Supporting Information for

Chiral Phosphoric Acid-Catalysed Friedel-Crafts Alkylation Reaction of Indoles with Racemic Spiro Indolin-3-ones

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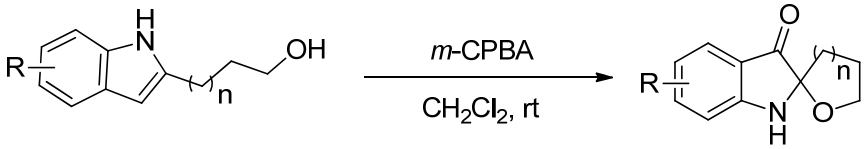
Contents

1. General considerations

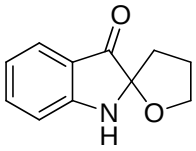
Unless stated otherwise, all reactions were carried out in flame-dried glassware under a dry argon atmosphere. All solvents were purified and dried according to standard methods prior to use. ^{1}H and ^{13}C NMR spectra were recorded on a Varian instrument (300 MHz and 75 MHz, 400 MHz and 100 MHz, respectively) and internally referenced to tetramethylsilane signal or residual protio solvent signals. Data for ^{1}H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet or unresolved, br = broad singlet, coupling constant(s) in Hz, integration). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm).

2. Experimental procedures, analytical and spectroscopic data

2.1. General procedure for preparation of spiro indolin-3-ones



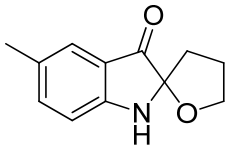
To 2-(3-hydroxylpropyl)indole[1] (n = 1) (10 mmol) in CH_2Cl_2 (50 mL) was slowly added a solution of *m*-CPBA (22 mmol) in CH_2Cl_2 (50 mL) at room temperature. The reaction was monitored by TLC. Upon consumption of the starting material (2 h), the mixture was added to a separatory funnel containing a saturated solution of Na_2SO_3 and extracted with CH_2Cl_2. The combined organic extracts were washed with brine, dried over $MgSO_4$, then the solvent was evaporated under reduced pressure and the residue was purified by flash chromatography (ethyl acetate/petroleum ether = 1/4, v/v) to afford the product.



4,5-Dihydro-3H-spiro[furan-2,2'-indolin]-3'-one (2a)

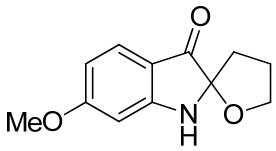
Yellow solid (33% yield) following silica gel column chromatography. Analytical data for **2a**: Mp = 57-59 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.99-2.12 (m, 2H), 2.27-2.34 (m, 2H), 4.09-4.16 (m, 2H), 4.73 (br, 1H), 6.76 (d, *J* = 8.4 Hz, 1H), 6.84 (t, *J* = 7.8 Hz, 1H), 7.44 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7, 34.0, 69.2, 95.0, 112.1, 118.9, 119.5, 124.9, 137.9, 159.7, 201.0; IR

(film) 3329, 2926, 2877, 1713, 1615, 1486, 1468, 1422, 1318, 1239, 1192, 1156, 1130, 1101, 1017, 988, 960, 945, 930, 747, 686 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{11}H_{12}NO_2^+$ (M+H) requires *m/z* 190.0863. Found *m/z* 190.0865.



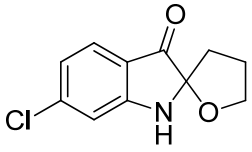
5'-Methyl-4,5-dihydro-3H-spiro[furan-2,2'-indolin]-3'-one (2b)

Yellow solid (31% yield) following silica gel column chromatography. Analytical data for **2b**: Mp = 88-90 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 1.92-2.14 (m, 2H), 2.17-2.31 (m, 5H), 4.03-4.15 (m, 2H), 4.95 (br, 1H), 6.68 (d, *J* = 8.4 Hz, 1H), 7.25 (d, *J* = 8.1 Hz, 1H), 7.34 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.3, 25.6, 34.1, 69.1, 95.4, 112.1, 119.1, 124.3, 128.9, 139.0, 158.1, 201.1; IR (film) 3304, 2918, 2868, 1705, 1619, 1586, 1494, 1436, 1293, 1118, 1061, 1019, 998, 973, 816, 774, 687 cm^{-1}; HRMS (EI) exact mass calcd for ($C_{12}H_{13}NO_2$) requires *m/z* 203.0946. Found *m/z* 203.0949.



6'-Methoxy-4,5-dihydro-3H-spiro[furan-2,2'-indolin]-3'-one (2c)

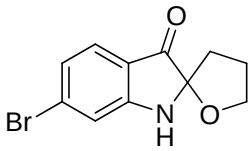
Pale yellow solid (26% yield) following silica gel column chromatography. Analytical data for **2c**: Mp = 133-135 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 1.97-2.10 (m, 2H), 2.26-2.34 (m, 2H), 3.83 (s, 3H), 4.08-4.15 (m, 2H), 4.78 (br, 1H), 6.19 (s, 1H), 6.40 (d, *J* = 8.4 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7, 34.1, 55.6, 69.3, 95.1, 95.7, 108.5, 112.3, 126.6, 162.0, 168.2, 198.4; IR (film) 3311, 2983, 2873, 1676, 1619, 1583, 1506, 1455, 1296, 1214, 1169, 1103, 1066, 1018, 974, 896, 820, 766, 694, 669 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{12}H_{14}NO_3^+$ (M+H) requires *m/z* 220.0968. Found *m/z* 220.0976.



6'-Chloro-4,5-dihydro-3H-spiro[furan-2,2'-indolin]-3'-one (2d)

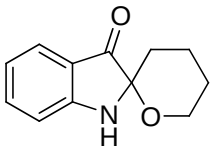
Pale yellow solid (36% yield) following silica gel column chromatography. Analytical data for **2d**: Mp = 137-139 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 1.97-2.11 (m, 2H), 2.18-2.30 (m, 2H), 4.04-4.11 (m, 2H), 5.17 (br, 1H), 6.73-6.78 (m, 2H), 7.47 (d, *J* =

7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.6, 34.0, 69.3, 95.3, 111.9, 117.2, 120.1, 126.0, 144.3, 160.0, 199.6; IR (film) 3367, 2987, 2898, 1704, 1606, 1572, 1453, 1390, 1242, 1187, 1103, 1063, 1025, 1003, 975, 920, 893, 852, 765, 688 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{11}H_{11}NO_2Cl^+$ (M+H) requires *m/z* 224.0473. Found *m/z* 224.0482.



6'-Bromo-4,5-dihydro-3H-spiro[furan-2,2'-indolin]-3'-one (2e)

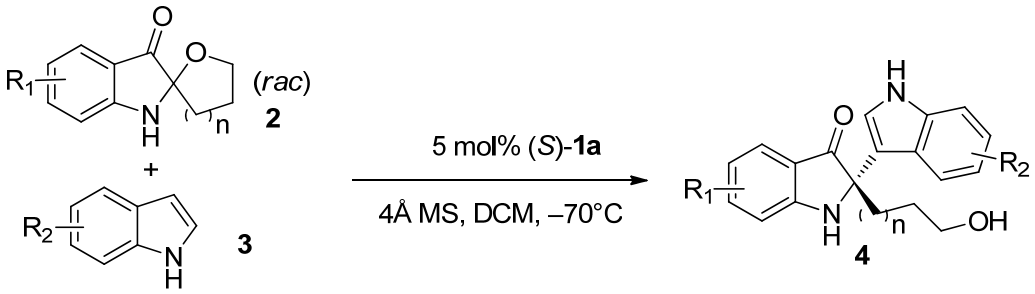
Pale yellow solid (36% yield) following silica gel column chromatography. Analytical data for **2e**: Mp = 149-151 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.98-2.11 (m, 2H), 2.24-2.29 (m, 2H), 4.08-4.16 (m, 2H), 4.83 (br, 1H), 6.95 (s, 1H), 6.96 (d, *J* = 8.1 Hz, 1H), 7.41 (d, *J* = 11.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.7, 34.0, 69.4, 95.2, 115.0, 117.6, 123.0, 126.0, 133.2, 160.0, 199.8; IR (film) 3363, 2987, 2901, 1703, 1664, 1603, 1568, 1453, 1407, 1310, 1262, 1066, 1053, 911, 855, 811, 763, 688 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{11}H_{11}NO_2Br^{+1}$ (M+H) requires *m/z* 267.9968. Found *m/z* 267.9979.



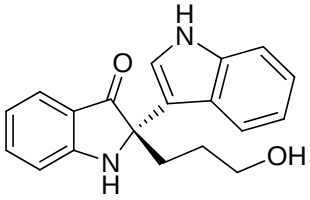
3',4',5',6'-Tetrahydrospiro[indoline-2,2'-pyran]-3-one (2f)

Pale yellow solid (59% yield) following silica gel column chromatography. Analytical data for **3f**: Mp = 117-119 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.55-1.73 (m, 4H), 1.98-2.11 (m, 2H), 3.82-3.86 (m, 1H), 4.10-4.14 (m, 1H), 6.83-6.88 (m, 2H), 7.46 (t, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 24.6, 30.4, 63.7, 87.5, 112.7, 119.6, 119.8, 125.3, 137.8, 159.5, 199.0; IR (film) 3324, 2936, 2848, 1713, 1614, 1488, 1468, 1439, 1321, 1295, 1253, 1205, 1189, 1164, 1137, 1099, 1040, 1004, 921, 760, 690 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{12}H_{13}NO_2Na^+$ (M+Na) requires *m/z* 226.0838. Found *m/z* 226.0848.

2.2. General procedure for the Friedel-Crafts alkylation reaction

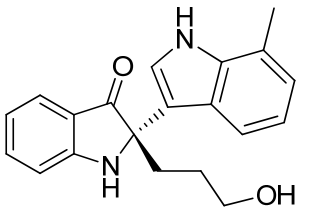


In a dry Schlenk tube, spiro indolin-3-one **2** (0.1 mmol), chiral phosphoric acid **1a** (0.005 mmol), 4Å MS (10 mg), and CH_2Cl_2 (1.0 mL) were added. The solution was cooled to -70 ℃. After 15 min, indole (0.2 mmol) was added in one portion. After the reaction was complete (monitored by TLC), the reaction mixture was diluted by adding acetone. Then the reaction mixture was filtered through a plug of silica gel (washed with acetone) and purified by column chromatography (acetone/petroleum ether = 1/4~1/2, v/v) to afford product.



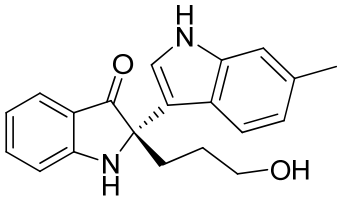
2-(3-Hydroxypropyl)-2-(1H-indol-3-yl)indolin-3-one (4a)

Yellow solid (97% yield) following silica gel column chromatography. Analytical data for **4a**: Mp = 197-199 ^oC; $[\alpha]_D^{20}$ = +635.3^o (c = 1.0 Acetone, 98% ee); ^1H NMR (400 MHz, CD_3OD) δ 1.34-1.48 (m, 1H), 1.58-1.66 (m, 1H), 2.19-2.39 (m, 2H), 3.54 (t, *J* = 6.4 Hz , 2H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.87 (t, *J* = 7.2 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 7.29-7.32 (m, 2H), 7.45-7.51 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 27.9, 34.5, 63.1, 70.5, 112.4, 113.1, 114.9, 118.7, 119.9, 120.4, 121.2, 122.5, 124.0, 125.4, 126.4, 138.7, 139.2, 163.4, 206.7; IR (film) 3674, 3250, 2987, 2901, 1709, 1664, 1614, 1492, 1465, 1409, 1328, 1242, 1128, 1049, 1008, 893, 755, 741, 715, 686 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{18}N_2O_2Na^+$ (M+Na) requires *m/z* 329.1261. Found *m/z* 329.1267. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.6 mL/min^{-1}, λ = 254 nm, t (major) = 22.89 min, t (minor) = 20.86 min.



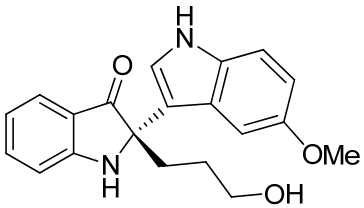
2-(3-Hydroxypropyl)-2-(7-methyl-1H-indol-3-yl)indolin-3-one (4b)

Yellow solid (98% yield) following silica gel column chromatography. Analytical data for **4b**: Decomposed temperature: 197 ^{o}C; $[\alpha]_D^{20}$ = +545.7^{o} (c = 1.0 Acetone, 98% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.34-1.47 (m, 1H), 1.58-1.64 (m, 1H), 2.22-2.39 (m, 2H), 2.43 (s, 3H), 3.54 (t, *J* = 6.3 Hz, 2H), 6.71-6.85 (m, 3H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.29-7.30 (m, 2H), 7.46-7.51 (m, 2H). ^{13}C NMR (75 MHz, CD_3OD) δ 16.9, 27.9, 34.5, 63.1, 70.5, 113.1, 115.2, 118.7, 118.9, 120.2, 120.5, 121.8, 123.0, 123.8, 125.4, 126.1, 138.0, 139.2, 163.4, 206.8; IR (film) 3493, 3393, 3383, 3238, 3046, 2955, 2874, 1660, 1613, 1580, 1493, 1465, 1434, 1327, 1154, 1103, 1050, 1015, 924, 892, 785, 756, 674, 625, 615 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{20}H_{20}N_2O_2Na^{+1}$ (M+Na) requires *m/z* 343.1417. Found *m/z* 343.1410. The enantiomeric ratio was determined by Daicel Chiralpak IC (25 cm), Hexanes / IPA = 80 / 20, 0.8 mL/min^{-1}, λ = 254 nm, t (major) = 29.97 min, t (minor) = 20.60 min.



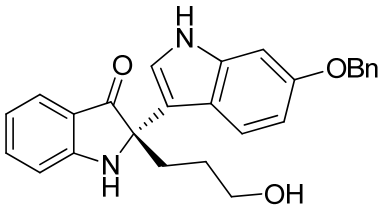
2-(3-Hydroxypropyl)-2-(6-methyl-1H-indol-3-yl)indolin-3-one (4c)

Yellow solid (92% yield) following silica gel column chromatography. Analytical data for **4c**: Mp = 193-195 ^{o}C; $[\alpha]_D^{20}$ = +291.7^{o} (c = 0.8 Acetone, 99% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 1.40-1.46 (m, 1H), 1.58-1.63 (m, 1H), 2.21-2.34 (m, 2H), 2.36 (s, 3H), 3.54 (t, *J* = 6.8 Hz, 2H), 6.71-6.76 (m, 2H), 6.96 (d, *J* = 8.4 Hz, 1H), 7.10 (s, 1H), 7.20 (s, 1H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.48-7.52 (m, 2H); ^{13}C NMR (100 MHz, CD_3OD) δ 21.7, 27.9, 34.5, 63.1, 70.6, 112.2, 113.1, 114.8, 118.7, 120.5, 120.9, 121.7, 123.3, 124.3, 125.4, 132.1, 139.1, 163.4, 206.7; IR (film) 3405, 3364, 3251, 2933, 2870, 1663, 1620, 1541, 1491, 1466, 1404, 1328, 1255, 1181, 1149, 1066, 1032, 954, 911, 886, 800, 750, 714, 686 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{20}H_{21}N_2O_2^{+1}$ (M+H) requires *m/z* 321.1598. Found *m/z* 321.1603. The enantiomeric ratio was determined by Daicel Chiralpak IC (25 cm), Hexanes / IPA = 80 / 20, 0.8 mL/min^{-1}, λ = 254 nm, t (major) = 36.52 min, t (minor) = 29.48 min.



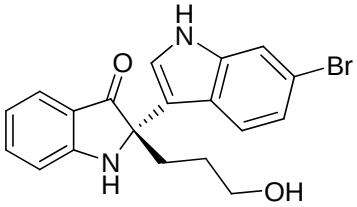
2-(3-Hydroxypropyl)-2-(5-methoxy-1H-indol-3-yl)indolin-3-one (4d)

Yellow solid (97% yield) following silica gel column chromatography. Analytical data for **4d**: Decomposed temperature: 205 ^{o}C; $[\alpha]_D^{20}$ = +332.1^{o} (c = 0.5 Acetone, 98% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.25-1.36 (m, 2H), 2.22-2.35 (m, 2H), 3.54-3.57 (m, 5H), 6.69 (dd, J_1 = 2.1 Hz, J_2 = 9.0 Hz, 1H), 6.76 (t, J = 7.2 Hz, 1H), 6.86 (d, J = 2.1 Hz, 1H), 6.98 (d, J = 8.4 Hz, 1H), 7.19 (d, J = 8.7 Hz, 1H), 7.28 (s, 1H), 7.50-7.55 (m, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.1, 34.3, 55.6, 62.7, 69.9, 103.5, 112.4, 112.9, 115.4, 118.4, 121.2, 124.4, 125.0, 126.7, 133.4, 137.9, 154.6, 162.3, 203.2; IR (film) 3664, 3375, 2960, 2902, 2499, 1675, 1615, 1481, 1463, 1323, 1210, 1177, 1065, 1028, 910, 890, 843, 826, 747, 680, 637 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{20}H_{20}N_2O_3Na^{+1}$ (M+Na) requires *m/z* 359.1366. Found *m/z* 359.1367. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) =34.05 min, t (minor) = 24.64 min.



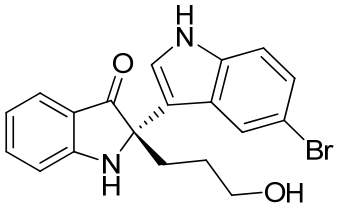
2-(6-(Benzyloxy)-1H-indol-3-yl)-2-(3-hydroxypropyl)indolin-3-one (4e)

Yellow solid (90% yield) following silica gel column chromatography. Analytical data for **4e**: Mp = 185-187 ^{o}C: $[\alpha]_D^{20}$ = +326.0^{o} (c = 0.8 Acetone, 99% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.34-1.45 (m, 1H), 1.57-1.61 (m, 1H), 2.19-2.33 (m, 2H), 3.54 (t, J = 6.3 Hz, 3H), 5.03 (s, 2H), 6.63-6.66 (dd, J_1 = 2.1 Hz, J_2 = 9.3 Hz, 2H), 6.74 (t, J = 7.2 Hz, 1H), 6.90-6.97 (m, 1H), 7.17 (s, 1H), 7.27-7.52 (m, 8H); ^{13}C NMR (100 MHz, CD_3OD) δ 27.9, 34.5, 63.1, 70.6, 71.4, 97.1, 110.8, 113.1, 115.0, 118.7, 120.4, 121.1, 121.9, 123.0, 125.5, 128.5, 128.7, 129.4, 139.1, 139.2, 139.4, 156.5, 163.4, 206.7; IR (film) 3663, 3410, 3349, 3233, 2987, 2908, 1661, 1620, 1580, 1490, 1463, 1407, 1379, 1326, 1299, 1282, 1259, 1178, 1065, 1036, 1017, 955, 912, 795, 753, 700, 624 cm^{-1}; HRMS (EI) exact mass calcd for $C_{26}H_{24}N_2O_3$ requires *m/z* 412.1787. Found *m/z* 412.1790. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 70 / 30, 0.6 mL/min^{-1}, λ = 254 nm, t (major) = 38.59 min, t (minor) = 30.85 min.



2-(6-Bromo-1H-indol-3-yl)-2-(3-hydroxypropyl)indolin-3-one (4f)

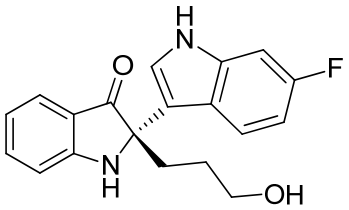
Yellow solid (90% yield) following silica gel column chromatography. Analytical data for **4f**: Decomposed temperature: 175 ^{o}C; $[\alpha]_D^{20}$ = +384.4^{o} (c = 1.0 Acetone, 97% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.34-1.47 (m, 1H), 1.53-1.61 (m, 1H), 2.15-2.36 (m, 2H), 3.53 (t, *J* = 6.6 Hz , 2H), 6.74 (t, *J* = 6.9 Hz, 1H), 6.95-7.02 (m, 2H), 7.31 (s, 1H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.48-7.53 (m, 3H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.1, 34.8, 62.6, 69.9, 112.9, 115.2, 115.4, 116.1, 118.6, 120.6, 122.7, 123.3, 124.7, 125.1, 125.4, 138.0, 139.2, 162.1, 203.0; IR (film) 3415, 2932, 2874, 2540, 2487, 1655, 1619, 1486, 1461, 1328, 1290, 1191, 1148, 1062, 1031, 928, 902, 804, 752, 672 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{17}N_2O_2NaBr^{+1}$ (M+Na) requires *m/z* 407.0365. Found *m/z* 407.0366. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 34.66 min, t (minor) = 25.00 min.



2-(5-Bromo-1H-indol-3-yl)-2-(3-hydroxypropyl)indolin-3-one (4g)

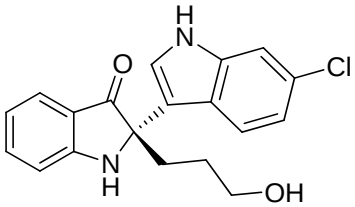
Yellow solid (99% yield) following silica gel column chromatography. Analytical data for **4g**: Decomposed temperature: 209 ^{o}C; $[\alpha]_D^{20}$ = +403.0^{o} (c = 1.0 Acetone, 98% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 1.39-1.46 (m, 1H), 1.54-1.62 (m, 1H), 2.17-2.34 (m, 2H), 3.54 (t, *J* = 6.4 Hz , 2H), 6.76 (t, *J* = 7.2 Hz, 1H), 6.99 (d, *J* = 8.4 Hz, 1H), 7.14 (dd, J_1 = 1.6 Hz, J_2 = 8.6 Hz, 1H), 7.24 (d, *J* = 8.8 Hz, 1H), 7.34 (s, 1H), 7.50-7.55 (m, 2H), 7.69 (d, *J* = 1.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.1, 35.0, 62.6, 69.9, 112.8, 112.9, 114.2, 115.7, 118.6, 120.6, 124.2, 124.9, 125.1, 125.3, 128.1, 137.0, 138.1, 162.1, 202.9; IR (film) 3440, 3234, 3033, 2945, 2851, 1650, 1617, 1498, 1463, 1332, 1300, 1156, 1117, 1102, 1054, 1020, 886, 864, 804, 788, 750, 720, 675 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{17}N_2O_2NaBr^{+1}$ (M+Na) requires *m/z* 407.0366. Found *m/z* 407.0370. The enantiomeric ratio was determined

by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 16.80 min, t (minor) = 13.04 min.



2-(6-Fluoro-1H-indol-3-yl)-2-(3-hydroxypropyl)indolin-3-one (4h)

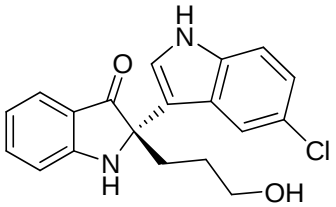
Yellow solid (96% yield) following silica gel column chromatography. Analytical data for **4h**: Decomposed temperature: 196 ^{o}C; $[\alpha]_D^{20}$ = +295.2^{o} (c = 1.0 Acetone, 98% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 1.28-1.36 (m, 1H), 1.45-1.52 (m, 1H), 2.07-2.26 (m, 2H), 3.43 (t, J = 6.4 Hz , 2H), 6.57 (dt, J_1 = 2.0 Hz, J_2 = 9.6 Hz, 1H), 6.64 (t, J = 7.6 Hz, 1H), 6.86 (d, J = 8.4 Hz, 1H), 6.90 (dd, J_1 = 2.4 Hz, J_2 = 9.6 Hz, 1H), 7.18 (s, 1H), 7.32-7.42 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 27.9, 34.6, 63.0, 70.4, 98.1, 98.4, 108.2, 108.4, 113.1, 115.3, 118.8, 120.3, 122.2, 122.3, 123.1, 124.5, 124.6, 125.5, 139.3, 163.4, 206.4; ^{19}F NMR(300 MHz, CD_3COCD_3) δ -127.9; IR (film) 3416, 3344, 2935, 2877, 1658, 1615, 1491, 1462, 1404, 1329, 1298, 1178, 1142, 1064, 1034, 960, 839, 756, 615 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{17}N_2O_2NaF^{+1}$ (M+Na) requires *m/z* 347.1166. Found *m/z* 347.1160. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 20.82 min, t (minor) = 17.86 min.



2-(6-Chloro-1H-indol-3-yl)-2-(3-hydroxypropyl)indolin-3-one (4i)

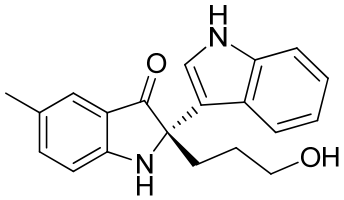
Yellow solid (88% yield) following silica gel column chromatography. Analytical data for **4i**: Mp = 220-222 ^{o}C; $[\alpha]_D^{20}$ = +278.3^{o} (c = 1.0 Acetone, 96% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 1.38-1.47 (m, 1H), 1.53-1.62 (m, 1H), 2.16-2.36 (m, 2H), 3.54 (t, J = 6.4 Hz , 2H), 6.75 (t, J = 7.6 Hz, 1H), 6.87 (dd, J_1 = 2.0 Hz, J_2 = 8.0 Hz, 1H), 6.97 (d, J = 8.4 Hz, 1H), 7.32 (s, 2H), 7.45-7.53 (m, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ 27.9, 34.6, 63.0, 70.3, 112.2, 113.1, 115.4, 118.9, 120.3, 120.4, 122.4, 124.9, 125.1, 125.5, 128.4, 139.1, 139.2, 163.3, 206.3; IR (film) 3415, 2932, 2874, 2541, 2487, 2411, 1656, 1617, 1487, 1463, 1328, 1291, 1193, 1150, 1062, 1032, 939,

907, 805, 752, 678 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{18}N_2O_2Cl^{+1}$ (M+H) requires *m/z* 341.1051. Found *m/z* 341.1062. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 28.25 min, t (minor) = 22.07 min.



2-(5-Chloro-1H-indol-3-yl)-2-(3-hydroxypropyl)indolin-3-one (4j)

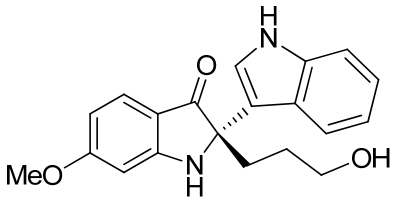
Yellow solid (97% yield) following silica gel column chromatography. Analytical data for **4j**: Mp = 219-221 °C; $[\alpha]_D^{20}$ = +520.3° (c = 1.0 Acetone, 98% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 1.39-1.47 (m, 1H), 1.53-1.61 (m, 1H), 2.15-2.35 (m, 2H), 3.54 (t, *J* = 6.6 Hz , 2H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.96-7.04 (m, 2H), 7.28 (d, *J* = 8.7 Hz, 1H), 7.35 (s, 1H), 7.49-7.53 (m, 3H); ^{13}C NMR (75 MHz, CD_3OD) δ 27.9, 34.7, 63.0, 70.3, 113.1, 113.6, 115.0, 118.9, 120.2, 120.8, 122.7, 125.5, 125.6, 125.7, 127.4, 137.1, 139.3, 163.4, 206.3; IR (film) 3489, 3415, 2945, 2428, 1654, 1618, 1489, 1457, 1329, 1195, 1135, 1107, 1051, 879, 864, 751, 717 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{18}N_2O_2Cl^{+1}$ (M+H) requires *m/z* 341.1051. Found *m/z* 341.1055. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 15.94 min, t (minor) = 12.84 min.



2-(3-Hydroxypropyl)-2-(1H-indol-3-yl)-5-methylindolin-3-one (4k)

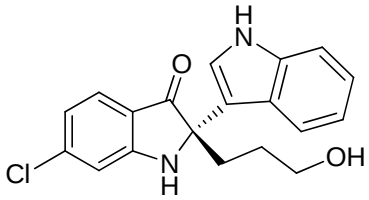
Yellow solid (95% yield) following silica gel column chromatography. Analytical data for **4k**: Mp = 182-184 °C; $[\alpha]_D^{20}$ = +296° (c = 0.1 Acetone, 96% ee); ^{1}H NMR (400 MHz, CD_3SOCD_3) δ 1.23-1.31 (m, 1H), 1.41-1.48 (m, 1H), 2.02-2.23 (m, 2H), 2.23 (s, 3H), 3.35-3.40 (m, 2H), 4.44 (t, *J* = 5.6 Hz, 1H), 6.84-6.89 (m, 2H), 7.03 (t, *J* = 7.6 Hz, 1H), 7.21 (s, 1H), 7.31-7.41 (m, 4H), 7.55 (s, 1H), 10.99 (br, 1H); ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 20.2, 27.1, 33.4, 61.1, 68.9, 111.6, 111.8, 114.1, 118.6, 119.0, 120.2, 121.1, 123.2, 123.3, 125.1, 125.8, 136.8, 138.9, 159.9, 202.9; IR (film) 3398, 3253, 2946, 2921, 1659, 1627, 1580, 1502, 1335, 1296, 1245, 1210, 1110, 1012,

826, 740 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{20}H_{21}N_2O_2^{+1}$ (M+H) requires *m/z* 321.1598. Found *m/z* 321.1605. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA =80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 20.11 min, t (minor) = 33.93 min.



2-(3-Hydroxypropyl)-2-(1H-indol-3-yl)-6-methoxyindolin-3-one (4l)

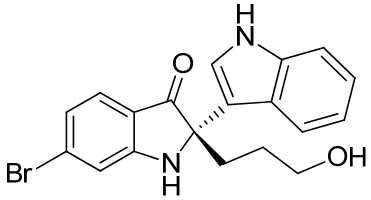
Gray solid (96% yield) following silica gel column chromatography. Analytical data for **4l**: Decomposed temperature: 220 °C; $[\alpha]_D^{20}$ = +458.0° (c = 0.5 Acetone, 97% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 1.41-1.47 (m, 1H), 1.58-1.64 (m, 1H), 2.20-2.38 (m, 2H), 3.55 (t, *J* = 6.4 Hz, 2H), 3.88 (s, 3H), 6.35 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 6.42 (d, *J* = 2.0 Hz, 1H), 6.87 (dt, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.04 (dt, J_1 = 1.2 Hz, J_2 = 6.8 Hz, 1H), 7.29 (s, 1H), 7.31 (d, *J* = 8.0 Hz, 1H), 7.39-7.43 (m, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.1, 34.8, 55.9, 62.8, 70.4, 95.0, 108.2, 112.3, 114.6, 116.3, 119.6, 121.6, 122.2, 123.6, 126.4, 126.6, 138.3, 164.2, 168.7, 200.6; IR (film) 3414, 3287, 2924, 2857, 1662, 1612, 1578, 1454, 1438, 1285, 1216, 1173, 1101, 1056, 1022, 903, 737 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{20}H_{21}N_2O_3^{+1}$ (M+H) requires *m/z* 337.1547. Found *m/z* 337.1552. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA =80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 28.95 min, t (minor) = 23.98 min.



6-Chloro-2-(3-hydroxypropyl)-2-(1H-indol-3-yl)indolin-3-one (4m)

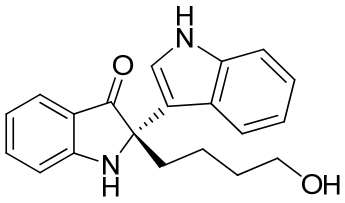
Yellow solid (92% yield) following silica gel column chromatography. Analytical data for **4m**: Decomposed temperature: 191 °C; $[\alpha]_D^{20}$ = +555.0° (c = 1.0 Acetone, 89% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.34-1.49 (m, 1H), 1.55-1.65 (m, 1H), 2.18-2.41 (m, 2H), 3.54 (t, *J* = 6.6 Hz, 2H), 6.72 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 6.91 (t, *J* = 6.6 Hz, 1H), 6.98 (d, *J* = 1.2 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.28 (s, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.0, 34.6, 62.6, 70.7, 112.3, 112.4, 115.2, 118.7, 119.5, 119.8, 121.4, 122.4, 123.8,

126.3, 126.5, 138.4, 143.6, 162.2, 201.8; IR (film) 3378, 2956, 2935, 2518, 1680, 1610, 1567, 1454, 1373, 1316, 1245, 1102, 1057, 1010, 1022, 926, 893, 751, 687 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{18}N_2O_2Cl^{+1}$ (M+H) requires *m/z* 341.1051. Found *m/z* 341.1056. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 25.29 min, t (minor) = 21.68 min.



6-Bromo-2-(3-hydroxypropyl)-2-(1H-indol-3-yl)indolin-3-one (4n)

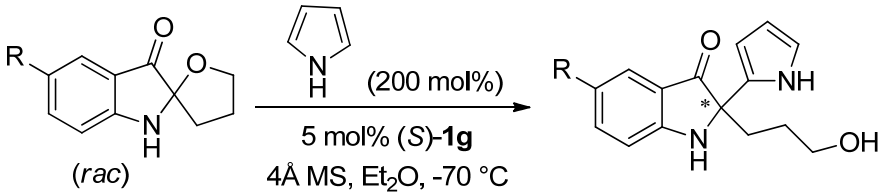
Yellow solid (95% yield) following silica gel column chromatography. Analytical data for **4n**: Decomposed temperature: 221 °C; $[\alpha]_D^{20}$ = +263.6° (c = 1.0 Acetone, 88% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.38-1.45 (m, 1H), 1.57-1.63 (m, 1H), 2.22-2.36 (m, 2H), 3.54 (t, *J* = 6.3 Hz, 2H), 6.85-6.93 (m, 2H), 7.06 (t, *J* = 7.2 Hz, 1H), 7.17 (s, 1H), 7.28 (s, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.46 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.1, 34.6, 62.6, 70.6, 112.4, 115.1, 115.4, 119.8, 121.4, 121.5, 122.4, 123.8, 126.3, 126.6, 132.5, 138.4, 143.6, 162.3, 202.0; IR (film) 3376, 2934, 2548, 2518, 1678, 1605, 1457, 1315, 1103, 1055, 1005, 913, 893, 750, 680 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{17}N_2O_2BrNa^{+1}$ (M+Na) requires *m/z* 407.0365. Found *m/z* 407.0377. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.7 mL/min^{-1}, λ = 254 nm, t (major) = 22.98 min, t (minor) = 19.37 min.



2-(4-Hydroxybutyl)-2-(1H-indol-3-yl)indolin-3-one (4o)

Yellow solid (98% yield) following silica gel column chromatography. Analytical data for **4o**: Decomposed temperature: 170 °C; $[\alpha]_D^{20}$ = +250.4° (c = 1.0 Acetone, 87% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 1.24-1.29 (m, 1H), 1.46-1.57 (m, 3H), 2.17-2.33 (m, 2H), 3.49 (t, *J* = 6.3 Hz , 2H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.87 (t, *J* = 7.5 Hz, 1H), 6.96 (d, *J* = 8.7 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 7.28 (s, 1H), 7.31 (d, *J* = 8.7 Hz, 1H), 7.44-7.53 (m, 3H); ^{13}C NMR (75 MHz, CD_3SOCD_3) δ 20.1, 32.9, 36.7, 60.6,

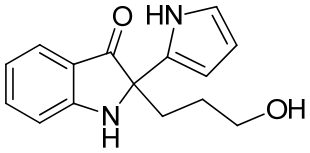
68.9, 111.6, 111.7, 113.9, 116.9, 118.5, 118.8, 120.2, 121.1, 123.2, 124.1, 125.0, 136.8, 137.4, 161.3, 202.8; IR (film) 3366, 3259, 2988, 2949, 1665, 1616, 1493, 1464, 1354, 1293, 1135, 1099, 1069, 990, 943, 891, 743, 692 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{20}H_{20}N_2O_2Na^{+1}$ (M+Na) requires *m/z* 343.1417. Found *m/z* 343.1417. The enantiomeric ratio was determined by Daicel Chiralpak IC (25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min^{-1}, λ = 254 nm, t (major) = 29.06 min, t (minor) = 12.58 min.



2a R = H
2b R = Me

4p R = H
4q R = Me

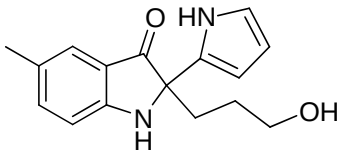
In a dry Schlenk tube, spiro indolin-3-one **2a** (18.9 mg, 0.1 mmol), chiral phosphoric acid **1g** (3.9 mg, 0.005 mmol), 4Å MS (10 mg), and Et_2O (1.0 mL) were added. The solution was cooled to -70 ℃. After 15 minute, pyrrole (13.4 mg, 0.2 mmol) was added in one portion. After the reaction was complete (monitored by TLC), the reaction mixture was diluted by adding acetone. Then the reaction mixture was filtered through a plug of silica gel (washed with acetone) and purified by column chromatography (acetone/petroleum ether = 1/4~1/2, v/v) to afford product.



2-(3-hydroxypropyl)-2-(1H-pyrrol-2-yl)indolin-3-one (4p)

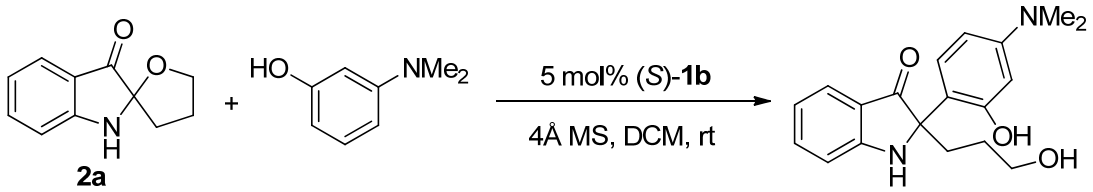
Yellow solid (92% yield) following silica gel column chromatography. Analytical data for **4p**: Mp = 61-63 °C; $[\alpha]_D^{20}$ = +683.5° (c = 1.0 Acetone, 96% ee); ^1H NMR (300 MHz, CD_3COCD_3) δ 1.27-1.42 (m, 2H), 1.89-2.00 (m, 2H), 3.35-3.41 (m, 2H), 3.48 (t, *J* = 5.1 Hz, 1H), 5.85 (m, 1H), 5.98 (br, 1H), 6.59-6.64 (m, 2H), 6.80 (br, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 7.30-7.37 (m, 2H), 9.80 (br, 1H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 28.1, 35.3, 62.4, 69.5, 105.8, 108.3, 113.1, 118.7, 118.9, 119.9, 125.2, 130.4, 137.9, 162.3, 201.9; IR (film) 3351, 2927, 2855, 1677, 1617, 1489, 1467, 1324, 1294, 1195, 1151, 1110, 1053, 887, 750, 721 cm^{-1}; HRMS (EI) exact mass calcd for $C_{15}H_{16}N_2O_2$ requires *m/z* 256.1212. Found *m/z* 256.1210. The enantiomeric ratio was

determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min^{-1}, λ = 254 nm, t (major) = 34.69 min, t (minor) = 9.01 min.

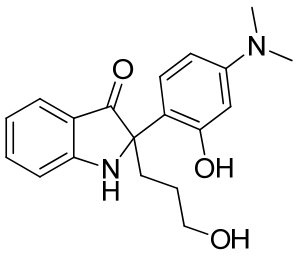


2-(3-hydroxypropyl)-5-methyl-2-(1H-pyrrol-2-yl)indolin-3-one (4q)

Yellow solid (90% yield) following silica gel column chromatography. Analytical data for **4q**: Mp = 48-50 °C; $[\alpha]_D^{20}$ = +523.8° (c = 1.0 Acetone, 97% ee); ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.29-1.41 (m, 2H), 1.89-2.00 (m, 2H), 2.13 (s, 3H), 3.36-3.41 (m, 2H), 3.45-3.47 (m, 1H), 5.86 (m, 1H), 5.98 (br, 1H), 6.59 (br, 2H), 6.81 (d, *J* = 5.4 Hz, 1H), 7.12 (s, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 9.79 (br, 1H); ^{13}C NMR (100 MHz, CD_3COCD_3) δ 20.4, 28.2, 35.4, 62.5, 69.8, 105.8, 108.3, 113.1, 118.8, 120.2, 124.5, 128.0, 130.7, 139.3, 160.9, 202.0; IR (film) 3359, 2924, 1672, 1625, 1499, 1432, 1271, 1213, 1055, 952, 902, 813, 723 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{16}H_{19}N_2O_2^{+1}$ (M+H) requires *m/z* 271.1441. Found *m/z* 271.1445. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min^{-1}, λ = 254 nm, t (major) = 11.70 min, t (minor) = 8.54 min.



