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J. Serb. Chem. Soc. 80 (7) S221–S245 (2015) *Supplementary material*

SUPPLEMENTARY MATERIAL TO

Synthesis and antimicrobial activity of azepine and thiepine derivatives

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ANALYTICAL AND SPECTRAL DATA OF THE COMPOUNDS

(2-Bromo-5-chlorophenyl)methanediyl diacetate. Yield: 1.31 g, 84 %; colourless powder; m.p.: 65–67 °C; IR (ATR, cm^{-1}): 3077, 2995, 1759, 1466, 1435, 1374, 1234, 1202, 1140, 1096, 1068, 1032, 1006, 880; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 7.85 (1H, *s*), 7.54–7.50 (2H, *m*), 7.27–7.22 (1H, *m*), 2.16 (6H, *s*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 168.23, 136.59, 134.30, 133.87, 131.12, 128.15, 120.33, 88.40, 20.66.

*2-Bromo-5-chlorobenzaldehyde (**19**).* White solid; m.p.; 72–74 °C; IR (ATR, cm^{-1}): 3351, 3060, 2884, 1689, 1578, 1455, 1390, 1283, 1248, 1188, 1125, 1091, 1031, 899, 820; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 10.30 (1H, *s*), 7.88 (1H, *d*, *J* = 2.5 Hz), 7.60 (1H, *d*, *J* = 8.5 Hz), 7.43 (1H, *dd*, *J* = 2.5 Hz, *J* = 8.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 190.49, 135.12, 135.03, 134.61, 134.44, 129.66, 124.61; GC-MS, *RT* 23 min (*m/z* (%)): 218.9 ([M^+] (100)), 190.9 (24), 138.0 (14), 110.0 (29), 84.0 (5), 75.0 (47), 50.0 (15).

*2-Bromo-5-methoxybenzaldehyde (**21**).* Colourless solid; m.p.: 76–78 °C; IR (ATR, cm^{-1}): 3339, 3095, 3074, 3008, 2981, 2944, 2876, 2845, 2746, 1890, 1677, 1689, 1600, 1570, 1471, 1419, 1384, 1301, 1281, 1243, 1200, 1169, 1136, 1061, 1014, 932, 866, 820; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 10.31 (1H, *s*), 7.52 (1H, *d*, *J* = 8.5 Hz), 7.42 (1H, *d*, *J* = 3.0 Hz), 7.03 (1H, *dd*, *J* = 3.0 Hz, *J* = 9.0 Hz), 3.84 (3H, *s*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 191.77, 159.25, 134.54, 133.95, 123.11, 117.95, 112.66, 55.71; GC-MS, *RT* 14.92 min (*m/z* (%)): 213.9 ([M^+] (100)), 184.9 (15), 171.9 (14), 156.9 (8), 144.9 (16), 134.0 (10), 106.0 (20), 92.0 (16), 75.0 (18), 63.0 (55), 50.0 (9).

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*3-[(Z)-2-(2-Bromo-5-chlorophenyl)ethenyl]-4-chloropyridine (**24**).* Colourless powder; m.p.: 65–67 °C; IR (ATR, cm^{-1}): 3107, 3081, 3054, 2967, 2928, 1754, 1732, 1639, 1572, 1546, 1471, 1449, 1404, 1386, 1309, 1267, 1224, 1204, 1166, 1109, 1087, 1023, 973, 936, 903, 882, 826; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.34 (1H, *d*, *J* = 5.5 Hz), 8.15 (1H, *s*), 7.51 (1H, *d*, *J* = 8.5 Hz), 7.34 (1H, *d*, *J* = 5.5 Hz), 7.07 (1H, *dd*, *J* = 2.0 Hz, *J* = 9.0 Hz), 6.92–6.89 (1H, *m*), 6.84 (1H, *d*, *J* = 11.5 Hz), 6.79 (1H, *d*, *J* = 12.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm) 150.92, 149.18, 143.29, 138.12, 133.99, 133.27, 132.17, 130.97, 130.12, 129.37, 126.03, 124.41, 121.77; (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 327.92899. Found: 327.92792.

*3-[(Z)-2-(2-Bromo-5-methoxyphenyl)ethenyl]-4-chloropyridine (**25**).* Colourless oil; IR (ATR, cm^{-1}): 3397, 3007, 2935, 2835, 2356, 1618, 1591, 1567, 1464, 1411, 1346, 1295, 1237, 1174, 1129, 1082, 1052, 1016, 934, 872, 821; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.32 (1H, *d*, *J* = 5.5 Hz), 8.21 (1H, *s*), 7.46 (1H, *d*, *J* = 8.5 Hz), 7.34 (1H, *d*, *J* = 5.5 Hz), 6.91 (1H, *d*, *J* = 12.0 Hz), 6.74 (1H, *d*, *J* = 12.0 Hz), 6.69–6.64 (1H, *m*), 6.46 (1H, *d*, *J* = 3.0 Hz), 3.53 (3H, *s*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 158.59, 150.82, 148.40, 143.60, 136.99, 133.63, 133.58, 131.75, 124.84, 124.42, 115.70, 115.56, 114.33, 55.24; (+)ESI-HRMS *m/z*: calcd. for [M + H$^+$]: 323.97853. Found: 323.97699.

*3-[(Z)-2-(2-Bromo-5-fluorophenyl)ethenyl]-4-chloropyridine (**26**).* Colourless powder; m.p.: 109–110 °C; IR (ATR, cm^{-1}): 3403, 3041, 2924, 2850, 1632, 1599, 1574, 1550, 1460, 1413, 1344, 1275, 1221, 1177, 1143, 1102, 1082, 1032, 962, 882, 819; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.33 (1H, *d*, *J* = 5.5 Hz), 8.16 (1H, *s*), 7.54 (1H, *dd*, *J* = 5.5 Hz, *J* = 8.5 Hz), 7.34 (1H, *d*, *J* = 5.5 Hz), 6.90–6.75 (3H, *m*), 6.64 (1H, *dd*, *J* = 3.0 Hz, *J* = 9.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 161.53 (*d*, *J* = 245.5 Hz), 150.98, 149.17, 143.29, 138.22 (*d*, *J* = 8.1 Hz), 134.18 (*d*, *J* = 8.1Hz), 132.46, 131.04, 125.93, 124.41, 118.20, 117.26 (*d*, *J* = 23.5), 116.67 (*d*, *J* = 22.6 Hz); (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 311.95854. Found: 311.95788.

*5-[3-(Pyrrolidin-1-yl)propyl]-5*H*-pyrido[4,3-*b*][1]benzazepine (**27**).* Yellow oil; IR (ATR, cm^{-1}): 3340, 3023, 2960, 2874, 2792, 1635, 1577, 1480, 1418, 1393, 1329, 1241, 1184, 1142, 1125, 1058, 912, 830; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.35 (1H, *d*, *J* = 5.5 Hz), 8.17 (1H, s), 7.29–7.23 (1H, *m*), 7.05––6.98 (2H, *m*), 6.94 (1H, *d*, *J* = 8.0 Hz), 6.81 (1H, *d*, *J* = 5.5 Hz), 6.74 (1H, *d*, *J* = = 11.0 Hz), 6.60 (1H, *d*, *J* = 11.5 Hz), 3.81–3.73 (2H, *m*), 2.57–2.50 (2H, *m*), 2.46–2.37 (4H, *m*), 1.85–1.77 (2H, *m*), 1.76–1.69 (4H, *m*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 158.79, 150.45, 150.08, 149.09, 134.12, 133.59, 129.47, 129.30, 129.19,129.06, 124.04, 121.08, 114.68, 54.23, 53.89, 48.50, 26.71, 23.37; (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 306.19647. Found: 306.19553.

*5-[3-(Pyrrolidin-1-yl)propyl]-5*H*-dipyrido[4,3-*b*:3',4'-*f*]azepine (**28**).* Yellow oil; IR (ATR, cm^{-1}): 3330, 3028, 2958, 2858, 2803, 1732, 1645, 1580, 1483,

1398, 1335, 1248, 1178, 1063, 929, 831; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.39 (2H, *d*, *J* = 5.5 Hz), 8.16 (2H, *s*), 6.76 (2H, *d*, *J* = 5.5 Hz), 6.64 (2H, *s*), 3.82–3.75 (2H, *m*), 2.58–2.52 (2H, *m*), 2.47–2.39 (4H, *m*), 1.86–1.79 (2H, *m*), 1.78–1.71 (4H, *m*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 157.08, 150.76, 150.74, 131.19, 128.68, 115.41, 54.24, 53.60, 48.08, 26.42,23.39; (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 307.19172. Found: 307.19048.

*3-(8-Chloro-5*H*-pyrido[4,3-*b*][1]benzazepin-5-yl)*-N,N-*dimethylpropan-1--amine (**29**)*. Yellow oil; IR (ATR, cm^{-1}): 3387, 3026, 2944, 2858, 2817, 2768, 1682, 1578, 1472, 1391, 1327, 1241, 1184, 1132, 1101, 1058, 920, 841; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.37 (1H, *d*, *J* = 5.5 Hz), 8.18 (1H, *s*), 7.21 (1H, *dd*, *J* = 2.5 Hz, *J* = 8.5 Hz), 6.99 (1H, *d*, *J* = 2.5 Hz), 6.86 (1H, *d*, *J* = 8.5 Hz), 6.80 (1H, *d*, *J* = 5.5 Hz), 6.64 (2H, *s*), 3.79–3.70 (2H, *m*), 2.41–2.30 (2H, *m*), 2.25–2.11 (6H, *m*), 1.76–1.68 (2H, *m*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 158.60, 150.62, 150.42, 147.46, 135.26, 132.73, 130.50, 129.34, 128.98, 128.96, 128.66, 122.27, 114.72, 56.89, 48.29, 45.45, 25.23; (+)ESI--HRMS *m/z*: calcd. for [M+H$^+$]: 314.14185. Found: 314.14336.

*3-(8-Methoxy-5*H*-pyrido[4,3-*b*][1]benzazepin-5-yl)*-N,N-*dimethylpropan-1--amine (**30**)*. Yellow oil; IR (ATR, cm^{-1}): 3381, 2944, 2858, 2819, 2768, 1674, 1634, 1578, 1480, 1394, 1322, 1276, 1244, 1206, 1038, 972, 938, 876; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.34 (1H, *d*, *J* = 5.5 Hz), 8.17 (1H, *s*), 6.87 (1H, *d*, *J* = 9.0 Hz), 6.85–6.78 (2H, *m*), 6.71 (1H, *d*, *J* = 11.5 Hz), 6.62 (1H, *d*, *J* = 11.5 Hz), 6.57 (1H, *d*, *J* = 3.0 Hz), 3.76 (3H, *s*), 3.73–3.68 (2H, *m*), 2.44–2.36 (2H, *m*), 2.20–2.15 (6H, *m*), 1.79–1.70 (2H, *m*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 159.36, 156.12, 150.53, 150.05, 141.73, 134.76, 133.68, 129.72, 128.82, 121.96, 114.69, 114.37, 114.08, 57.07, 55.47, 48.32, 45.50, 25.40; (+)ESI-HRMS *m/z*: calcd. for [M + H$^+$]: 310.19139. Found: 310.19142.

