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Chiral vicinal diamines as promising ligands in Pd-catalyzed reductive Heck type cyclizations

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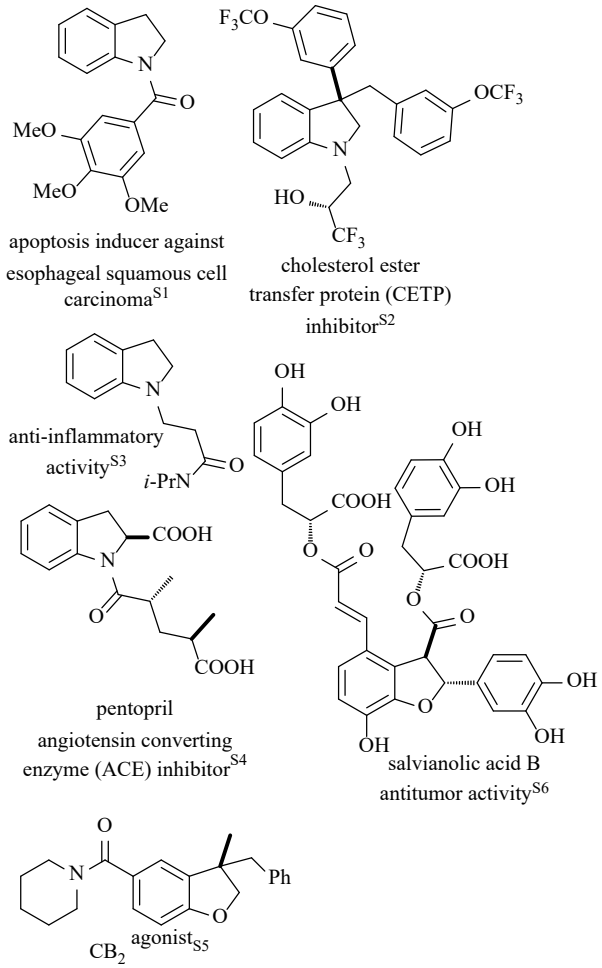


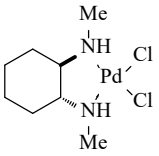
Figure S1. Representative bioactive compounds containing indoline and 2,3-dihydrobenzofuran core

1. General information

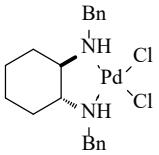
All commercial reagents were used without further purification. All solvents were distilled prior to use. {*N,N′*-Bis[(1*S*)-1-phenylethyl]ethane-1,2-diamine-κ^2*N,N′*}(dichloro)palladium,[S7] (1*R*,2*R*)-*N,N′*-dimethylcyclohexane-1,2-diamine,[S8] (1*R*,2*R*)-*N,N′*-dibenzylcyclohexane-1,2-diamine,[S9] (1*R*,2*R*)-*N,N′*-bis(4-methylbenzyl)-1,2-diphenylethane-1,2-diamine[S10] were obtained according to the reported procedures. Melting points were measured with an OptiMelt automated melting point system. All reactions were monitored by TLC, performed on precoated silica gel plates (Sorbfil); compounds were made visible with I_2. ^{1}H, ^{13}C NMR spectra were recorded with a JEOL JNM-ECX400 spectrometer at 400, 100.5 MHz, respectively, in $CDCl_3$ solution. Elemental analysis was performed with a EuroVector EA-3000 analyzer. Optical rotations were measured with Rudolph Research Analytical (Autopol V Plus Automatic Polarimeter). The enantiomeric purity of the products was determined by HPLC analysis on Shimadzu Prominence LC-20AD (Spd-20auv vis detector, Cto-20a column over, Dgu-20a degasing unit) equipped with a chiral stationary phase column (ChiralPAK AD-3) with hexane/2-propanol as eluent and with a chiral stationary phase column ChiralPAK AD-3R with water/acetonitrile as eluent. The high resolution mass spectra (HRMS) of compounds **2a-f** were obtained on an Agilent AccuTOF 6230 mass-spectrometer. The high resolution mass spectra (HRMS) of compounds **4,5,6** were obtained on a Bruker Ultraflex III MALDI-TOF/TOF mass spectrometer in the reflectron mode. The device is equipped with a solid-state laser Nd:YAG laser (λ = 355 nm, repetition rate 100 Hz). Measurements were made in the range *m/z* 200-1000. A mixture of the sample in $CHCl_3$ and calibrant PEG-400 (0.1 mg ml^{-1}, MeCN) was prepared to determine the exact mass values. *p*-Nitroaniline (10 mg ml^{-1}, MeCN) was used as a matrix. Portions (0.5 μl) of the matrix solution and the analyzed mixture were sequentially applied to the target and evaporated. The metal target MTP AnchorChipTM was used. The data was obtained using the FlexControl program (Bruker Daltonik GmbH, Germany) and processed using the FlexAnalysis 3.0 program (Bruker Daltonik GmbH, Germany). IR spectra were obtained on a Shimadzu IRAffinity-1 instrument using a Specac® Quest ATR ATR attachment.

2. Experimental procedures

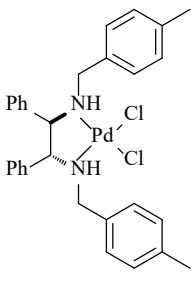
General procedure for catalysts synthesis. To a solution of diamine (0.757 mmol) in CH_2Cl_2 (4 ml) was added [$PdCl_2$(cod)] (0.19 g, 0.690 mmol) in CH_2Cl_2 (6 ml) and boiled for 1 h. The solvent was distilled off under reduced pressure. Diethyl ether was added to the residue. The formed precipitate was filtered off and washed with diethyl ether. Dried in vacuum.



((*R*,*R*)-*N*,*N*-Dimethylcyclohexane-1,2-diamine-κ^2-*N*,*N′*)(dichloro)palladium (4). This compound was prepared in accordance with the general procedure from (*R,R*)-*N,N*-dimethylcyclohexane-1,2-diamine (0.11 g, 0.757 mmol). Yield: 0.18 g (84%), yellow crystals, mp 281-282 ºC (decomp.). **IR (*ν*/cm^{-1}):** 3113 (s), 2935 (m), 2862 (m), 2360 (w), 1454 (m), 1161 (w), 1076 (m), 1006 (m), 952 (s), 910 (w), 894 (w), 848 (w), 794 (w), 736 (w), 590 (s). MALDI-TOF HRMS (*m/z*): [M+K]$^+$ calcd. for [$C_8H_{18}Cl_2N_2Pd$+K]$^+$ 356.9513, found 356.9543.



((*R*,*R*)-*N*,*N*-Dibenzylcyclohexane-1,2-diamine-κ^2-*N*,*N′*)(dichloro)palladium (5). This compound was prepared in accordance with the general procedure from (*R,R*)-*N,N*-dibenzylcyclohexane-1,2-diamine (0.22 g, 0.757 mmol). Yield: 0.20 g (62%), yellow crystals, mp 232-233ºC (decomp.), $[\alpha]_D^{20}$ = +190.9 (*c* 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 0.72-0.82 (m, 1H, CH_2), 1.00-1.65 (m, 6H, CH_2), 1.95-2.05 (m, 1H, CH_2), 2.40-2.60 (m, 1H, C<u>H</u>-N), 3.35-3.47 (m, 1H, C<u>H</u>$_2$Ph), 3.79 (d, 1H, *J* 13.2 Hz, C<u>H</u>$_2$Ph), 4.21-4.25 (m, 2H, C<u>H</u>$_2$Ph, C<u>H</u>-N), 4.36 (d, 1H, *J* 13.2 Hz, C<u>H</u>$_2$Ph), 5.49 (br s, 1H, NH), 5.64 (br s, 1H, NH), 7.20-7.55 (m, 8H, Ph), 8.05 (d, 2H, *J* 7.2 Hz, Ph). **^{13}C NMR (100.5 MHz, $CDCl_3$) *δ*:** 24.3 (CH_2), 24.4 (CH_2), 30.2 (CH_2), 31.5 (CH_2), 51.2 (<u>C</u>H$_2$Ph), 52.2 (<u>C</u>H$_2$Ph), 62.4 (<u>C</u>H-N), 66.5 (<u>C</u>H-N), 128.1 (CH_{Ar}), 128.7 (CH_{Ar}), 128.8 (CH_{Ar}), 128.9 (CH_{Ar}), 129.0 (CH_{Ar}), 130.8 (CH_{Ar}),), 135.3 (C_{Ar}), 137.3 (C_{Ar}). **IR (*ν*/cm^{-1}):** 3437 (w), 3074 (m), 2941 (w), 1602 (w), 1496 (s), 1454 (s), 1286 (w), 1207 (w), 1128 (w), 1111 (w), 939 (m), 871 (m), 736 (vs), 696 (vs). MALDI-TOF HRMS (*m/z*): [M+K]$^+$ calcd. for [$C_{20}H_{26}Cl_2N_2Pd$+K]$^+$ 509.0139, found 509.0164.



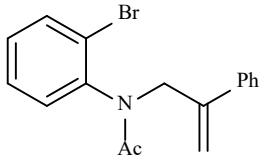
((1*R*,2*R*)-*N*^{1},*N*^{2}-bis(4-methylbenzyl)-1,2-diphenylethane-1,2-diamine-κ^2-N,N′)(dichloro)palladium (6). This compound was prepared in accordance with the general procedure from (1*R*,2*R*)-*N*^{1},*N*^{2}-bis(4-methylbenzyl)-1,2-diphenylethane-1,2-diamine (0.32 g, 0.757 mmol). Yield: 0.30 g (74%), yellow crystals, mp 238-239 ºC

(decomp.), $[\alpha]_D^{20}$ = +220.0 (*c* 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 2.20 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 3.16 (d, 1H, *J* 12.0 Hz, CH_2), 3.64 (dd, 1H, *J* 14.2, 7.4 Hz, CH_2), 4.31-4.41 (m, 2H, CH, CH_2), 4.74 (d, 1H, *J* 12.0 Hz, CH_2), 5.92 (dd, 1H, J 12.8, 4.6 Hz, CH), 6.05 (br s, 1H, NH), 6.32 (br s, 1H, NH), 6.81-7.22 (m, 12H, aromatic), 7.39 (d, 2H, *J* 7.8 Hz, aromatic), 7.60 (d, 2H, *J* 7.2 Hz, aromatic), 8.37 (d, 2H, *J* 7.8 Hz, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) *δ*:** 21.2 (CH_3), 21.5 (CH_3), 51.2 (CH_2), 51.5 (CH_2), 66.9 (CH), 68.6 (CH), 128.1 (CH_{Ar}), 128.4 (CH_{Ar}), 128.6 (CH_{Ar}), 128.8 (CH_{Ar}), 129.0 (CH_{Ar}), 129.1 (CH_{Ar}), 129.7 (CH_{Ar}), 130.4 (CH_{Ar}), 130.9 (CH_{Ar}), 131.1 (C_{Ar}), 132.7 (C_{Ar}), 133.1 (C_{Ar}), 134.9 (C_{Ar}), 136.7 (C_{Ar}), 138.5 (C_{Ar}). **IR (*ν*/cm^{-1}):** 3122 (w), 2920 (w), 1516 (m), 1498 (m), 1456 (m), 1444 (m), 1373 (w), 1209 (w), 1184 (w), 1120 (w), 1018 (w), 883 (m), 840 (w), 796 (s), 763 (s), 752 (s), 700 (vs), 574 (m), 522 (s). MALDI-TOF HRMS (*m/z*): $[M+K]^+$ calcd. for $[C_{30}H_{32}Cl_2N_2Pd+K]^+$ 635.0609, found 635.0611.

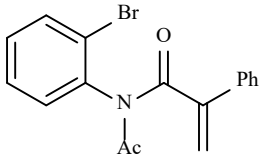
General procedure for the synthesis of compounds 1a,b,e

Sodium hydride (60% dispersion in mineral oil, 0.73 g, 18.30 mmol) was added portionwise with stirring to a solution of the corresponding amide (16.70 mmol) in dry THF (50 ml). The mixture was stirred for 10 min and then a solution of (3-bromoprop-1-en-2-yl)benzene (3.94 g, 20.0 mmol) or 2-phenylacrylic acid chloride (3.6 g, 21.71 mmol) in dry THF (20 ml) was added. The resulting mixture was stirred at room temperature for 96 hours. The reaction mixture was poured into water (150 ml) and extracted with ethyl acetate (2×25 ml). The extract was dried over sodium sulfate and the solvent was distilled off under reduced pressure.

