Supporting Information

Enantioselective synthesis of spiro[*4H*-pyran-3,3'-oxindole] derivatives catalyzed by cinchona alkaloid thioureas: Significant water effects on the enantioselectivity

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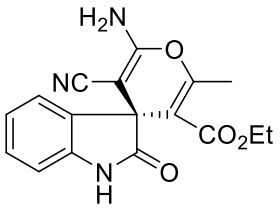
Table of Contents

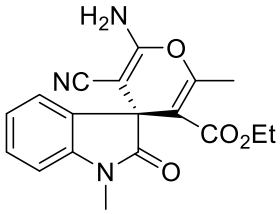
Compound Characterization Data

Ethyl (*S*)-2'-amino-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9a)[67]



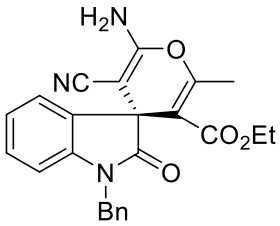
White solid, 27.1 mg, 84% yield; $[\alpha]^{24}_{D}$ = +15.5 (c 1.0, MeOH, 72% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.40 (s, 1H), 7.19 (dd, J = 7.6, 1.3 Hz, 2H), 7.14 (s, 2H), 7.06 (dd, J = 7.4, 1.2 Hz, 1H), 6.95 (dd, J = 7.6, 1.0 Hz, 1H), 6.80 (d, J = 7.7 Hz, 1H), 3.77 (dd, J = 14.9, 7.2 Hz, 2H), 2.32 (s, 3H), 0.79 (t, J = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 179.04, 164.95, 159.39, 158.96, 142.59, 134.99, 129.00, 123.84, 122.32, 117.94, 109.78, 105.10, 60.71, 56.96, 49.41, 19.02, 13.44. Enantiomeric excess of **9a** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 23.6 min, minor enantiomer: t_R = 13.6 min.

Ethyl (*R*)-2'-amino-3'-cyano-1,6'-dimethyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9b)[68]



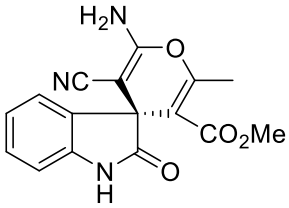
White solid, 27.3 mg, 81% yield; $[\alpha]^{24}_{D}$ = +14.7 (c 1.0, MeOH, 28% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.29 (dd, J = 7.7, 1.3 Hz, 1H), 7.20 (s, 2H), 7.13 (dd, J = 7.3, 1.2 Hz, 1H), 7.06 – 6.98 (m, 2H), 3.72 (dd, J = 7.1, 2.0 Hz, 2H), 3.14 (s, 3H), 2.33 (s, 3H), 0.73 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 177.41, 164.79, 159.42, 143.94, 134.18, 129.36, 129.22, 128.67, 123.57, 123.08, 117.77, 108.71, 104.86, 60.66, 56.61, 48.97, 26.76, 19.09, 13.66. Enantiomeric excess of **9b** was determined by chiral stationary phase HPLC analysis using a ChiralPak AD-H column (80:20 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 11.2 min, minor enantiomer: t_R = 9.3 min.

Ethyl (*R*)-2'-amino-1-benzyl-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9c)[68]



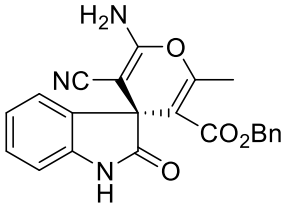
White solid, 33.3 mg, 80% yield; $[\alpha]^{24}_D$ = +20.4 (c 1.4, MeOH, 71% ee) [lit. $[\alpha]^{24}_D$ = +21.3 (c 1.4, MeOH, 74% ee) [8]]; ^{1}H NMR (500 MHz, DMSO-d_6) δ 7.48 (d, J = 7.4 Hz, 2H), 7.35 – 7.15 (m, 8H), 7.02 (d, J = 7.5 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 5.02 (d, J = 16.0 Hz, 1H), 4.79 (d, J = 15.8 Hz, 1H), 3.79 (dd, J = 10.9, 6.7 Hz, 1H), 3.54 (dd, J = 10.9, 6.6 Hz, 1H), 2.35 (s, 3H), 0.59 (t, J = 7.0 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 177.67, 164.84, 159.66, 159.33, 143.21, 136.62, 134.11, 129.36, 129.11, 128.86, 128.67, 127.99, 127.81, 125.77, 123.79, 123.19, 118.03, 109.36, 105.02, 60.58, 56.62, 49.01, 43.88, 21.51, 19.12, 13.55. Enantiomeric excess of **9c** was determined by chiral stationary phase HPLC analysis using a ChiralPak AD-H column (80:20 hexanes /*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 19.6 min, minor enantiomer: t_R = 11.6 min.

Methyl (*S*)-2'-amino-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9d)[67]



White solid, 24.2 mg, 78% yield; $[\alpha]^{24}_D$ = -19.5 (c 1.0, MeOH, 64% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.33 (s, 1H), 7.16 – 7.03 (m, 3H), 6.98 (dd, J = 7.5, 1.2 Hz, 1H), 6.86 (d, J = 1.1 Hz, 1H), 6.73 (d, J = 7.7 Hz, 1H), 3.27 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.95, 165.56, 159.39, 158.90, 142.40, 134.87, 129.36, 129.03, 128.67, 125.78, 123.81, 122.33, 117.91, 109.77, 105.33, 79.62, 56.95, 51.87, 49.51, 21.51, 19.27. Enantiomeric excess of **9d** was determined by chiral stationary phase HPLC analysis using a ChiralPak IC column (60:40 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 36.5 min, minor enantiomer: t_R = 15.2 min.

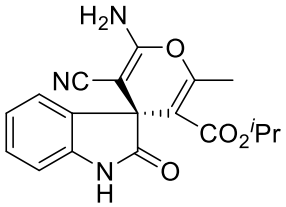
Benzyl (*S*)-2'-amino-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9e)



White solid, 30.9 mg, 80% yield; mp: 194-196 °C; $[\alpha]^{24}_D$ = +26.9 (c 1.0, MeOH, 53% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.36 (s, 1H), 7.43 – 7.10 (m, 6H), 7.15 – 6.85 (m, 5H), 6.72 (d, J = 7.7 Hz, 1H), 4.86 (d, J = 2.1 Hz, 2H), 2.32 (s, 3H).; ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.86,

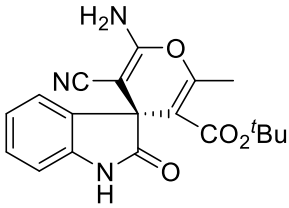
164.94, 159.44, 159.29, 142.39, 135.69, 134.92, 128.98, 128.71, 128.31, 128.06, 123.87, 122.32, 117.88, 110.00, 104.91, 66.42, 57.18, 49.45, 19.38. ν_{max} (neat, cm^{-1}): 3472, 2221, 1716, 1673, 1596, 1208, 1060, 886; HRMS (ESI): m/z calcd. for $C_{22}H_{18}N_3O_4$ ($[M+H]^+$): 388.1292; found 388.1289. Enantiomeric excess of **9e** was determined by chiral stationary phase HPLC analysis using a ChiralPak AD-H column (80:20 hexanes /*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 18.6 min, minor enantiomer: t_R = 15.2 min.

Isopropyl (*S*)-2'-amino-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9f)[27]



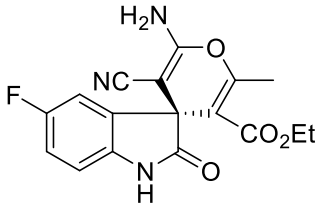
White solid, 27.8 mg, 82% yield; $[\alpha]^{24}_D$ = -42.3 (c 1.0, MeOH, 87% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.39 (s, 1H), 7.22 – 7.04 (m, 4H), 6.97 – 6.75 (m, 2H), 4.80 – 4.45 (m, 1H), 2.32 (s, 3H), 0.97 (d, *J* = 6.3 Hz, 3H), 0.55 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.11, 164.33, 159.36, 158.92, 142.75, 137.81, 135.17, 129.36, 128.93, 128.67, 125.77, 123.84, 122.24, 117.96, 109.78, 105.09, 68.25, 56.97, 49.35, 21.31, 20.59, 18.86. Enantiomeric excess of **9f** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 31.1 min, minor enantiomer: t_R = 12.0 min.

***tert*-Butyl (*S*)-2'-amino-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9g)[67]**



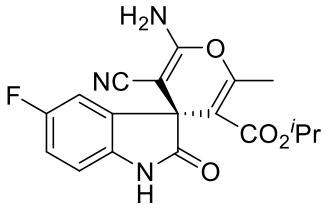
White solid, 26.8 mg, 76% yield; $[\alpha]^{24}_D$ = +16.7 (c 1.0, MeOH, 82% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (s, 1H), 7.21 (td, J = 7.7, 1.3 Hz, 1H), 7.15 – 7.04 (m, 3H), 6.96 (td, *J* = 7.5, 1.0 Hz, 1H), 6.81 (d, *J* = 7.7 Hz, 1H), 2.25 (s, 3H), 1.02 (s, 9H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.89, 164.24, 159.59, 157.65, 142.77, 134.79, 129.02, 124.01, 122.25, 118.03, 109.87, 106.26, 81.73, 56.85, 49.37, 27.38, 18.61. Enantiomeric excess of **9g** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 33.8 min, minor enantiomer: t_R = 8.5 min.

Ethyl (*S*)-2'-amino-3'-cyano-5-fluoro-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9h)[67]



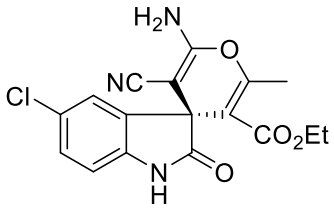
White solid, 29.3 mg, 86%yield; $[\alpha]^{24}_{D}$ = -18.9 (c 1.0, MeOH, 60% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.38 (s, 1H), 7.16 (s, 2H), 6.98 (ddt, J = 8.3, 6.8, 4.1 Hz, 2H), 6.74 (dd, J = 8.3, 4.3 Hz, 1H), 3.76 (dd, J = 18.0, 7.1 Hz, 2H), 2.29 (s, 3H), 0.78 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.09, 164.81, 159.53 (d, $J_{C\text{-}F}$ = 37 Hz), 157.71, 138.76, 136.85 (d, $J_{C\text{-}F}$ = 8 Hz), 129.01 (d, $J_{C\text{-}F}$= 87 Hz), 117.81, 115.20 (d, $J_{C\text{-}F}$= 23 Hz), 111.81, 110.50 (d, $J_{C\text{-}F}$ = 8 Hz), 104.41, 60.80, 56.51, 49.96, 19.17, 13.49. Enantiomeric excess of **9h** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 24.3 min, minor enantiomer: t_R = 11.4 min.

Isopropyl (*S*)-2'-amino-3'-cyano-5-fluoro-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9i)



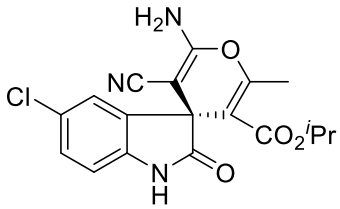
White solid, 28.9 mg, 81% yield; mp: 224- 226 °C; $[\alpha]^{24}_{D}$ = -15.2 (c 1.0, MeOH, 71% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.42 (s, 1H), 7.20 (s, 2H), 7.11 – 6.98 (m, 2H), 6.83 – 6.76 (m, 1H), 4.71 – 4.59 (m, 1H), 2.33 (s, 3H), 0.99 (d, J = 6.3 Hz, 3H), 0.61 (d, J = 6.2 Hz, 3H).; ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.18, 164.18, 159.50 (d, $J_{C\text{-}F}$ = 35 Hz), 157.77, 138.90, 137.02 (d, $J_{C\text{-}F}$ = 8 Hz), 129.02 (d, $J_{C\text{-}F}$ = 87 Hz), 117.84, 115.13 (d, $J_{C\text{-}F}$ = 24 Hz), 111.72 (d, $J_{C\text{-}F}$ = 24 Hz), 110.51 (d, $J_{C\text{-}F}$ = 8 Hz), 104.38, 68.34, 56.49, 49.89, 21.29, 20.73, 19.00. ν_{max} (neat, cm^{-1}): 3232, 2203, 1717, 1672, 1592, 1205, 1069, 886; HRMS (ESI): m/z calcd. for $C_{18}H_{17}FN_3O_4$ ([M+H]$^+$): 358.1198; found 358.1195. Enantiomeric excess of **9i** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 33.8 min, minor enantiomer: t_R = 10.2 min.

Ethyl (*S*)-2'-amino-5-chloro-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9j)[28]



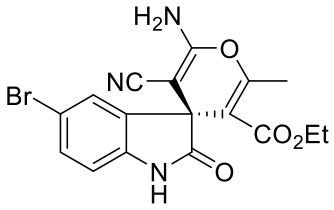
White solid, 29.2 mg, 82% yield; $[\alpha]^{24}_D$ = -21.7 (c 1.0, MeOH, 59% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.55 (s, 1H), 7.29 – 7.15 (m, 4H), 6.82 (d, J = 8.2 Hz, 1H), 3.82 (dd, J = 14.3, 7.1 Hz, 2H), 2.34 (s, 3H), 0.84 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.84, 164.80, 159.95, 159.36, 141.47, 137.27, 128.87, 126.23, 124.03, 117.81, 111.22, 104.18, 60.87, 56.37, 49.74, 19.23, 13.51. Enantiomeric excess of **9j** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 19.7 min, minor enantiomer: t_R = 11.7 min.

Isopropyl (*S*)-2'-amino-5-chloro-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9k)[27]



White solid, 29.0 mg, 78% yield; $[\alpha]^{24}_D$ = +31.6 (c 1.0, MeOH, 74% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.31 – 7.08 (m, 4H), 6.82 (d, J = 8.2 Hz, 1H), 4.75 – 4.62 (m, 1H), 2.34 (s, 3H), 0.99 (d, J = 6.2 Hz, 3H), 0.62 (d, J = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.89, 164.15, 159.87, 159.35, 141.61, 137.41, 128.79, 126.23, 124.04, 117.84, 111.22, 104.18, 68.38, 56.34, 49.67, 21.29, 20.75, 19.04. Enantiomeric excess of **9k** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 25.8 min, minor enantiomer: t_R = 10.1 min.

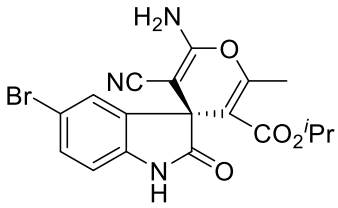
Ethyl (*S*)-2'-amino-5-bromo-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9l)[28, 67]



White solid, 32.1 mg, 80% yield; $[\alpha]^{24}_D$ = +34.3 (c 1.0, MeOH, 59% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.56 (s, 1H), 7.37 (dd, J = 8.2, 2.0 Hz, 1H), 7.30 (d, J = 2.0 Hz, 1H), 7.23 (s, 2H), 6.78 (d, J = 8.2 Hz, 1H), 3.95 – 3.74 (m, 2H), 2.34 (s, 3H), 0.84 (t, J = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.71, 164.80, 160.00, 159.35, 141.87, 137.66, 131.73, 126.71, 117.82, 113.89, 111.77, 104.16, 60.88, 56.39, 49.69, 19.25, 13.51. Enantiomeric excess of **9l** was

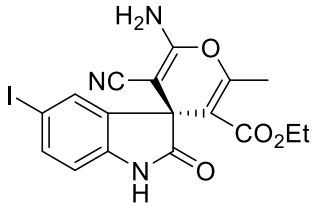
determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 18.0 min, minor enantiomer: t_R = 11.8 min.

Isopropyl (*S*)-2'-amino-5-bromo-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9m)



White solid, 34.6 mg, 83% yield; mp: 250- 252 °C; $[\alpha]^{24}_D$ = +30.6 (c 1.0, MeOH, 58% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.38 (dd, *J* = 8.2, 2.1 Hz, 1H), 7.30 (d, *J* = 2.1 Hz, 1H), 7.22 (s, 2H), 6.78 (d, *J* = 8.2 Hz, 1H), 4.67 (p, *J* = 6.2 Hz, 1H), 2.34 (s, 3H), 0.99 (d, *J* = 6.3 Hz, 3H), 0.63 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO) δ 178.76, 164.16, 159.90, 159.35, 142.03, 137.81, 131.65, 126.72, 117.85, 113.84, 111.76, 104.17, 68.39, 56.36, 49.62, 21.29, 20.75, 19.05. ν_{max} (neat, cm^{-1}): 3234, 2208, 1714, 1636, 1592, 1229, 1069, 868; HRMS (ESI): m/z calcd. for $C_{18}H_{17}BrN_3O_4$ ([M+H]$^+$): 418.0397; found 418.0400. Enantiomeric excess of **9m** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 22.6 min, minor enantiomer: t_R = 9.9 min.

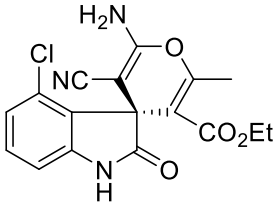
Ethyl (*S*)-2'-amino-3'-cyano-5-iodo-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9n)



White solid, 41.3 mg, 92% yield; mp: 246 - 248 °C; $[\alpha]^{24}_D$ = +17.8 (c 1.0, MeOH, 65% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.54 (s, 1H), 7.53 (dd, *J* = 8.1, 1.8 Hz, 1H), 7.40 (d, *J* = 1.8 Hz, 1H), 7.22 (s, 2H), 6.67 (d, *J* = 8.0 Hz, 1H), 3.82 (dd, *J* = 14.4, 7.1 Hz, 2H), 2.34 (s, 3H), 0.84 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.49, 164.82, 159.93, 159.33, 142.34, 137.88, 137.56, 132.07, 117.84, 112.30, 104.22, 84.95, 60.87, 56.46, 49.47, 19.24, 13.51. ν_{max} (neat, cm^{-1}): 3237, 2201, 1718, 1629, 1589, 1213, 1068, 864; HRMS (ESI): m/z calcd. for $C_{17}H_{15}IN_3O_4$ ([M+H]$^+$): 452.0102; found 452.0101. Enantiomeric excess of **9n** was determined

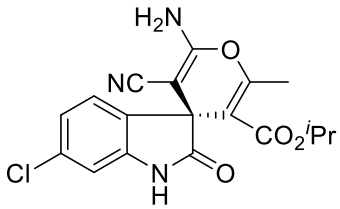
by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 17.2 min, minor enantiomer: t_R = 13.1 min.

Ethyl (*S*)-2'-amino-4-chloro-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9o)



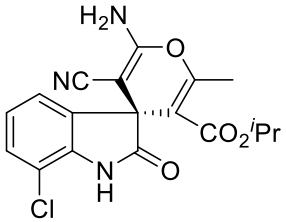
White solid, 27.8 mg, 78% yield; mp: 242 -244 °C; $[\alpha]^{24}_D$ = +28.2 (c 1.0, MeOH, 44% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.67 (s, 1H), 7.33 – 7.14 (m, 3H), 7.02 – 6.88 (m, 1H), 6.80 (d, *J* = 7.7 Hz, 1H), 3.85 (t, *J* = 7.2 Hz, 2H), 2.34 (s, 3H), 0.87 (t, *J* = 7.1 Hz, 3H).; ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.26, 164.74, 160.37, 160.10, 144.40, 130.69, 130.15, 129.86, 129.36, 128.67, 122.69, 117.68, 108.89, 103.18, 60.88, 54.30, 50.05, 19.20, 13.54. ν_{max} (neat, cm^{-1}): 3294, 2195, 1698, 1591, 1375, 1212, 1065, 899; HRMS (ESI): m/z calcd. for $C_{17}H_{15}ClN_3O_4$ ([M+H]$^+$): 360.0746; found 360.0745. Enantiomeric excess of **9o** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 21.2 min, minor enantiomer: t_R = 13.8 min.

Isopropyl (*S*)-2'-amino-6-chloro-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9p)



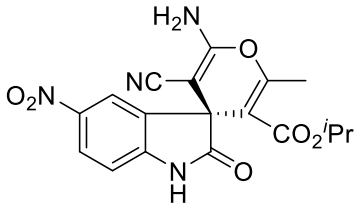
White solid, 29.8 mg, 80% yield; mp: 182-184 °C; $[\alpha]^{24}_D$ = +13.2 (c 1.0, MeOH, 62% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.56 (s, 1H), 7.20 (s, 2H), 7.08 (d, *J* = 7.9 Hz, 1H), 6.97 (dd, *J* = 7.9, 2.0 Hz, 1H), 6.82 (d, *J* = 2.0 Hz, 1H), 4.80 – 4.45 (m, 1H), 2.31 (s, 3H), 0.98 (d, *J* = 6.3 Hz, 3H), 0.61 (d, *J* = 6.2 Hz, 3H).; ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.07, 164.15, 159.55, 159.36, 144.24, 134.14, 133.14, 129.35, 128.66, 125.34, 121.95, 117.82, 109.83, 104.47, 68.44, 56.36, 49.11, 21.33, 20.72, 18.97. ν_{max} (neat, cm^{-1}): 3181, 2195, 11707, 1670, 1598, 1208, 1063, 869; HRMS (ESI): m/z calcd. for $C_{18}H_{17}ClN_3O_4$ ([M+H]$^+$): 374.0902; found 374.0899. Enantiomeric excess of **9p** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (80:20 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 15.8 min, minor enantiomer: t_R = 20.1 min.

Isopropyl (*S*)-2'-amino-7-chloro-3'-cyano-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9q)



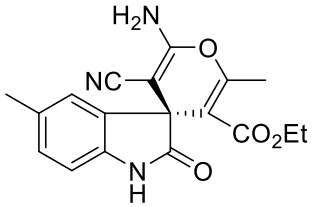
White solid, 29.0 mg, 78% yield; mp: 170-172 °C; $[\alpha]^{24}_{D}$ = +22.9 (c 1.0, MeOH, 83% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.86 (s, 1H), 7.33 – 7.16 (m, 3H), 7.05 (dd, *J* = 7.5, 1.1 Hz, 1H), 7.01 – 6.88 (m, 1H), 4.62 (p, *J* = 6.2 Hz, 1H), 2.32 (s, 3H), 0.98 (d, *J* = 6.3 Hz, 3H), 0.55 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.14, 164.07, 159.65, 159.34, 140.45, 137.04, 128.88, 123.63, 122.54, 117.81, 114.20, 104.51, 68.38, 56.34, 50.23, 21.36, 20.62, 18.93. ν_{max} (neat, cm^{-1}): 3164, 2022, 1746, 1674, 1567, 1215, 1076, 851; HRMS (ESI): m/z calcd. for $C_{18}H_{17}ClN_3O_4$ ([M+H]$^+$): 374.0902; found 374.0899. Enantiomeric excess of **9q** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 10.5 min, minor enantiomer: t_R = 15.5 min.

Isopropyl (*S*)-2'-amino-3'-cyano-6'-methyl-5-nitro-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9r)



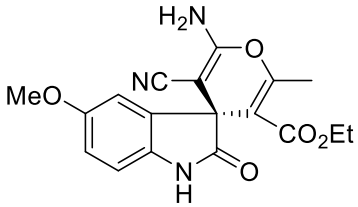
White solid, 30.7 mg, 80% yield; mp: 200-202 °C; $[\alpha]^{24}_{D}$ = +26.4 (c 1.0, MeOH, 67% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 11.13 (s, 1H), 8.15 (dd, *J* = 8.6, 2.4 Hz, 1H), 7.98 (d, *J* = 2.4 Hz, 1H), 7.29 (s, 2H), 6.98 (d, *J* = 8.6 Hz, 1H), 4.61 (p, *J* = 6.2 Hz, 1H), 2.32 (s, 2H), 0.92 (d, *J* = 6.2 Hz, 3H), 0.55 (d, *J* = 6.2 Hz, 3H)·; ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.66, 163.94, 160.93, 159.45, 149.16, 142.89, 136.60, 126.45, 119.56, 117.66, 110.08, 103.38, 68.60, 55.61, 49.56, 21.28, 20.86, 19.22. ν_{max} (neat, cm^{-1}): 3217, 2198, 1718, 1672, 1519, 1220, 1074, 866; HRMS (ESI): m/z calcd. for $C_{18}H_{17}N_4O_6$ ([M+H]$^+$): 385.1143; found 385.1154. Enantiomeric excess of **9r** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 19.9 min, minor enantiomer: t_R = 9.3 min.

Ethyl (*S*)-2'-amino-3'-cyano-5,6'-dimethyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9s)[69]



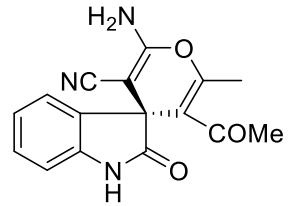
White solid, 26.9 mg, 80% yield; $[\alpha]^{24}_{D}$ = -24.0 (c 1.0, MeOH, 71% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.24 (s, 1H), 7.07 (s, 2H), 7.02 – 6.90 (m, 1H), 6.83 (d, *J* = 1.7 Hz, 1H), 6.64 (d, *J* = 7.8 Hz, 1H), 3.74 (dd, *J* = 8.3, 7.1 Hz, 2H), 2.28 (s, 3H), 2.18 (s, 3H), 0.77 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 179.01, 164.98, 159.31, 158.93, 140.10, 137.81, 135.16, 131.10, 129.36, 129.21, 128.67, 125.78, 124.38, 118.00, 109.51, 105.15, 60.71, 57.20, 49.47, 21.08, 19.06, 13.45. Enantiomeric excess of **9s** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 24.0 min, minor enantiomer: t_R = 13.6 min.

Ethyl (*S*)-2'-amino-3'-cyano-5-methoxy-6'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carboxylate (9t)[70]



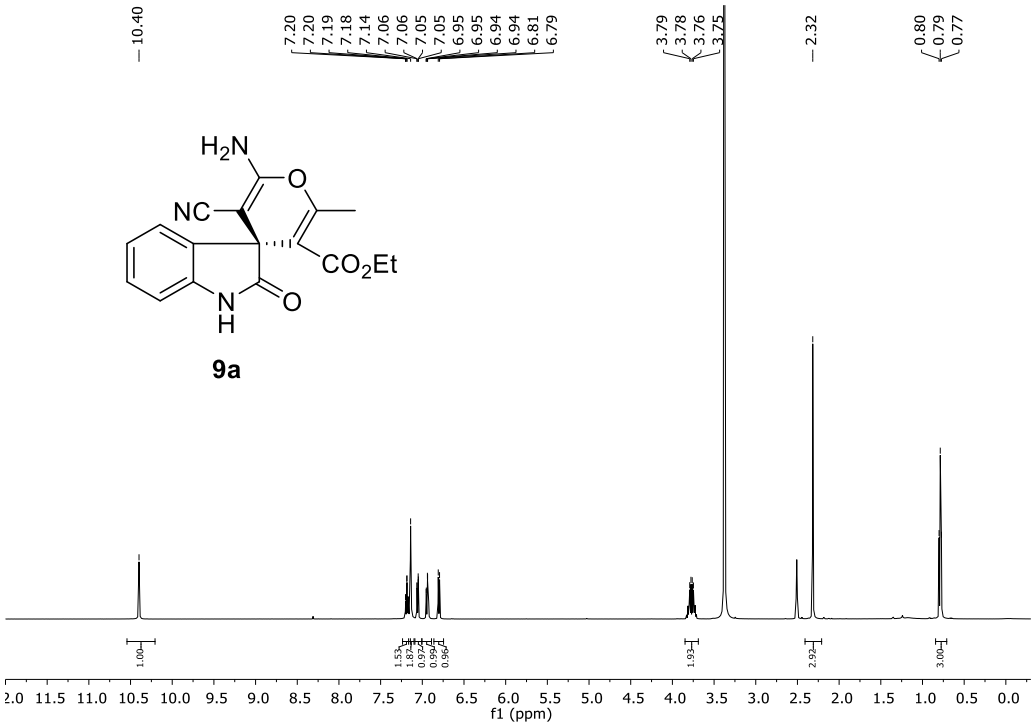
White solid, 27.5 mg, 78% yield; $[\alpha]^{24}_{D}$ = +32.2 (c 1.0, MeOH, 60% ee); ^{1}H NMR (500 MHz, DMSO-d_6) δ 10.22 (s, 1H), 7.14 (s, 2H), 6.79 – 6.64 (m, 3H), 3.79 (dd, *J* = 13.3, 6.9 Hz, 2H), 3.68 (s, 3H), 2.32 (s, 3H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (126 MHz, DMSO-d_6) δ 178.94, 164.95, 159.34, 159.05, 155.53, 136.30, 135.90, 129.36, 128.67, 125.78, 117.97, 113.60, 110.71, 110.16, 105.00, 60.70, 57.09, 55.92, 49.90, 19.06, 13.48. Enantiomeric excess of **9t** was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, λ = 254 nm), major enantiomer: t_R = 31.4 min, minor enantiomer: t_R = 15.6 min.

