Supporting Information

A family of site selective molecular optical switches

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General experimental. ^{1}H NMR spectra were measured on a Brucker Ac 300 MHz; mass spectra were carried out on a Micromass AutoSpec for EI, a Micromass LCT for ESI, or a Bruker REFLEX II for MALDI. Absorption spectra were recorded on a Hewlett-Packard 82152 diode array spectrophotometer or a Shimadzu 1601PC instrument. The starting materials for the following syntheses are all commercially available.

8-(Chloromethyl)spirobenzopyran (2) A THF solution (10 ml) of 3-chloromethyl-5-nitrosalicylaldehyde (50 mg, 0.23 mmol) and 1,3,3-trimethyl-2-methyleneindoline (40 mg, 0.23 mmol) was refluxed for 4 h. Evaporation of the solvent gave **2** (90 mg) as a crude product, which was used for the subsequent reaction without further purification. MS(EI): 370(M^+, 45), 336(72), 159(73); HRMS(EI): M^+370.1096 (Calc. 370.1084); ^{1}H NMR ($CDCl_3$) δ 1.22 (s, 3H), 1.32 (s, 3H), 2.71, (s, 3H), 4.32 (d, *J* = 11.7 Hz, 1H), 4.38 (d, *J* = 11.7 Hz, 1H), 5.92 (d, *J* = 10.3 Hz, 1H), 6.55 (d, *J* = 7.3 Hz, 1H), 6.89 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.95 (d, *J* = 10.3 Hz, 1H), 7.09 (d, *J* = 7.3 Hz, 1H), 7.19 (dd, *J* = 7.3, 7.3 Hz, 1H), 8.00 (d, *J* = 2.8, 1H), 8.14 (d, *J* = 2.8 Hz, 1H).

8-(Iodomethyl)spirobenzopyran (3). An acetone solution (5 ml) of crude product **2** (56 mg, ca. 0.15mmol) and NaI (70 mg, 0.47 mmol) was stirred overnight. After evaporation, the residue was purified by column chromatography (silica gel; eluent, CH_2Cl_2) to afford **3** (55 mg, 78%; based on 1-3,3-trimethyl-2-methyleneindoline). MS(EI): 335($[M-I]^+$, 23), 159(13), 71(100); HRMS: $[M-I]^+$335.1385 (calc. 335.1396); ^{1}H NMR ($CDCl_3$) δ 1.24 (s, 3H), 1.38 (s, 3H), 2.77, (s, 3H), 4.13 (d, *J* = 9.3 Hz, 1H), 4.22 (d, *J* = 9.3 Hz, 1H), 5.94 (d, *J* = 10.4 Hz, 1H), 6.59 (d, *J* = 7.5 Hz, 1H), 6.91 (dd, *J* = 7.5, 7.5

Hz, 1H), 6.95 (d, *J* = 10.4 Hz, 1H), 7.12 (dd, *J* = 1.0, 7.5 Hz, 1H), 7.21 (ddd, *J* = 1.0, 7.5, 7.5 Hz, 1H), 7.95 (d, *J* = 2.8, 1H), 8.08 (d, *J* = 2.8 Hz, 1H).

1'-(Hydroxyethyl)spirobenzopyran (5). A solution of 2,3,3-trimethyl-3*H*-indole (1 ml, 6.3 mmol) and 2-iodoethanol (0.56 ml, 8.8 mmol) in MeCN (4 mL) was refluxed for 1 day. After being cooled to r.t., the reaction mixture was suspended in hexane, and the precipitated solid was sonicated and filtered. A part of the obtained purple solid (53 mg out of 1.37 g) was dissolved in 1N KOH (2 mL) and stirred at r.t. for 30 min. After extraction with ether, the organic layer was evaporated to afford **4** as a yellow oil. A solution of 5-nitrososalicylaldehyde (38 mg, 0.23 mmol) and the obtained crude **4** in EtOH (5 mL) was refluxed for 4 h. The mixture was evaporated and purified by column chromatography (silica gel; eluent, hexane:AcOEt=1:1) to afford purple crystal **5** (56 mg, 66 % based on 2,3,3-trimethyl-3*H*-indole). MS(EI): 352(M^+, 15), 337(5), 321(9), 83(100); HRMS(EI): M^+352.1411 (calc.352.1423); ^{1}H NMR ($CDCl_3$) δ 1.20 (s, 3H), 1.30 (s, 3H), 3.34 (ddd, *J* = 5.1, 5.1, 14.7 Hz, 1H), 3.47 (ddd, *J* = 5.5, 7.3, 14.7 Hz, 1H), 3.69-3.82 (m, 2H), 5.89 (d, *J* = 10.5 Hz, 1H), 6.67 (d, *J* = 7.5 Hz, 1H), 6.77 (d, *J* = 8.5 Hz, 1H), 6.90 (dd, *J* = 7.5, 7.5 Hz, 1H), 6.91 (d, *J* = 10.5 Hz, 1H), 7.10 (dd, *J* = 1.1, 7.5 Hz, 1H), 7.50 (ddd, *J* = 1.1, 7.5, 7.5 Hz, 1H), 8.00 (d, *J* = 2.5, 1H), 8.03 (dd, *J* = 2.5, 8.5 Hz, 1H).

1'-(Maleimidoethyl)spirobenzopyran (6). To a dry THF (1 ml) solution of PPh_3 (25 mg, 95 μmol) was added DIAD (18 ul, 95 μmol) over 2 min at -78°C, and the reaction mixture was stirred for 5 min. To this solution, **5** (32 mg, 91 μmol) in dry THF (0.3 ml) was added over 2 min, and the mixture was stirred for 5 m. Neopentyl alcohol (4 mg, 4

μmol) and maleimide (9 mg, 9 μmol) were added sequentially to the reaction mixture as solids. After stirred for 5 min, the reaction mixture was allowed to warm up to r.t. and stirred for additional 1hour. The reaction mixture was concentrated and then applied to preparative TLC twice (silica gel; hexane:EtOAc = 2:1, then CH_2Cl_2) to afford **6** (6 mg, 15 %). MS(MALDI): 432 $[M+H]^+$; HRMS(ESI): $[M+Na+MeOH]^+$ 486.1657 (calc.486.1641); ^{1}H NMR ($CDCl_3$) δ 1.18 (s, 3H), 1.31 (s, 3H), 3.43 (t, *J* = 6.7 Hz, 1H), 3.77 (t, *J* = 6.7 Hz, 1H), 5.98 (d, *J* = 10.4 Hz, 1H), 6.68 (dd, *J* = 1.0, 7.5 Hz, 1H), 6.72 (s, 2H), 6.79 (d, *J* = 10.1 Hz, 1H), 6.92 (ddd, *J* = 1.0, 7.5, 7.5 Hz, 1H), 6.97 (d, *J* = 10.4 Hz, 1H), 7.12 (dd, *J* = 1.3, 7.5 Hz, 1H), 7.23 (ddd, *J* = 1.3, 7.5, 7.5 Hz, 1H), 8.05 (d, *J* = 2.5, 1H), 8.06 (dd, *J* = 2.5, 10.1 Hz, 1H).

4-(Hydroxymethyl)-2,3,3-trimethyl-3*H*-indole (14) and 6-(hydroxymethyl)-2,3,3-trimethyl-3*H*-indole (15). To 3-aminobenzylalcohol (2.0 g, 16 mmol) in conc. HCl (6.4 mL) was added an aqueous solution (5.6 mL) of $NaNO_2$ (1.1 g, 16 mmol) at 0°C. After 30 min, $SnCl_2{\cdot}2H_2O$ (10 g, 44 mmol) in conc. HC1 (11 mL) was added to the reaction mixture. The reaction mixture was stirred for an additional 30 min, then washed with ether, neutralized with NaOH, and extracted with ether. The ether extract was evaporated to afford 3-hydrazinobenzyl alcohol, which was used for the next reaction without further purification. The obtained 3-hydrazinobenzyl alcohol was dissolved in EtOH (10 mL) and refluxed with 3-methyl-2-butanone (1.7 ml, 16 mmol) and concentrated H_2SO_4 (1 ml) for 17 h. After concentration, the reaction mixture was washed with CH_2Cl_2, basified with Sat. Na_2CO_3, and extracted with CH_2Cl_2. The CH_2Cl_2 extract was subjected to column chromatography (silica gel; eluent, EtOAc) and preparative TLC (silica gel;

EtOAc) to give **14** (86 mg, 3% based on 3-aminobenzyl alcohol) and the isomer **15** (131 mg, 4%). **14**: MS(EI): 189 (M^+,88), 174 (48), 156 (36), 83 (100); HRMS(EI): M^+189.1161 (calc.189.1154); ^{1}H NMR (CDC13) δ 1.43(s, 6H), 2.29(s, 3H), 4.88(2H, s), 7.26 (d, *J* = 7.5 Hz, 1H), 7.35 (dd, *J* = 7.5 Hz, 1H), 7.50 (d, *J*=7.5 Hz, 1H). **15**: MS(EI): 189(M^+,100), 174 (56), 158(19), 144(18); HRMS(EI): M^+189.1155 (calc.189.1154); ^{1}H NMR ($CDC1_3$) δ 1.29(s, 6H), 2.27(s, 3H), 4.73(s, 2H), 7.22 (d, *J* = 7.6 Hz, 1H), 7.25 (d, *J* = 7.6 Hz, 1H), 7.54 (s, 1H).