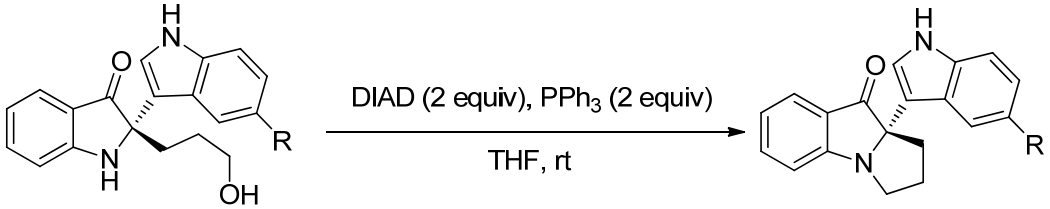
In a dry Schlenk tube, spiro indolin-3-one **2a** (18.9 mg, 0.1 mmol), chiral phosphoric acid **1b** (4.4 mg, 0.005 mmol), 4Å MS (10 mg), and 3-(dimethylamino)phenol (27.4 mg, 0.2 mmol) were stirred in CH_2Cl_2 (1.0 mL) at room temperature. After the reaction was complete (monitored by TLC), the reaction mixture was filtered through a plug of silica gel (washed with DCM) and purified by column chromatography (acetone/petroleum ether = 1/4~1/2, v/v) to afford product **4r**.



2-(4-(dimethylamino)-2-hydroxyphenyl)-2-(3-hydroxypropyl)indolin-3-one (4r)

Yellow solid (93% yield) following silica gel column chromatography. Analytical data for **4r**: Mp = 72-74 °C; $[\alpha]_D^{20}$ = +173.3° (c = 1.0 Acetone, 50% ee); ^{1}H NMR (300 MHz, CD_3COCD_3) δ 1.20-1.30 (m, 2H), 1.94-2.00 (m, 1H), 2.06-2.12 (m, 1H), 2.70 (s, 6H), 3.29-3.35 (m, 2H), 3.46 (t, *J* = 5.4 Hz, 1H), 6.05 (dd, J_1 = 2.7 Hz, J_2 = 9.0 Hz, 1H), 6.10 (d, *J* = 2.7 Hz, 1H), 6.60 (t, *J* = 7.5 Hz, 1H), 6.88 (d, *J* = 8.7 Hz, 1H), 7.10 (s, 1H), 7.12 (d, *J* = 2.1 Hz, 1H), 7.32-7.37 (m, 2H), 9.60 (s, 1H); ^{13}C NMR (75 MHz, CD_3COCD_3) δ 28.4, 34.3, 40.4, 62.4, 73.0, 102.9, 105.1, 113.2, 113.6, 118.8, 119.7, 125.3, 128.4, 139.0, 152.6, 157.5 162.1, 206.6; IR (film) 2959, 1659, 1613, 1523, 1490, 1468, 1361, 1327, 1239, 1056, 987, 752 cm^{-1}; HRMS (EI) exact mass calcd for $C_{19}H_{22}N_2O_3$ requires *m/z* 326.1630. Found *m/z* 326.1631. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.8 mL/min^{-1}, λ = 254 nm, t (major) = 14.52 min, t (minor) = 12.13 min.

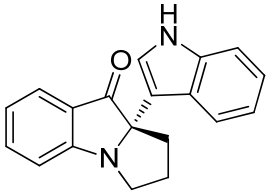
2.3. General procedure for transformation of 4a and 4g



4a R = H
4g R = Br

5a R = H
5g R = Br

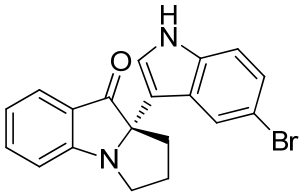
In a dry Schlenk tube, compoumd **4a** (30.6 mg, 0.1 mmol), DIAD (40.4 mg, 0.2 mmol) and PPh_3 (52.5 mg, 0.2 mmol) were dissolved in 1.0 mL THF at room temperature. After 48 hours, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography (ethyl acetate/petroleum ether = 1/5, v/v) to afford product **5a**.



(S)-9a-(1H-Indol-3-yl)-2,3-dihydro-1H-pyrrolo[1,2-a]indol-9(9aH)-one (5a)

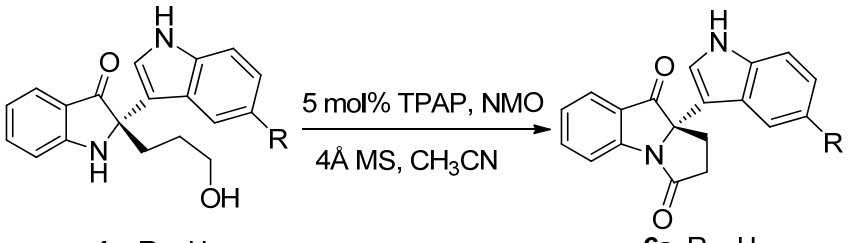
Pale yellow solid (64% yield) following silica gel column chromatography. Analytical data for **5a**: Mp = 190-192 °C; $[\alpha]_D^{20}$ = +74.1° (c = 0.5 Acetone, 92% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96-2.16 (m, 3H), 2.50-2.54 (m, 1H), 3.31-3.36 (m, 1H), 3.62-3.67 (m, 1H), 6.90-7.00 (m, 2H), 7.04-7.17 (m, 3H), 7.25-7.30 (m, 1H), 7.54-7.59 (m,

2H), 7.83 (d, *J* = 7.8 Hz, 1H), 8.24 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.1, 33.0, 50.3, 77.8, 111.2, 113.7, 114.6, 119.7, 120.3, 121.0, 122.1, 122.3, 122.4, 125.2, 125.4, 137.1, 137.2, 164.7, 203.8; IR (film) 3673, 3290, 2973, 2924, 1682, 1608, 1475, 1457, 1324, 1152, 1105, 1077, 1011, 984, 889, 770, 743, 697 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{17}N_2O^{+1}$ (M+H) requires *m/z* 289.1335. Found *m/z* 289.1332. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 70 / 30, 0.8 mL/min^{-1}, λ = 254 nm, t (major) = 14.29 min, t (minor) = 26.73 min.



(S)-9a-(5-Bromo-1H-indol-3-yl)-2,3-dihydro-1H-pyrrolo[1,2-a]indol-9(9aH)-one (5g)

Pale yellow solid (55% yield) following silica gel column chromatography. Analytical data for **5g**: Mp = 181-183 °C; $[\alpha]_D^{20}$ = +373° (c = 0.3 Acetone, 94% ee); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.05-2.13 (m, 3H), 2.47-2.49 (m, 1H), 3.35-3.38 (m, 1H), 3.66-3.69 (m, 1H), 6.95-7.02 (m, 2H), 7.16-7.29 (m, 3H), 7.57-7.59 (m, 1H), 8.06 (s, 1H), 8.15-8.17 (br, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.0, 33.3, 50.3, 77.6, 112.7, 112.9, 113.8, 114.3, 120.6, 122.2, 123.4, 124.9, 125.1, 127.0, 135.7, 137.5, 164.7, 203.7; IR (film) 3673, 3425, 2971, 2923, 1688, 1606, 1475, 1456, 1318, 1101, 1067, 1006, 990, 883, 863, 806, 757, 696 cm^{-1}; HRMS (MALDI/DHB) exact mass calcd for $C_{19}H_{16}N_2OBr^{+1}$(M+H) requires *m/z* 367.0440. Found *m/z* 367.0439. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 0.8 mL/min^{-1}, λ = 254 nm, t (major) = 15.51 min, t (minor) = 11.38 min.

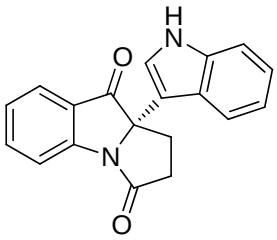


4a R = H
4g R = Br

6a R = H
6g R = Br

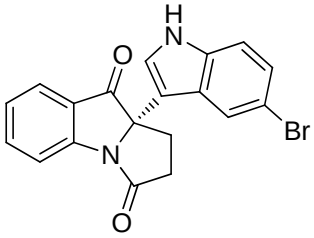
In a dry Schlenk tube, 4Å molecular sieves (10 mg), N-methylmorpholine N-oxide (35 mg, 0.3 mmol), and **4a** (30.6 mg, 0.1 mmol) were stirred in 1 mL acetonitrile at

25°C. Tetrapropylammonium perruthenate (2 mg, 0.005 mmol) was added and the mixture was stirred for 15-45 minutes until consumption of the alcohol was complete (as monitored by TLC). The reaction mixture was filtered through a plug of silica gel (washed with ethyl acetate) and purified by column chromatography (ethyl acetate/petroleum ether = 1/5, v/v) to afford product **6a**.



(S)-9a-(1H-indol-3-yl)-1H-pyrrolo[1,2-a]indole-3,9(2H,9aH)-dione (6a)

White solid (77% yield) following silica gel column chromatography. Analytical data for **6a**: Mp = 208-210 °C; $[\alpha]_D^{20}$ = +162.1° (c = 1.0 Acetone, 97% ee); ^{1}H NMR (300 MHz, CD_3OD) δ 2.50-2.59 (m, 2H), 2.77-2.90 (m, 2H), 7.01 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.23-7.28 (m, 2H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.70-7.79 (m, 2H), 7.92 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, CD_3SOCD_3) δ 28.3, 34.4, 73.5, 111.0, 112.1, 116.2, 119.2, 119.8, 121.6, 123.2, 123.4, 124.4, 124.7, 125.0, 137.1, 137.3, 149.7, 173.5, 199.1; IR (film) 3332, 2926, 2853, 1709, 1602, 1460, 1430, 1341, 1219, 1179, 1095, 837, 750, 674 cm^{-1}; HRMS (EI) exact mass calcd for $C_{19}H_{14}N_2O_2$ requires *m/z* 302.1055. Found *m/z* 302.1057. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min^{-1}, λ = 254 nm, t (major) = 19.83 min, t (minor) = 17.70 min.

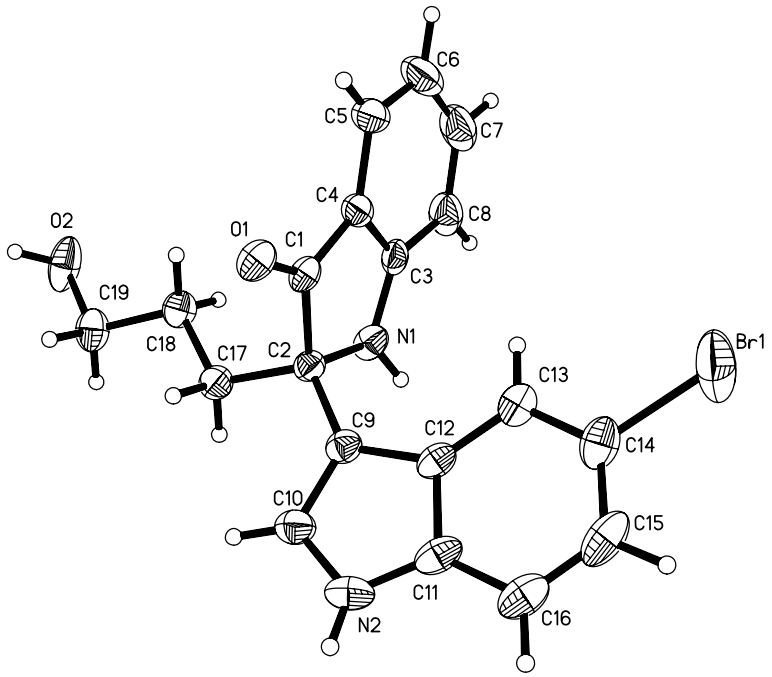


(S)-9a-(5-bromo-1H-indol-3-yl)-1H-pyrrolo[1,2-a]indole-3,9(2H,9aH)-dione (6g)

White solid (72% yield) following silica gel column chromatography. Analytical data for **6g**: Mp = 132-134 °C; $[\alpha]_D^{20}$ = +239° (c = 0.3 Acetone, 98% ee); ^{1}H NMR (400 MHz, CD_3OD) δ 2.51-2.60 (m, 2H), 2.72-2.76 (m, 1H), 2.86-2.95 (m, 1H), 7.21 (dd, J_1 = 2.0 Hz, J_2 = 8.4 Hz, 1H), 7.25-7.29 (m, 2H), 7.31 (s, 1H), 7.63 (dd, J_1 = 0.8 Hz, J_2 = 8.8 Hz, 1H), 7.74 (dt, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 1H), 7.96 (d, *J* = 2.0 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 30.1, 35.4, 75.3, 112.5, 113.8, 114.5,

117.6, 123.8, 125.1, 125.9, 126.2, 126.2, 126.4, 127.6, 137.8, 138.1, 150.9, 175.7, 200.6; IR (film) 2926, 2853, 1704, 1602, 1464, 1339, 1230, 1216, 1177, 1099, 982, 880, 797, 670 cm^{-1}; HRMS (EI) exact mass calcd for $C_{19}H_{13}N_2O_2Br$ requires *m/z* 380.0160. Found *m/z* 380.0157. The enantiomeric ratio was determined by Daicel Chiralpak AD-H (25 cm), Hexanes / IPA = 80 / 20, 1.0 mL/min^{-1}, λ = 254 nm, t (major) = 36.45 min, t (minor) = 14.58 min.

3. Crystal data and structure refinement for (*S*)-5g



ORTEP diagram at 30% thermal ellipsoids (CCDC 808591)

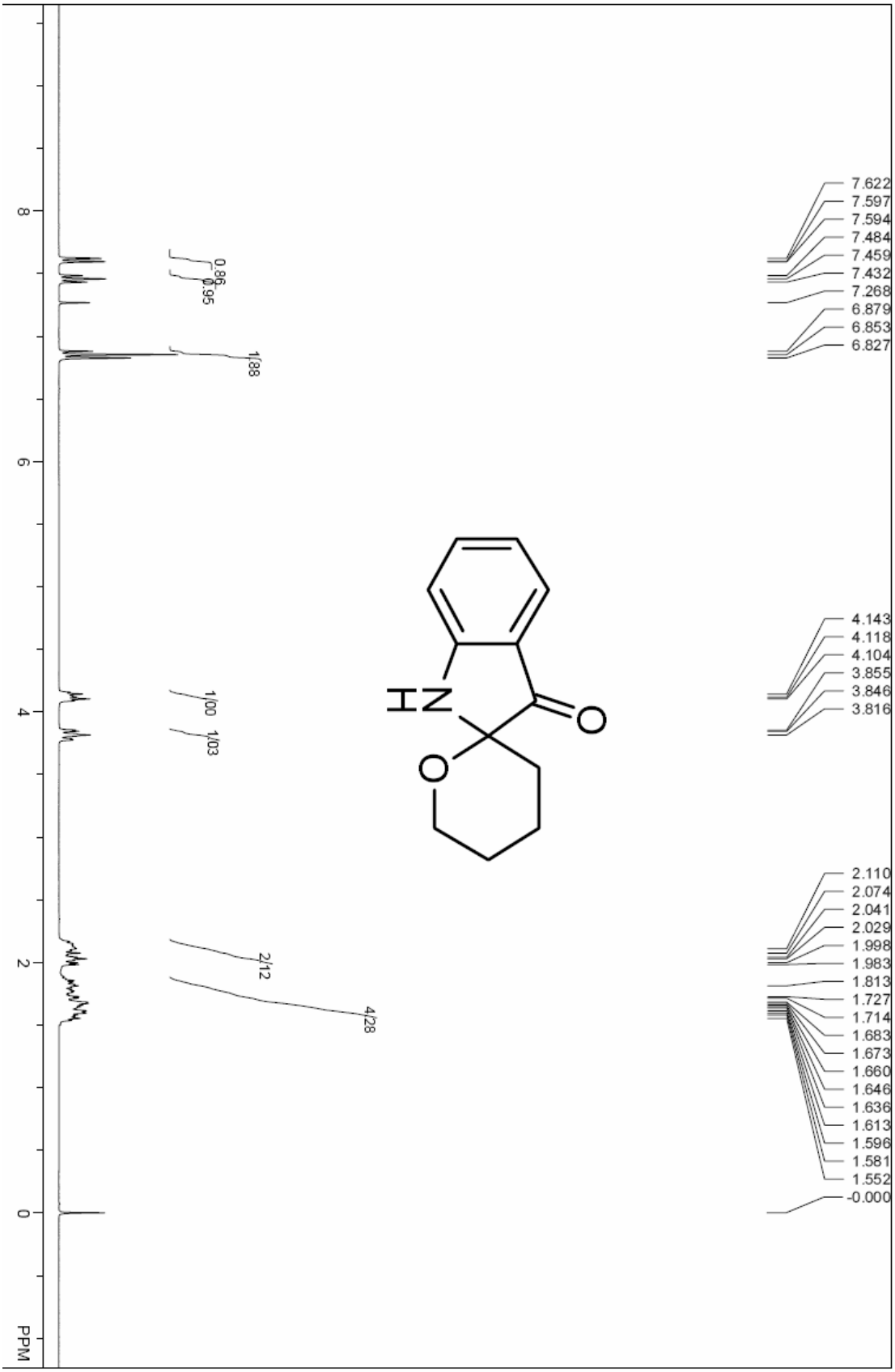
Table 1. Crystal data and structure refinement for cd201665.

Identification code	cd201665
Empirical formula	C19 H17 Br N2 O2
Formula weight	385.26
Temperature	293(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 7.8404(7) A alpha = 90 deg. b = 10.9935(10) A beta = 90 deg. c = 20.0870(18) A gamma = 90 deg.
Volume	1731.4(3) A^3
Z, Calculated density	4, 1.478 Mg/m^3

Absorption coefficient	2.387 mm^-1
F(000)	784
Crystal size	0.304 x 0.171 x 0.156 mm
Theta range for data collection	2.03 to 27.50 deg.
Limiting indices	-10<=h<=9, -14<=k<=12, -14<=l<=25
Reflections collected / unique	10420 / 3934 [R(int) = 0.0324]
Completeness to theta = 27.50	99.7 %
Absorption correction	Empirical
Max. and min. transmission	1.0000 and 0.5638
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3934 / 3 / 229
Goodness-of-fit on F^2	1.027
Final R indices [I>2sigma(I)]	R1 = 0.0459, wR2 = 0.1043
R indices (all data)	R1 = 0.0764, wR2 = 0.1173
Absolute structure parameter	0.005(11)
Largest diff. peak and hole	0.506 and -0.289 e.A^-3

Reference:

1. A. Tsotinis, P. A. Afroudakis, K. Davidson, A.Prashar and D. Sugden, *J. Med. Chem.* 2007, **50**, 6436-6440.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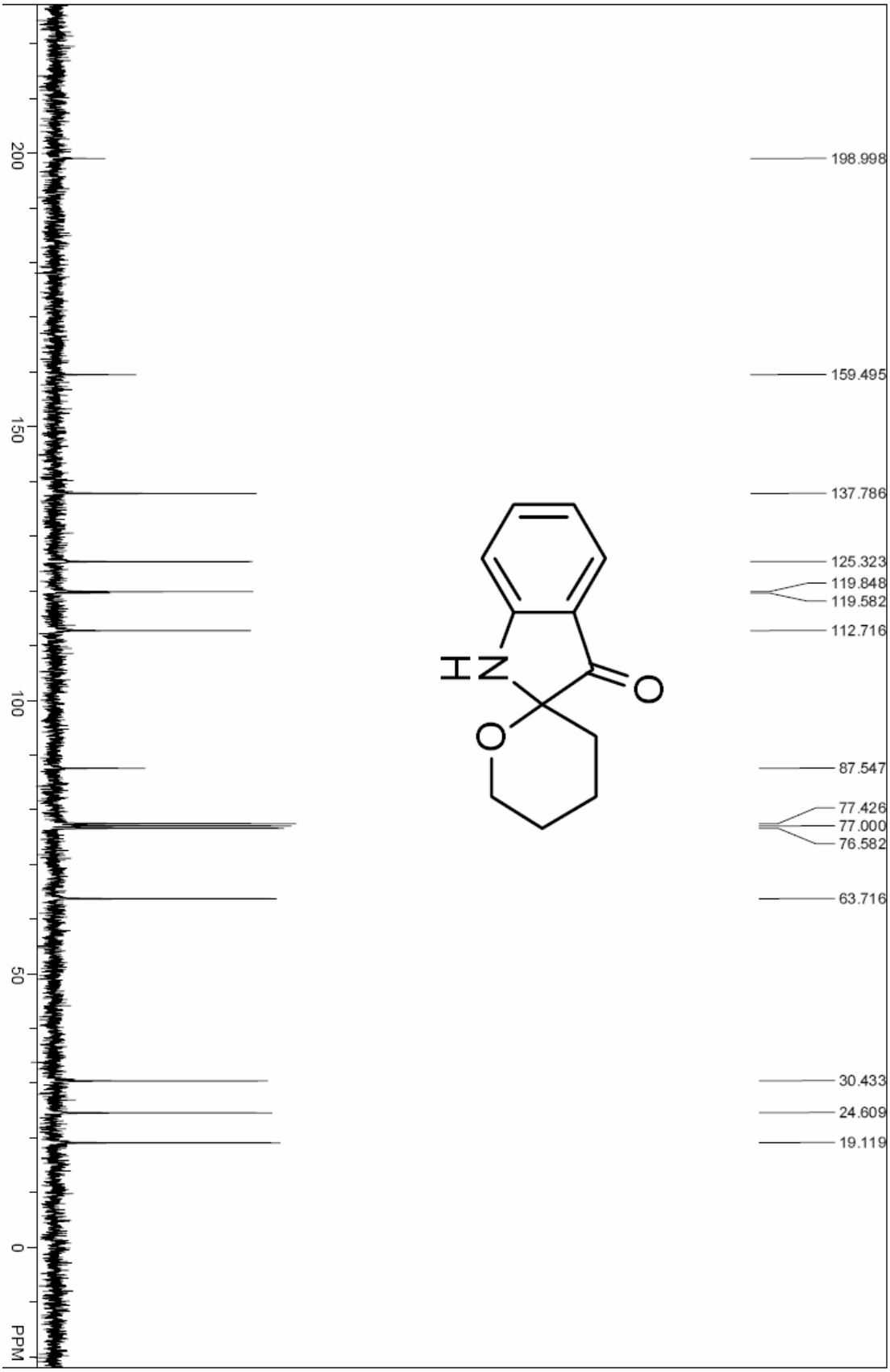
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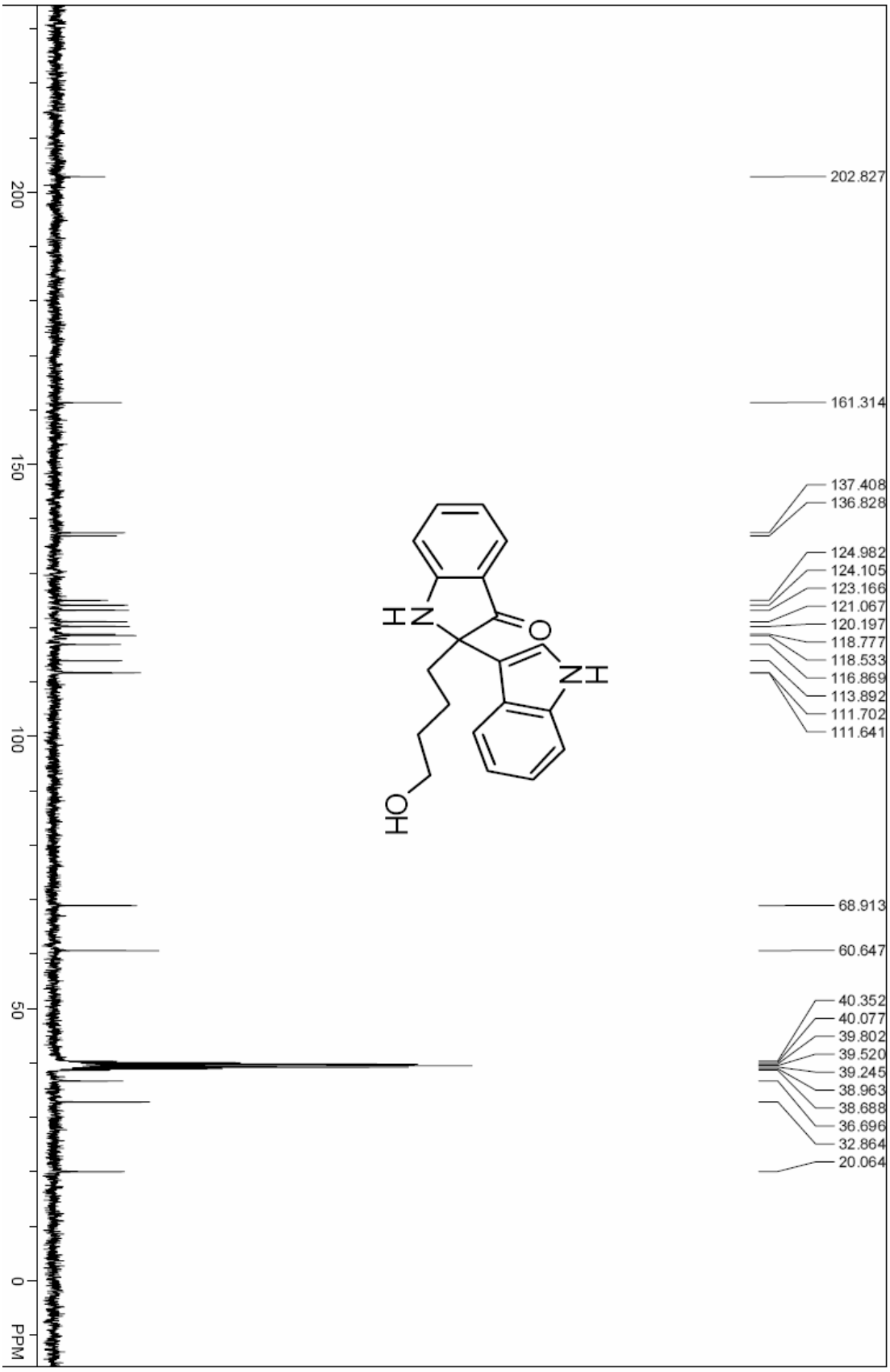

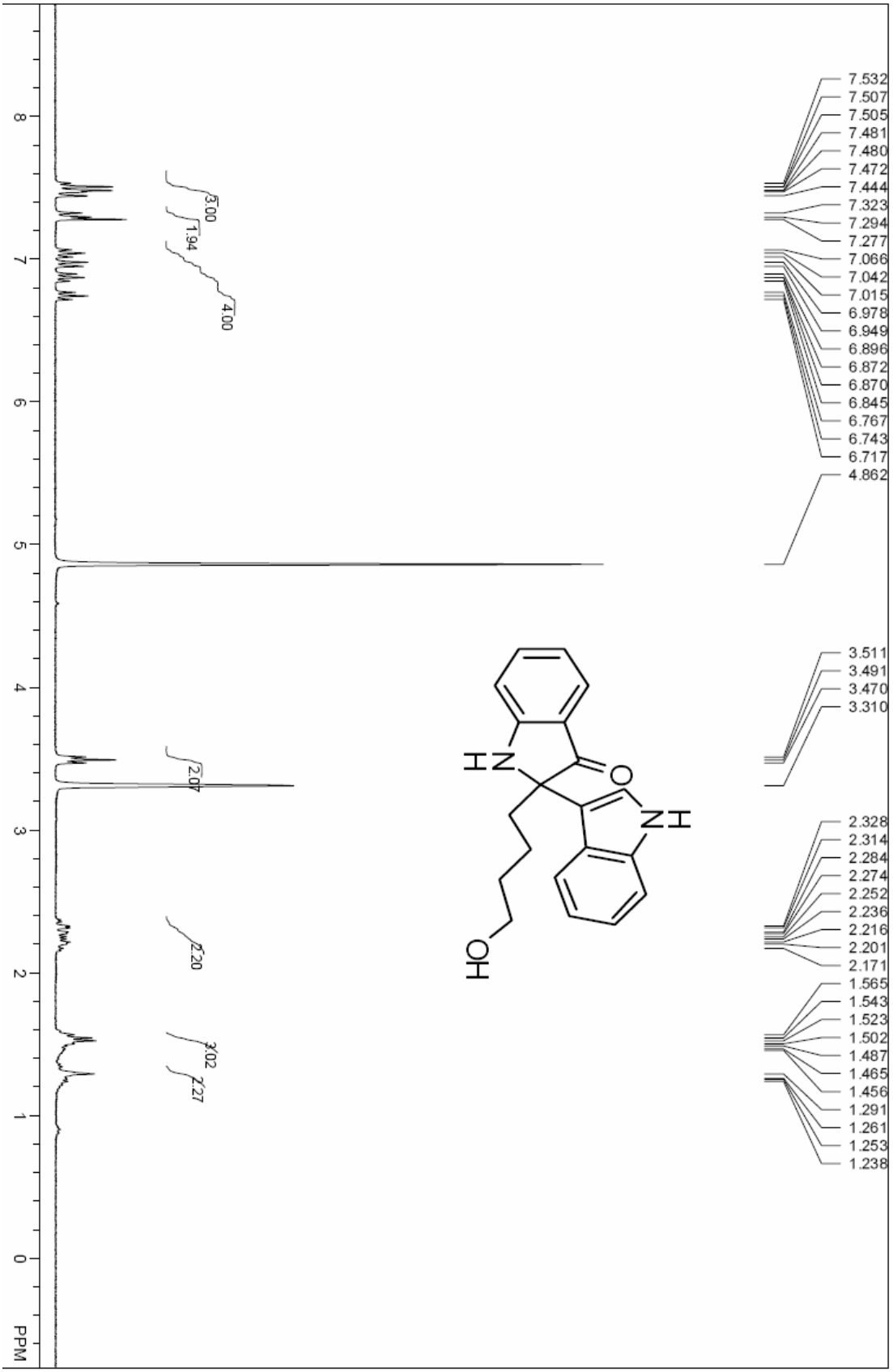
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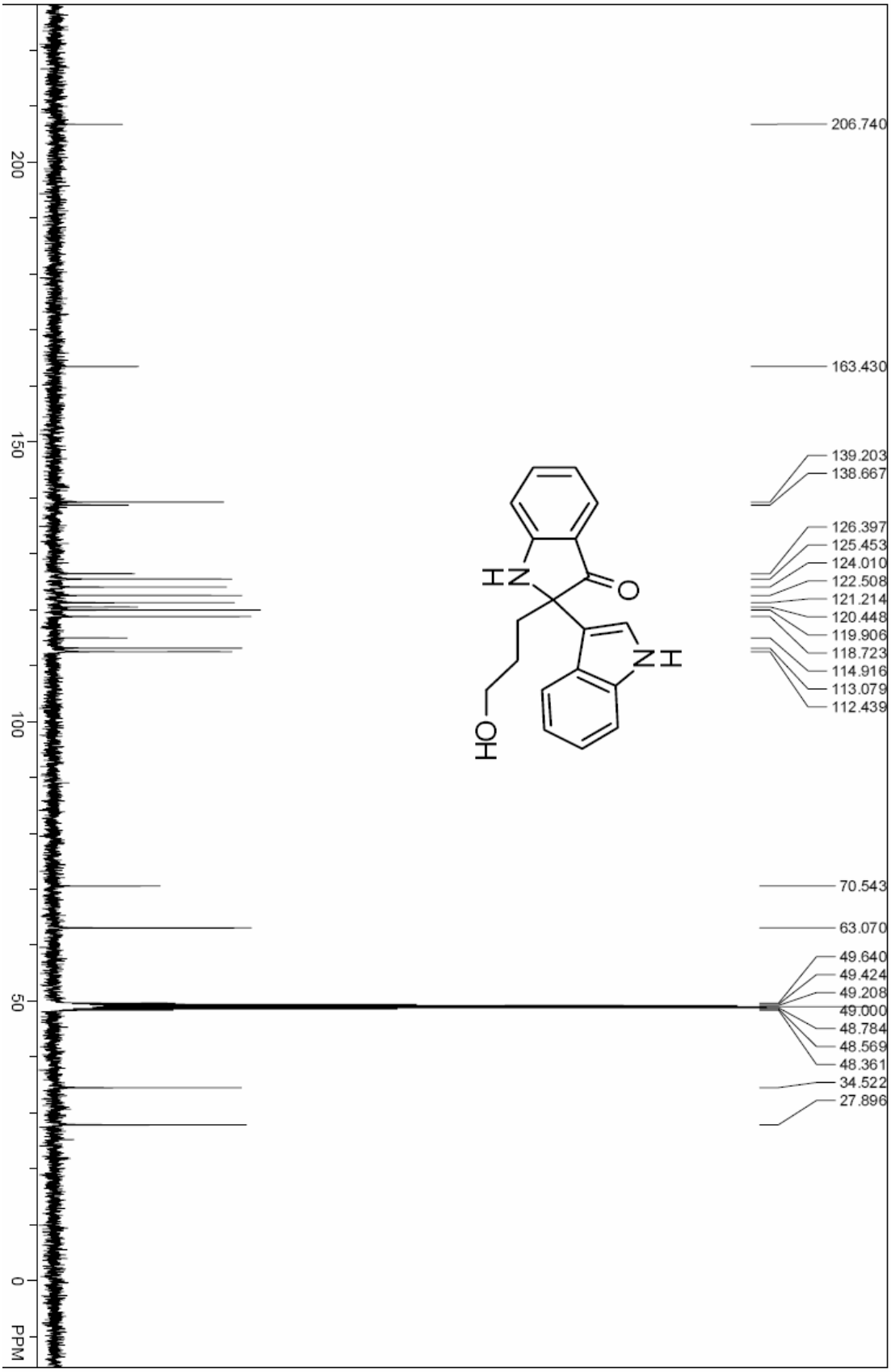
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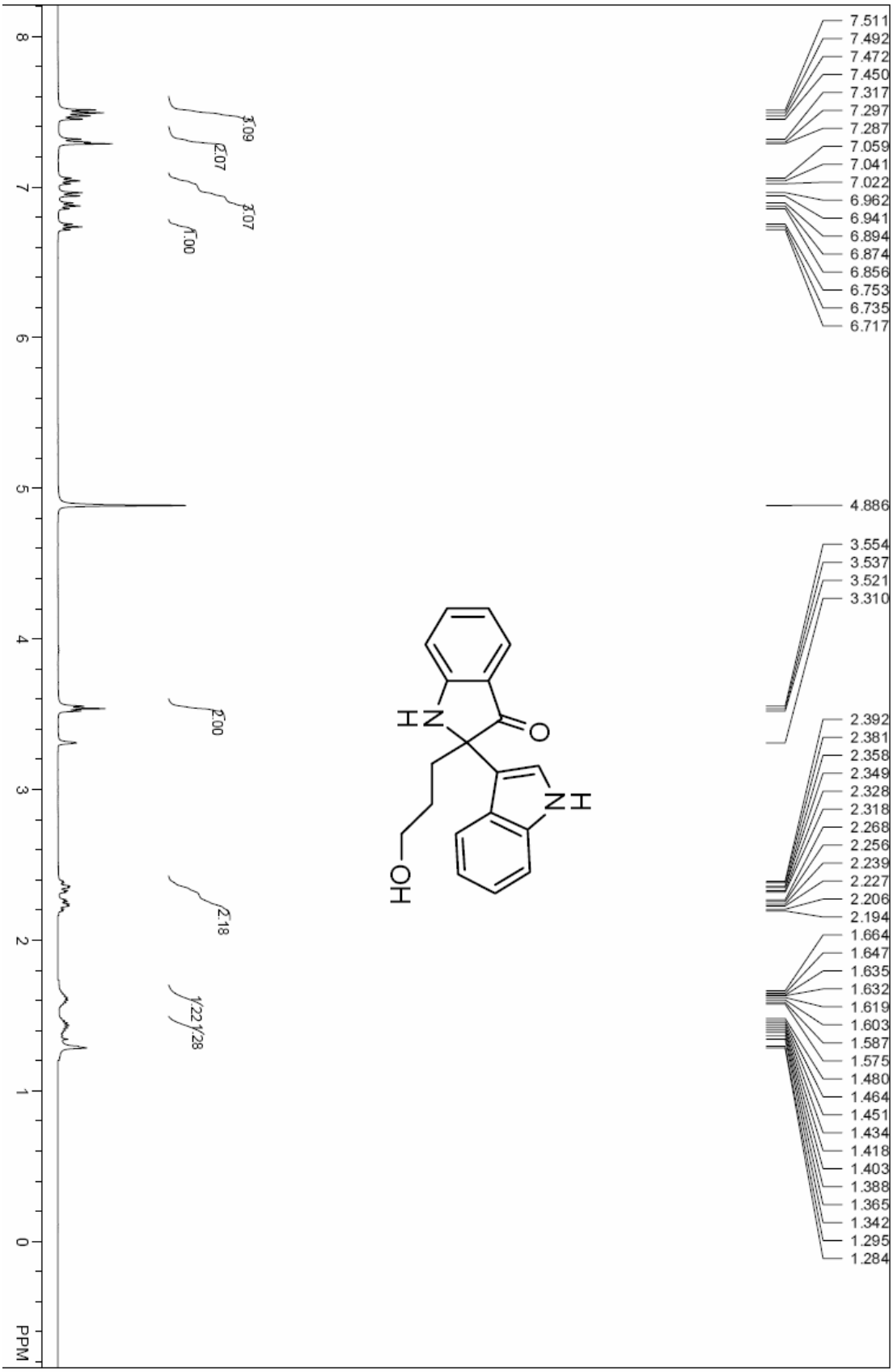