(*S*)-3'-Acetyl-6'-amino-2'-methyl-2-oxospiro[indoline-3,4'-pyran]-5'-carbonitrile (9u)[29]



White solid, 21.0 mg, 71% yield; m.p. 238-240 ˚C; ^{1}H NMR (500 MHz, DMSO-d_6 and $CDCl_3$) δ 10.38 (s, 1H), 7.16 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.11 (s, 2H), 7.04 (dd, *J* = 7.4, 1.2 Hz, 1H), 6.93 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.85 – 6.71 (m, 1H), 2.29 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (126 MHz, DMSO-d_6 and $CDCl_3$) δ 197.9, 178.9, 159.7, 156.5, 142.4, 134.5, 128.9, 123.8, 122.3, 118.0, 115.3, 109.9,

79.6, 57.1, 49.8, 31.7, 19.8. Enantiomeric excess was determined by chiral stationary phase HPLC analysis using a ChiralPak IB column (70:30 hexanes/*i*-PrOH at 1.0 mL·min^{-1}, $\lambda = 254$ nm), major enantiomer: $t_R = 15.6$ min, minor enantiomer: $t_R = 20.8$ min.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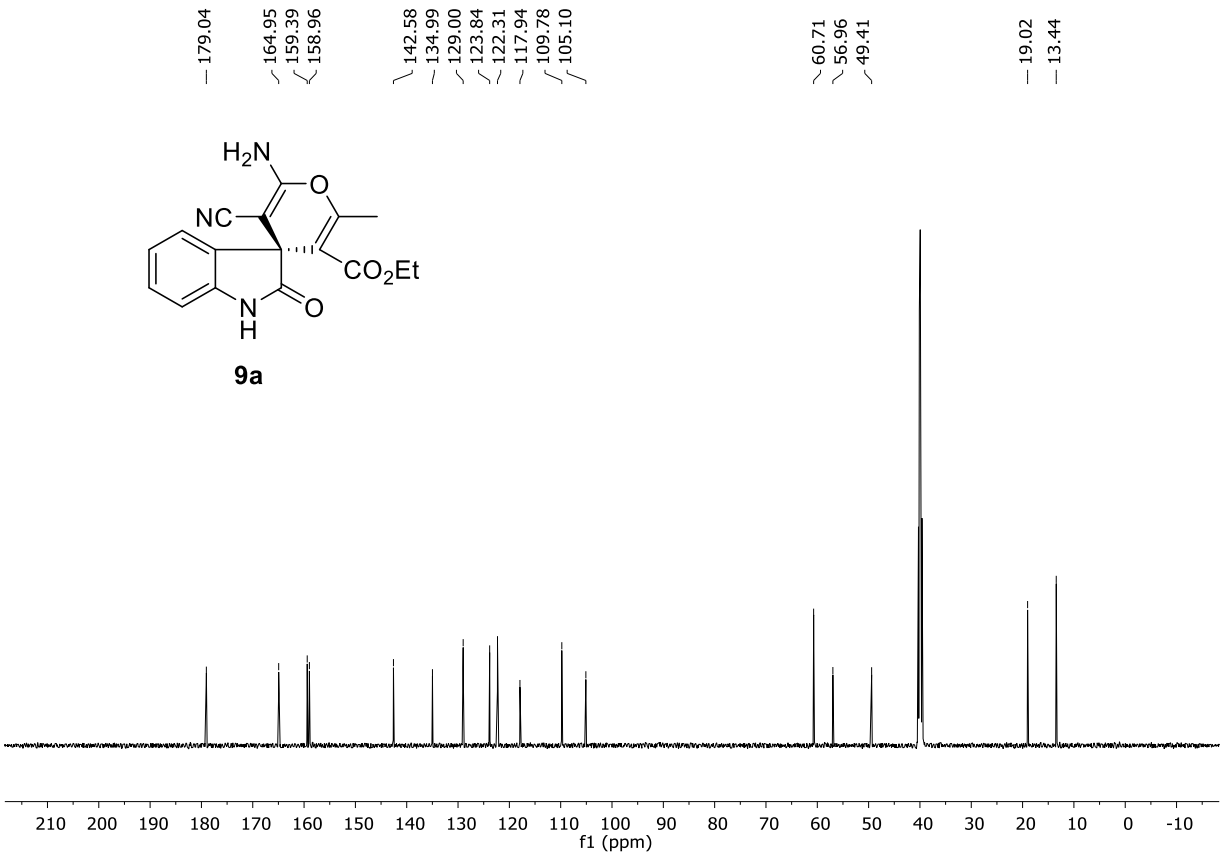
7.20
7.20
7.19
7.18
7.14
7.06
7.06
7.05
7.05
6.95
6.95
6.94
6.94
6.81
6.79
3.79
3.78
3.76
3.75
2.32
0.80
0.79
0.77
H2N
O
NC
CO2Et
N
H
O
9a
f1 (ppm)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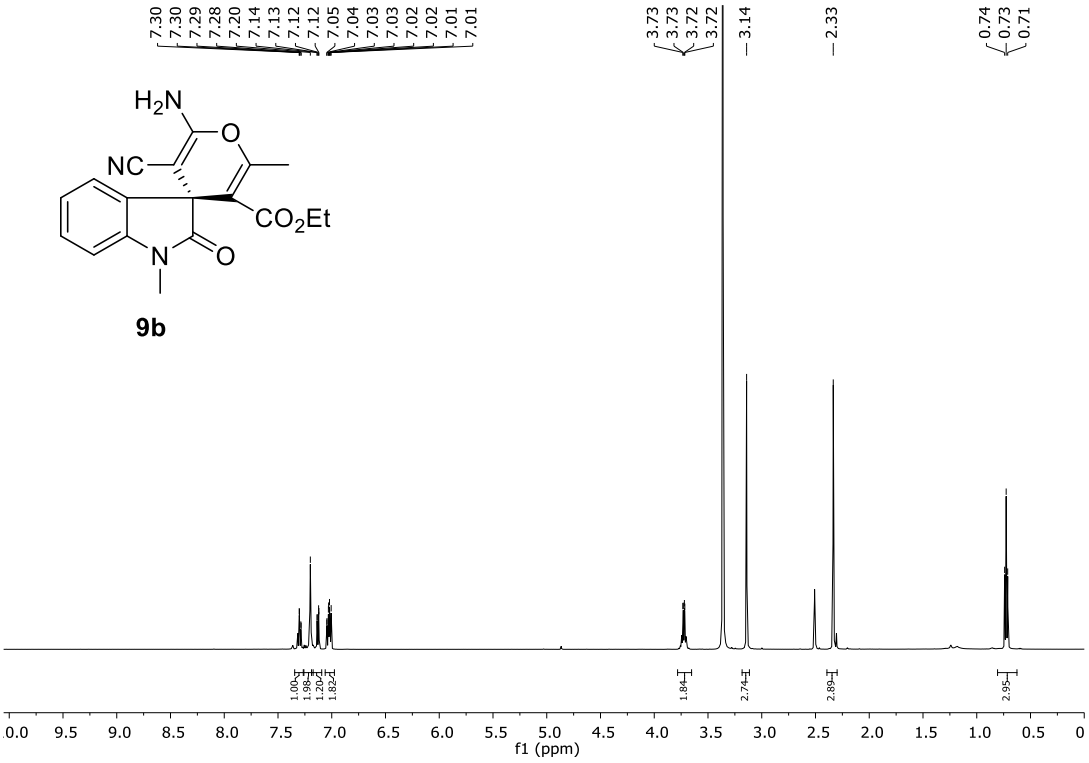
158.96
142.58
134.99
129.00
123.84
122.31
117.94
109.78
105.10
60.71
56.96
49.41
19.02
13.44
H2N
O
NC
CO2Et
N
H
O
9a
f1 (ppm)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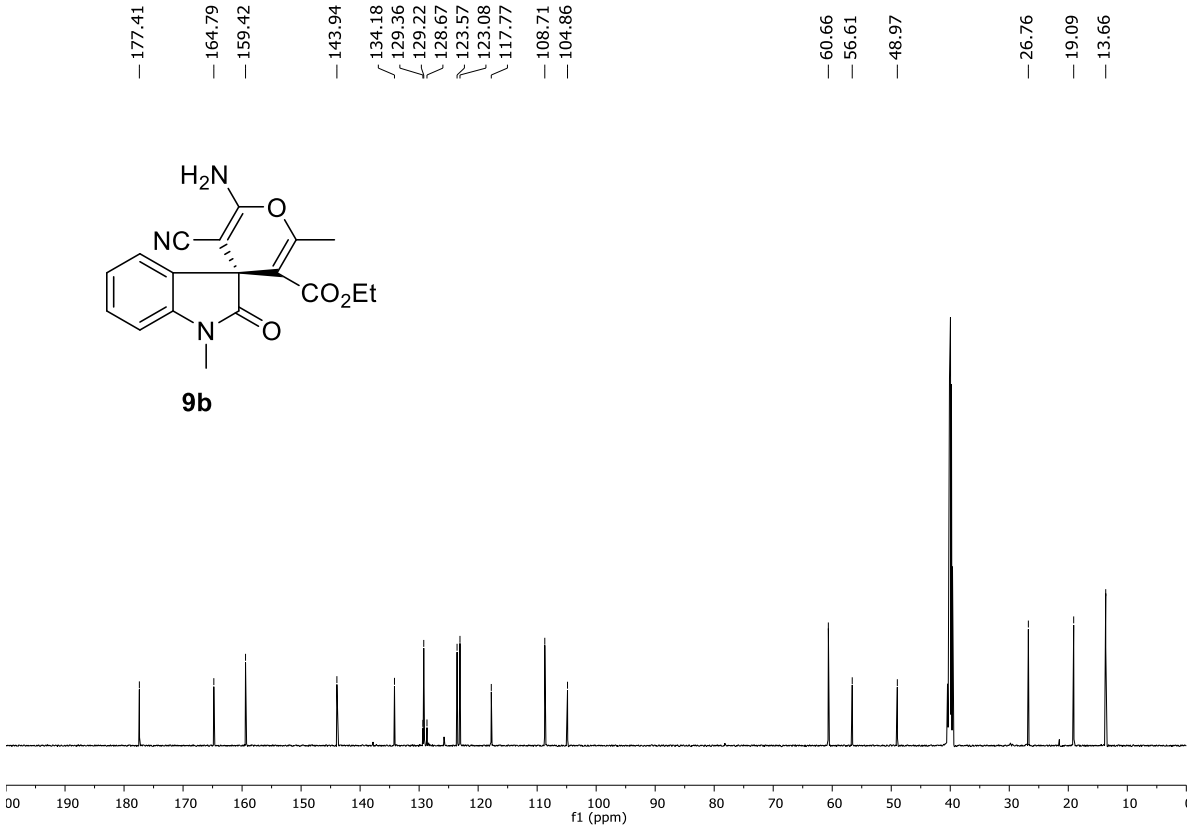
7.30
7.29
7.28
7.20
7.14
7.13
7.12
7.12
7.05
7.04
7.03
7.03
7.02
7.02
7.01
7.01
3.73
3.73
3.72
3.72
3.14
2.33
0.74
0.73
0.71
H2N
O
NC
CO2Et
N
O
1.00
1.98
1.20
1.82
1.84
2.74
2.89
2.95
f1 (ppm)

9b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128.67
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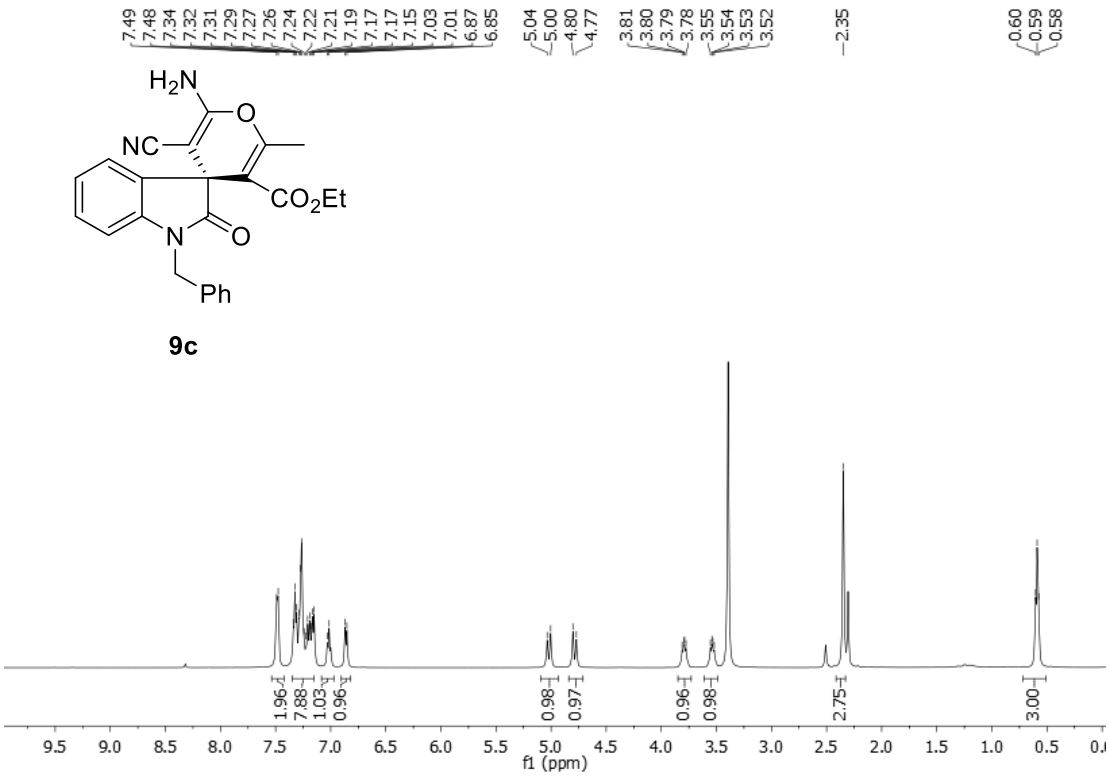
123.08
117.77
108.71
104.86
60.66
56.61
48.97
26.76
19.09
13.66
H2N
O
NC
CO2Et
N
O
f1 (ppm)

9b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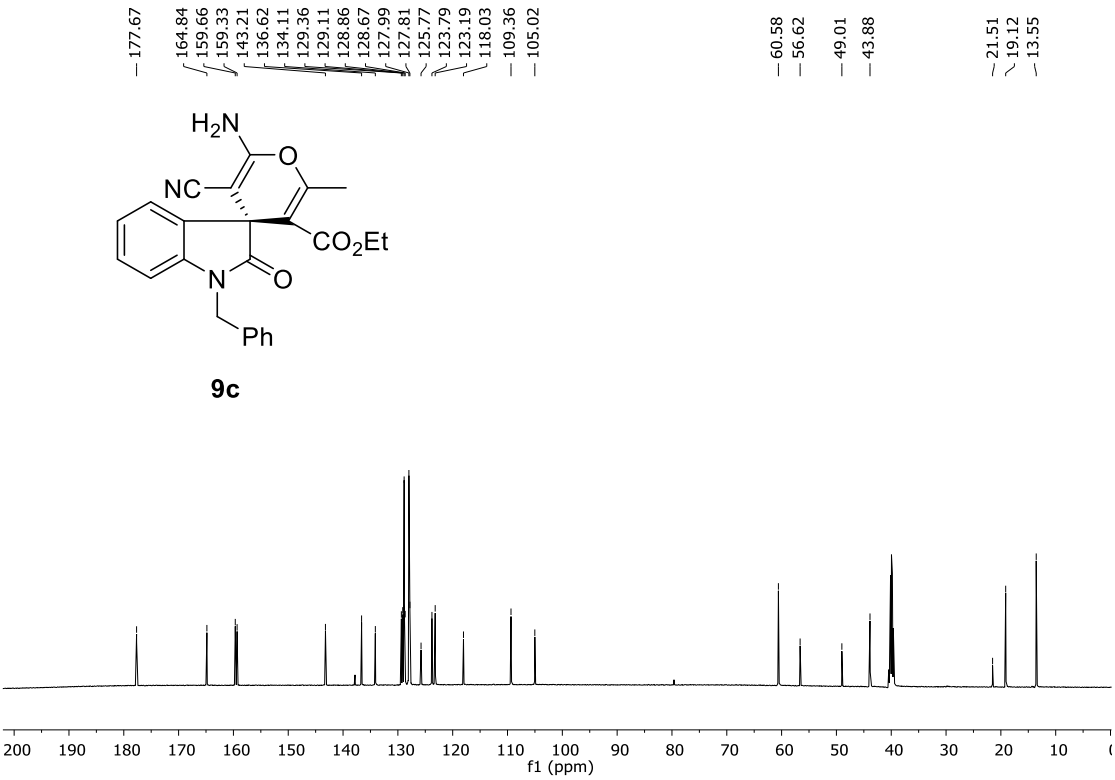
7.17
7.15
7.03
7.01
6.87
6.85
5.04
5.00
4.80
4.77
3.81
3.80
3.79
3.78
3.55
3.54
3.53
3.52
2.35
0.60
0.59
0.58
H2N
O
NC
CO2Et
N
O
Ph
1.96
7.88
1.03
0.96
0.98
0.97
0.96
0.98
2.75
3.00
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

9c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159.66
159.33
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136.62
134.11
129.36
129.11
128.86
128.67
127.99
127.81
125.77
123.79
123.19
118.03
109.36
105.02
60.58
56.62
49.01
43.88
21.51
19.12
13.55
H2N
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CO2Et
N
O
Ph
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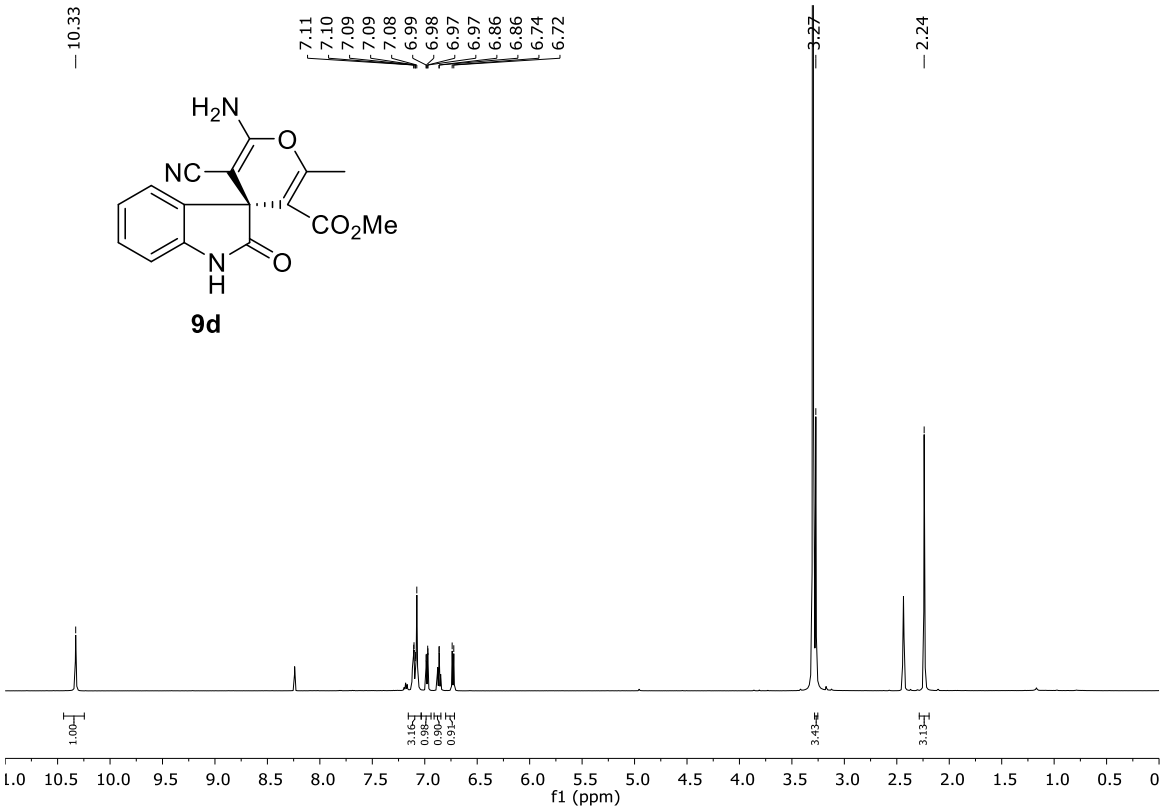
f1 (ppm)

9c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6.72
3.27
2.24
H2N
O
NC
CO2Me
N
H
O
9d
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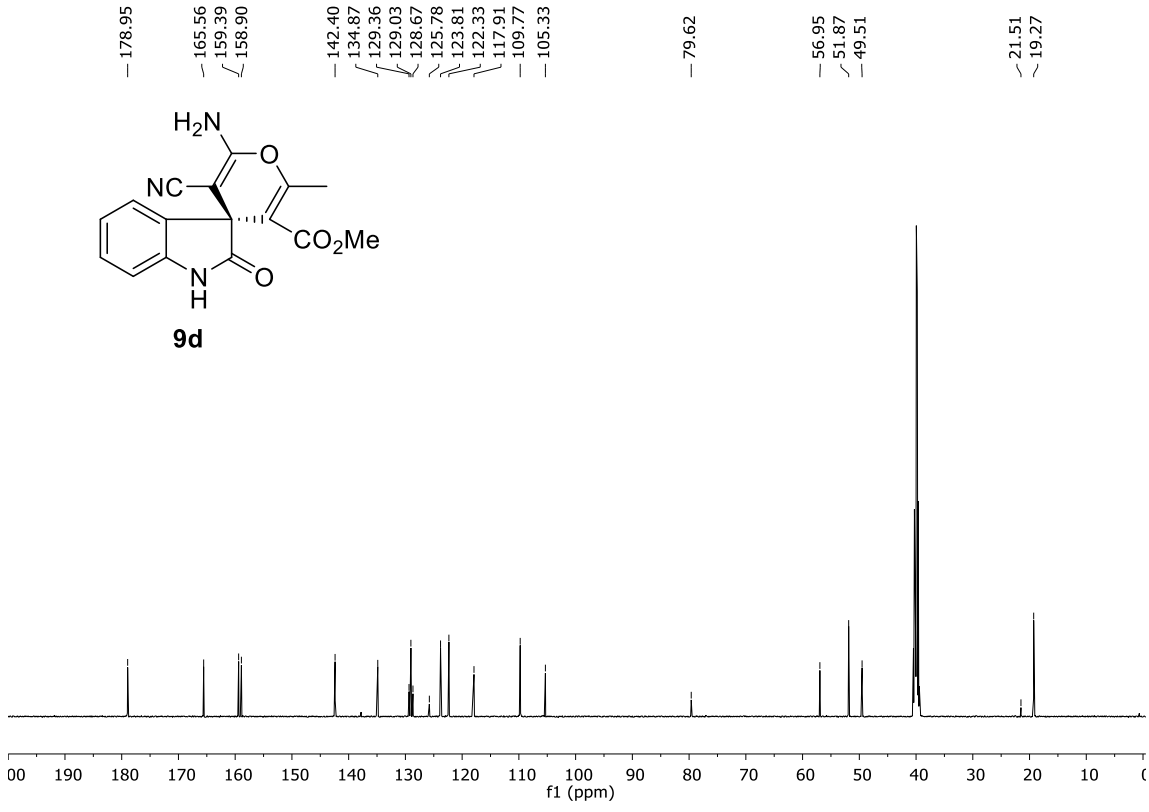
0.90
0.91
3.43
3.13
f1 (ppm)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109.77
105.33
79.62
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21.51
19.27
H2N
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CO2Me
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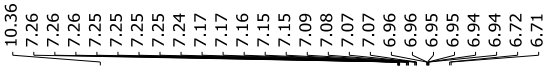
9d
f1 (ppm)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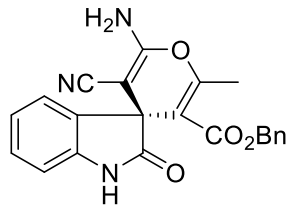
6.94
6.72
6.71
4.87
4.86
2.32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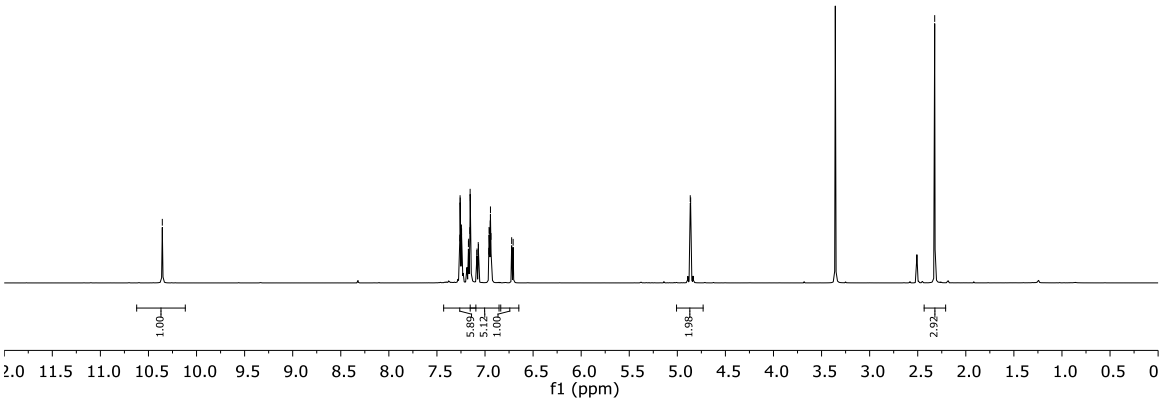
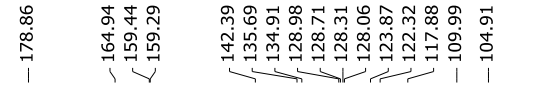
O
NC
CO2Bn
N
H
O

9e


1.00
5.89
5.12
1.00
1.98
2.92
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)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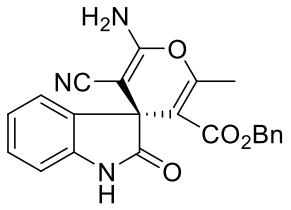
57.18
49.45
19.38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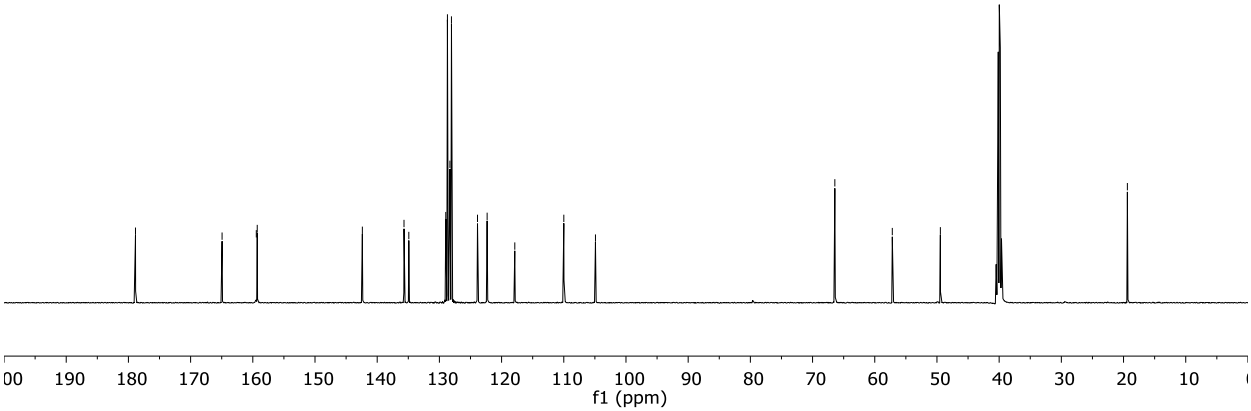
O
NC
CO2Bn
N
H
O

9e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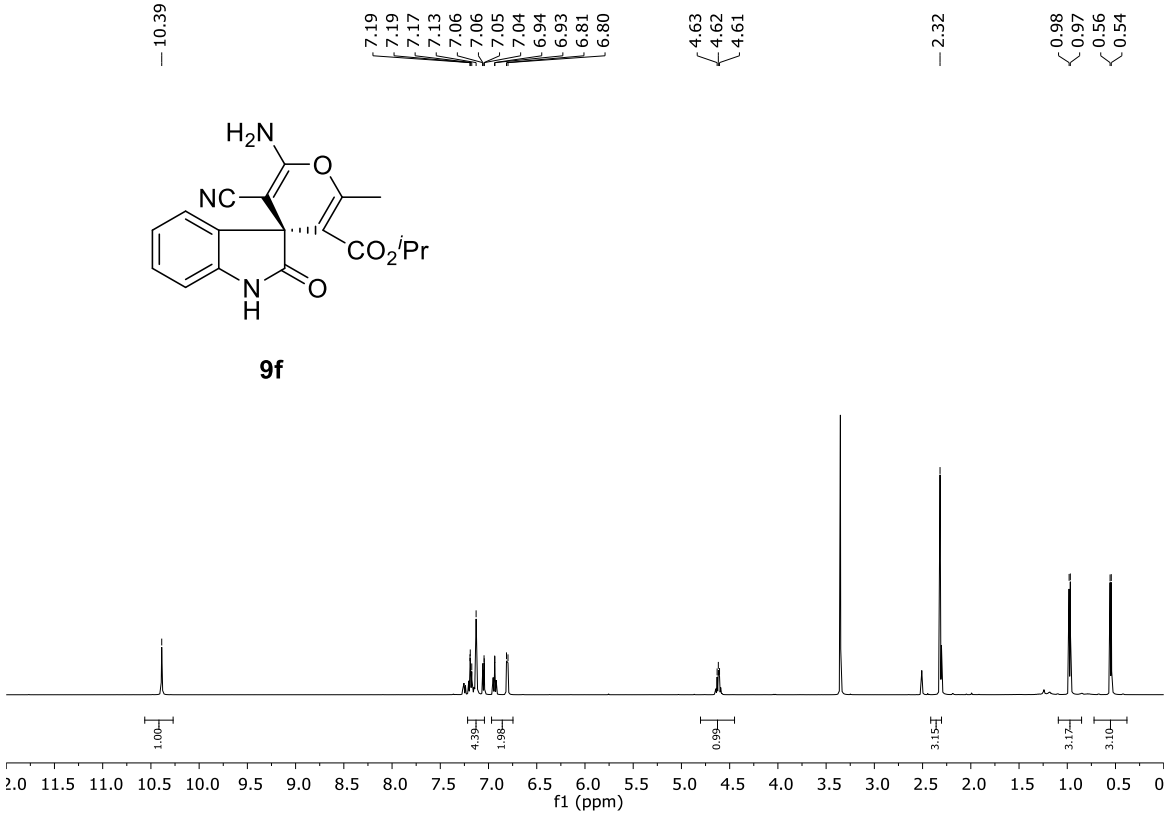
f1 (ppm)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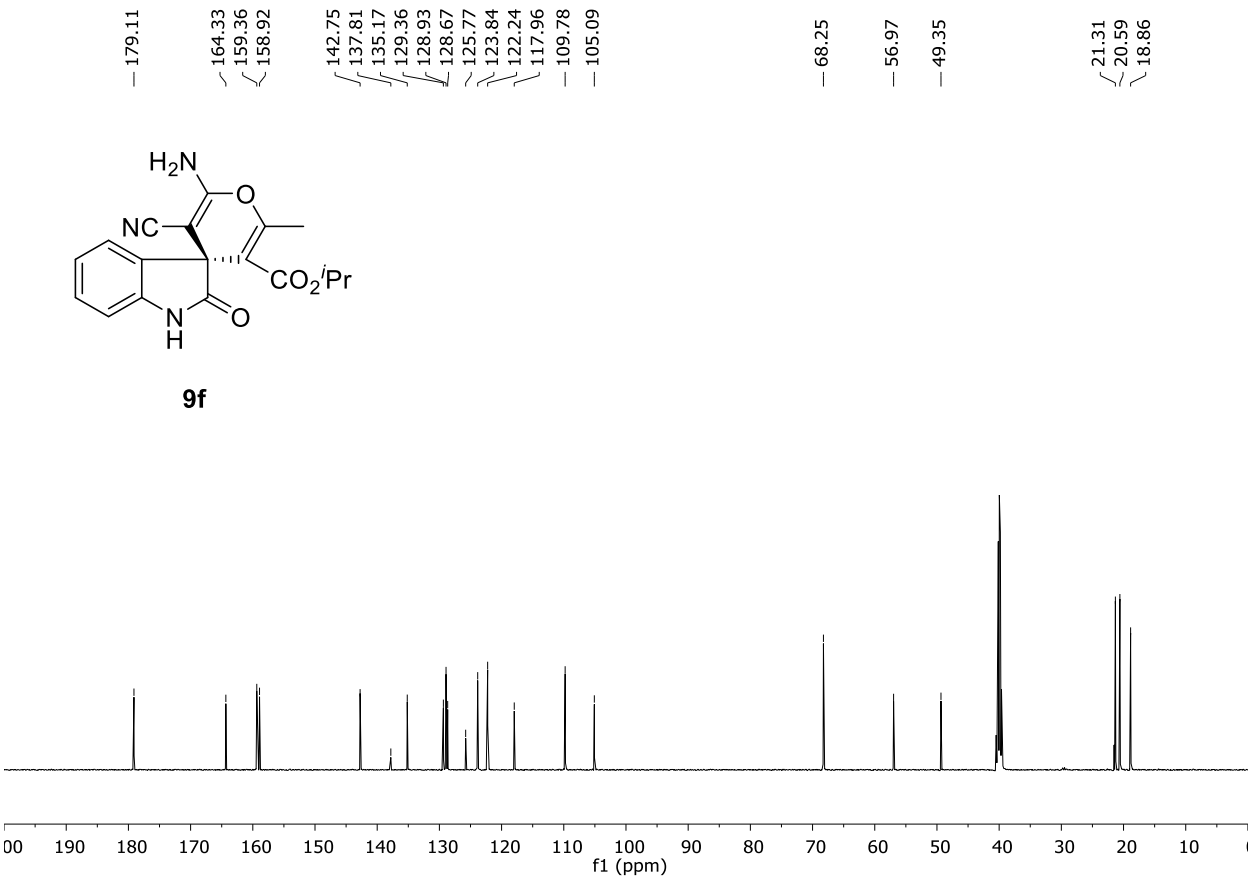
7.06
7.06
7.05
7.04
6.94
6.93
6.81
6.80
4.63
4.62
4.61
2.32
0.98
0.97
0.56
0.54
H2N
O
NC
CO2iPr
N
H
O
1.00
4.39
1.98
0.99
3.15
3.17
3.10
f1 (ppm)