***N*-(2-Bromophenyl)-*N*-(2-phenylallyl)acetamide (1a).** This compound was prepared in accordance with the general procedure from *N*-(2-bromophenyl)acetamide (3.25 g, 16.70 mmol). The product was purified by recrystallization from hexane. Yield: 3.13 g (57%), colorless cryst., m.p. 58-61 °C. **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.73 (s, 3H, CH_3), 3.92 (d, 1H, *J* 14.8 Hz, $\underline{CH_2}$-N), 5.00 (s, 1H, =CH_2), 5.35 (s, 1H, =CH_2), 5.74 (d, 1H, *J* 14.8 Hz, $\underline{CH_2}$-N), 6.67-6.69 (m, 1H, aromatic), 7.14-7.17 (m, 2H, aromatic), 7.27-7.34 (m, 3H, aromatic), 7.42-7.45 (m, 2H, aromatic), 7.62-7.64 (m, 1H, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) *δ*:** 22.7 (CH_3), 50.0 ($\underline{CH_2}$-N), 116.9 (=CH_2), 123.7 (C_{Ar}), 126.4 (2C, CH_{Ar}), 128.0 (CH_{Ar}), 128.2 (CH_{Ar}), 128.6 (2C, CH_{Ar}), 129.8 (CH_{Ar}), 131.6 (CH_{Ar}), 133.8 (CH_{Ar}), 138.5 ($\underline{C}$=CH_2), 140.5 (C-N), 143.5 (C_{Ar}), 170.4 (C=O). **IR (*ν*/cm^{-1}):** 3283 (w), 3059 (w), 2963 (w), 2916 (w), 1659 (vs), 1470 (s), 1381 (vs), 1277 (vs), 1249 (s), 1091 (m), 1015 (s), 907 (vs), 775 (vs), 752 (vs), 709 (vs), 682 (vs), 613 (m), 594 (m), 559 (s). **MS, *m*/*z* (I_{rel}, %):** 329$[M]^+$ (8), 289 (90), 287 (100), 250 (40), 206 (30), 196 (30), 186 (50), 184 (62), 155 (10), 130 (15), 117 (40), 115 (55), 103 (25), 91 (35), 77 (32). Anal. calcd for $C_{17}H_{16}BrNO$: C 61.83; H 4.88; N 4.24. Found: C 61.88, H 4.92, N 4.34.



***N*-(2-Bromophenyl)-*N*-(2-phenylallyl)benzamide (1b).** This compound was prepared in accordance with the general procedure from *N*-(2-bromophenyl)benzamide (4.59 g, 16.70 mmol). The product was purified by column chromatography (eluent petroleum ether). Yield: 4.11 g (63%), colorless cryst., m.p. 102-104 °C. **^{1}H NMR (400 MHz, $CDCl_3$) *δ*:** 4.17 (d, 1H, *J* 15.2 Hz, $\underline{CH_2}$-N), 5.16 (s, 1H, =CH_2), 5.41 (s, 1H, =CH_2), 5.97 (d, 1H, *J* 15.2 Hz, $\underline{CH_2}$-N), 6.51 (dd, 1H, *J* 7.4 Hz, 1.4 Hz, aromatic), 6.90-6.98 (m, 2H, aromatic), 7.05-7.09 (m, 2H, aromatic), 7.13-7.20 (m, 3H, aromatic), 7.28-7.37 (m, 3H, aromatic), 7.43-7.52 (m, 3H, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) *δ*:** 50.6 ($\underline{CH_2}$-N), 116.8 (=CH_2), 123.4 (C_{Ar}), 126.6 (CH_{Ar}), 127.5 (CH_{Ar}), 127.6 (CH_{Ar}), 127.7 (CH_{Ar}), 128.1 (CH_{Ar}), 128.6 (CH_{Ar}), 129.2 (CH_{Ar}), 129.6 (CH_{Ar}), 132.7 (CH_{Ar}), 133.4 (CH_{Ar}), 136.1 (C_{Ar}), 138.6 ($\underline{C}$=CH_2), 140.7 (C-N), 143.6 (C_{Ar}), 170.8 (C=O). **IR (*ν*/cm^{-1}):** 3071 (w), 3024 (w), 2970 (w), 2943 (w), 1632 (vs), 1574 (m), 1474 (s), 1447 (m), 1369 (vs), 1350 (vs), 1281 (s), 1254 (s), 1219 (m), 1150 (m), 1065 (m), 1030 (m), 987 (m), 907 (s), 791 (s), 768 (s), 741 (s), 710 (vs), 691 (vs), 667 (m), 640 (m), 567 (s), 532 (m). **MS, *m*/*z* (I_{rel}, %):** 391 $[M]^+$ (8), 312 (12), 286 (8), 260 (18), 258 (20), 207 (8), 115 (10), 105 (100), 77 (41). Anal. calcd for $C_{22}H_{18}BrNO$: C 67.36; H 4.63; N 3.57. Found: C 67.41, H 4.66, N 3.59.

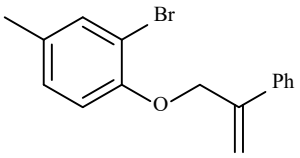


***N*-Acetyl-*N*-(2-bromophenyl)-2-phenylacrylamide (1e).** This compound was prepared in accordance with the general procedure from *N*-(2-bromophenyl)acetamide (3.25 g, 16.70 mmol). The reaction mixture was stirred for 12 hours. The product was purified by column chromatography (eluent petroleum ether/EtOAc 5:1). Yield: 2.46 g (43%), colorless cryst., m.p. 90-92 °C. **^{1}H NMR (400 MHz, $CDCl_3$) *δ*:** 2.47 (s, 3H, CH_3), 5.49 (s, 1H, =CH_2), 5.74 (s, 1H, =CH_2), 6.81-6.83 (m, 1H, aromatic), 7.12-7.17 (m, 4H, aromatic), 7.25-7.28 (m, 3H, aromatic), 7.53-7.56 (m, 1H, aromatic).

^{13}C NMR (100.5 MHz, $CDCl_3$) δ: 26.4 (CH_3), 118.7 (=CH_2), 124.3 (C_{Ar}), 126.3 (CH_{Ar}), 128.1 (CH_{Ar}), 128.5 (CH_{Ar}), 128.6 (CH_{Ar}), 130.2 (CH_{Ar}), 131.3 (CH_{Ar}), 133.5 (CH_{Ar}), 135.8 (C_{Ar}), 137.3 (C=CH_2), 146.1 (C_{Ar}–N), 171.3 (C=O), 172.4 (C=O). **IR (ν/cm^{-1}):** 3101 (w), 3059 (w), 3032 (w), 1718 (s), 1689 (vs) , 1614 (m), 1575 (m), 1498 (m), 1471 (s), 1433 (m), 1365 (s), 1332 (m), 1288 (m), 1251 (m), 1228 (vs), 1161 (s), 1026 (s), 925 (m), 915 (m), 786 (m), 765 (s), 758 (s). **MS, m/z (I_{rel}, %):** 345 $[M]^+$ (8), 343 (8), 317 (10), 315 (10) 301 (7), 222 (42), 196 (10), 193 (8), 131 (4), 104 (10), 103 (100), 90 (8), 77 (30), 76 (10). Anal. calcd for $C_{17}H_{14}BrNO_2$: C 59.32; H 4.10; N 4.07. Found: C 59.37; H 4.17; N 4.16.

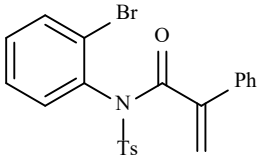
***N*-(2-Bromophenyl)-4-methyl-*N*-(2-phenylallyl)benzenesulfonamide (1c)** was obtained according to reported procedures.[S11] Yield: 57%.

2-Bromo-4-methyl-1-(2-phenylallyloxy)benzene (1d) was obtained according to reported procedures.[S12] The product was purified by column chromatography (eluent CCl_4). Yield: 76%, colorless oil.



^{1}H NMR (400 MHz, $CDCl_3$) δ: 2.29 (s, 3H, CH_3), 4.93 (s, 2H, CH_2O), 5.58 (s, 1H, =CH_2), 5.62 (s, 1H, =CH_2), 6.86 (d, 1H, *J* 8.0 Hz, aromatic), 7.04 (d, 1H, *J* 8.0 Hz, aromatic), 7.38-7.39 (m, 4H, aromatic), 7.50 (m, 2H, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 20.3 (CH_3), 70.8 (CH_2O), 112.3 (C_{Ar}), 113.9 (CH_{Ar}), 114.7 (=CH_2), 126.2 (2C, CH_{Ar}), 128.1 (CH_{Ar}), 128.6 (2C, CH_{Ar}), 128.9 (CH_{Ar}), 132.0 (C_{Ar}), 133.9 (CH_{Ar}), 138.5 (C_{Ar}), 142.7 (C=CH_2), 152.9 (C_{Ar}-O). **IR (ν/cm^{-1}):** 1605 (m), 1493 (vs), 1450 (m), 1382 (w), 1285 (m), 1250 (s), 1053 (s), 1023 (m), 907 (m), 775 (s), 752 (vs), 702 (vs). **MS, m/z (I_{rel}, %):** 302 $[M]^+$ (10), 287 (8), 224 (12), 209 (52), 208 (20), 179 (14), 165 (14), 152 (8), 145 (18), 115 (42), 103 (100), 91 (74), 78 (22), 77 (90), 65 (38), 63 (16), 51 (26). Anal. calcd for $C_{16}H_{15}BrO$: C 63.38; H 4.99. Found: C 63.42; H 4.97.

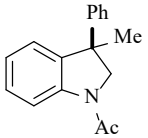
***N*-(2-Bromophenyl)-2-phenyl-*N*-tosylacrylamide (1f).** A solution of 2-phenylacrylic acid chloride (1.46 g, 8.78 mmol) in CH_2Cl_2 (0.4 M) was added dropwise to a mixture of *N*-(2-bromophenyl)-4-methylbenzenesulfonamide (2.20 g, 6.75 mmol) and Et_3N (1.02 g, 10.1 mmol) cooled to 0 °C in 42 mL CH_2Cl_2. The reaction mass was stirred for 12 hours at room temperature, then extracted with ethyl acetate (3x15 ml). Organic extracts were combined and washed with $NaHCO_3$, dried over sodium sulfate. The solvent was evaporated under reduced pressure. The product was purified by column chromatography (eluent petroleum ether/EtOAc 7%). Yield: 1.47 g (48%), colorless cryst., m.p. 141-143°C. **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 2.46 (s, 3H, CH_3), 5.37 (s, 1H, =CH_2), 5.73 (s, 1H, =CH_2), 6.71 (dd, 1H, *J* 8.0, 1.6 Hz, aromatic), 6.89-6.93 (m, 3H, aromatic), 7.07-7.12 (m, 1H, aromatic), 7.14-7.18 (m, 2H, aromatic), 7.21-7.23 (m, 1H, aromatic), 7.34 (d, 2H, *J* 8.0, aromatic), 7.47 (dd, 1H, *J* 8.0, 1.6 Hz, aromatic), 8.01 (d, 2H, *J* 8.4 Hz, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 21.8 (CH_3), 120.9 (CH_2), 125.2 (C_{Ar}), 126.0 (CH_{Ar}), 127.3 (CH_{Ar}), 128.5 (CH_{Ar}), 128.6 (CH_{Ar}), 129.3 (CH_{Ar}), 130.0 (CH_{Ar}), 130.7 (CH_{Ar}), 133.4 (CH_{Ar}), 133.8 (CH_{Ar}), 134.8 (C_{Ar}), 135.6 (C_{Ar}), 135.9 (C_{Ar}), 144.9 (C=CH_2), 145.3 (C_{Ar}–N), 168.9 (C=O). **IR (ν/cm^{-1}):** 3061 (w), 3026 (w), 2922 (w), 2852 (w), 1695 (s), 1476 (m), 1363 (s), 1168 (s), 1155 (vs), 1082 (vs), 968 (m), 929 (m), 815 (m), 761 (s), 704 (s). Anal. calcd for $C_{22}H_{18}BrNO_3S$: C 57.90; H 3.98; N 3.07; S 7.03. Found: C 57.95; H 3.95; N 3.17; S 7.13.