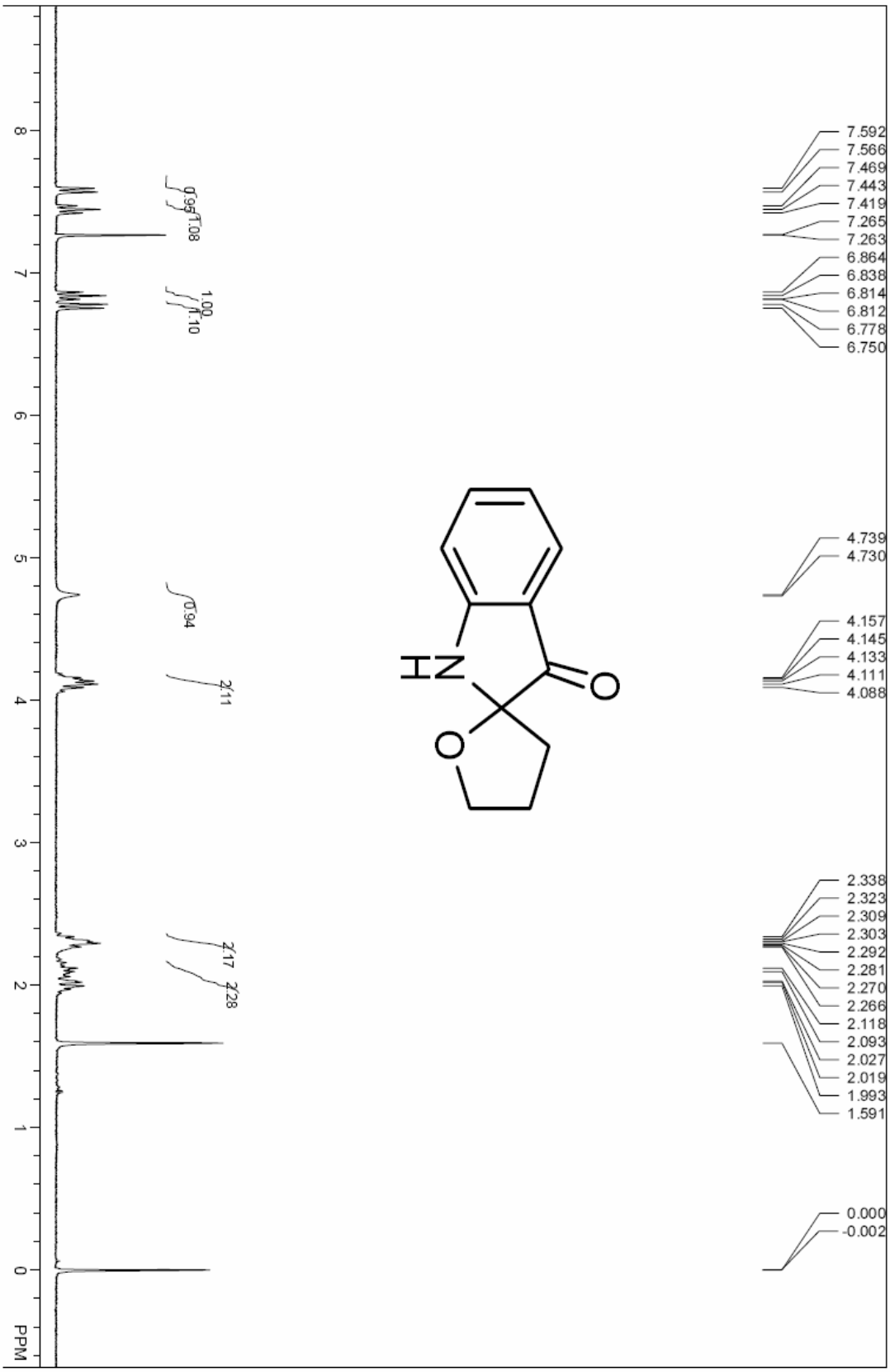

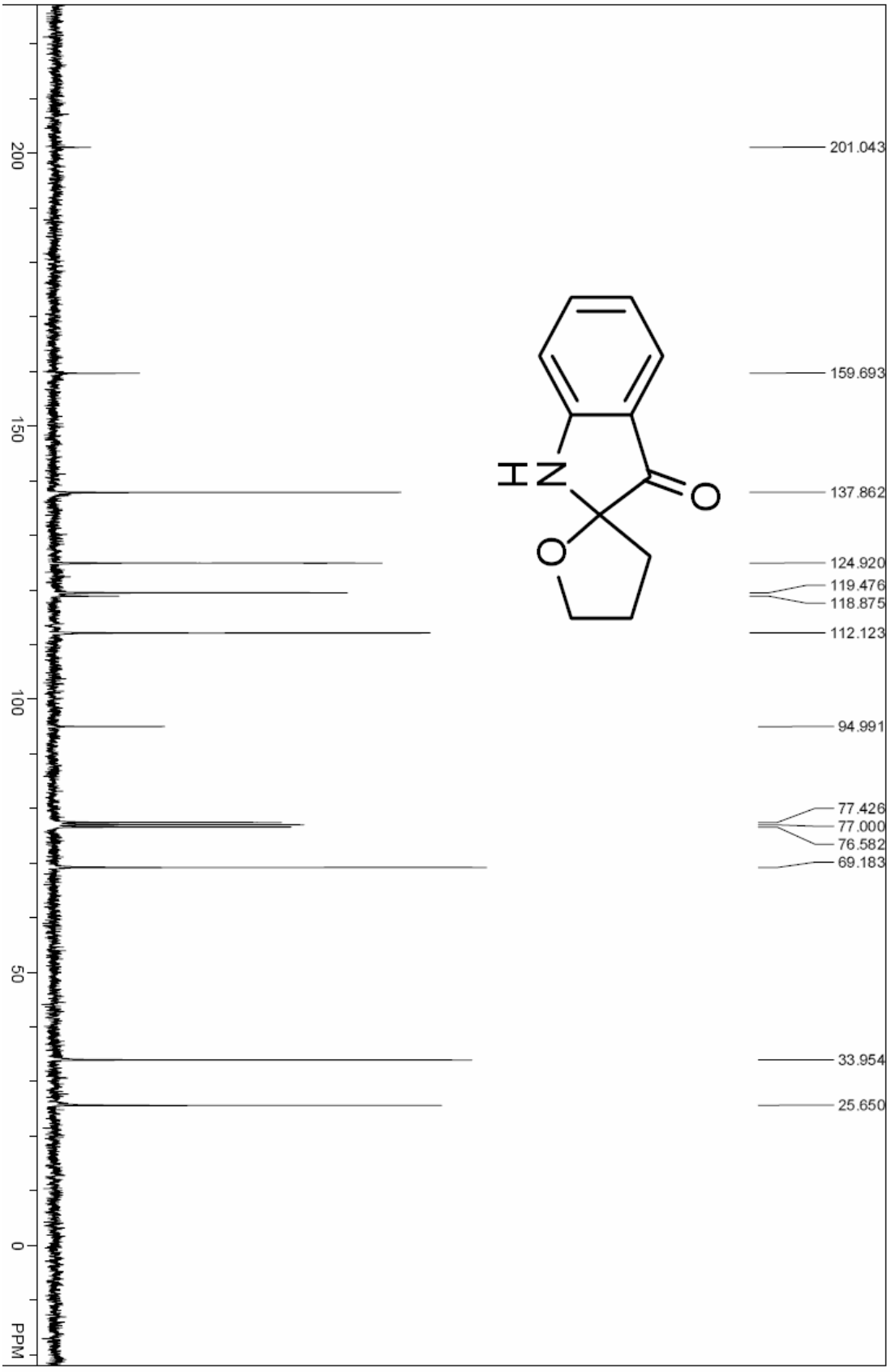
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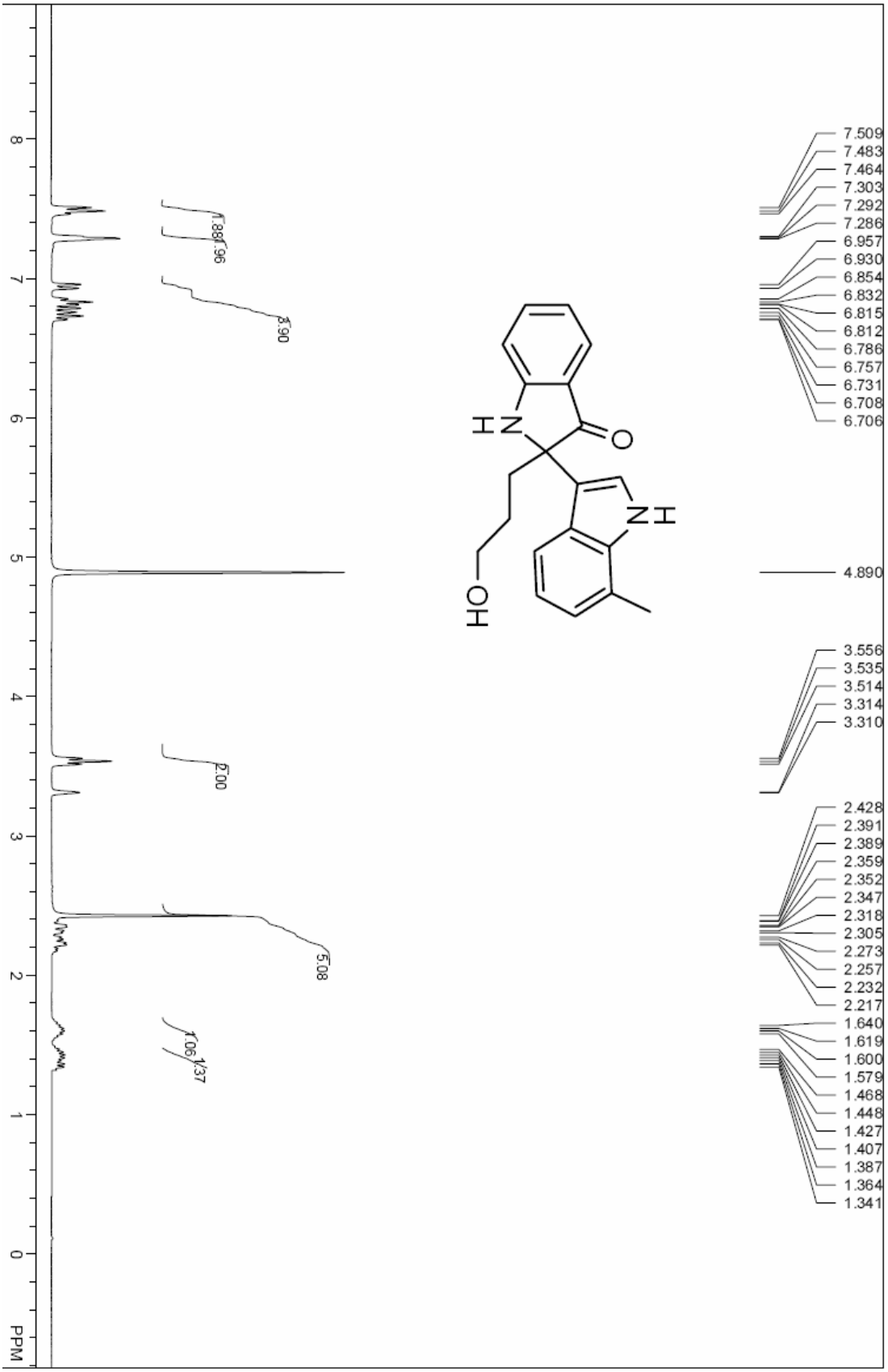
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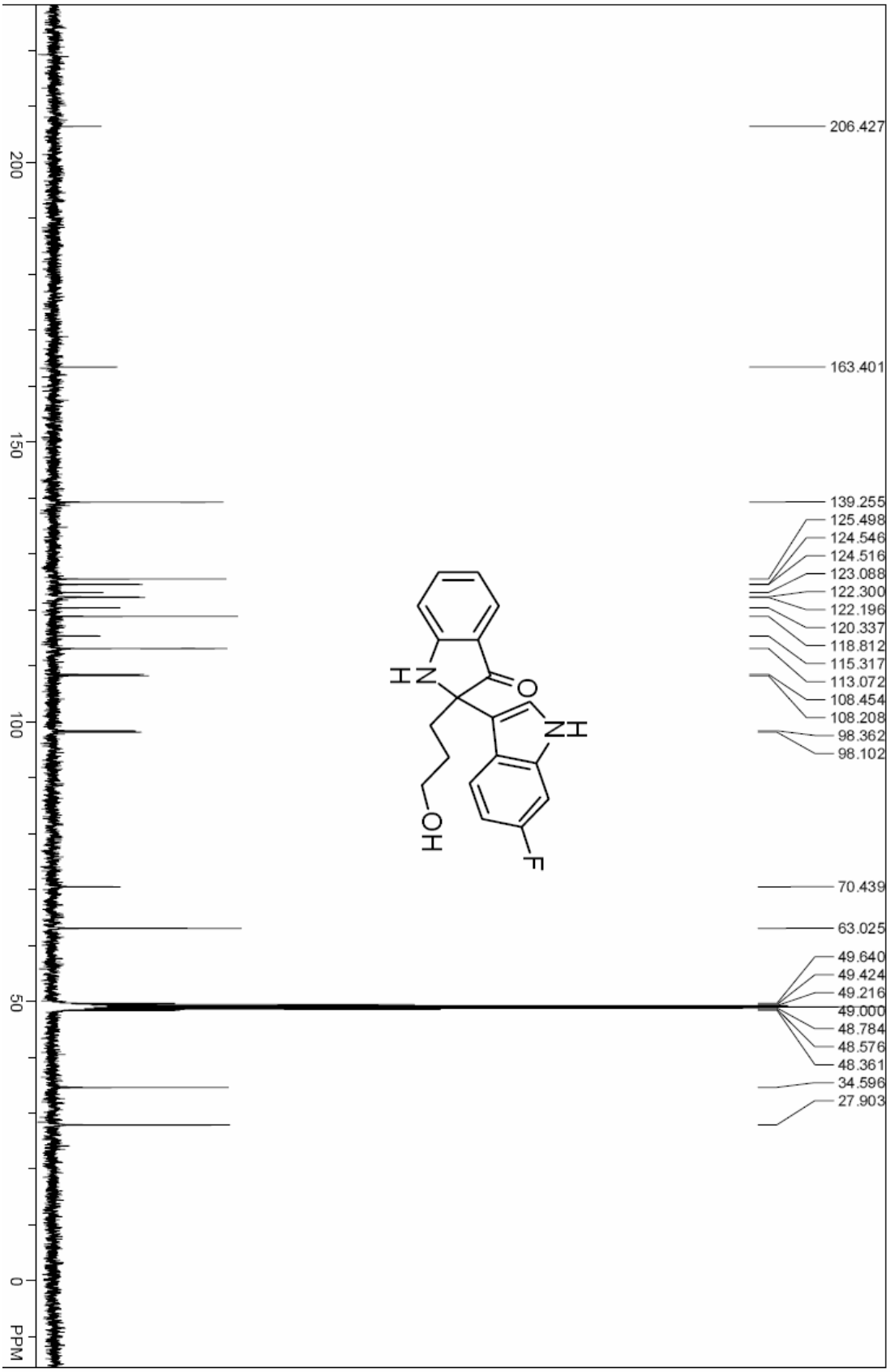

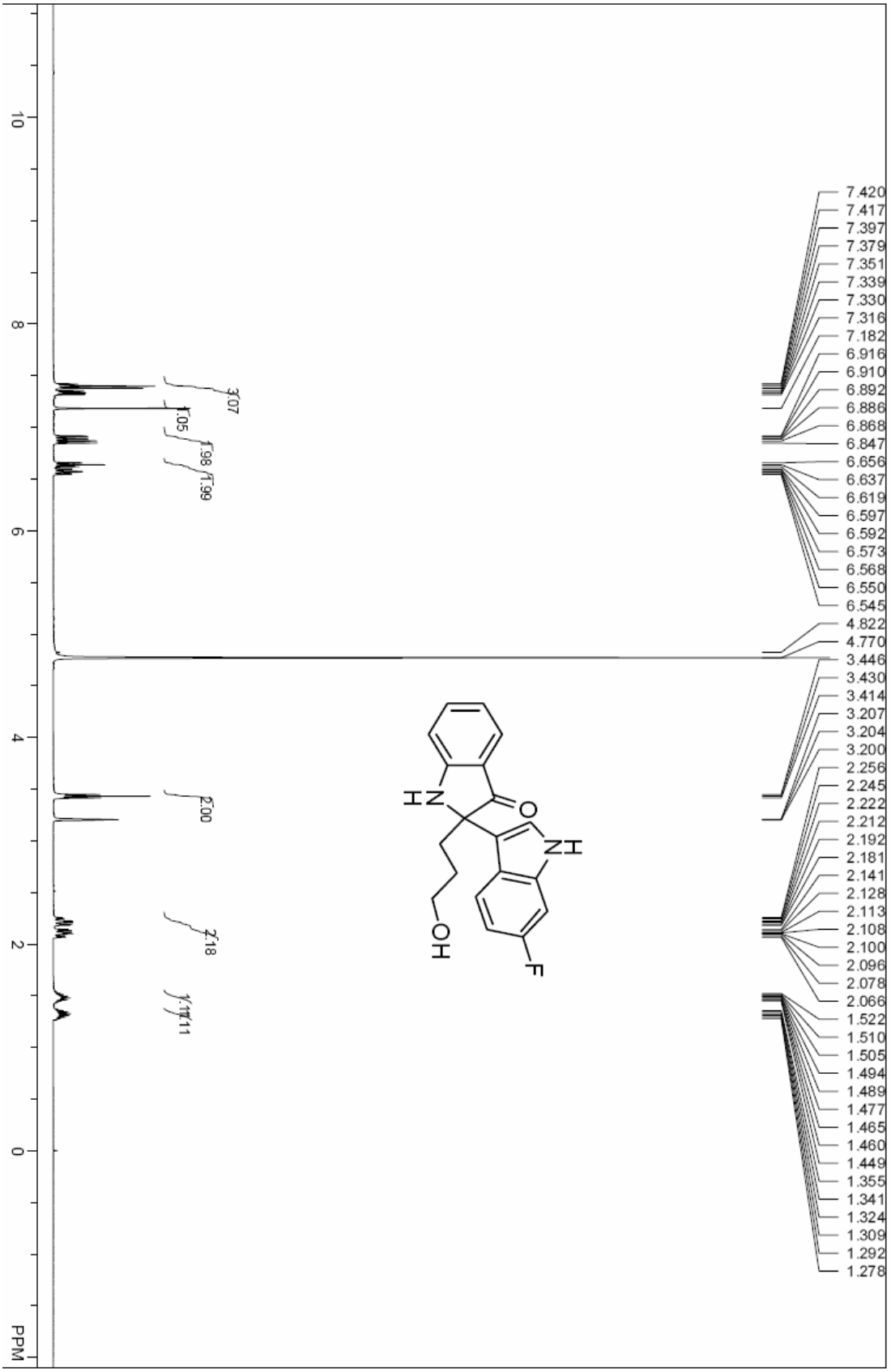
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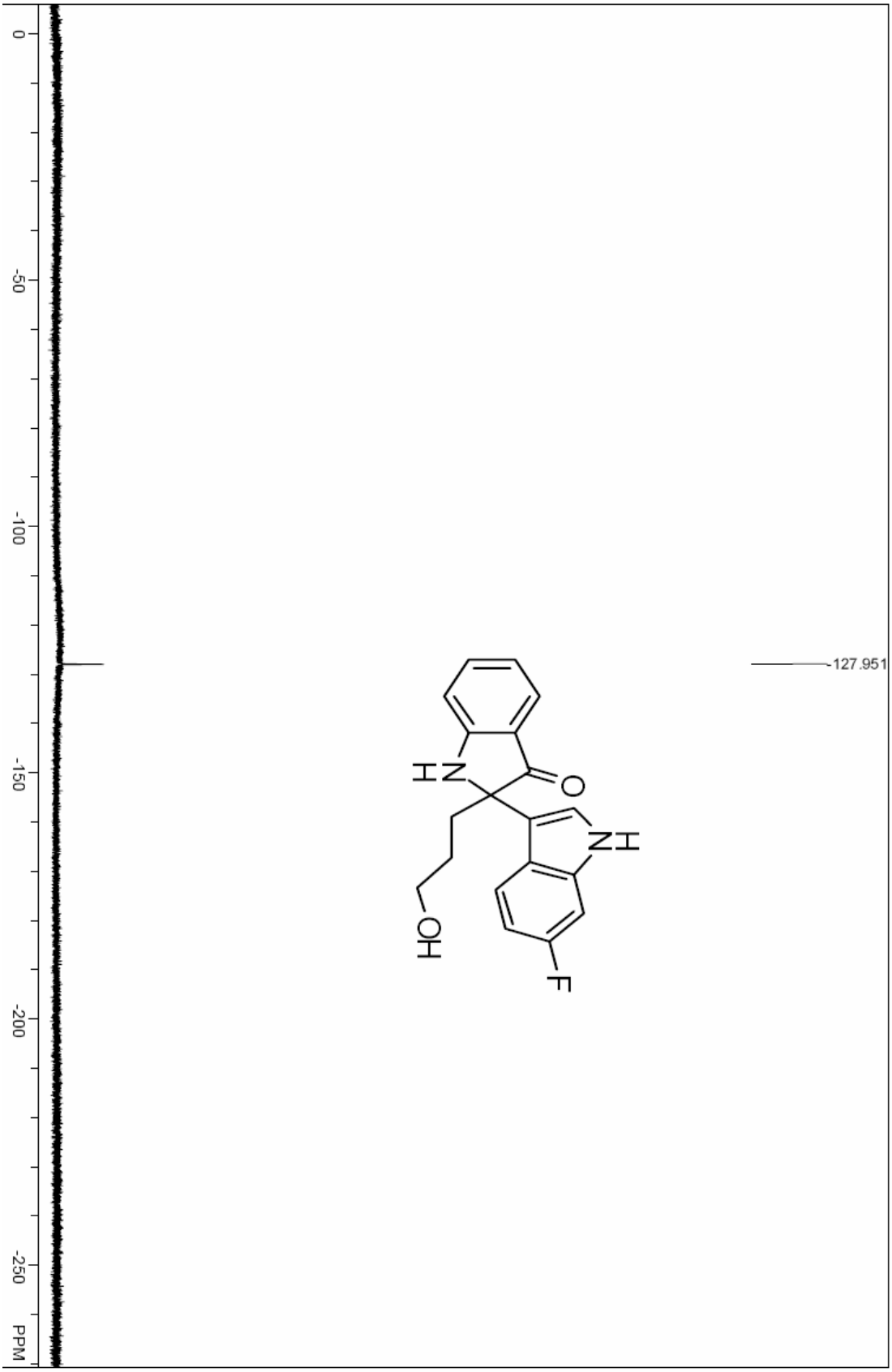
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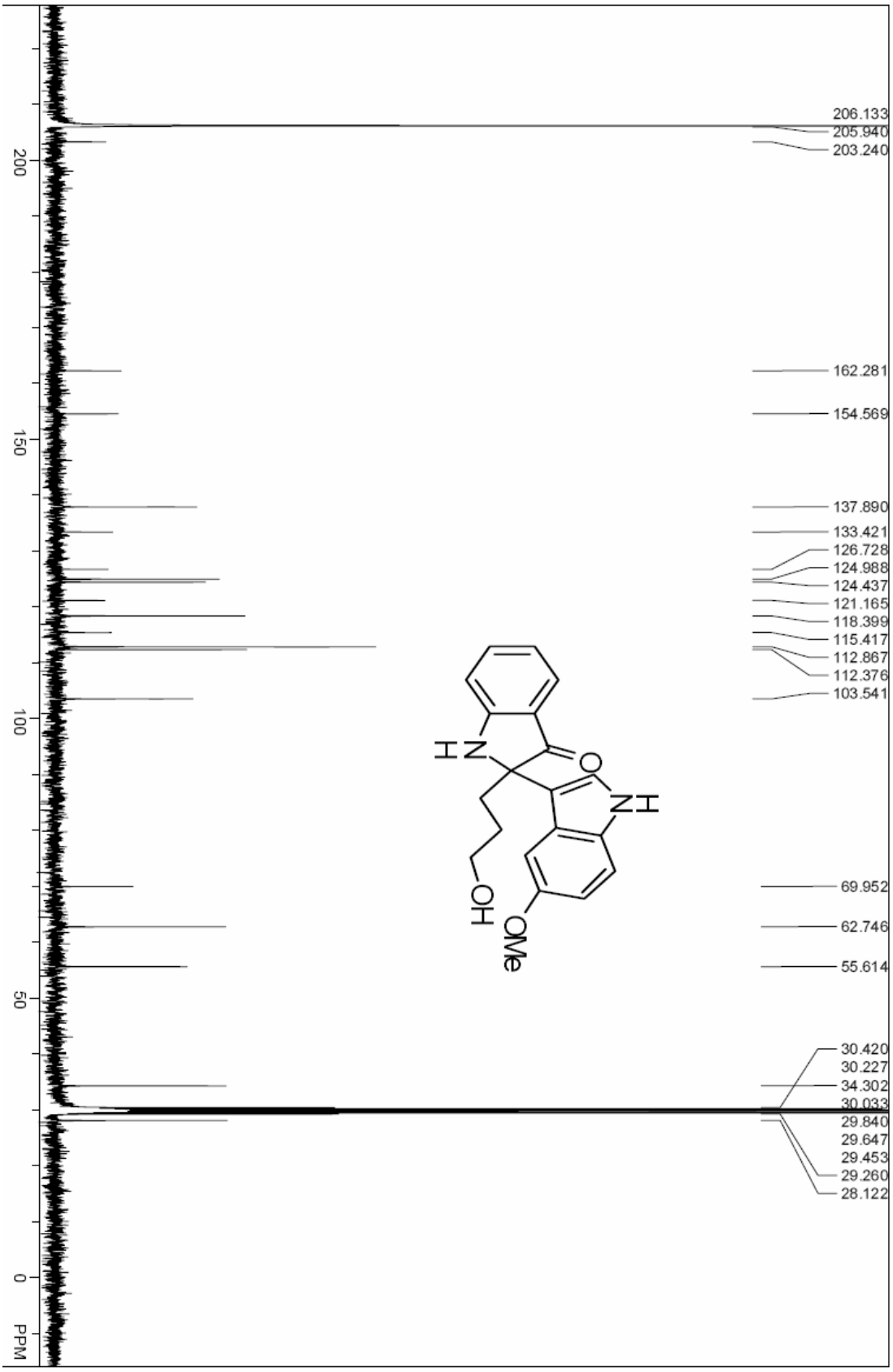
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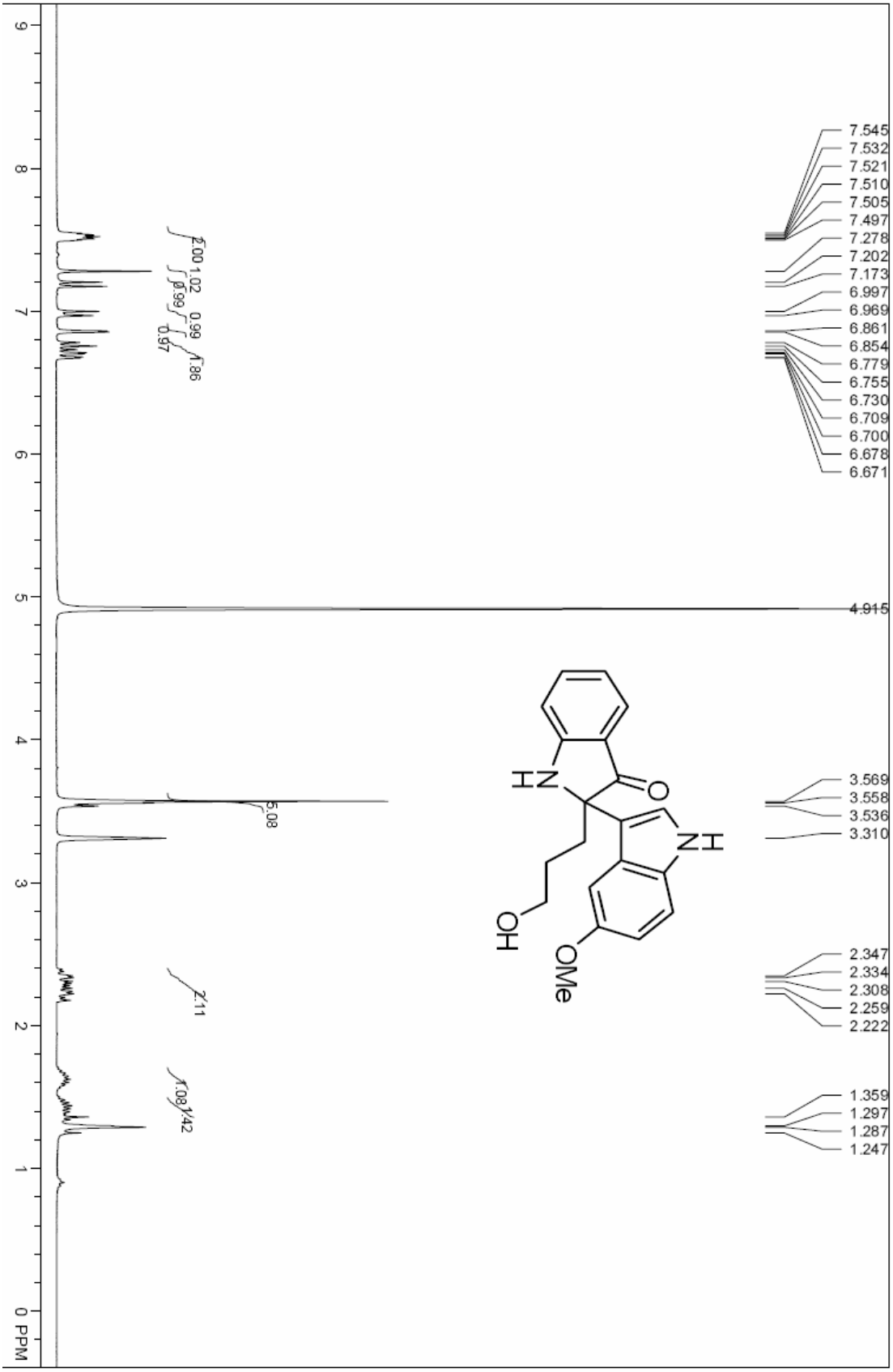
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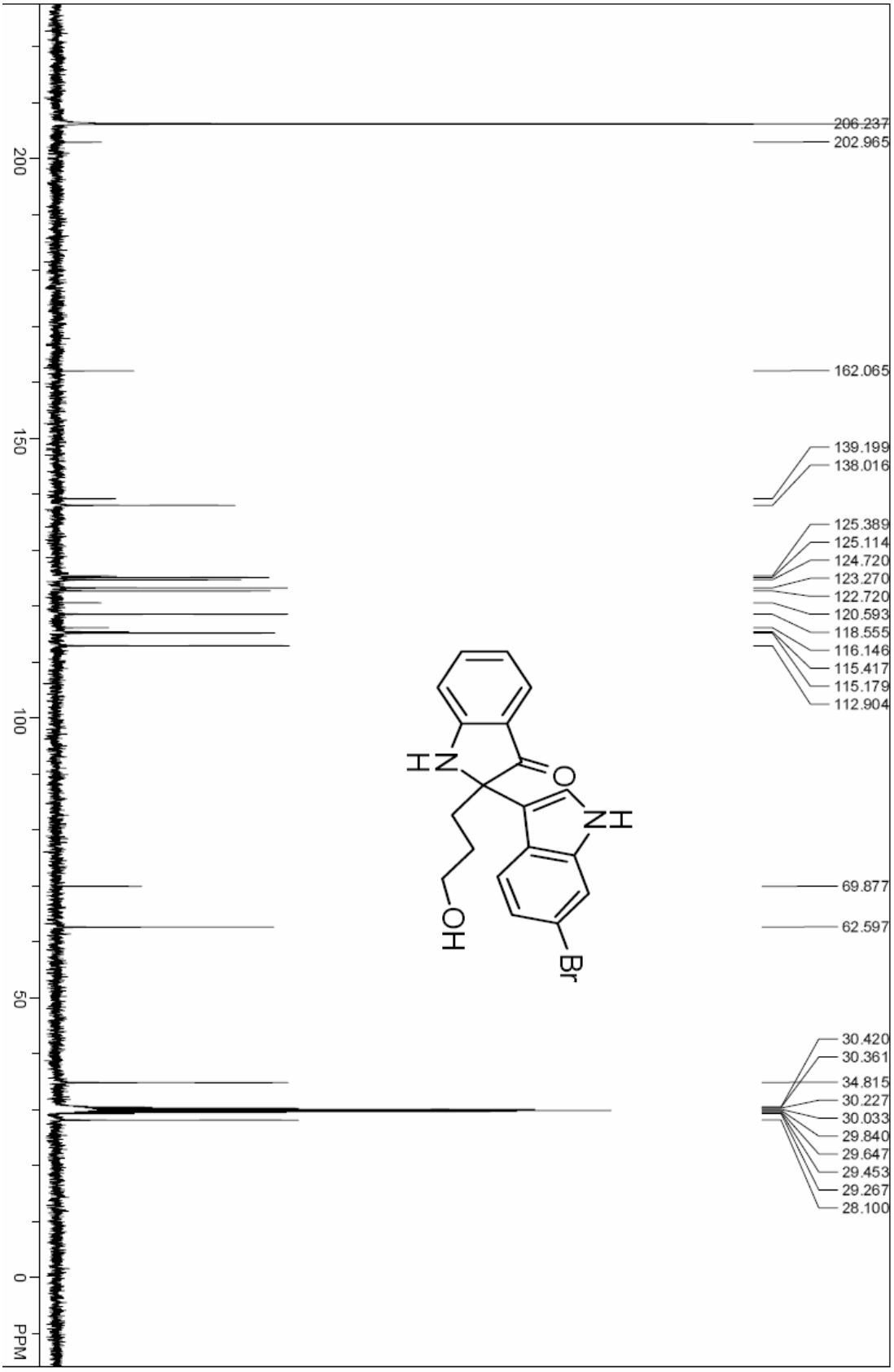
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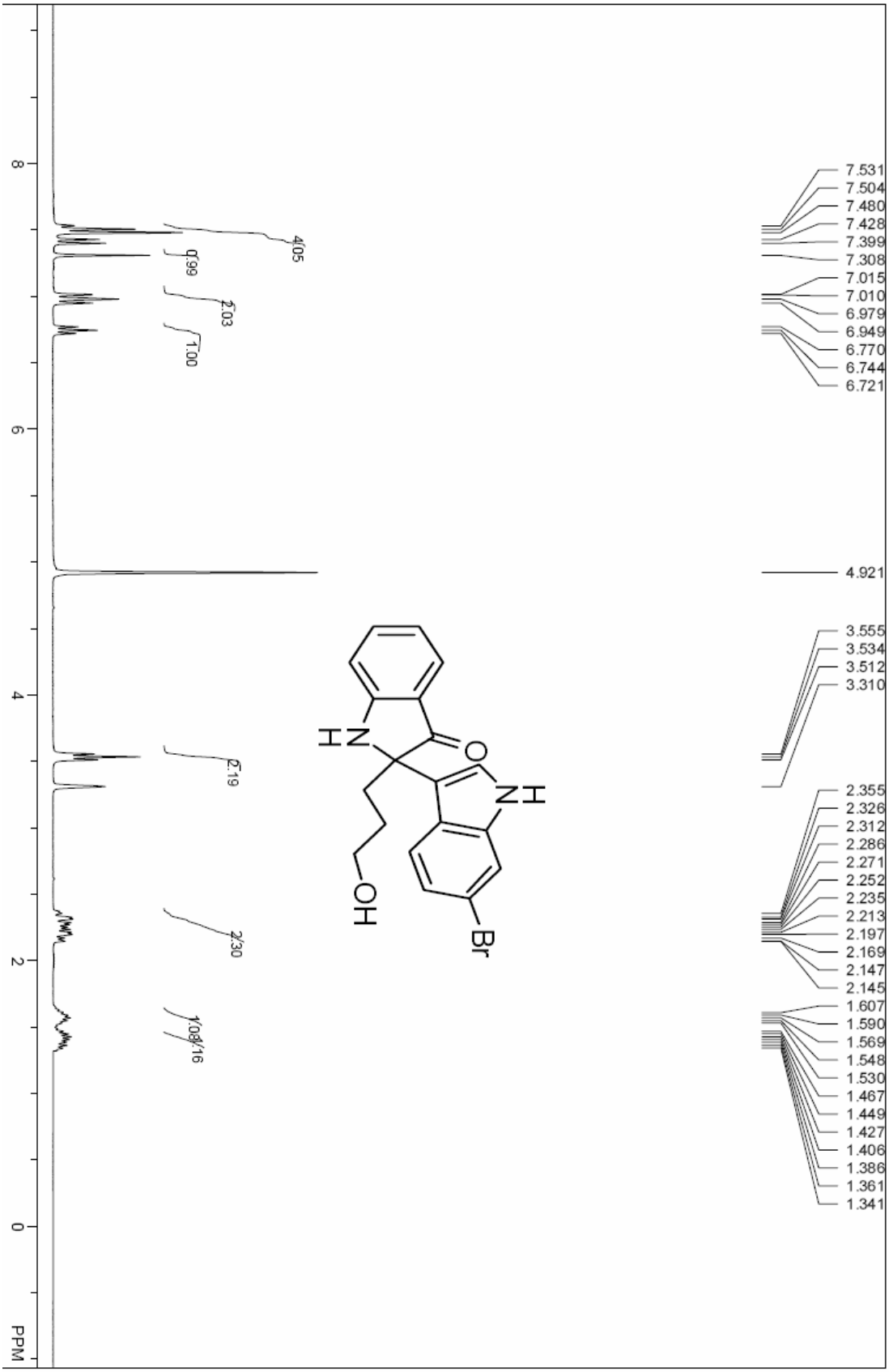
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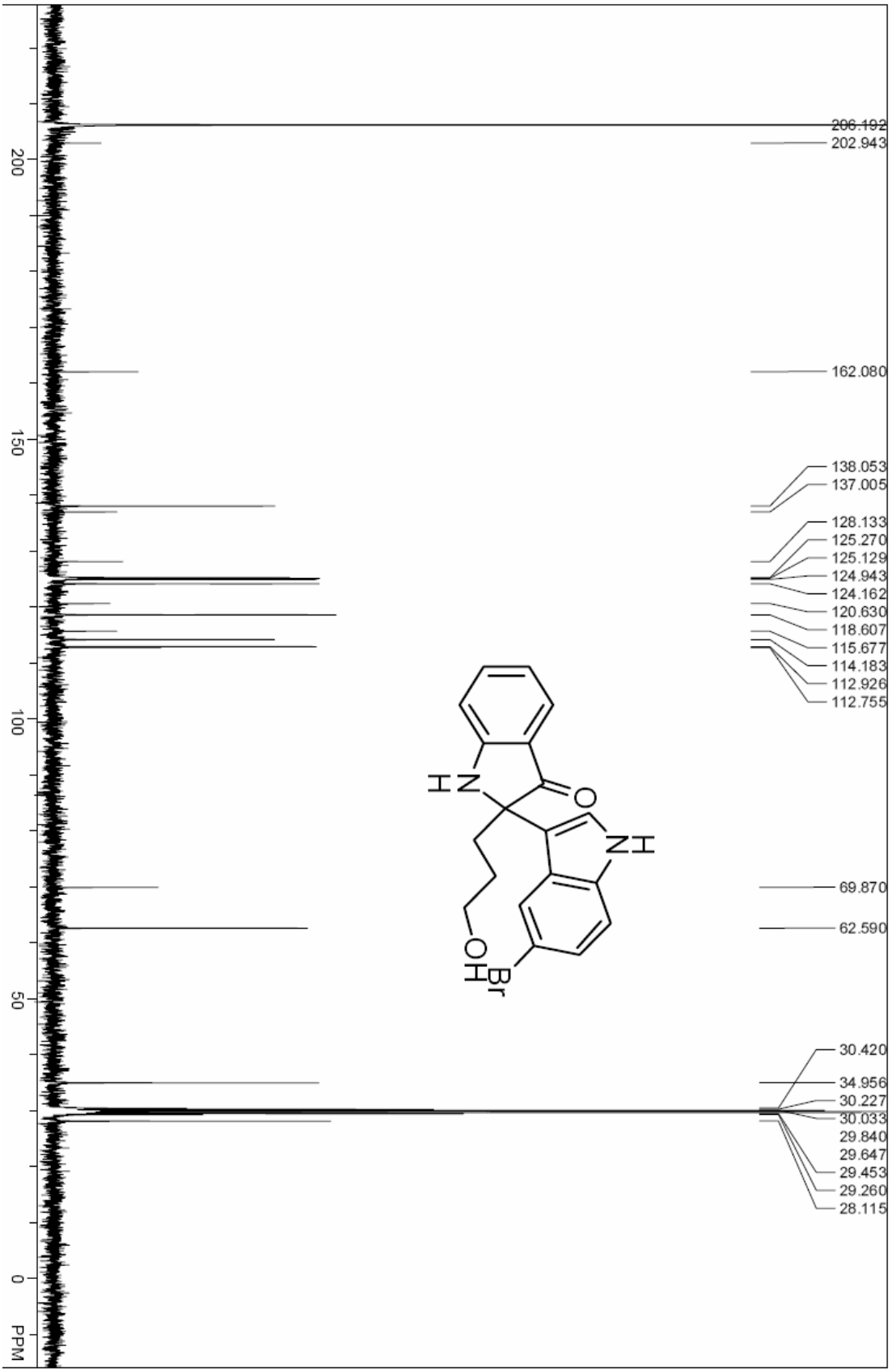
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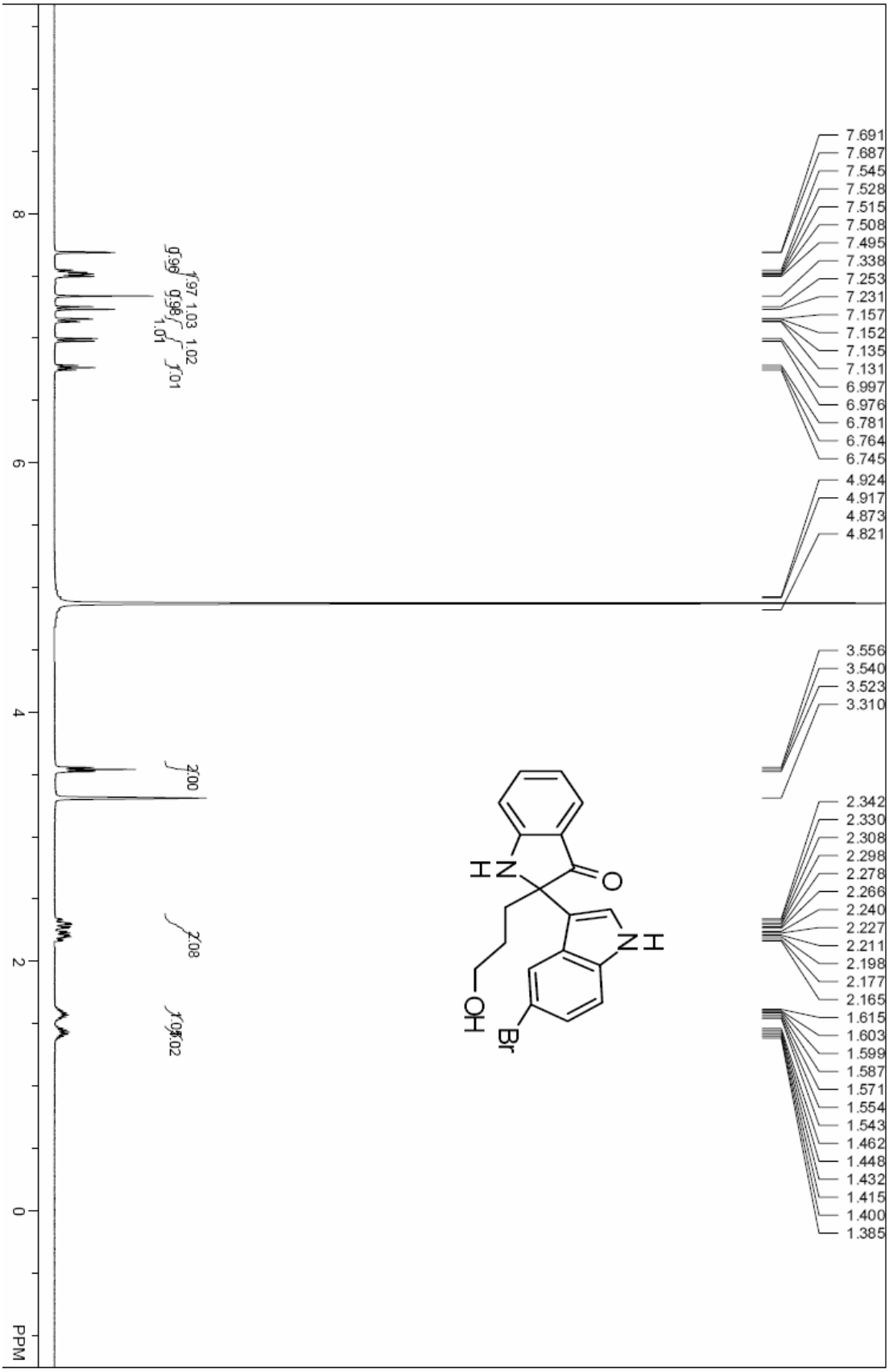
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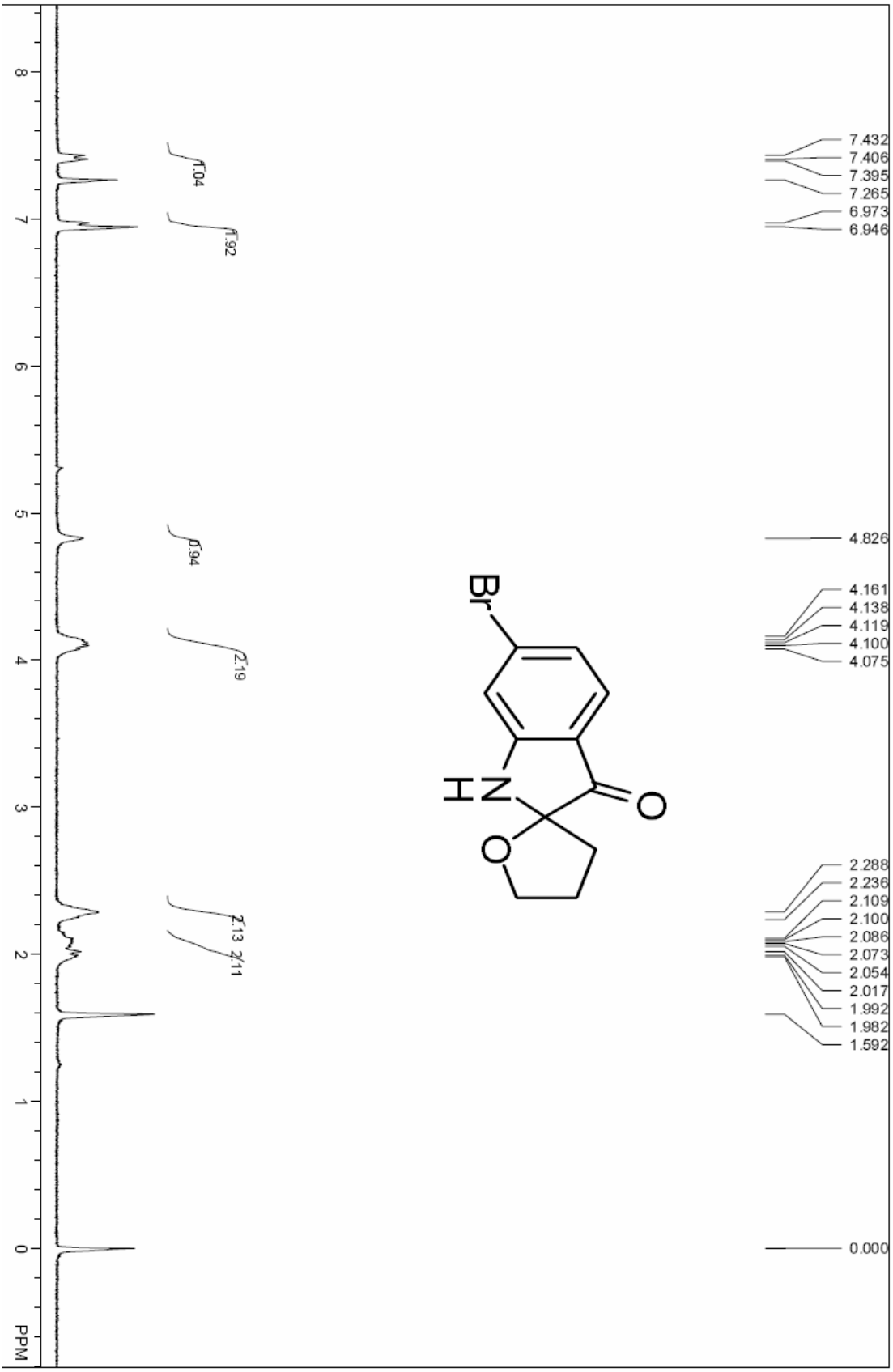
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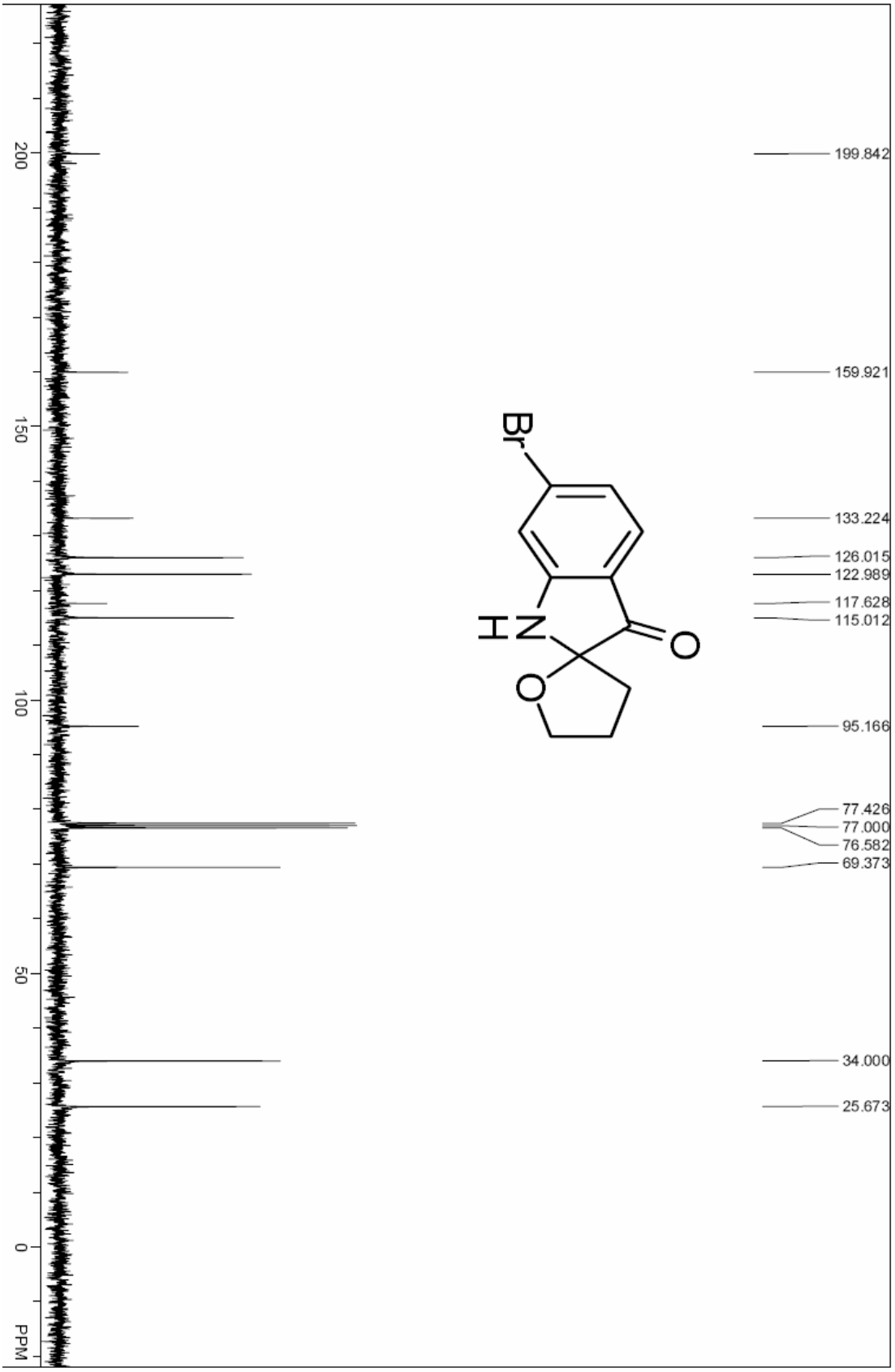
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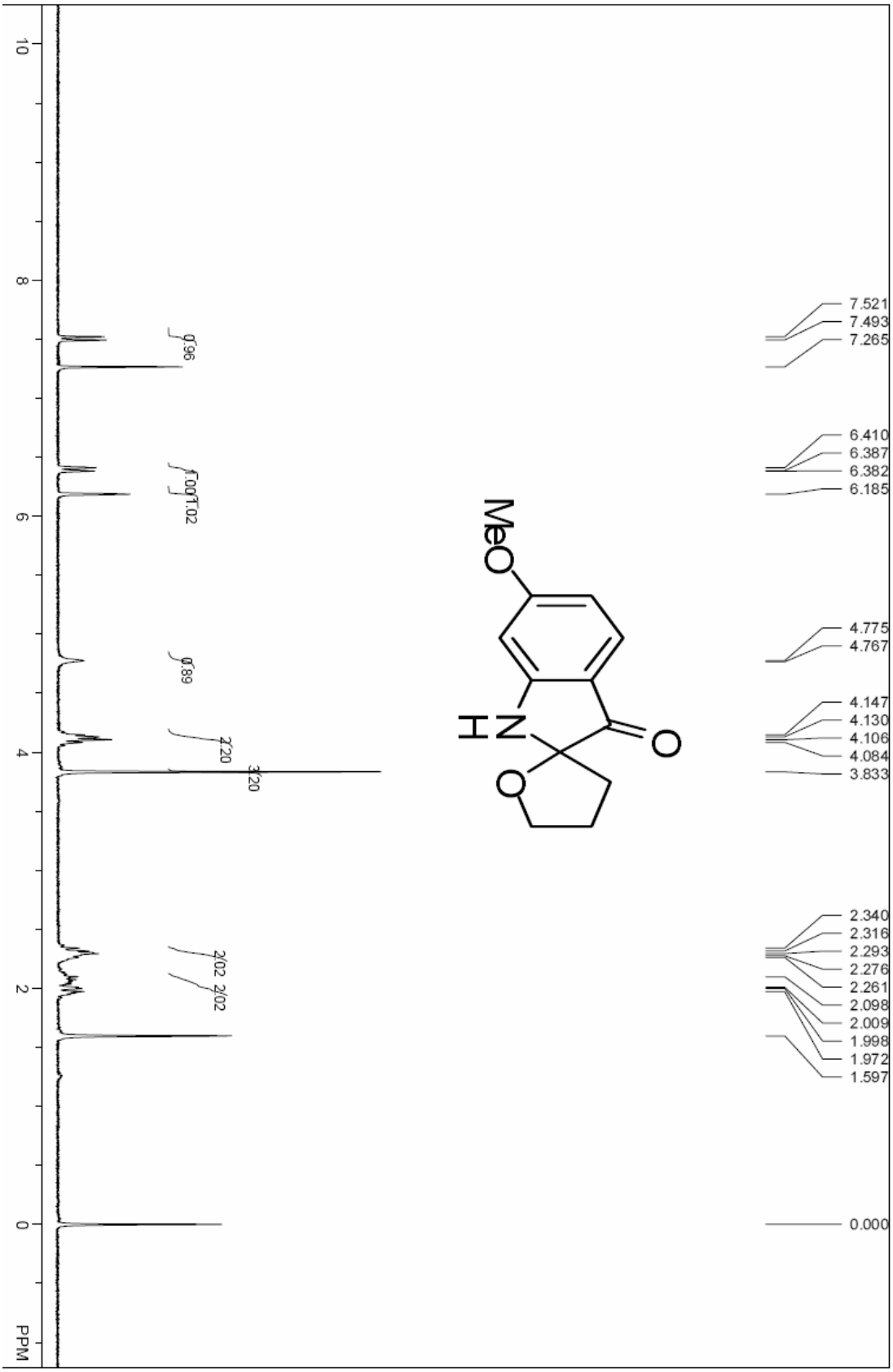
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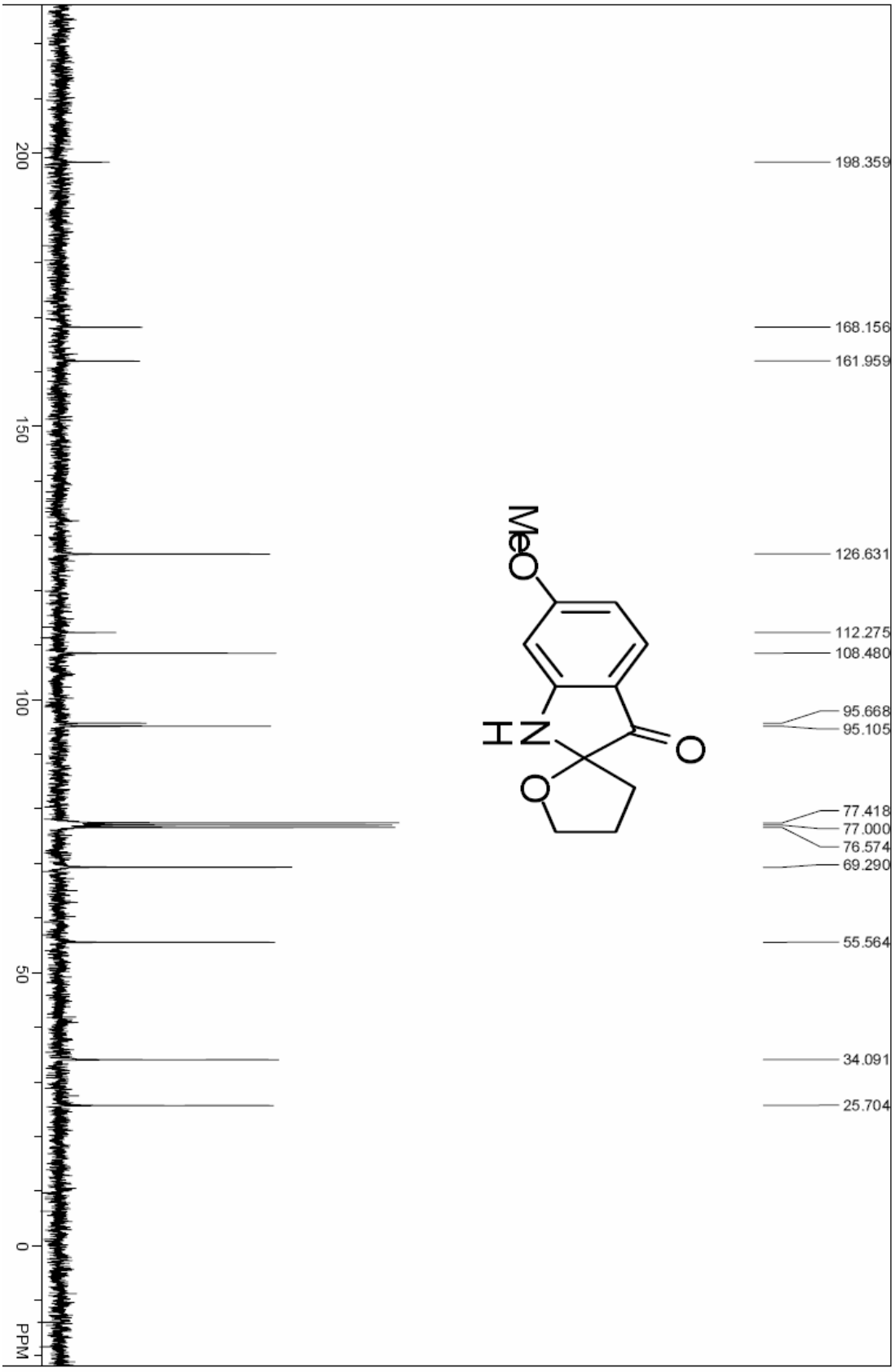
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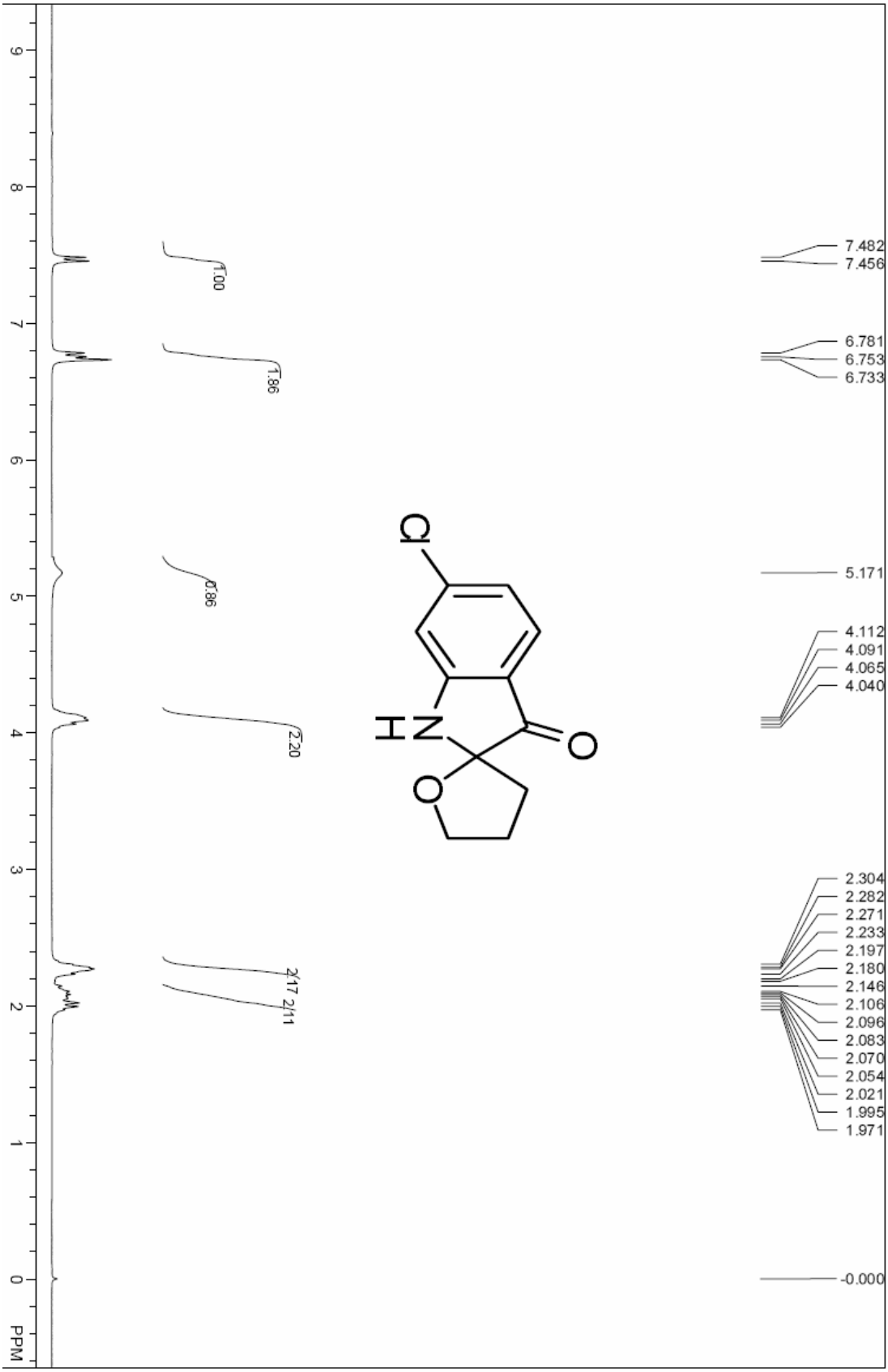