4'-(Hydroxymethyl)spirobenzopyran (8). A solution of **14** (51 mg, 0.27 mmol) and CH_3I (0.15 ml**,** 2.4 mmol) in CH_2Cl_2 (1 mL) was refluxed for overnight. The reaction mixture was filtered, and the filtrate was dissolved in 0.5 N KOH (1 ml) and stirred for 15 min. After extraction with CH_2Cl_2, the extract was evaporated to afford oil **7** as a crude product. With 5-nitrosalicylaldehyde (45 mg, 0.27 mmol), **7** was stirred in EtOH (2 mL) at r.t. over night. The reaction mixture was evaporated and subjected to column chromatography (silica gel; eluent, EtOAc) to afford **8** (34 mg, 36 % based on **14**). MS(EI): 352 (M^+, 22), 337 (4), 189 (10), 83 (100); HRMS(EI): M^+352.1408 (calc.352.1423); ^{1}H NMR (CDC13) 1.25 (s, 3H), 1.28 (s, 3H), 2.74 (s, 3H), 4.74 (d, *J* = 12.5 Hz, 1H), 4.82 (d, *J* = 12.5 Hz, 1H), 5.85 (d, *J* = 10.4 Hz, 1H), 6.55 (d, *J* = 7.7 Hz, 1H), 6.77 (d, *J* = 9.0 Hz, 1H), 6.93 (d, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 10.4 Hz, 1H), 7.23 (dd, *J* = 7.7, 7.7 Hz, 1H), 8.01 (d, *J* = 2.8, 1H), 8.02 (dd, *J* = 2.8, 9.0 Hz, 1H).

4'-(Bromomethyl)spirobenzopyran (9). To a THF solution (1 mL) of **8** (34 mg, 97 μmol) and CBr_4, (70 mg, 211 μmol) was dropped Ph_3P (50 mg, 191 μmol) at 0^o. The

reaction mixture was stirred at 0°C for 30 min and at r.t. overnight. After evaporation of the reaction mixture, the residue was subjected to column chromatography (silica gel; eluent, hexane:EtOAc = 5:1) to afford **9** (24 mg, 60%). MS(EI): 416 (76), 414 (M^+, 74), 335 (41), 85 (100), 83 (99); HRMS(EI): M^+414.0580 (calc.414.0579); ^{1}H NMR ($CDC1_3$) 1.25 (s, 3H), 1.32 (s, 3H), 2.73 (s, 3H), 4.51 (d, *J* = 10.3 Hz, 1H), 4.65 (d, *J* = 10.3 Hz, 1H), 5.84 (d, *J* = 10.1 Hz, 1H), 6.51 (d, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.97 (d, *J* = 10.1 Hz, 1H), 7.20 (dd, *J* = 7.8, 7.8 Hz, 1H), 8.01 (s, 1H), 8.03 (dd, *J* = 2.8, 8.5 Hz, 1H).

6'-(Hydroxymethyl)spirobenzopyran (11). A solution of **15** (50 mg, 0.27 mmol) and CH_3I (100 ul**,** 1.6 mmol) in CH_2Cl_2 (2 mL) was refluxed for 12 h. The reaction mixture was filtered, and the filtrate was dissolved in 0.5 N NaOH and stirred for 15 min. After extraction with CH_2Cl_2, the extract was evaporated to afford oil **10** as a crude product. With 5-nitrosalicylaldehyde (50 mg, 0.30 mmol), **10** was refluxed in EtOH (2 mL) for 2 h, and then the reaction mixture was evaporated and subjected to column chromatography (silica gel; eluent, EtOAc) to afford **11** (70 mg, 75 % based on **15**). MS(EI): 352 (M^+, 10), 337 (4), 83 (100); HRMS(EI): M^+352.1434 (calc.352.1423); ^{1}H NMR (CDC13) 1.19 (s, 3H), 1.30 (s, 3H), 2.76 (s, 3H), 4.70 (s, 2H), 5.87 (d, *J* = 10.5 Hz, 1H), 6.62 (s, 1H), 6.77 (d, *J* = 8.7 Hz, 1H), 6.94 (d, *J* = 10.5 Hz, 1H), 7.07 (d, *J* = 7.2 Hz, 1H), 8.01 (d, *J* = 2.4, 1H), 8.02 (dd, *J* = 2.4, 8.7 Hz, 1H).

6'-(Maleimidomethyl)spirobenzopyran (12). To a dry THF (1 ml) solution of PPh_3 (25 mg, 95 μmol), was added DIAD (18 ul, 95 μmol) over 2 min at -78°C, and the

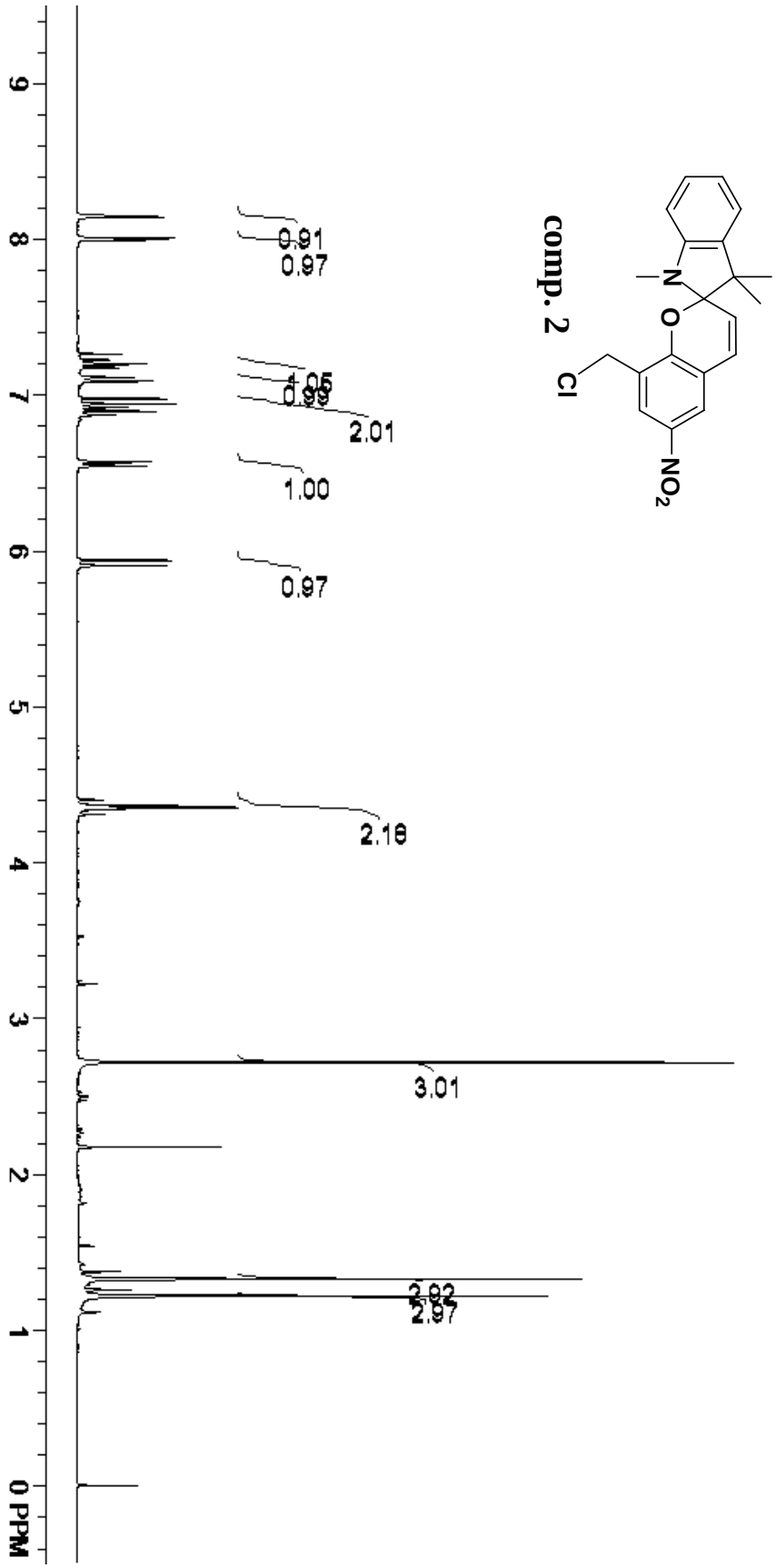
reaction mixture was stirred for 5 min. To this solution **11** (34 mg, 97 μmol) in dry THF (0.3 ml) was added over 2 min, and the mixture was stirred for 5 min. Neopentyl alcohol (4 mg, 4 μmol) and maleimide (9 mg, 9 μmol) were added sequentially to the reaction mixture as solids. After stirred for 5 min, the reaction mixture was allowed to warm up to r.t. and stirred for additional 1h. The reaction mixture was concentrated and then applied to preparative TLC (silica gel; hexane:EtOAc = 1:1) to afford **12** (10 mg, 24 %). MS(EI): 431(M^+, 10), 416 (3), 268 (8), 83 (100); HRMS(EI) M^+431.1497 (calc.431.1481); ^{1}H NMR ($CDCl_3$) δ 1.61 (s, 3H), 1.27 (s, 3H), 2.74 (s, 3H), 5.84 (d, *J* = 10.2 Hz, 1H), 6.54 (s, 1H), 6.73 (s, 2H), 6.78 (d, *J* = 8.6 Hz, 1H), 6.88 (d, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 10.2 Hz, 1H), 7.02 (d, *J* = 7.6 Hz, 1H), 8.01 (d, *J* = 2.4, 1H), 8.03 (dd, *J* = 2.4, 8.6 Hz, 1H).