General procedure of reductive Heck reaction:

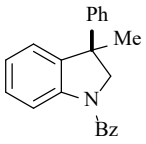
Catalyst **5** (10 mol.%, 0.052 mmol) and DMF (1 ml) were added to an ampule filled with argon. The mixture was stirred until complete dissolution of the catalyst. Then sodium acetate (0.11 g, 1.29 mmol), sodium formate (70 mg, 1.03 mmol), compound **1a-f** (0.52 mmol) and a solution of 15-crown-5 (11 mg, 0.052 mmol) in DMF (1 ml) were added. The reaction mixture was stirred for 24 h at a temperature of 80 °C in a sealed ampoule in an argon atmosphere. After cooling, the reaction mixture was poured into 5 ml of water and extracted with ethyl acetate (3×5 ml).

1-Acetyl-3-methyl-3-phenylindoline (2a). The product was purified by column chromatography (eluent petroleum ether/EtOAc 10:1). Yield: 86 mg (66%), colorless cryst, m.p. 81-83 °C, $[\alpha]_D^{20}$ = -6.2 (*c* 1.0, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.77 (s, 3H, CH_3), 2.18 (s, 3H, CH_3), 4.03 (d, 1H, *J* 11.4 Hz, CH_2), 4.15 (d, 1H, *J* 11.4 Hz, CH_2), 6.97-7.07 (m, 2H, aromatic), 7.23-7.30 (m, 6H, aromatic), 8.27 (d, 1H, *J* 8.4 Hz, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 24.3 (CH_3), 27.2 (CH_3), 48.0 (C-3), 65.9 (C-2), 117.1 (CH_{Ar}), 124.0 (CH_{Ar}), 124.2 (CH_{Ar}), 126.5 (2CH_{Ar}), 126.8 (CH_{Ar}), 128.2 (CH_{Ar}), 128.6 (2CH_{Ar}), 139.5 (C_{Ar}), 142.4 (C_{Ar}), 146.9 (C_{Ar}), 168.7 (C=O). **IR (ν/cm^{-1}):** 2970 (w), 2882 (w), 1655 (vs), 1593 (m), 1481 (s), 1400 (vs), 1358 (m),

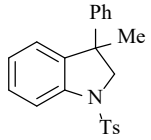


1339 (s), 1281 (s), 1130 (m), 1099 (m), 1057 (m), 1026 (s), 942 (w), 922 (w), 817 (s), 764 (vs), 752 (vs), 698 (vs), 556 (s). **MS, *m*/*z* (I_{rel}, %):** 251 $[M]^+$ (44), 209 (8), 195 (10), 194 (100), 165 (10), 132 (8), 91 (6), 77 (5). APPI-HRMS (*m*/*z*): calcd. for $[C_{17}H_{17}NO+H]^+$ 252.1383; found 252.1385. HPLC (Chiralpak AD-3R, H_2O/MeCN, 0.25 mL/min, λ = 210, 230 nm), retention times: (*R*) (major) 18.9 min, (*S*) (minor) 20.5 min.

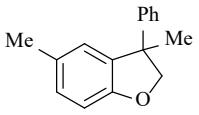
1-Benzoyl-3-methyl-3-phenylindoline (2b). The product was purified by column chromatography (eluent CCl_4). Yield: 81 mg (50%), colorless cryst. m.p. 132-133 °C, $[\alpha]_D^{20} = 5.54$ (*c* 0.33, $CHCl_3$). **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.74 (s, 3H, CH_3), 4.05 (s, 1H, CH_2), 4.23 (s, 1H, CH_2), 7.03-7.05 (m, 2H, aromatic), 7.20-7.32 (m, 6H, aromatic), 7.39-7.51 (m, 6H, aromatic). **IR (*ν*/cm^{-1}):** 2962 (w), 2924 (w), 2885 (w), 1720 (m), 1647 (vs), 1597 (m), 1477 (s), 1446 (m), 1373 (vs), 1334 (m), 1284 (m), 1257 (m), 1157 (m), 1072 (m), 1049 (w), 1026 (m), 925 (w), 864 (w), 790 (m) , 752 (s), 649 (vs), 663 (s), 609 (m), 578 (m). **MS, m/z (Irel, %):** 313 $[M]^+$ (50), 298 (10), 281 (8), 207 (18), 165 (8), 130 (8), 105 (100), 91 (8), 77 (38). APPI-HRMS (*m*/*z*): calcd. for $[C_{22}H_{19}NO+H]^+$ 314.1539; found 314.1532. HPLC (Chiralpak AD-3, hexane/2-propanol, 95:5; 1.2 mL/min; λ = 230, 254 nm), retention times: (*S*) (minor) 24.1 min, (*R*) (major) 35.9 min.



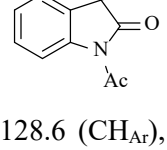
3-Methyl-3-phenyl-1-tosylindoline (2c). The product was purified by column chromatography (eluent CCl_4:$CHCl_3$ (5%)). Yield: 115 mg (61%), colorless cryst., m.p. 119-120 °C. **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.55 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 3.95 (d, 1H, *J* 10.6 Hz, CH_2), 4.05 (d, 1H, *J* 10.6 Hz, CH_2), 6.88-7.01 (m, 4H, aromatic), 7.14-7.28 (m, 6H, aromatic), 7.62 (d, 2H, *J* 7.6 Hz, aromatic), 7.73 (d, 1H, ^3J 7.6 Hz, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 21.6 (CH_3), 27.2 (CH_3), 48.0 (C-3), 66.0 (C-2), 114.9 (CH_{Ar}), 124.1 (CH_{Ar}), 124.8 (CH_{Ar}), 126.5 ($4CH_{Ar}$), 127.3 ($2CH_{Ar}$), 128.4 ($2CH_{Ar}$), 129.7 ($2CH_{Ar}$), 134.0 (C_{Ar}), 139.6 (C_{Ar}), 141.5 (C_{Ar}), 144.1 (C_{Ar}), 146.5 (C_{Ar}). **IR (*ν*/cm^{-1}):** 2963 (w), 1593 (w), 1493 (w), 1474 (w), 1458 (w), 1377 (w), 1354 (s), 1165 (vs), 1111 (w), 1088 (m), 1022 (m), 976 (m), 906 (w), 814 (m), 768 (vs), 729 (s), 706 (s), 660 (vs), 629 (m), 575 (vs), 540 (vs). **MS, *m*/*z* (I_{rel}, %):** 363 $[M]^+$ (50), 348 (20), 281 (16), 253 (10), 209 (20), 208 (60), 207 (100), 193 (26), 165 (18), 155 (10), 130 (28), 115 (15), 91 (55). APPI-HRMS (*m*/*z*): calcd. for $[C_{22}H_{21}NO_2S+H]^+$ 364.1366; found 364.1361. HPLC (Chiralpak AD-3, hexane/2-propanol, 97:3; 1.2 mL/min; λ = 230, 254 nm), retention times: first enantiomer 16.9 min, second enantiomer 19.6 min.



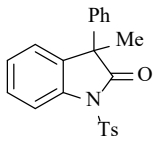
3,5-Dimethyl-3-phenyl-2,3-dihydrobenzofuran (2d). The product was purified by column chromatography (eluent petroleum ether). Yield: 61 mg (53%), yellow oil. **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.75 (s, 3H, CH_3), 2.28 (s, 3H, CH_3), 4.45 (d, 1H, *J* 8.9 Hz, CH_2), 4.58 (d, 1H, *J* 8.9 Hz, CH_2), 6.78-6.83 (m, 2H, aromatic), 6.98-6.99 (m, 1H, aromatic), 7.23-7.32 (m, 5H, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 21.0 (CH_3), 26.1 (CH_3), 50.0 (C-3), 86.3 (C-2), 109.5 (CH_{Ar}), 124.7 (CH_{Ar}), 126.7 ($3CH_{Ar}$), 128.5 ($2CH_{Ar}$), 128.9 (CH_{Ar}), 130.3 (C_{Ar}), 135.7 (C_{Ar}), 146.5 (C_{Ar}), 157.7 (C_{Ar}). **IR (*ν*/cm^{-1}):** 2967 (w), 2878 (w), 1655 (w), 1597 (m), 1489 (vs), 1466 (s), 1447 (s), 1377 (w), 1331 (m), 1277 (m), 1242 (m), 1215 (s), 1153 (m), 1114 (m), 1053 (m), 980 (s), 841 (m), 806 (vs), 764 (vs), 741 (s), 694 (vs), 590 (w), 556 (m). **MS, *m*/*z* (I_{rel}, %):** 224 $[M]^+$ (80), 209 (100), 181 (60), 165 (30), 147 (10), 115 (10), 103 (12), 91 (10), 77 (10). Anal. calcd. for $C_{16}H_{16}O$: C 85.68; H 7.19. Found: C 85.79; H 7.11.



1-Acetyl-3-methyl-3-phenylindolin-2-one (2e). The product was purified by column chromatography (eluent CCl_4:$CHCl_3$ (5%)). Yield: 65 mg (47%), colorless cryst., m.p. 111-112 °C. **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.87 (s, 3H, CH_3), 2.64 (s, 3H, CH_3), 7.18-7.20 (m, 1H, aromatic), 7.23-7.33 (m, 6H, aromatic), 7.35-7.39 (m, 1H, aromatic), 8.33 (d, 1H, *J* 8.0 Hz, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 24.5 (CH_3), 26.7 (CH_3), 52.6(C-3), 116.9 (CH_{Ar}), 124.1 (CH_{Ar}), 125.6 (CH_{Ar}), 126.8 (2C, CH_{Ar}), 127.8 (CH_{Ar}), 128.6 (CH_{Ar}), 128.8 (2C, CH_{Ar}), 133.7(C_{Ar}), 139.6 (C_{Ar}) , 140.4 (C_{Ar}), 171.2 (C=O), 180.1 (C=O). **IR (*ν*/cm^{-1}):** 3005 (w), 2974 (w), 2931 (w), 2851 (w), 1751 (vs), 1709 (vs), 1604 (m), 1493 (m), 1477 (s), 1458 (s), 1442 (s), 1416 (m), 1369 (vs), 1338 (s), 1303 (s), 1269 (vs), 1196 (m), 1168 (vs), 1018 (vs), 760 (vs), 729 (vs), 698 (vs), 675 (s), 625 (m), 590 (vs). **MS, *m*/*z* (I_{rel}, %):** 265 $[M]^+$ (22), 223 (100), 208 (98), 193 (40), 180 (16), 165 (12), 152 (10), 116 (12), 77 (10). APPI-HRMS (*m*/*z*): calcd. for $[C_{17}H_{15}NO_2\text{-}CH_3CO+2H]^+$ 224.1070; found 224.1066. HPLC (Chiralpak AD-3, hexane/2-propanol, 98:2; 1.2 mL/min; λ = 230, 254 nm), retention times: first enantiomer 7.4 min, second enantiomer 8.1 min.