*[1]Benzothiepino[3,2-*c*]pyridine (**16**)*. Colourless solid; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.49–8.42 (2H, *m*), 7.49–7.43 (1H, *m*), 7.38–7.29 (3H, *m*), 7.28–7.23 (1H, *m*), 7.13 (1H, *d*, *J* = 12.0 Hz), 6.99 (1H, *d*, *J* = 12.0 Hz); (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 212.05354. Found: 212.05354.

*Pyrido[3',4':6,7]thiepino[3,2-*c*]pyridine (**17**)*. Colourless solid; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.51 (2H, *d*, *J* = 5.5 Hz), 8.47 (2H, *s*), 7.32 (2H, *d*, *J* = 5.0 Hz), 7.09 (2H, *s*); (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 213.04810. Found: 213.04861.

*8-Chloro[1]benzothiepino[3,2-*c*]pyridine (**31**)*. Colourless solid; m.p.: 132––136 °C; IR (ATR, cm^{-1}): 3965, 3356, 3080, 3048, 3021, 2959, 2928, 2855, 2024, 1989, 1952, 1919, 1894, 1852, 1812, 1754, 1676, 1630, 1569, 1546, 1468, 1395, 1362, 1306, 1273, 1195, 1163, 1099, 1053, 1027, 976, 946; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.48 (1H, *d*, *J* = 5.0 Hz), 8.46 (1H, *s*), 7.38 (1H, *d*, *J* = = 8.5 Hz), 7.34 (1H, *d*, *J* = 5.0 Hz), 7.29 (1H, *dd*, *J* = 2.0 Hz, *J* = 8.0 Hz), 7.25––7.22 (1H, *m*), 7.03 (2H, *s*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 150.16,

150.03, 144.42, 141.10, 135.08, 134.91, 134.75, 134.06, 131.67, 131.06, 129.68, 129.34, 126.27; (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 246.01387. Found: 246.01318.

*8-Methoxy[1]benzothiepino[3,2-*c*]pyridine (**32**).* Colourless oil; IR (ATR, cm^{-1}): 3597, 3392, 3022, 2928, 2841, 1710, 1591, 1564, 1471, 1389, 1324, 1278, 1243, 1210, 1176, 1153, 1068, 1030, 926, 857, 829; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm); 8.49–8.42 (2H, *m*), 7.38–7.32 (2H, *m*), 7.08 (1H, *d*, *J* = 12.5 Hz), 6.98 (1H, *d*, *J* = 12.0 Hz), 6.87 (1H, *dd*, *J* = 3.0 Hz, *J* = 8.5 Hz), 6.78 (1H, *d*, *J* = 3.0 Hz), 3.79 (3H, *s*); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 160.12, 149.96, 149.74, 145.36, 140.92, 135.88, 135.36, 134.14, 130.71, 126.05, 123.70, 115.60, 114.72, 55.43; (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 242.06341. Found: 242.06256.

*8-Fluoro[1]benzothiepino[3,2-*c*]pyridine (**33**).* Colourless solid; m.p.: 110––112 °C; IR (ATR, cm^{-1}): 3336, 2923, 2854, 1740, 1682, 1647, 1598, 1568, 1468, 1391, 1310, 1245, 1205, 1177, 1121, 1058; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.48 (1H, *d*, *J* = 5.5 Hz), 8.47 (1H, *s*), 7.42 (1H, *dd*, *J* = 5.5 Hz, *J* = 8.5 Hz), 7.35 (1H, *d*, *J* = 5.0 Hz), 7.09–7.01 (3H, *m*), 6.96 (1H, *dd*, *J* = 2.5 Hz, *J* = = 9.0 Hz); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 162.95 (*d*, *J* = 247.2 Hz), 150.12, 150.02, 144.73, 141.66 (*d*, *J* = 8.1 Hz), 135.13, 134.92, 134.62 (*d*, *J* = 8.1 Hz), 131.54, 127.88, 126.21, 116.81 (*d*, *J* = 21.8 Hz), 116.18 (*d*, *J* = 22.5 Hz); (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 230.04342. Found: 230.04321.

*8-Chloro-2-methyl-1,2,3,4-tetrahydro[1]benzothiepino[3,2-*c*]pyridine (**34**).* Pale yellow oil. IR (ATR, cm^{-1}): 3012, 2922, 2844, 2784, 2384, 1735, 1636, 1575, 1546, 1461, 1375, 1290, 1263, 1188, 1150, 1128, 1097, 1065, 813; ^{1}H--NMR (500 MHz, $CDCl_3$, δ / ppm): 7.28–7.22 (2H, *m*), 7.16 (1H, *s*), 6.88 (1H, *d*, *J* = 12.5), 6.27 (1H, *d*, *J* = 12.0), 2.99 (2H, *s*), 2.52 (4H, *s*), 2.34 (3H, *s*); ^{13}C--NMR (125 MHz, $CDCl_3$, δ / ppm) 142.04, 135.71, 133.88, 133.42, 133.36, 133.33, 132.48, 129.68, 129.16, 128.24, 58.28, 52.12, 45.15, 34.51; (+)ESI--HRMS *m/z*: calcd. for [M+H$^+$]: 264.06082. Found: 264.06121.

*8-Phenyl[1]benzothiepino[3,2-*c*]pyridine (**35**).* Colourless foam; IR (ATR, cm^{-1}): 3389, 3026, 2925, 2852, 1670, 1565, 1542, 1470, 1389 ,1265, 1174, 1069, 1045, 836; ^{1}H-NMR (500 MHz, $CDCl_3$, δ / ppm): 8.51–8.44 (2H, *m*), 7.59–7.34 (9H, *m*), 7.19 (1H, *d*, *J* = 12.5), 7.03 (1H, *d*, *J* = 12.0); ^{13}C-NMR (125 MHz, $CDCl_3$, δ / ppm): 150.00, 149.90, 144.72, 141.95, 140.00, 139.71, 136.09, 135.40, 133.38, 131.59, 130.71, 128.90, 128.52, 128.41, 127.87, 127.04, 126.27; (+)ESI-HRMS *m/z*: calcd. for [M+H$^+$]: 288.08415. Found: 288.08543.

THE SPECTRA

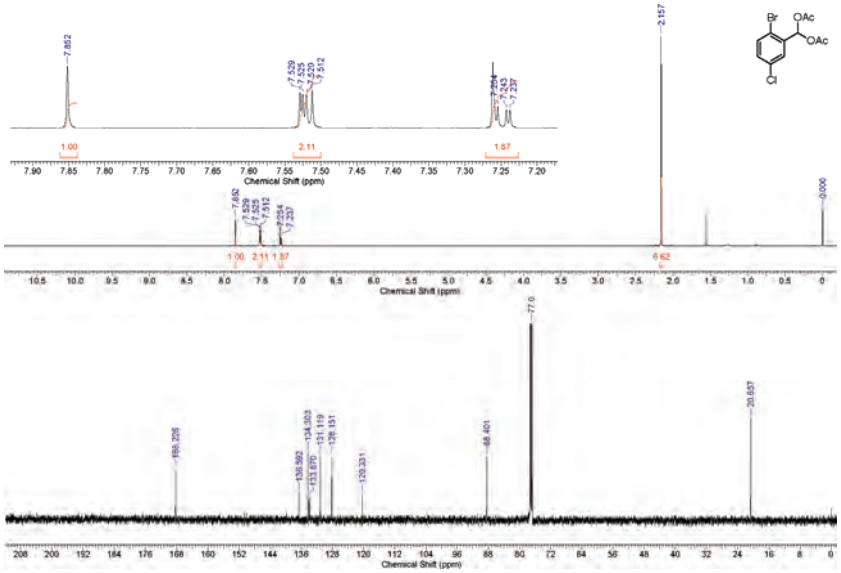


Fig. S-1. The ^{1}H- and ^{13}C-NMR spectra for (2-bromo-5-chlorophenyl)methanediyl diacetate.

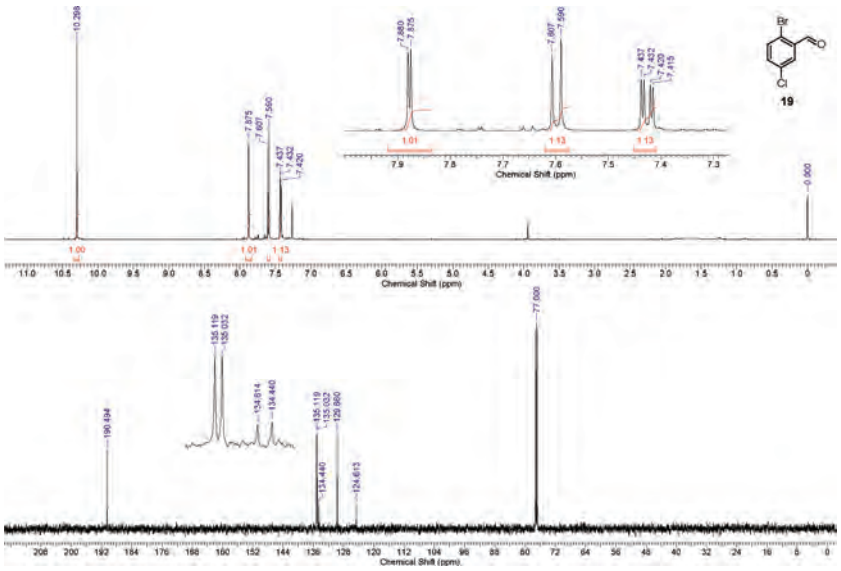


Fig. S-2. The ^{1}H- and ^{13}C-NMR spectra for compound **19**.

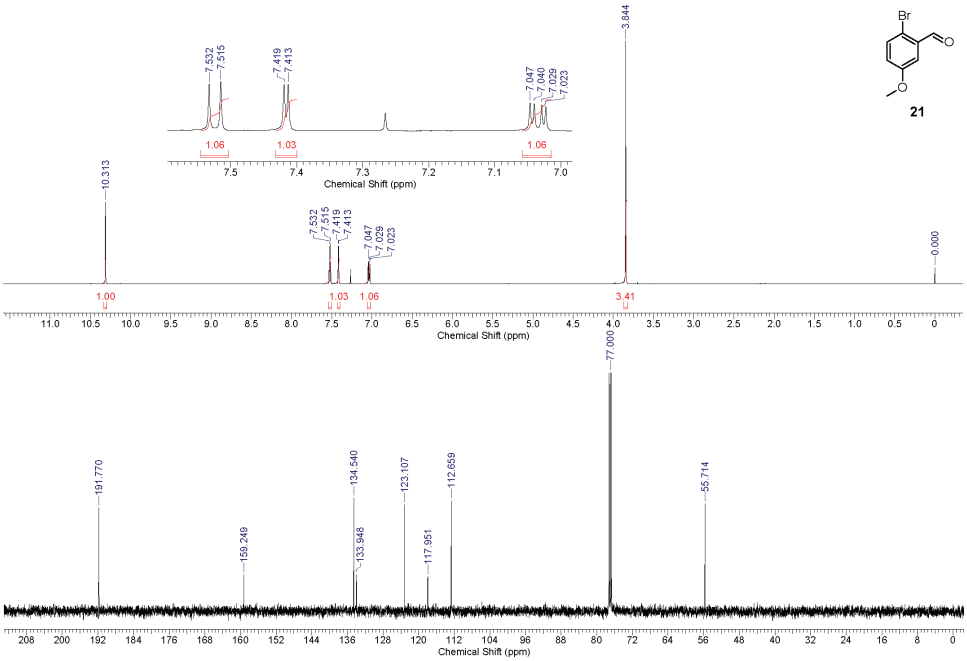


Fig. S-3. The ^{1}H- and ^{13}C-NMR spectra for compound **21**.

