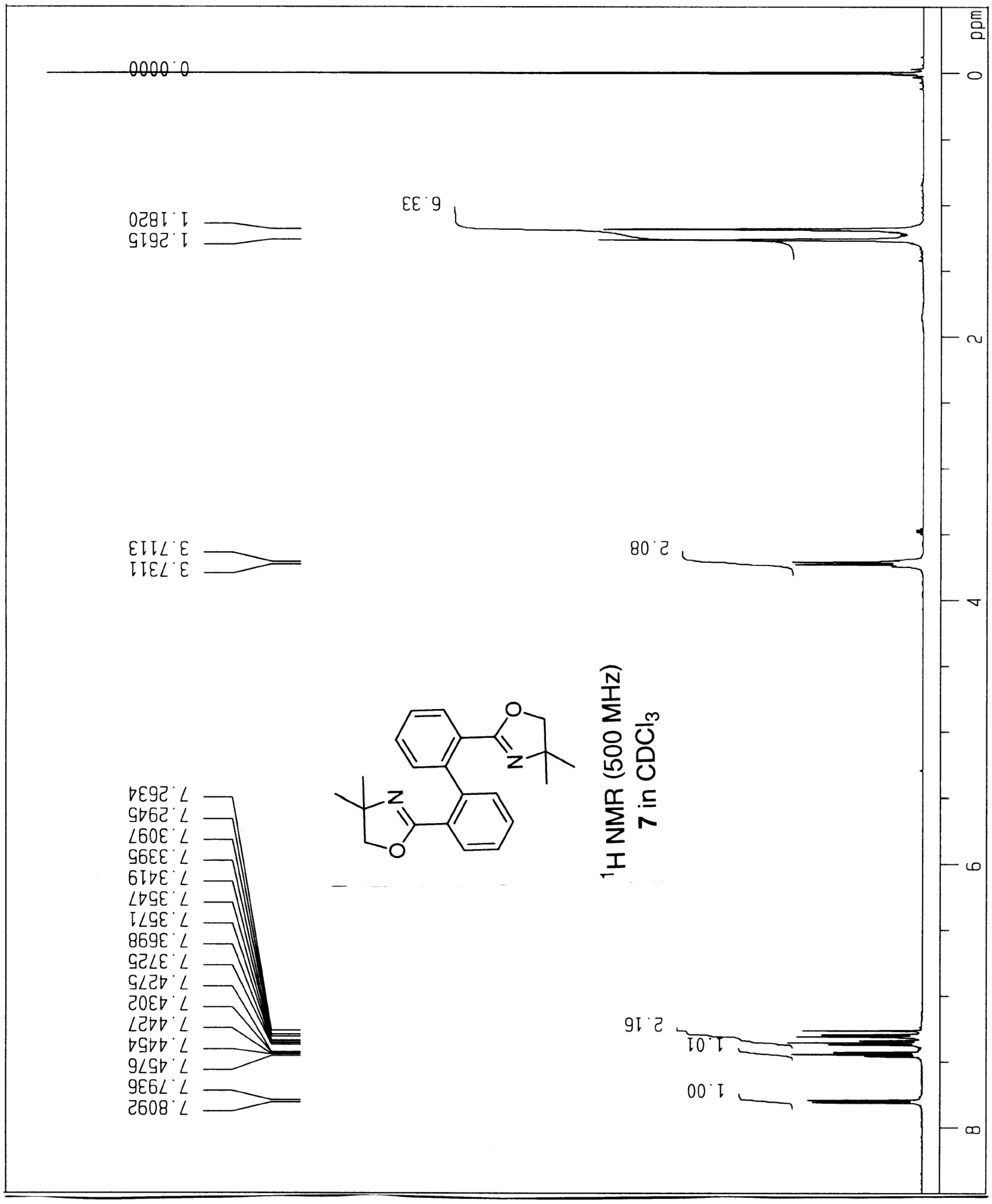
6
4
2
0
ppm



^{1}H NMR (500 MHz)

7 in $CDCl_3$