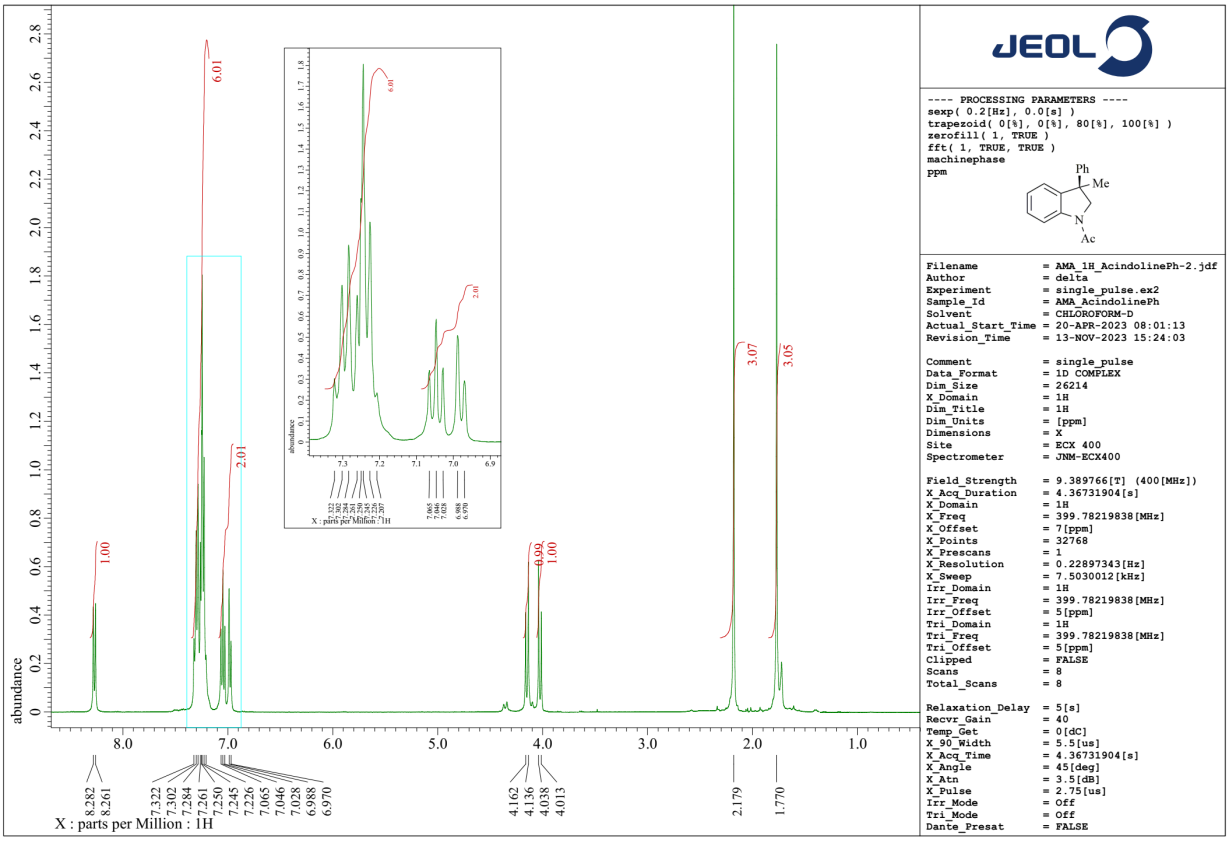
3-Methyl-3-phenyl-1-tosylindolin-2-one (2f). The product was purified by column chromatography (eluent CCl_4). Yield: 98 mg (50%), colorless cryst., m.p. 111-112 °C. **^{1}H NMR (400 MHz, $CDCl_3$) δ:** 1.69 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 7.01-7.04 (m, 2H, aromatic), 7.09-7.11 (m 1H, aromatic), 7.17-7.21 (m, 4H, aromatic), 7.26 (d, 2H, *J* 8.2



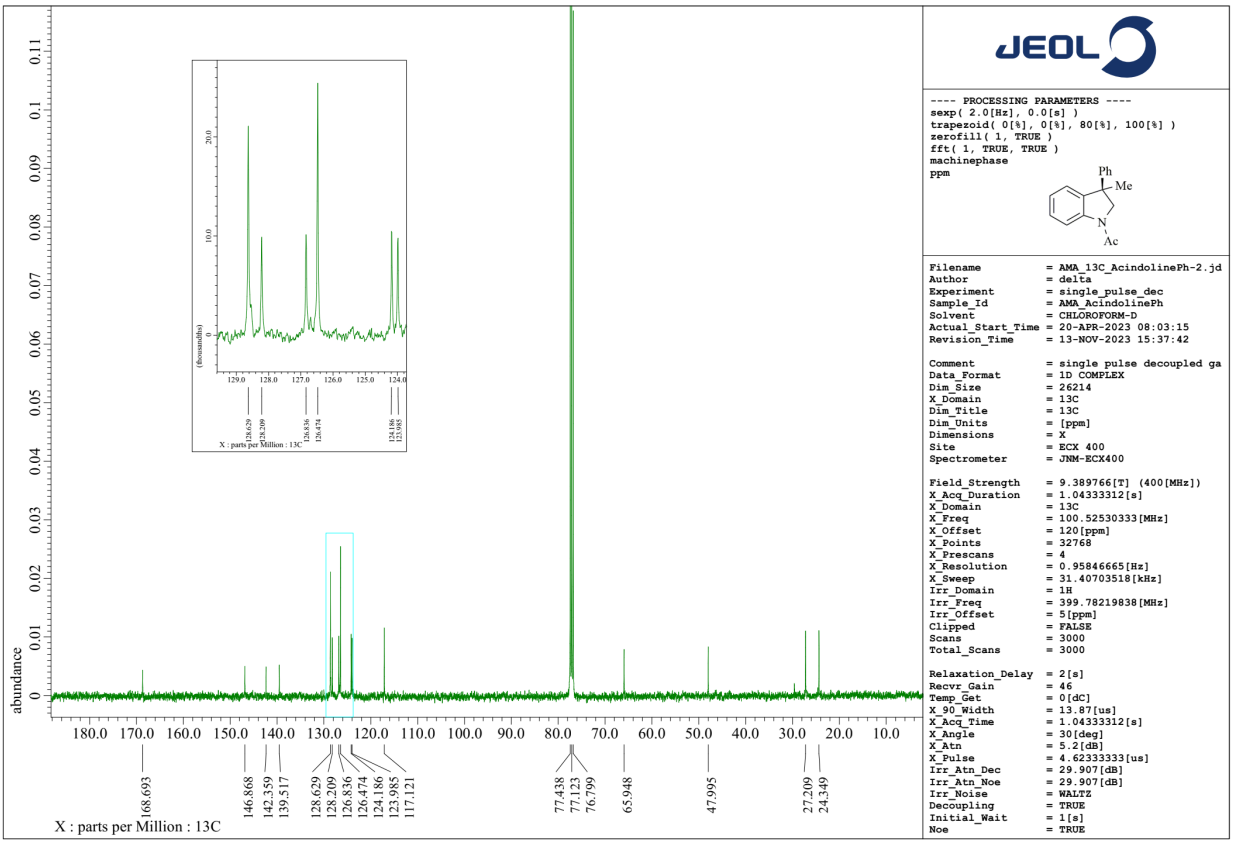
Hz, aromatic), 7.35-7.39 (m, 1H, aromatic), 7.93 (d, 2H, *J* 8.5 Hz, aromatic), 8.01 (d, 1H, CH, *J* 8.2 Hz, aromatic). **^{13}C NMR (100.5 MHz, $CDCl_3$) δ:** 21.8 (CH_3), 23.8 (CH_3), 52.5 (C), 114.1 (CH_{Ar}), 124.6 (CH_{Ar}), 125.3 (CH_{Ar}), 126.5 (2C, CH_{Ar}), 127.7 (CH_{Ar}), 127.8 (2C, CH_{Ar}), 128.7 (2C, CH_{Ar}), 128.9 (CH_{Ar}), 129.8 (2C, CH_{Ar}), 133.8 (C_{Ar}), 135.1 (C_{Ar}), 138.5 (C_{Ar}), 139.9 (C_{Ar}), 145.6 (C_{Ar}), 177.6 (C=O). **IR (ν/cm^{-1}):** 3080 (w), 3020 (w), 2980 (w), 2924 (w), 1755 (s), 1597 (m), 1462 (m), 1369 (s), 1230 (s), 1161 (s), 1087 (m), 1060 (s), 960 (m), 813 (m), 783 (m),759 (s), 690 (s), 655 (s), 563 (vs), 543 (vs). APPI-HRMS (*m*/*z*): calcd for $[C_{22}H_{19}NO_3S+H]^+$ 378.1158; found 378.1158. HPLC (Chiralpak AD-3, hexane/2-propanol, 97.5:2.5; 1.2 mL/min; λ = 230, 254 nm), retention times: first enantiomer 27.4 min, second enantiomer 35.2 min.

3. Copies of NMR spectra for compounds 2a–f

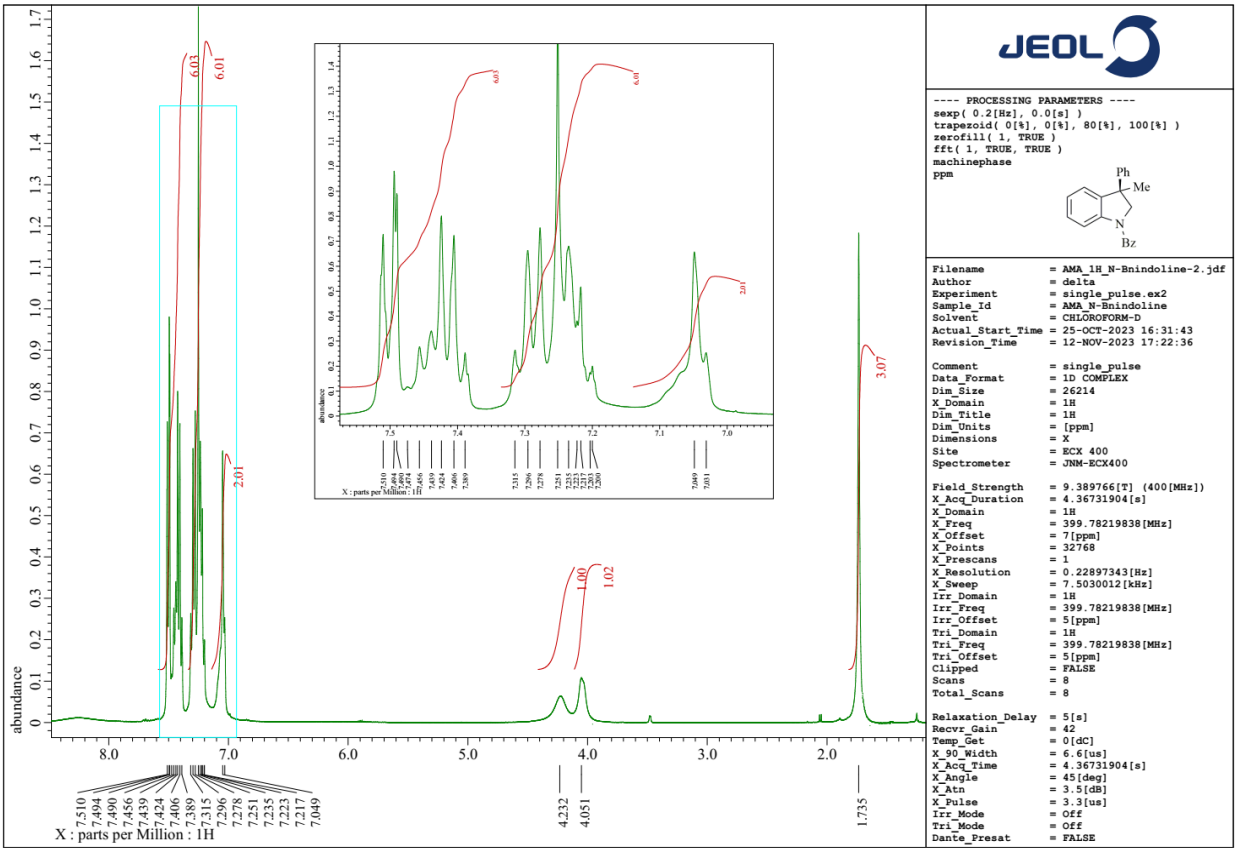
^{1}H NMR spectrum of 1-acetyl-3-methyl-3-phenylindoline (**2a**) in $CDCl_3$