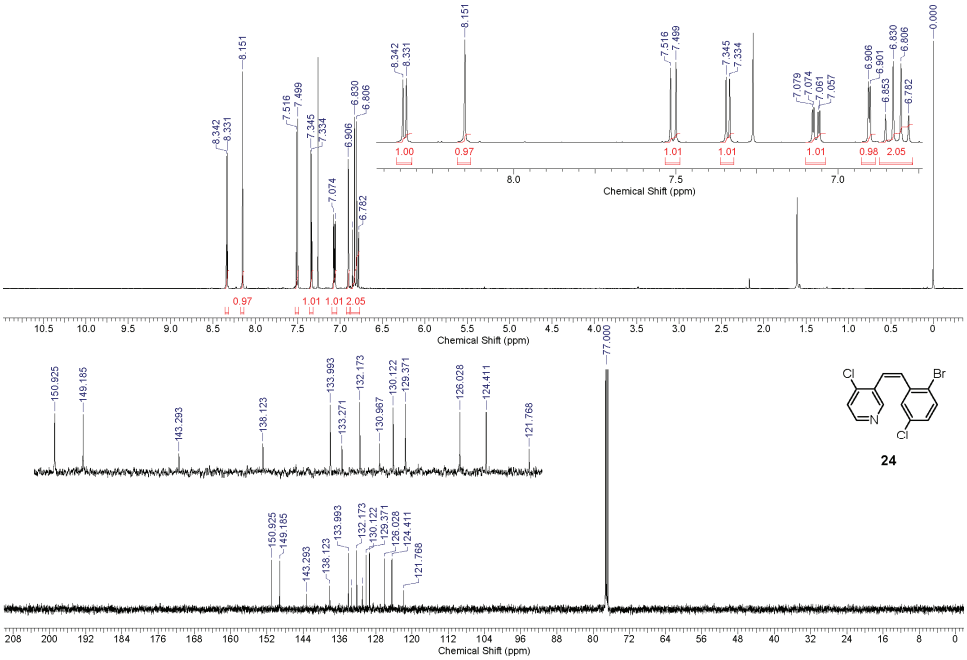


Fig. S-4. The ^{1}H- and ^{13}C-NMR spectra for compound **24**.

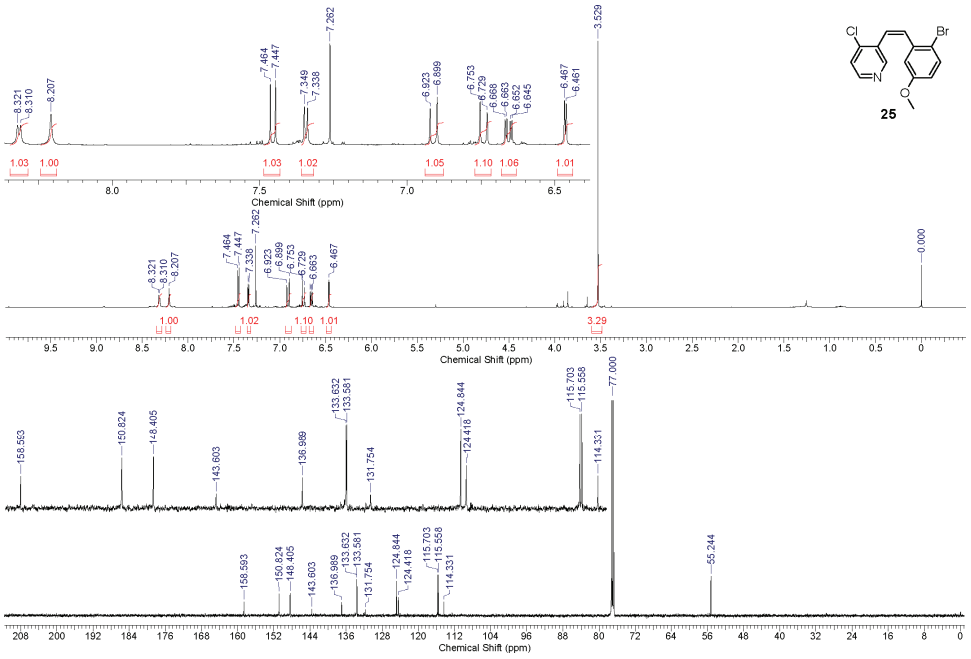


Fig. S-5. The ^{1}H- and ^{13}C-NMR spectra for compound **25**.

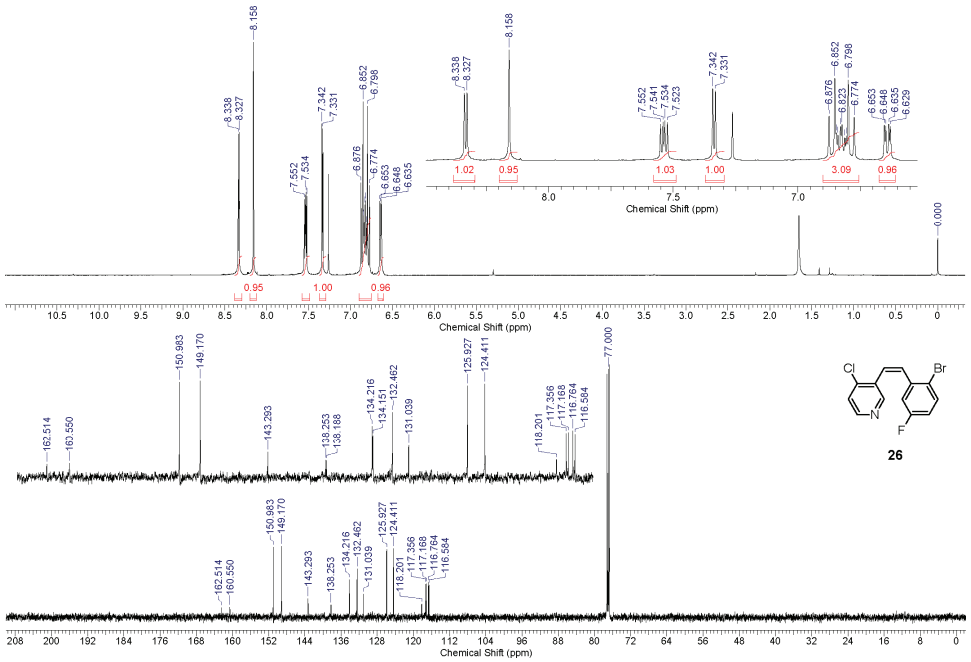


Fig. S-6. The ^{1}H- and ^{13}C-NMR spectra for compound **26**.

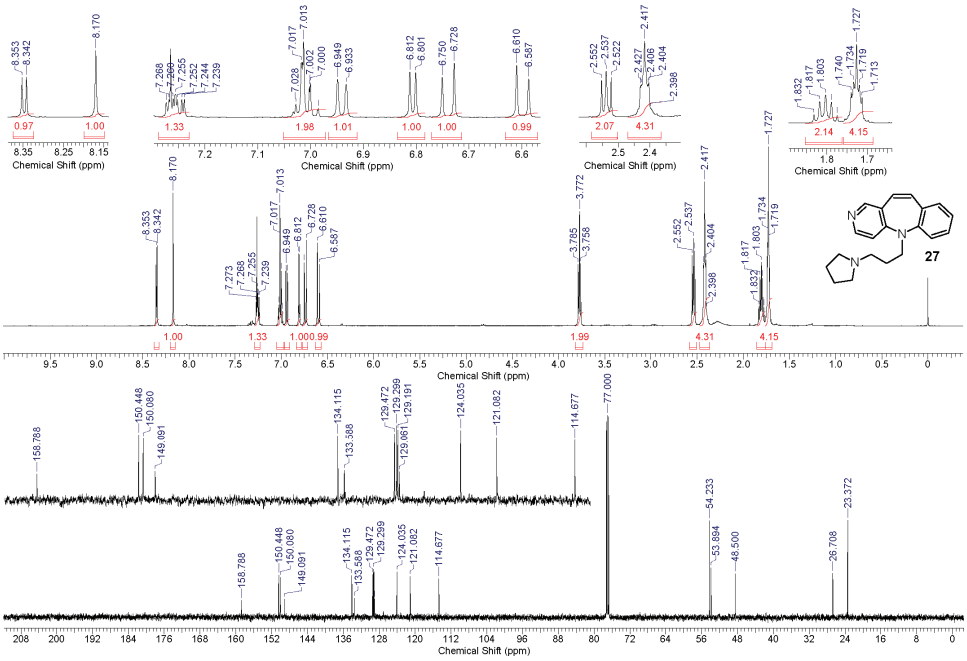


Fig. S-7. The ^{1}H- and ^{13}C-NMR spectra for compound **27**.

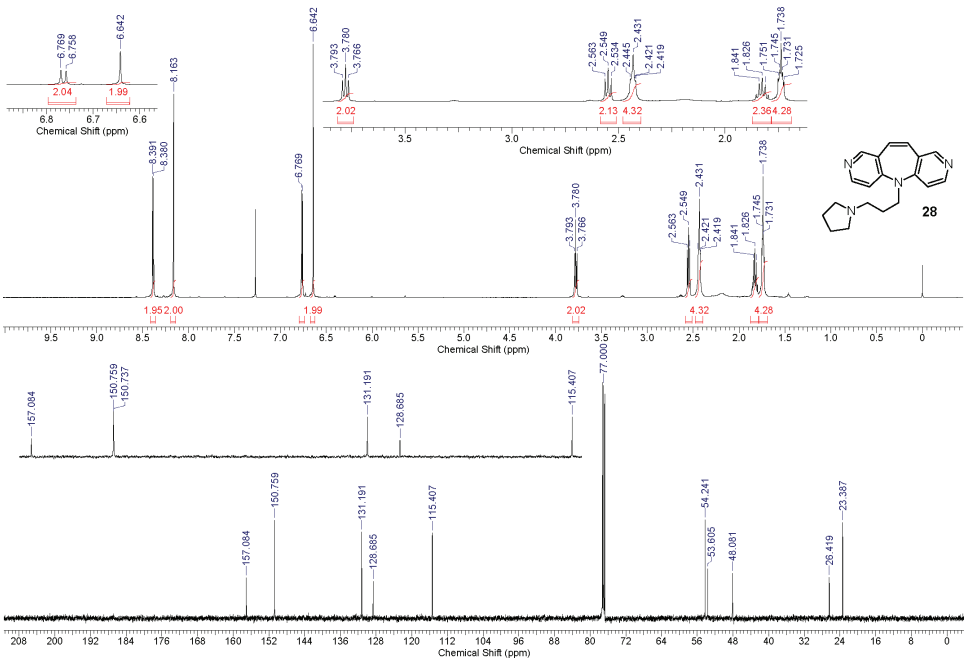


Fig. S-8. The ^{1}H- and ^{13}C-NMR spectra for compound **28**.