9f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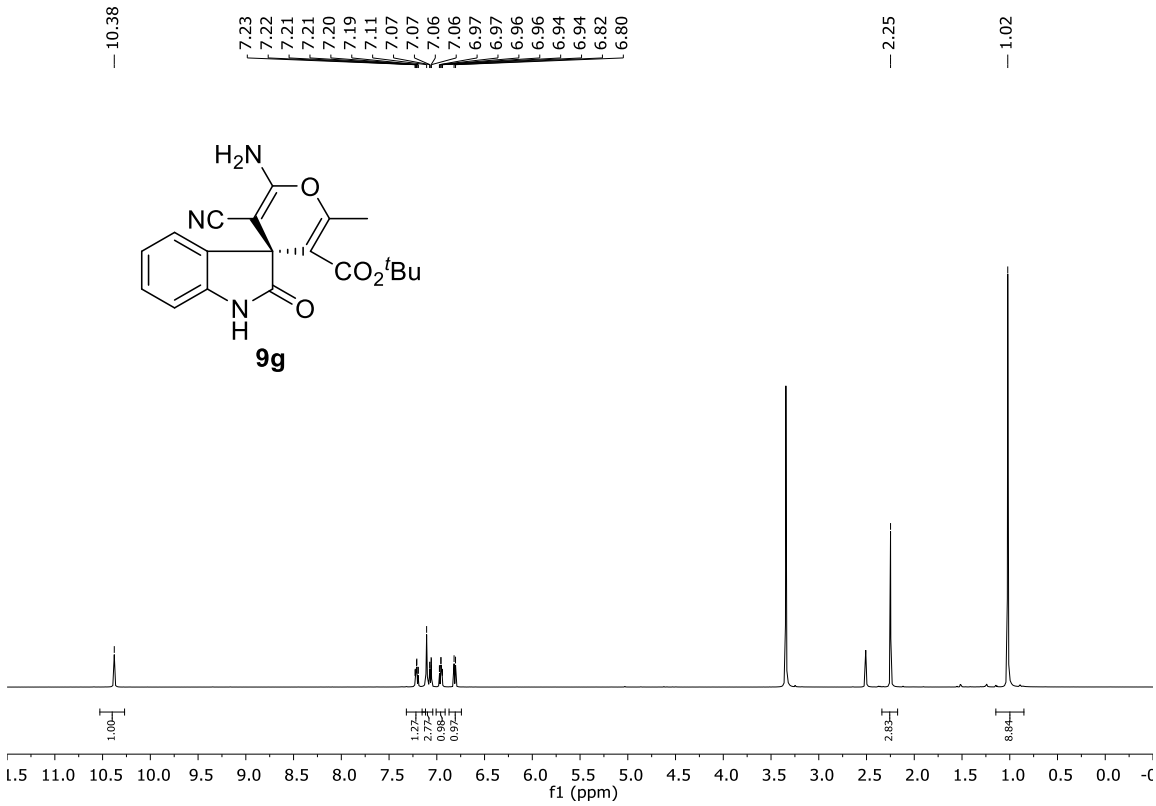
164.33
159.36
158.92
142.75
137.81
135.17
129.36
128.93
128.67
125.77
123.84
122.24
117.96
109.78
105.09
68.25
56.97
49.35
21.31
20.59
18.86
H2N
O
NC
CO2iPr
N
H
O
f1 (ppm)

9f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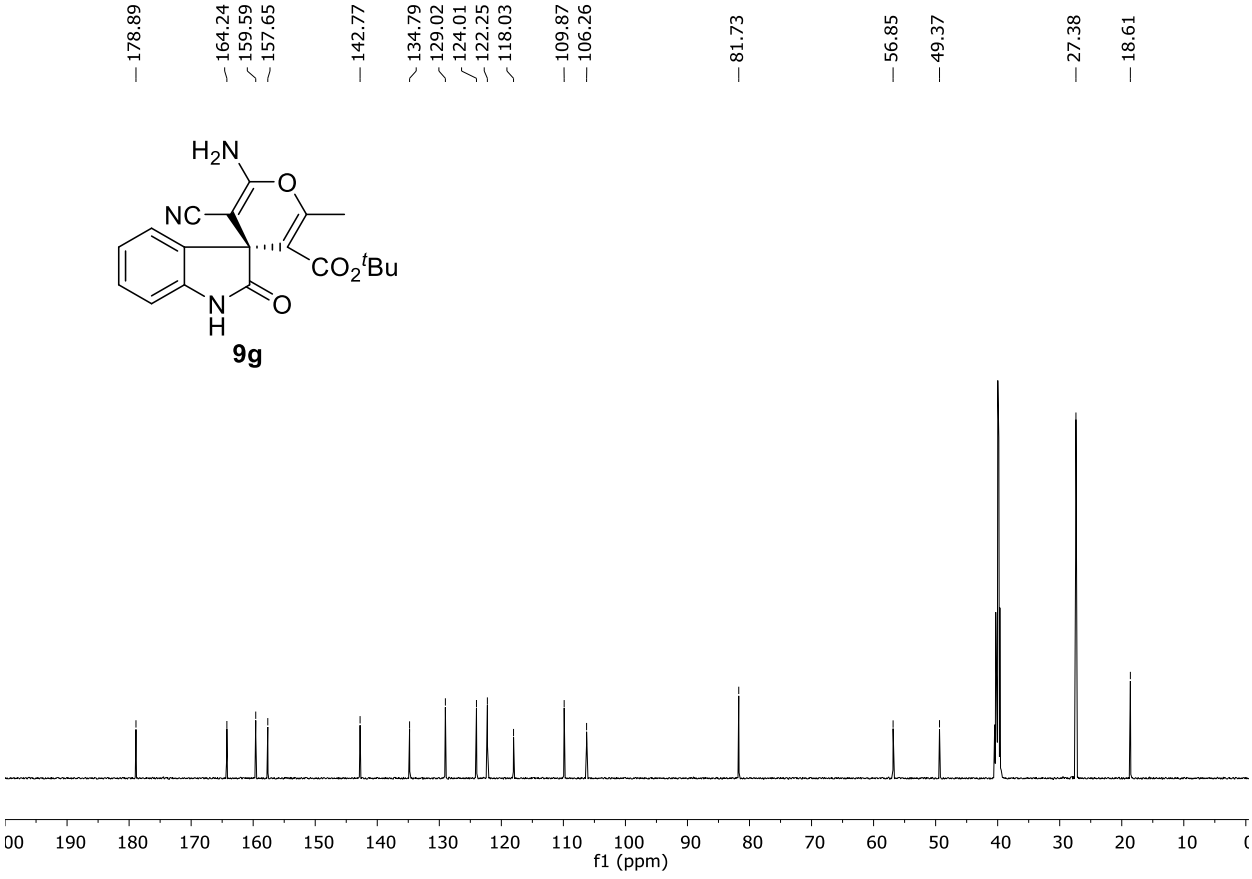
7.23
7.22
7.21
7.21
7.20
7.19
7.11
7.07
7.07
7.06
7.06
6.97
6.97
6.96
6.96
6.94
6.94
6.82
6.80
2.25
1.02
H2N
O
NC
CO2tBu
N
H
O
9g
1.00
1.27
2.77
0.98
0.97
2.83
8.84
f1 (ppm)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164.24
159.59
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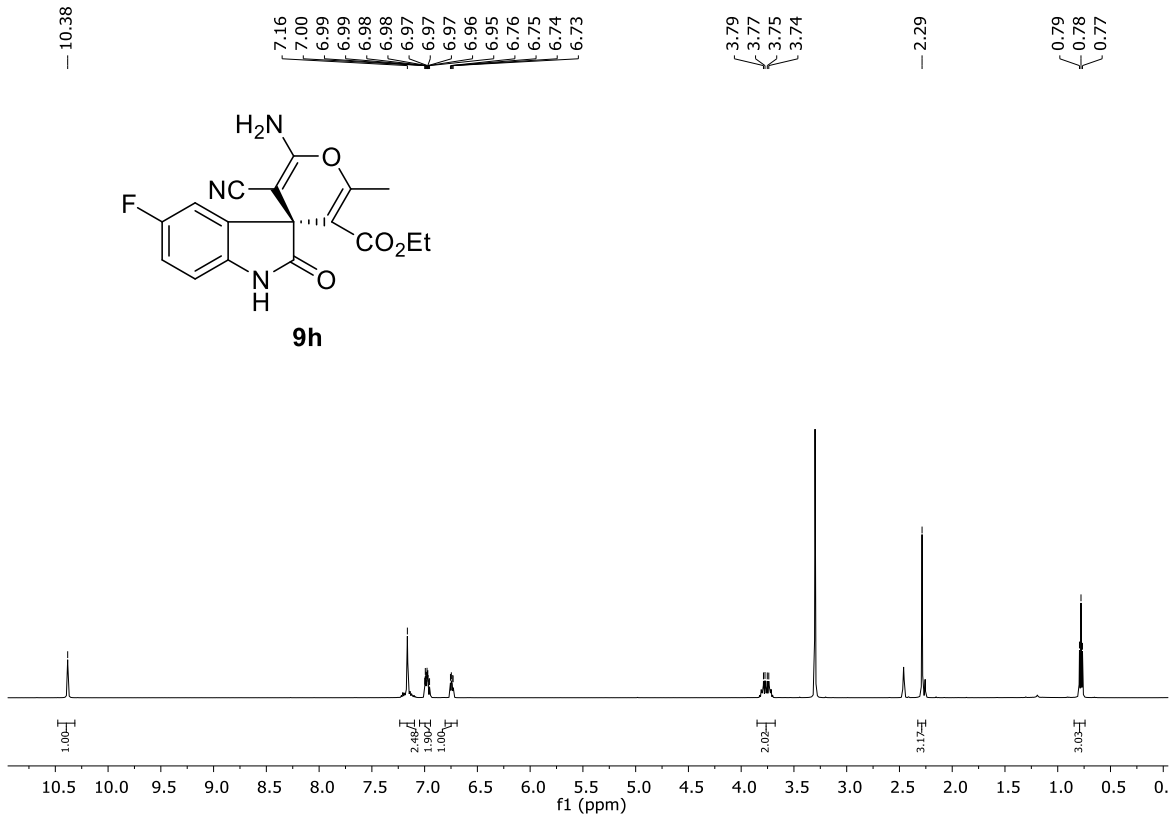
134.79
129.02
124.01
122.25
118.03
109.87
106.26
81.73
56.85
49.37
27.38
18.61
H2N
O
NC
CO2tBu
N
H
O
9g
f1 (ppm)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7.16
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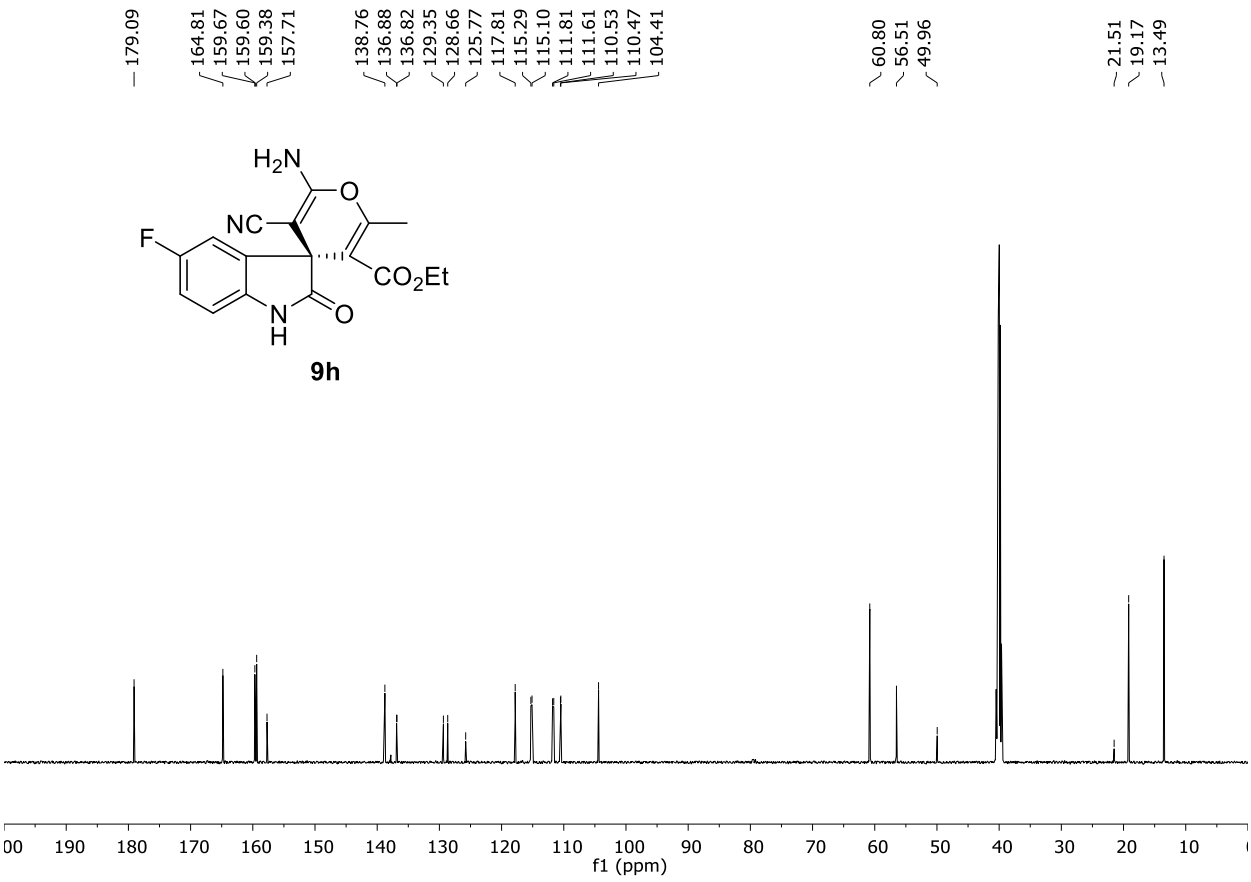
6.98
6.98
6.97
6.97
6.97
6.96
6.95
6.76
6.75
6.74
6.73
3.79
3.77
3.75
3.74
2.29
0.79
0.78
0.77
H2N
O
NC
F
CO2Et
N
H
O
1.00
2.48
1.90
1.00
2.02
3.17
3.03
10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.
f1 (ppm)

9h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164.81
159.67
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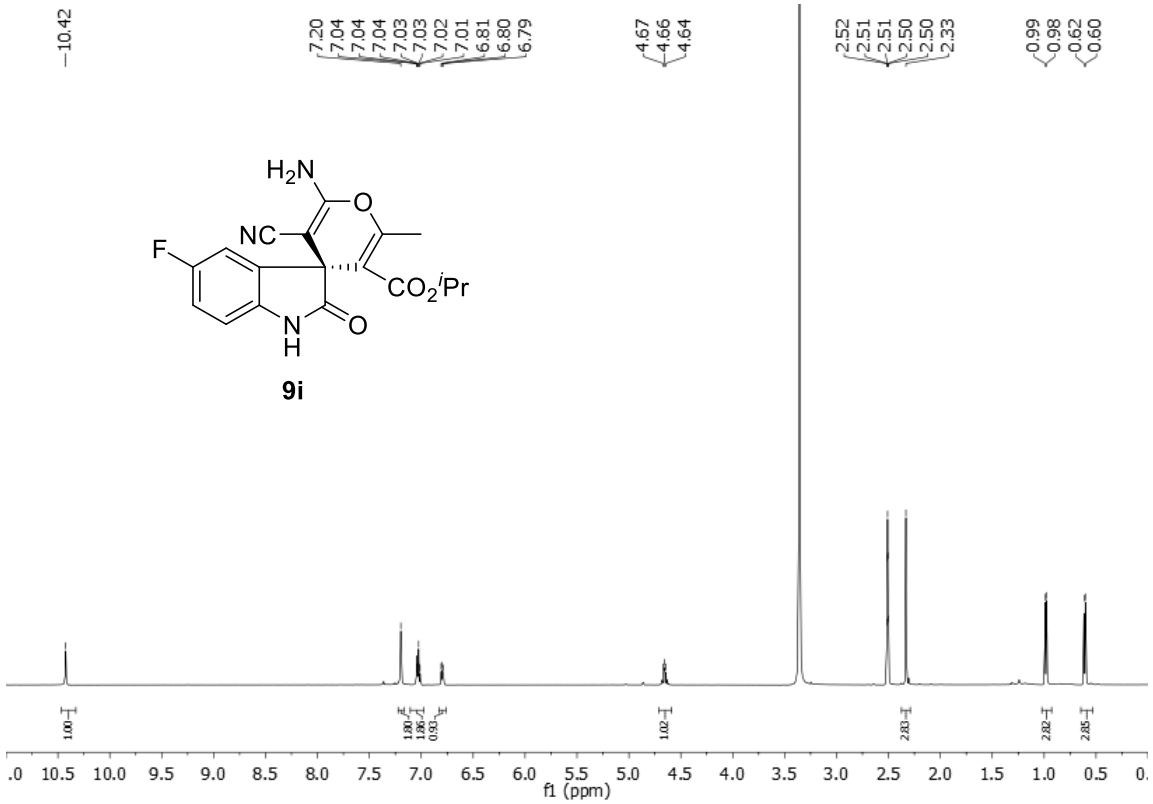
159.38
157.71
138.76
136.88
136.82
129.35
128.66
125.77
117.81
115.29
115.10
111.81
111.61
110.53
110.47
104.41
60.80
56.51
49.96
21.51
19.17
13.49
H2N
O
NC
F
CO2Et
N
H
O
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

9h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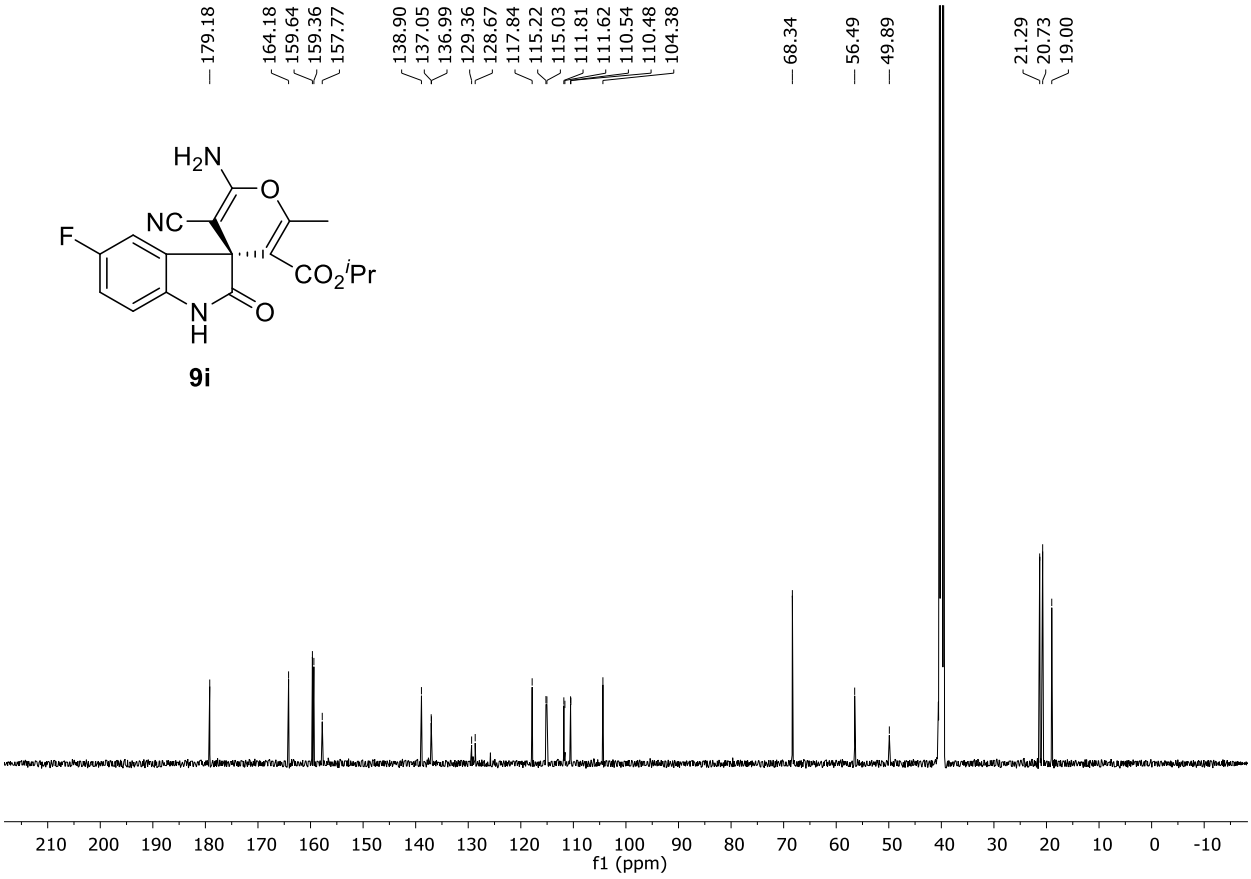
7.20
7.04
7.04
7.04
7.03
7.03
7.02
7.01
6.81
6.80
6.79
4.67
4.66
4.64
2.52
2.51
2.51
2.50
2.50
2.33
0.99
0.98
0.62
0.60
H2N
O
NC
F
CO2iPr
N
H
O
9i
f1 (ppm)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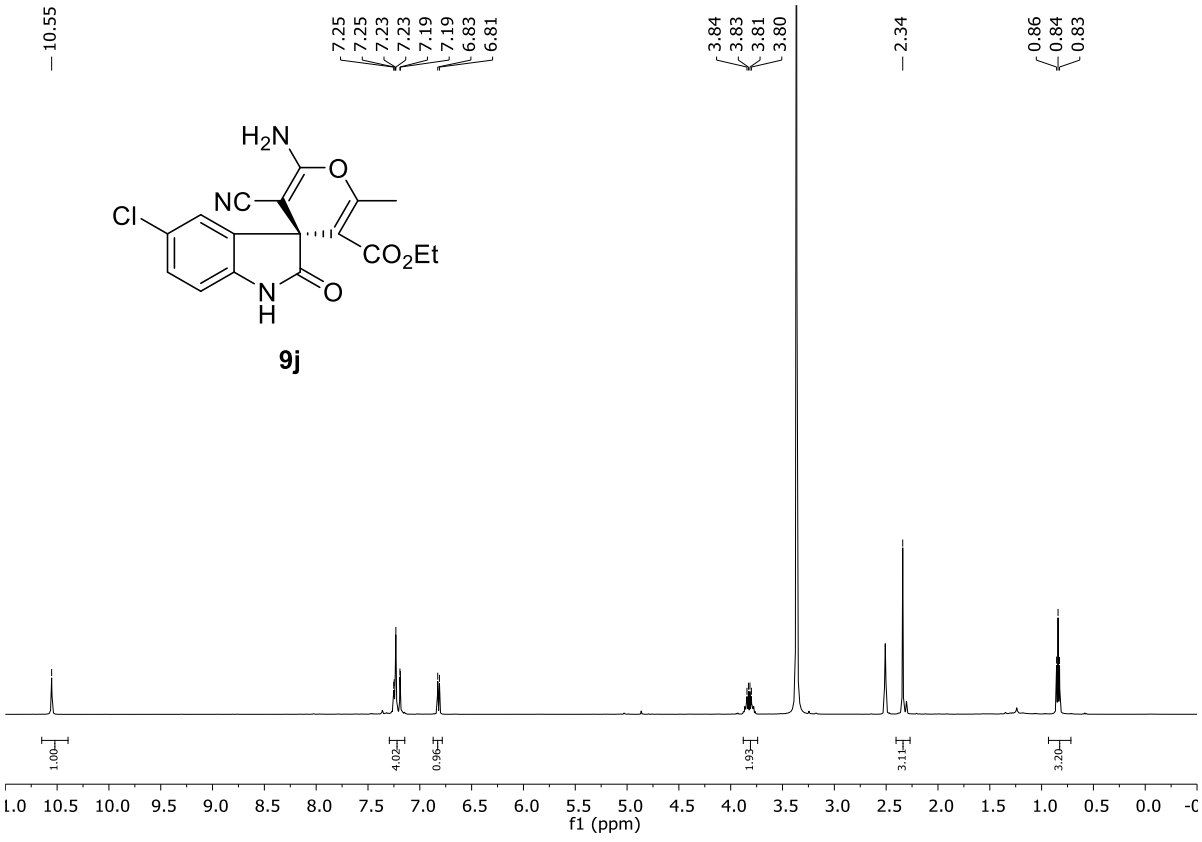
138.90
137.05
136.99
129.36
128.67
117.84
115.22
115.03
111.81
111.62
110.54
110.48
104.38
68.34
56.49
49.89
21.29
20.73
19.00
H2N
O
NC
F
CO2iPr
N
H
O
9i
f1 (ppm)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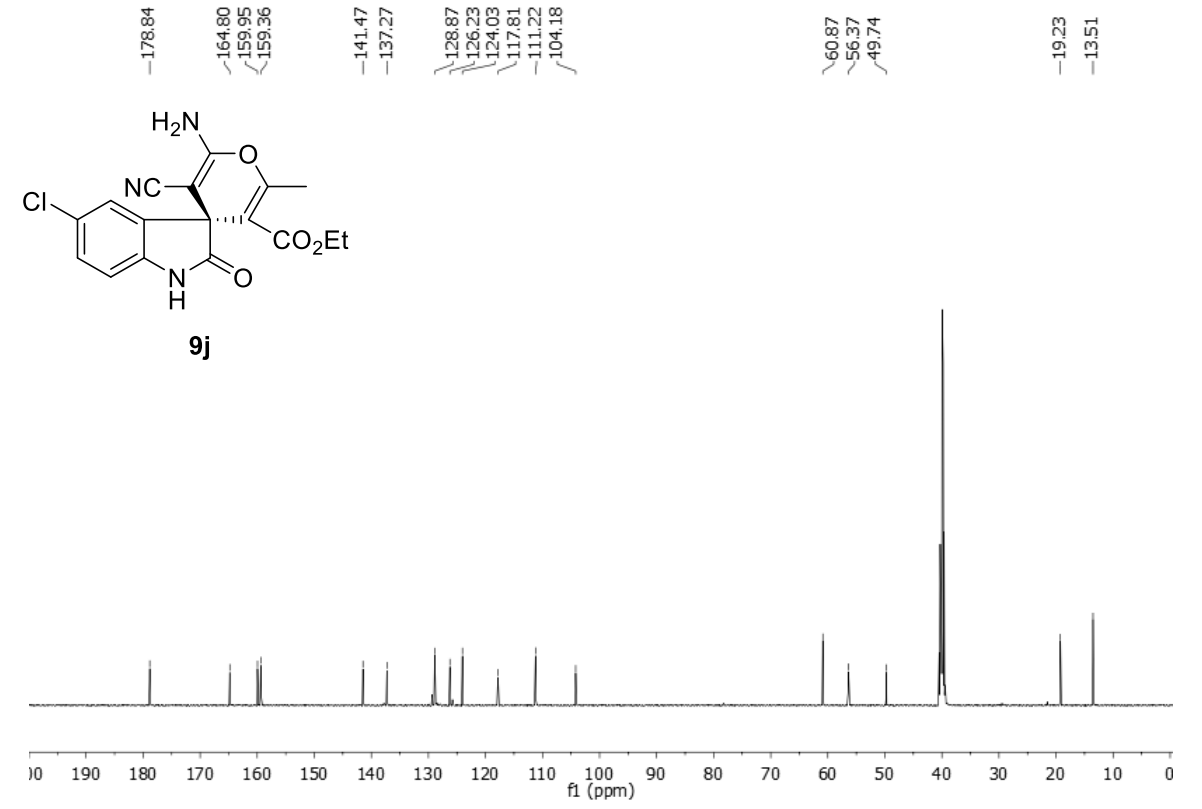
7.25
7.25
7.23
7.23
7.19
7.19
6.83
6.81
3.84
3.83
3.81
3.80
2.34
0.86
0.84
0.83
H2N
O
NC
Cl
CO2Et
N
H
O
1.00
4.02
0.96
1.93
3.11
3.20
f1 (ppm)