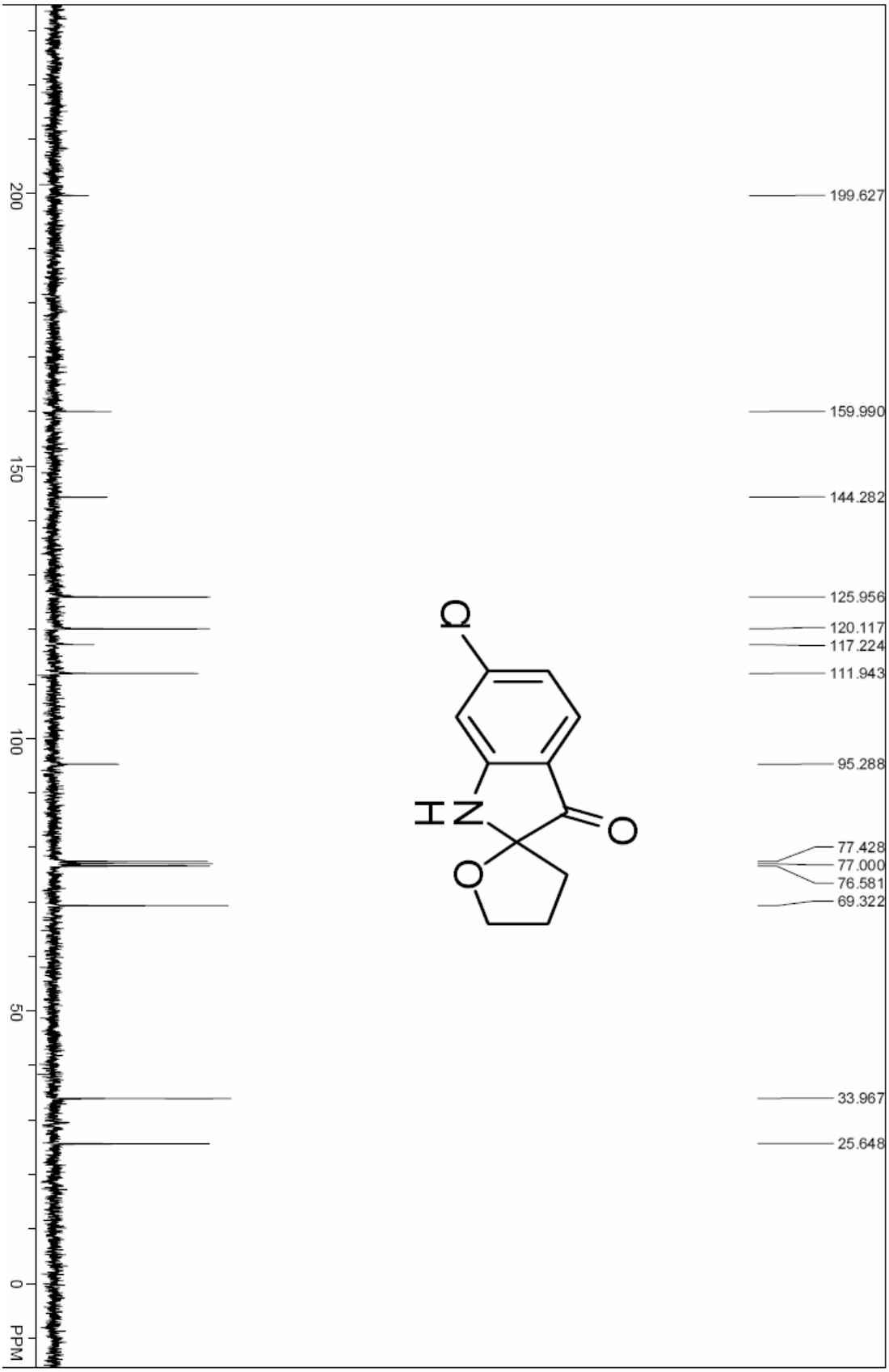

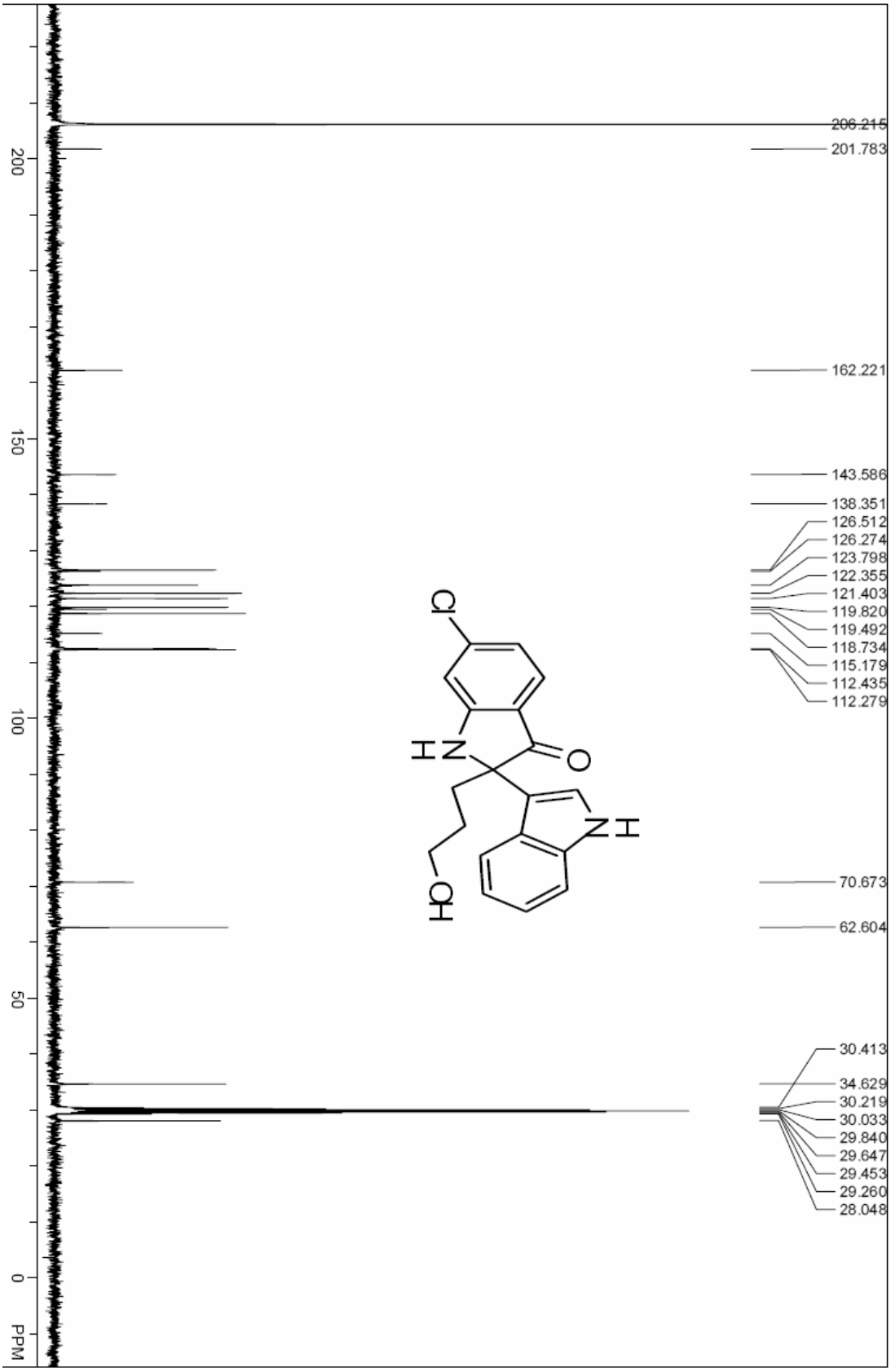

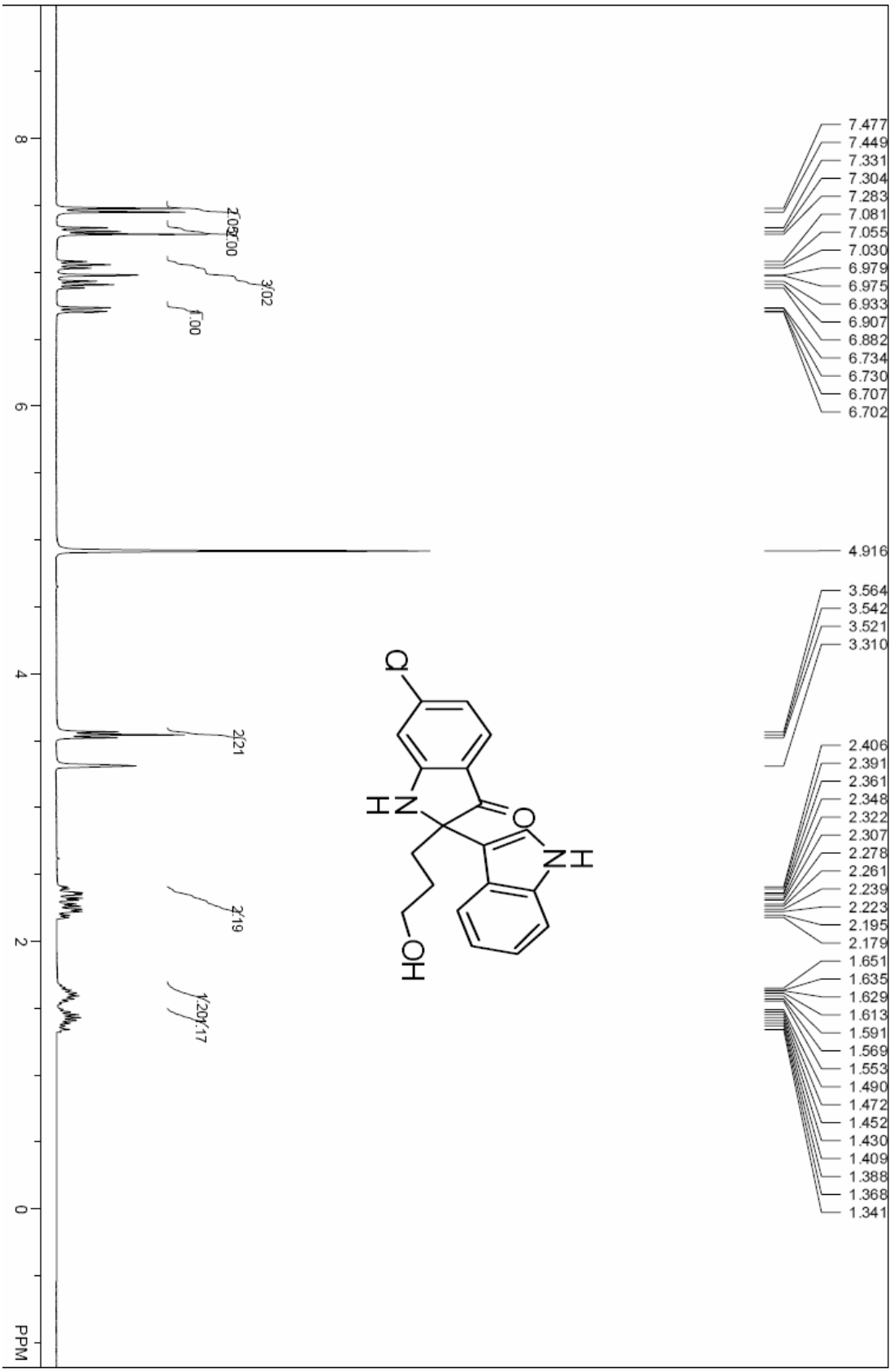
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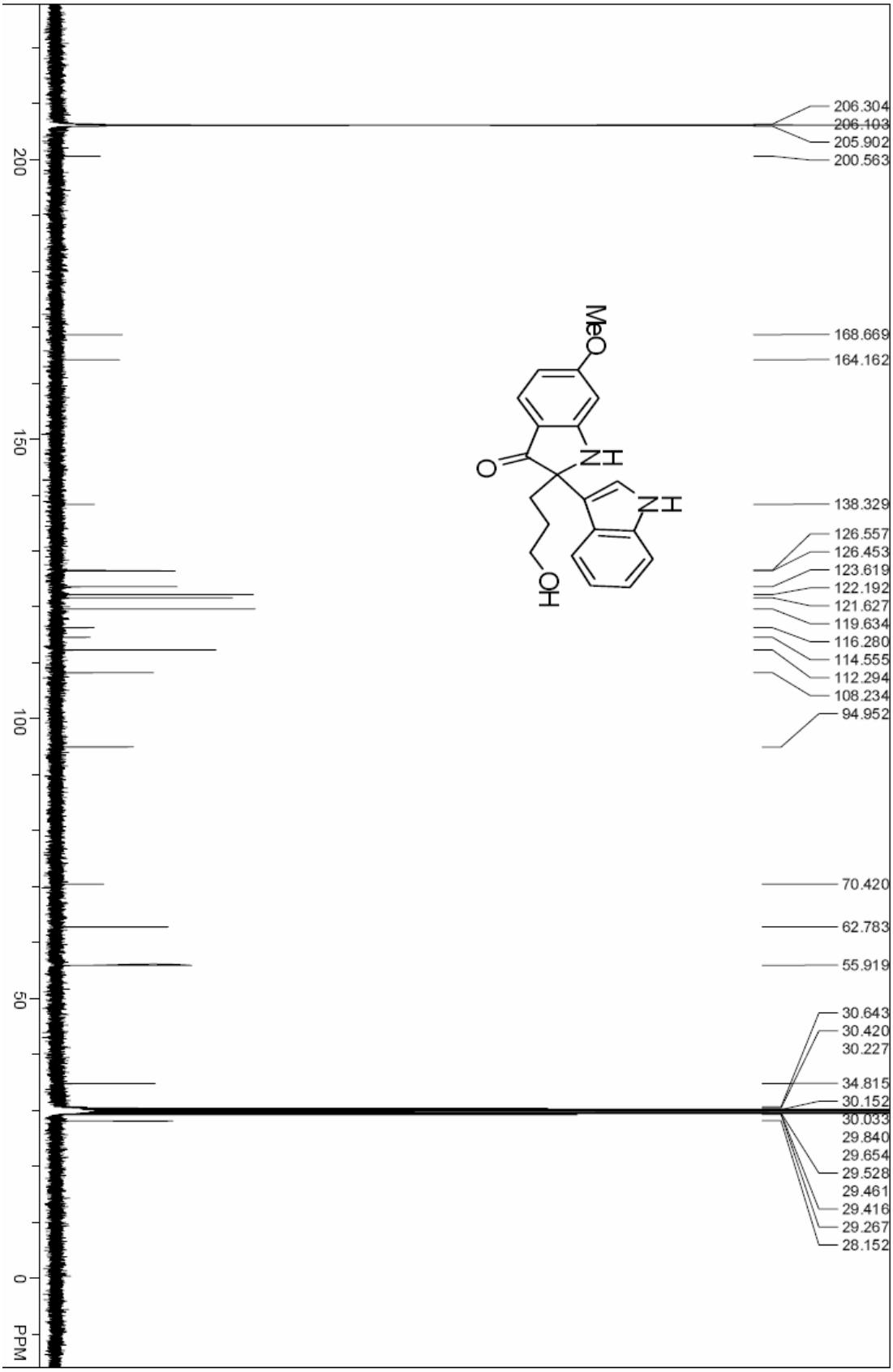
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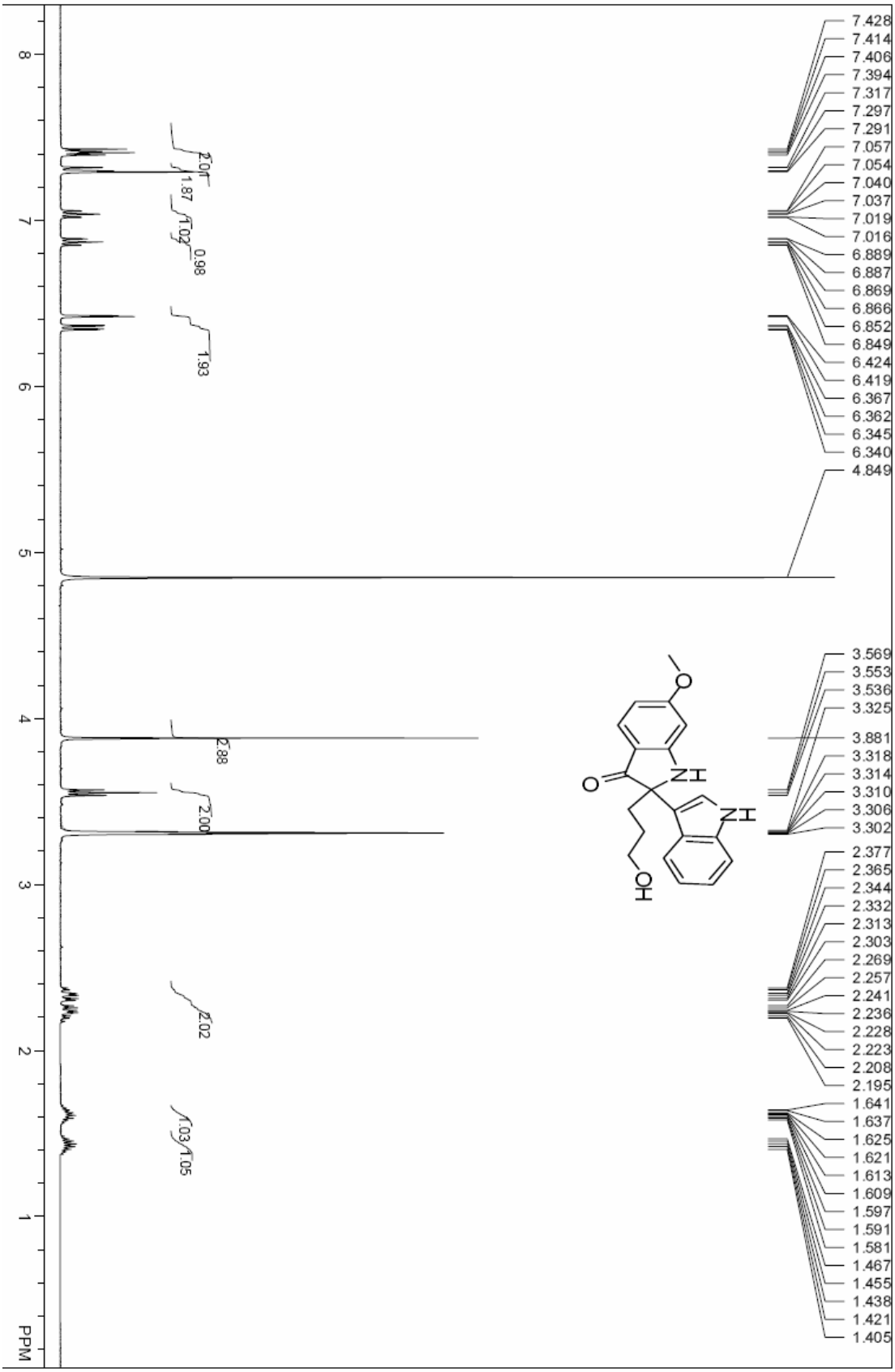
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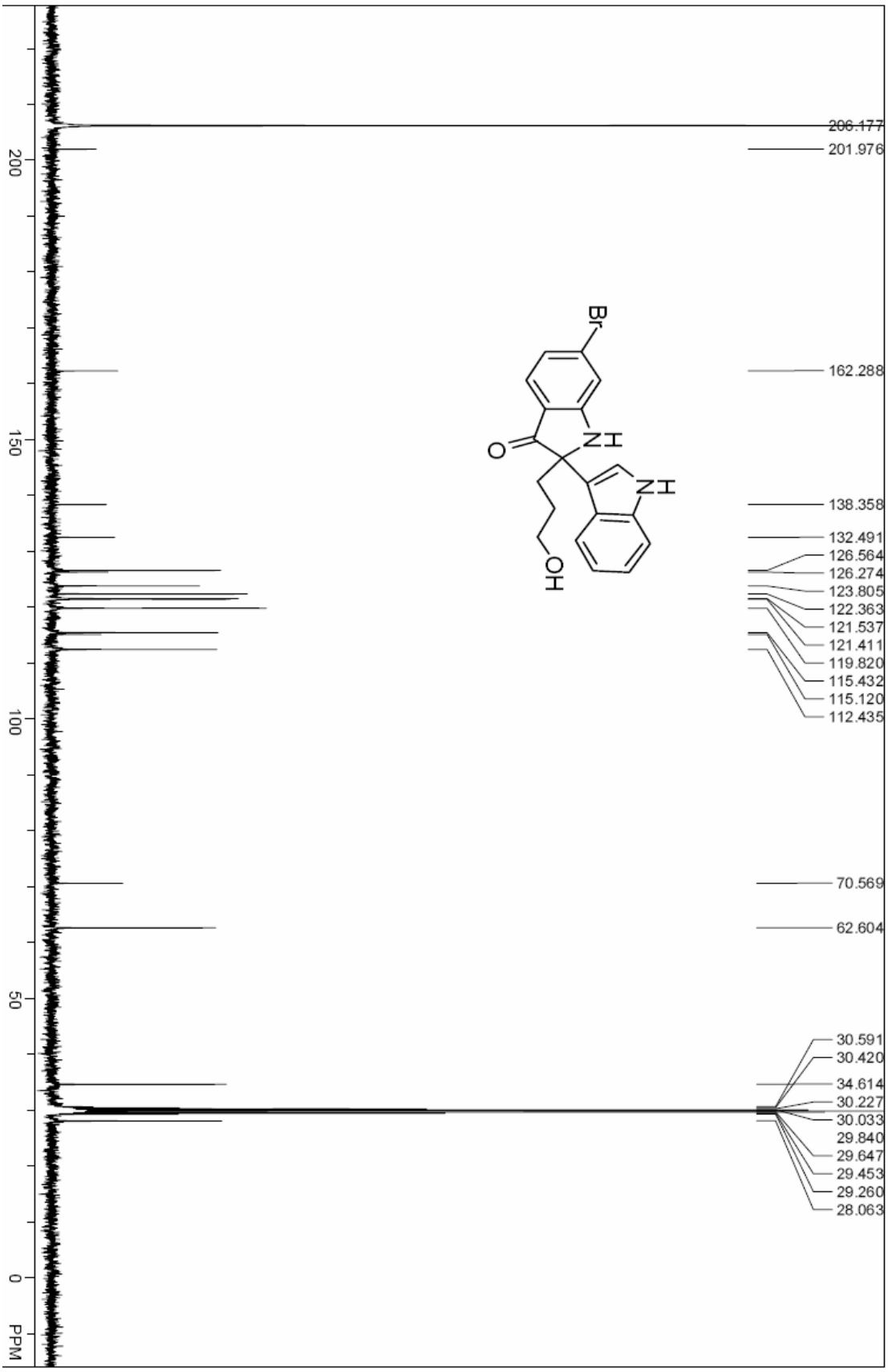
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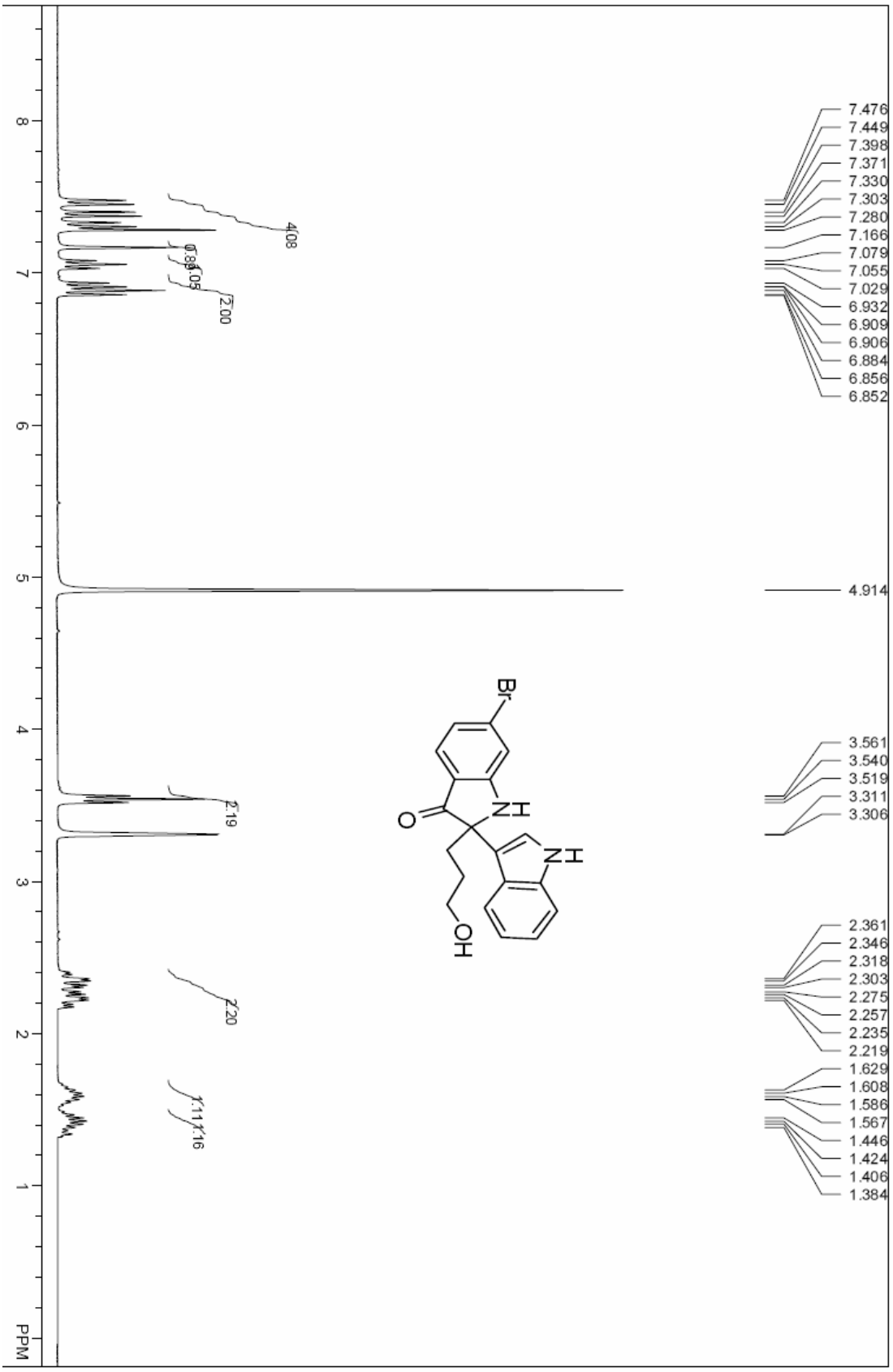
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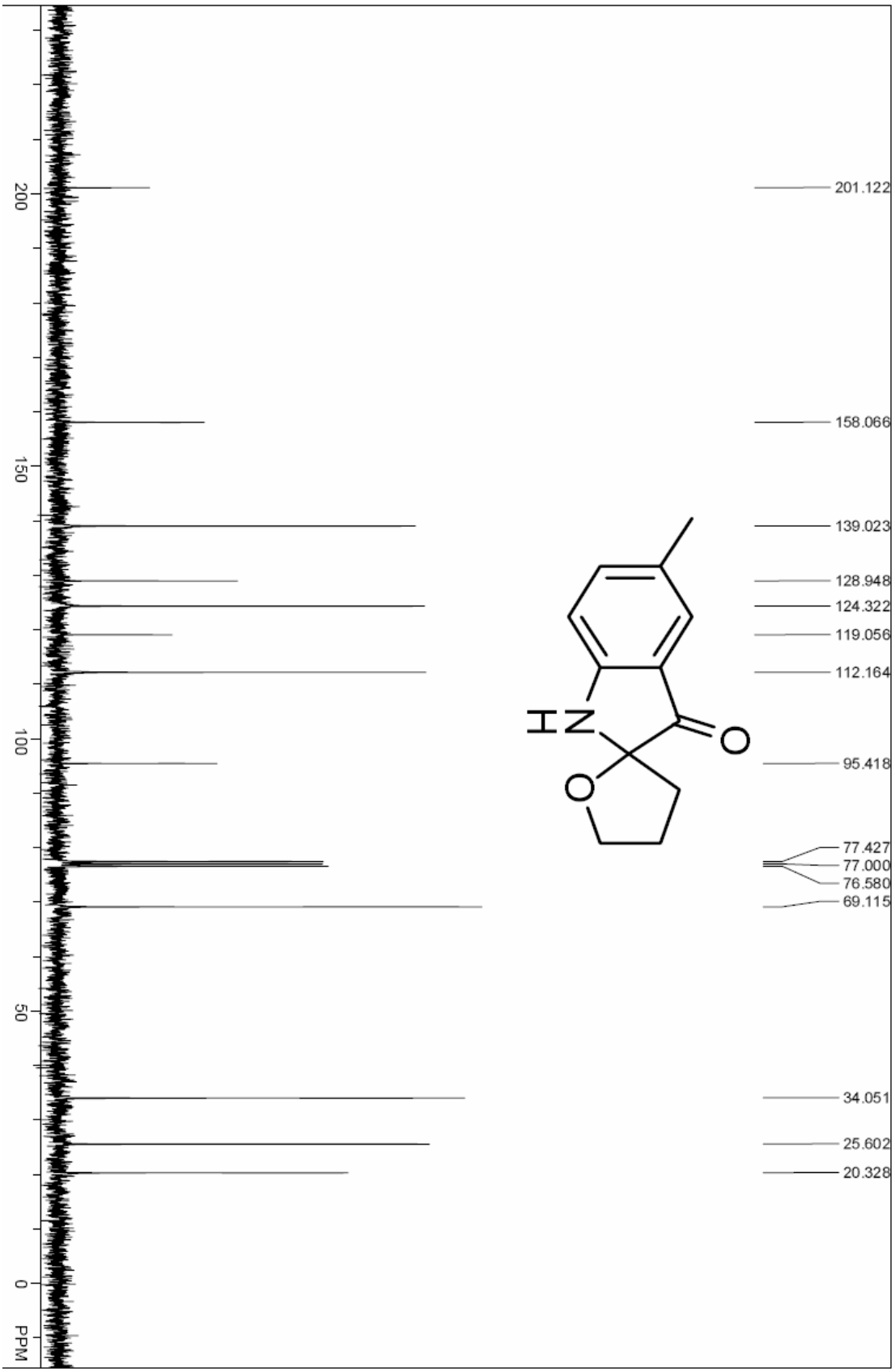
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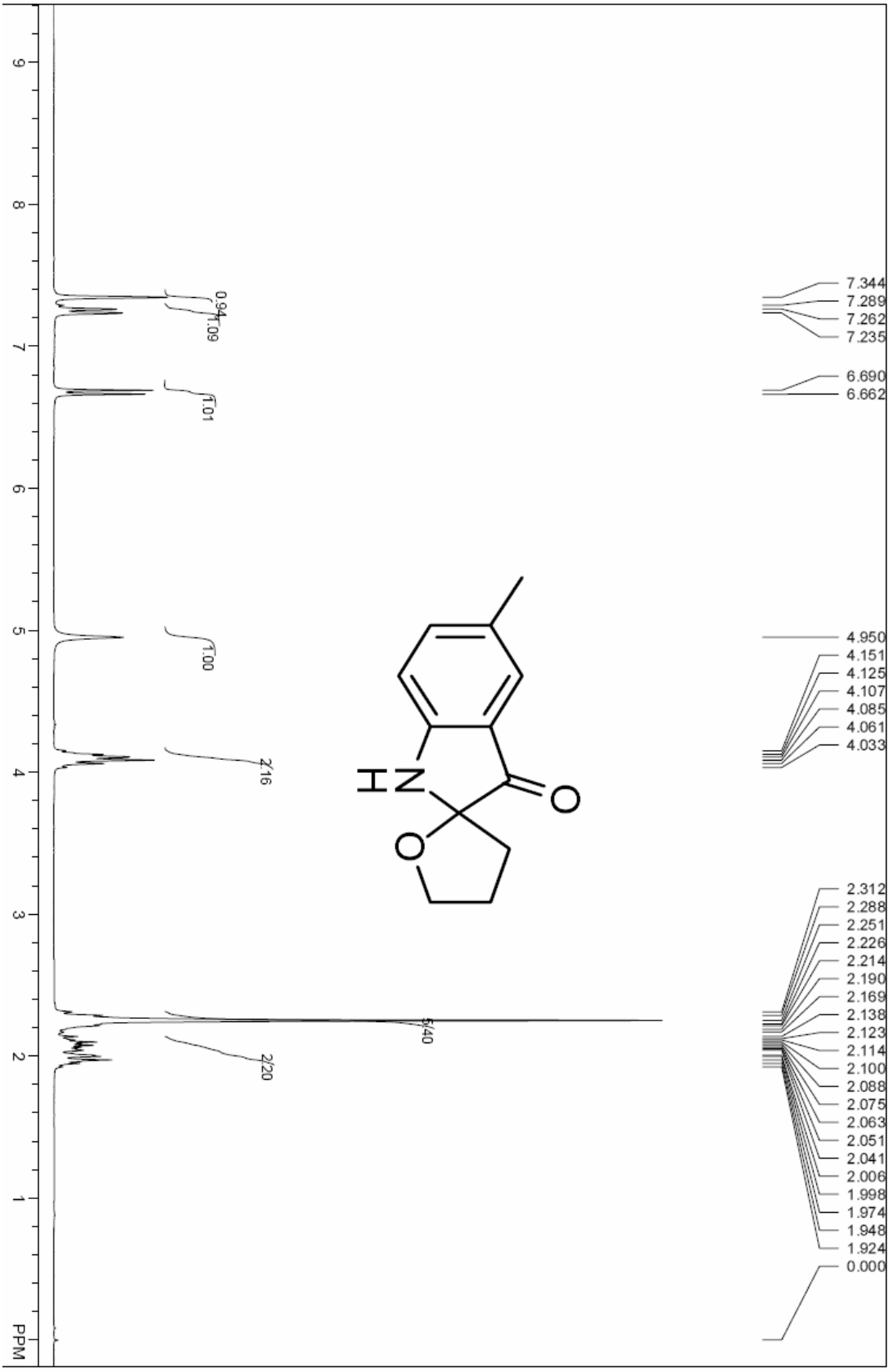
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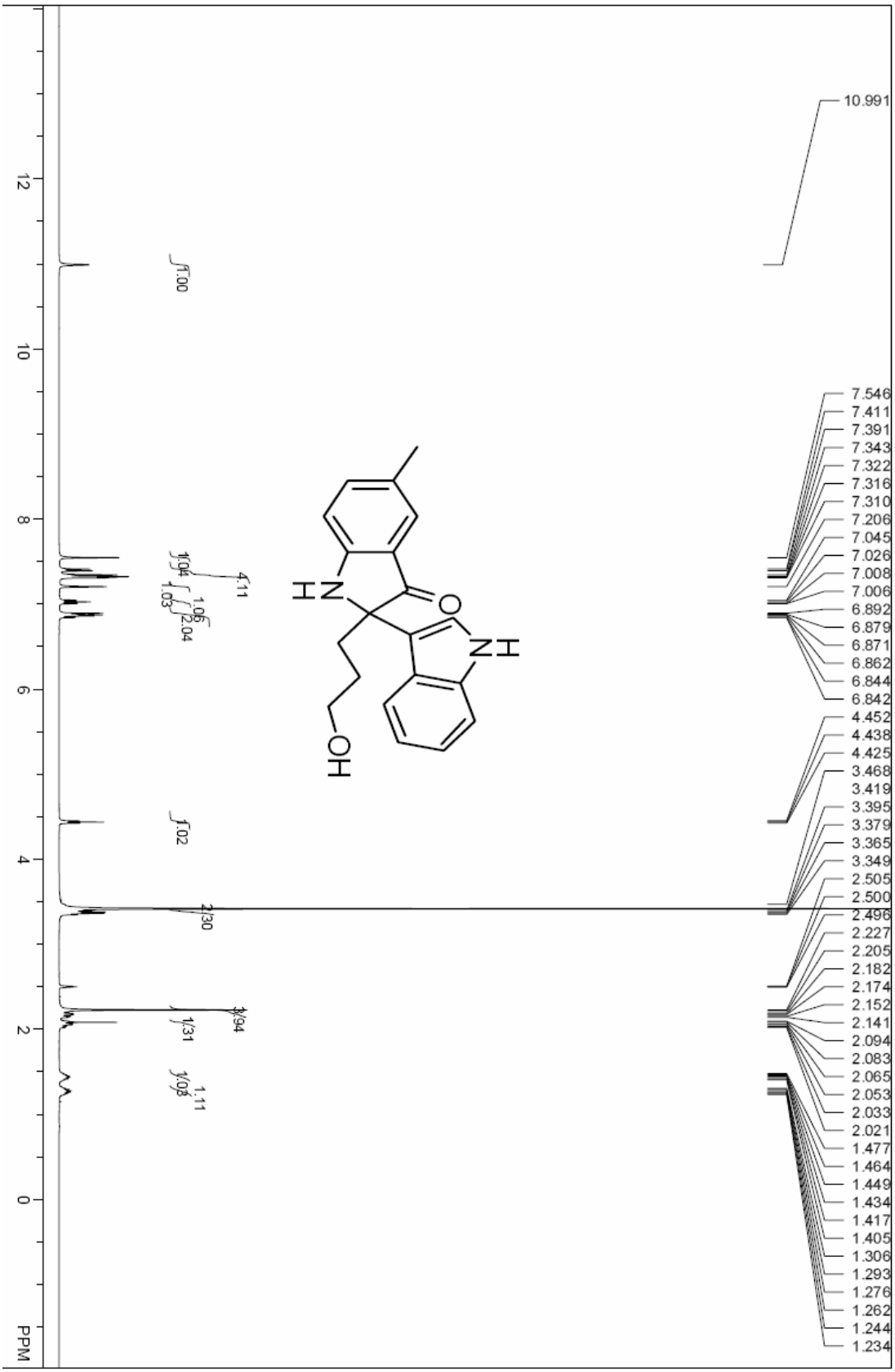
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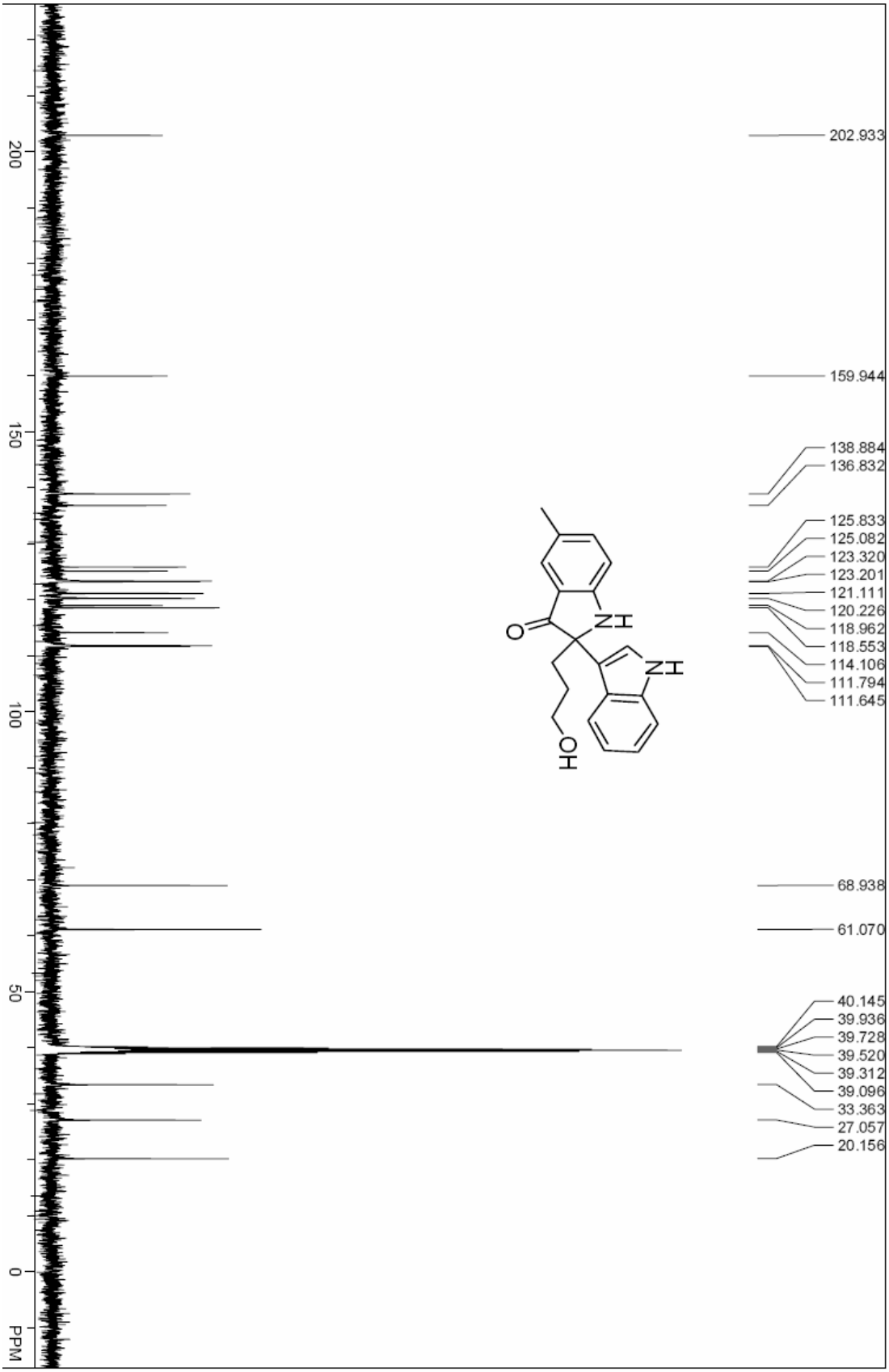