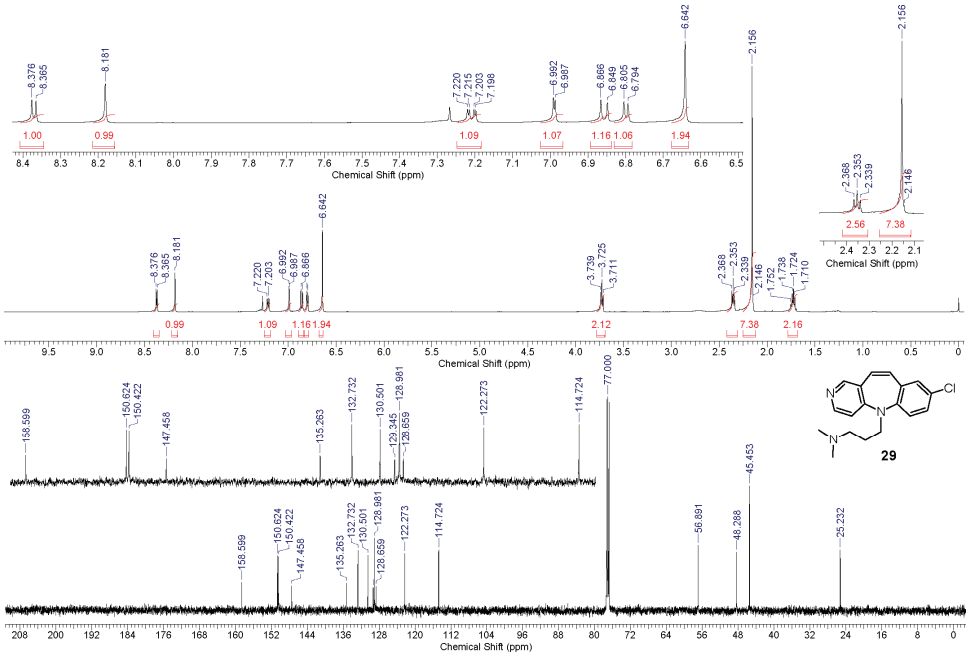


Fig. S-9. The ^{1}H- and ^{13}C-NMR spectra for compound **29**.

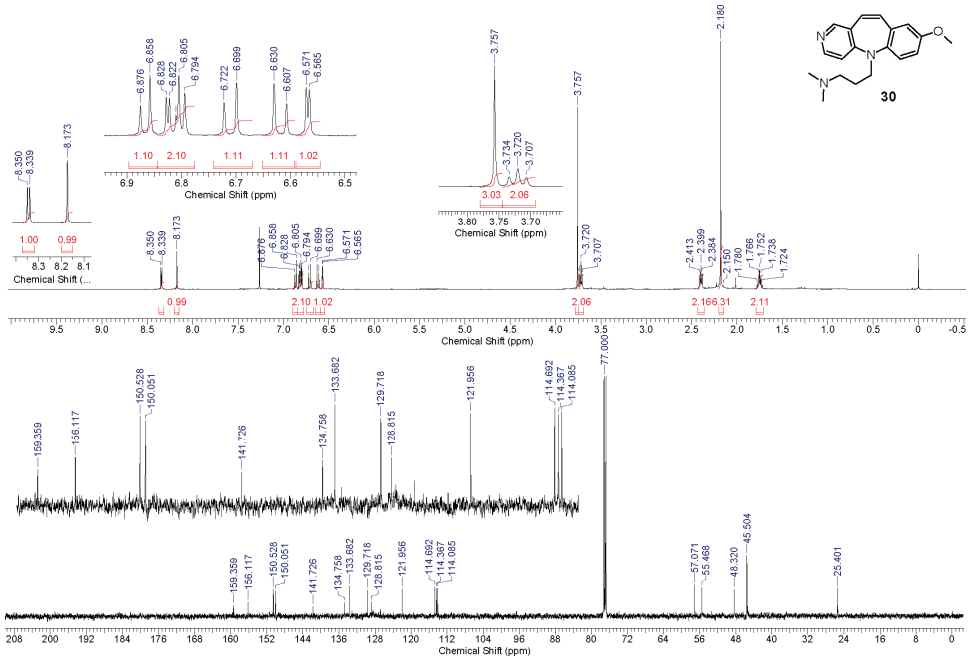


Fig. S-10. The ^{1}H- and ^{13}C-NMR spectra for compound **30**.

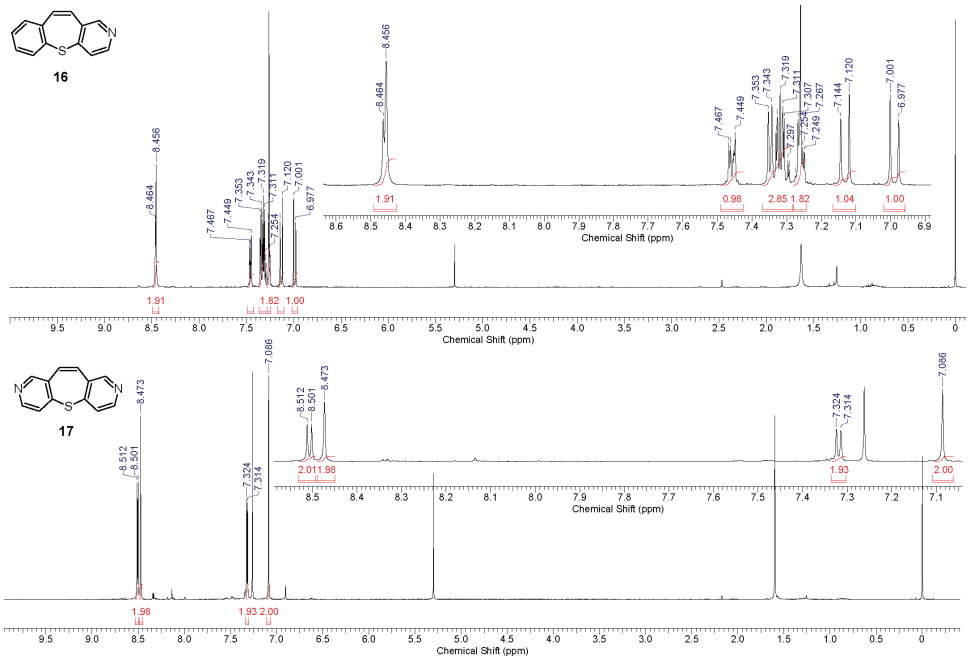


Fig. S-11. The ^{1}H-NMR spectra for compounds **16** and **17**.

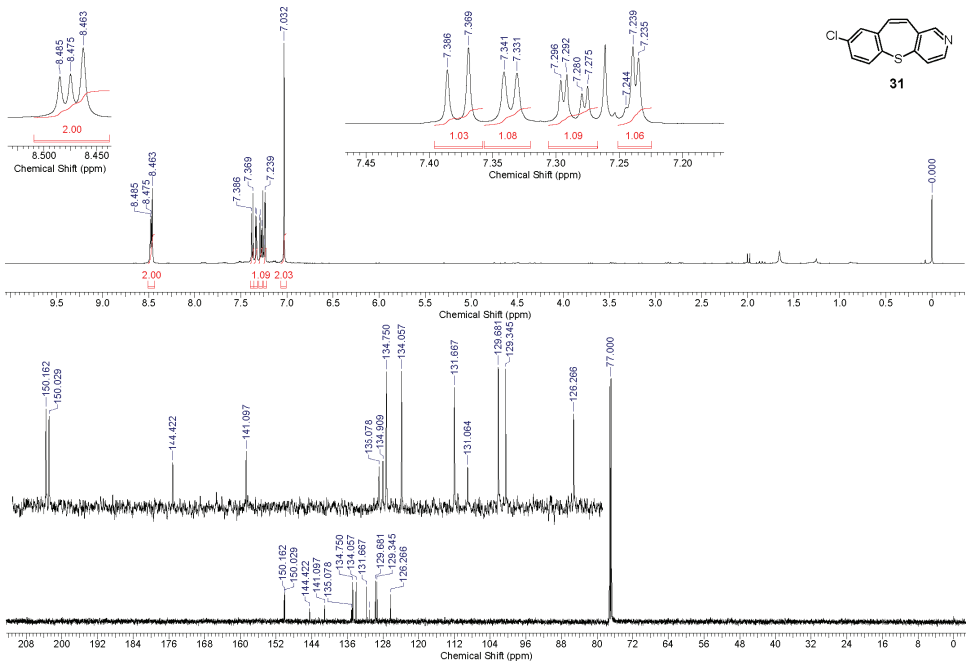


Fig. S-12. The ^{1}H- and ^{13}C-NMR spectra for compound **31**.

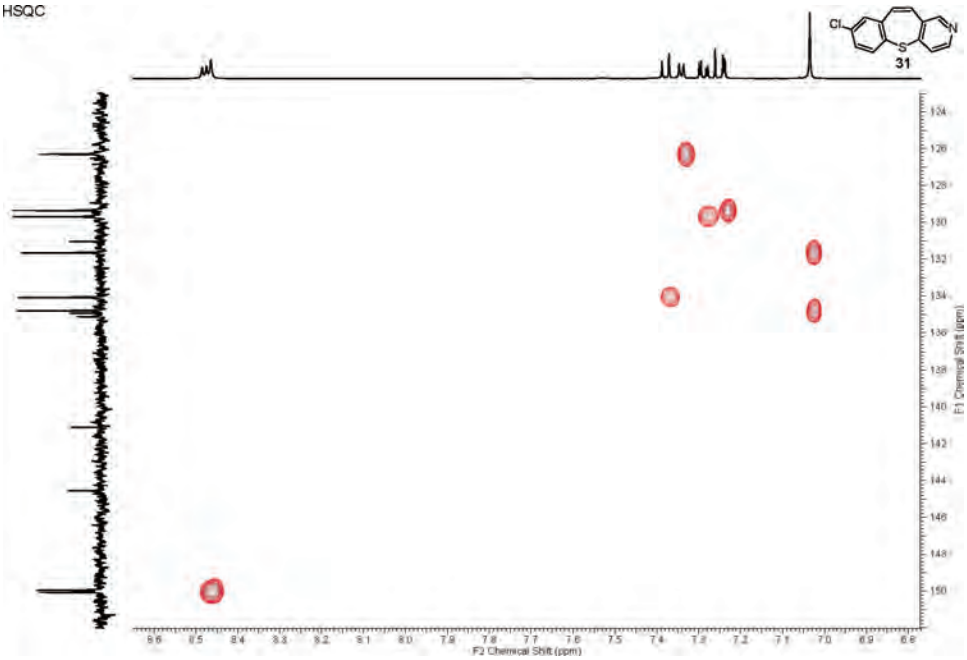


Fig. S-13. 2D ^{1}H-^{13}C HSQC spectrum for compound **31**.