9j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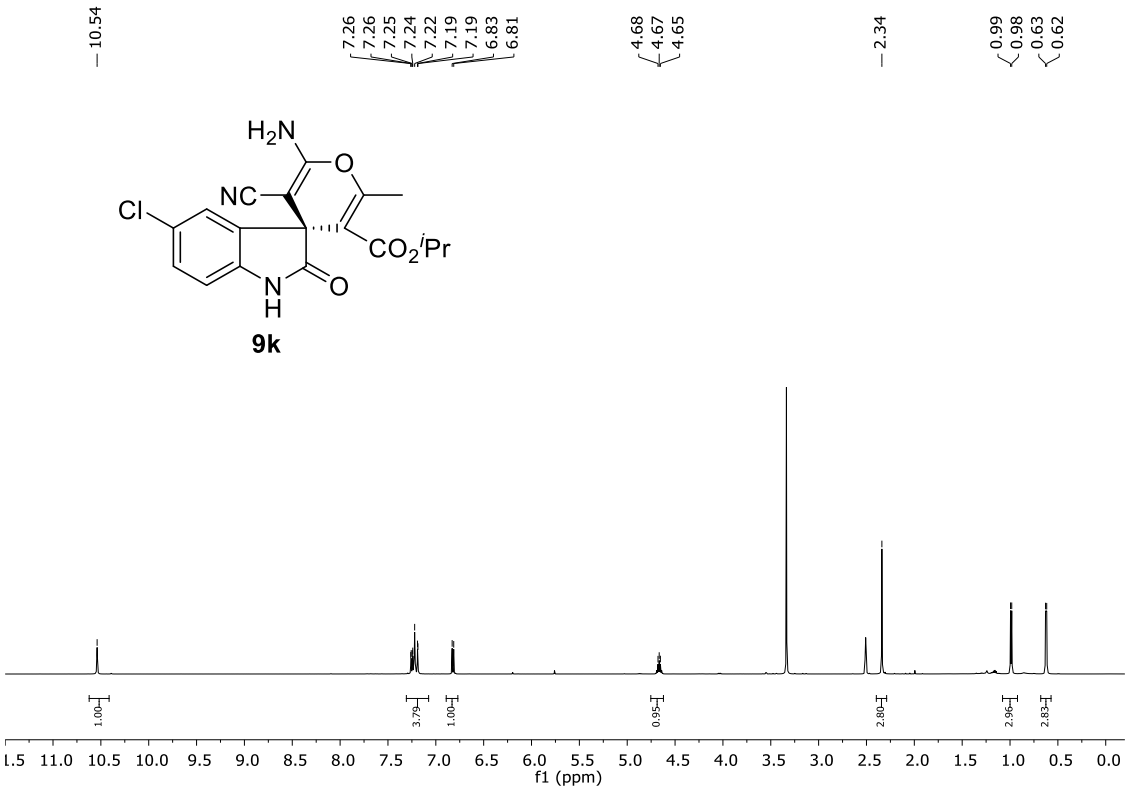
159.36
141.47
137.27
128.87
126.23
124.03
117.81
111.22
104.18
60.87
56.37
49.74
19.23
13.51
H2N
O
NC
Cl
CO2Et
N
H
O
f1 (ppm)

9j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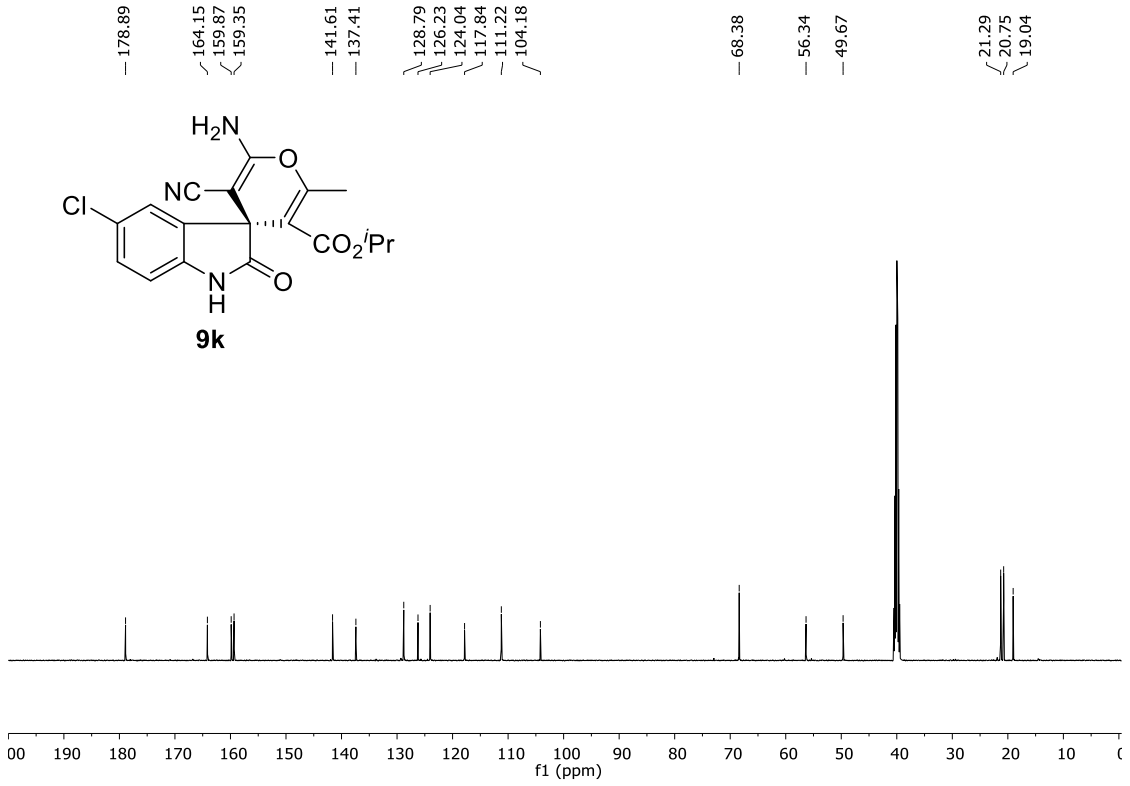
7.26
7.26
7.25
7.24
7.22
7.19
7.19
6.83
6.81
4.68
4.67
4.65
2.34
0.99
0.98
0.63
0.62
H2N
O
NC
Cl
CO2iPr
N
H
O
9k
1.00
3.79
1.00
0.95
2.80
2.96
2.83
f1 (ppm)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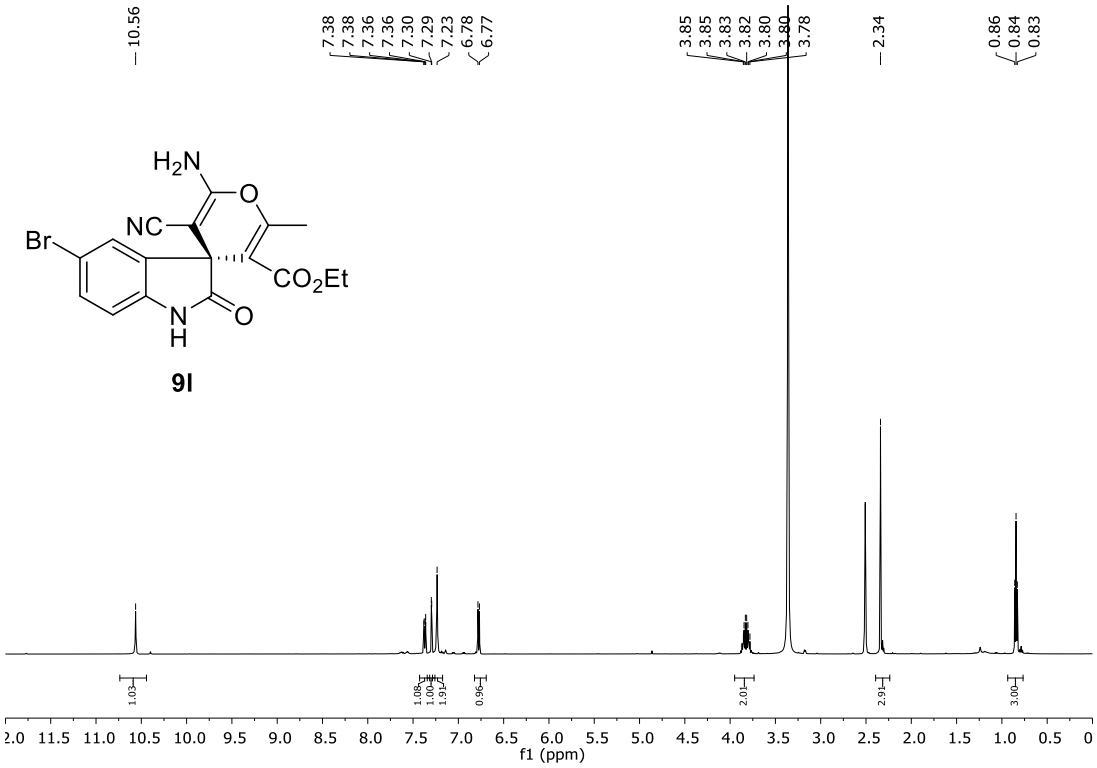
164.15
159.87
159.35
141.61
137.41
128.79
126.23
124.04
117.84
111.22
104.18
68.38
56.34
49.67
21.29
20.75
19.04
H2N
O
NC
Cl
CO2iPr
N
H
O
9k
f1 (ppm)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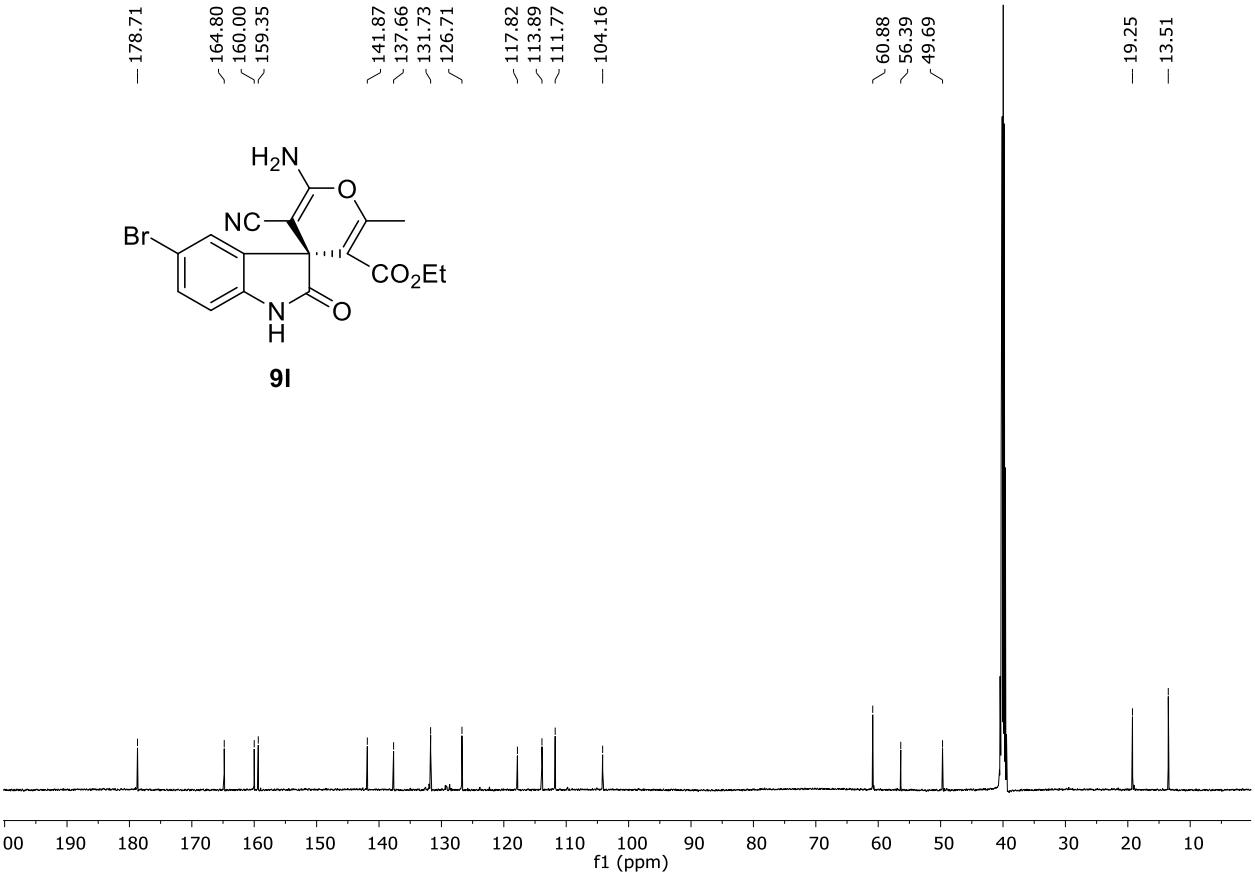
7.38
7.38
7.36
7.36
7.30
7.29
7.23
6.78
6.77
3.85
3.85
3.83
3.82
3.80
3.80
3.78
2.34
0.86
0.84
0.83
H2N
O
NC
Br
CO2Et
N
H
O
1.03
1.08
1.00
1.91
0.96
2.01
2.91
3.00
f1 (ppm)

9l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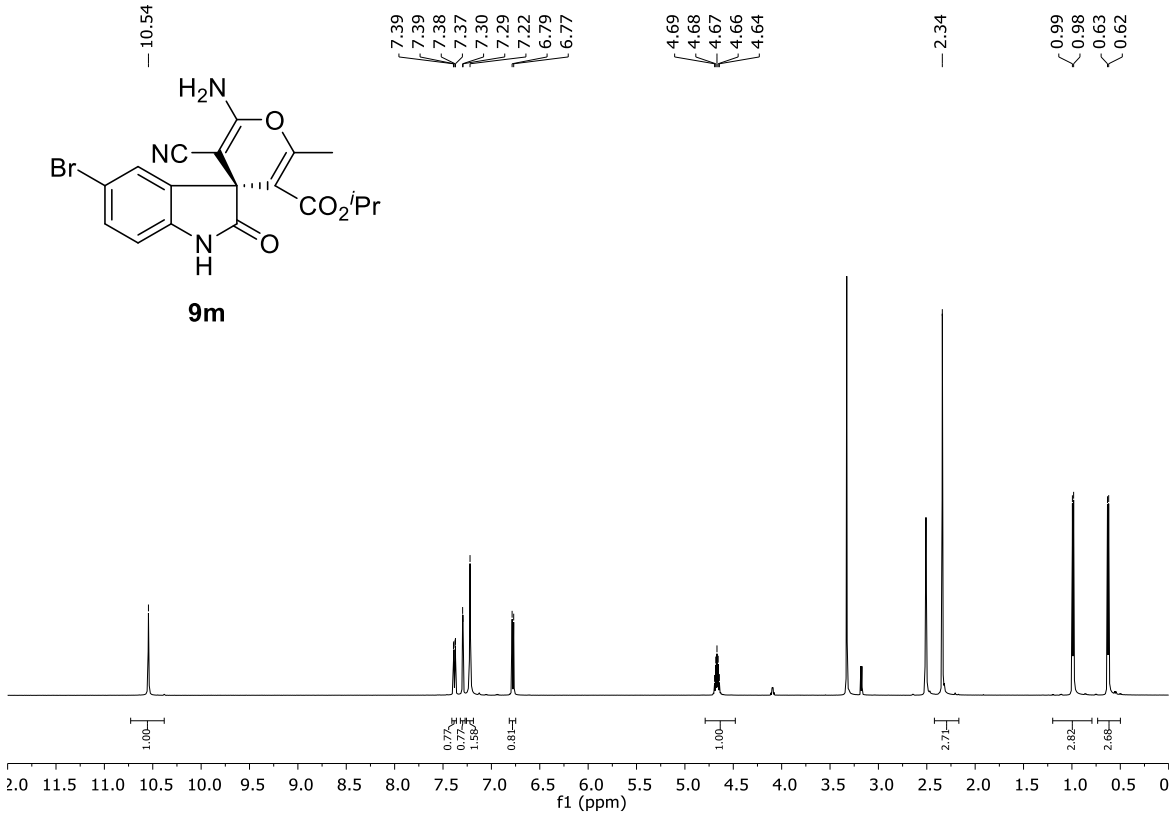
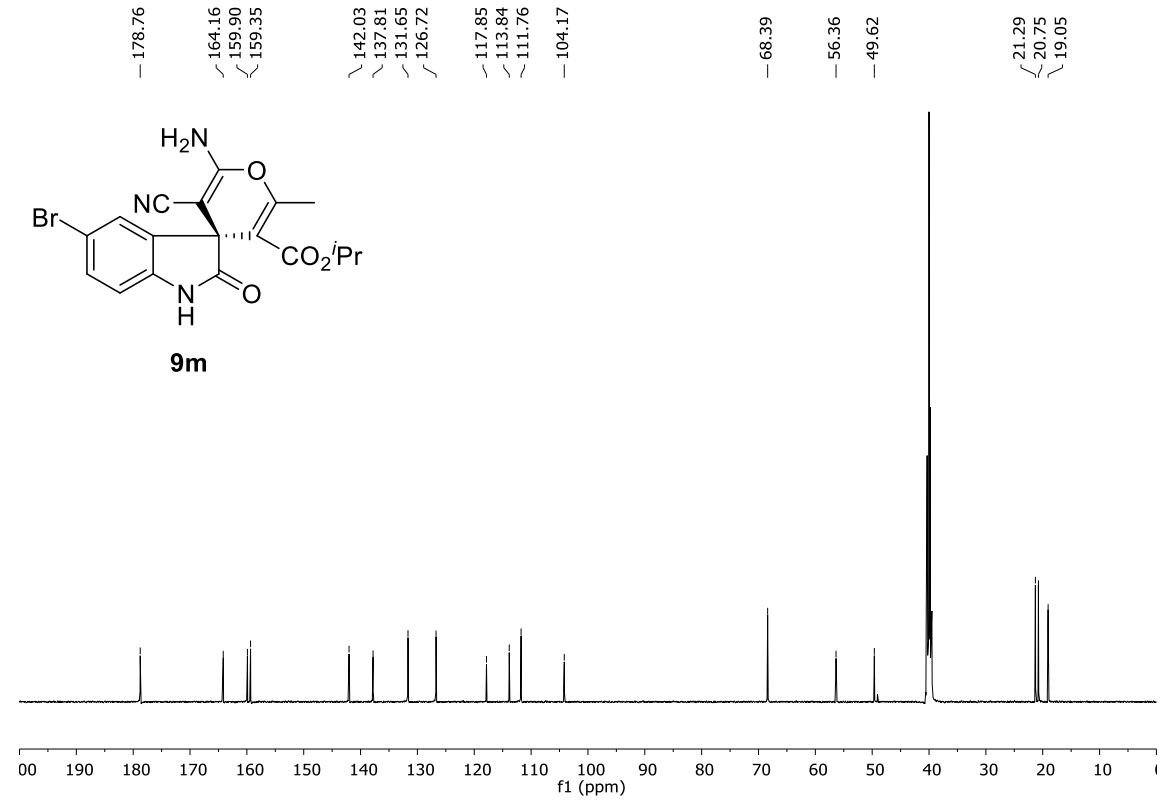
164.80
160.00
159.35
141.87
137.66
131.73
126.71
117.82
113.89
111.77
104.16
60.88
56.39
49.69
19.25
13.51
H2N
O
NC
Br
CO2Et
N
H
O
f1 (ppm)

9l


10.54
7.39
7.39
7.38
7.37
7.30
7.29
7.22
6.79
6.77
4.69
4.68
4.67
4.66
4.64
2.34
0.99
0.98
0.63
0.62
H2N
O
NC
Br
CO2iPr
N
H
O
9m
1.00
0.77
0.77
1.58
0.81
1.00
2.71
2.82
2.68
f1 (ppm)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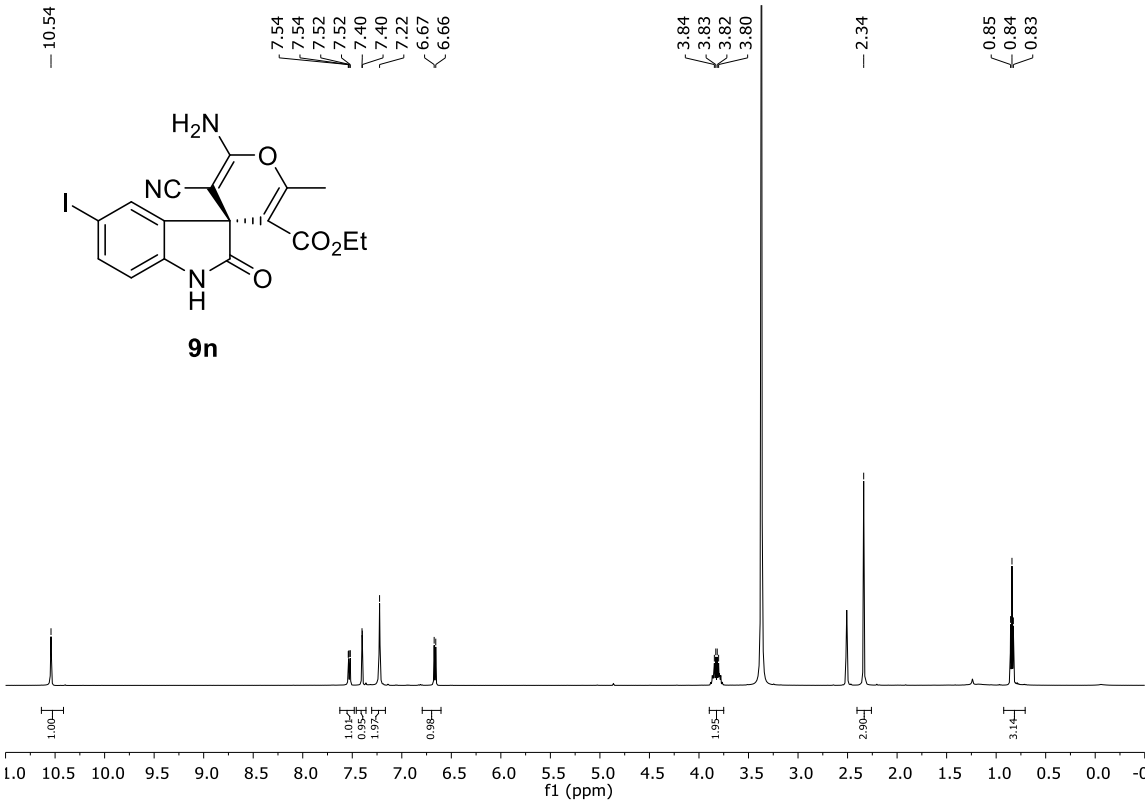
164.16
159.90
159.35
142.03
137.81
131.65
126.72
117.85
113.84
111.76
104.17
68.39
56.36
49.62
21.29
20.75
19.05
H2N
O
NC
Br
CO2iPr
N
H
O
9m
f1 (ppm)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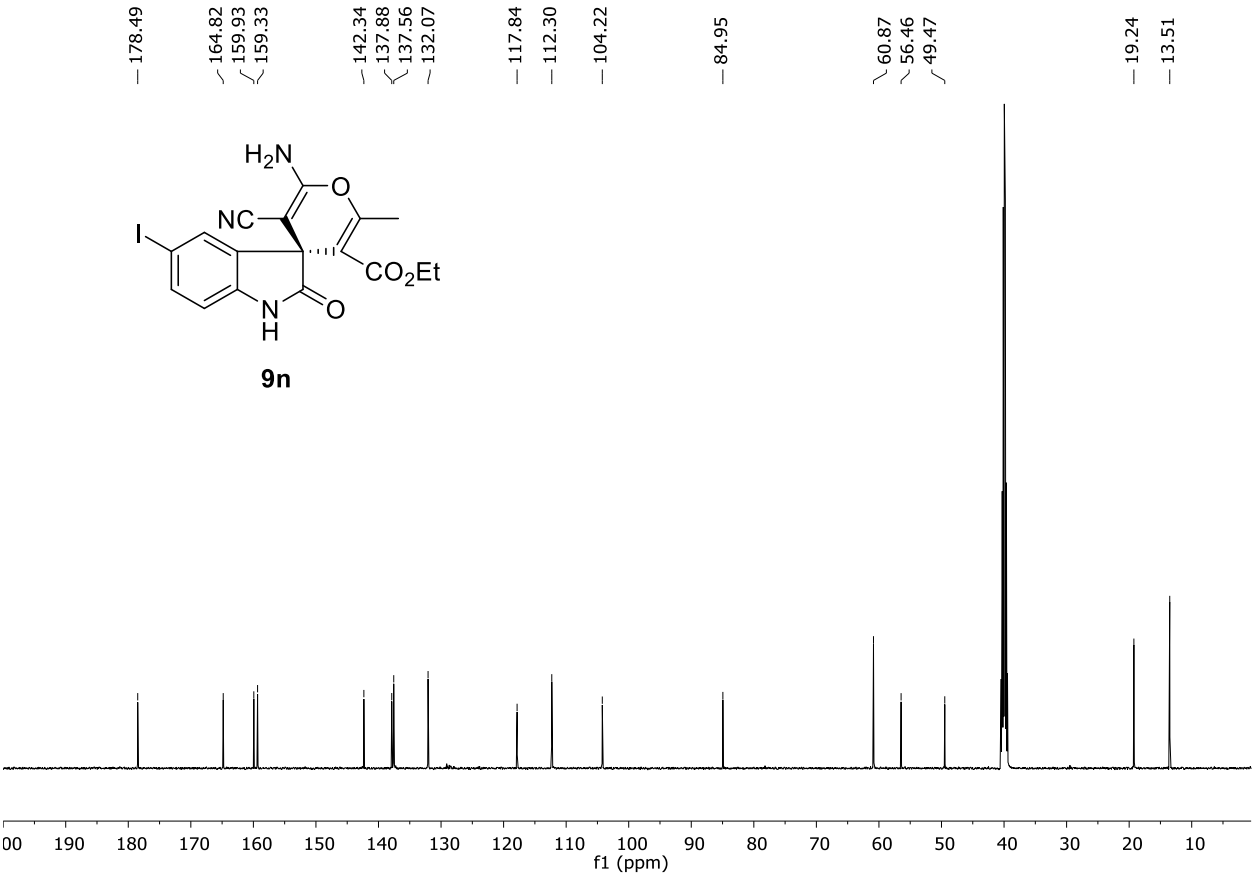
7.54
7.54
7.52
7.52
7.40
7.40
7.22
6.67
6.66
3.84
3.83
3.82
3.80
2.34
0.85
0.84
0.83
H2N
O
NC
I
CO2Et
N
H
O
1.00
1.01
0.95
1.97
0.98
1.95
2.90
3.14
f1 (ppm)

9n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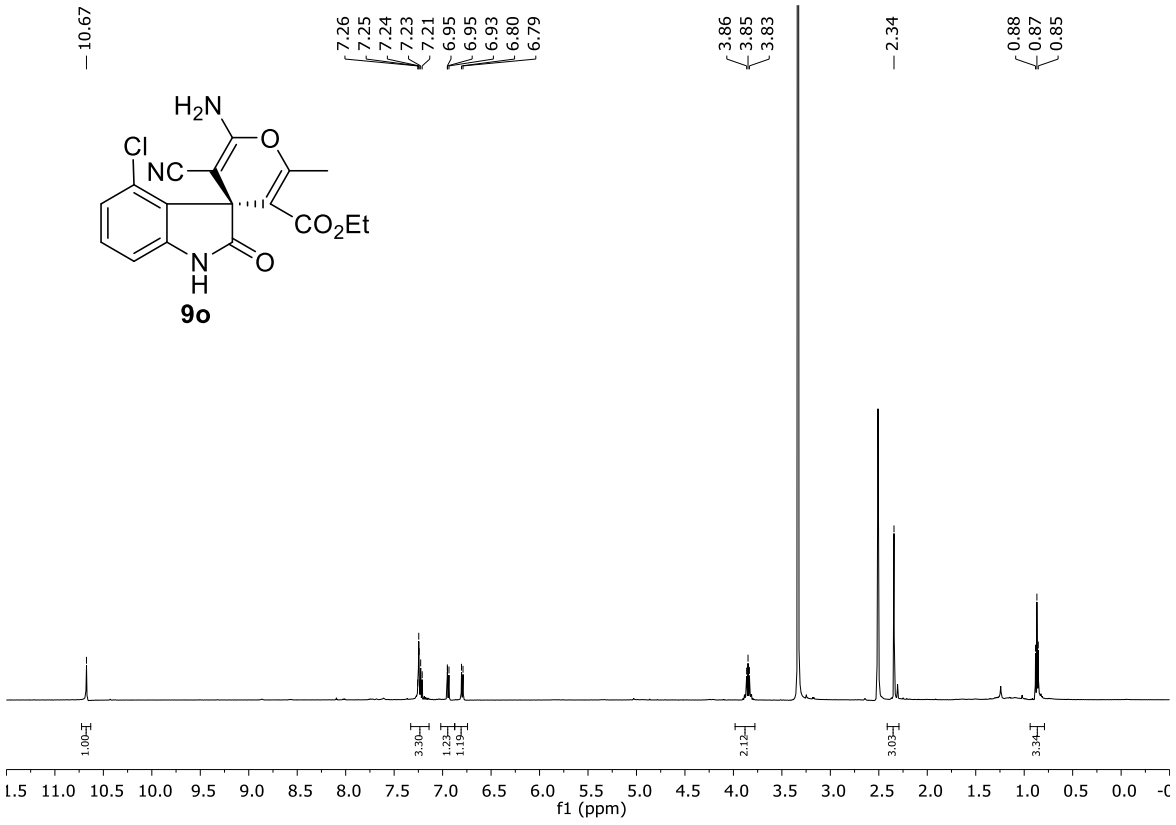
142.34
137.88
137.56
132.07
117.84
112.30
104.22
84.95
60.87
56.46
49.47
19.24
13.51
H2N
O
NC
I
CO2Et
N
H
O
f1 (ppm)