6'-(Bromomethyl)spirobenzopyran (13). To a THF solution (1.5 mL) of **11** (28 mg, 78 μmol) and CBr_4, (53 mg, 160 μmol) was dropped a THF solution (0.5 mL) of Ph_3P (42 mg, 160 μmol) at 0 C. The reaction mixture was stirred at 0°C for 30 min and at r.t. overnight. after evaporation of the reaction mixture, the residue was subjected to column chromatography (silica gel; eluent, hexane:EtOAc = 5:1) to afford **13** (18mg, 55%) with recovered **11** (10 mg, 36%). MS(EI): 416 (1), 414(M^+, 1), 335 (2); HRMS(EI): M^+414.0577 (calc.414.0579); ^{1}H NMR ($CDC1_3$) 1.19 (s, 3H), 1.29 (s, 3H), 2.76 (s, 3H), 4.52 (d, *J* = 10.5 Hz, 1H), 4.56 (d, *J* = 10.5 Hz, 1H), 5.86 (d, *J* = 10.2 Hz, 1H), 6.58 (d, *J* = 1.3 Hz, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.92 (dd, *J* = 1.3, 7.3 Hz, 1H), 6.94 (d, *J* = 10.3 Hz, 1H), 7.04 (d, *J* = 7.3 Hz, 1H), 8.01 (d, *J* = 3.2, 1H), 8.04 (dd, *J* = 3.2, 8.4 Hz, 1H).

6'-(Hydroxymethyl)spironaphthoxazine (16). A solution of **15** (62 mg, 0.33 mmol) and CH_3I (150 µl**,** 2.4 mmol) in CH_2Cl_2 (1 mL) was refluxed for 12 h. The reaction mixture was filtered, and the filtrate was dissolved in 0.5 N NaOH and stirred for 15 min. After extraction with CH_2Cl_2, the extract was evaporated to afford oil **10** (43 mg) as a crude product. With 1-nitroso-2-naphthol (39 mg, 0.23 mmol), **10** was refluxed in EtOH (10 mL) for 3 h, and then the reaction mixture was evaporated and subjected to column chromatography (silica gel; hexane:EtOAc 3:1) and preparative TLC (silica gel; hexane:EtOAc 2:1) to afford **16** (43 mg, 53 % based on **15**). MS(EI): 358(M^+, 20), 343(15), 189(20), 83 (100); HRMS(EI): M^+358.1670 (calc.358.1681); ^{1}H NMR (CDC13) 1.35 (s, 3H), 1.36 (s, 3H), 2.78 (s, 3H), 4.70 (m, 2H), 6.63 (s, 1H), 6.88 (d, *J* = 7.3 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 7.07 (d, *J* = 7.3 Hz, 1H), 7.40 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.58 (dd, *J* = 7.9, 7 .9 Hz, 1H), 7.67 (d, *J* = 8.9 Hz, 1H), 7.75 (s, 1H), 7.75 (d, *J* = 7.9 Hz, 1H), 8.56 (d, *J* = 7.9 Hz, 1H)

6'-(Bromomethyl)spironaphthoxazine (17). To a THF solution (1 mL) of **16** (16 mg, 45 µmol) and CBr_4, (30 mg, 91 µmol) was dropped a THF solution (0.5 mL) of Ph_3P (23 mg, 88 µmol) at 0 C. The reaction mixture was stirred at 0°C for 30 min and at r.t. overnight. after evaporation of the reaction mixture, the residue was subjected to preparative TLC (silica gel; hexane:EtOAc = 2:1) to afford **17** (3 mg, 15%) with recovered **16** (11 mg, 69%). MS(EI): 422 (6), 420 (M^+, 6), 407(4), 405(4), 199(40), 83(100); HRMS(EI): M^+420.0839 (calc. 420.0837); ^{1}H NMR ($CDC1_3$) 1.33 (s, 3H), 1.35 (s, 3H), 2.77 (s, 3H), 4.51 (d, *J* = 10.2 Hz, 1H), 4.55 (d, *J* = 10.2 Hz, 1H), 6.59 (d, *J* = 1.6 Hz, 1H), 6.92 (dd, *J* = 1.5, 7.4 Hz, 1H), 7.00 (d, *J* = 9.2 Hz, 1H), 7.03 (d, *J* = 7.9 Hz, 1H),