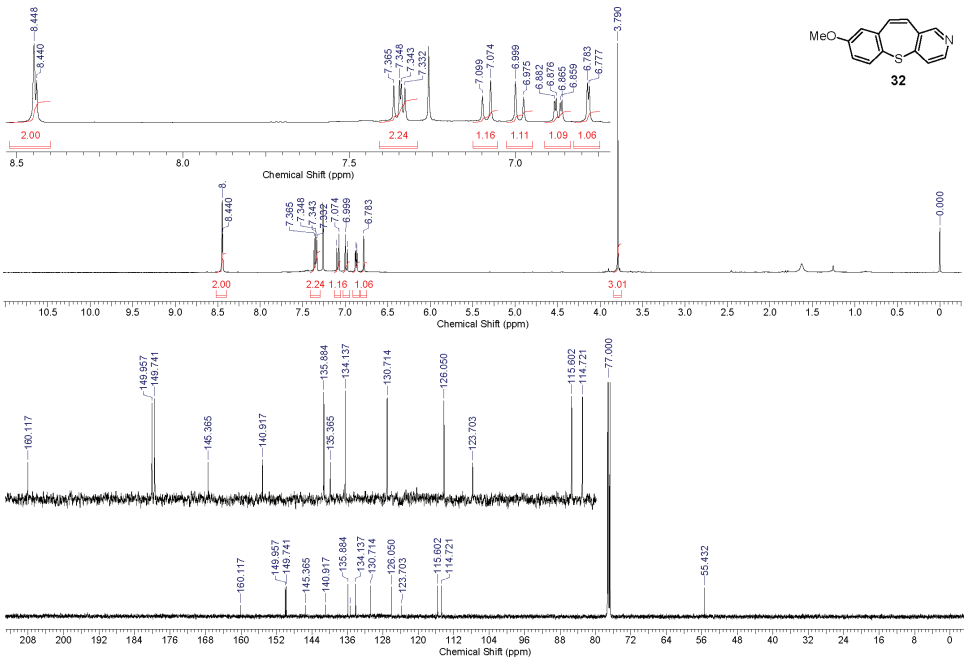


Fig. S-14. The ^{1}H- and ^{13}C-NMR spectra for compound **32**.

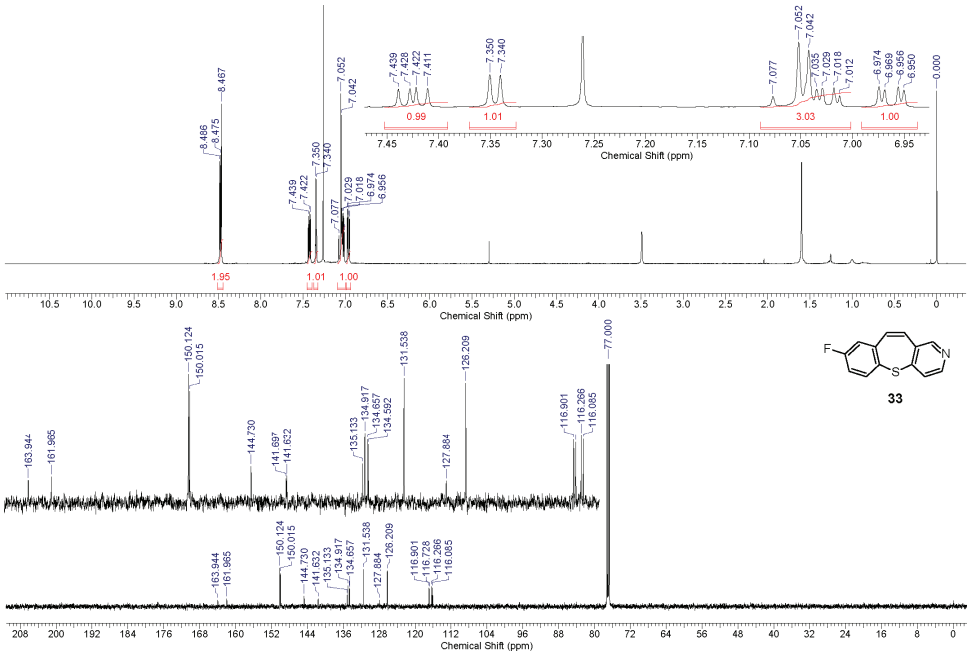


Fig. S-15. The ^{1}H- and ^{13}C-NMR spectra for compound **33**.

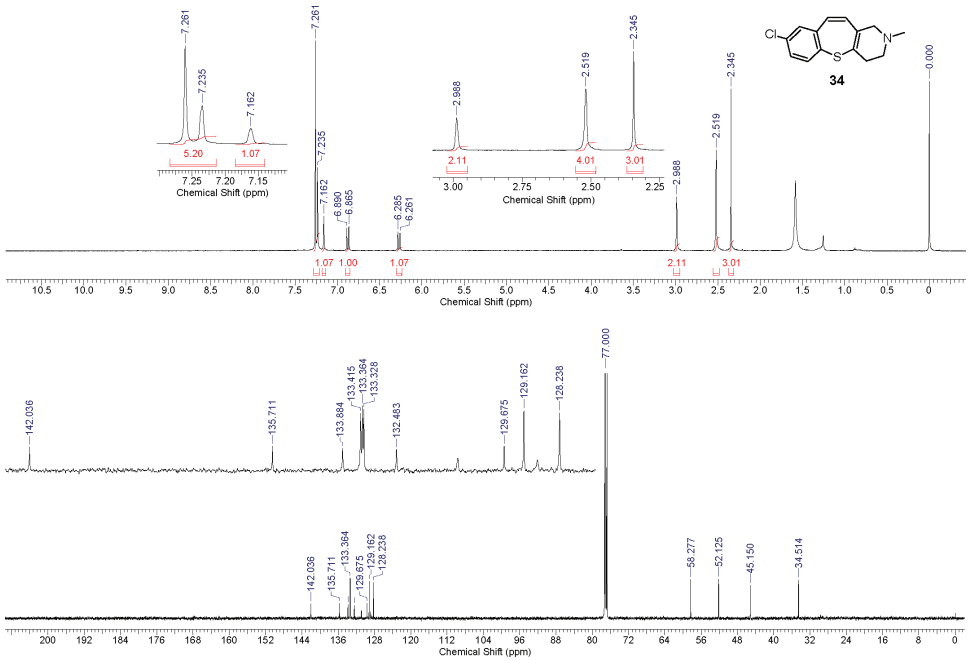


Fig. S-16. The ^{1}H- and ^{13}C-NMR spectra for compound **34**.

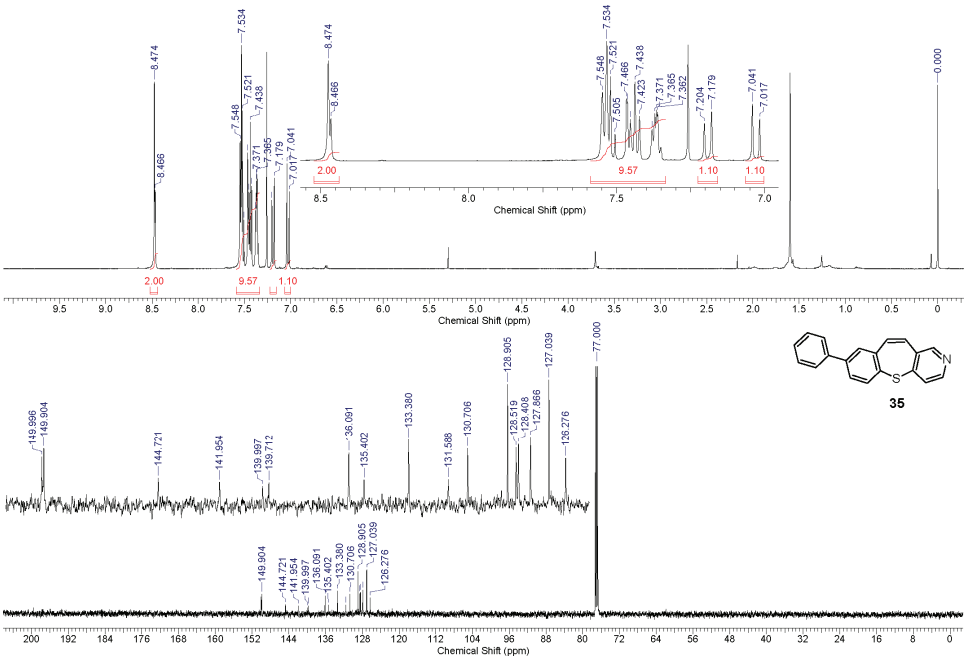


Fig. S-17. The ^{1}H- and ^{13}C-NMR spectra for compound **35**.

HPLC ANALYSES FOR PURITY

Compounds were analyzed for purity (HPLC) using a Agilent 1200 HPLC system equipped with Quat pump (G1311B), injector (G1329B) 1260 ALS, TCC 1260 (G1316A) and detector 1260 DAD VL + (G1315C). All compounds were >95 % pure. The HPLC analyses were performed in diverse systems:

Method A

Zorbax Eclipse Plus C18 4.6×150 mm, 1.8 µ, S.N. USWKY01594 was used as the stationary phase. The eluent was made from the following solvents: 0.2 % formic acid in water (A) and methanol (B). The analysis were performed at the UV max of the compounds (at 250 nm, 254 nm or 270 nm) to maximize selectivity. The compounds were dissolved in methanol; the final concentrations were ≈1 mg ml^{-1}. The flow rate was 0.5 ml min^{-1}.

Compounds **8**–**15**, **27**, **29**, **30** and **34** were eluted using the gradient protocol: 0 – 1 min 95 % A, 1 – 5 min 95 % A → 5 % A, 5 – 14 min 5 % A, 14 – 15 min 5% A → 95 % A, 15 – 16 min 95 % A.

Compounds **16**, **17**, **31**, **32** and **33** were eluted using the gradient protocol: 0 – 1.5 min 95 % A, 1.5 – 5 min 95 % A → 5 % A, 5 – 16 min 5 % A, 16 – 18 min 5 % A → 95 % A.

Compound **35** was eluted using gradient protocol: 0 – 1.5 min 50 % A, 1.5 – 3 min 50 % A → 30 % A, 3 – 6 min 30 % A → 0 % A, 6 – 9 min 0 % A → 50 % A, 9 – 12 min 50 % A.

Method B

Zorbax Eclipse Plus C18 4.6×150 mm, 1.8 µ, S.N. USWKY01594 was used as the stationary phase. The eluent was made from the following solvents: 0.2 % formic acid in water (A) and acetonitrile (B). The analyses were performed at the UV max of the compounds

to maximize selectivity. The compounds were dissolved in methanol; the final concentrations were ≈1 mg ml^{-1}. The flow rate was 0.5 ml min^{-1}.

Compounds **8 – 15**, **27**–**30** and **34** were eluted using the gradient protocol: 0 – 1 min 95 % A, 1 – 6 min 95 % A → 5 % A, 6 – 11 min 5 % A, 11 – 14 min 5 % A → 95 % A, 14 – 15 min 95 % A.