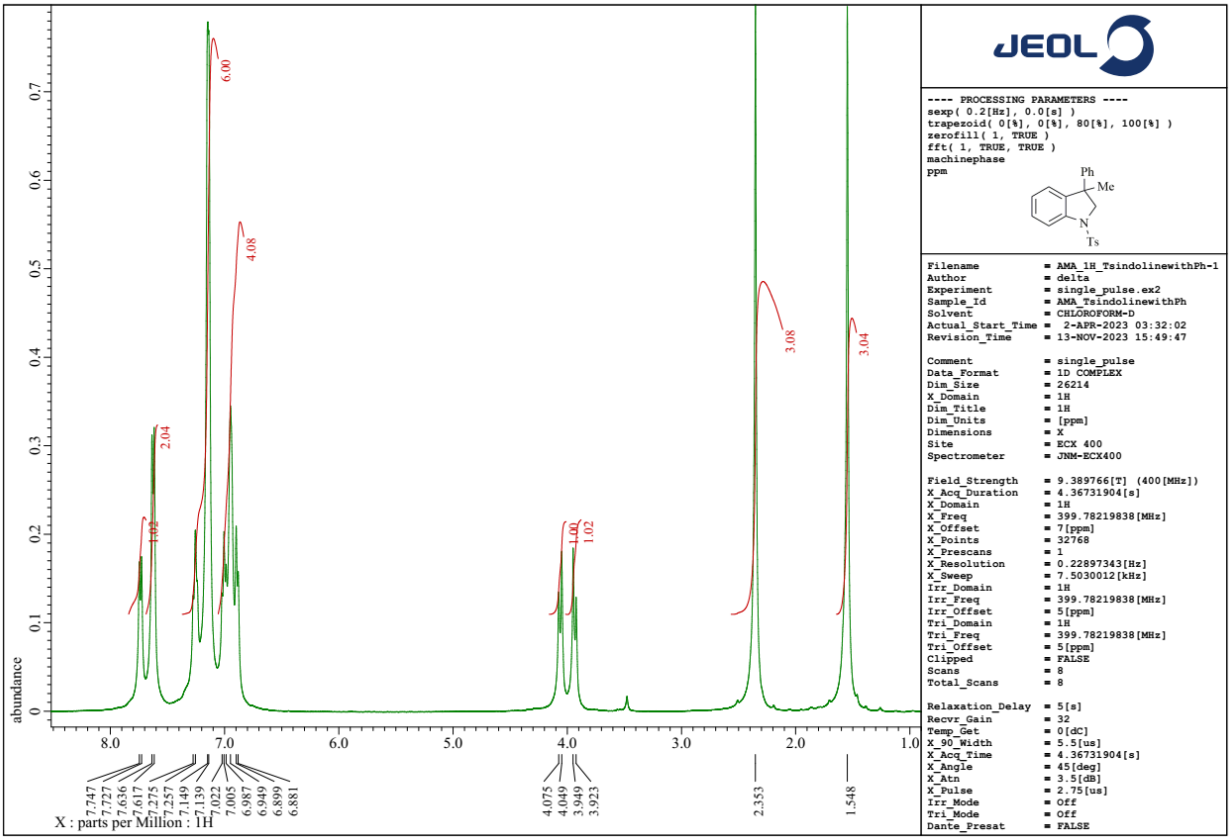
^{13}C NMR spectrum of 1-acetyl-3-methyl-3-phenylindoline (**2a**) in $CDCl_3$



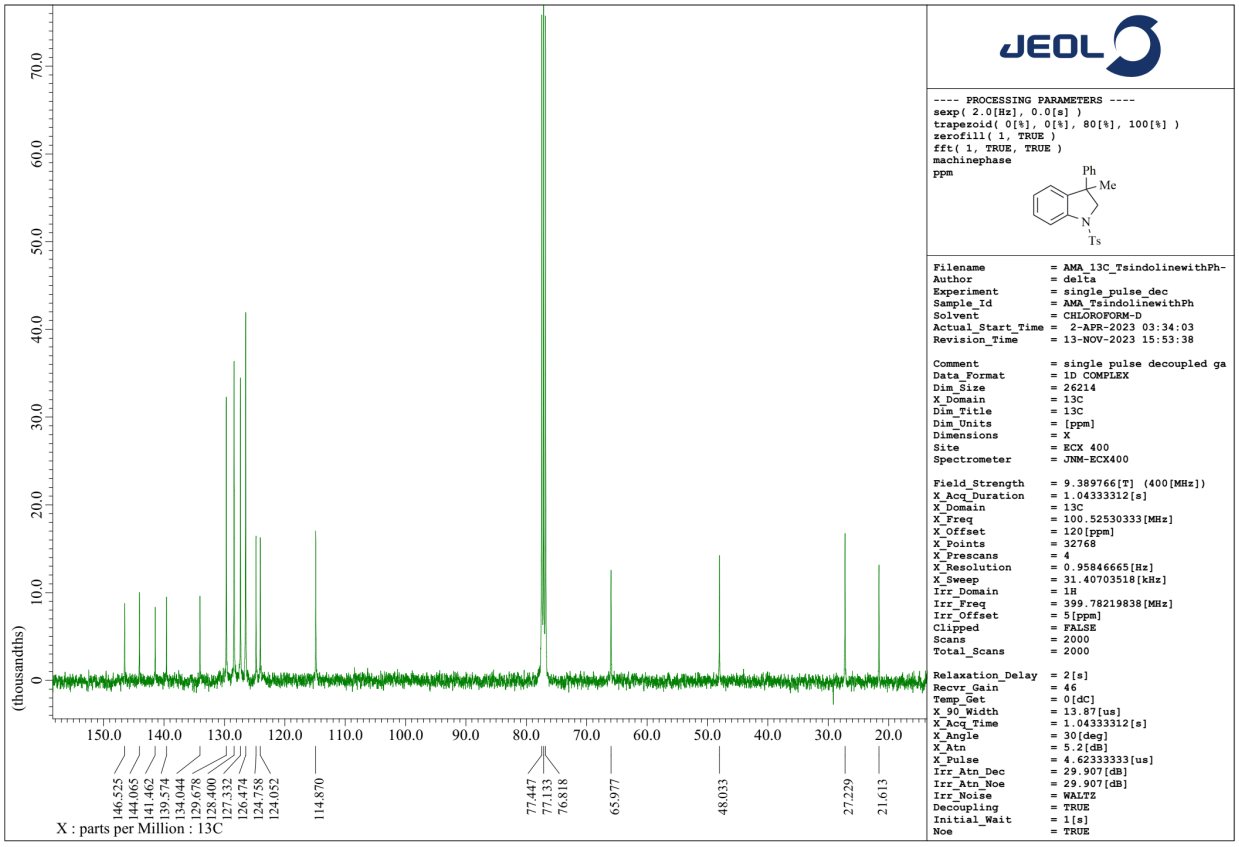
^{1}H NMR spectrum of 1-benzoyl-3-methyl-3-phenylindoline (**2b**) in $CDCl_3$



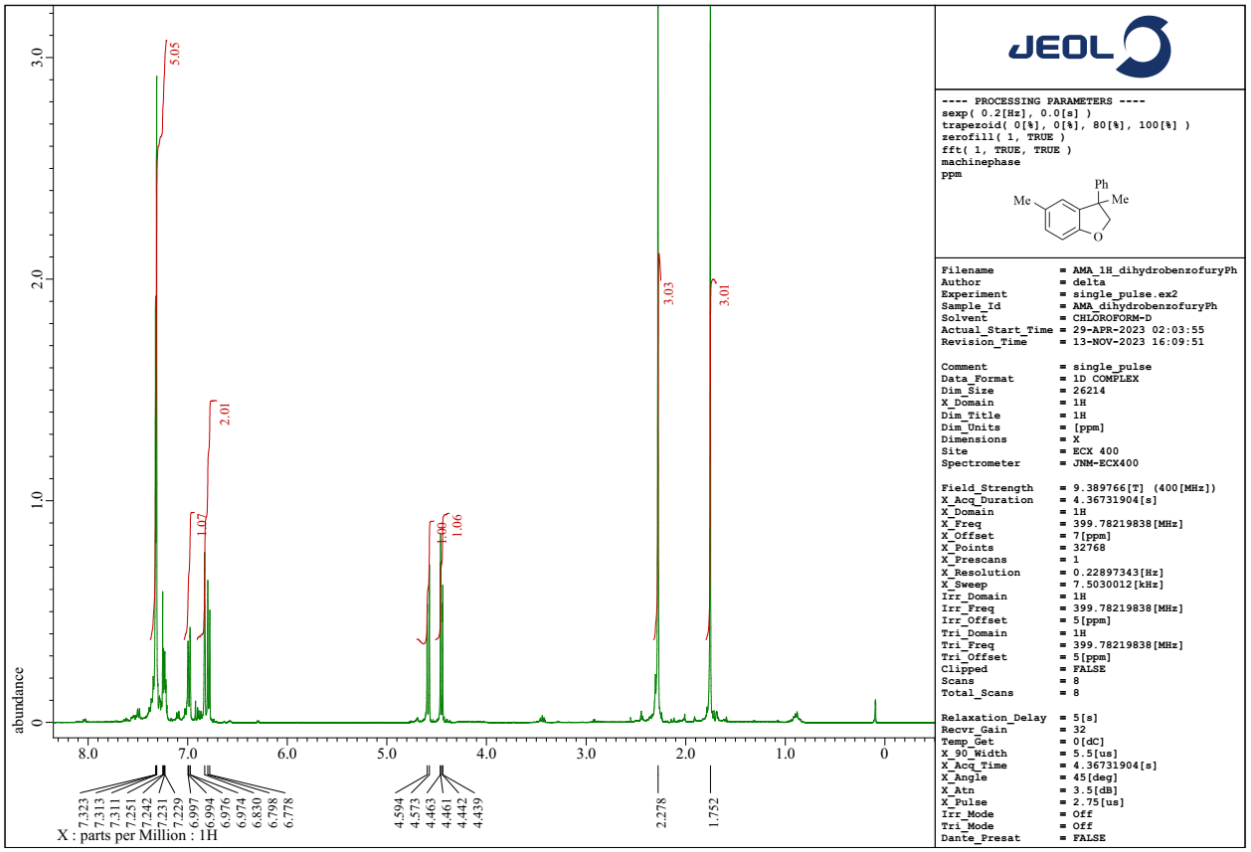
^{1}H NMR spectrum of 3-methyl-3-phenyl-1-tosylindoline (**2c**) in $CDCl_3$



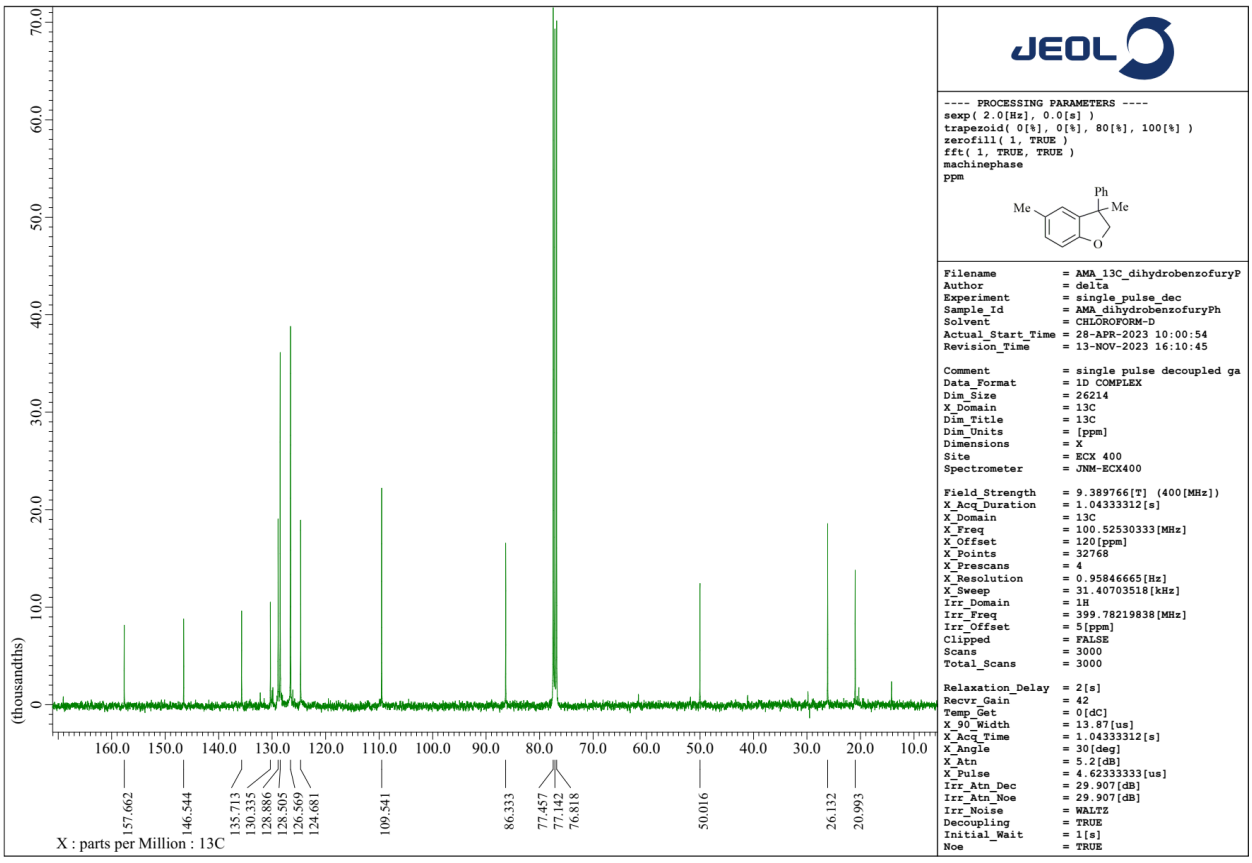
^{13}C NMR spectrum of 3-methyl-3-phenyl-1-tosylindoline (**2c**) in $CDCl_3$