7.40 (ddd, *J* = 1.1, 7.0, 8.2 Hz, 1H), 7.58 (ddd, *J* = 1.5, 7.0, 8.2 Hz, 1H), 7.67 (d, *J* = 9.2 Hz, 1H), 7.73 (s, 1H), 7.75 (d, *J* = 8.2 Hz, 1H), 8.55 (d, *J* = 8.2 Hz, 1H)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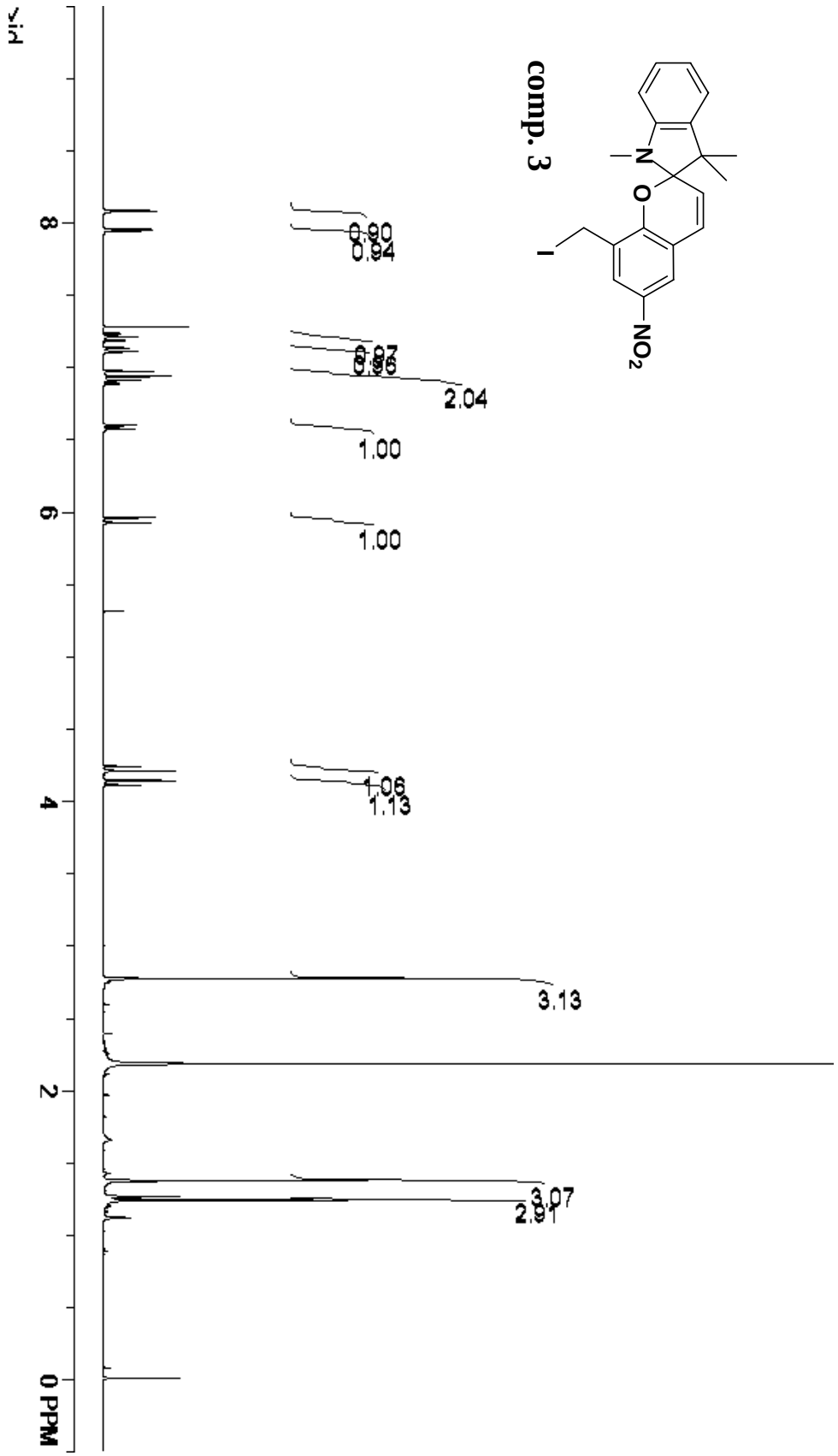
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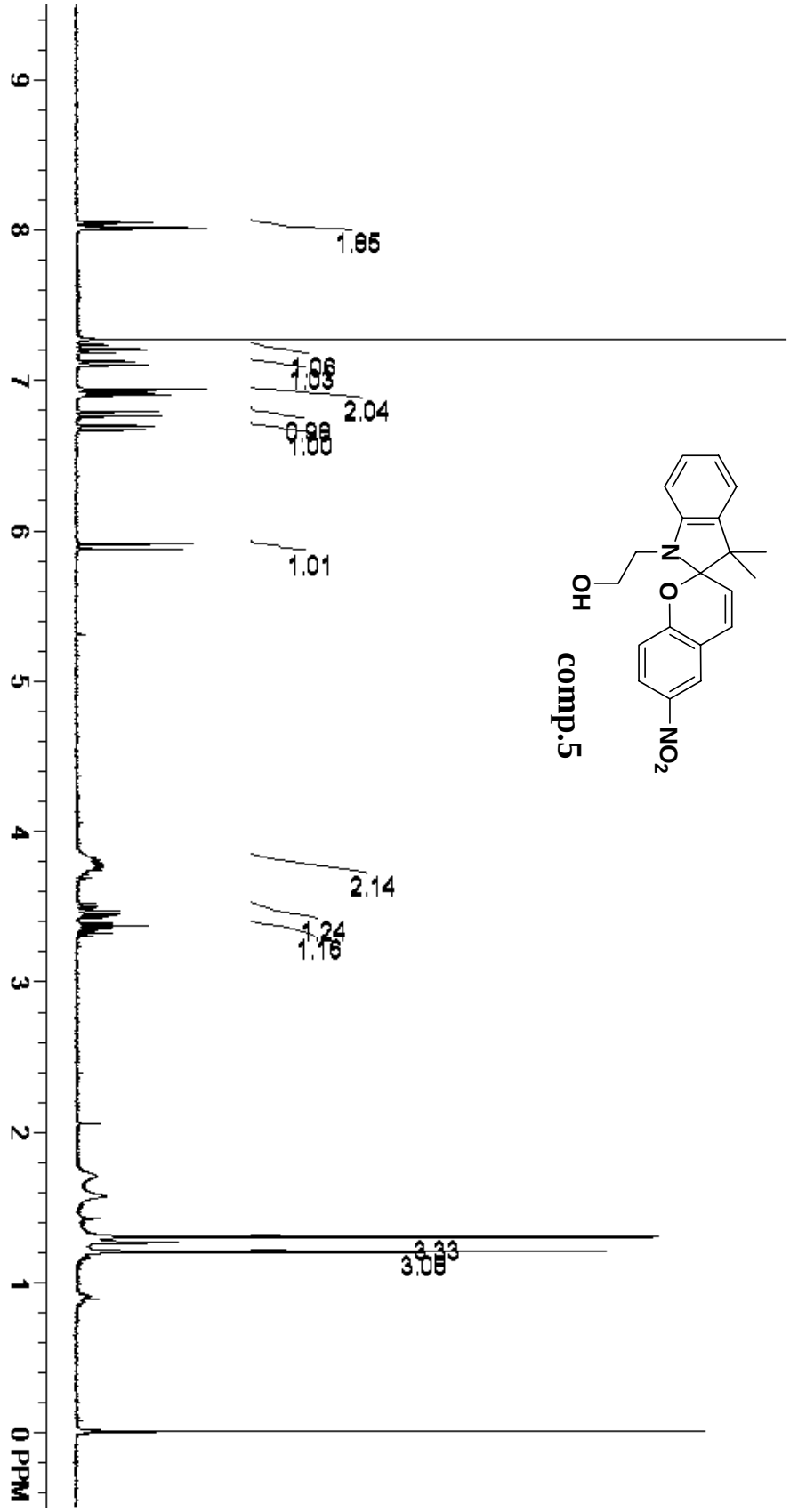