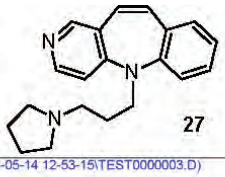
Compounds **31** and **32** were eluted using the gradient protocol: 0 – 1.5 min 95 % A, 1.5 – 5 min 95 % A → 5 % A, 5 – 16 min 5 % A, 16 – 18 min 5 % A → 95 % A, 18 – 21 min 95 % A.

Compounds **16**, **17**, **33** and **35** were eluted using the gradient protocol: 0 – 1.5 min 50 % A, 1.5 – 3 min 50 % A → 30 % A, 3 – 6 min 30 % A → 0 % A, 6 – 9 min 0 % A → 50 % A, 9 – 12 min 50 % A.

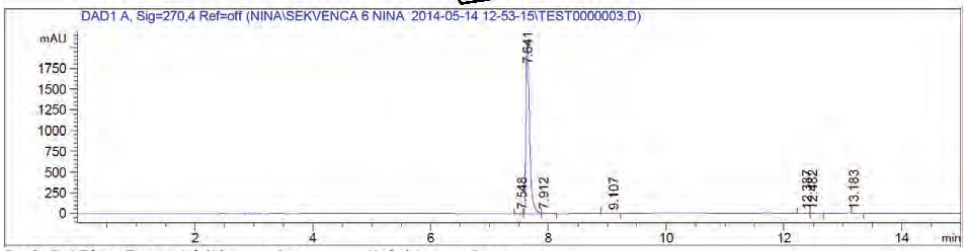
Method C

Zorbax Eclipse Plus C18 2.1 × 100 mm, 1.8 µ, was used as the stationary phase. The eluent was made from the following solvents: 0.2 % formic acid in water (A) and acetonitrile (B). The analysis was performed at the UV max of the compound to maximize selectivity. The compound was dissolved in methanol; the final concentrations were ≈1 mg ml^{-1}. The flow rate was 0.5 ml min^{-1}.

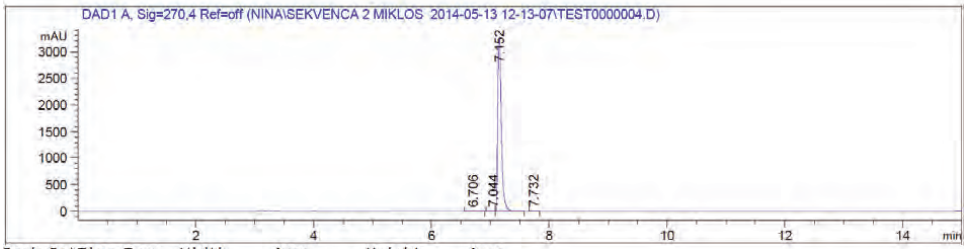
Compound **28** was eluted using gradient protocol: 0 – 1 min 95 % A, 1 – 6 min 95 % A→ 5 % A, 6 – 11 min 5 % A, 11 – 14 min 5 % A→ 95 % A, 14 – 15 min 95 % A.



27

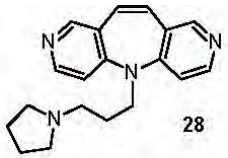


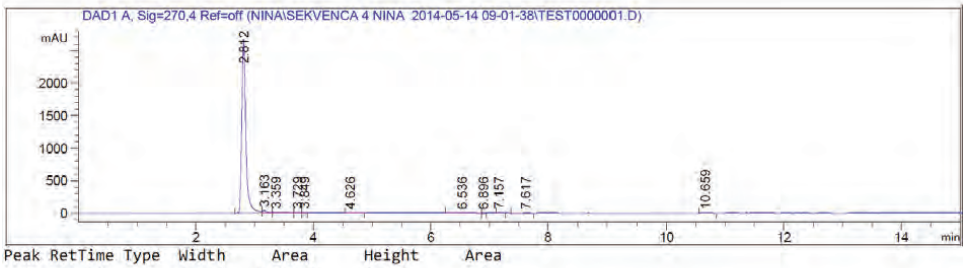
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.548	BV	0.0421	27.47963	9.67868	0.3071
2	7.641	VV	0.0643	8849.70117	2092.66846	98.8875
3	7.912	VB	0.0695	38.02967	7.71260	0.4249
4	9.107	BB	0.0676	8.57053	1.69131	0.0958
5	12.387	BV	0.0789	10.66416	1.63973	0.1192
6	12.482	VB	0.0758	8.40187	1.31871	0.0939
7	13.183	VB	0.0655	6.41428	1.18783	0.0717



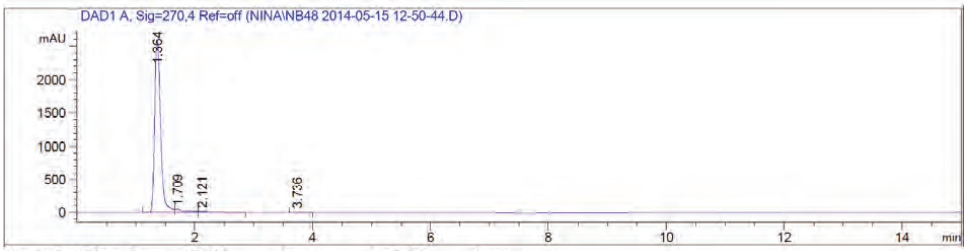
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.706	BB	0.1018	60.67188	8.06409	0.4295
2	7.044	BV	0.0583	17.64050	4.75640	0.1249
3	7.152	VB	0.0668	1.40376e4	3254.58472	99.3648
4	7.732	BB	0.0534	11.42744	3.18306	0.0809

Fig. S-18. HPLC elution profiles for compound **27**, upper method A and lower method B.



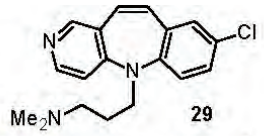


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.812	BV	0.0720	1.29263e4	2668.47119	96.7264
2	3.163	VV	0.0680	181.72783	36.25947	1.3599
3	3.359	VB	0.1323	77.69334	7.38394	0.5814
4	3.729	BV	0.0746	11.18529	1.79814	0.0837
5	3.849	VB	0.0528	13.06463	3.47869	0.0978
6	4.626	BB	0.0670	12.05556	2.26718	0.0902
7	6.536	BB	0.2034	70.80660	4.10196	0.5298
8	6.896	BV	0.0403	12.08752	4.57284	0.0904
9	7.157	VB	0.0537	30.49500	8.73818	0.2282
10	7.617	BB	0.1465	21.70231	1.85542	0.1624
11	10.659	BB	0.0706	6.65240	1.12362	0.0498

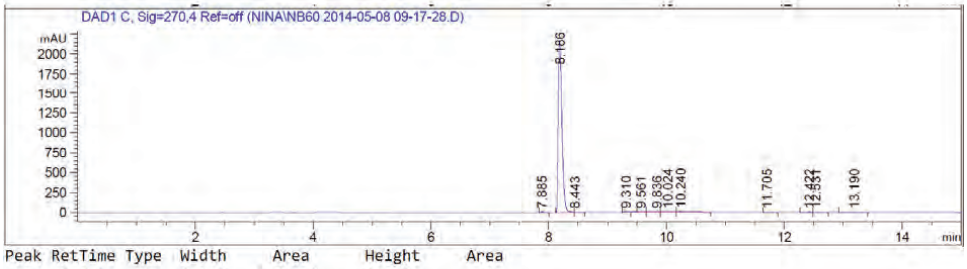


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	1.364	BV	0.1094	1.83442e4	2595.84497	96.1463
2	1.709	VV	0.1494	534.30261	46.38500	2.8004
3	2.121	VB	0.1905	181.87314	11.31421	0.9532
4	3.736	BB	0.1143	19.09738	1.97568	0.1001

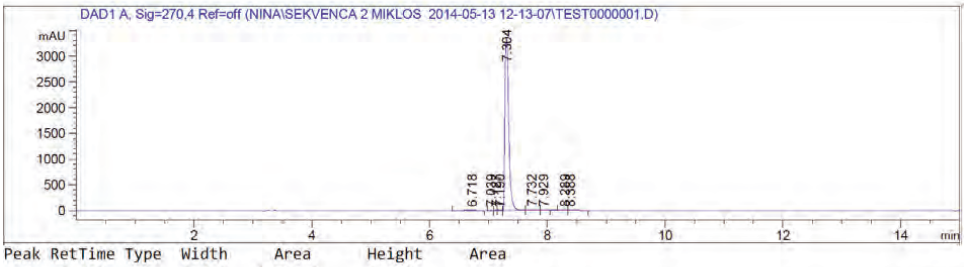
Fig. S-19. HPLC elution profiles for compound **28**, upper method B and lower method C.



29

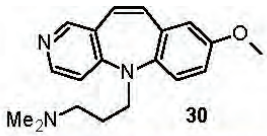


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.885	BB	0.0521	30.19774	8.46898	0.3108
2	8.186	BV	0.0686	9514.95703	2173.33716	97.9212
3	8.443	VB	0.0594	12.54330	2.71250	0.1291
4	9.310	VV	0.0665	15.16273	3.15939	0.1560
5	9.561	BB	0.0557	8.65833	2.33926	0.0891
6	9.836	BV	0.0888	10.26755	1.43848	0.1057
7	10.024	VV	0.1446	30.93267	2.65173	0.3183
8	10.240	VB	0.1266	49.72878	5.34056	0.5118
9	11.705	BB	0.0903	7.55613	1.07135	0.0778
10	12.422	BV	0.0827	12.88099	2.22059	0.1326
11	12.531	VB	0.0779	10.59624	1.65074	0.1090
12	13.190	BB	0.1318	13.47426	1.24490	0.1387

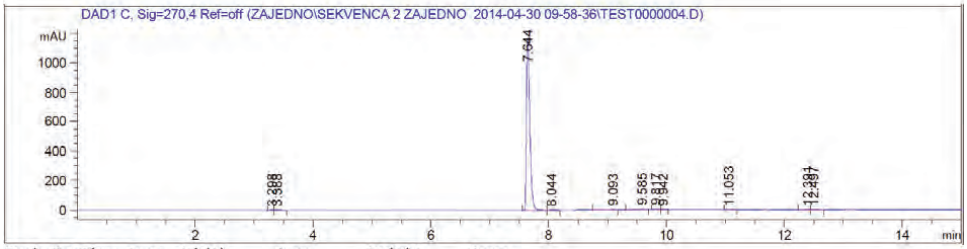


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.718	BB	0.1330	91.36644	8.49679	0.5849
2	7.039	BV	0.0464	9.06460	2.90784	0.0580
3	7.127	VV	0.0434	9.76251	3.31010	0.0625
4	7.190	VB	0.0506	12.45709	3.53889	0.0798
5	7.304	BV	0.0605	1.53765e4	3353.64990	98.4409
6	7.732	VV	0.1027	58.05438	7.46597	0.3717
7	7.929	VB	0.0614	25.94724	6.25671	0.1661
8	8.289	BV	0.0665	11.27498	2.34898	0.0722
9	8.388	VV	0.0794	25.60482	4.49576	0.1639

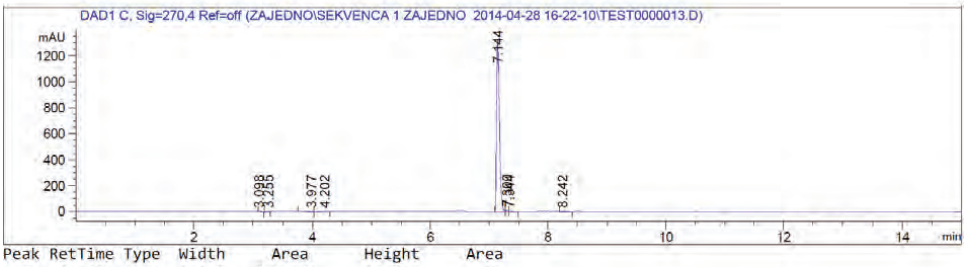
Fig. S-20. HPLC elution profiles for compound **29**, upper method A and lower method B.