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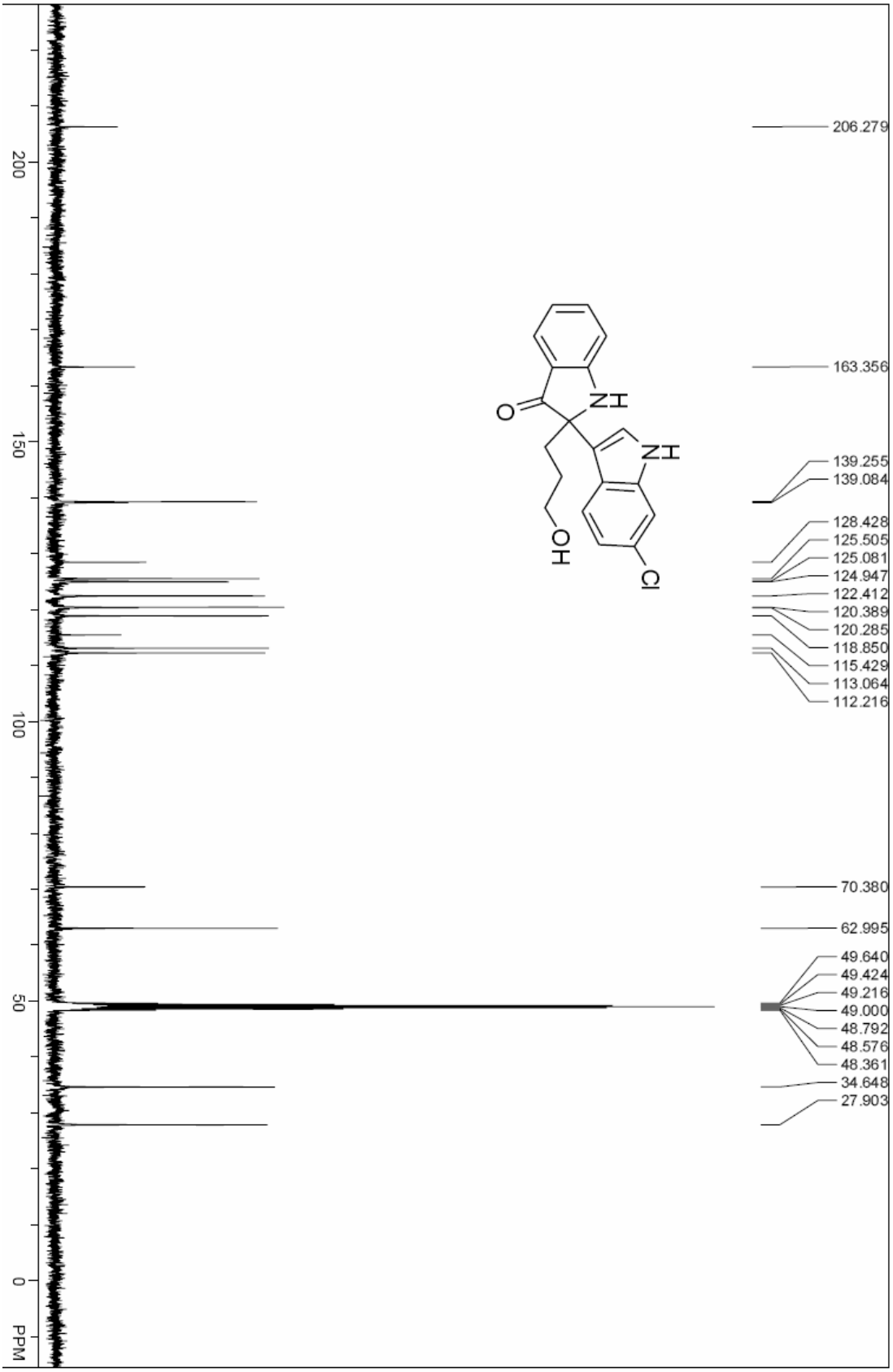
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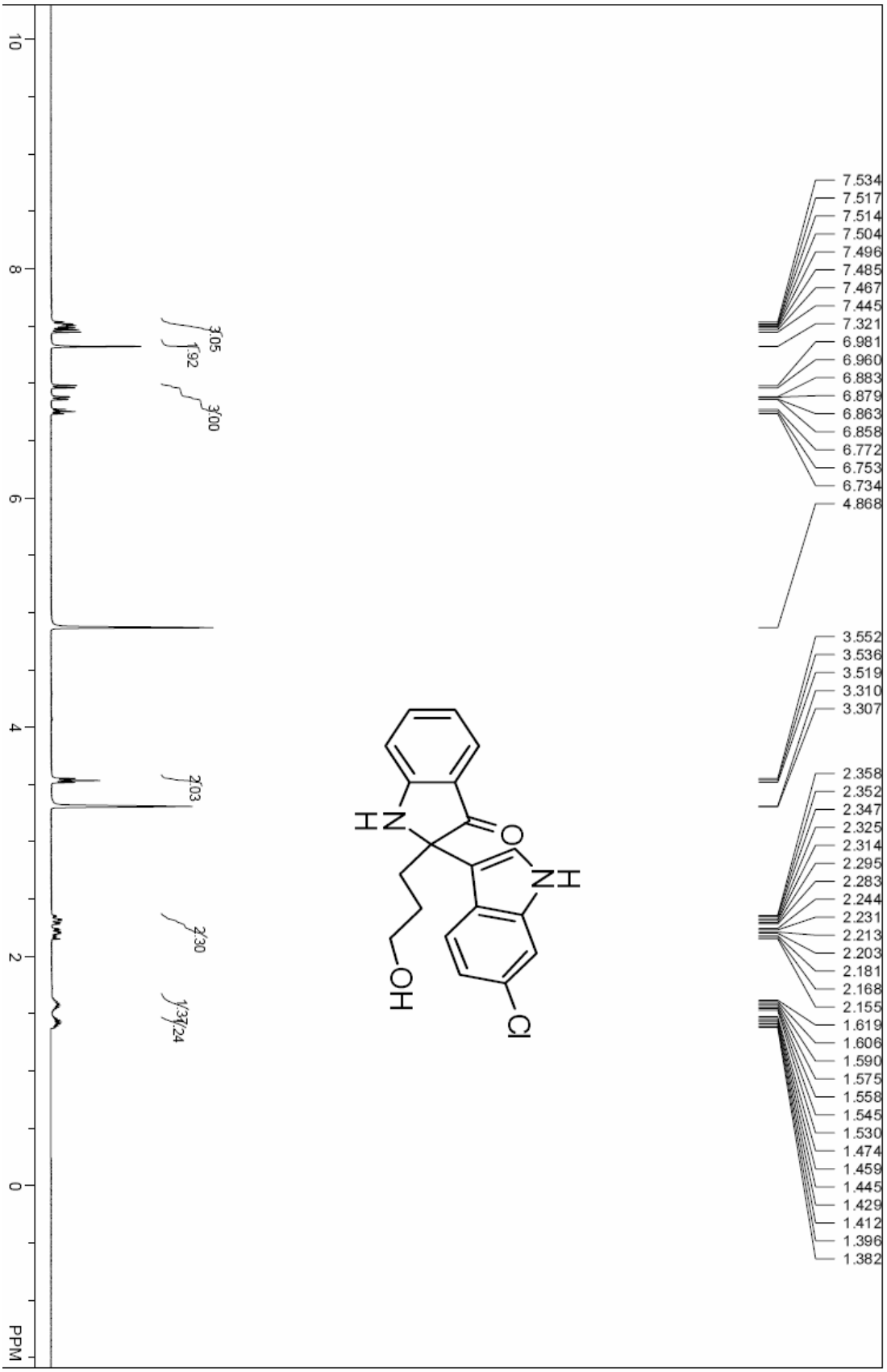
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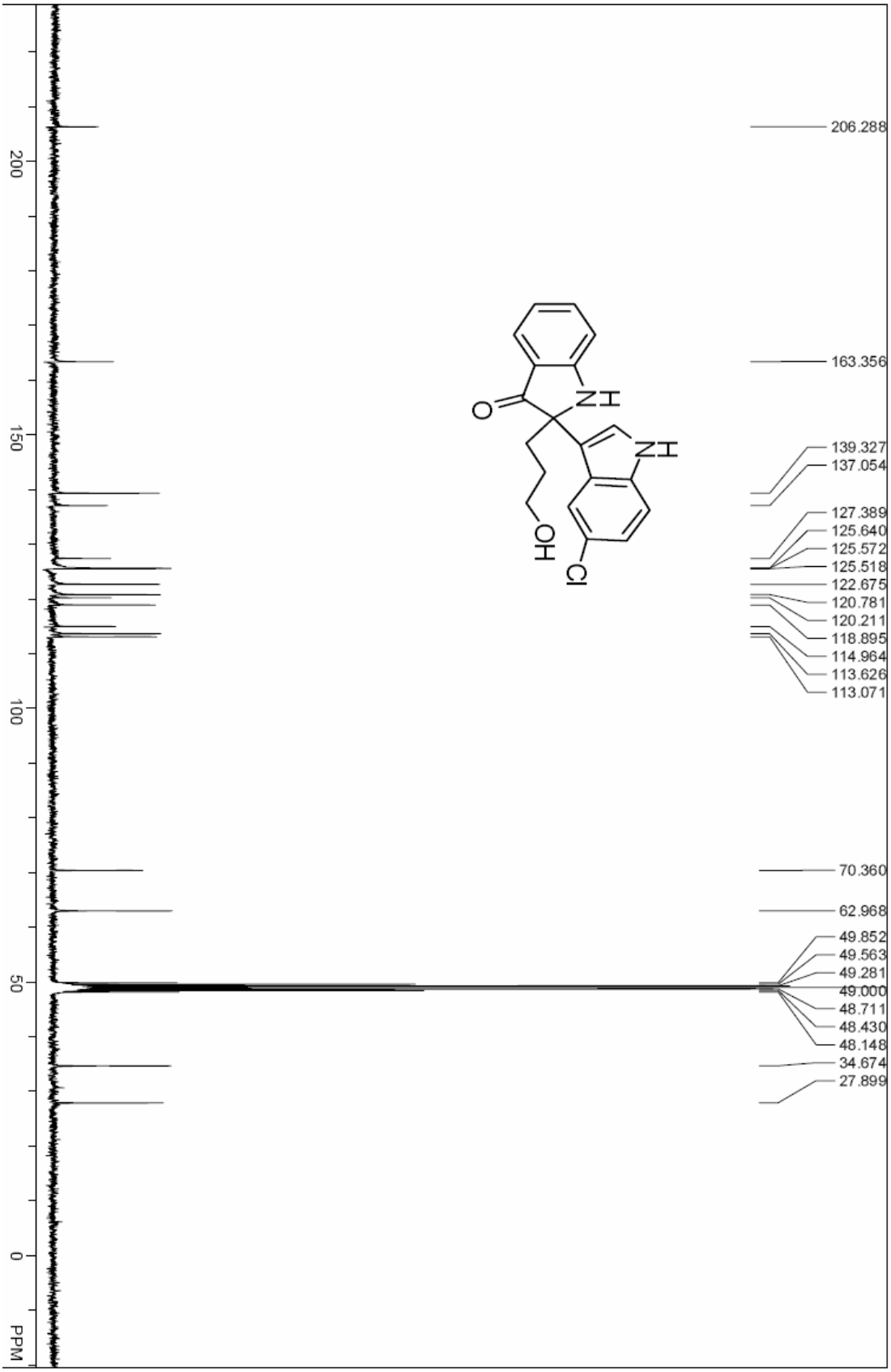
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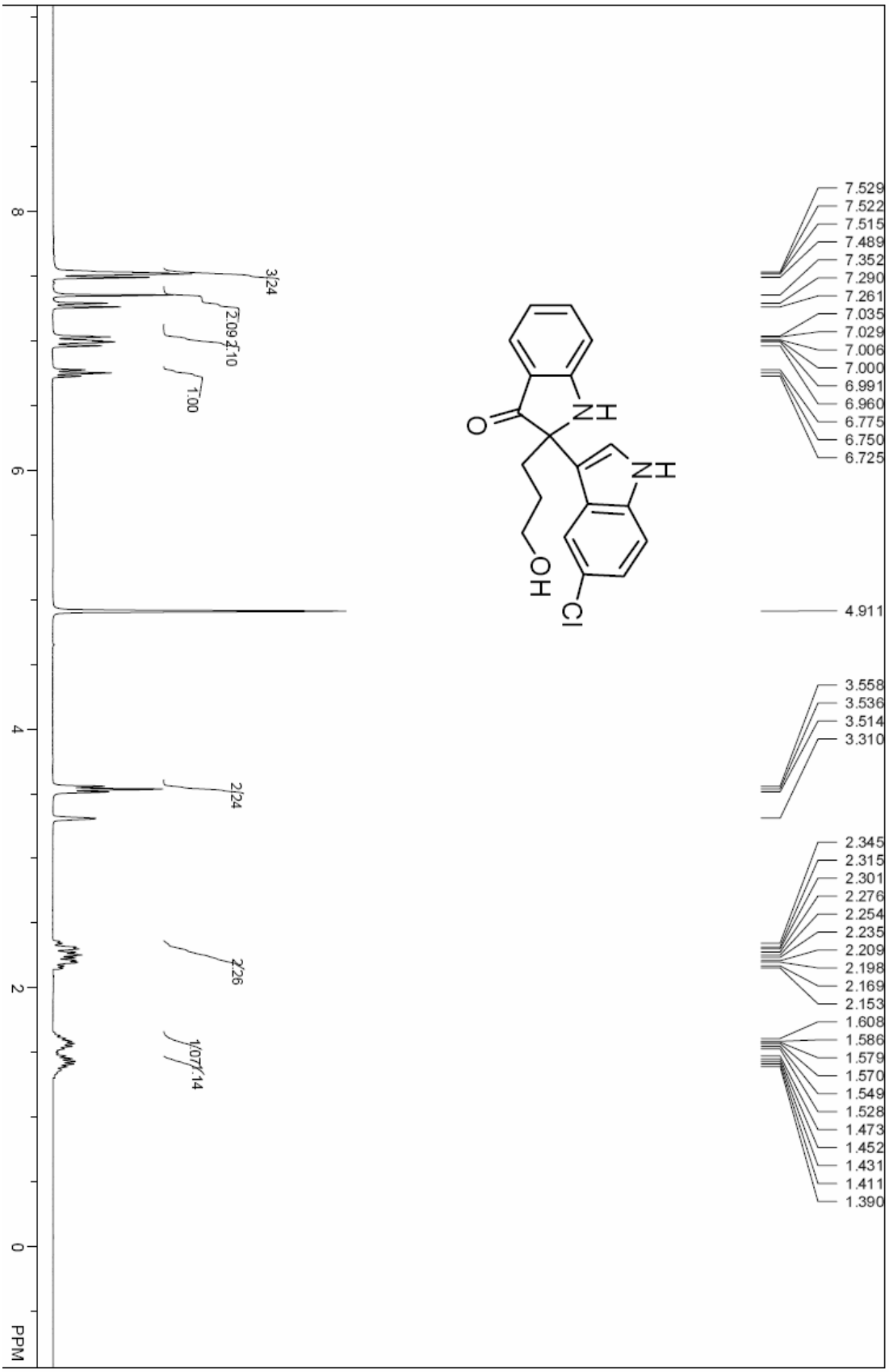
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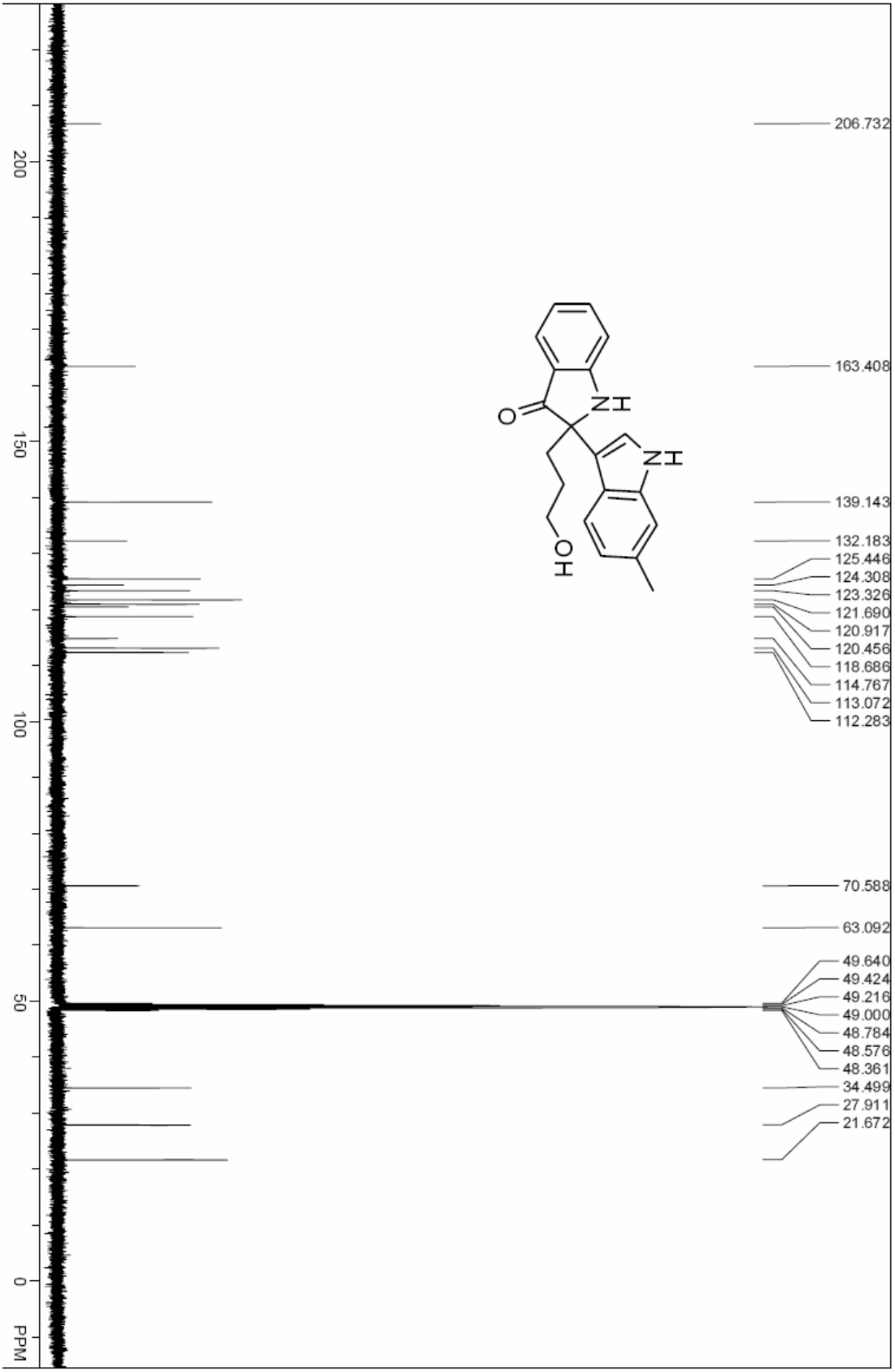
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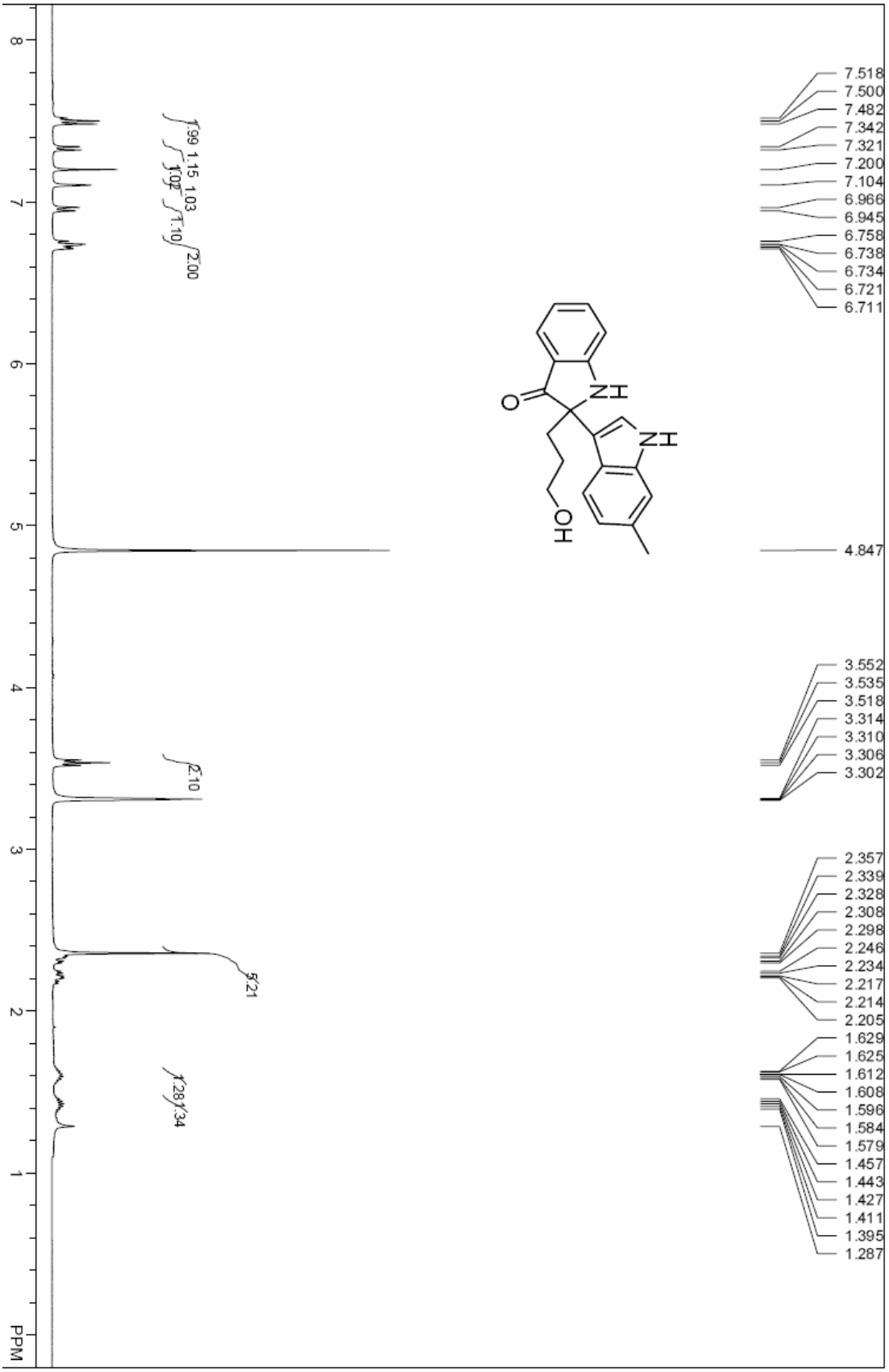
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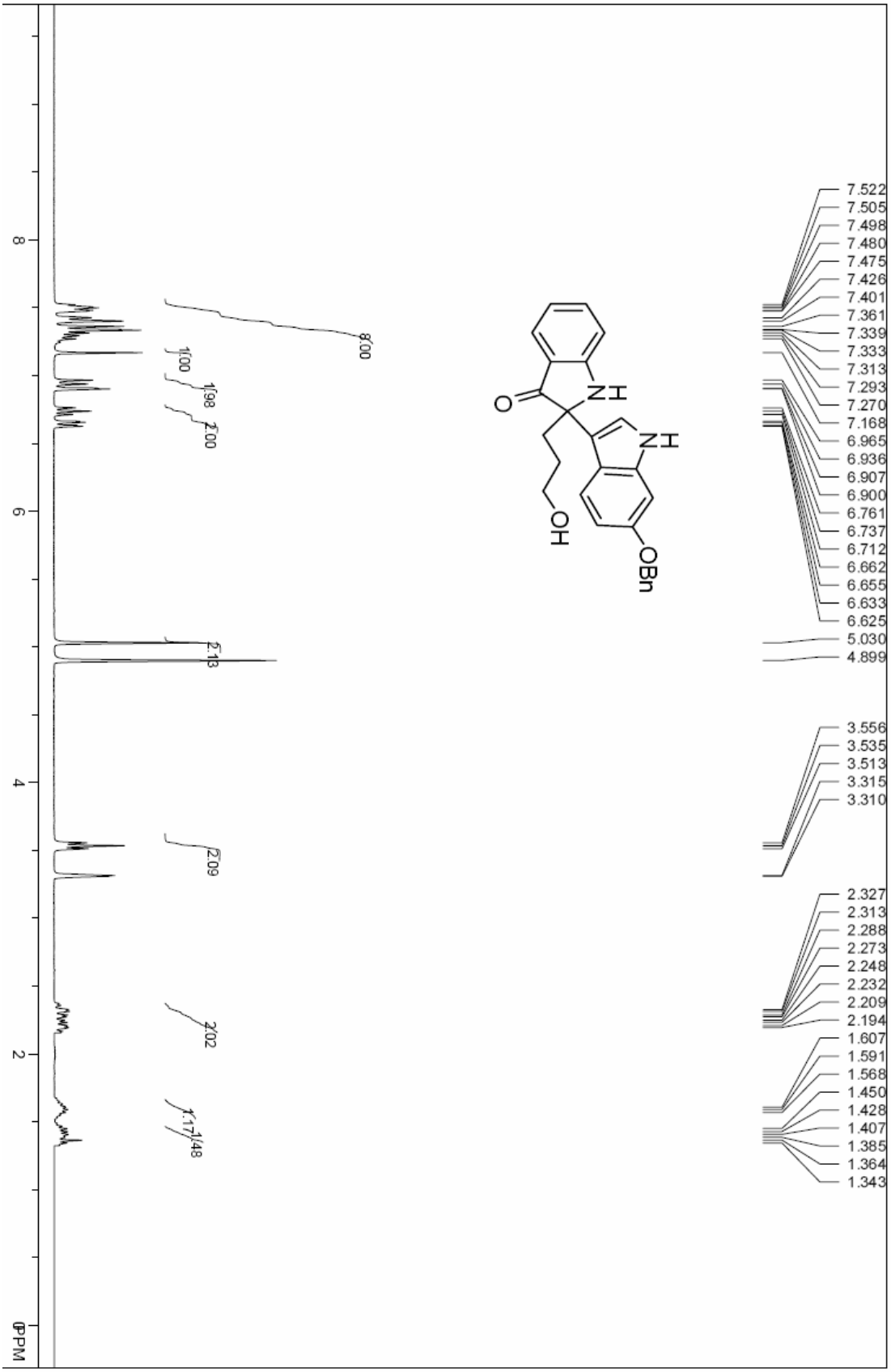
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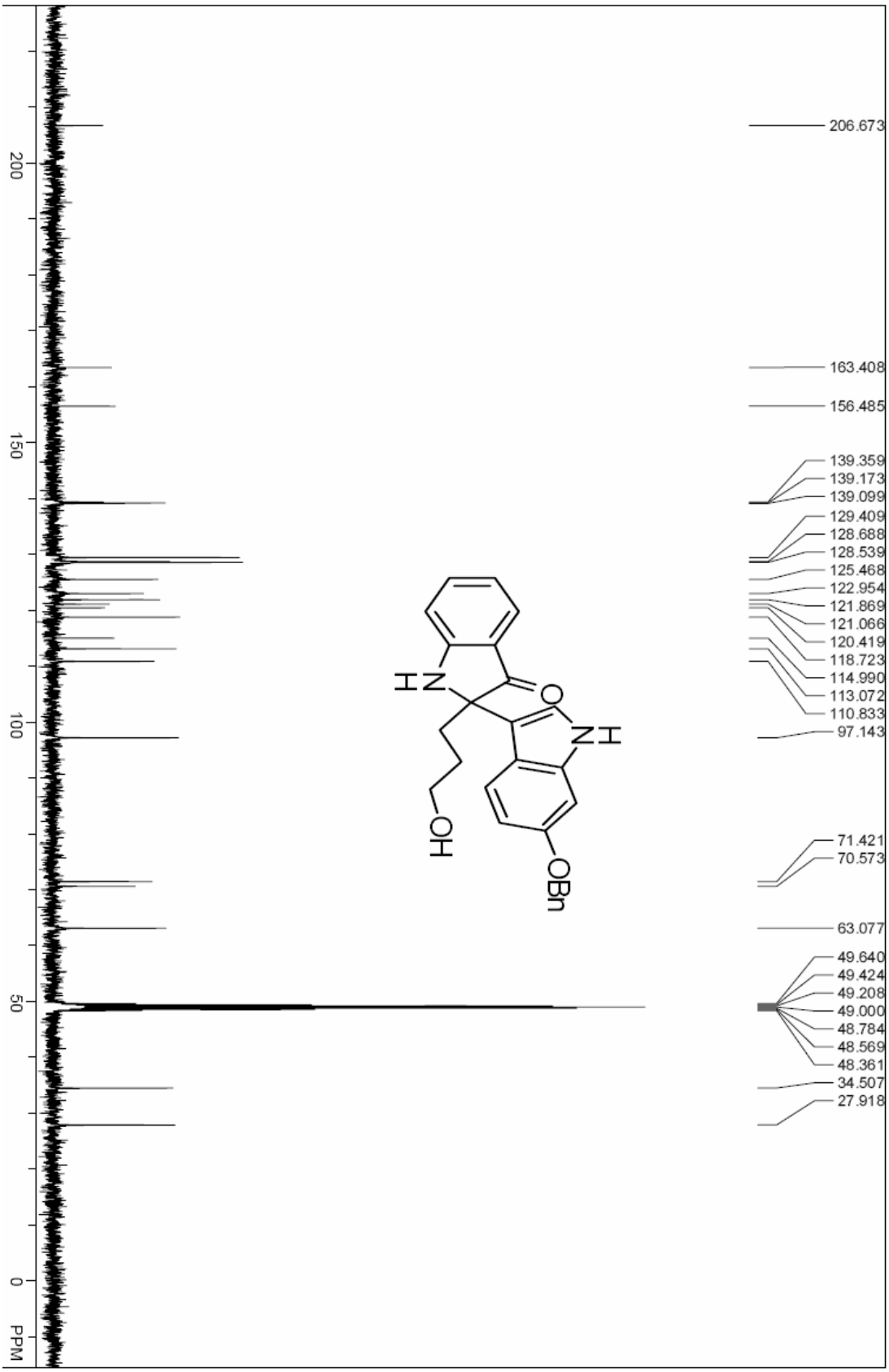
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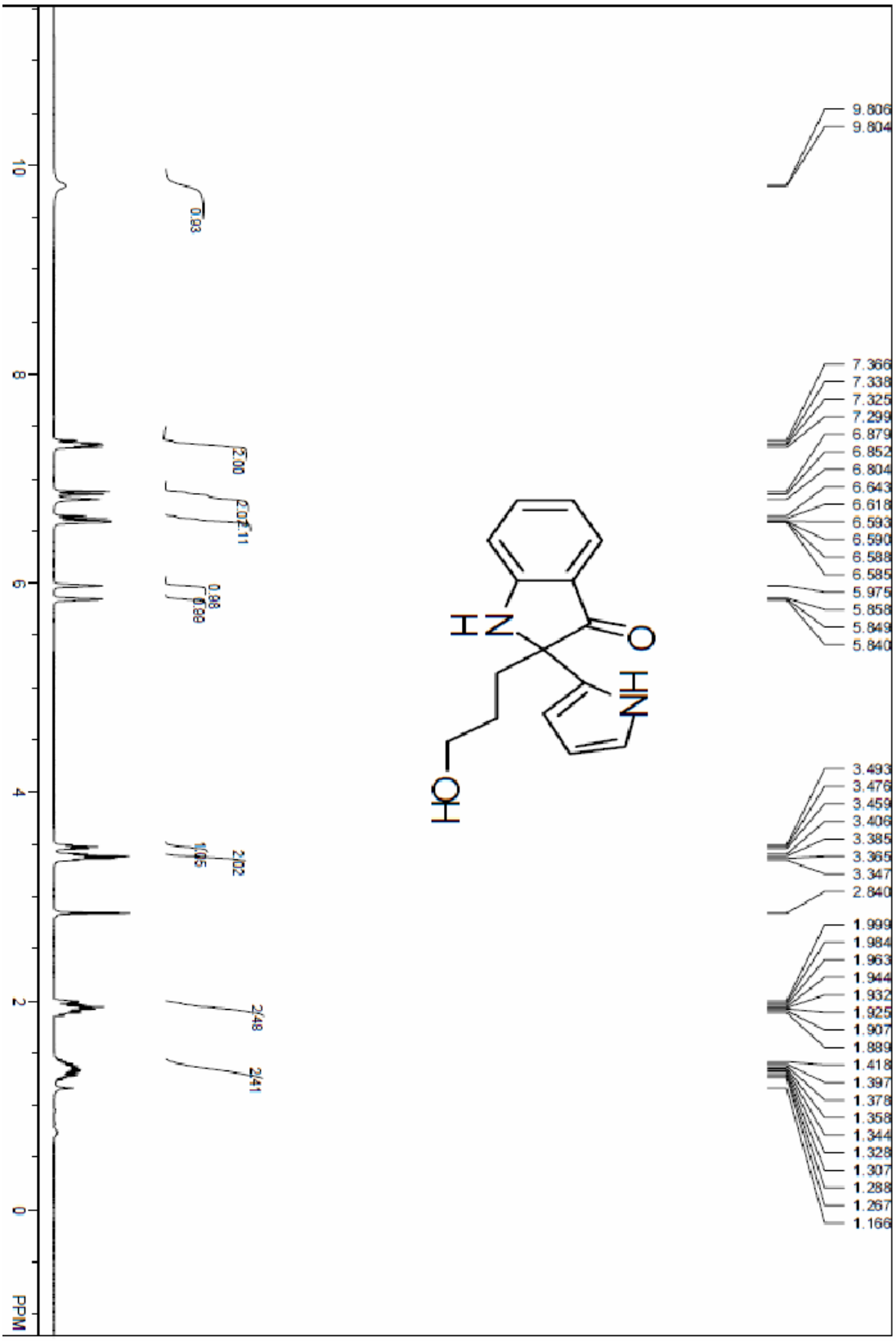
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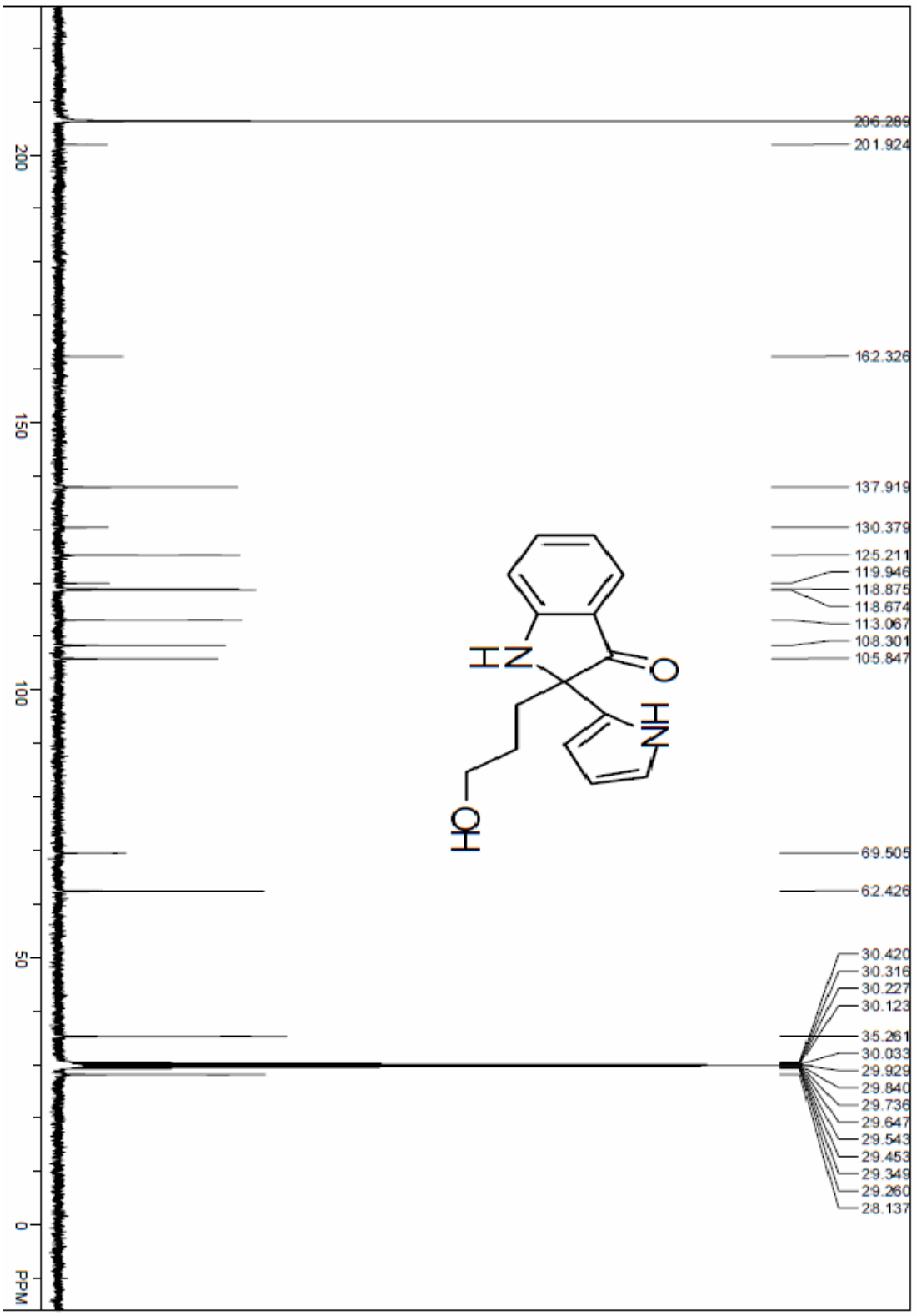