9n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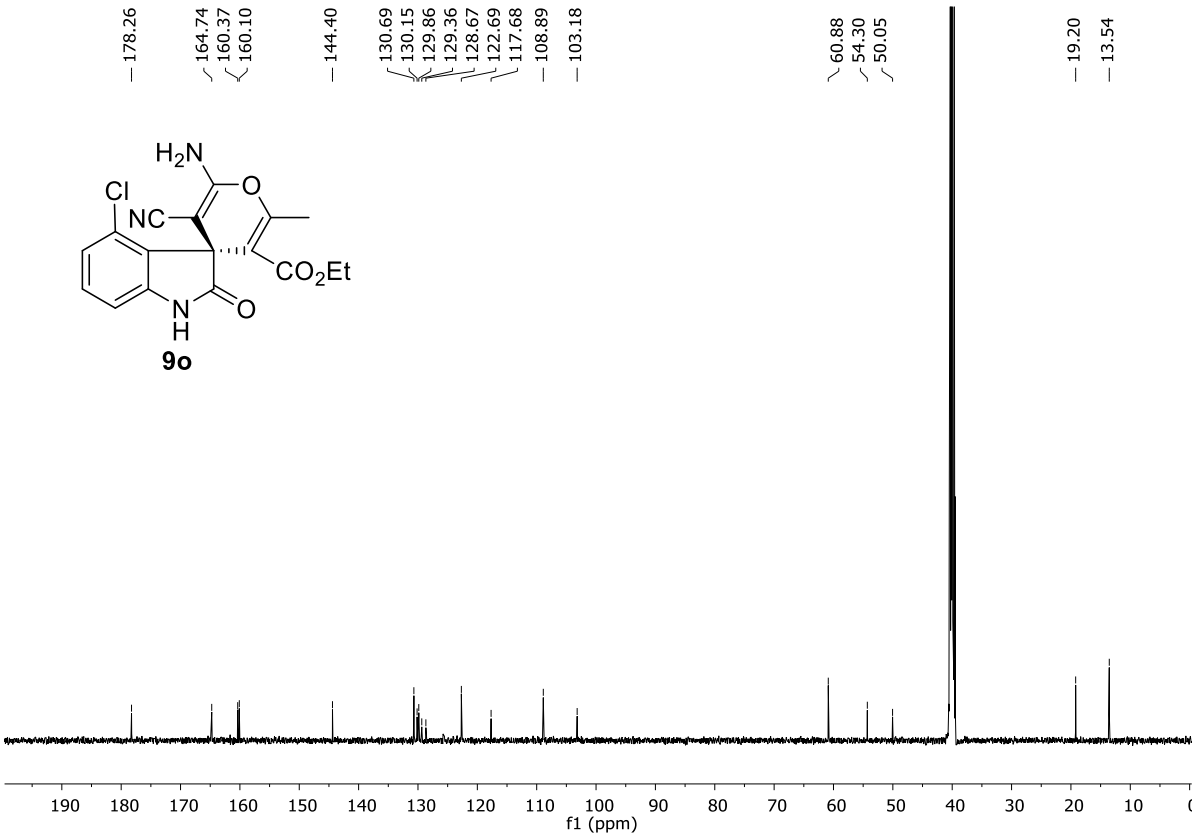
7.25
7.24
7.23
7.21
6.95
6.95
6.93
6.80
6.79
3.86
3.85
3.83
2.34
0.88
0.87
0.85
1.00
3.30
1.23
1.19
2.12
3.03
3.34
f1 (ppm)
9o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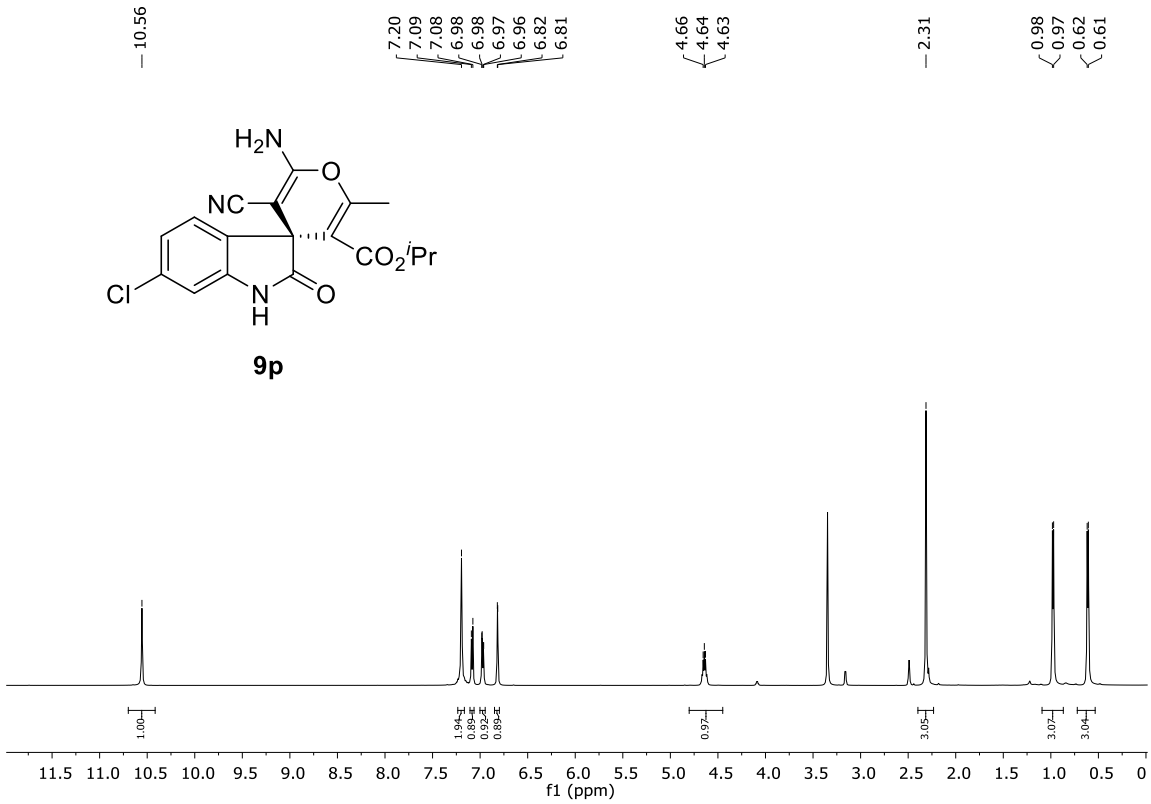
130.69
130.15
129.86
129.36
128.67
122.69
117.68
108.89
103.18
60.88
54.30
50.05
19.20
13.54
f1 (ppm)
9o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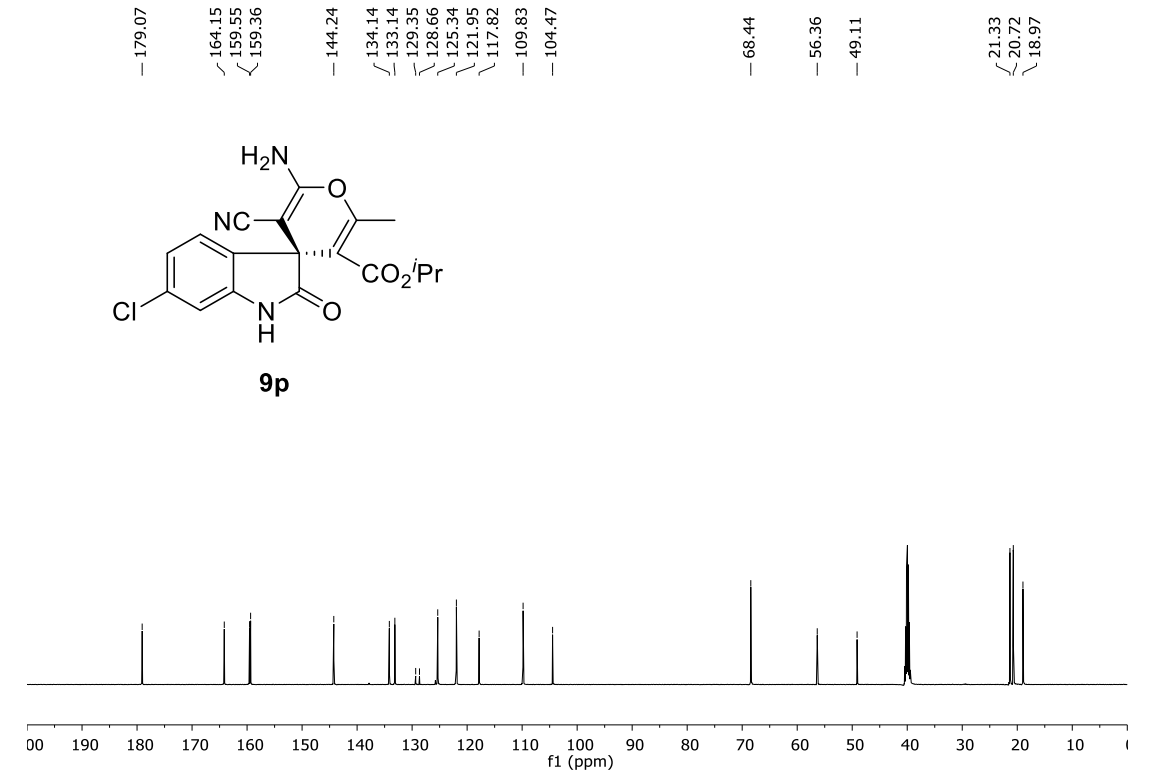
7.09
7.08
6.98
6.98
6.97
6.96
6.82
6.81
4.66
4.64
4.63
2.31
0.98
0.97
0.62
0.61
H2N
O
NC
CO2iPr
Cl
N
H
O
1.00
1.94
0.89
0.92
0.89
0.97
3.05
3.07
3.04
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0
f1 (ppm)

9p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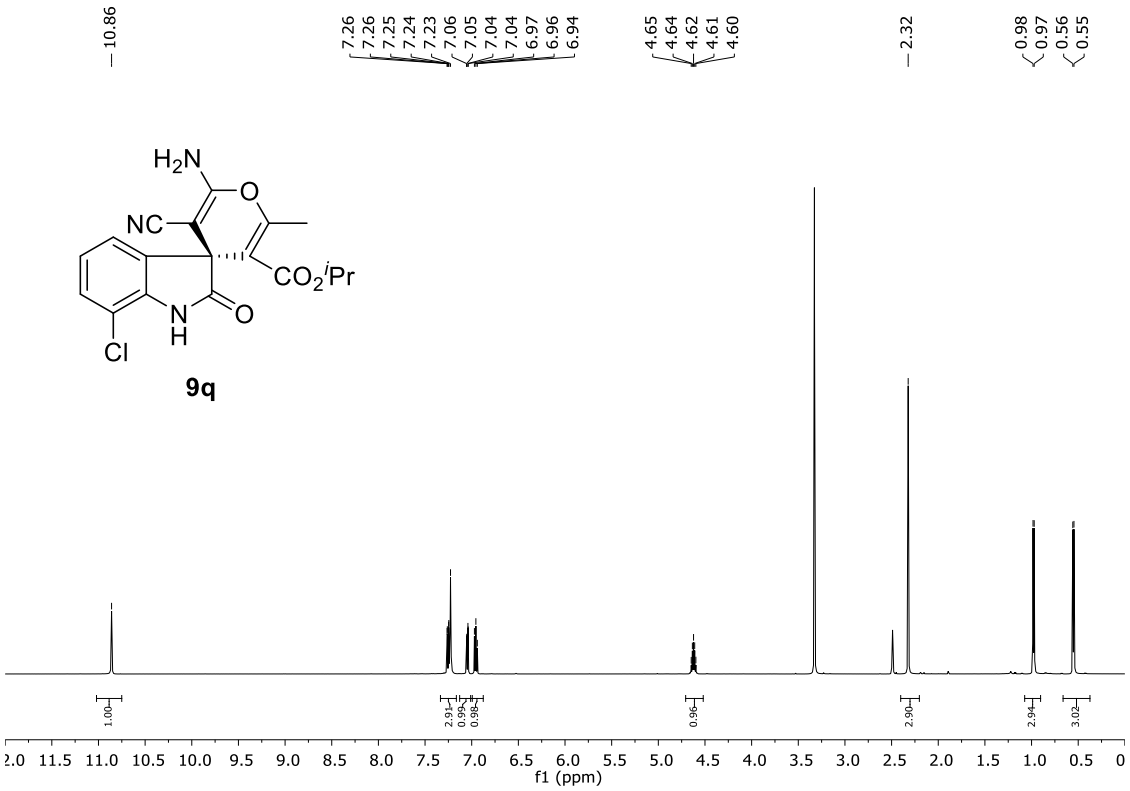
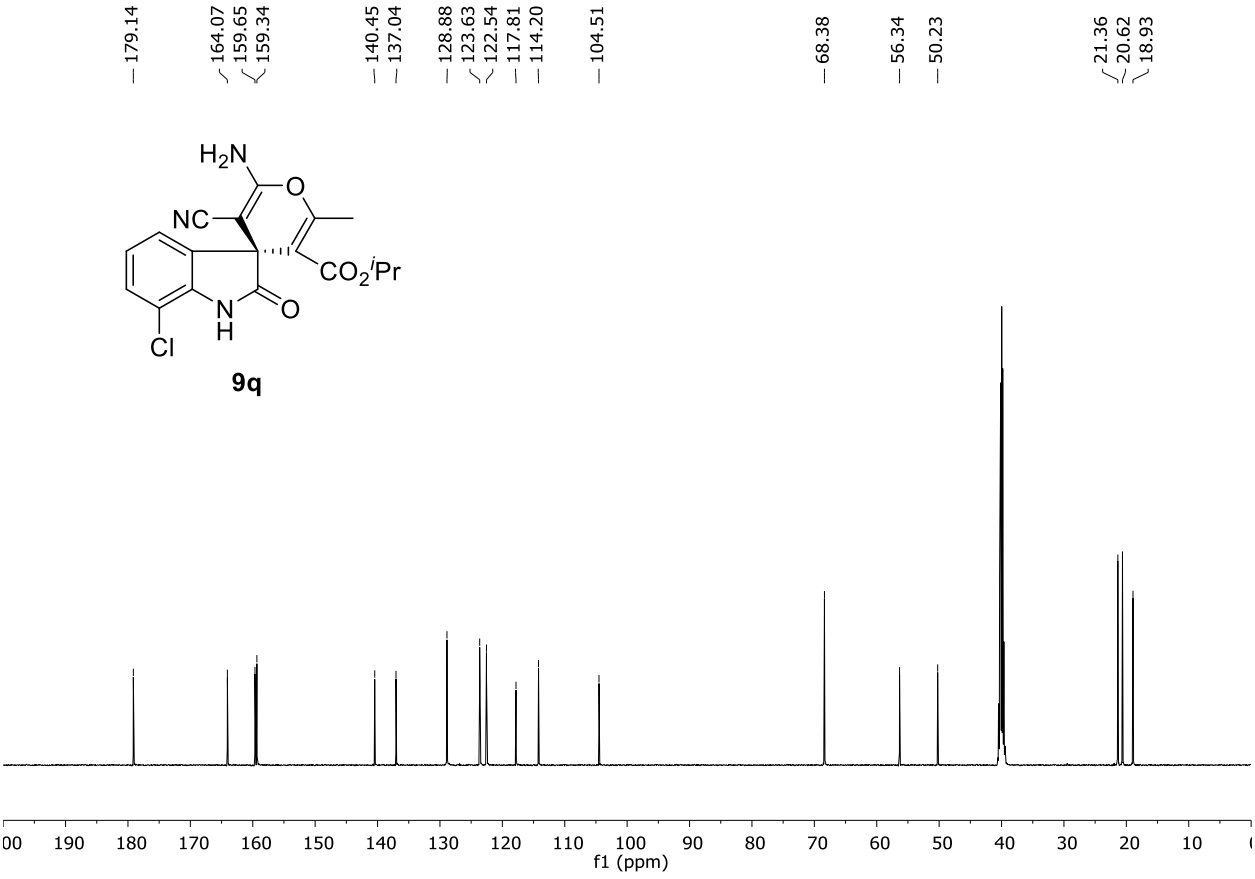
159.36
144.24
134.14
133.14
129.35
128.66
125.34
121.95
117.82
109.83
104.47
68.44
56.36
49.11
21.33
20.72
18.97
H2N
O
NC
CO2iPr
Cl
N
H
O
00 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

9p


10.86
7.26
7.26
7.25
7.24
7.23
7.06
7.05
7.04
7.04
6.97
6.96
6.94
4.65
4.64
4.62
4.61
4.60
2.32
0.98
0.97
0.56
0.55
H2N
O
NC
CO2iPr
N
H
O
Cl
9q
1.00
2.91
0.99
0.98
0.96
2.90
2.94
3.02
f1 (ppm)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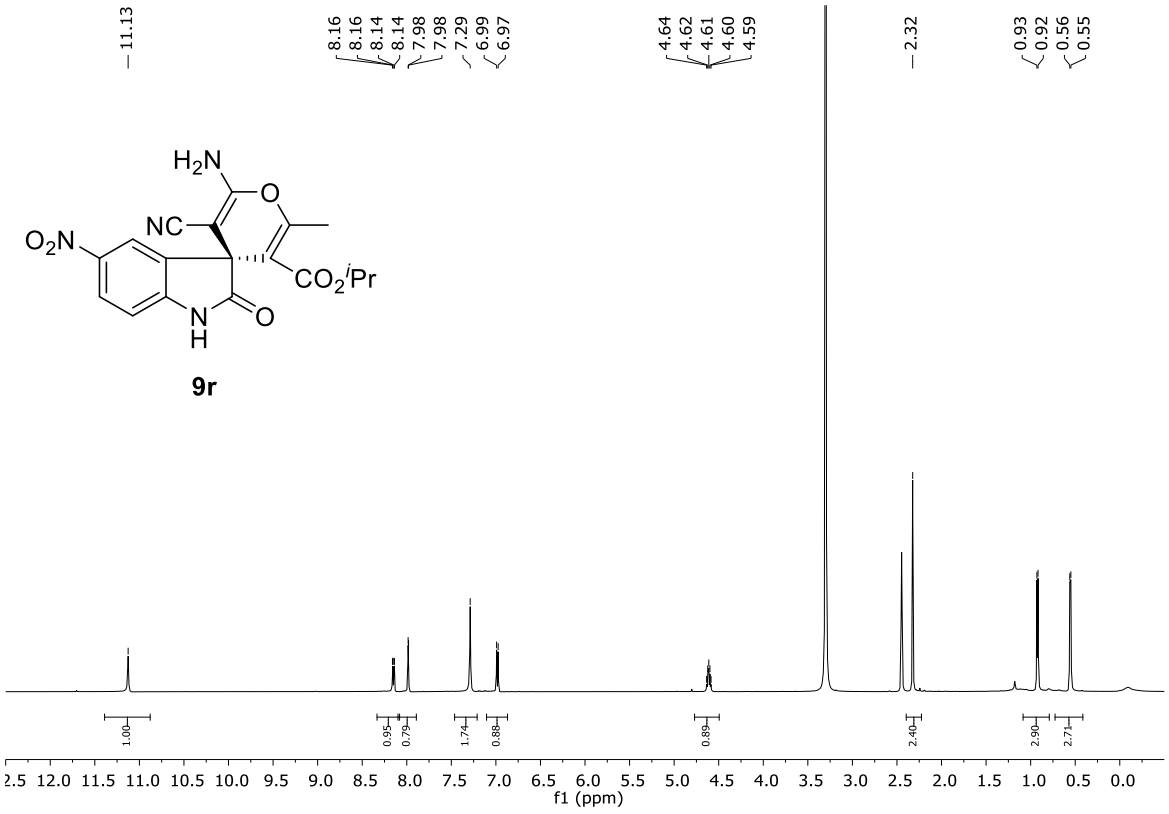
159.65
159.34
140.45
137.04
128.88
123.63
122.54
117.81
114.20
104.51
68.38
56.34
50.23
21.36
20.62
18.93
H2N
O
NC
CO2iPr
N
H
O
Cl
9q
f1 (ppm)


11.13
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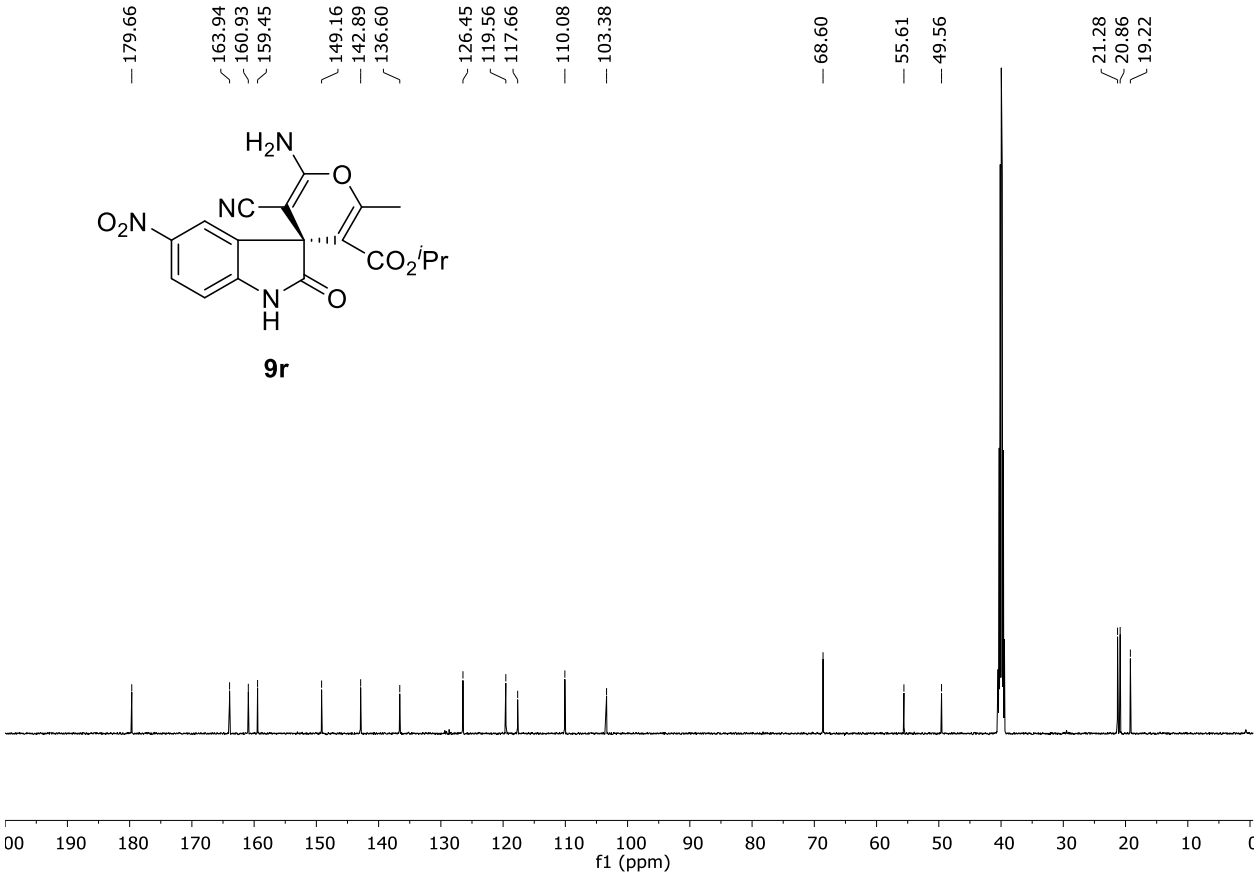
8.16
8.14
8.14
7.98
7.98
7.29
6.99
6.97
4.64
4.62
4.61
4.60
4.59
2.32
0.93
0.92
0.56
0.55
H2N
O
NC
O2N
CO2iPr
N
H
O
9r
1.00
0.95
0.79
1.74
0.88
0.89
2.40
2.90
2.71
f1 (ppm)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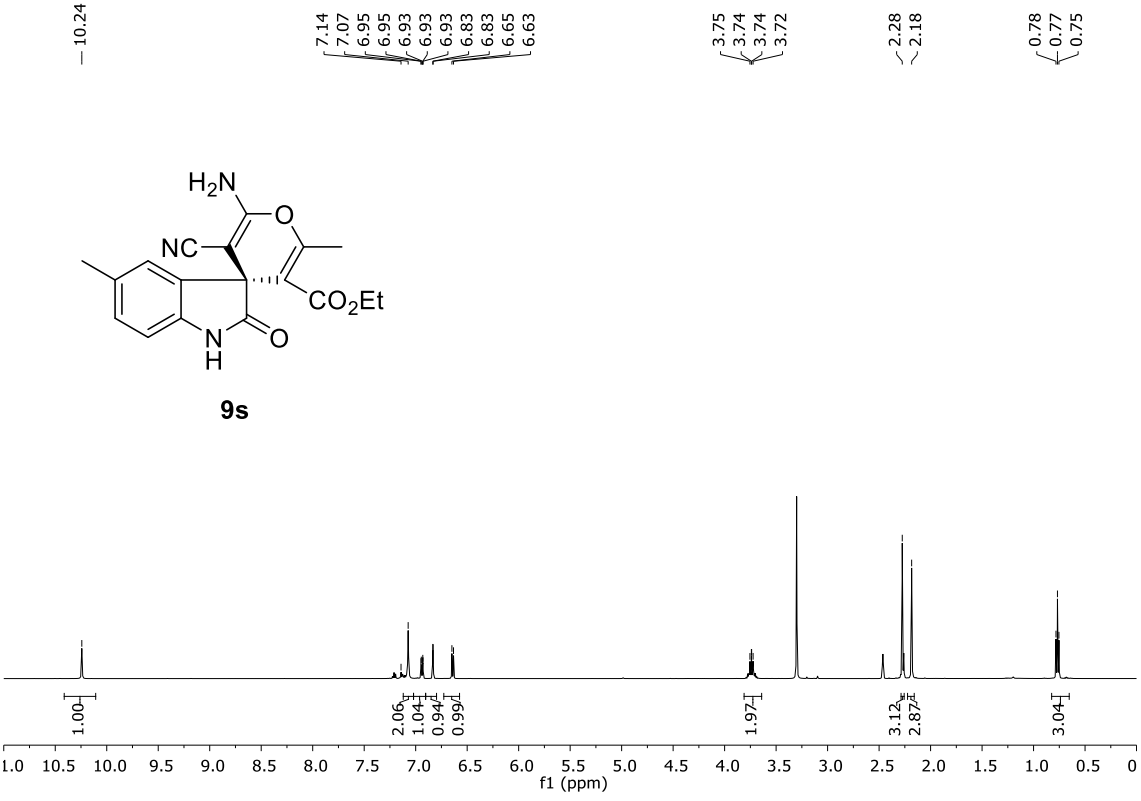
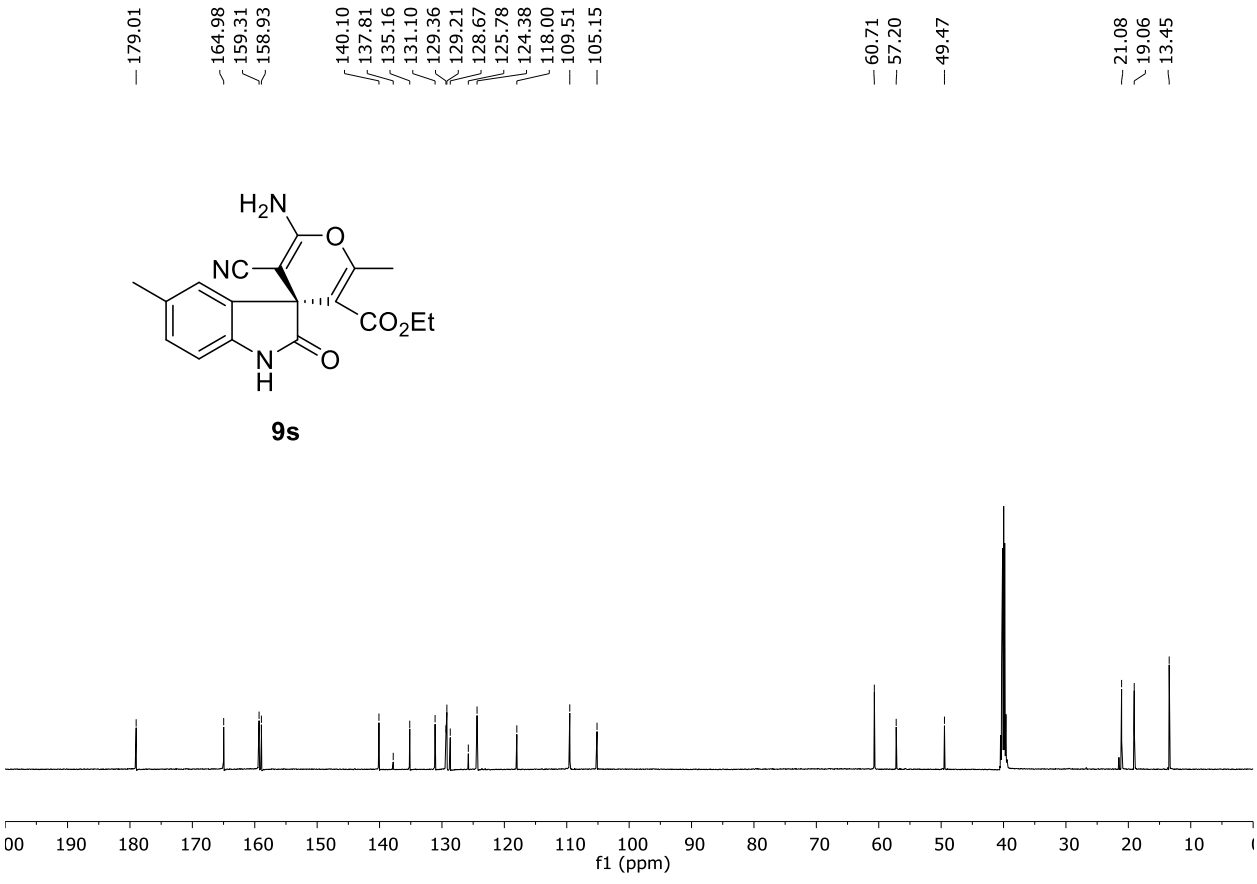
160.93
159.45
149.16
142.89
136.60
126.45
119.56
117.66
110.08
103.38
68.60
55.61
49.56
21.28
20.86
19.22
H2N
O
NC
O2N
CO2iPr
N
H
O
9r
f1 (ppm)


10.24
7.14
7.07
6.95
6.95
6.93
6.93
6.93
6.83
6.83
6.65
6.63
3.75
3.74
3.74
3.72
2.28
2.18
0.78
0.77
0.75
H2N
O
NC
CO2Et
N
H
O
1.00
2.06
1.04
0.94
0.99
1.97
3.12
2.87
3.04
f1 (ppm)

9s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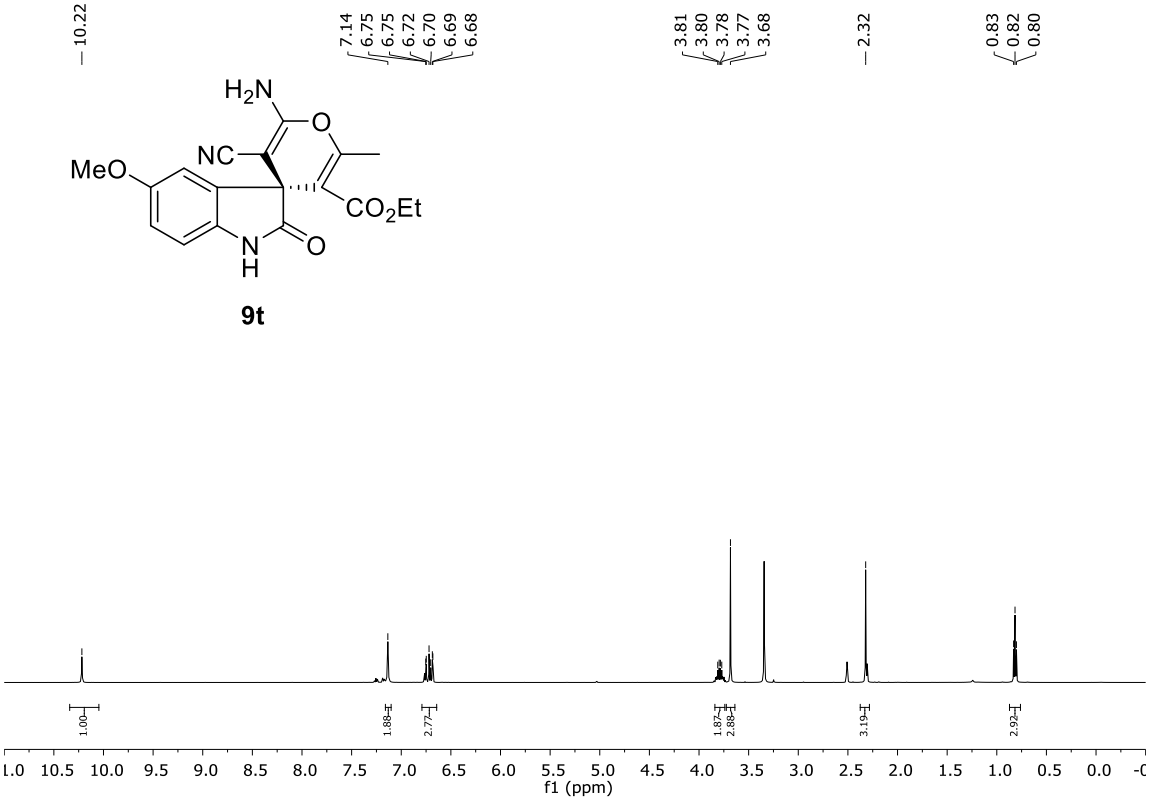
137.81
135.16
131.10
129.36
129.21
128.67
125.78
124.38
118.00
109.51
105.15
60.71
57.20
49.47
21.08
19.06
13.45
H2N
O
NC
CO2Et
N
H
O
f1 (ppm)