30

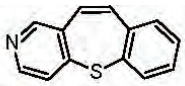


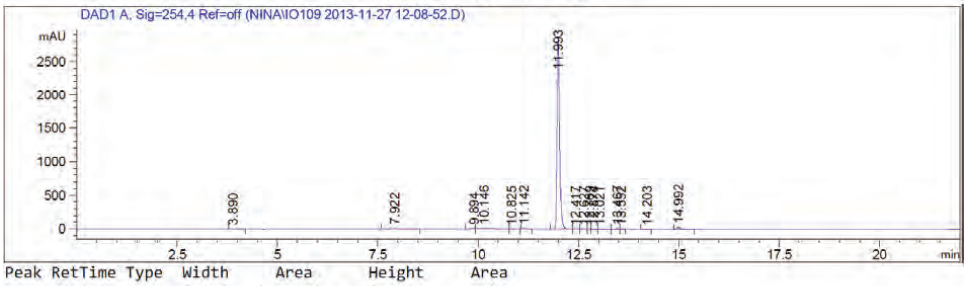
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.298	BV	0.0541	19.86989	4.44590	0.4148
2	3.388	VB	0.0957	25.92024	3.28044	0.5411
3	7.644	BB	0.0609	4654.91016	1170.44666	97.1709
4	8.044	BB	0.0542	9.56042	2.46893	0.1996
5	9.093	BV	0.0765	14.69546	2.54153	0.3068
6	9.585	BV	0.0967	21.04048	2.86450	0.4392
7	9.817	VV	0.0818	14.01601	2.18601	0.2926
8	9.942	VV	0.0729	7.21489	1.17937	0.1506
9	11.053	BB	0.0598	6.15833	1.36199	0.1286
10	12.391	BV	0.0779	9.03729	1.60000	0.1887
11	12.497	VB	0.0769	8.01088	1.24010	0.1672



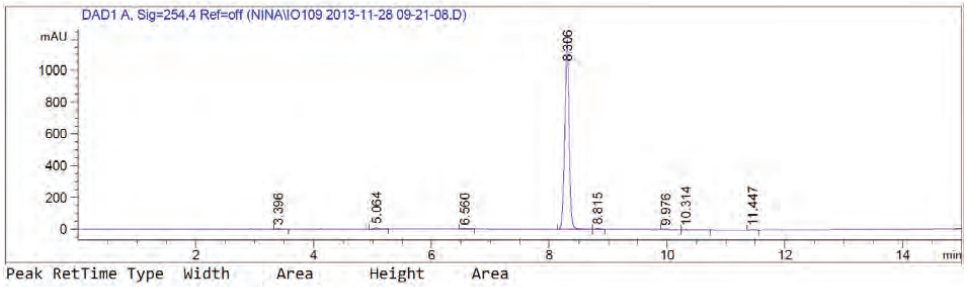
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.098	BB	0.2107	17.90455	1.00548	0.3835
2	3.255	BV	0.0575	31.74411	8.52148	0.6799
3	3.977	BB	0.1110	37.12119	4.31019	0.7951
4	4.202	BB	0.2120	24.82742	1.37625	0.5318
5	7.144	BV	0.0529	4503.91650	1332.61279	96.4647
6	7.300	VV	0.0456	28.15750	9.09036	0.6031
7	7.344	VB	0.0447	16.08459	5.32594	0.3445
8	8.242	VB	0.0552	9.22391	2.46256	0.1976

Fig. S-21. HPLC elution profiles for compound **30**, upper method A and lower method B.



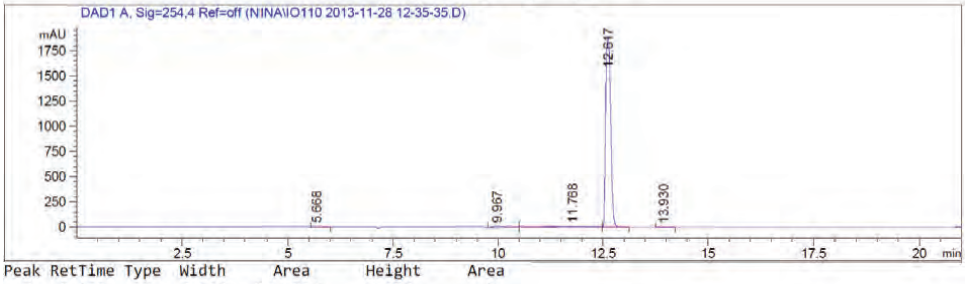


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.890	BB	0.1354	51.10493	4.46830	0.3845
2	7.922	BB	0.2849	89.93788	3.74178	0.6766
3	9.894	BV	0.0994	17.91653	2.14572	0.1348
4	10.146	VV	0.3010	158.23694	6.43204	1.1905
5	10.825	VB	0.0886	14.11954	2.01784	0.1062
6	11.142	BB	0.0718	47.00090	9.73345	0.3536
7	11.993	BV	0.0664	1.26492e4	2841.25220	95.1628
8	12.417	VB	0.0714	10.71146	2.07020	0.0806
9	12.627	BV	0.0756	13.77031	2.60825	0.1036
10	12.769	VV	0.0645	9.50805	1.83435	0.0715
11	12.874	VV	0.0792	21.27560	3.80838	0.1601
12	13.021	VB	0.0869	7.94873	1.23026	0.0598
13	13.467	BV	0.0704	33.00604	7.07205	0.2483
14	13.552	VV	0.0711	21.05645	4.30051	0.1584
15	14.203	BB	0.0792	6.62382	1.17682	0.0498
16	14.992	BB	0.0836	140.74380	25.42936	1.0588

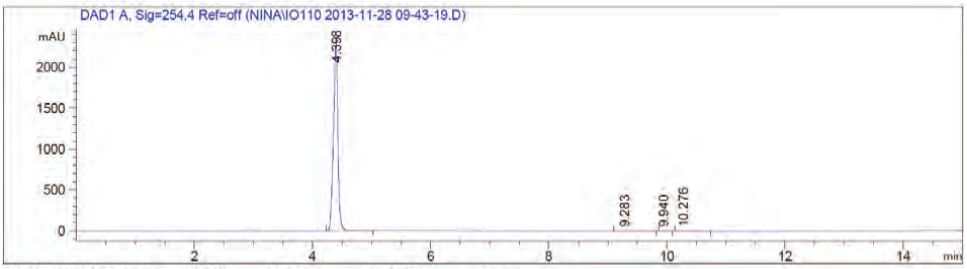


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.396	BB	0.0720	15.29431	3.13193	0.2476
2	5.064	BB	0.0776	40.54786	7.81269	0.6565
3	6.560	BB	0.0741	6.97794	1.30133	0.1130
4	8.306	BV	0.0744	6071.65381	1201.72729	98.3038
5	8.815	VB	0.0699	17.48453	3.67874	0.2831
6	9.976	BV	0.0849	8.77334	1.47549	0.1420
7	10.314	VB	0.1007	9.81294	1.31997	0.1589
8	11.447	BB	0.0769	5.87038	1.07236	0.0950

Fig. S-22. HPLC elution profiles for compound **16**, upper method A and lower method B.

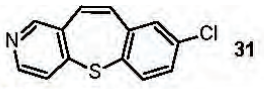


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.668	BB	0.1665	55.44031	3.93163	0.3390
2	9.967	BB	0.2480	212.26466	10.25258	1.2980
3	11.768	BV	0.8591	528.61047	7.19939	3.2324
4	12.617	VB	0.1346	1.55389e4	1886.19885	95.0201
5	13.930	BB	0.1145	18.06047	1.89800	0.1104

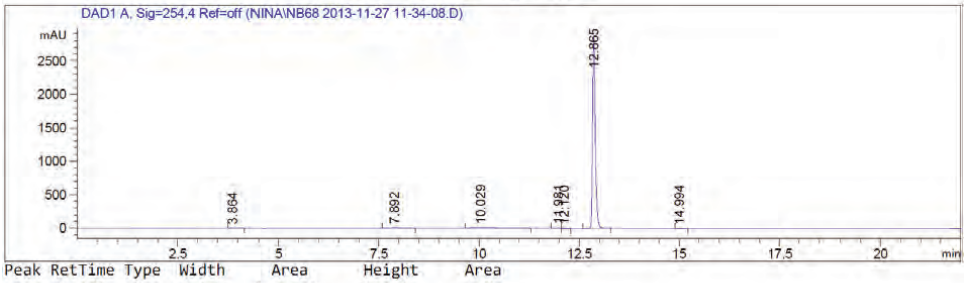


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.398	BB	0.0756	1.20603e4	2343.01733	99.5661
2	9.283	BB	0.1323	15.04413	1.34216	0.1242
3	9.940	BB	0.0625	6.53773	1.45172	0.0540
4	10.276	BB	0.1134	30.97738	3.47744	0.2557

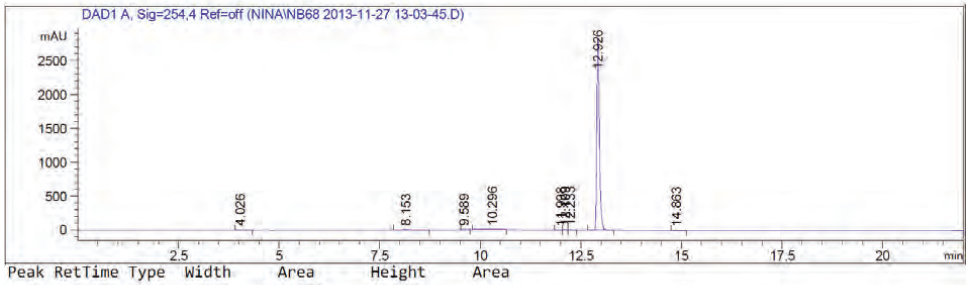
Fig. S-23. HPLC elution profiles for compound **17**, upper method A and lower method B.