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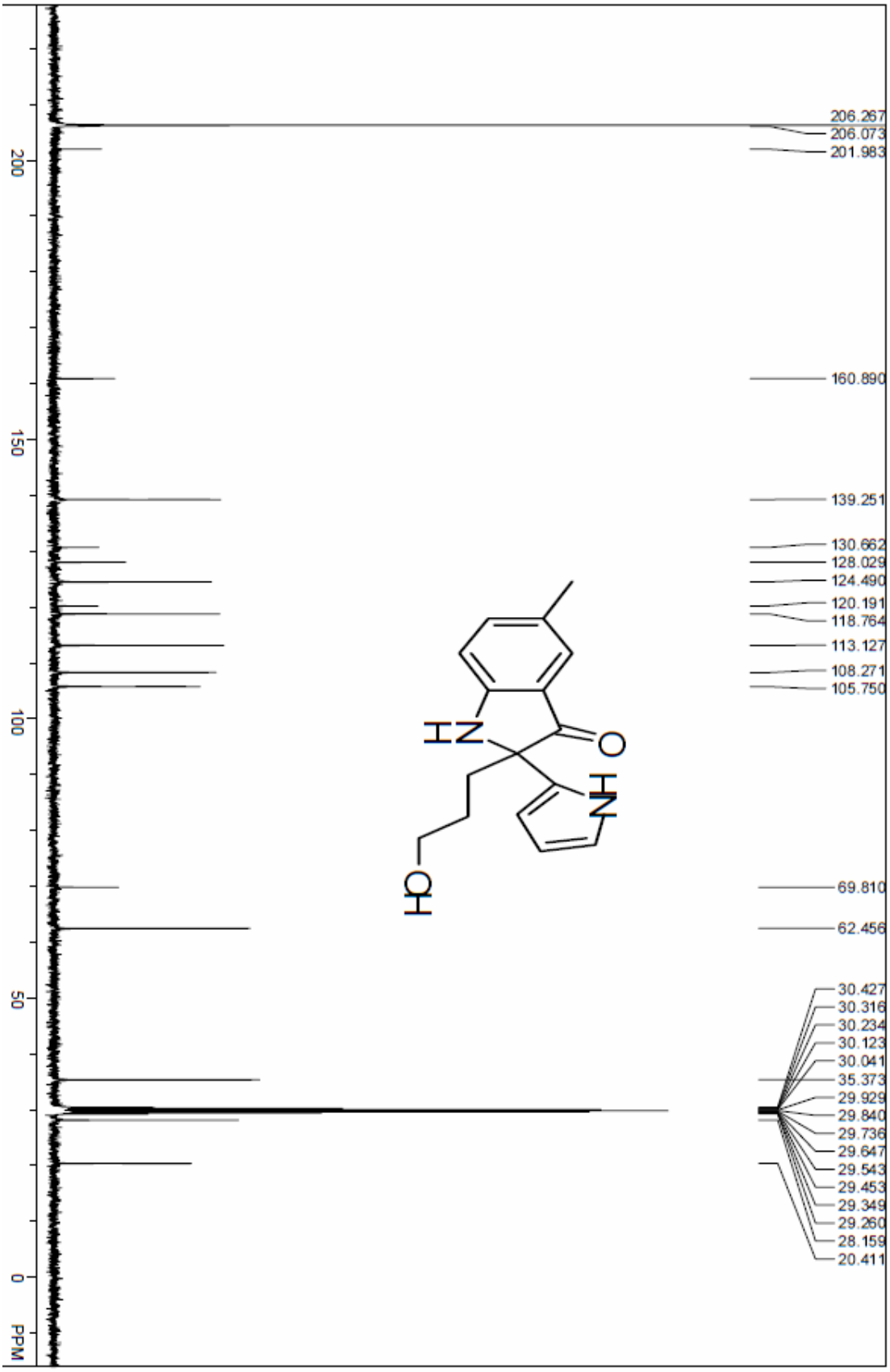
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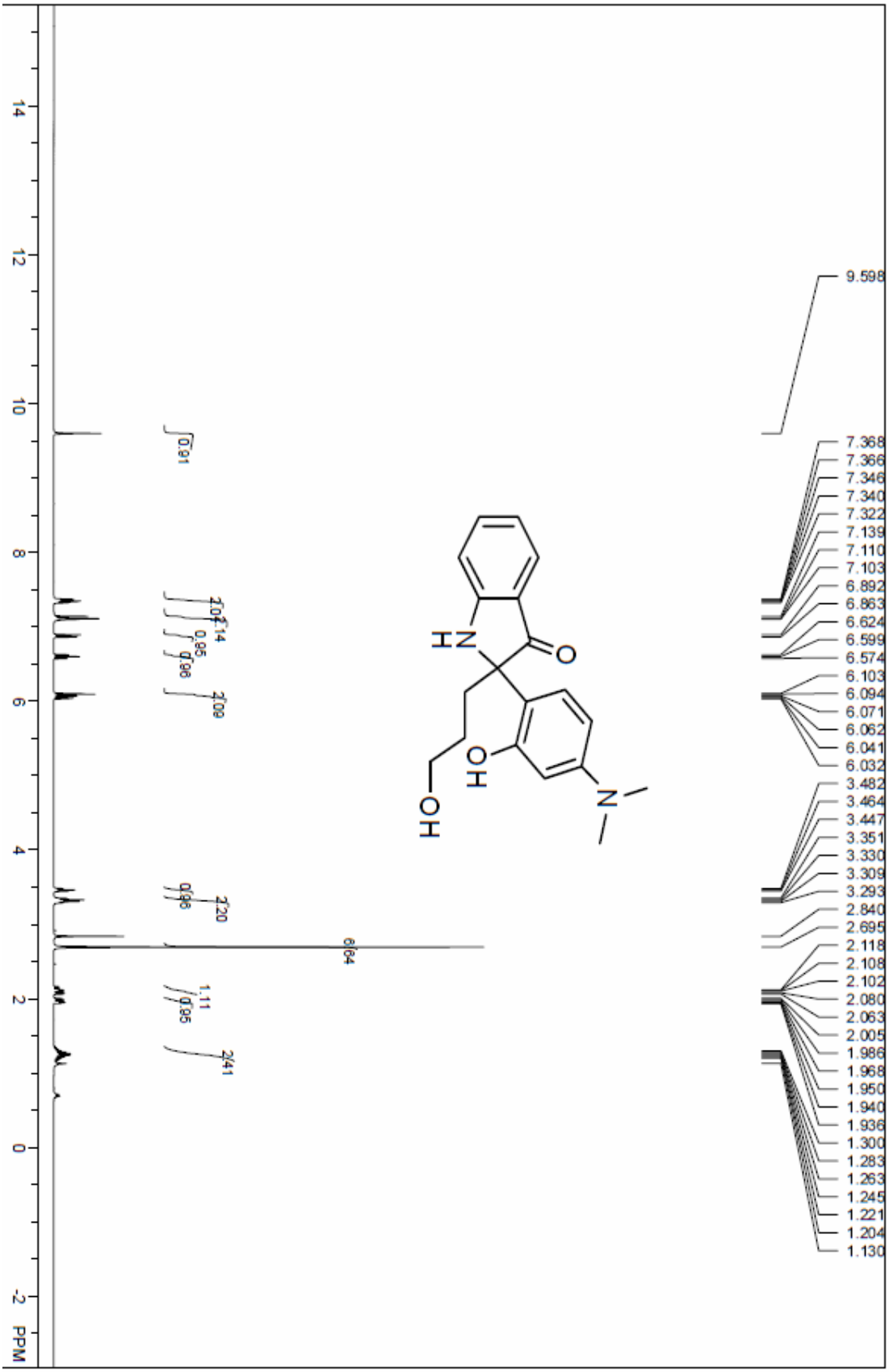
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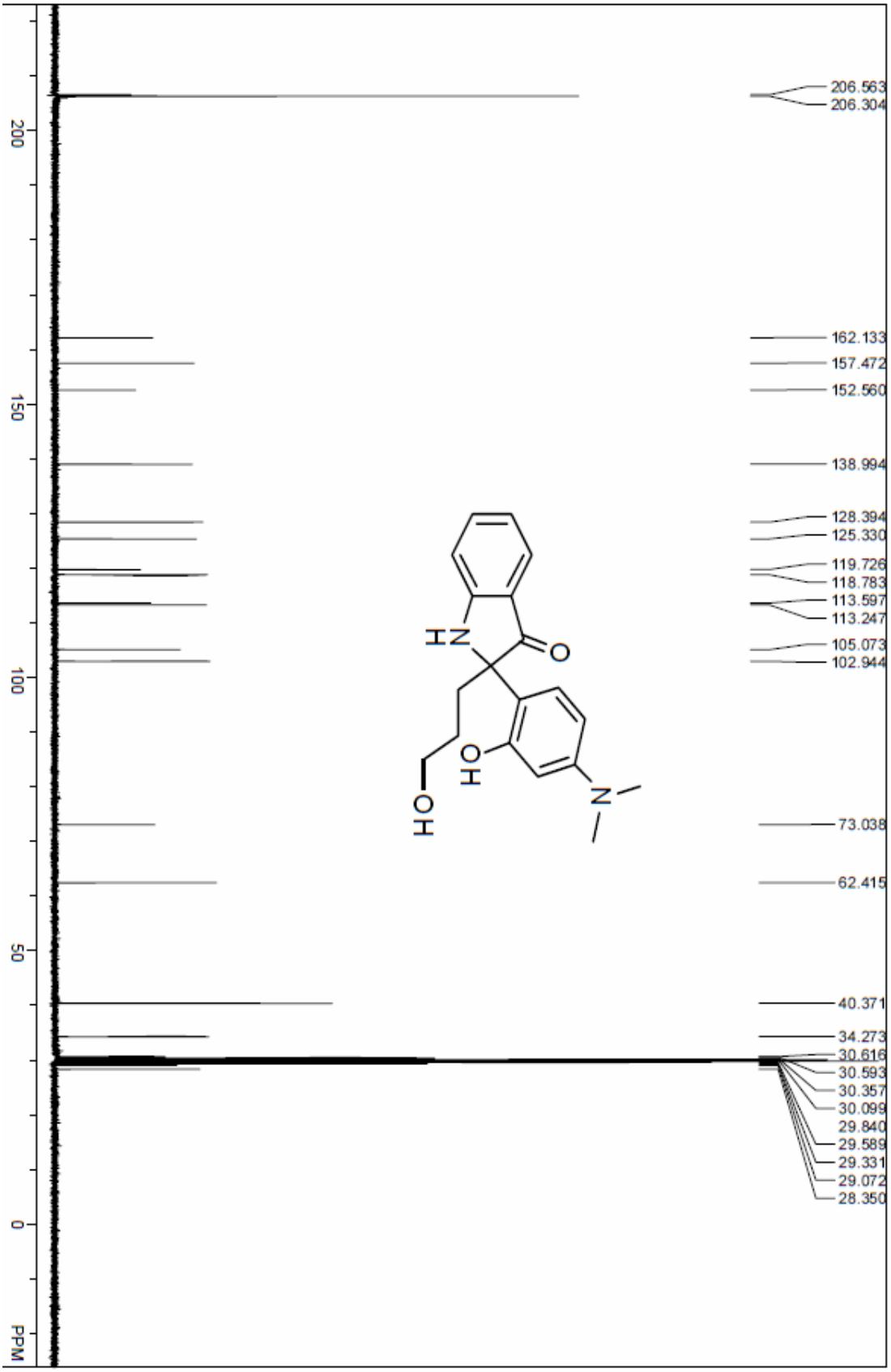
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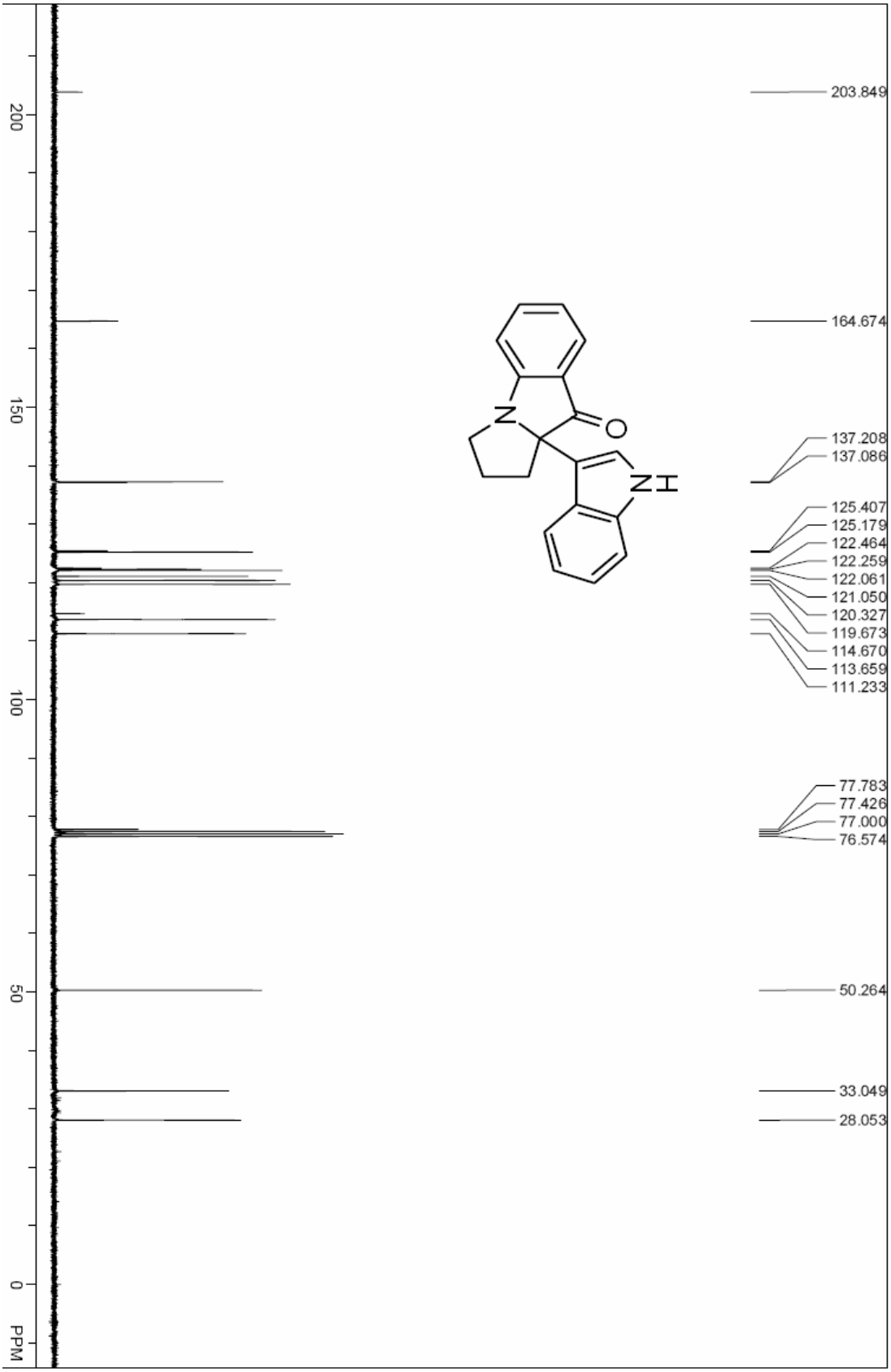
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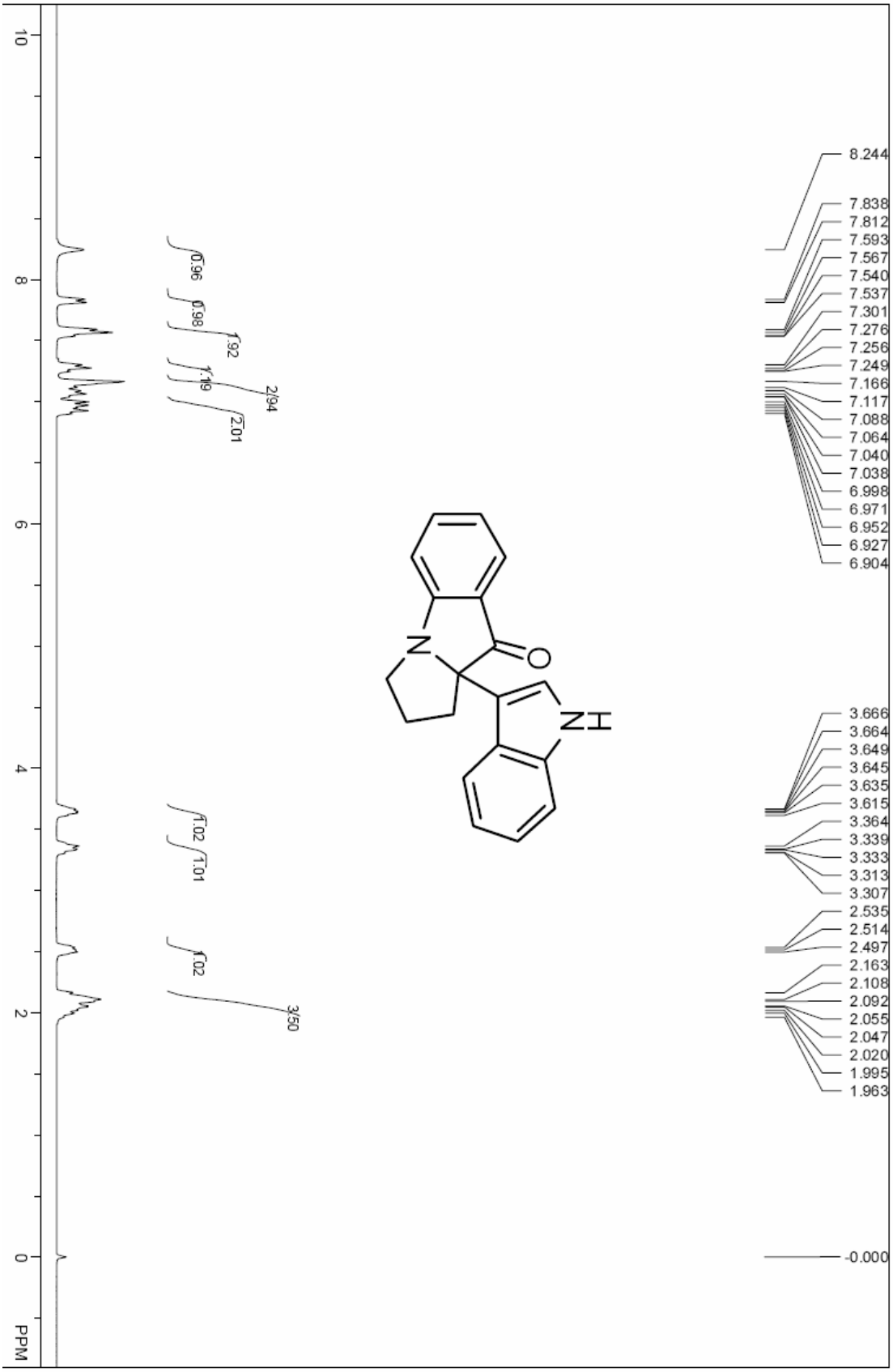
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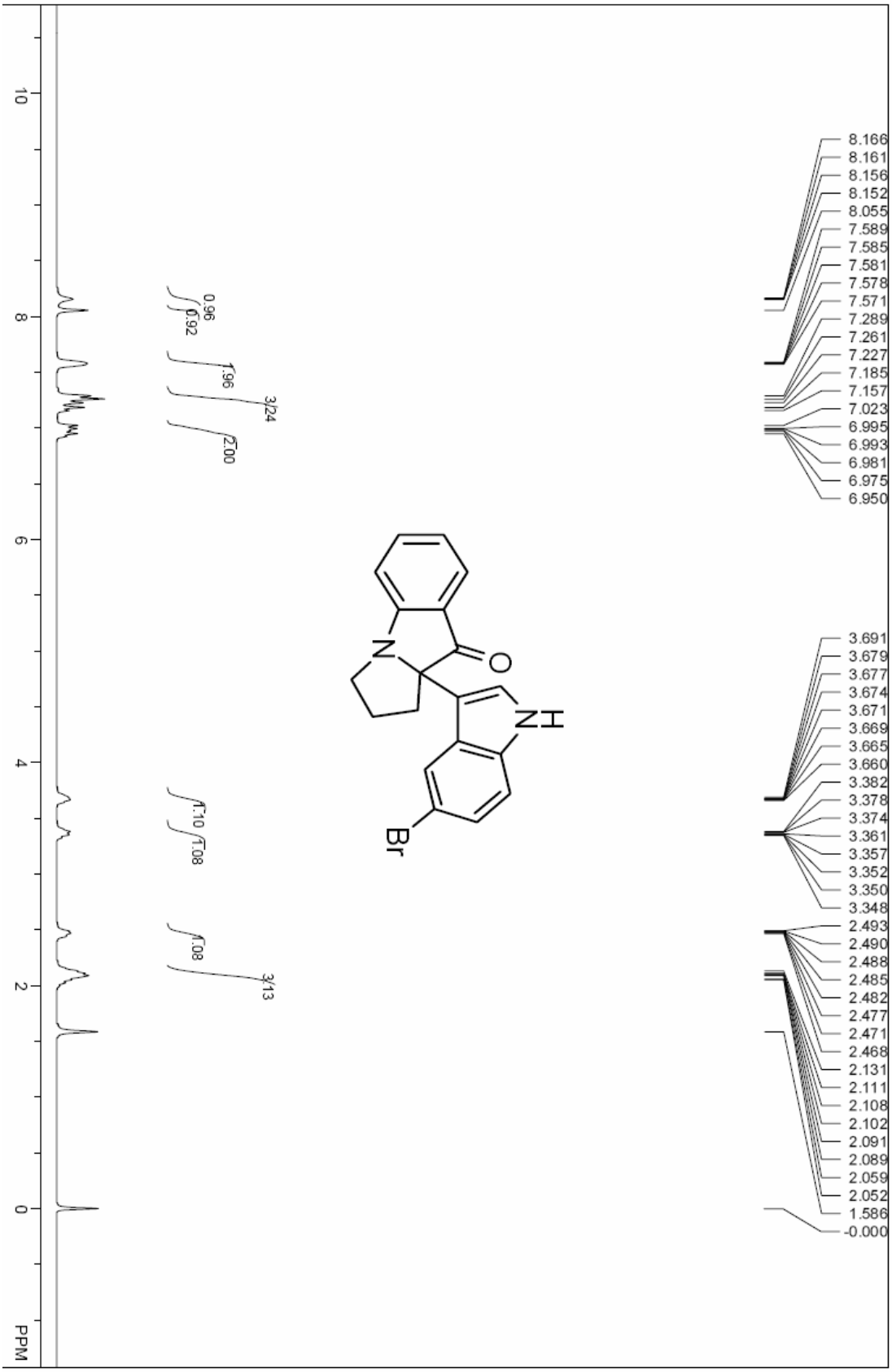
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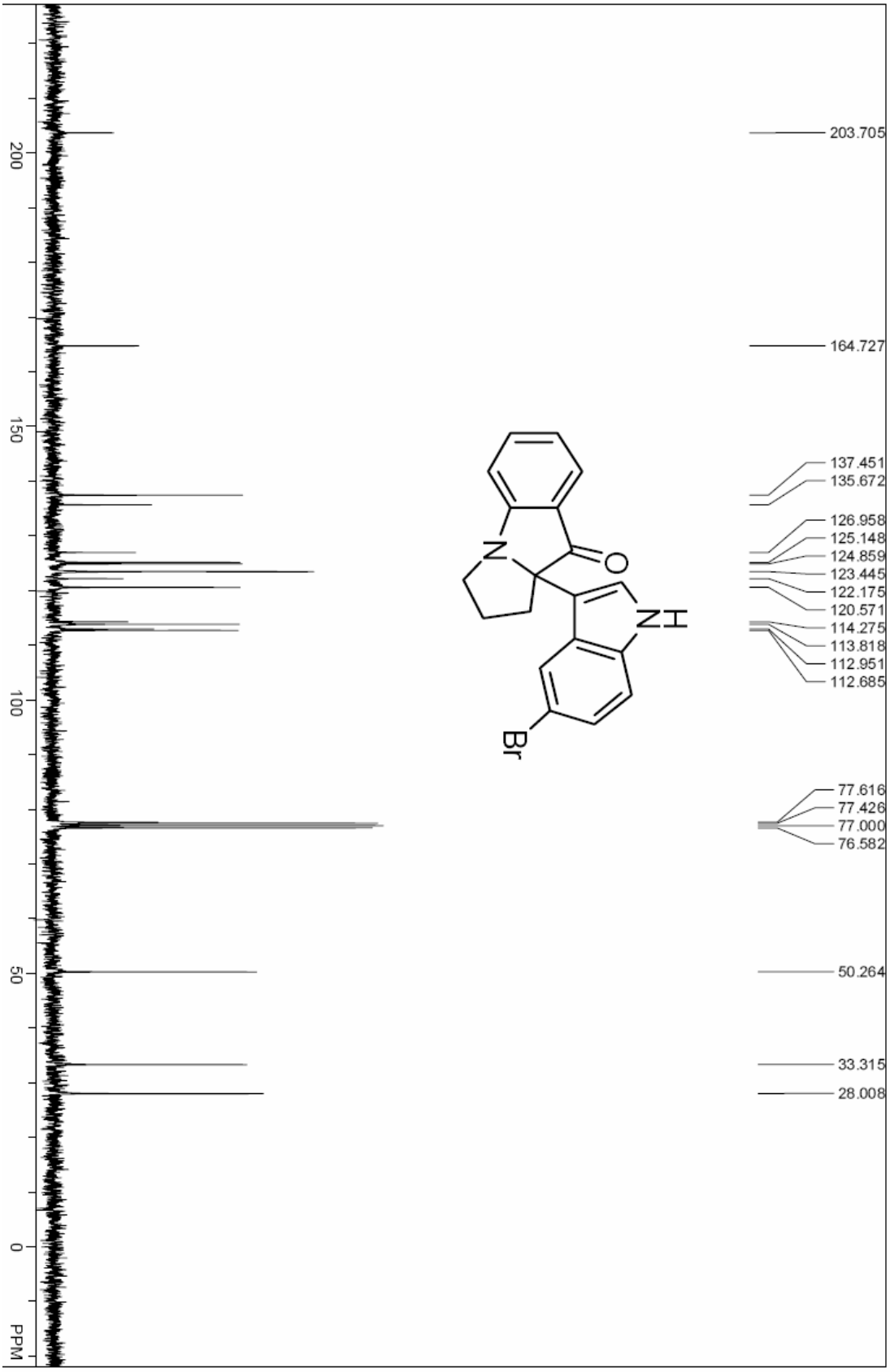
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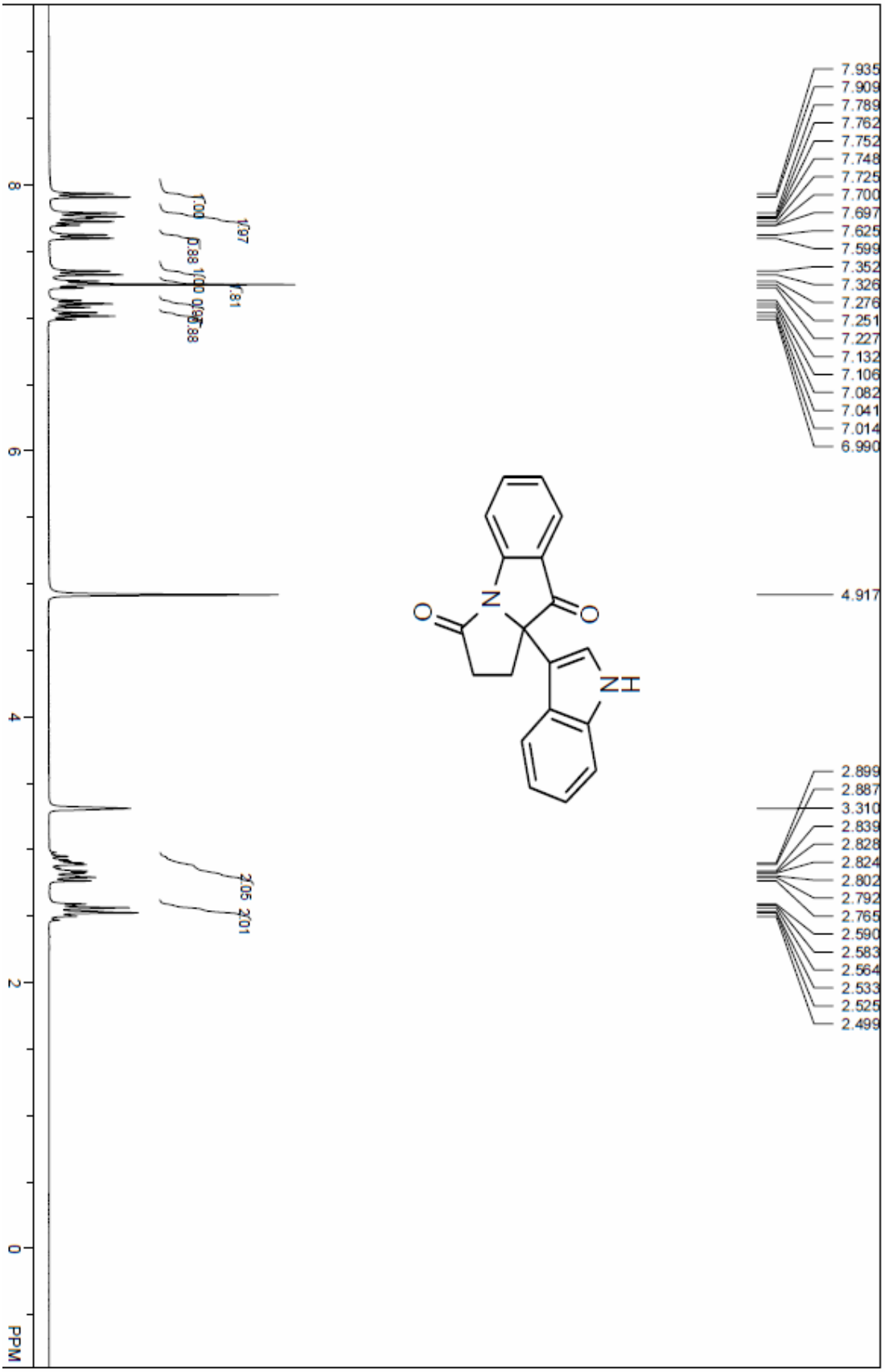
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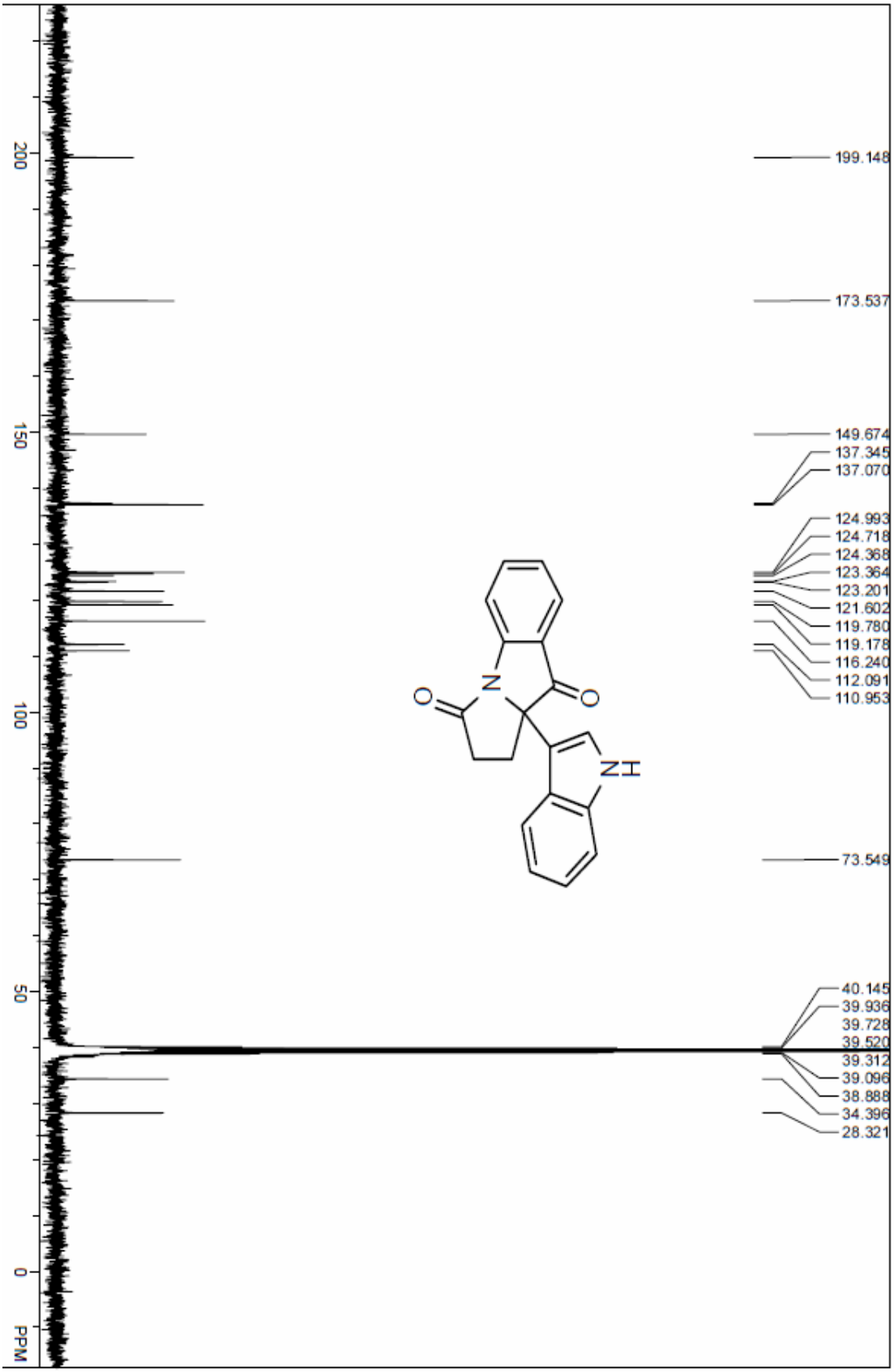