9s


10.22
7.14
6.75
6.75
6.72
6.70
6.69
6.68
3.81
3.80
3.78
3.77
3.68
2.32
0.83
0.82
0.80
H2N
O
NC
MeO
CO2Et
N
H
O
1.00
1.88
2.77
1.87
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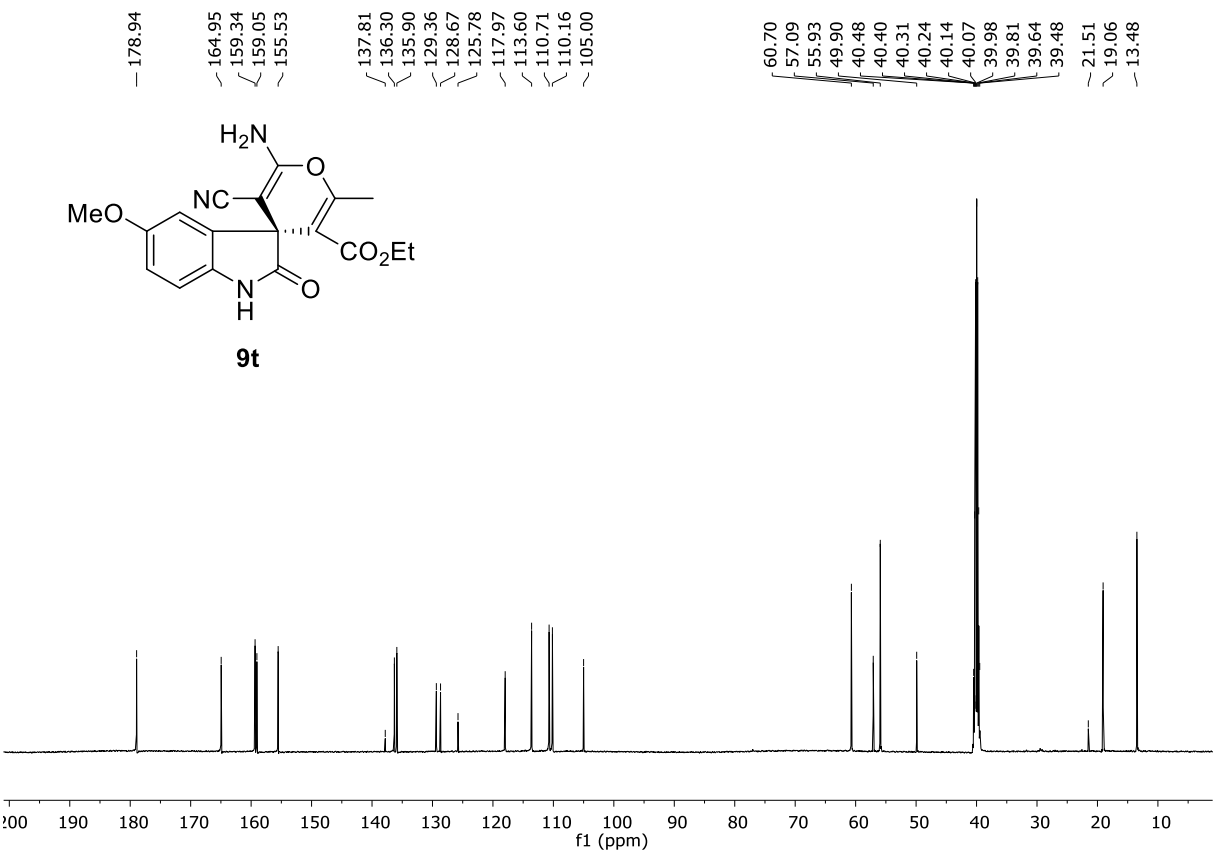
9t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159.05
155.53
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128.67
125.78
117.97
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110.71
110.16
105.00
60.70
57.09
55.93
49.90
40.48
40.40
40.31
40.24
40.14
40.07
39.98
39.81
39.64
39.48
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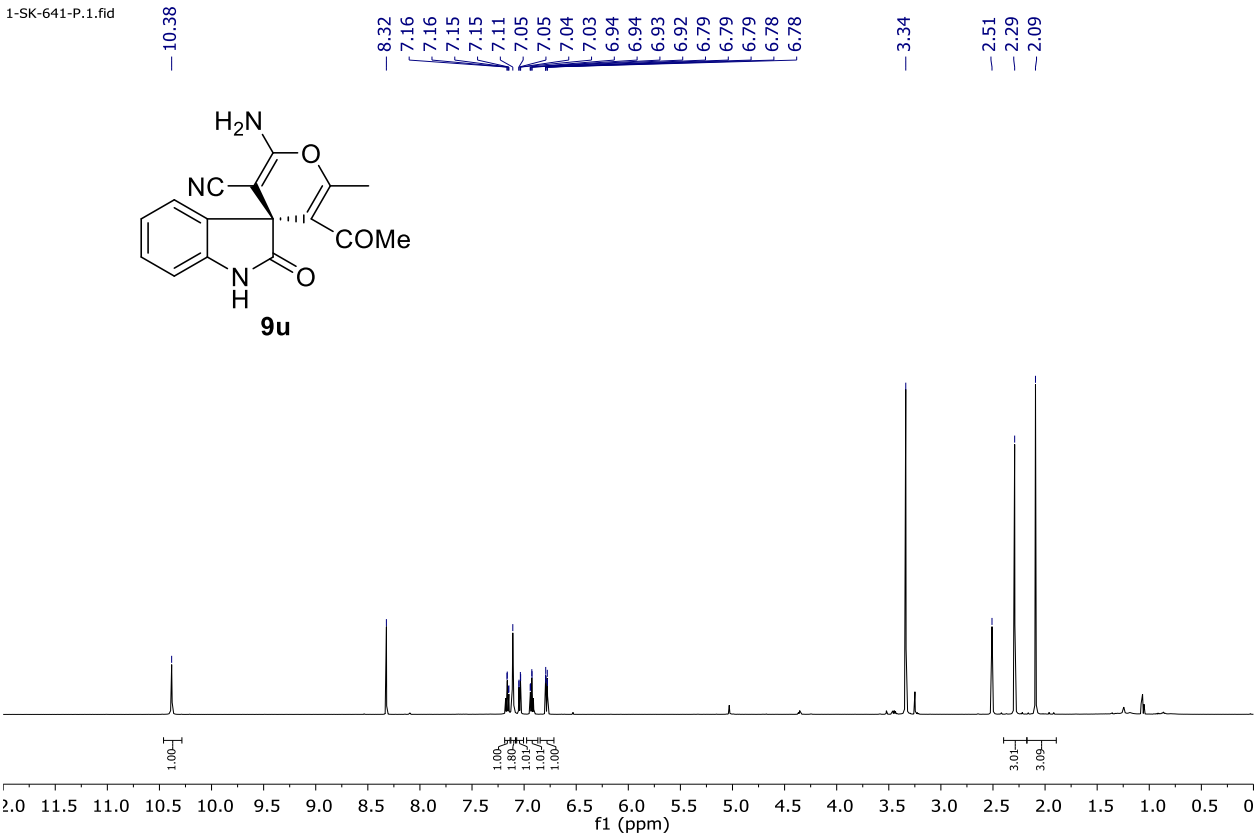
H2N
O
NC
MeO
CO2Et
N
H
O
f1 (ppm)

9t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6.92
6.79
6.79
6.79
6.78
6.78
3.34
2.51
2.29
2.09
H2N
O
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N
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O
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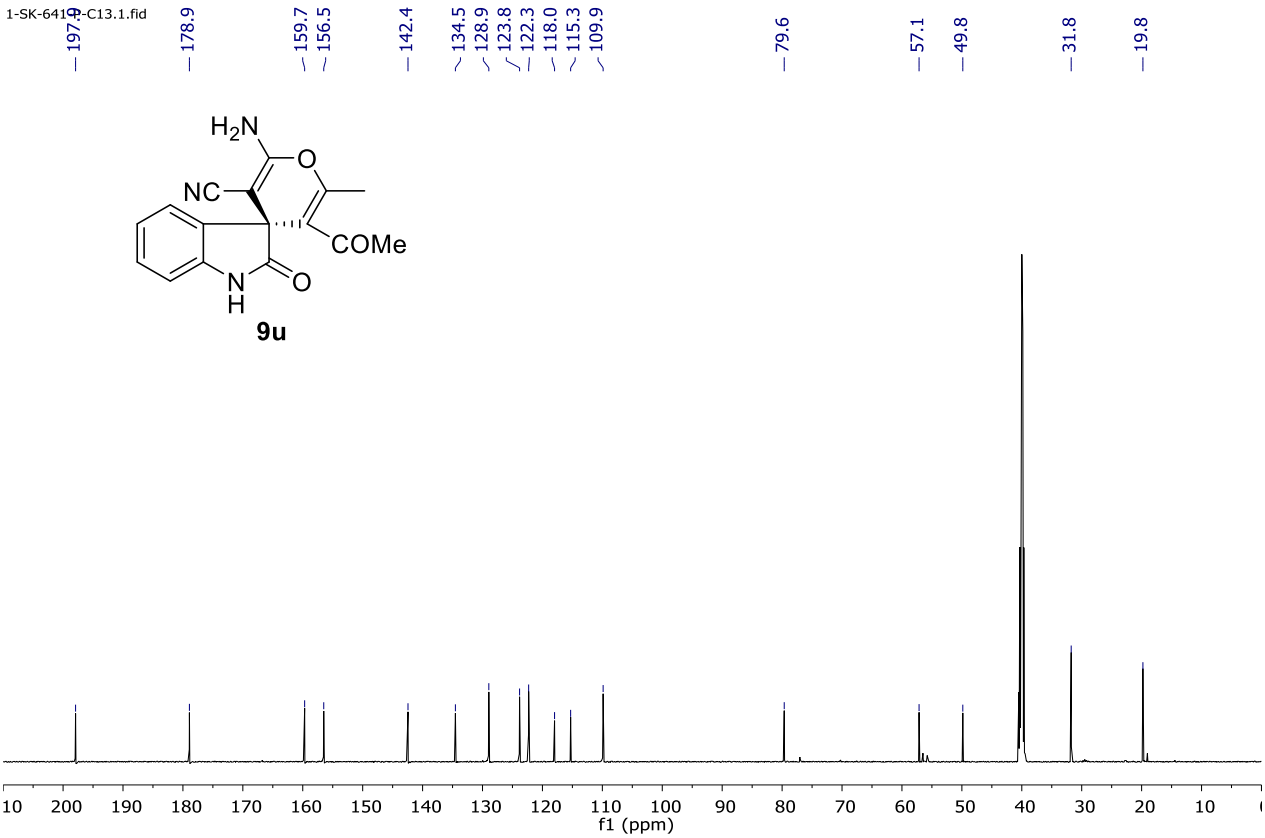
1.01
1.00
3.01
3.09
f1 (ppm)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109.9
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49.8
31.8
19.8
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N
H
O
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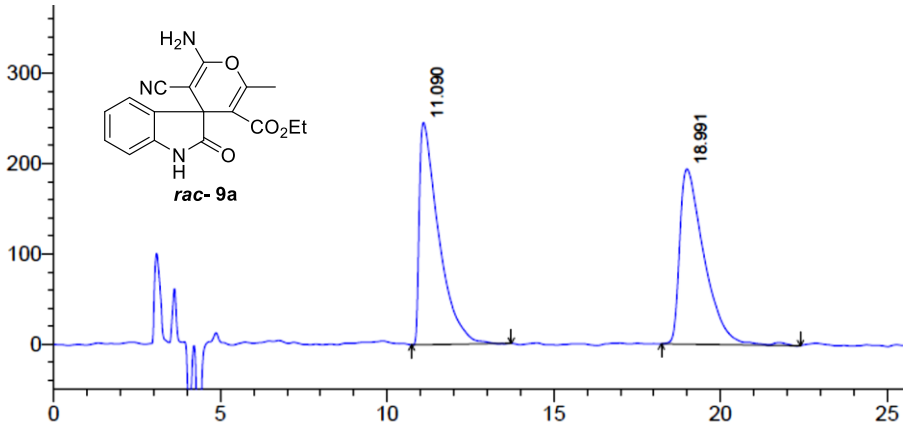
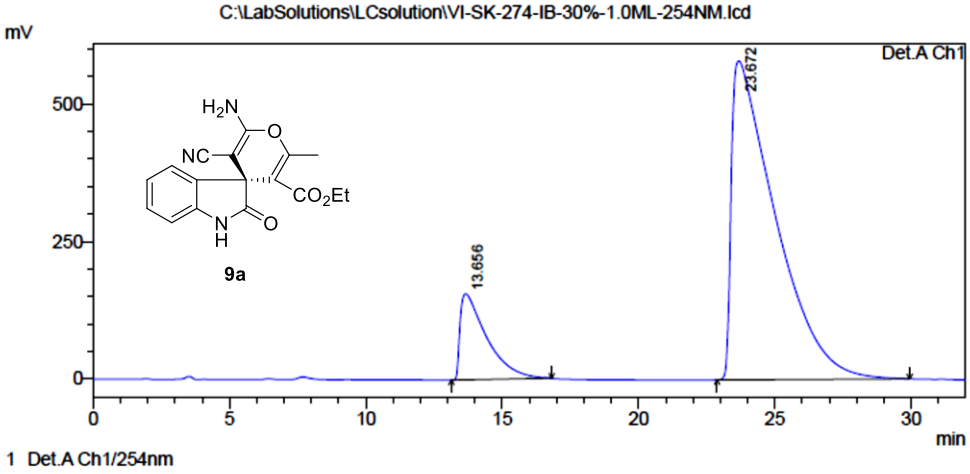
f1 (ppm)



PeakTable

Detector A Ch1 254nm

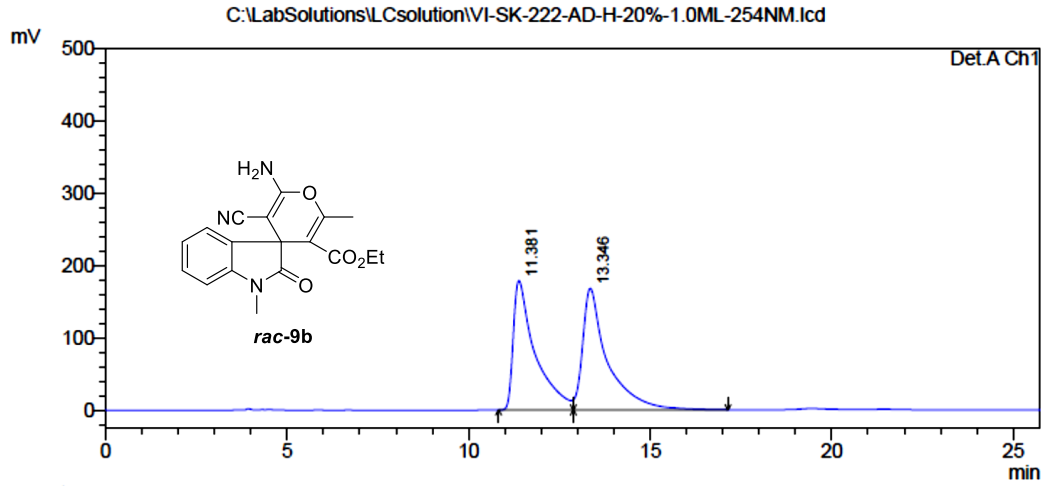
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.090	9941351	245727	50.135	55.902
2	18.991	9887719	193841	49.865	44.098
Total		19829070	439568	100.000	100.000



PeakTable

Detector A Ch1 254nm

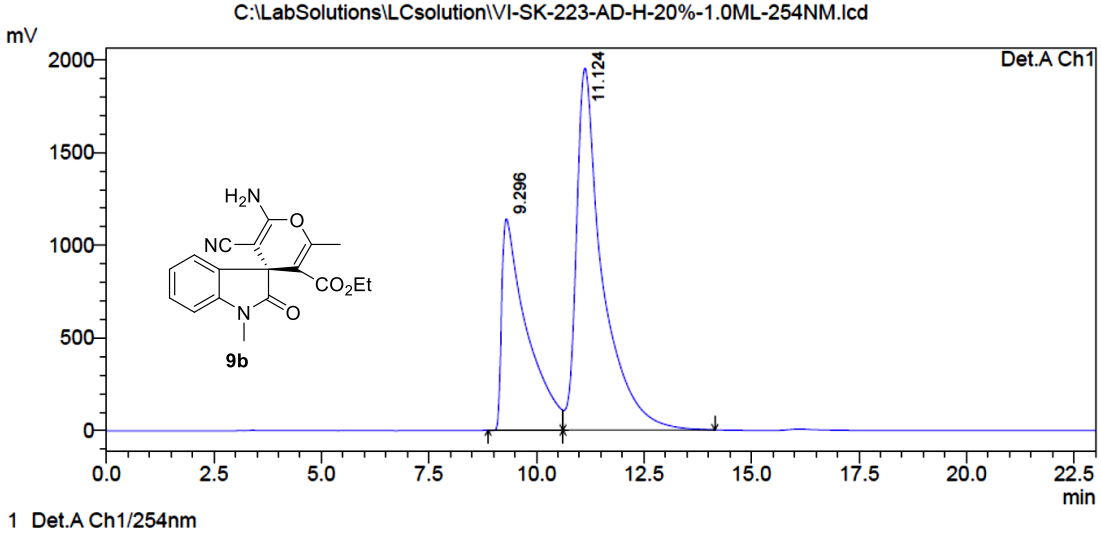
Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.656	10594998	156465	13.987	21.242
2	23.672	65151449	580105	86.013	78.758
Total		75746448	736570	100.000	100.000



PeakTable

Detector A Ch1 254nm

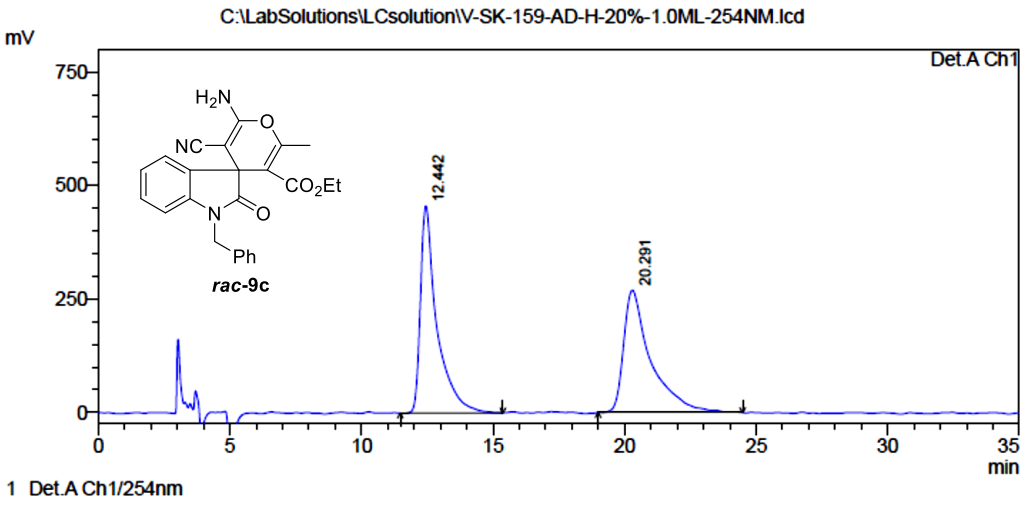
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.381	7468443	178527	48.492	51.559
2	13.346	7933036	167729	51.508	48.441
Total		15401479	346256	100.000	100.000



PeakTable

Detector A Ch1 254nm

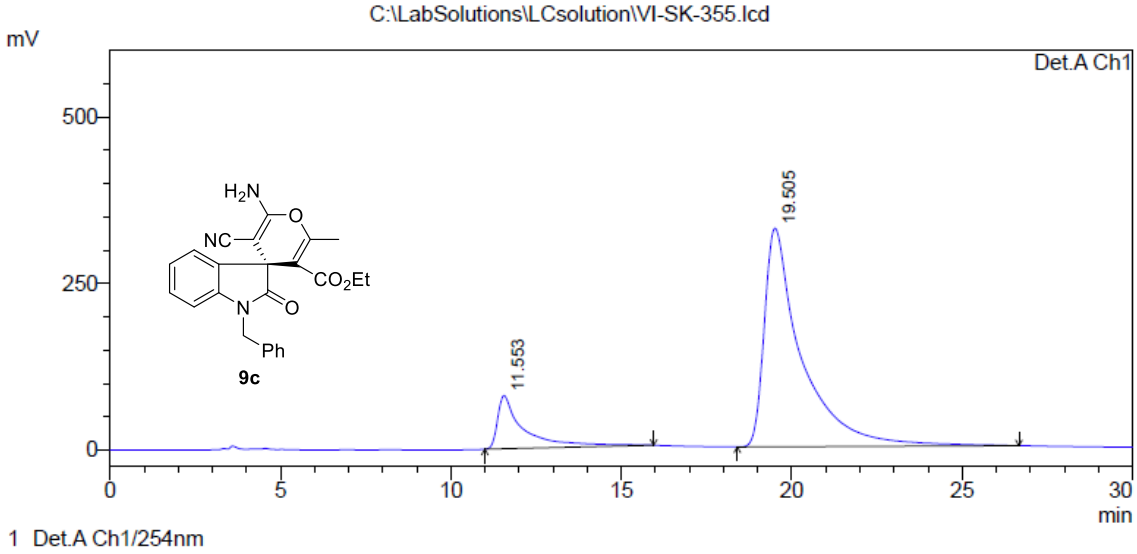
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.296	46008220	1139532	35.888	36.874
2	11.124	82190106	1950805	64.112	63.126
Total		128198326	3090337	100.000	100.000



PeakTable

Detector A Ch1 254nm

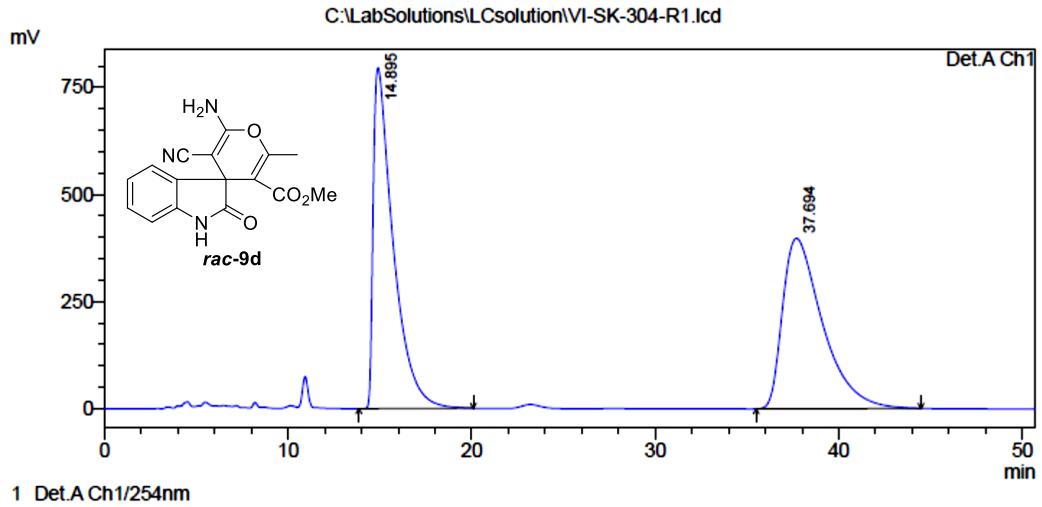
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.442	19831263	456048	50.553	62.865
2	20.291	19397254	269390	49.447	37.135
Total		39228518	725438	100.000	100.000



PeakTable

Detector A Ch1 254nm

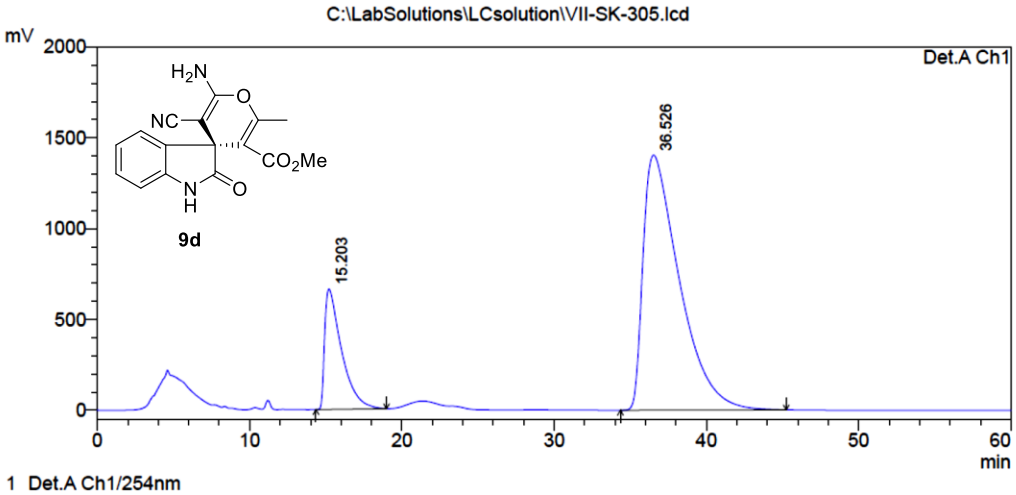
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.553	4336347	79907	14.713	19.573
2	19.505	25136634	328350	85.287	80.427
Total		29472981	408258	100.000	100.000



PeakTable

Detector A Ch1 254nm

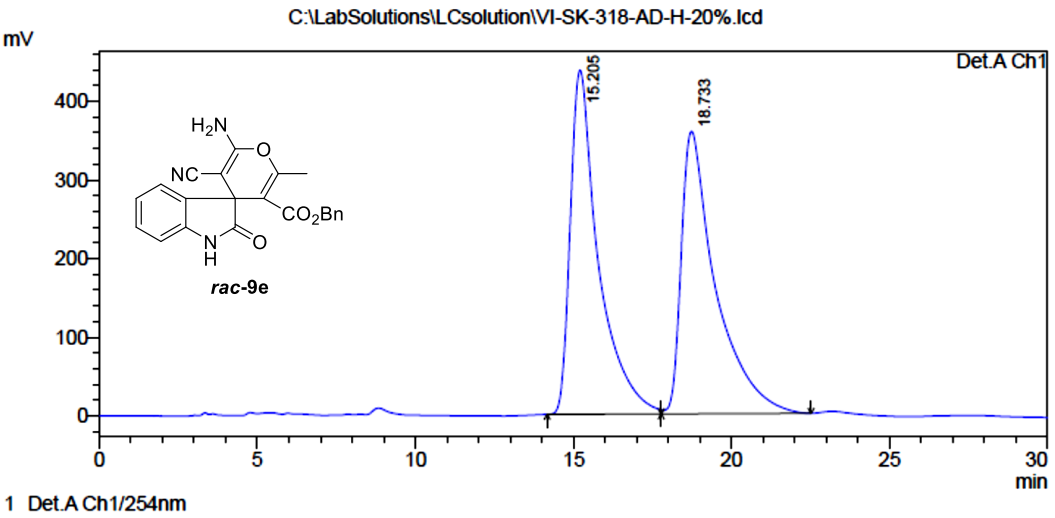
Peak#	Ret. Time	Area	Height	Area %	Height %
1	14.895	60019083	795265	49.874	66.662
2	37.694	60321922	397712	50.126	33.338
Total		120341004	1192977	100.000	100.000



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.203	51101823	663812	17.998	32.087
2	36.526	232825248	1404978	82.002	67.913
Total		283927071	2068790	100.000	100.000

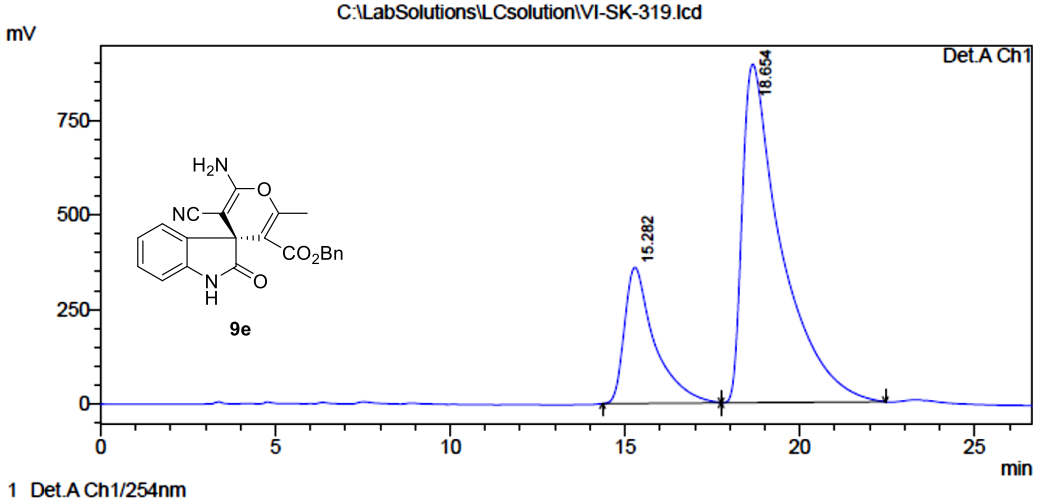


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.205	27059867	437381	49.969	54.925
2	18.733	27092973	358942	50.031	45.075
Total		54152841	796323	100.000	100.000