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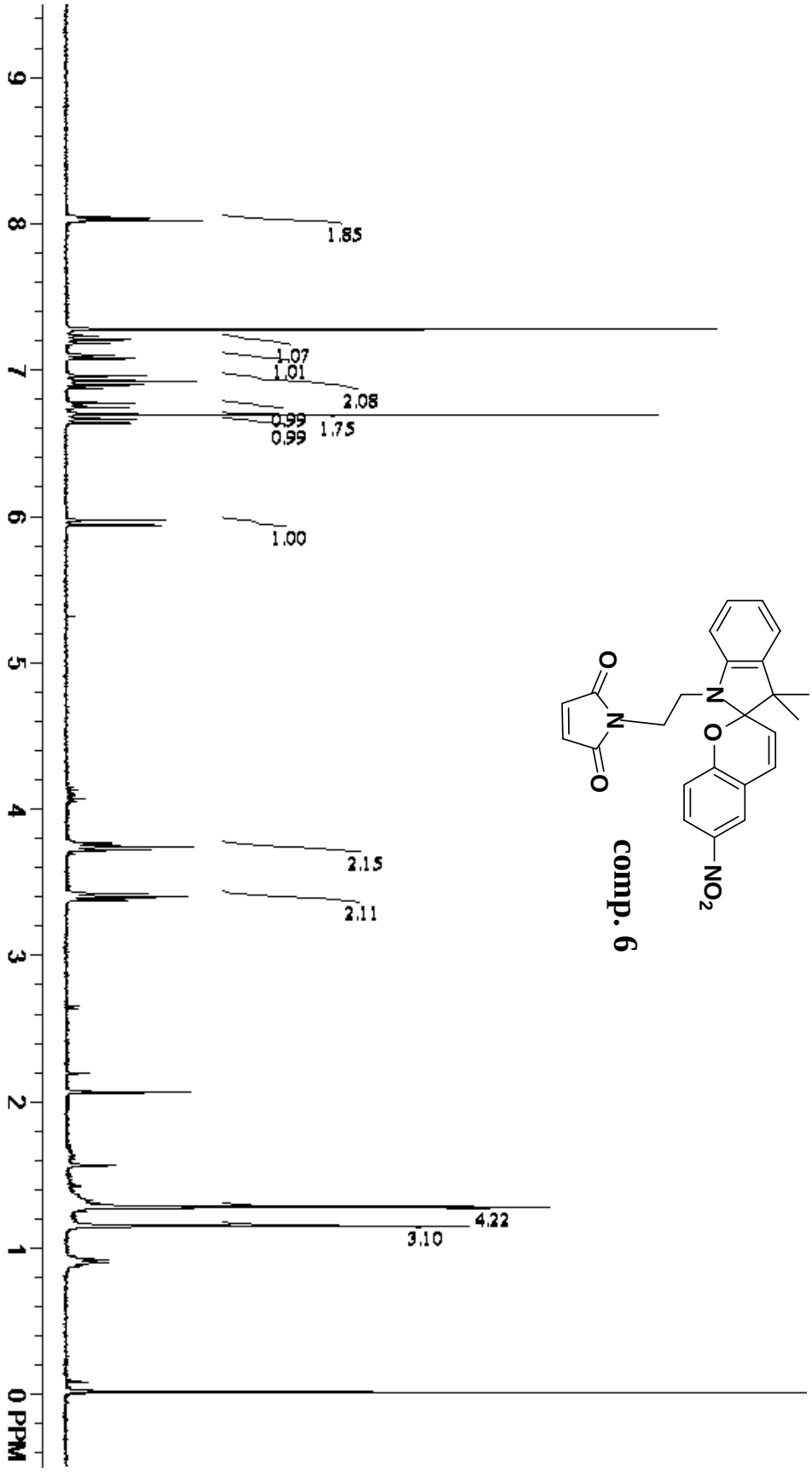
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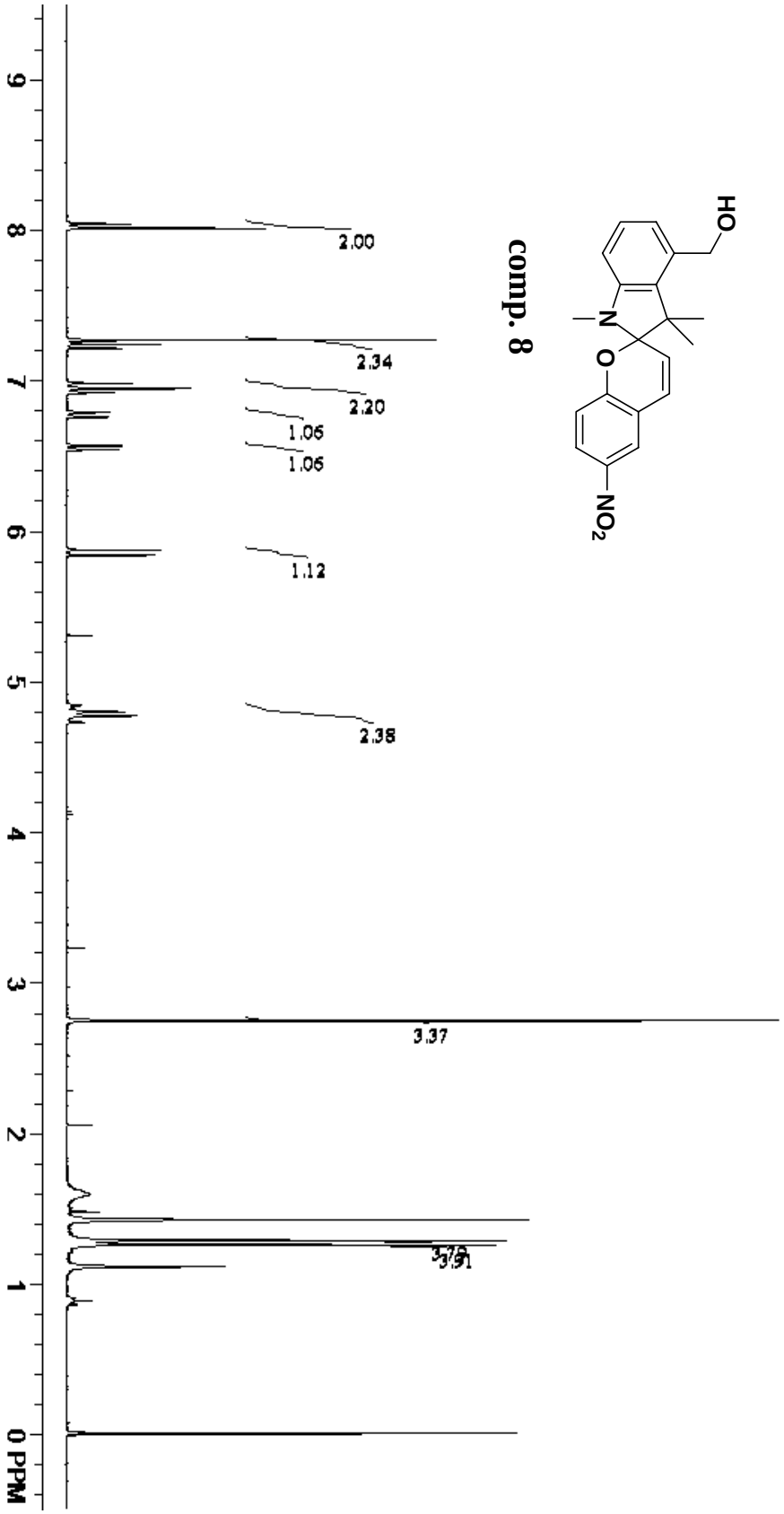
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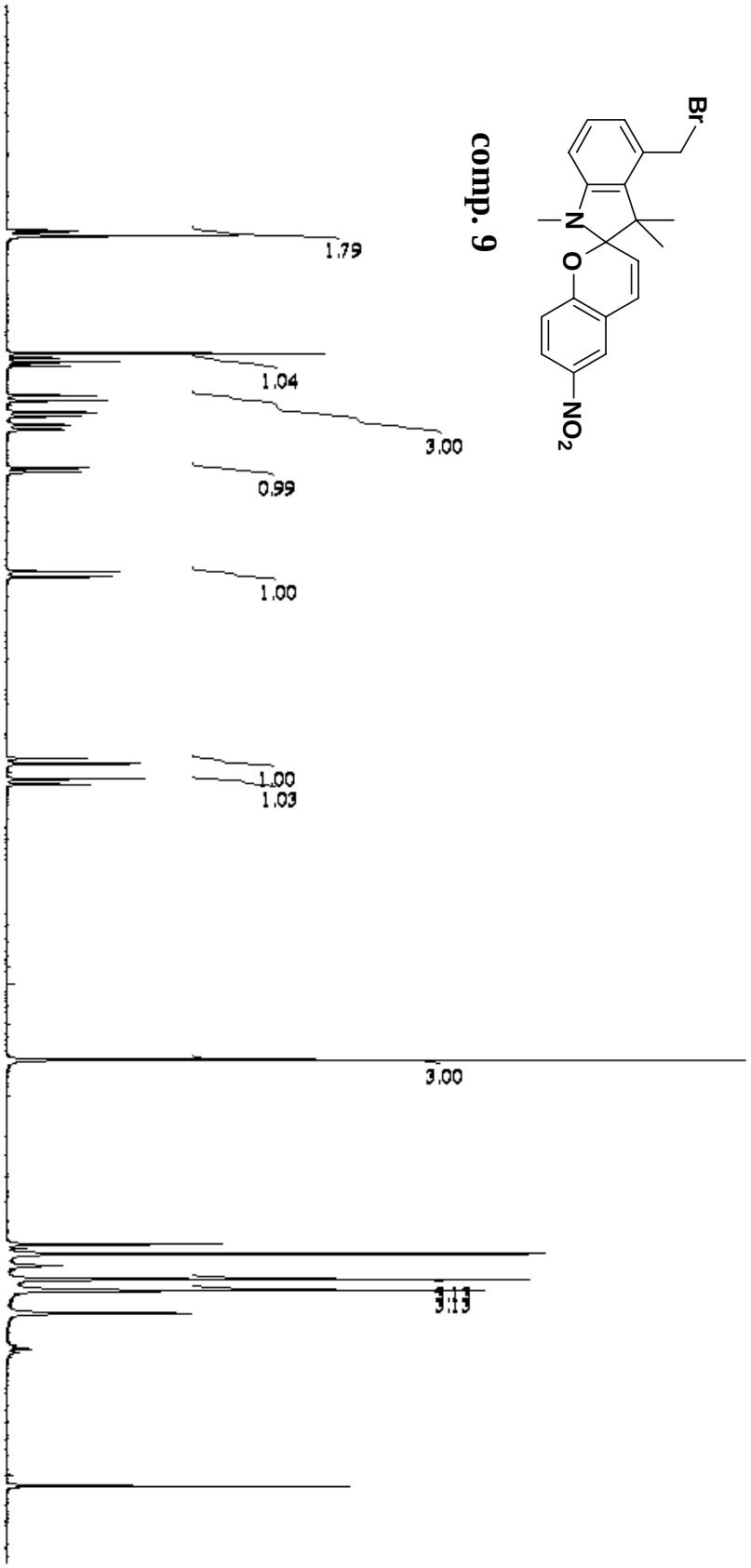