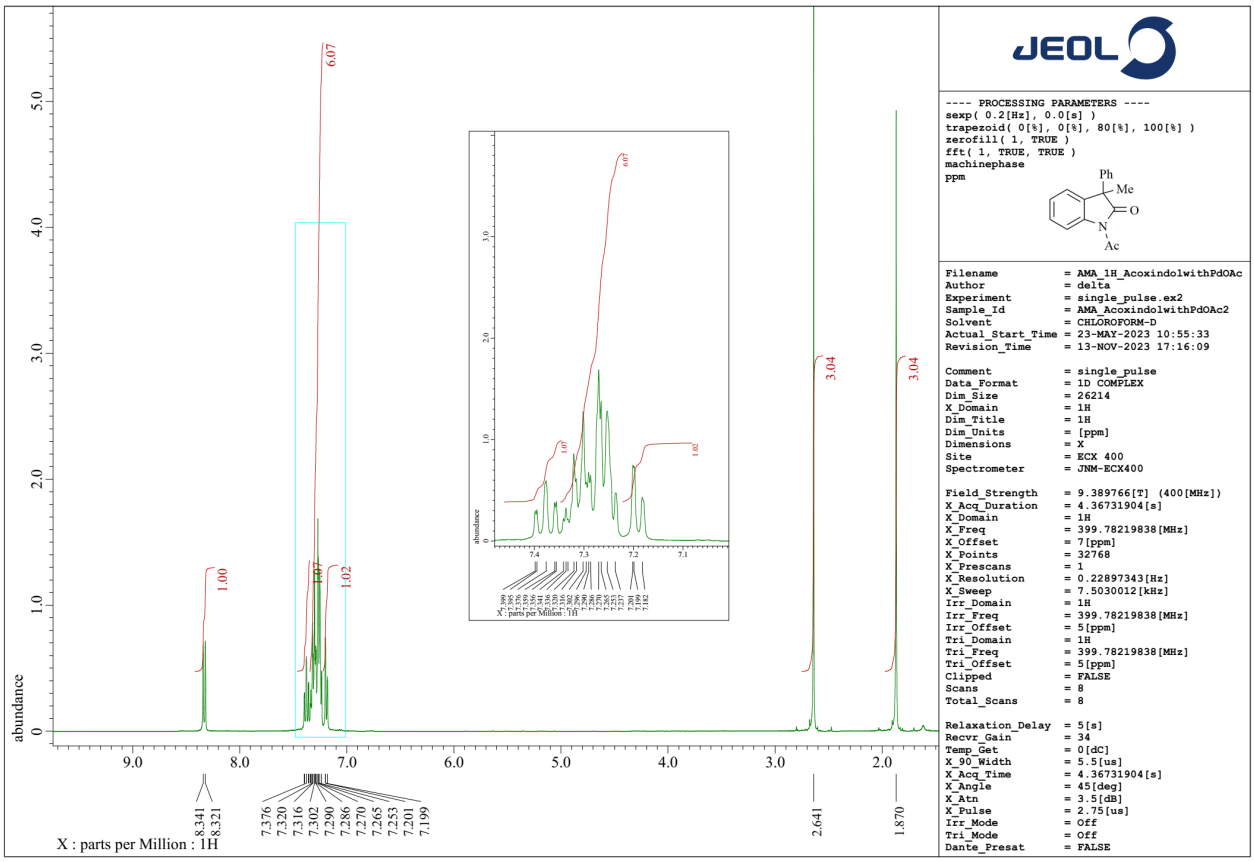
^{1}H NMR spectra of 3,5-dimethyl-3-phenyl-2,3-dihydrobenzofuran (**2d**) in $CDCl_3$



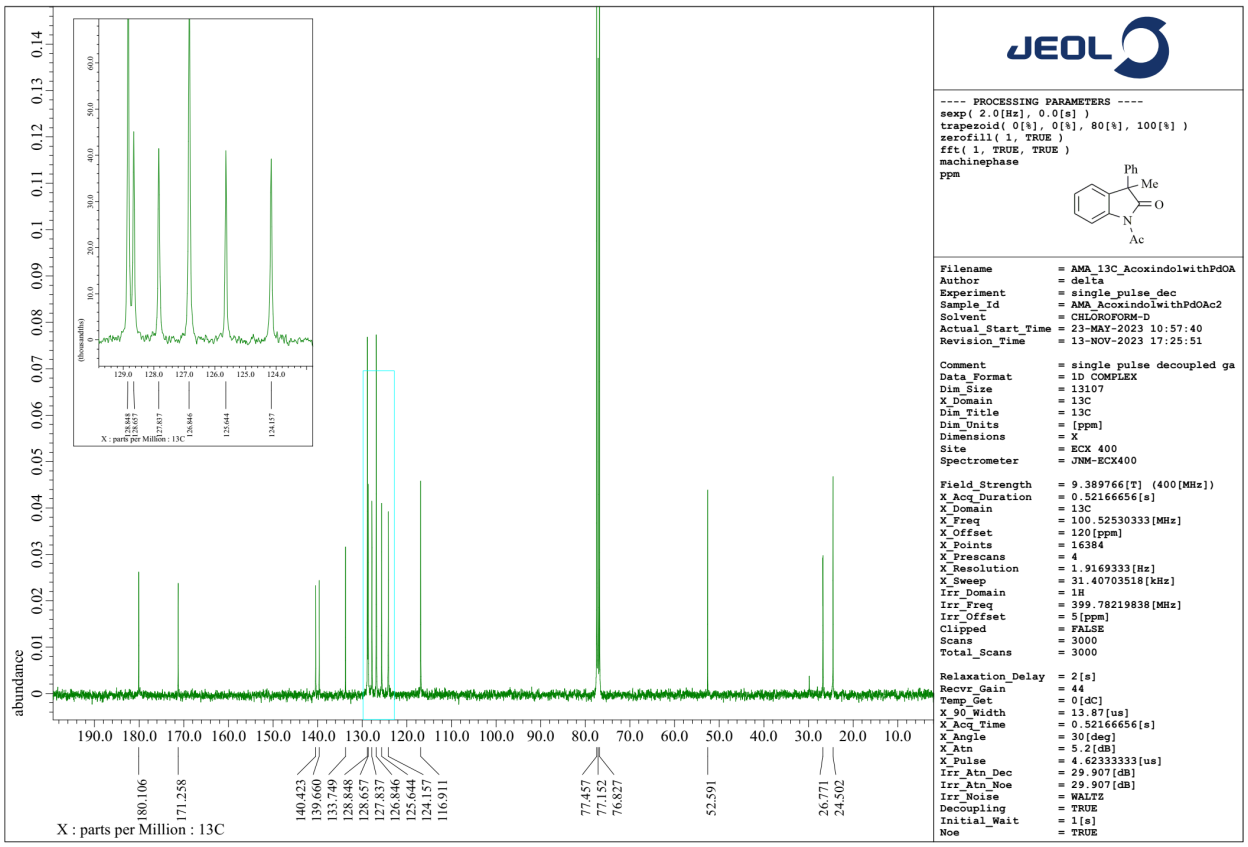
^{13}C NMR spectrum of 3,5-dimethyl-3-phenyl-2,3-dihydrobenzofuran (**2d**) in $CDCl_3$



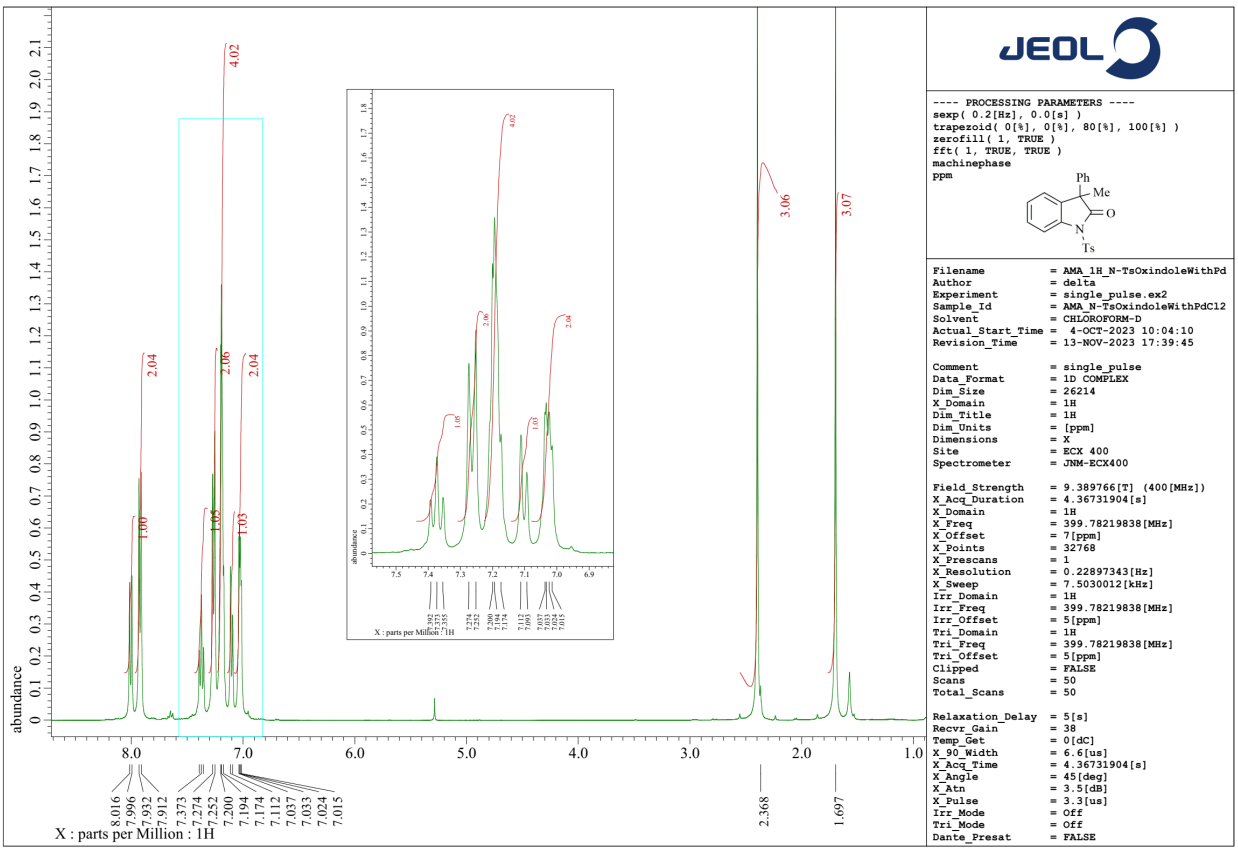
^{1}H NMR spectrum of 1-acetyl-3-methyl-3-phenylindolin-2-one (**2e**) in $CDCl_3$