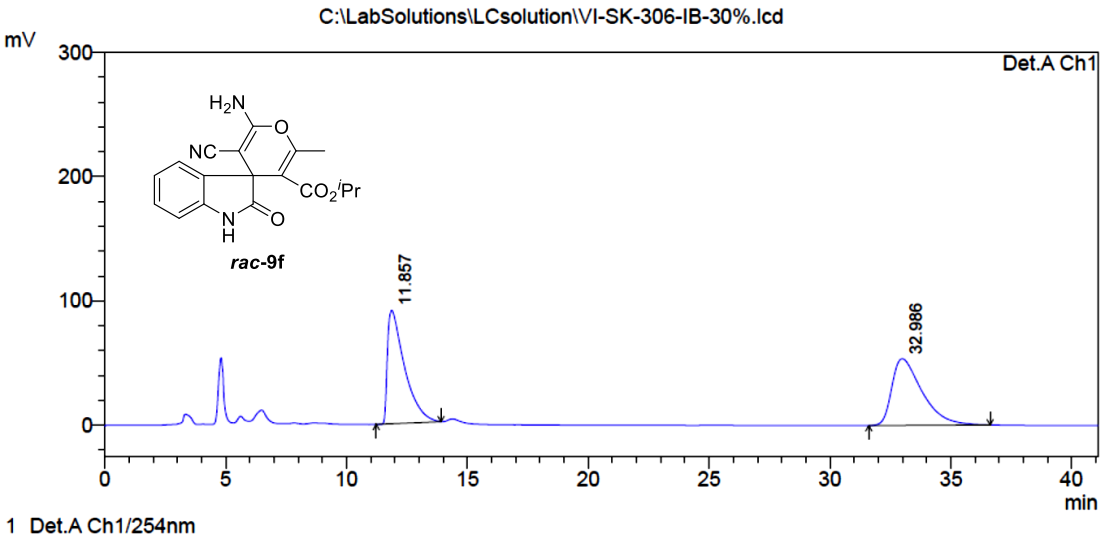


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

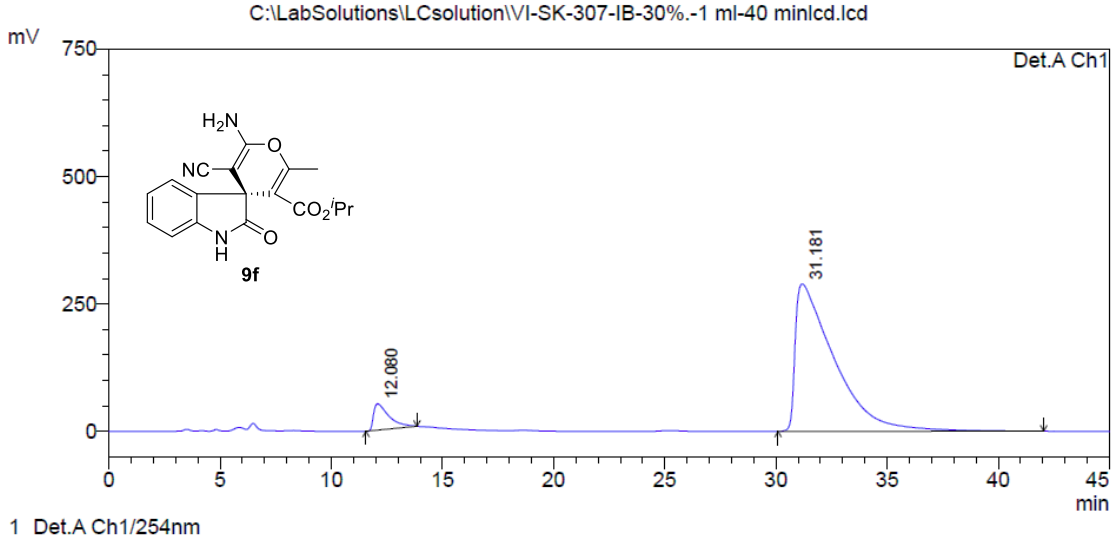
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.282	21500392	359561	23.599	28.682
2	18.654	69606879	894065	76.401	71.318
Total		91107271	1253626	100.000	100.000



PeakTable

Detector A Ch1 254nm

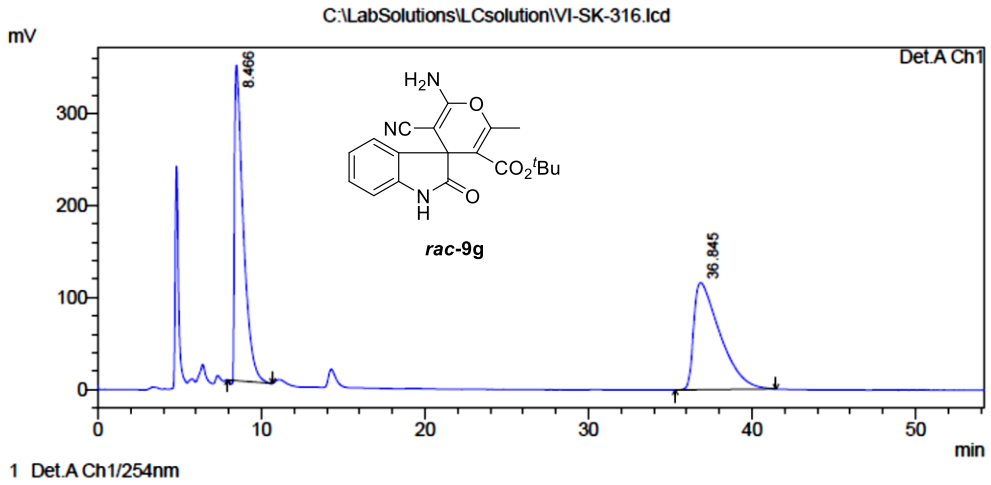
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.857	4496239	91371	48.998	63.024
2	32.986	4680171	53608	51.002	36.976
Total		9176410	144979	100.000	100.000



PeakTable

Detector A Ch1 254nm

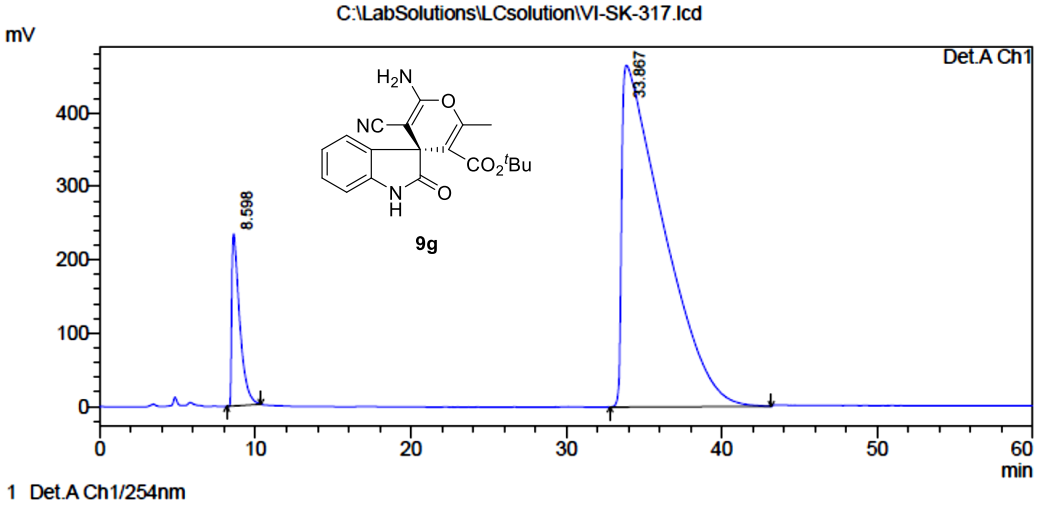
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.080	2506040	51700	6.635	15.161
2	31.181	35261746	289300	93.365	84.839
Total		37767785	341000	100.000	100.000



PeakTable

Detector A Ch1 254nm

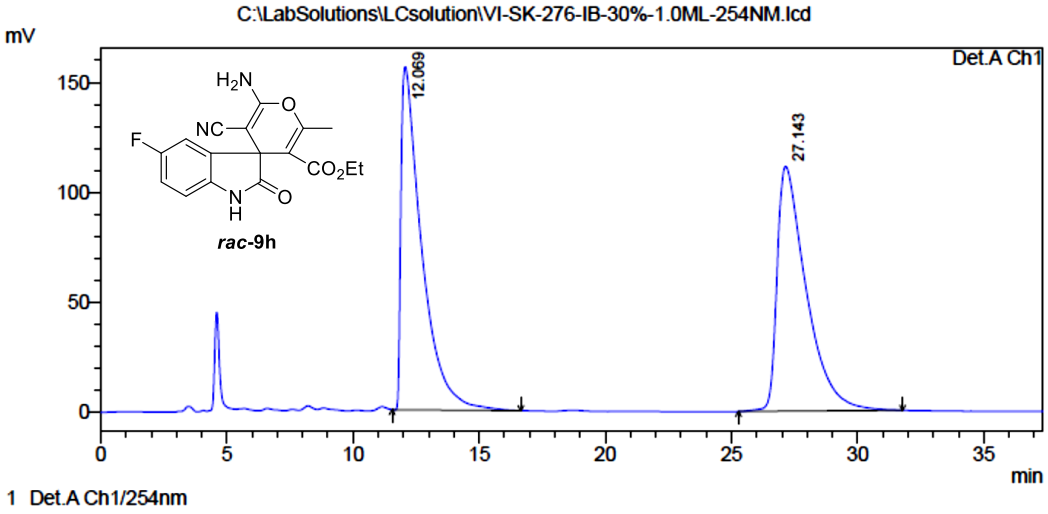
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.466	12737671	343568	49.380	74.685
2	36.845	13057360	116454	50.620	25.315
Total		25795031	460022	100.000	100.000



PeakTable

Detector A Ch1 254nm

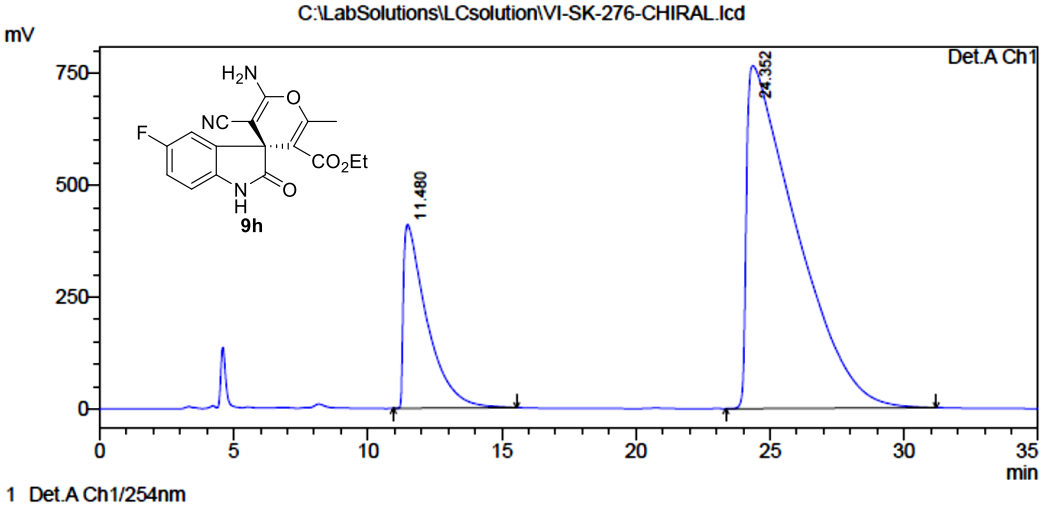
Peak#	Ret. Time	Area	Height	Area %	Height %
1	8.598	8360045	234649	8.790	33.509
2	33.867	86747834	465596	91.210	66.491
Total		95107879	700245	100.000	100.000



PeakTable

Detector A Ch1 254nm

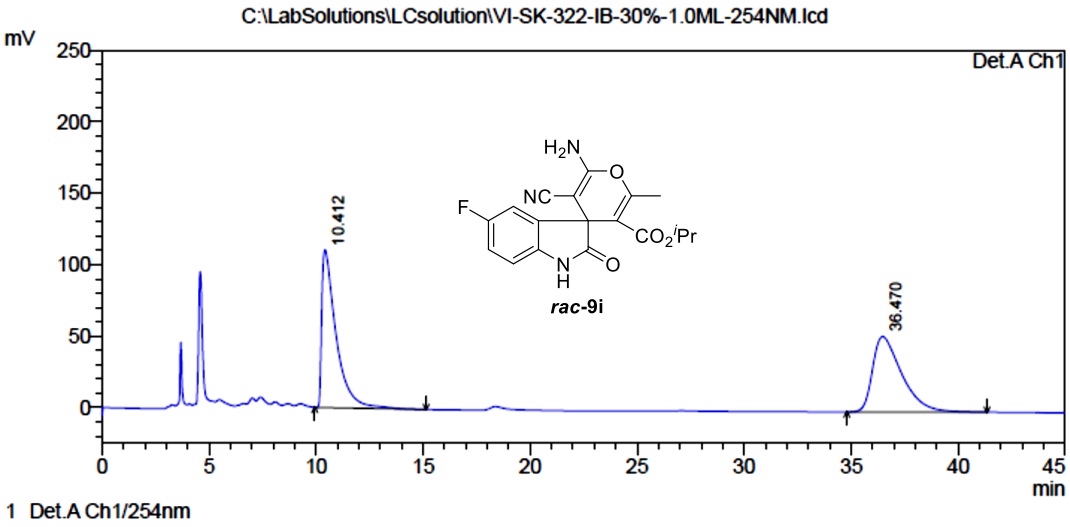
Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.069	8873346	155943	49.766	58.368
2	27.143	8956953	111230	50.234	41.632
Total		17830299	267173	100.000	100.000



PeakTable

Detector A Ch1 254nm

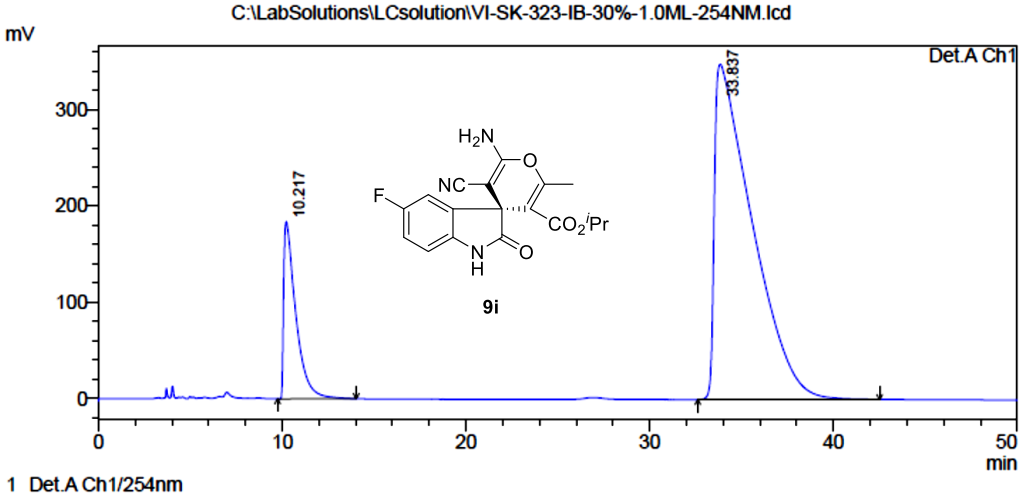
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.480	25063034	411106	20.114	34.882
2	24.352	99544867	767466	79.886	65.118
Total		124607901	1178573	100.000	100.000



PeakTable

Detector A Ch1 254nm

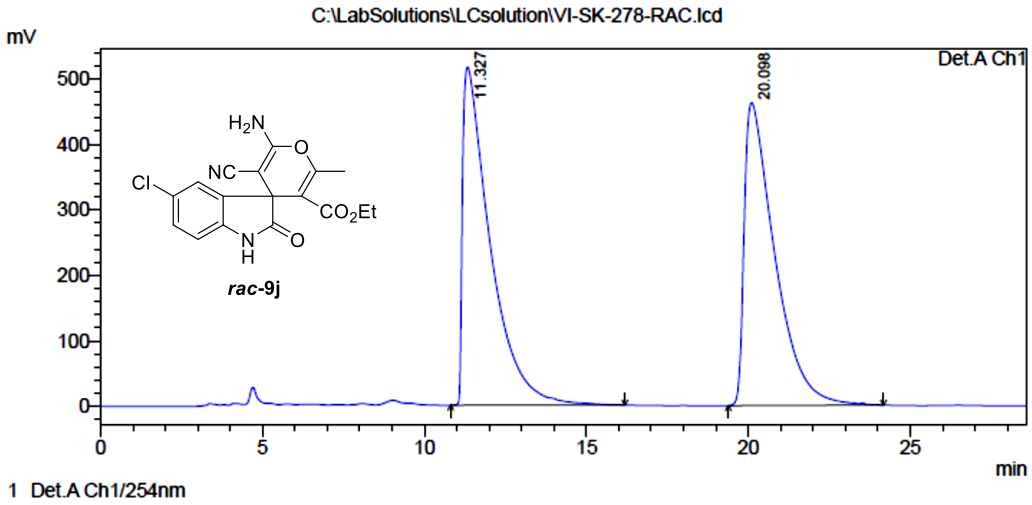
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.412	5134098	110412	50.593	67.630
2	36.470	5013721	52846	49.407	32.370
Total		10147819	163258	100.000	100.000



PeakTable

Detector A Ch1 254nm

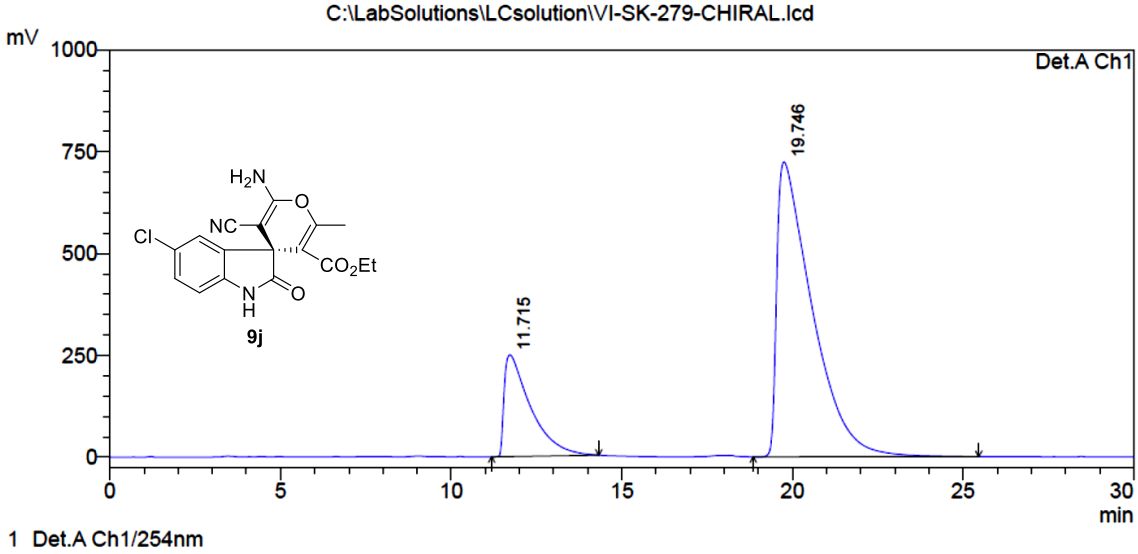
Peak#	Ret. Time	Area	Height	Area %	Height %
1	10.217	8459170	183837	14.554	34.562
2	33.837	49663688	348070	85.446	65.438
Total		58122858	531907	100.000	100.000



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.327	30514046	515872	50.220	52.738
2	20.098	30246708	462313	49.780	47.262
Total		60760755	978185	100.000	100.000



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.715	13488623	250158	20.543	25.652
2	19.746	52171621	725035	79.457	74.348
Total		65660245	975193	100.000	100.000

Data Filename : VI-SK-336-R.lcd
Method Filename : IB-30%-1.0 mL-254 nm-40-MIN.lcm
Batch Filename :
Vial # : 1-1 Sample Type : Unknown
Injection Volume : 10 uL
Date Acquired : 8/27/2018 3:54:00 PM Acquired by : nzc766
Date Processed : 8/27/2018 4:50:41 PM Processed by : nzc766

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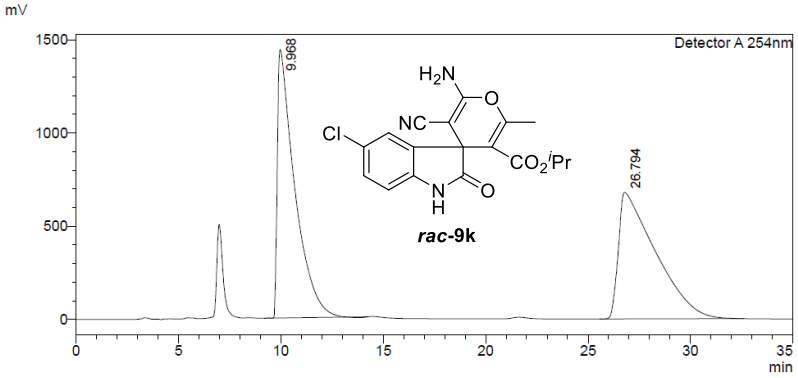

<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Height%
1	9.968	84801573	1439724	49.769	49.769	67.962
2	26.794	85587354	678710	50.231	50.231	32.038
Total		170388927	2118435		100.000	100.000

Data Filename : VI-SK-327-C.lcd
Method Filename : IB-30%-1.0 mL-254 nm-40-MIN.lcm
Batch Filename :
Vial # : 1-1 Sample Type : Unknown
Injection Volume : 10 uL
Date Acquired : 8/27/2018 12:22:42 PM Acquired by : nzc766
Date Processed : 8/27/2018 1:17:46 PM Processed by : nzc766

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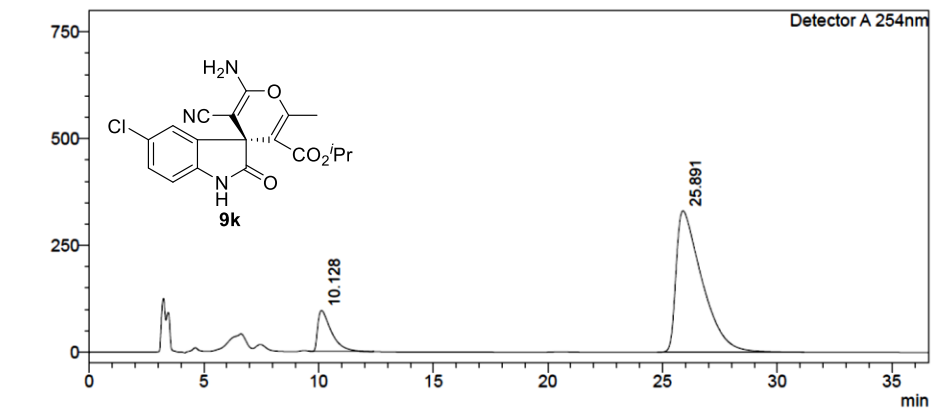
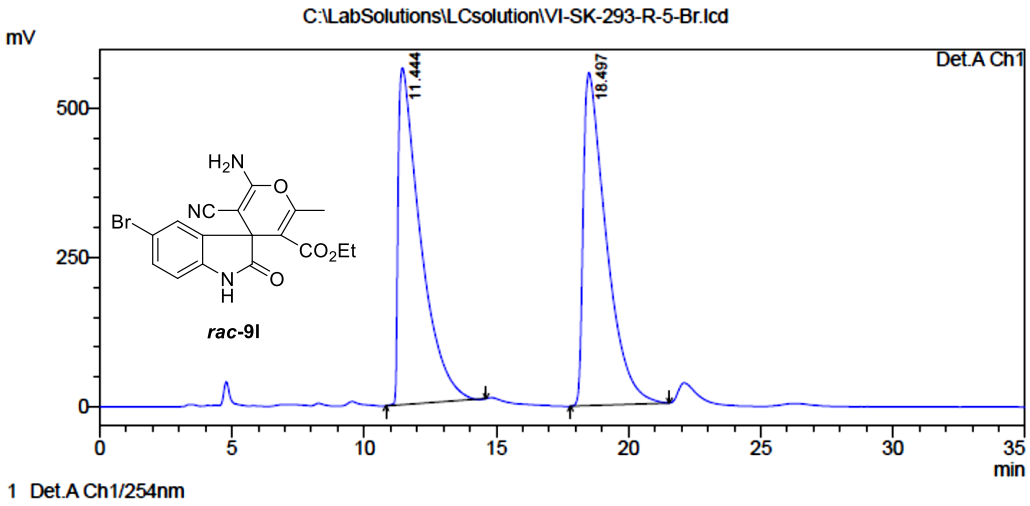


<Peak Table>

Detector A 254nm

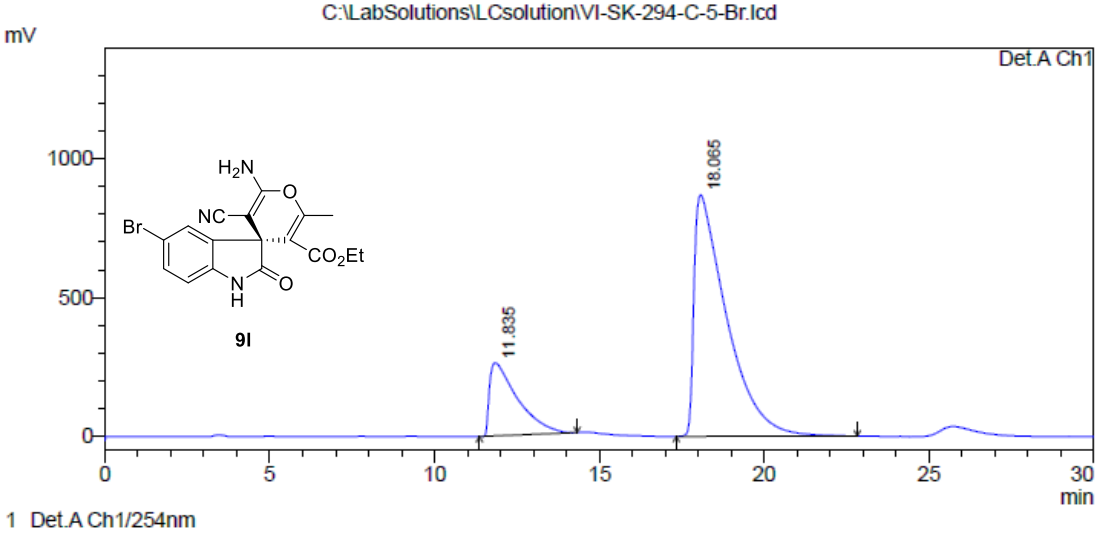
Peak#	Ret. Time	Area	Height	Height%	Area%
1	10.128	3927565	95733	22.403	13.091
2	25.891	26074165	331595	77.597	86.909
Total		30001730	427328	100.000	100.000



PeakTable

Detector A Ch1 254nm

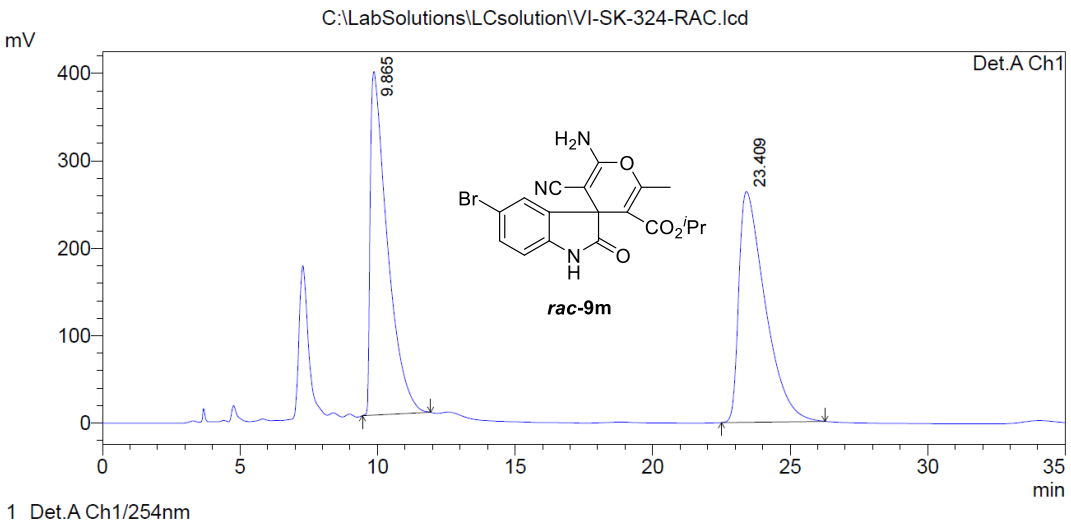
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.444	33040182	564029	49.506	50.267
2	18.497	33699596	558036	50.494	49.733
Total		66739777	1122064	100.000	100.000



PeakTable

Detector A Ch1 254nm

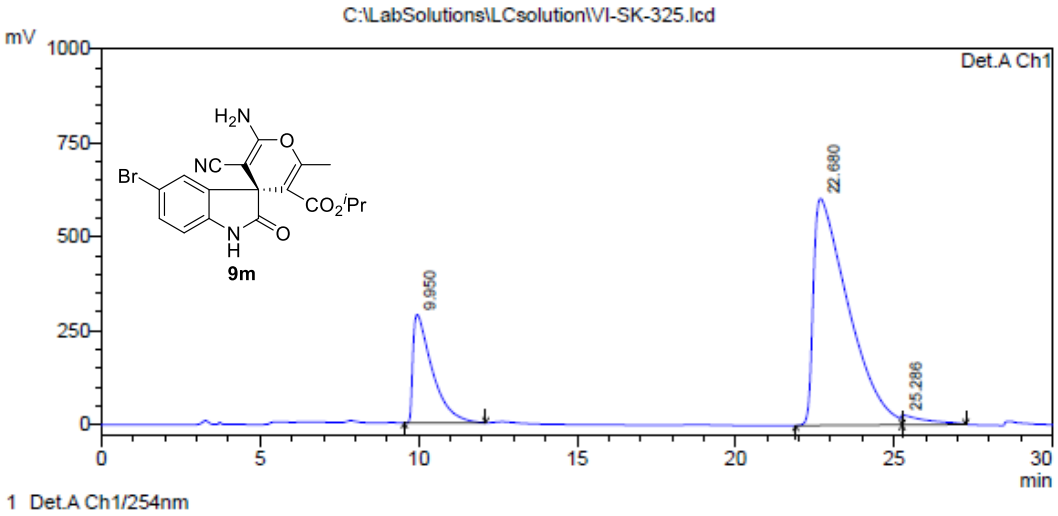
Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.835	15540638	263512	20.645	23.259
2	18.065	59734079	869422	79.355	76.741
Total		75274718	1132933	100.000	100.000