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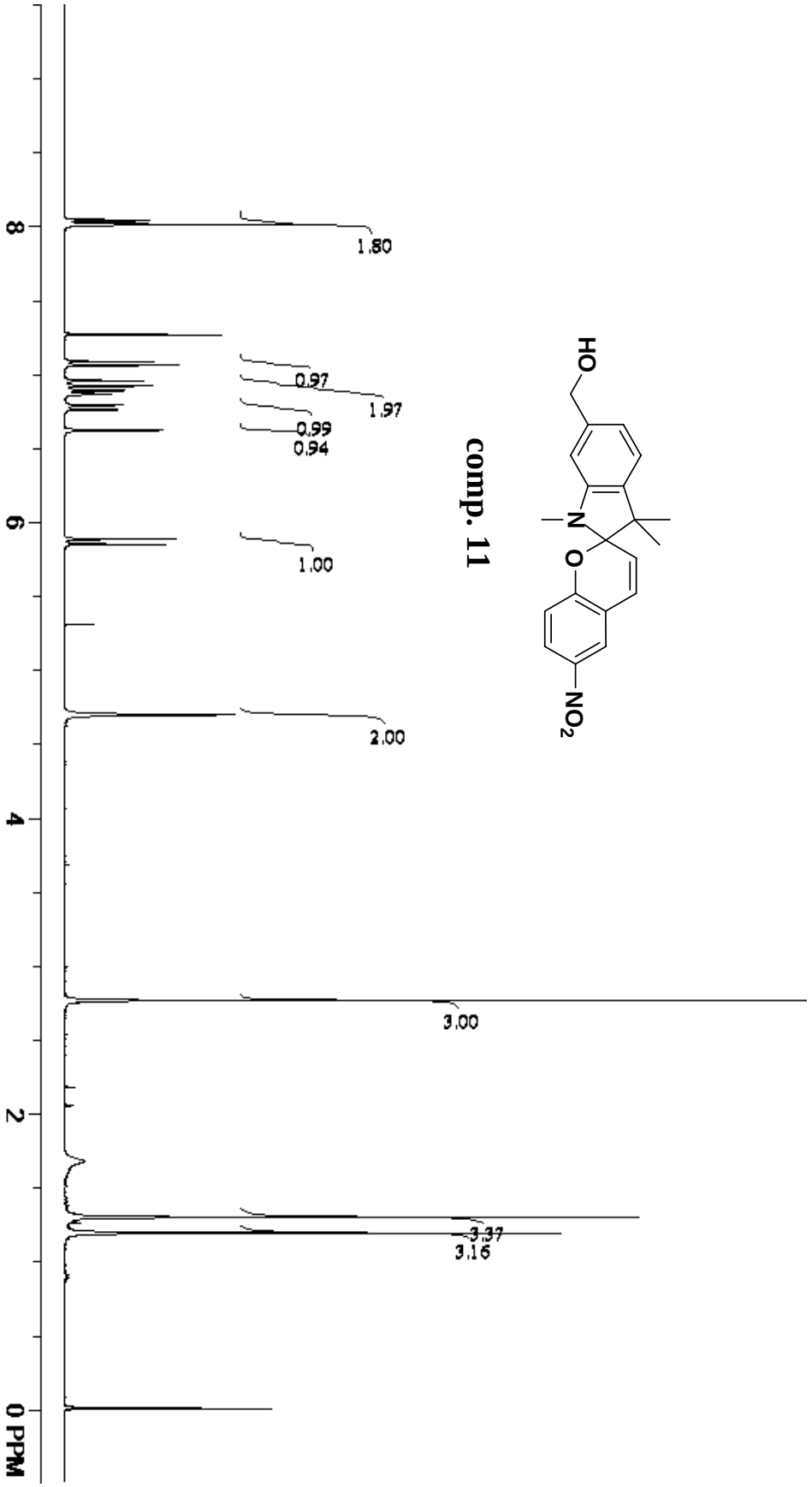
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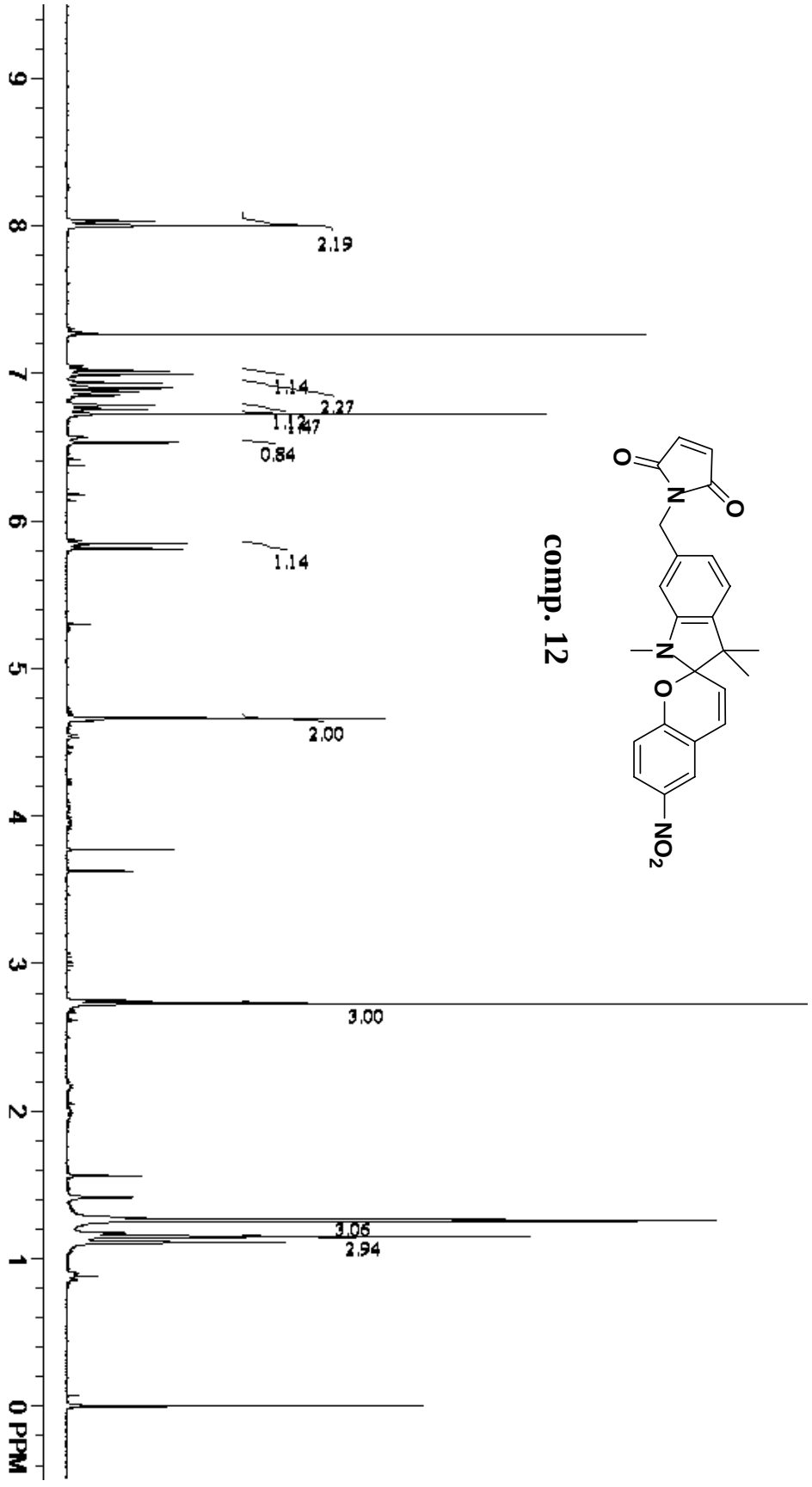
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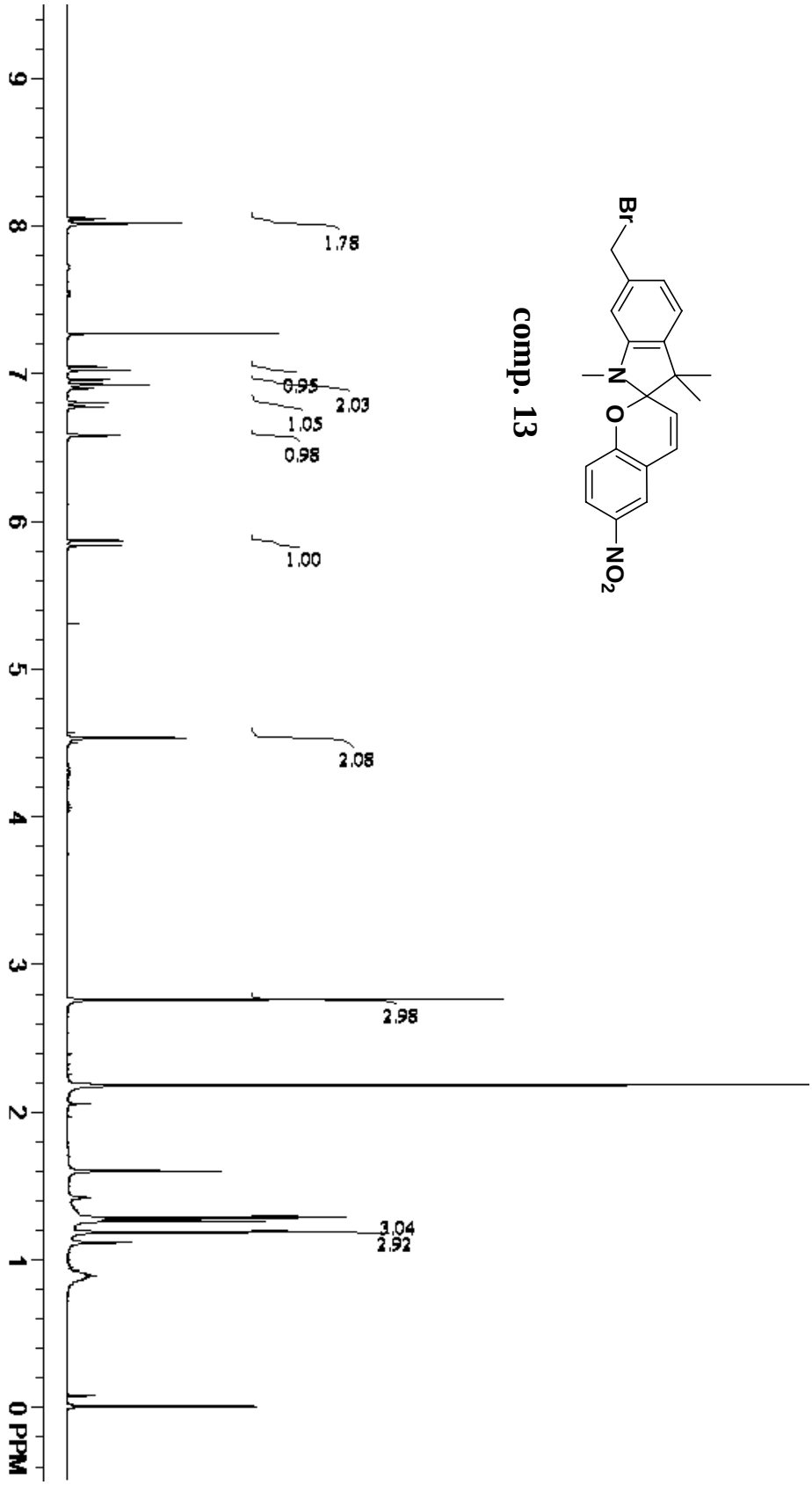
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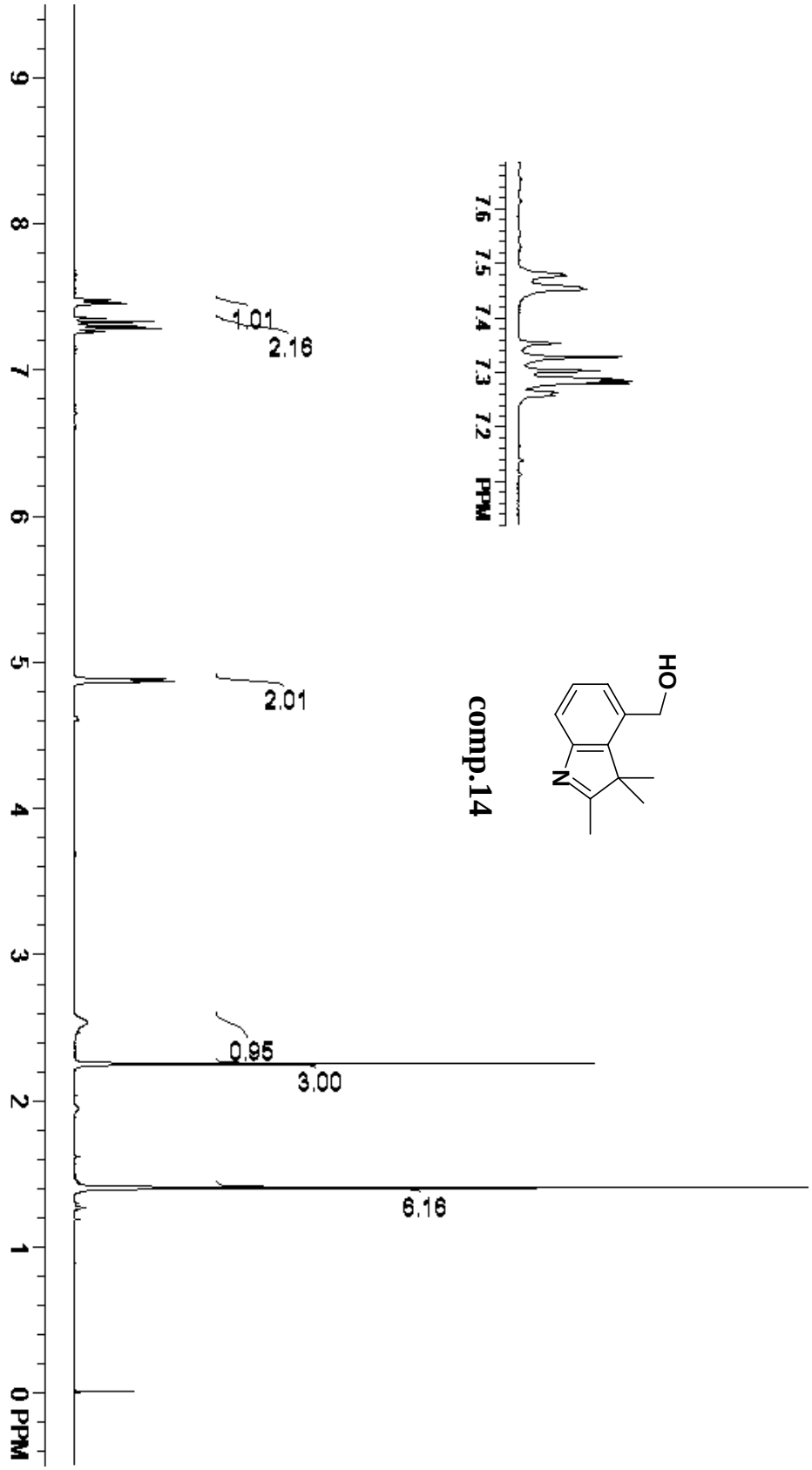