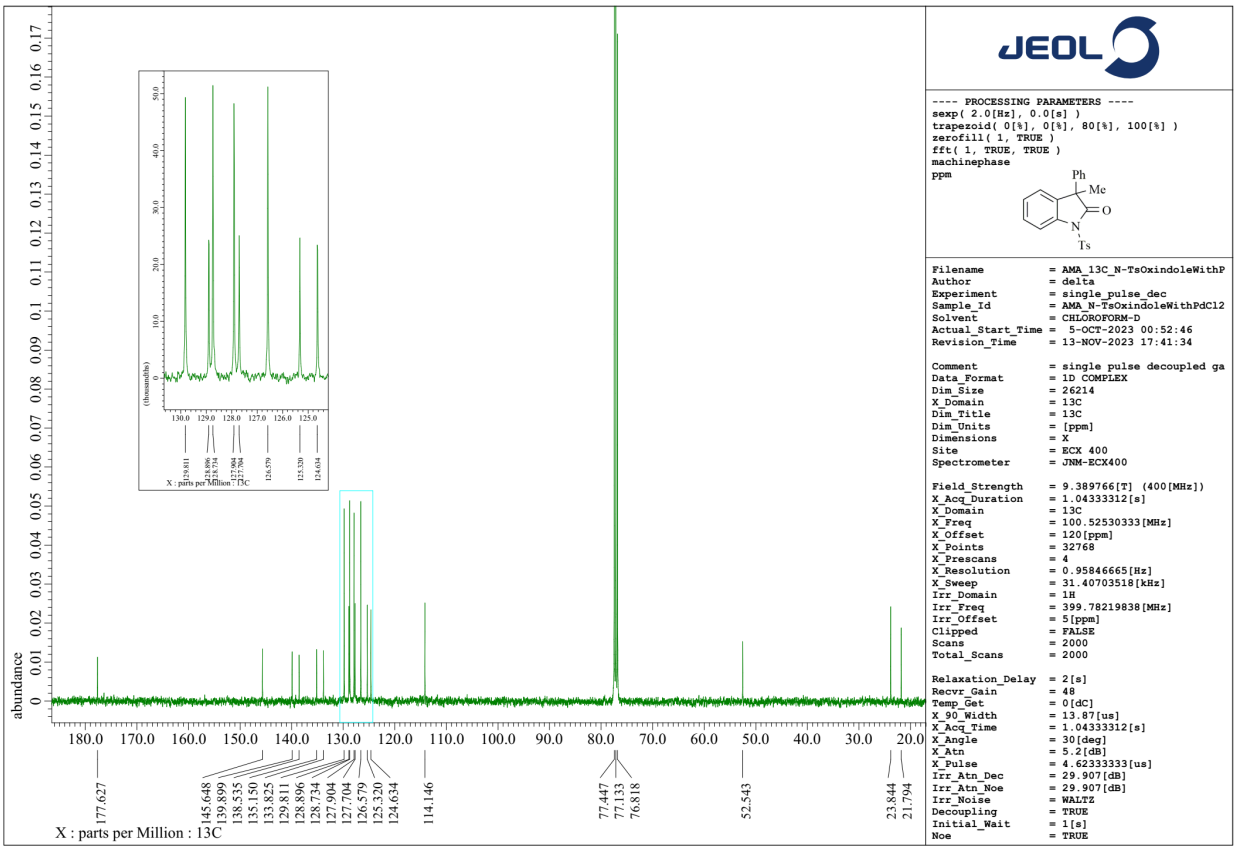
^{13}C NMR spectrum of 1-acetyl-3-methyl-3-phenylindolin-2-one (**2e**) in $CDCl_3$



^{1}H NMR spectrum of 3-methyl-3-phenyl-1-tosylindolin-2-one (**2f**) in $CDCl_3$

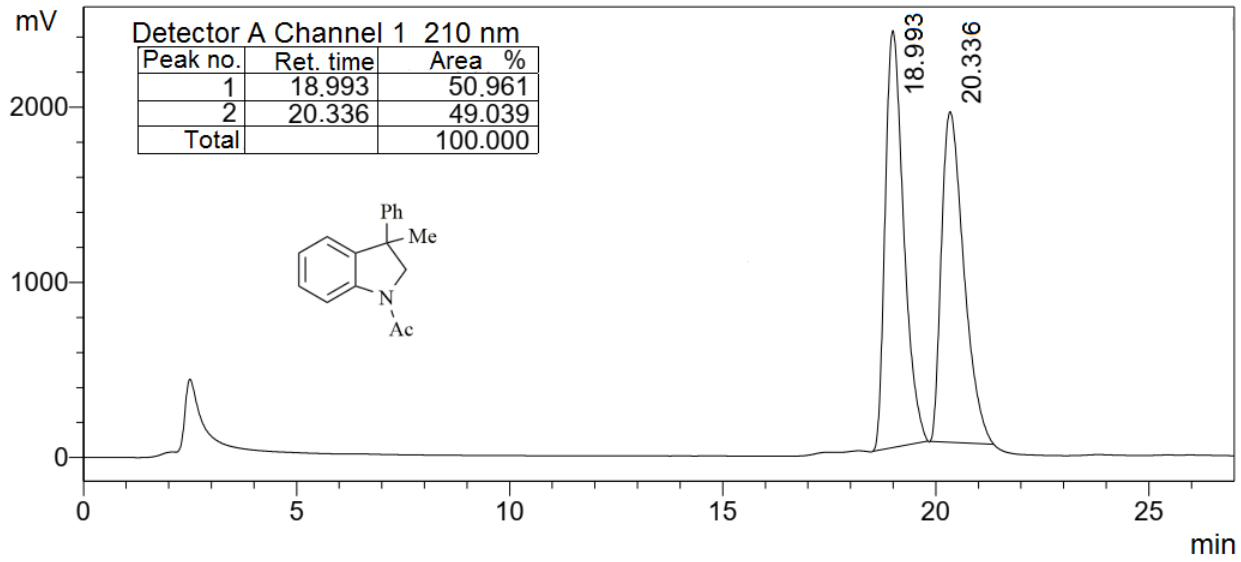


^{13}C NMR spectrum of 3-methyl-3-phenyl-1-tosylindolin-2-one (**2f**) in $CDCl_3$

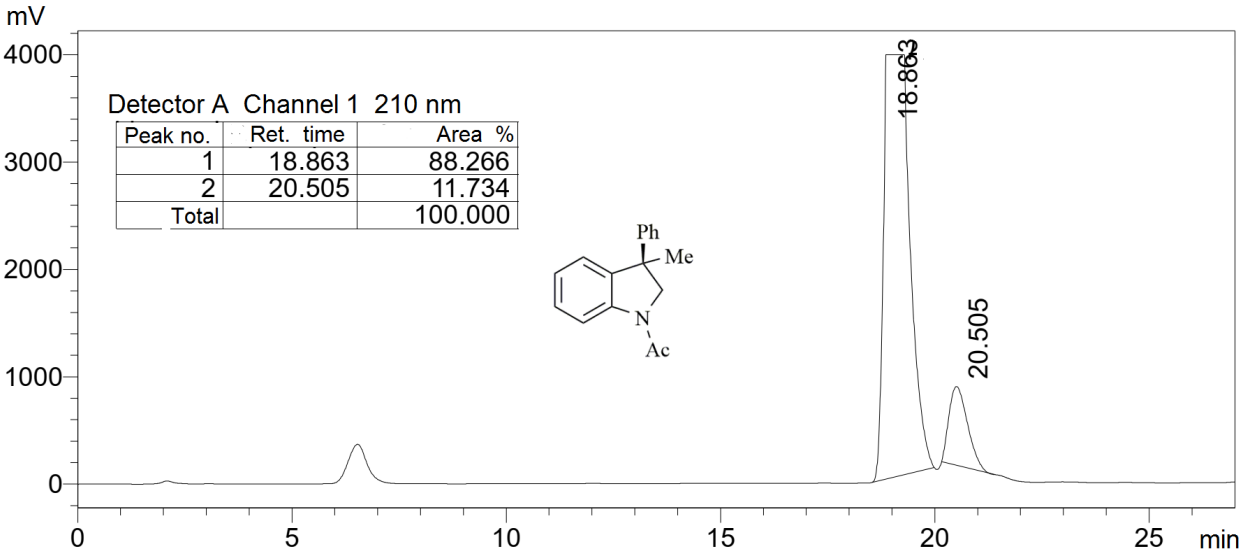


4. Copies of HPLC chromatograms for compounds 2a,b,c,e,f

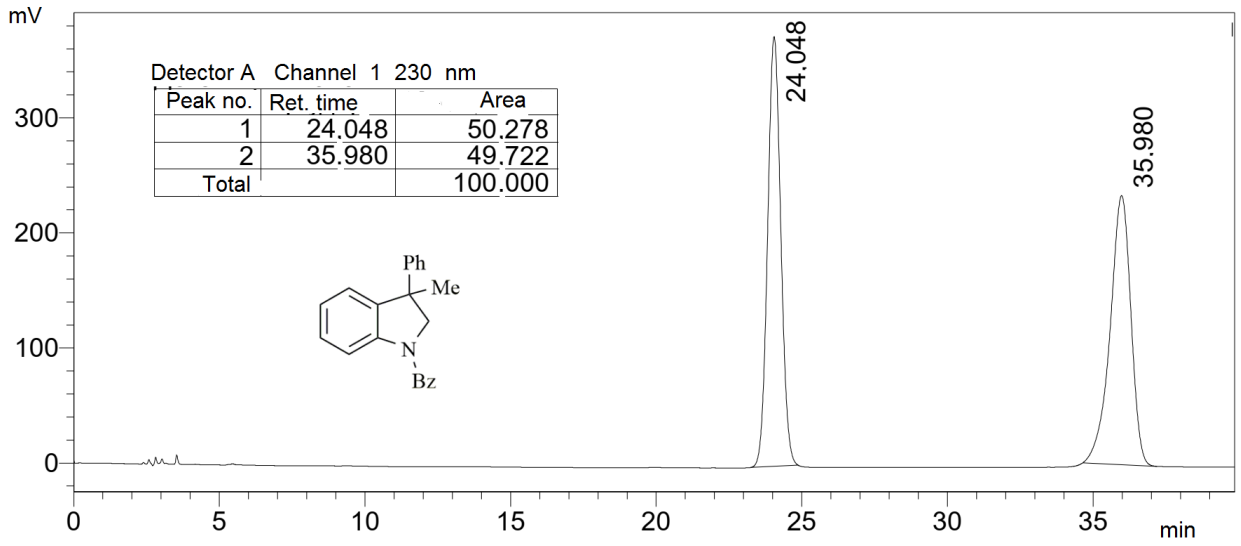
HPLC for racemic 1-acetyl-3-methyl-3-phenylindoline (**2a**)



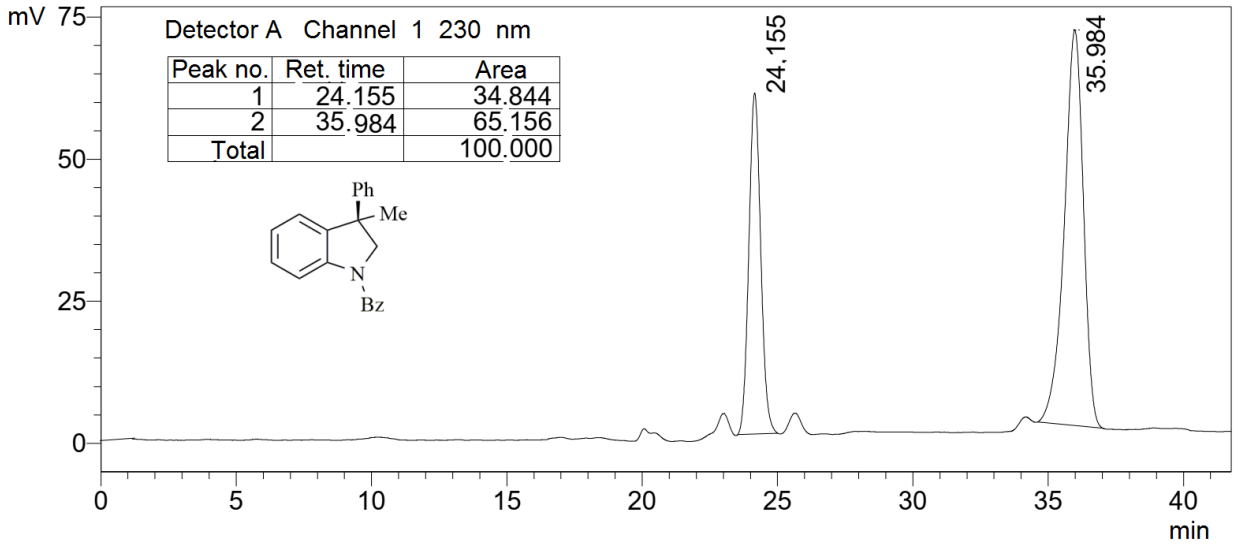
HPLC for (*R*)-1-acetyl-3-methyl-3-phenylindoline (**2a**)