PeakTable

Detector A Ch1 254nm

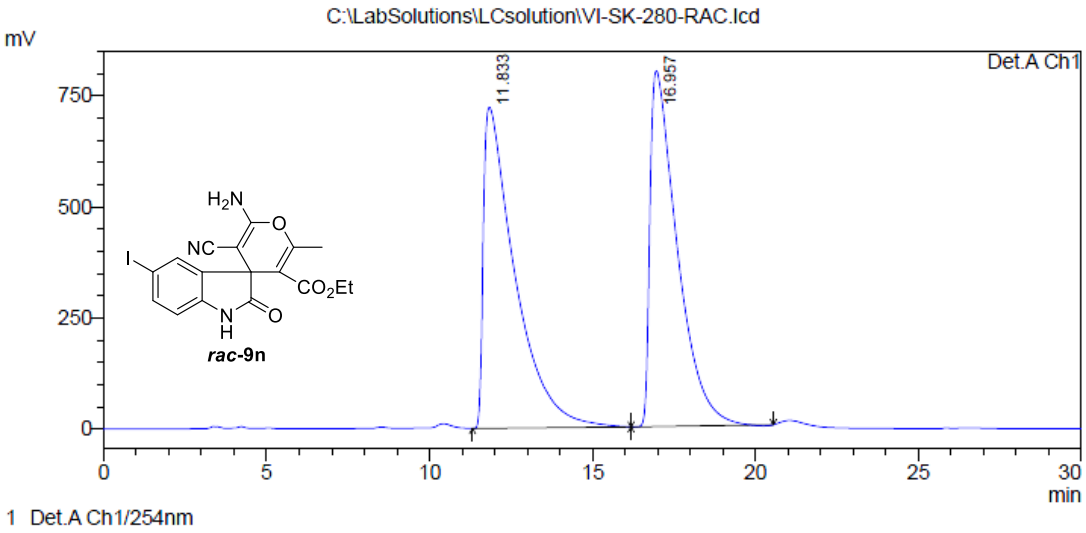
Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.865	17022687	393079	49.201	59.817
2	23.409	17575634	264055	50.799	40.183
Total		34598321	657134	100.000	100.000



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	9.950	12246813	288311	20.472	31.432
2	22.680	46272140	603535	77.350	65.797
3	25.286	1302993	25416	2.178	2.771
Total		59821946	917262	100.000	100.000

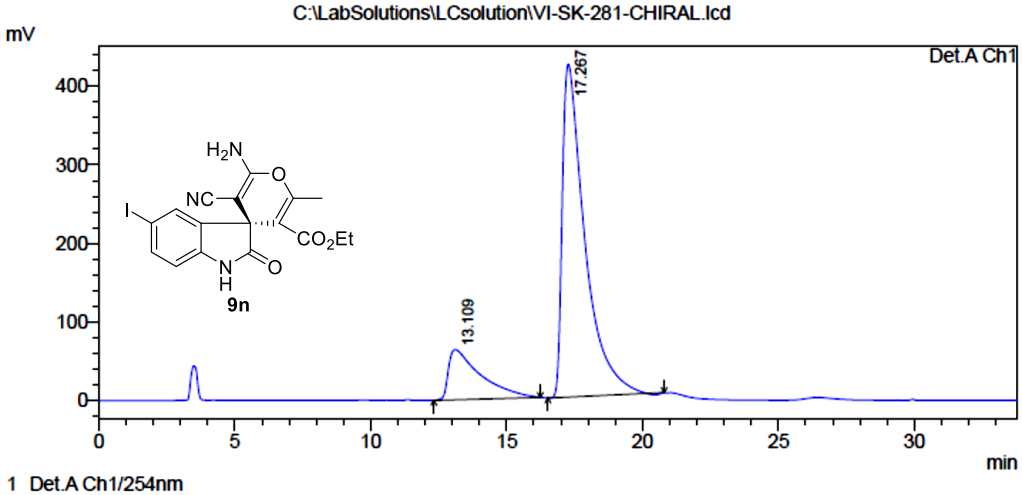


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	11.833	48550382	722069	51.138	47.427
2	16.957	46390022	800426	48.862	52.573
Total		94940404	1522496	100.000	100.000

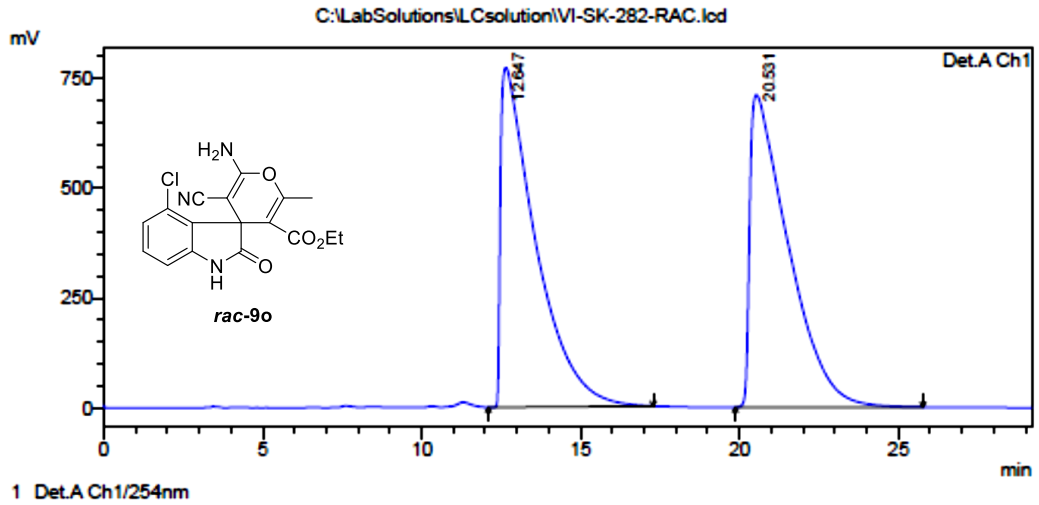


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.109	5255502	63875	17.757	13.102
2	17.267	24341135	423650	82.243	86.898
Total		29596637	487524	100.000	100.000

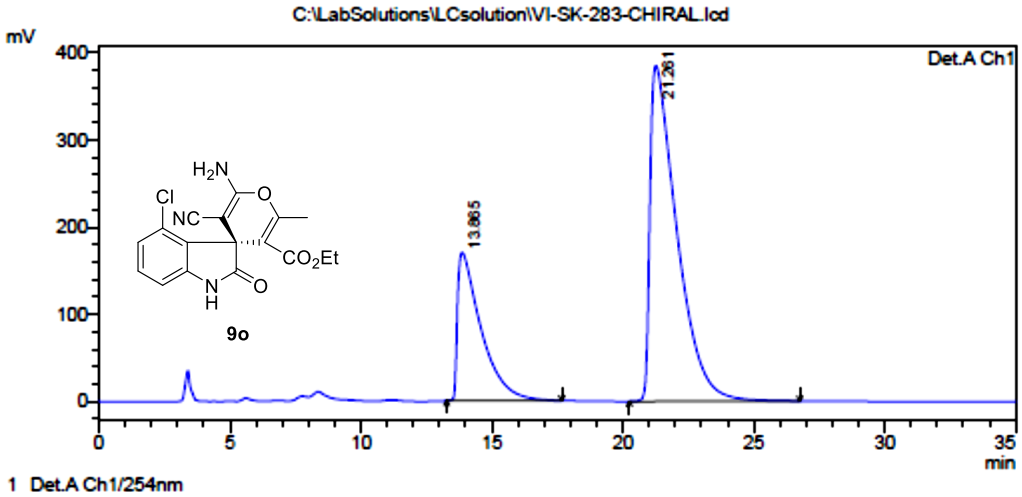


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	12.647	59252343	773686	49.721	52.080
2	20.531	59916520	711880	50.279	47.920
Total		119168863	1485567	100.000	100.000



1 Det.A Ch1/254nm

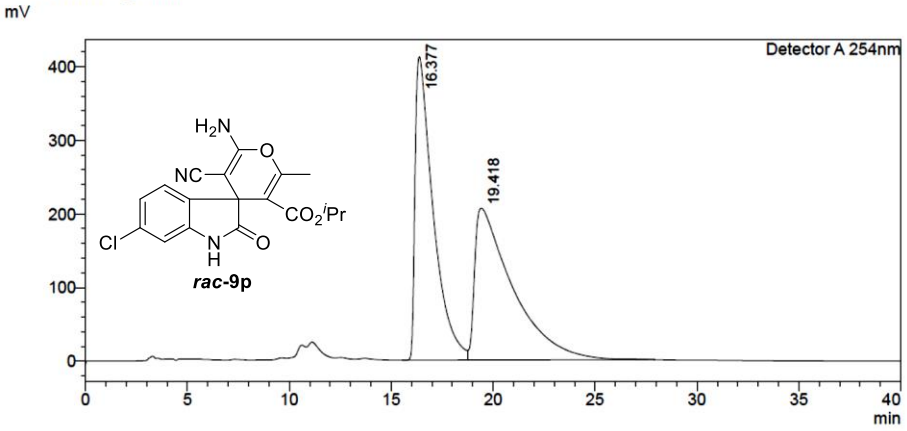
PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.865	10624851	169656	27.869	30.603
2	21.261	27499293	384719	72.131	69.397
Total		38124144	554375	100.000	100.000

Data Filename : VI-SK-338-R.lcd
Method Filename : IB-20%-1.0 mL-254 nm-40-MIN.lcm
Batch Filename :
Vial # : 1-1 Sample Type : Unknown
Injection Volume : 10 uL
Date Acquired : 8/27/2018 1:34:26 PM Acquired by : nzc766
Date Processed : 8/27/2018 2:14:28 PM Processed by : nzc766

<Chromatogram>



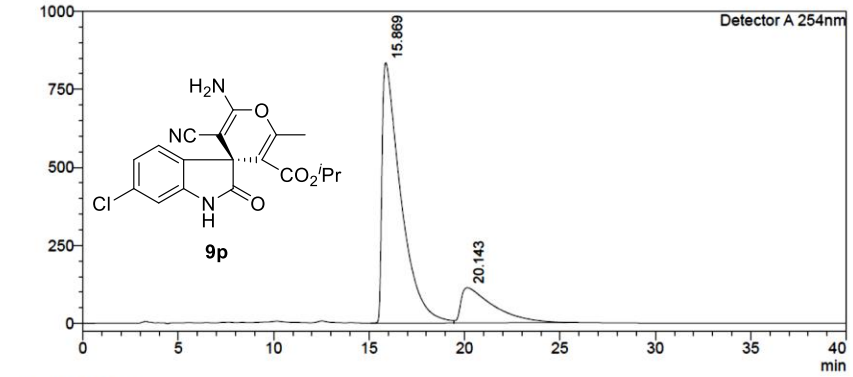
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Conc.	Area%	Height%
1	16.377	25418486	412177	48.621	48.621	66.652
2	19.418	26860231	206222	51.379	51.379	33.348
Total		52278717	618400		100.000	100.000

Data Filename : VI-SK-339-6-Cl-Chiral.lcd
Method Filename : IB-20%-1.0 mL-254 nm-40-MIN.lcm
Batch Filename :
Vial # : 1-1 Sample Type : Unknown
Injection Volume : 10 uL
Date Acquired : 8/27/2018 2:29:53 PM Acquired by : nzc766
Date Processed : 8/27/2018 3:26:32 PM Processed by : nzc766

<Chromatogram>



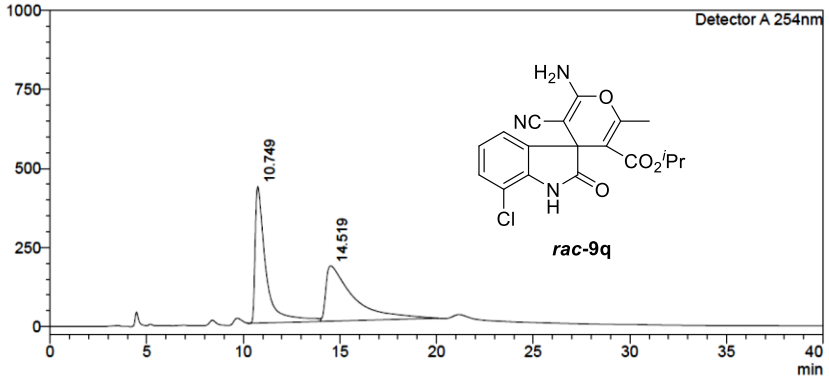
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	15.869	57173946	834730	81.087	88.128
2	20.143	13335641	112450	18.913	11.872
Total		70509587	947180	100.000	100.000

Data Filename : VI-SK-340-RAC.lcd
Method Filename : IB-30%-1.0 mL-254 nm-40-MIN.lcm
Batch Filename :
Vial # : 1-1 Sample Type : Unknown
Injection Volume : 10 uL
Date Acquired : 8/27/2018 5:11:02 PM Acquired by : nzc766
Date Processed : 9/24/2018 10:26:53 AM Processed by : nzc766

<Chromatogram>



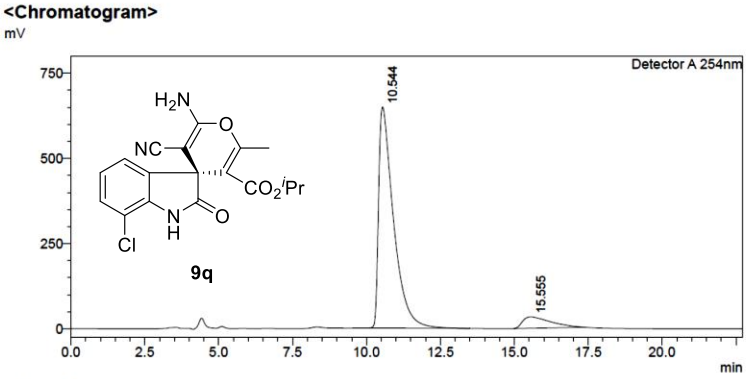
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	10.749	16805770	431736	49.173	71.212
2	14.519	17371118	174529	50.827	28.788
Total		34176888	606265	100.000	100.000

Data Filename : VI-SK-341-C.lcd
Method Filename : IB-30%-1.0 mL-254 nm-40-MIN.lcm
Batch Filename :
Vial # : 1-1 Sample Type : Unknown
Injection Volume : 10 uL
Date Acquired : 8/27/2018 6:40:23 PM Acquired by : nzc766
Date Processed : 8/27/2018 7:06:36 PM Processed by : nzc766

<Chromatogram>



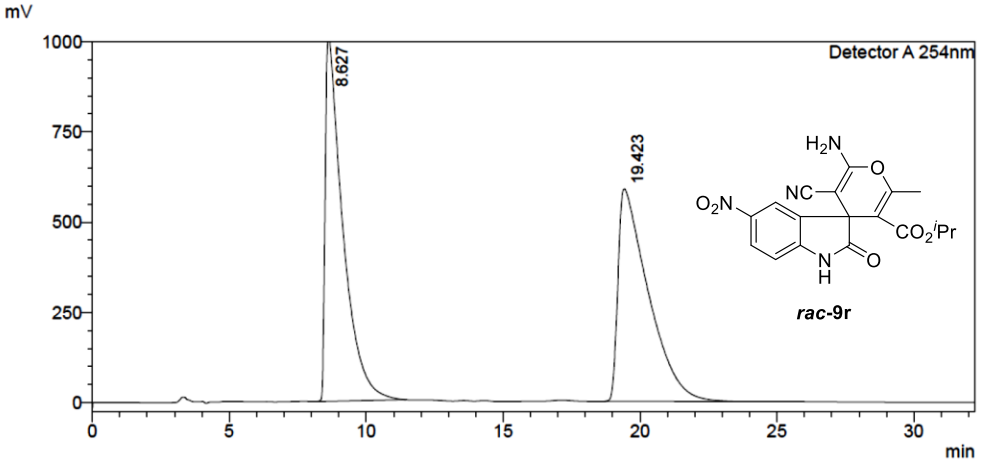
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	10.544	22774117	649500	91.272	95.139
2	15.555	2177836	33182	8.728	4.861
Total		24951954	682682	100.000	100.000

Data Filename	: VI-SK-330-RACEMIC.lcd		
Method Filename	: IB-30%-1.0 mL-254 nm-40-MIN.lcm		
Batch Filename	:		
Vial #	: 1-1	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 8/28/2018 9:21:28 AM	Acquired by	: nzc766
Date Processed	: 8/28/2018 12:11:35 PM	Processed by	: nzc766

<Chromatogram>



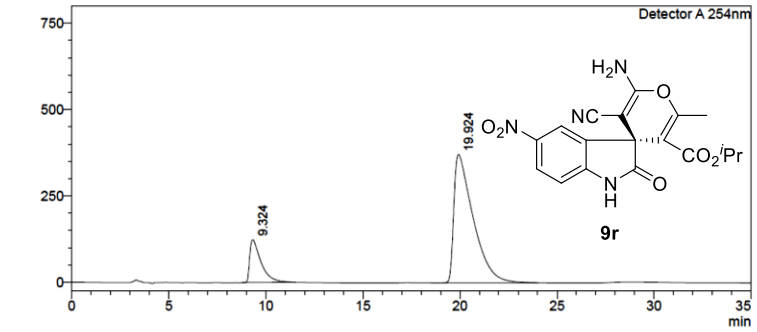
<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	8.627	45018840	1010820	49.839	63.170
2	19.423	45308940	589348	50.161	36.830
Total		90327780	1600168	100.000	100.000

Data Filename	: VI-SK-331-CHIRAL.lcd		
Method Filename	: IB-30%-1.0 mL-254 nm-40-MIN.lcm		
Batch Filename	:		
Vial #	: 1-1	Sample Type	: Unknown
Injection Volume	: 10 uL		
Date Acquired	: 8/28/2018 9:55:29 AM	Acquired by	: nzc766
Date Processed	: 8/28/2018 12:14:42 PM	Processed by	: nzc766

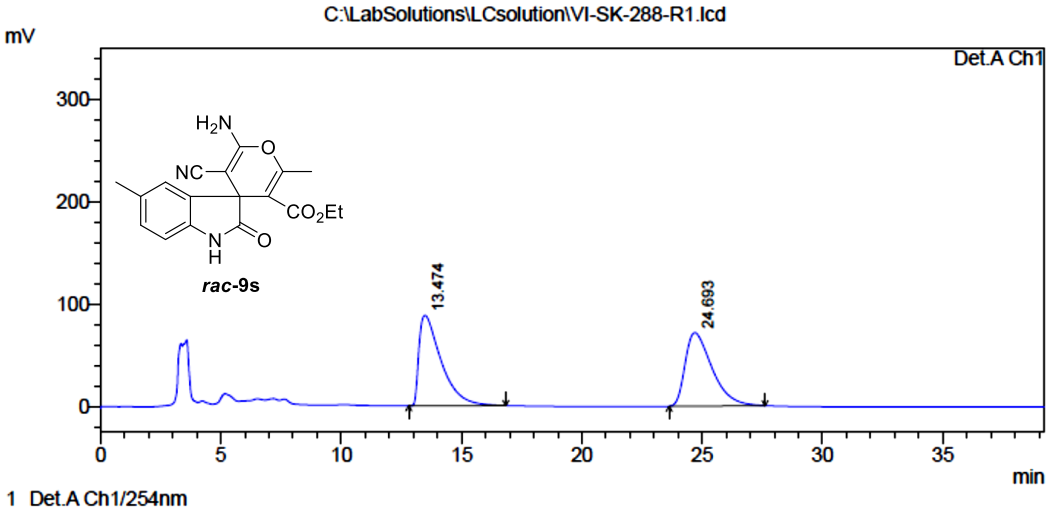
<Chromatogram>



<Peak Table>

Detector A 254nm

Peak#	Ret. Time	Area	Height	Area%	Height%
1	9.324	5017947	124136	16.284	25.004
2	19.924	25797168	372319	83.716	74.996
Total		30815116	496455	100.000	100.000

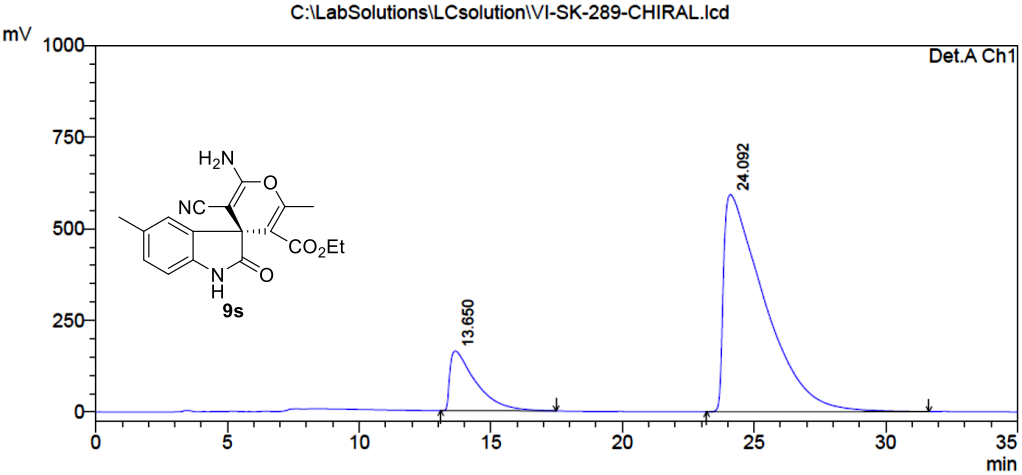


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.474	5654589	88276	50.334	55.207
2	24.693	5579485	71625	49.666	44.793
Total		11234074	159901	100.000	100.000

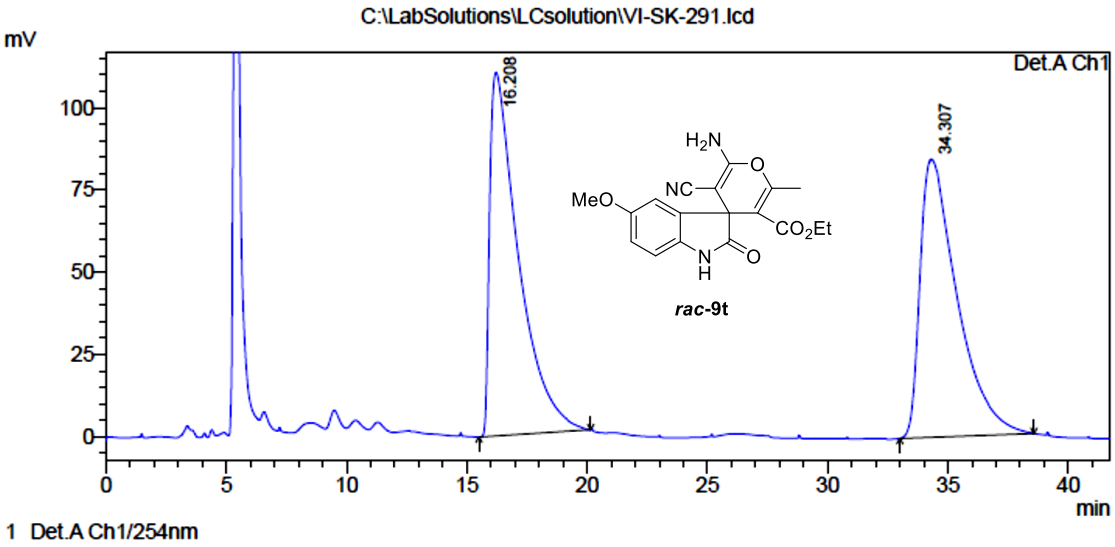


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	13.650	11130240	163010	14.742	21.553
2	24.092	64372269	593322	85.258	78.447
Total		75502509	756332	100.000	100.000

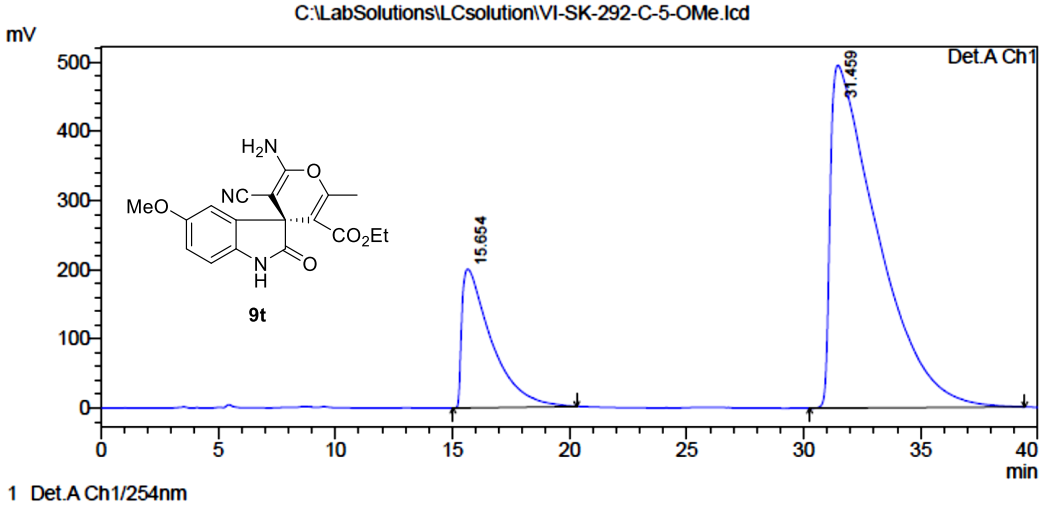


1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.208	9192258	110509	50.411	56.653
2	34.307	9042302	84552	49.589	43.347
Total		18234559	195061	100.000	100.000



1 Det.A Ch1/254nm

PeakTable

Detector A Ch1 254nm

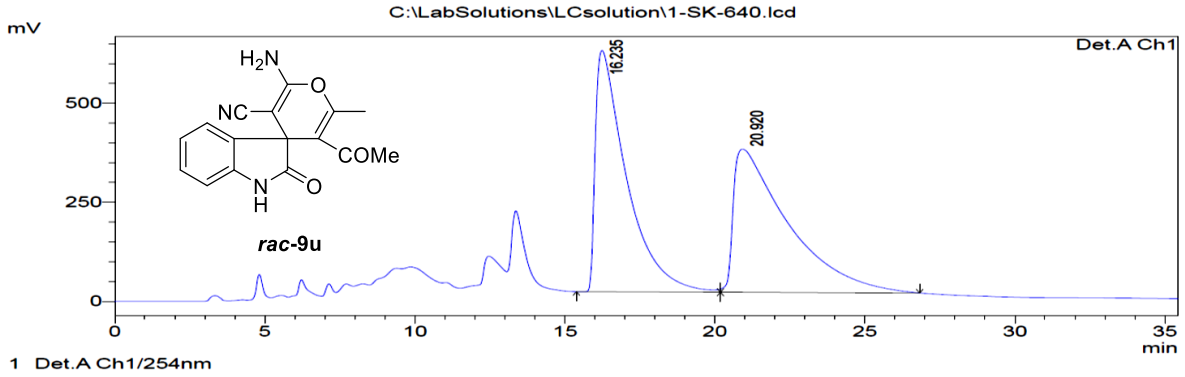
Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.654	17725510	200718	20.263	28.826
2	31.459	69750007	495585	79.737	71.174
Total		87475517	696303	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-SK-640.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-SK-640.lcd
Method File Name	: ChiralPak IB-30%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 7/13/2019 12:12:50 PM
Data Processed	: 7/13/2019 12:51:49 PM

<Chromatogram>



PeakTable

Detector A Ch1 254nm

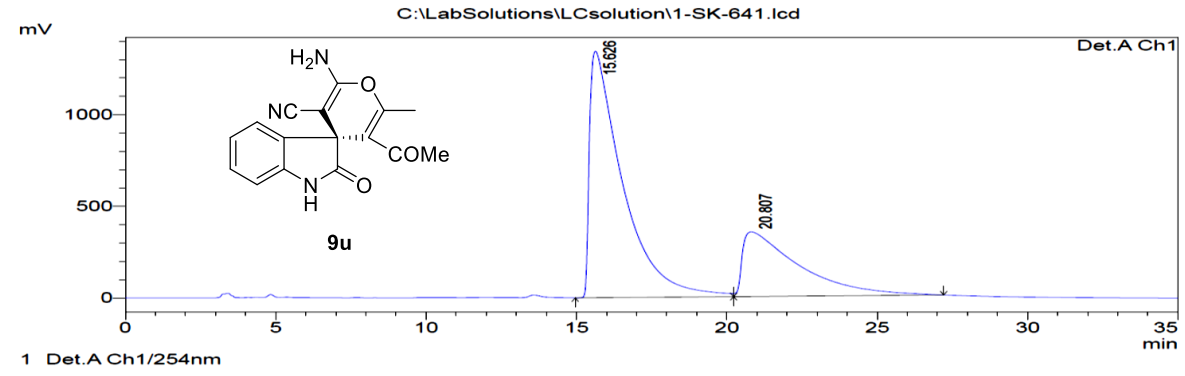
Peak#	Ret. Time	Area	Height	Area %	Height %
1	16.235	44011393	609023	48.969	62.762
2	20.920	45865022	361344	51.031	37.238
Total		89876414	970366	100.000	100.000

==== Shimadzu LCsolution Analysis Report ====

C:\LabSolutions\LCsolution\1-SK-641.lcd

Acquired by	: Admin
Sample Name	:
Sample ID	:
Vail #	:
Injection Volume	: 1 uL
Data File Name	: 1-SK-641.lcd
Method File Name	: ChiralPak IB-30%-1.0 mL-254nm.lcm
Batch File Name	:
Report File Name	: Default.lcr
Data Acquired	: 7/13/2019 1:01:16 PM
Data Processed	: 7/13/2019 1:37:29 PM

<Chromatogram>



PeakTable

Detector A Ch1 254nm

Peak#	Ret. Time	Area	Height	Area %	Height %
1	15.626	103177973	1344502	69.125	79.218
2	20.807	46084545	352711	30.875	20.782
Total		149262518	1697213	100.000	100.000

Additional References

[67] Brahmachari, G.; Banerjee, B. Facile and Chemically Sustainable One-Pot Synthesis of a Wide Array of Fused *O*- and *N*-Heterocycles Catalyzed by Trisodium Citrate Dihydrate under Ambient Conditions. *Asian J. Org. Chem*. **2016**, *5*, 271-286.

[68] Dworczak, R.; Sterk, H.; Kratky, C.; Junek, H. Uber Spirocindan-pyrane] und Inden-propellane-Addukte von 1,3-Dicarbonylverbindungen an 2-(Dicyanmethylen)-1,3-indandion *Chem. Ber.* **1989**, *122*, 1323-1328.

[69] Zhao, L.; Zhou, B.; Li, Y. Synthesis of spirooxindole derivatives under solvent- and catalyst-free conditions. *Youji Huaxue*, **2011**, *31*, 553- 556.

[70] Chai, S.-J.; Lai, Y.-F.; Xu, J.-C.; Zheng, H.; Zhu, Q.; Zhang, P. F. One-Pot Synthesis of Spirooxindole Derivatives Catalyzed by Lipase in the Presence of Water. *Adv. Synth. Catal*. **2011**, *353*, 371-375.