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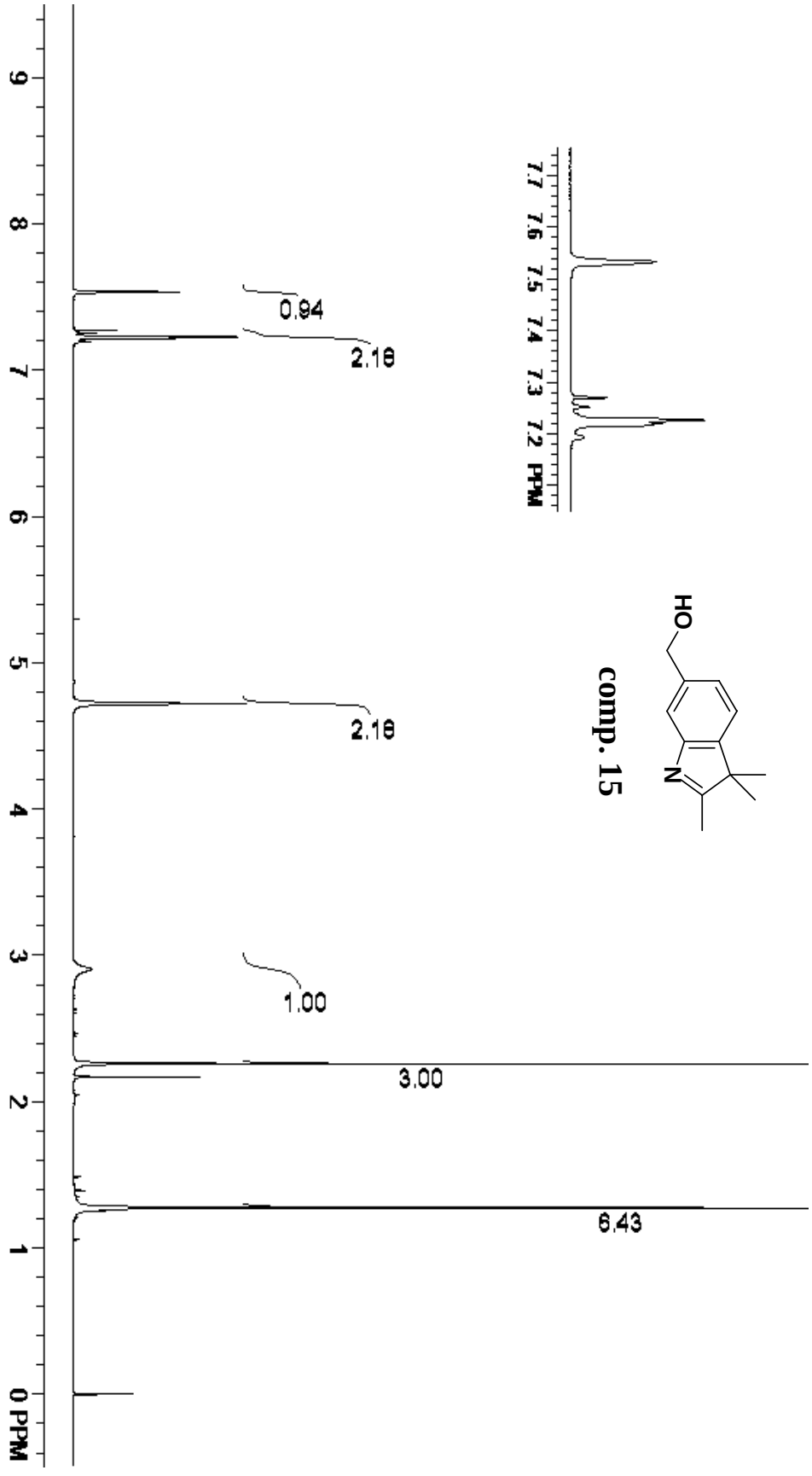
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2.16
2.16
1.00
3.00
6.43
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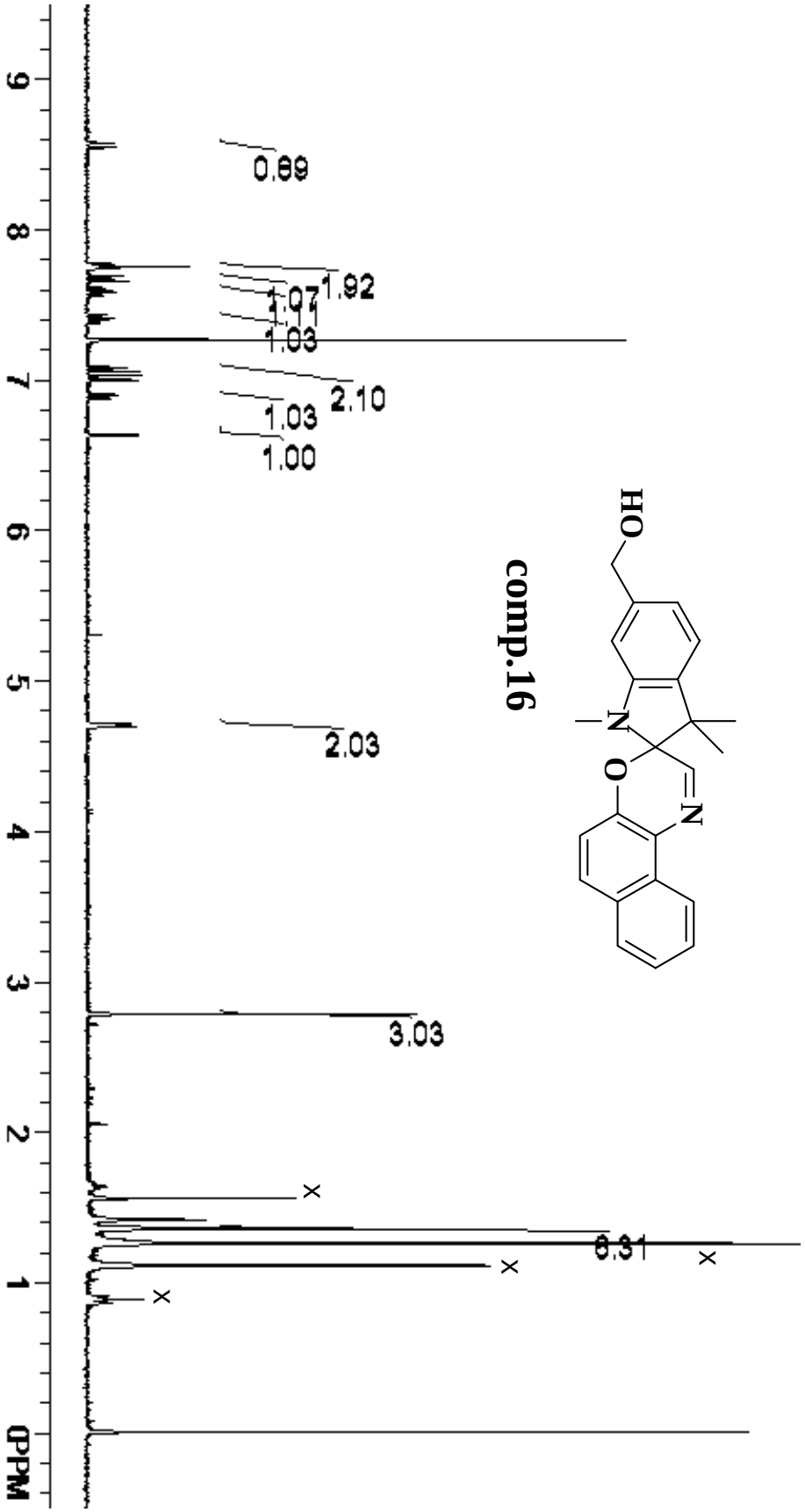
3
4
5
6
7
8
9
7.7 7.6 7.5 7.4 7.3 7.2 PPM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2.03