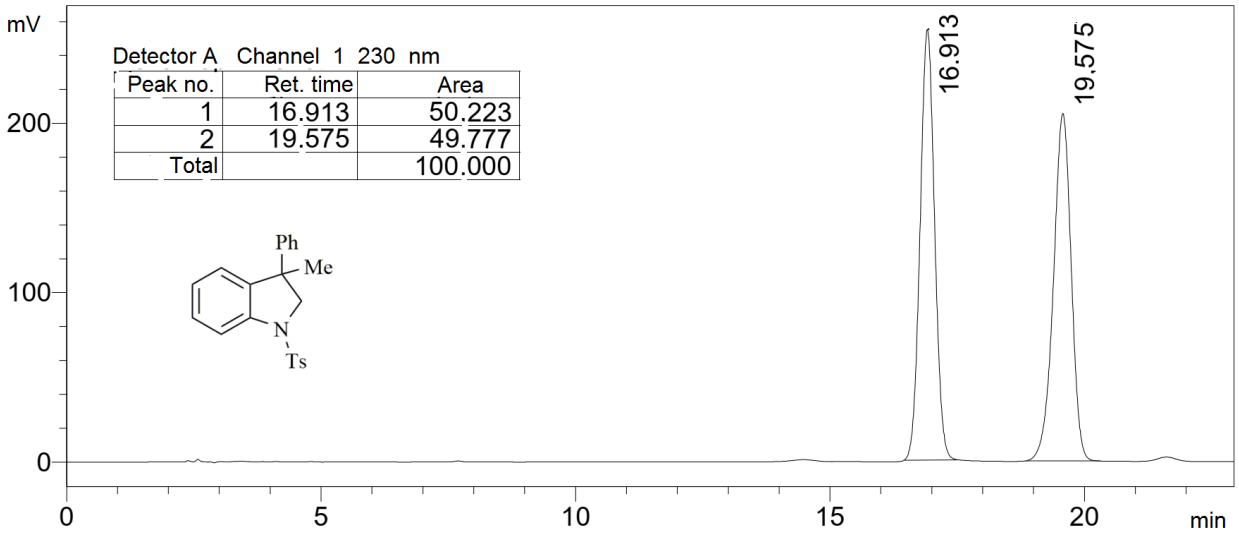
HPLC for racemic 1-benzoyl-3-methyl-3-phenylindoline (**2b**)



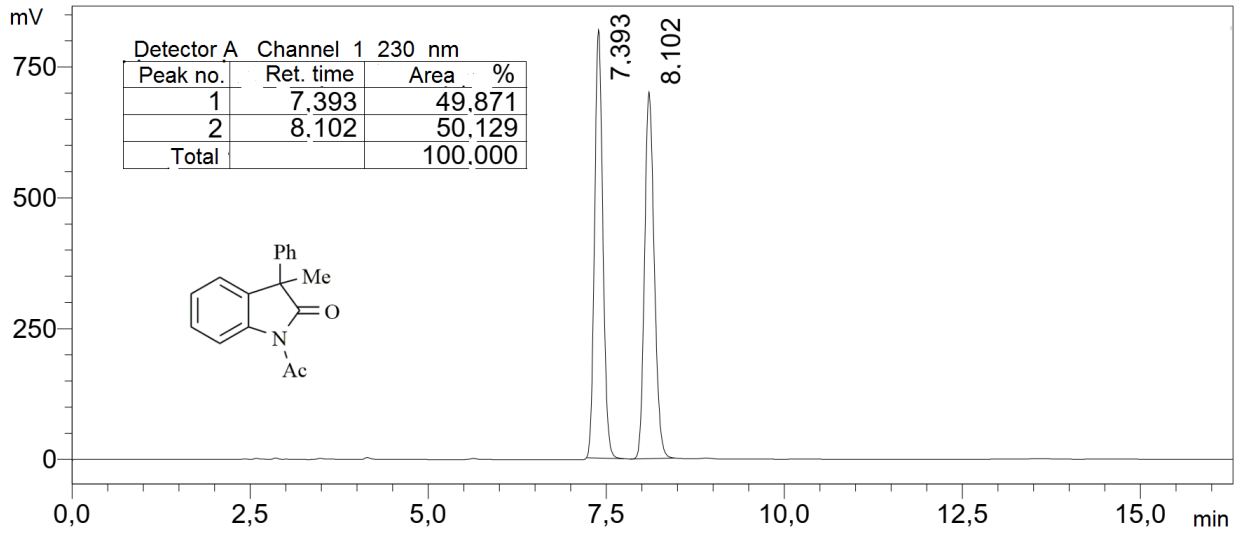
HPLC for enantiomerically enriched 1-benzoyl-3-methyl-3-phenylindoline (**2b**)



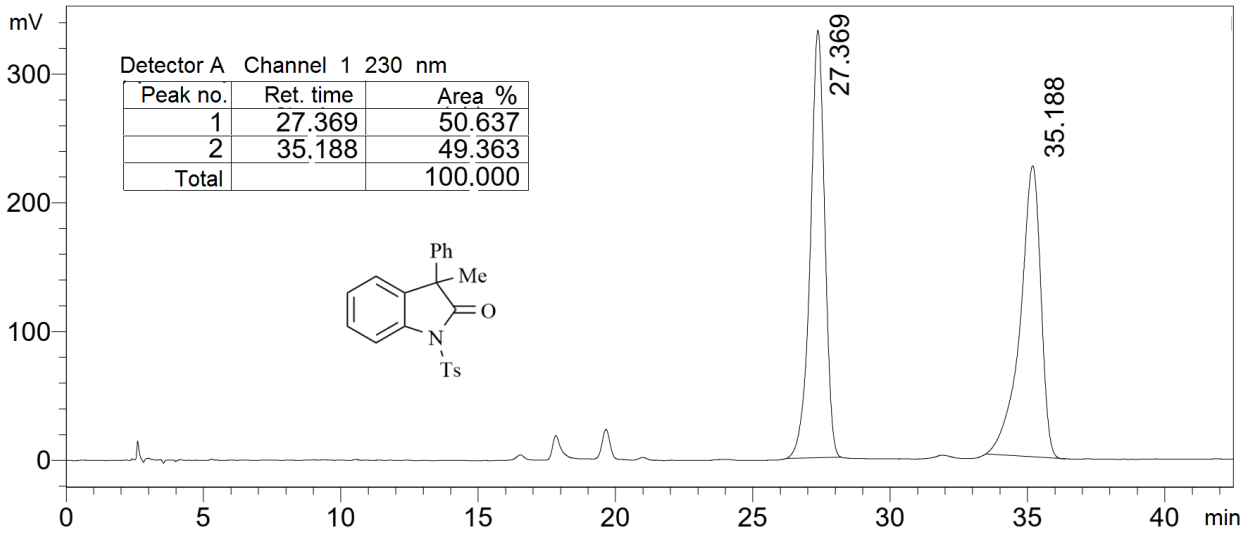
HPLC for racemic 3-methyl-3-phenyl-1-tosylindoline (**2c**)



HPLC for racemic 1-acetyl-3-methyl-3-phenylindolin-2-one (**2e**)



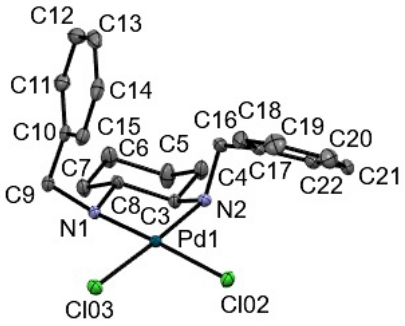
HPLC for racemic 3-methyl-3-phenyl-1-tosylindolin-2-one (**2f**)

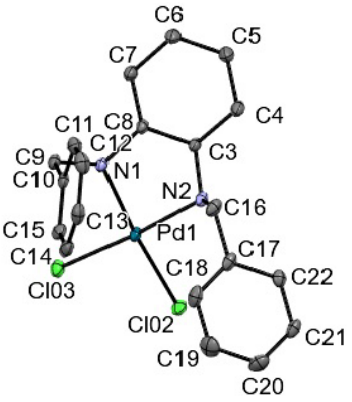


5. Crystal data and structure refinement for 2b, 5

The single crystal of compounds **5** and **2b** were prepared from $CHCl_3$/MeOH and cyclohexane solutions respectively. X-ray data for compounds **5** and **2b** were obtained with a Bruker D8 QUEST diffractometer. CCDC 2307155 (compound **5**) and CCDC 2307152 (compound **2b**) deposits contain the supplementary crystallographic data for this article. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* https://www.ccdc.cam.ac.uk

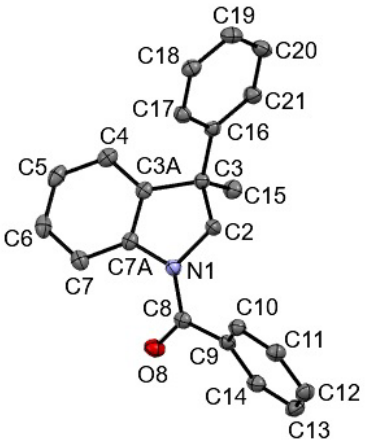
Table S1. Crystallographic data for compound **5**





CCDC	
Empirical formula	$C_{20}H_{26}Cl_2N_2Pd$
Formula weight	471.73
Temperature/K	102(2)
Wavelength	0.71073 (MoK\a)
Crystal system	orthorhombic
Space group	P 2_1 2_1 2_1
Unit cell dimensions:	
a/Å	10.3396(12)
b/Å	10.8284(11)
c/Å	18.9391(19)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2120.4(4)
Z	4
Absorption coefficient/ mm^{-1}	1.132
Reflections collected	69147
R indices (all data)	0.0239

Table S2. Crystallographic data for compound **2b**



CCDC	
Empirical formula	$C_{22}H_{19}NO$
Formula weight	313.38
Temperature/K	102(2)
Wavelength	0.71073 (MoK\a)
Crystal system	orthorhombic
Space group	P b c a
Unit cell dimensions:	
a/Å	8.3006(9)
b/Å	18.1475(19)
c/Å	21.510(2)
α/°	90
β/°	90
γ/°	90
Volume/$Å^3$	3240.2(6)
Z	8
Absorption coefficient/ mm^{-1}	0.078
Reflections collected	83254
R indices (all data)	0.0618

6. Calculation of specific rotation

The absolute (*R*)-configuration of the predominant enantiomer in compound **2a** was assumed based on correlation of computed specific rotation with experimental data. The optimization of geometry and calculation of specific rotation were performed using the B3LYP functional and the 6-311++G(2d,2p) basis set.[S13-S16] The calculation results and the experimental data obtained are presented in the table S1.

Table S3. Experimental and calculated values for the specific rotation of **2a**

λ, nm	Calculated $[\alpha]^{20}$ for (*S*)-isomer	Calculated $[\alpha]^{20}$ for (*R*)-isomer	Experimental $[\alpha]^{20}$ for **2a** with 35% *ee*	Experimental $[\alpha]^{20}$ for **2a** with correction for optical purity
436	+21.22	-21.22	-8.56	-24.5
546	+10.89	-10.89	-7.52	-21.5
589	+9.03	-9.03	-6.84	-19.5
633	+7.65	-7.65	-6.00	-17.1

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