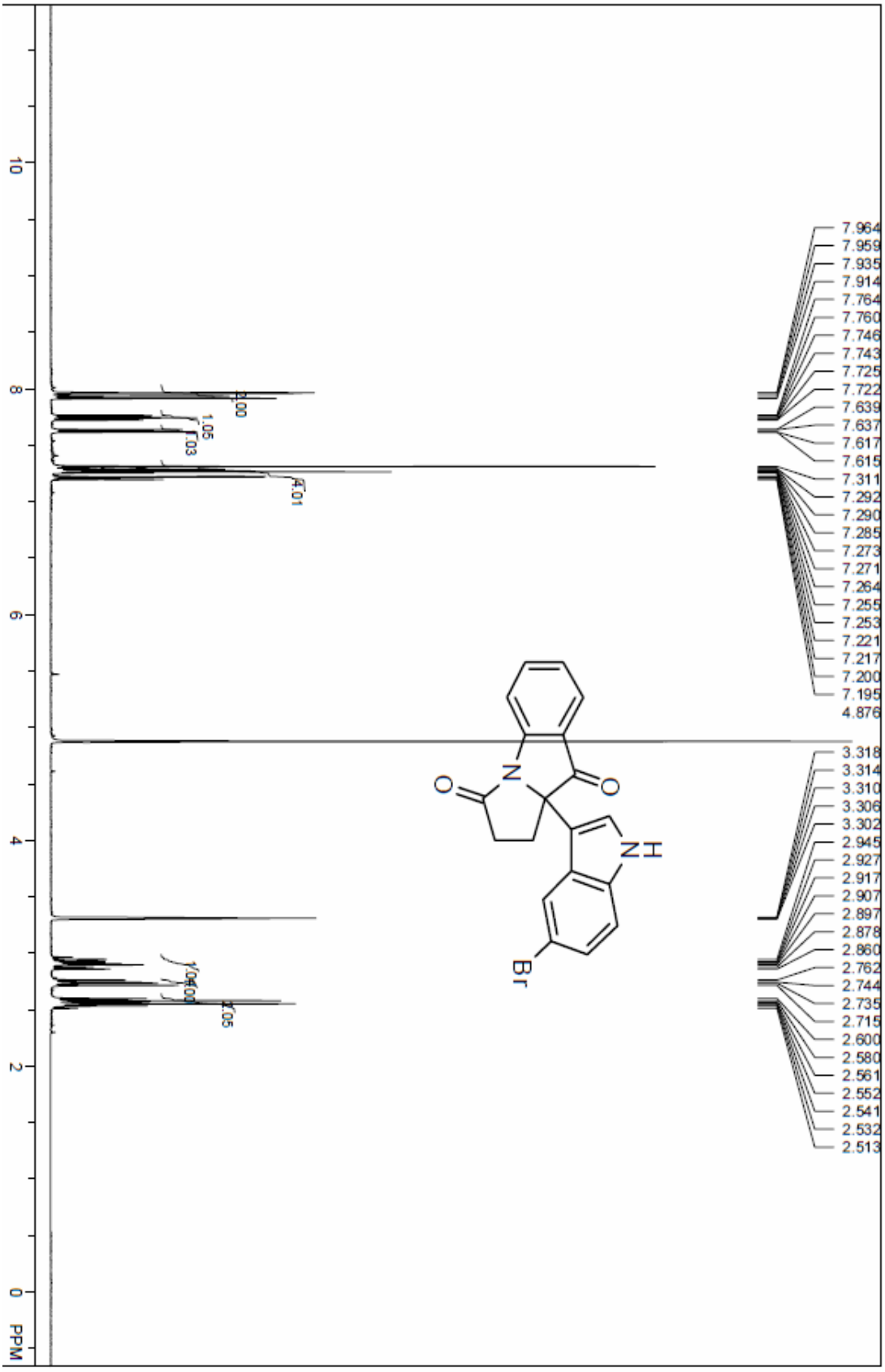
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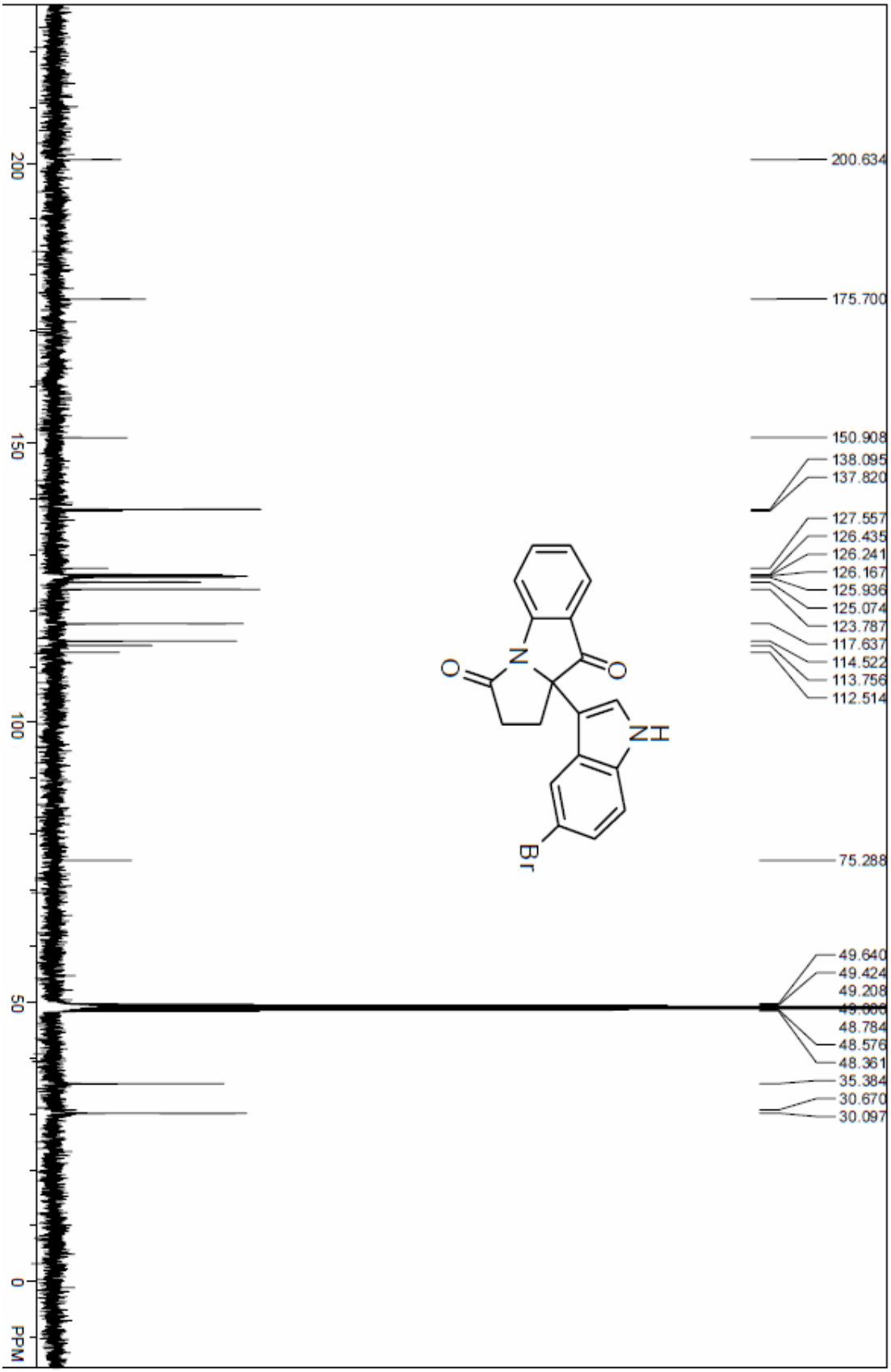
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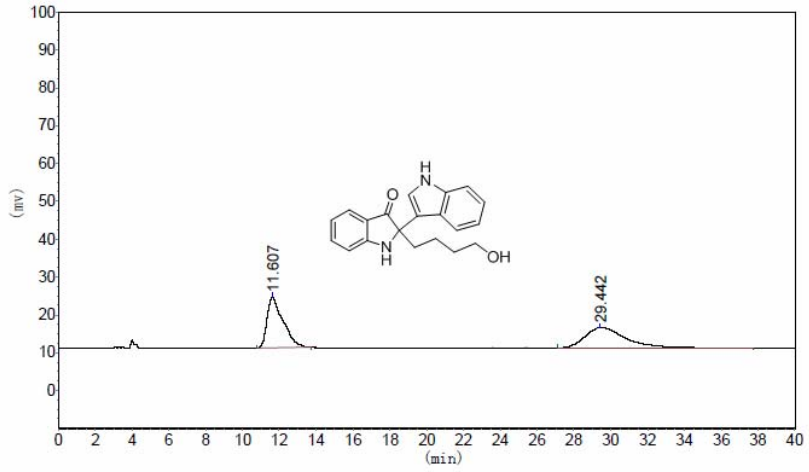
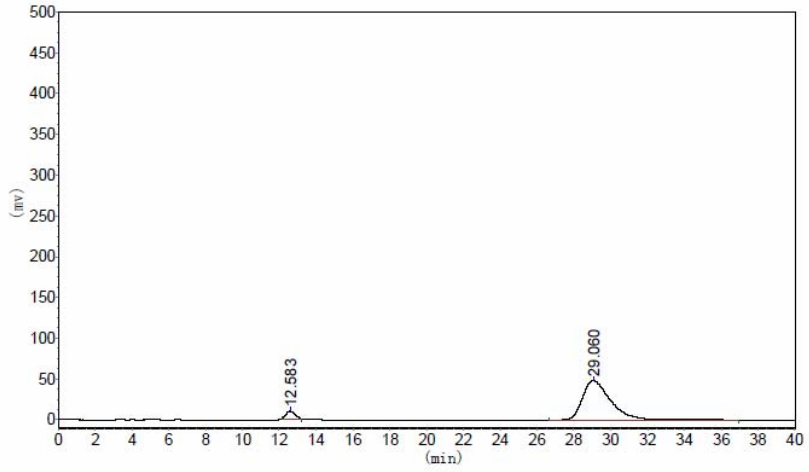
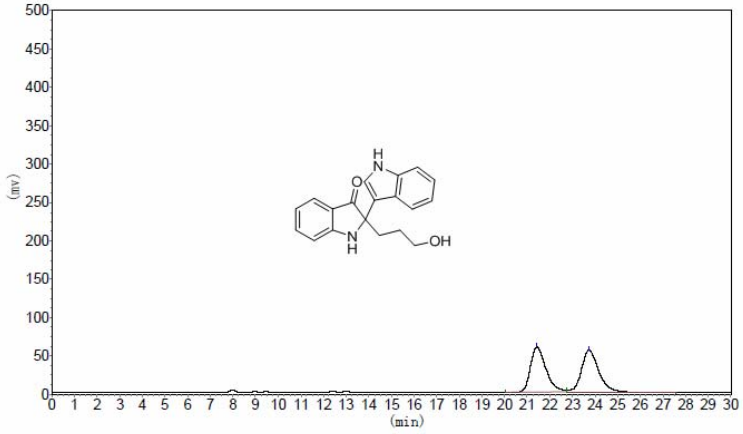


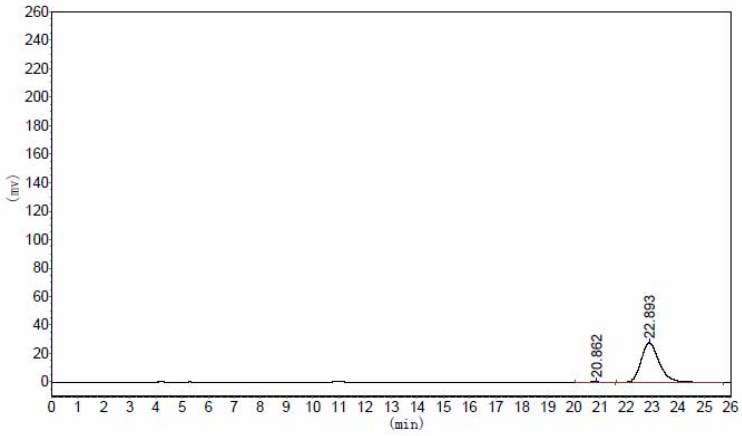
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	11.607	13375.315	802348.375	49.9414
2	29.442	5319.501	804231.188	50.0586
Total		18694.817	1606579.563	100.0000



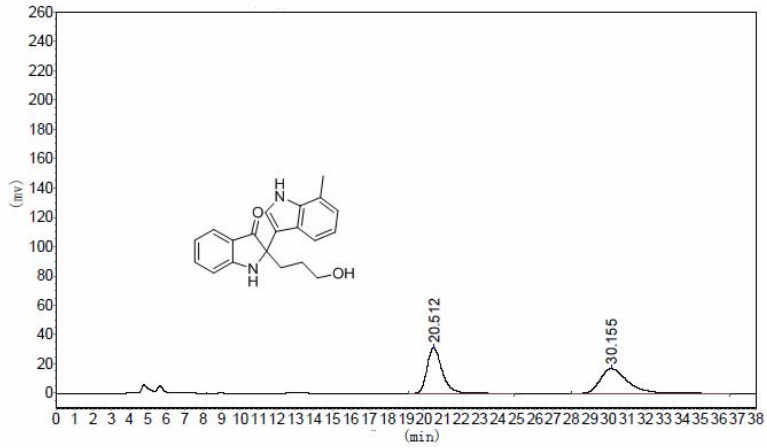
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	12.583	9968.079	322831.000	5.8669
2	29.060	48199.848	5179714.500	94.1331
Total		58167.927	5502545.500	100.0000



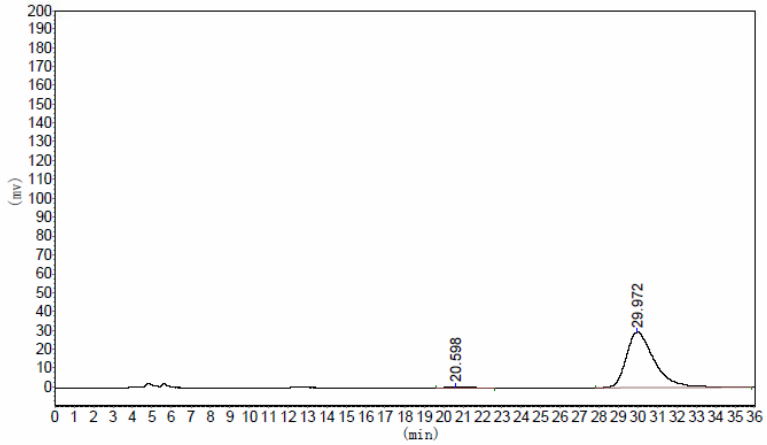
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	21.430	58587.496	2773874.500	49.0880
2	23.732	54104.691	2876941.750	50.9120
Total		112692.188	5650816.250	100.0000



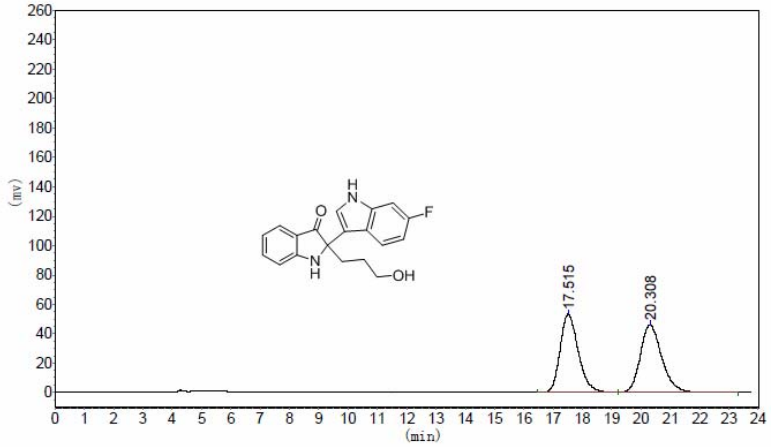
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	20.862	210.112	8782.251	0.6576
2	22.893	27628.193	1326682.500	99.3424
Total		27838.305	1335464.751	100.0000



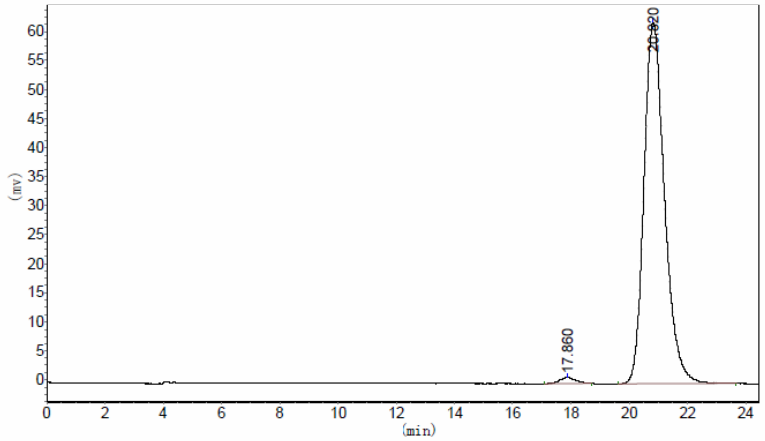
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	20.512	31226.230	1800871.000	50.3036
2	30.155	16978.963	1779135.375	49.6964
Total		48205.193	3580006.375	100.0000



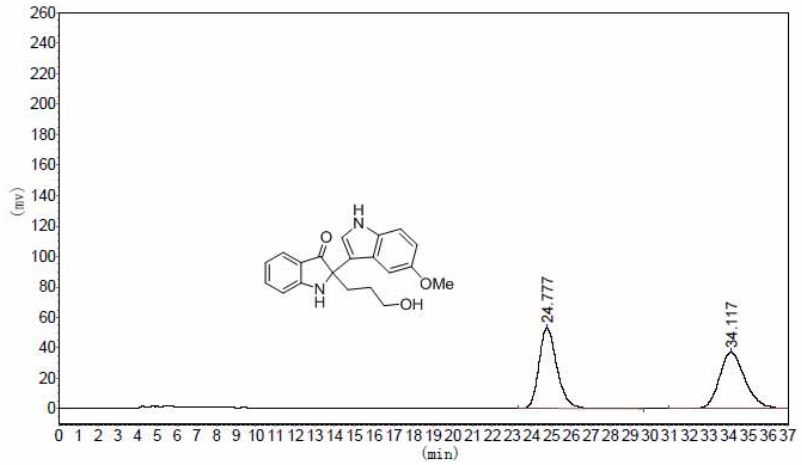
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	20.598	389.005	24284.148	0.8200
2	29.972	29408.941	2937228.000	99.1800
Total		29797.946	2961512.148	100.0000



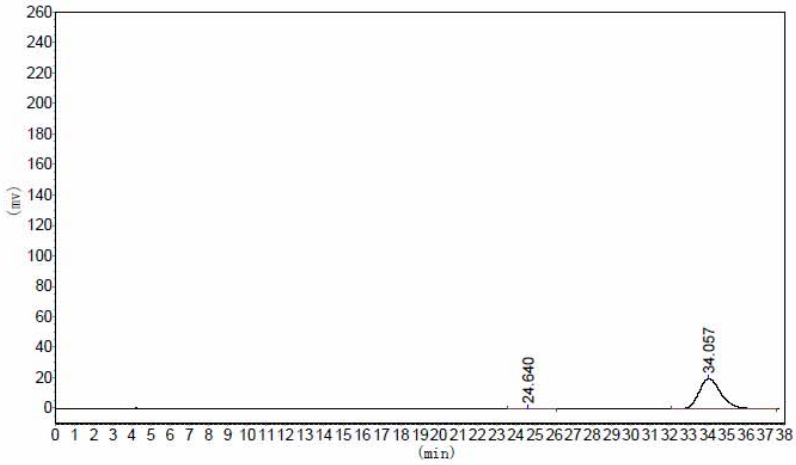
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	17.515	53373.727	2305946.750	49.4984
2	20.308	45969.375	2352679.250	50.5016
Total		99343.102	4658626.000	100.0000



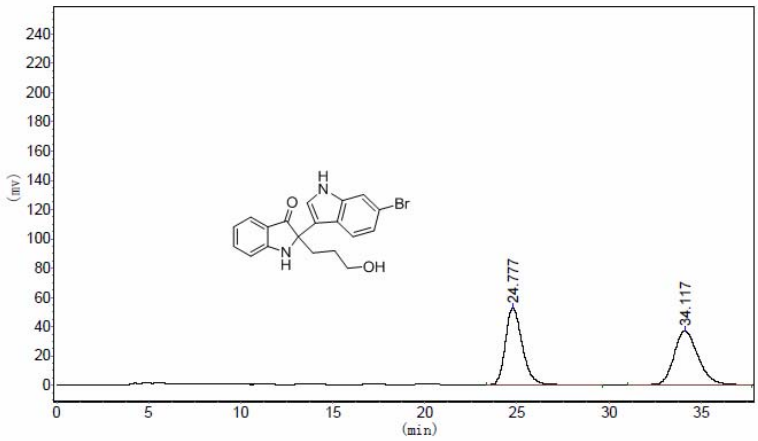
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	17.860	1018.834	39118.500	1.2681
2	20.820	62225.559	3045794.500	98.7319
Total		63244.393	3084913.000	100.0000



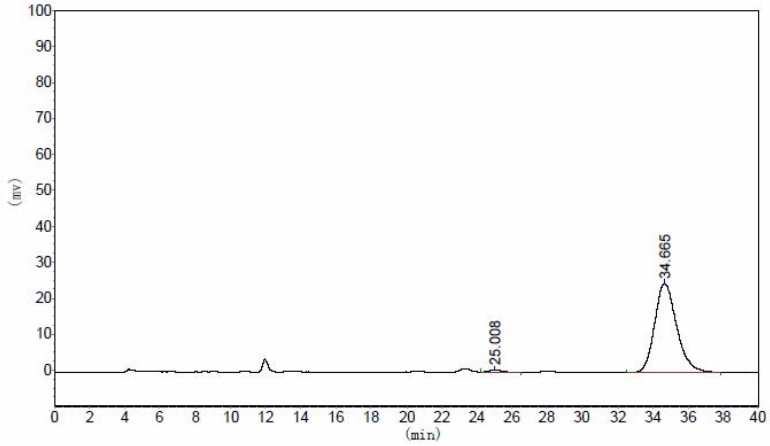
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	24.777	52786.324	3340727.250	49.9674
2	34.117	36850.055	3345089.250	50.0326
Total		89636.379	6685816.500	100.0000



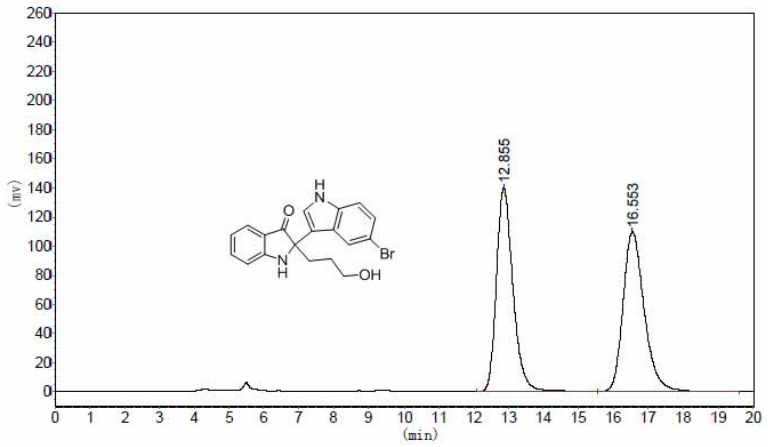
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	24.640	246.090	14912.805	0.9194
2	34.057	19900.135	1607048.000	99.0806
Total		20146.225	1621960.805	100.0000