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6.31
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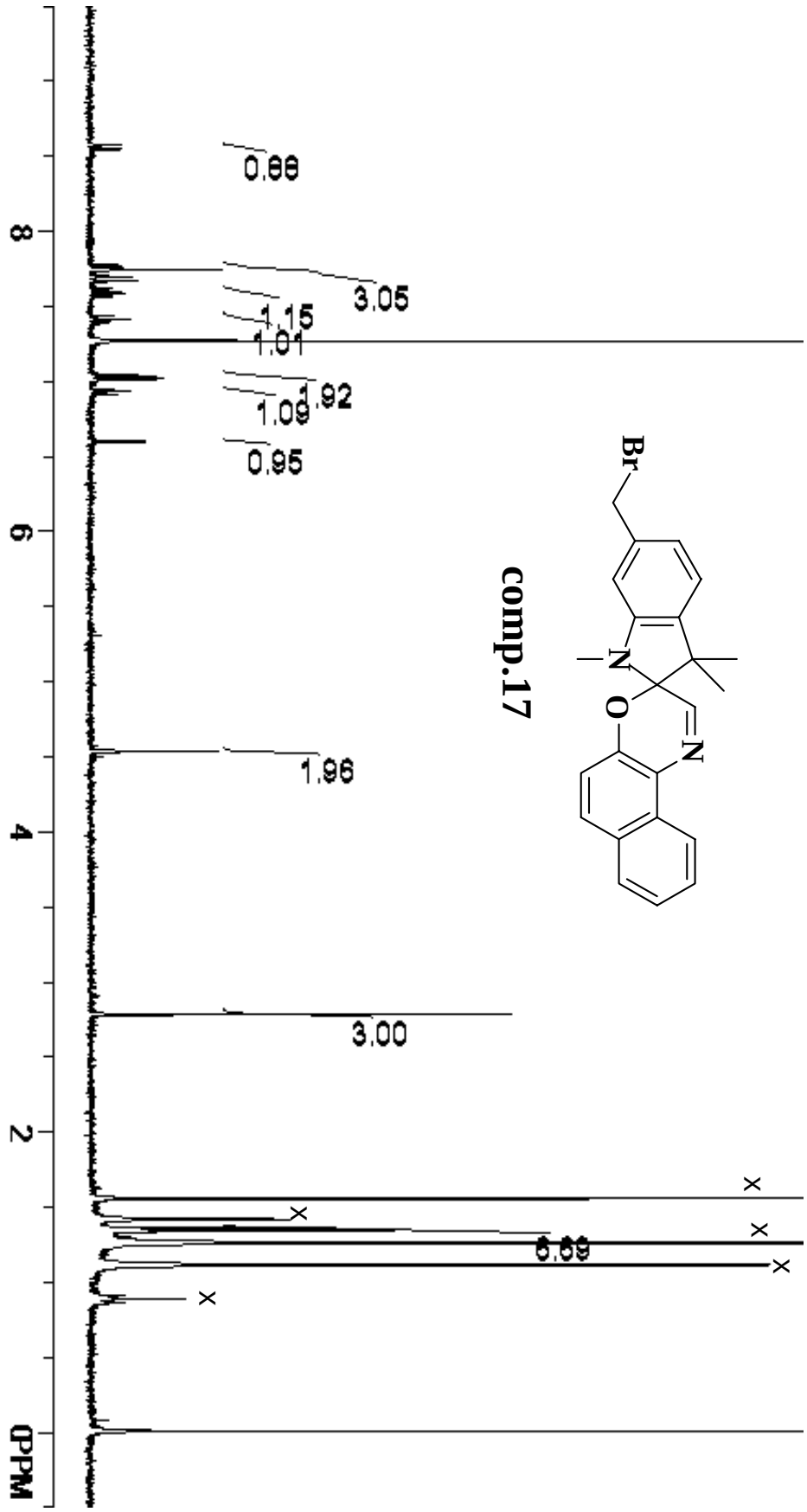
HO
N
O
N
PPM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1.92
1.09
0.95
1.96
3.00
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8
6
4
2
PPM
comp.17
Br
N
O
N