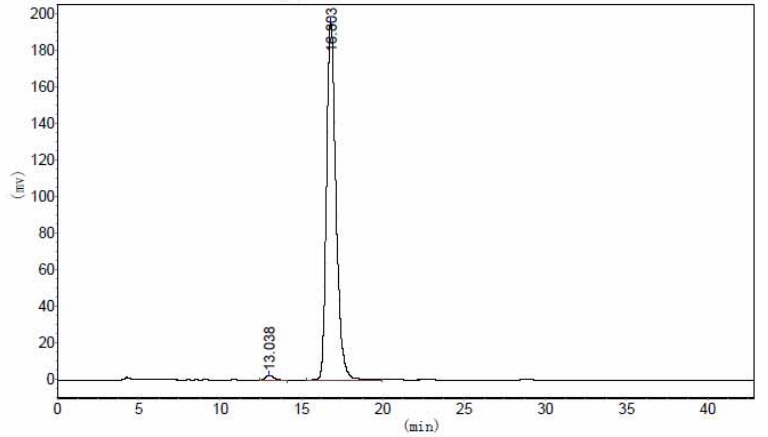
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	24.777	52786.324	3340727.250	49.9674
2	34.117	36850.055	3345089.250	50.0326
Total		89636.379	6685816.500	100.0000



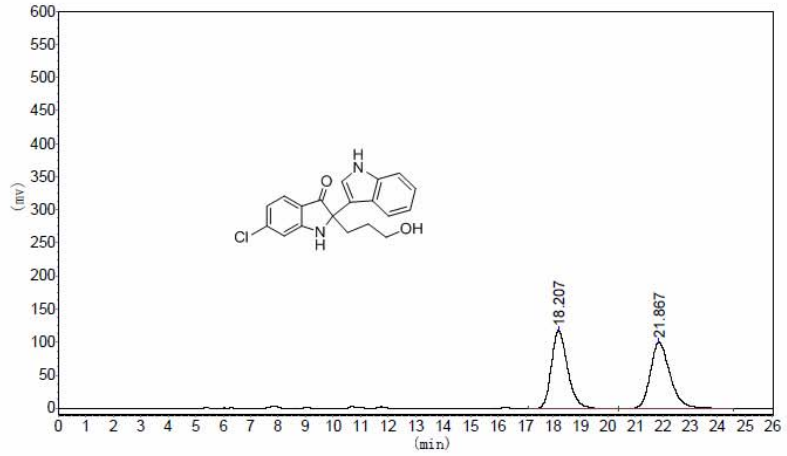
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	25.008	520.615	30568.508	1.3983
2	34.665	24693.051	2155519.500	98.6017
Total		25213.665	2186088.008	100.0000



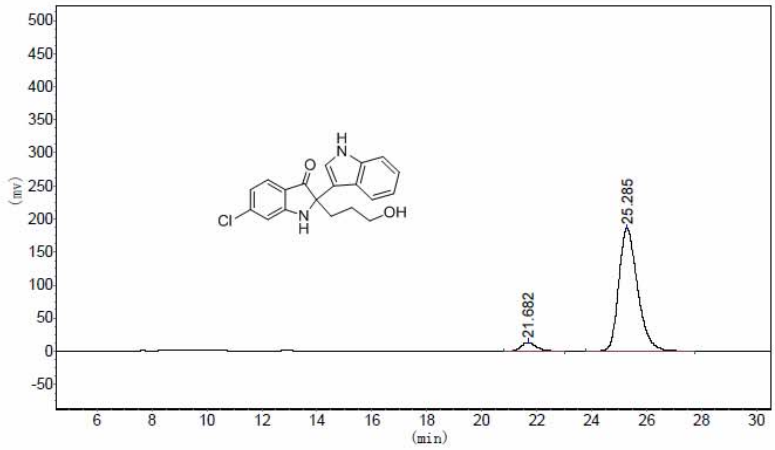
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	12.855	139742.859	4630792.500	49.9649
2	16.553	109522.313	4637306.500	50.0351
Total		249265.172	9268099.000	100.0000



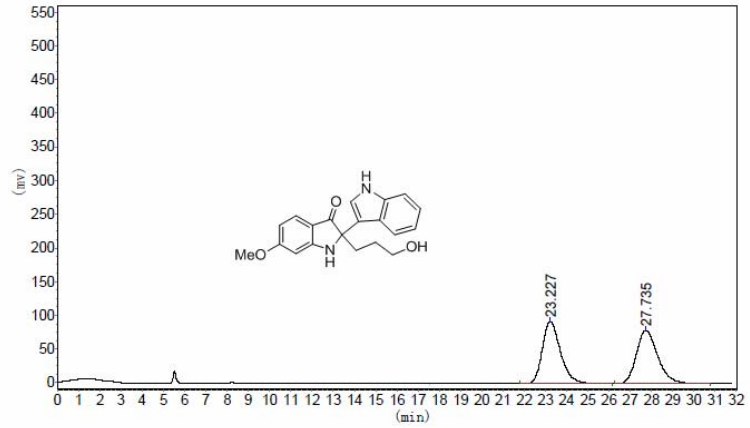
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	13.038	2492.940	78088.898	0.9745
2	16.803	195839.047	7935084.000	99.0255
Total		198331.987	8013172.898	100.0000



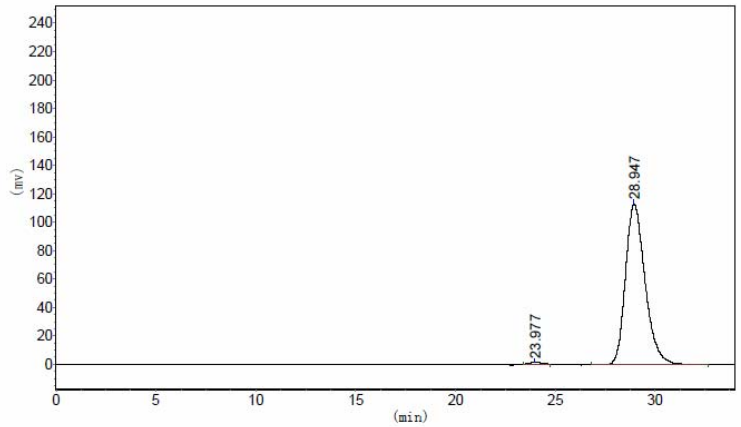
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	18.207	118180.836	4876387.500	49.2440
2	21.867	100128.313	5026114.500	50.7560
Total		218309.148	9902502.000	100.0000



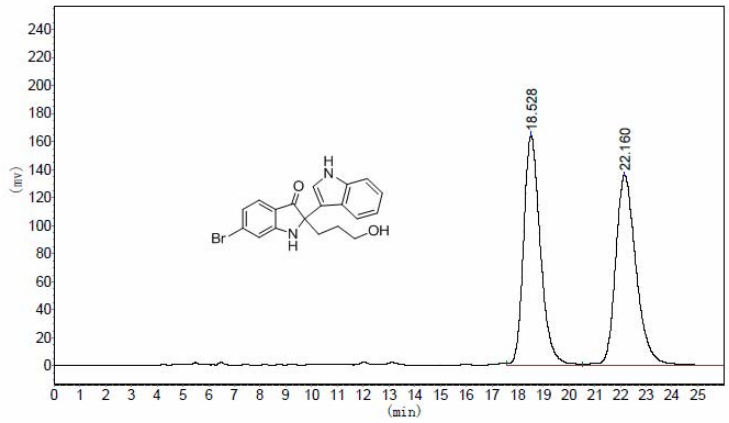
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	21.682	12955.536	503844.000	5.4001
2	25.285	185135.719	8826447.000	94.5999
Total		198091.255	9330291.000	100.0000



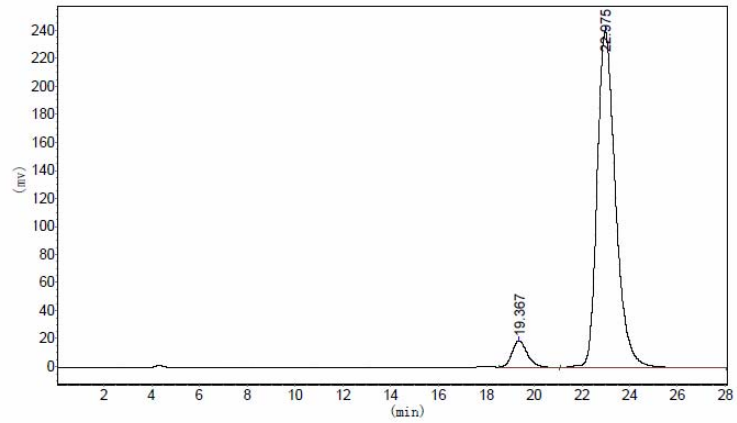
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	23.227	92586.289	5527307.000	49.9691
2	27.735	79403.813	5534144.000	50.0309
Total		171990.102	11061451.000	100.0000



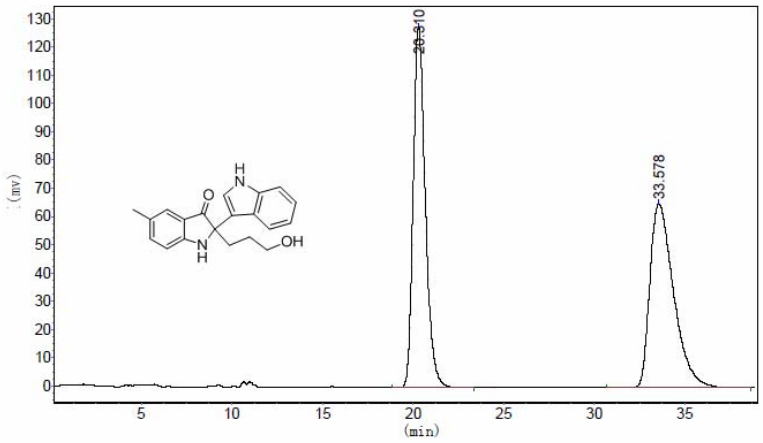
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	23.977	1422.088	61849.402	0.7929
2	28.947	113220.938	7738811.000	99.2071
Total		114643.026	7800660.402	100.0000



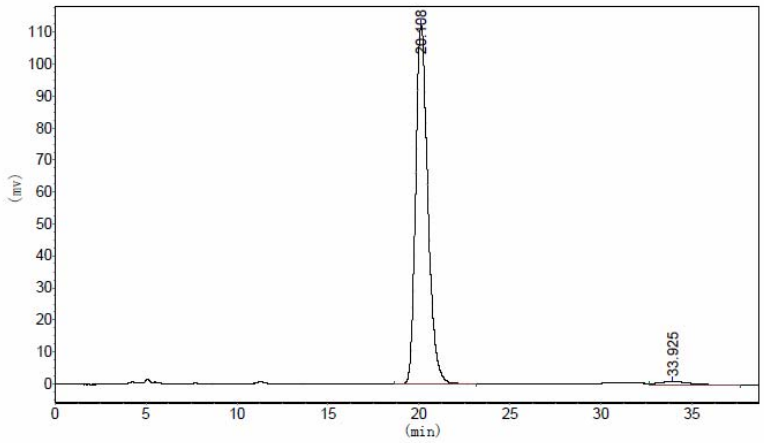
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	18.528	163850.656	7404722.000	49.6948
2	22.160	135587.844	7495676.500	50.3052
Total		299438.500	14900398.500	100.0000

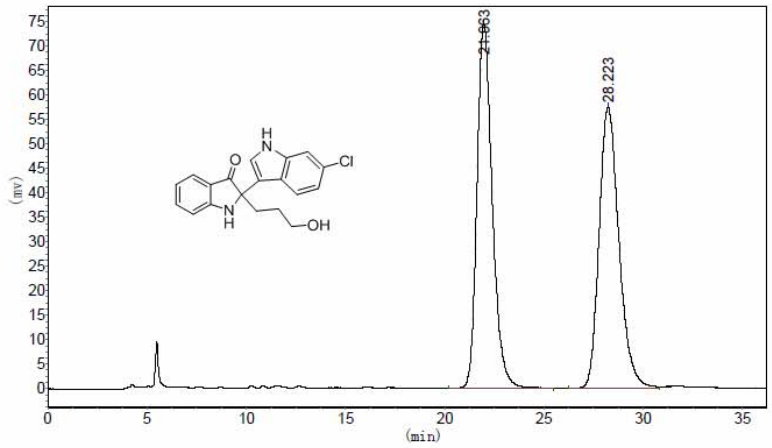


Peak No.	R. Time	Peak Height	Peak Area	Percent
1	19.367	19104.143	858139.375	6.2798
2	22.975	239823.406	12807024.000	93.7202
Total		258927.549	13665163.375	100.0000

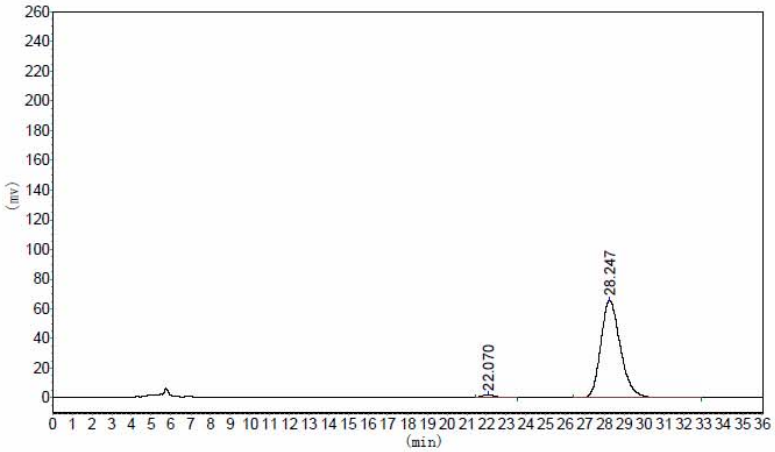


Peak No.	R. Time	Peak Height	Peak Area	Percent
1	20.310	127546.203	5957971.000	50.0292
2	33.578	65197.488	5951026.000	49.9708
Total		192743.691	11908997.000	100.0000

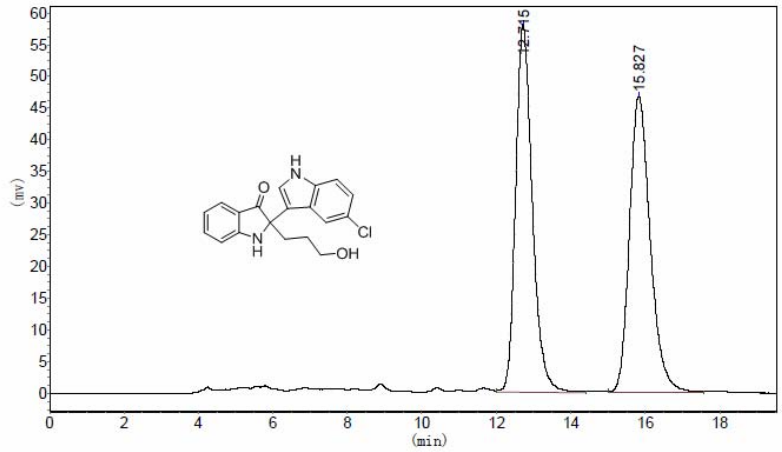




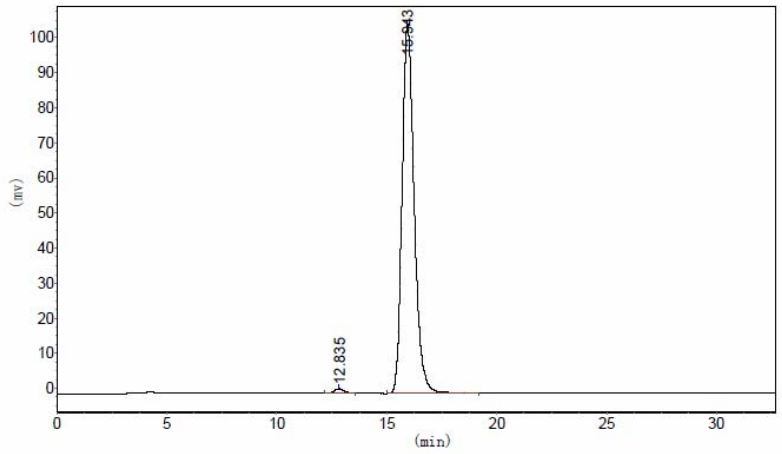
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	21.963	74299.680	3980636.500	49.9603
2	28.223	57458.410	3986955.250	50.0397
Total		131758.090	7967591.750	100.0000



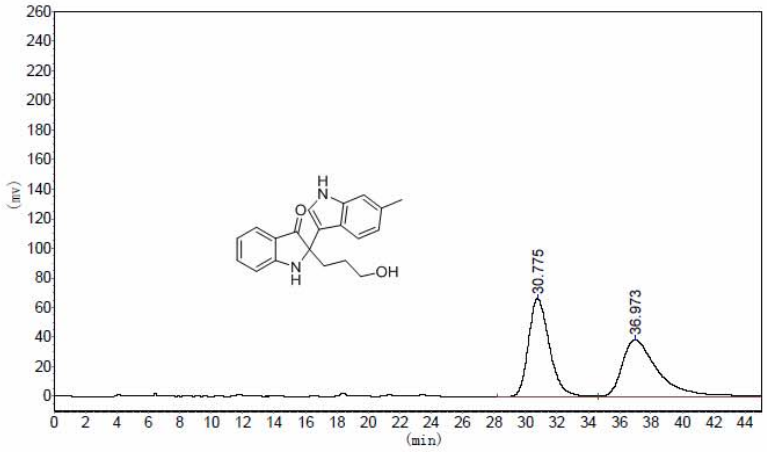
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	22.070	1879.476	99128.086	2.1307
2	28.247	65788.648	4553201.500	97.8693
Total		67668.124	4652329.586	100.0000



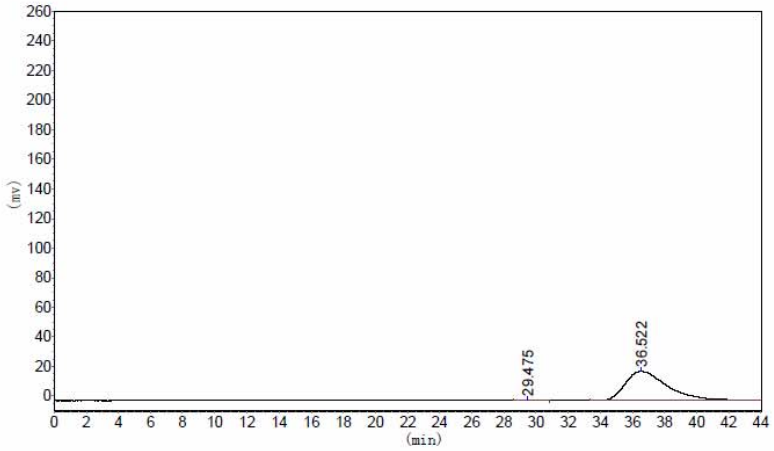
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	12.715	57997.797	1812165.125	49.9356
2	15.827	46770.836	1816837.000	50.0644
Total		104768.633	3629002.125	100.0000



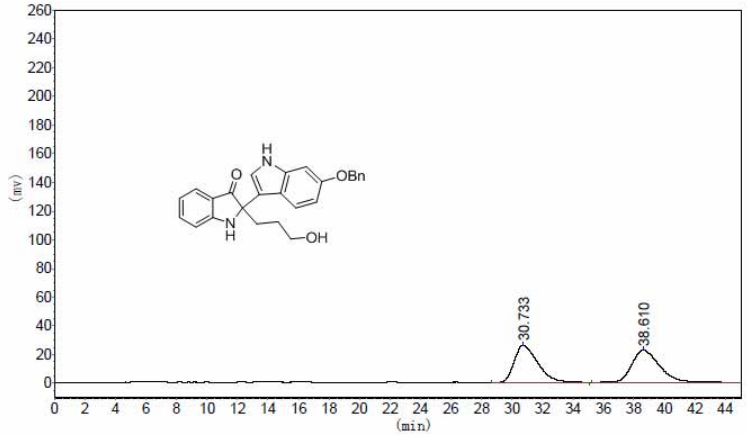
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	12.835	1332.311	40204.500	0.9889
2	15.943	105119.906	4025223.500	99.0111
Total		106452.217	4065428.000	100.0000



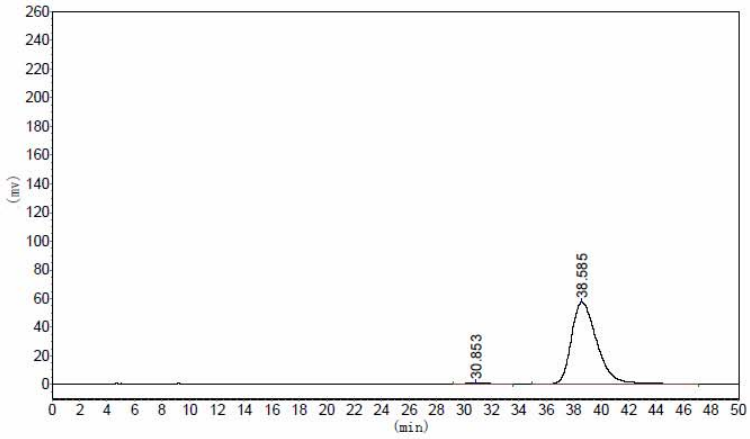
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	30.775	66262.813	6135610.000	50.1635
2	36.973	38569.965	6095603.000	49.8365
Total		104832.777	12231213.000	100.0000



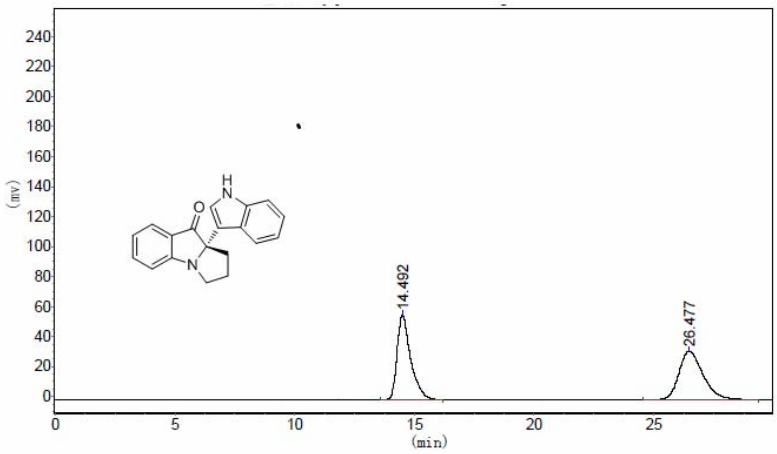
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	29.475	258.437	21069.072	0.5552
2	36.522	20032.404	3773486.500	99.4448
Total		20290.841	3794555.572	100.0000



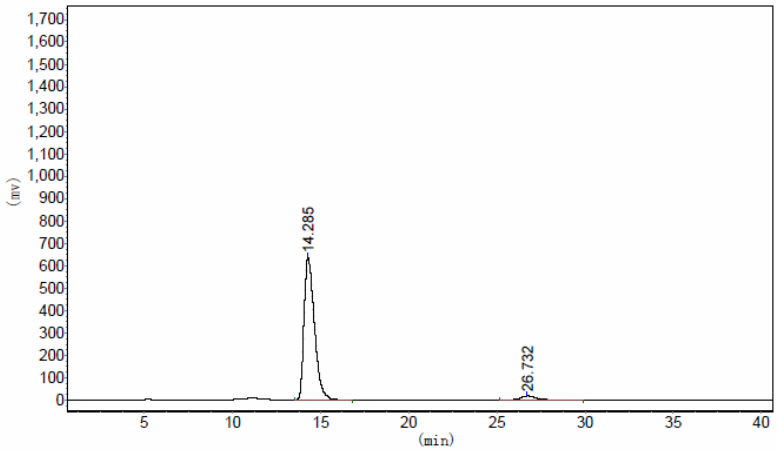
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	30.733	25686.350	2755605.250	49.1632
2	38.610	22261.916	2849406.750	50.8368
Total		47948.266	5605012.000	100.0000



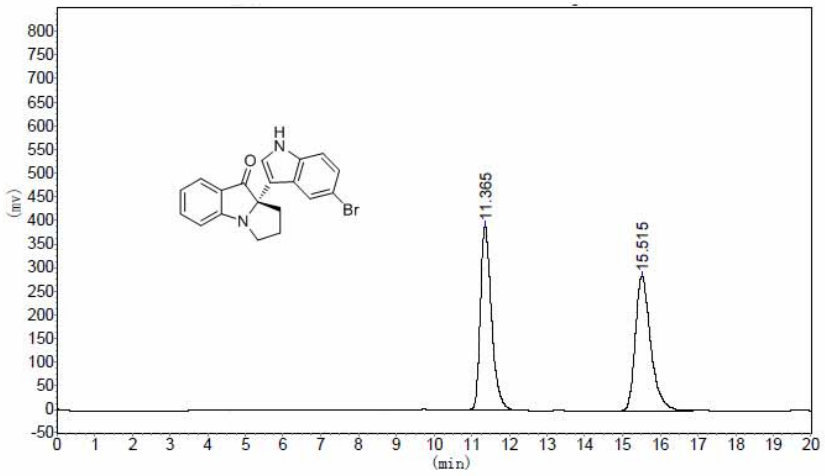
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	30.853	407.058	42328.141	0.5801
2	38.585	56848.852	7254308.000	99.4199
Total		57255.909	7296636.141	100.0000



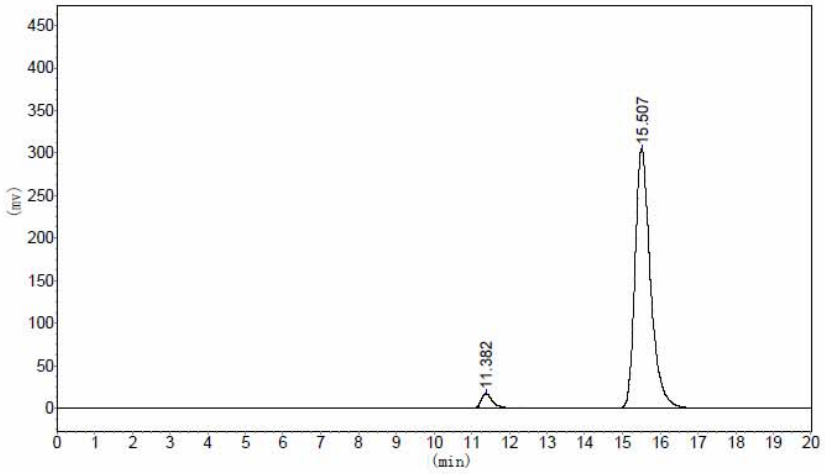
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	14.492	56551.066	2201083.500	49.9544
2	26.477	32120.406	2205098.500	50.0456
Total		88671.473	4406182.000	100.0000



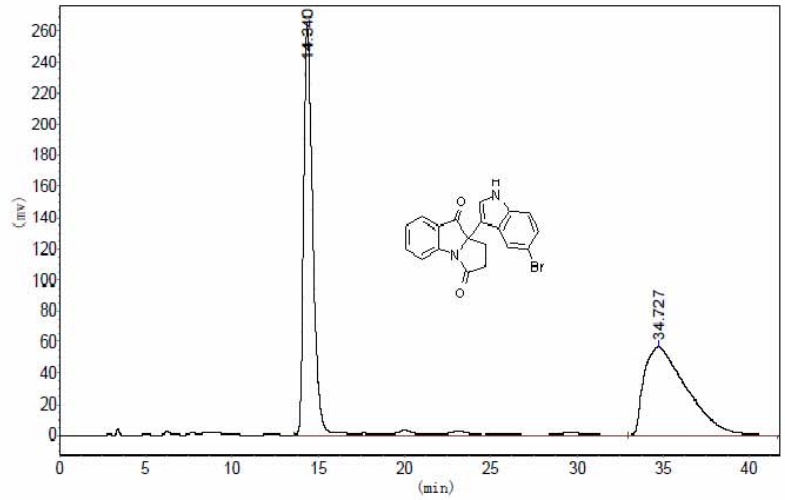
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	14.285	637539.625	25837352.000	95.7817
2	26.732	16893.996	1137902.125	4.2183
Total		654433.621	26975254.125	100.0000



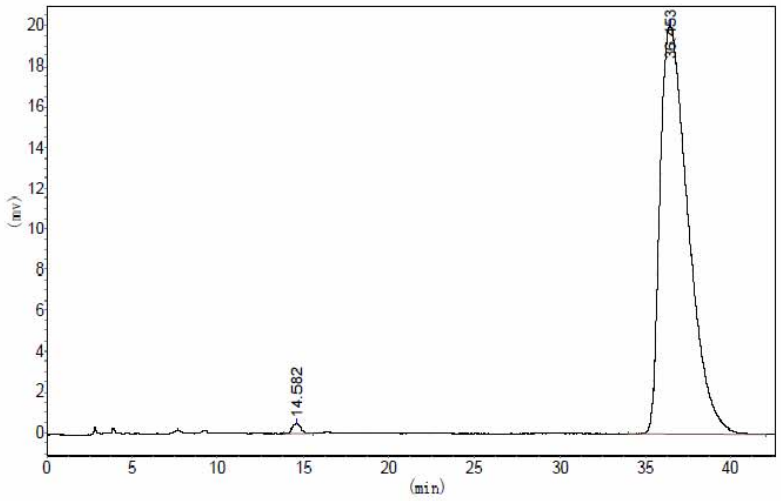
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	11.365	392977.563	8067949.500	49.8494
2	15.515	285332.844	8116697.000	50.1506
Total		678310.406	16184646.500	100.0000



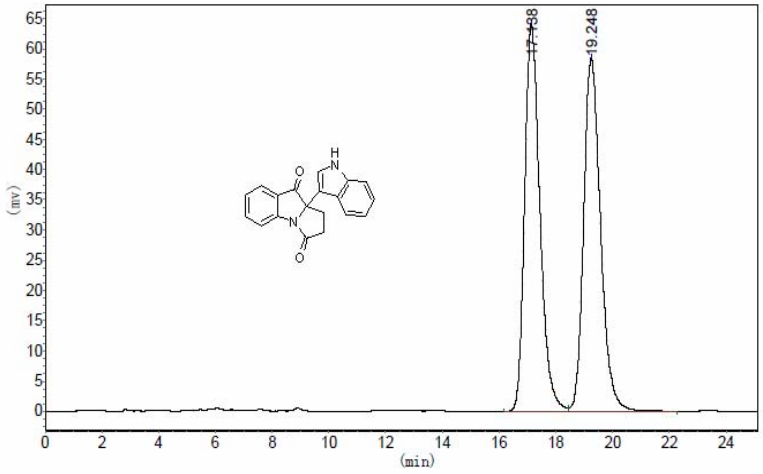
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	11.382	15256.477	270073.406	3.0446
2	15.507	304082.344	8600630.000	96.9554
Total		319338.820	8870703.406	100.0000



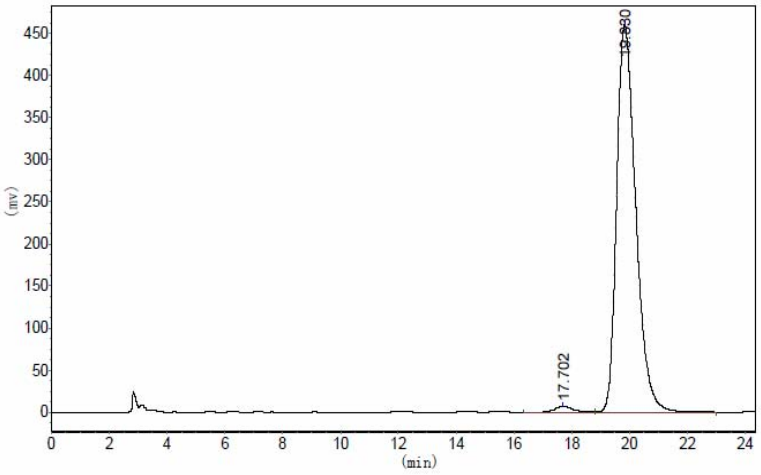
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	14.340	263503.844	10211640.000	51.3137
2	34.727	57606.629	9688763.000	48.6863
Total		321110.473	19900403.000	100.0000



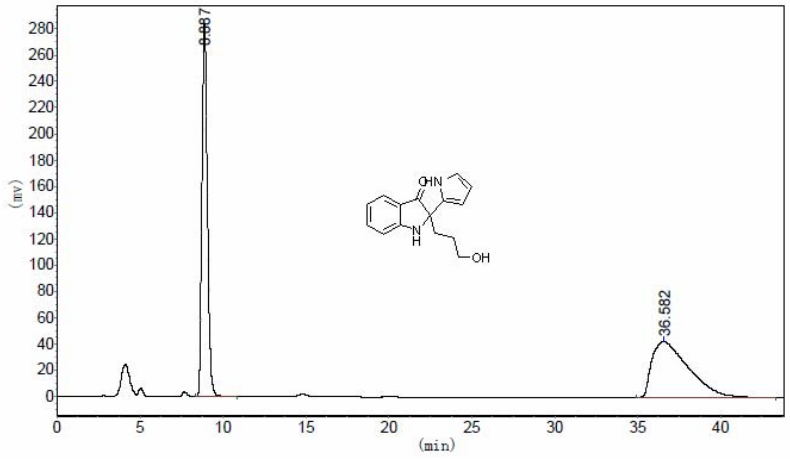
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	14.582	491.161	17505.338	0.7570
2	36.453	20052.432	2295056.750	99.2430
Total		20543.593	2312562.088	100.0000



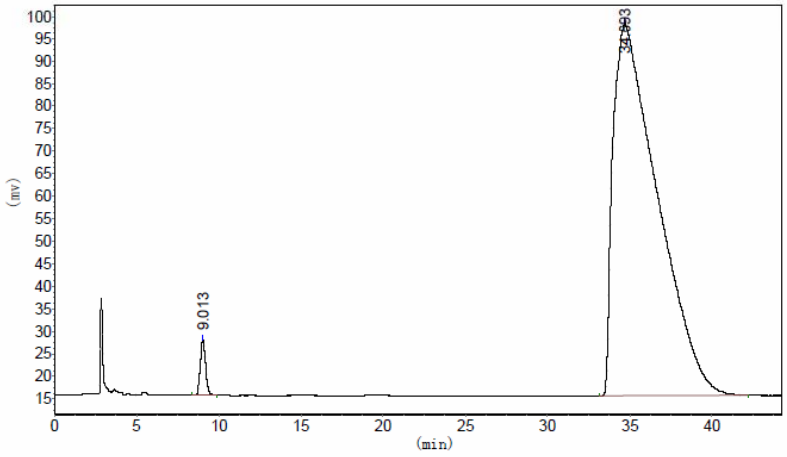
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	17.138	64042.281	2388759.000	49.7543
2	19.248	58401.031	2412355.000	50.2457
Total		122443.313	4801114.000	100.0000



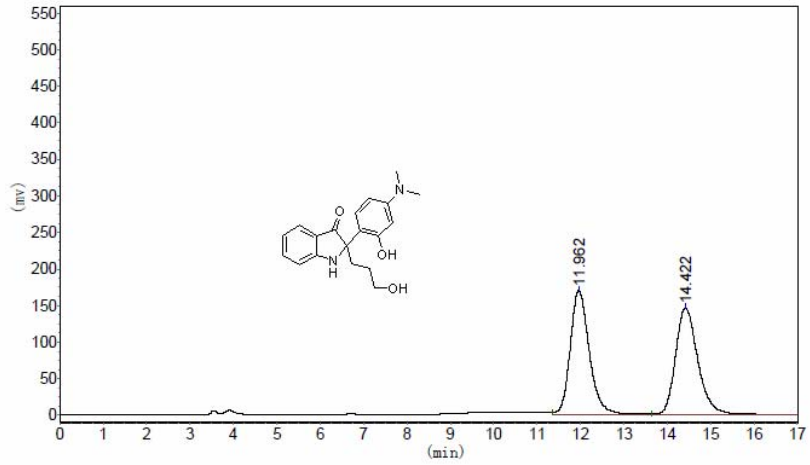
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	17.702	6954.414	288466.656	1.3521
2	19.830	459248.469	21045834.000	98.6479
Total		466202.883	21334300.656	100.0000



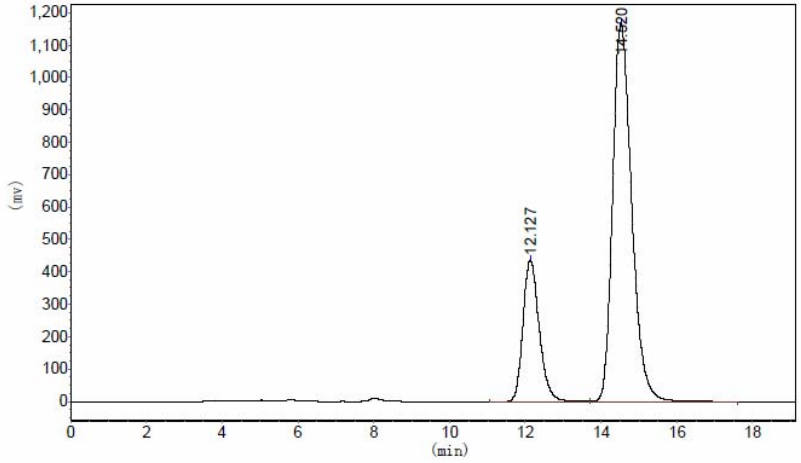
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	8.887	284042.563	6430490.000	49.9665
2	36.582	42674.875	6439116.000	50.0335
Total		326717.438	12869606.000	100.0000



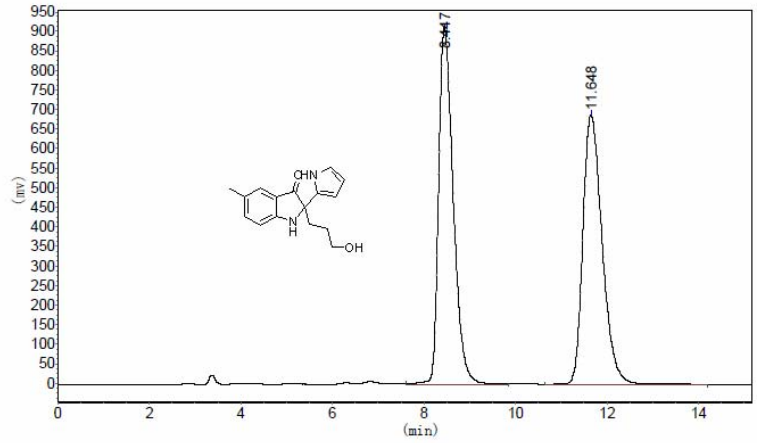
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	9.013	12378.948	277429.344	1.7632
2	34.693	82793.688	15457338.000	98.2368
Total		95172.636	15734767.344	100.0000



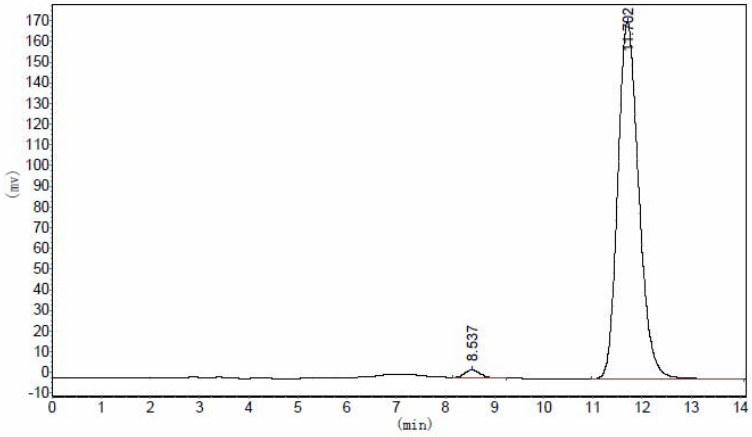
Peak No.	R. Time	Peak Height	Peak Area	Percent
1	11.962	170045.844	5229244.500	50.0188
2	14.422	146159.984	5225309.000	49.9812
Total		316205.828	10454553.500	100.0000



Peak No.	R. Time	Peak Height	Peak Area	Percent
1	12.127	437730.813	13062735.000	24.2723
2	14.520	1167121.000	40754680.000	75.7277
Total		1604851.813	53817415.000	100.0000



Peak No.	R. Time	Peak Height	Peak Area	Percent
1	8.447	910868.625	20190214.000	50.1948
2	11.648	689591.438	20033536.000	49.8052
Total		1600460.063	40223750.000	100.0000



Peak No.	R. Time	Peak Height	Peak Area	Percent
1	8.537	3888.046	89009.711	1.7143
2	11.702	172333.000	5103309.500	98.2857
Total		176221.046	5192319.211	100.0000