31

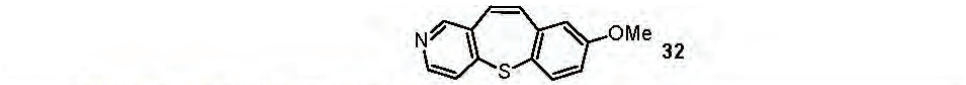


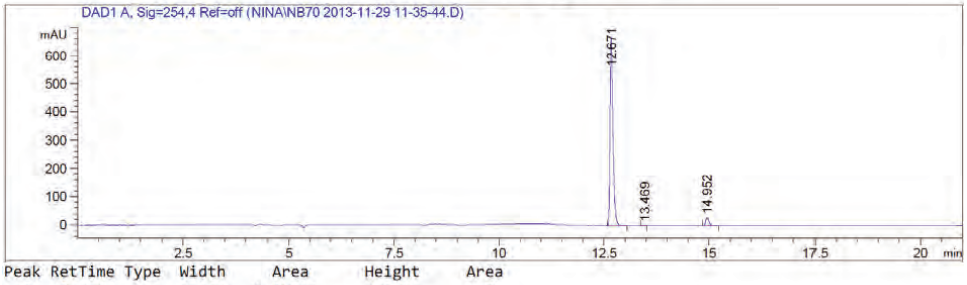
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.864	BB	0.1363	51.03075	4.51642	0.3738
2	7.892	BB	0.2642	83.32990	3.70753	0.6103
3	10.029	BB	0.5818	165.40530	3.33676	1.2115
4	11.981	BV	0.0749	48.58148	9.53649	0.3558
5	12.120	VB	0.0766	28.84962	5.55861	0.2113
6	12.865	BB	0.0702	1.32392e4	2847.47290	96.9678
7	14.994	BB	0.0845	36.79321	6.60021	0.2695



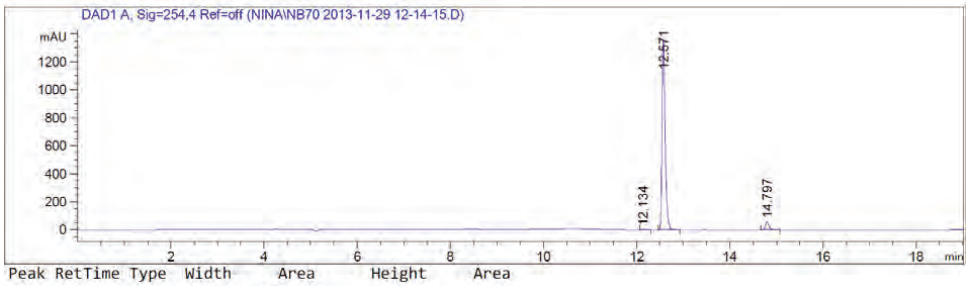
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.026	BB	0.1429	54.69809	4.53009	0.4222
2	8.153	BB	0.2723	87.95848	3.78935	0.6789
3	9.589	BB	0.0896	7.88486	1.05052	0.0609
4	10.296	BB	0.2664	62.62362	2.76284	0.4834
5	11.998	BV	0.0696	7.87534	1.45576	0.0608
6	12.109	VV	0.0690	44.50266	9.61065	0.3435
7	12.233	VB	0.0706	32.70956	6.51745	0.2525
8	12.926	BB	0.0676	1.26211e4	2826.88281	97.4177
9	14.863	BB	0.0809	36.30520	6.78889	0.2802

Fig. S-24. HPLC elution profiles for compound **31**, upper method A and lower method B.



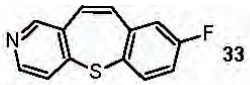


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.671	VB	0.0719	3203.70923	668.97974	95.0268
2	13.469	BV	0.0602	5.36811	1.07582	0.1592
3	14.952	BB	0.0843	162.29872	28.98040	4.8140

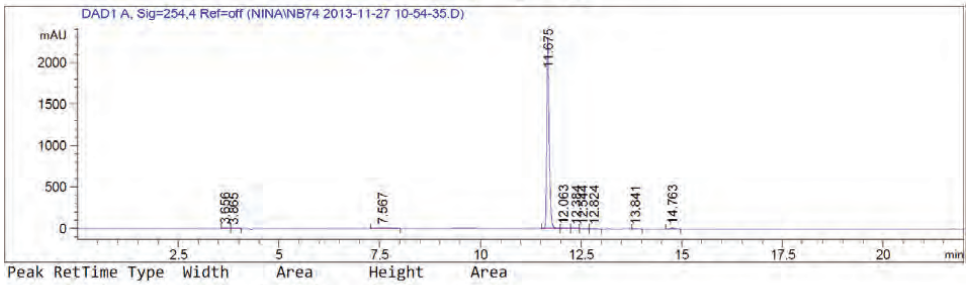


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.134	BB	0.0664	7.48816	1.63641	0.1128
2	12.571	VV	0.0695	6308.89600	1362.75183	95.0506
3	14.797	BB	0.0826	321.02032	58.44611	4.8365

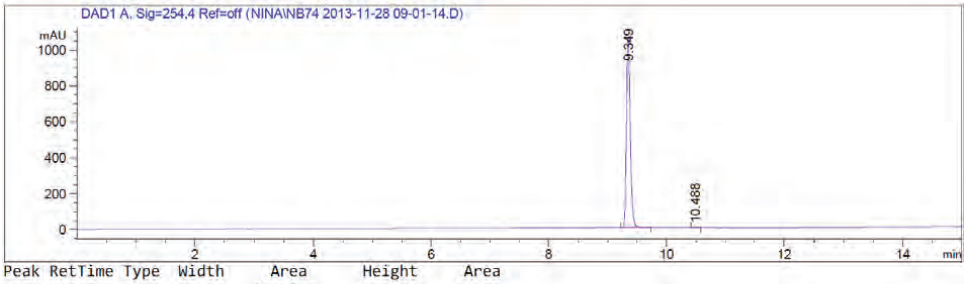
Fig. S-25. HPLC elution profiles for compound **32**, upper method A and lower method B.



33

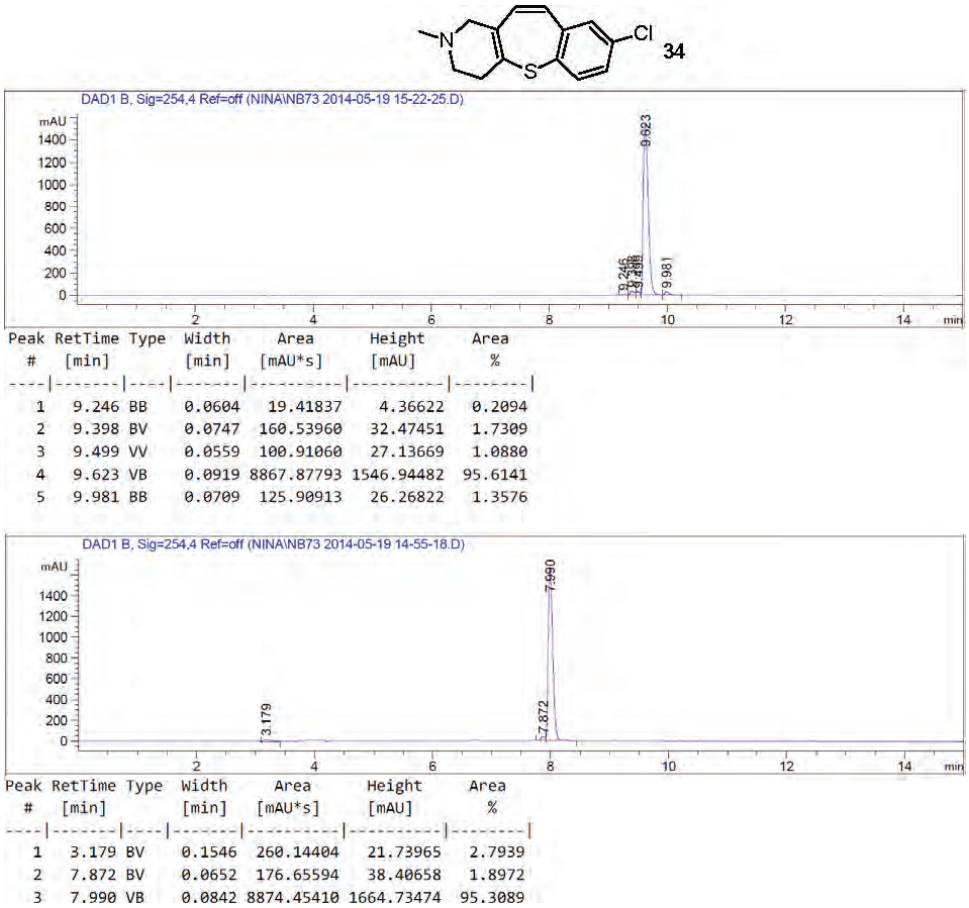


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.656	BV	0.1137	37.60769	4.07236	0.3791
2	3.865	VB	0.0988	15.03811	1.86089	0.1516
3	7.567	BB	0.2690	66.57471	2.90348	0.6711
4	11.675	VV	0.0635	9657.76074	2298.79932	97.3485
5	12.063	VB	0.0686	28.64441	6.06960	0.2887
6	12.384	BV	0.0865	7.78985	1.06921	0.0785
7	12.544	VB	0.0897	11.56906	1.54753	0.1166
8	12.824	BB	0.0816	12.90930	2.07346	0.1301
9	13.841	BB	0.0744	23.91412	4.90121	0.2411
10	14.763	BB	0.0788	59.00208	11.42182	0.5947



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.349	BB	0.0681	4770.22705	1057.27808	99.6944
2	10.488	BV	0.0546	14.62429	3.86562	0.3056

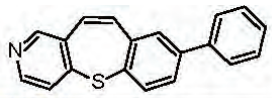
Fig. S-26. HPLC elution profiles for compound **33**, upper method A and lower method B.



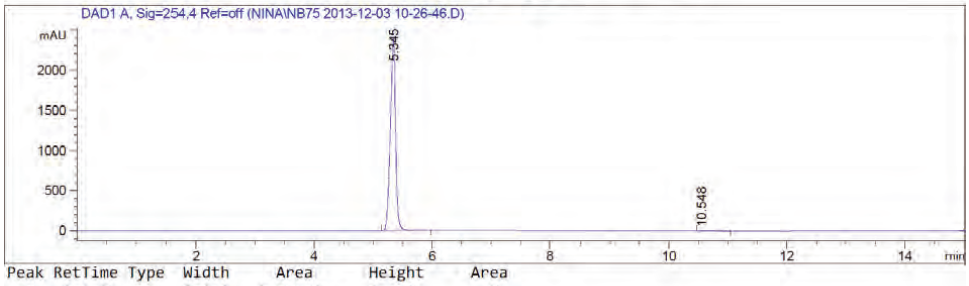
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.246	BB	0.0604	19.41837	4.36622	0.2094
2	9.398	BV	0.0747	160.53960	32.47451	1.7309
3	9.499	VV	0.0559	100.91060	27.13669	1.0880
4	9.623	VB	0.0919	8867.87793	1546.94482	95.6141
5	9.981	BB	0.0709	125.90913	26.26822	1.3576

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.179	BV	0.1546	260.14404	21.73965	2.7939
2	7.872	BV	0.0652	176.65594	38.40658	1.8972
3	7.990	VB	0.0842	8874.45410	1664.73474	95.3089

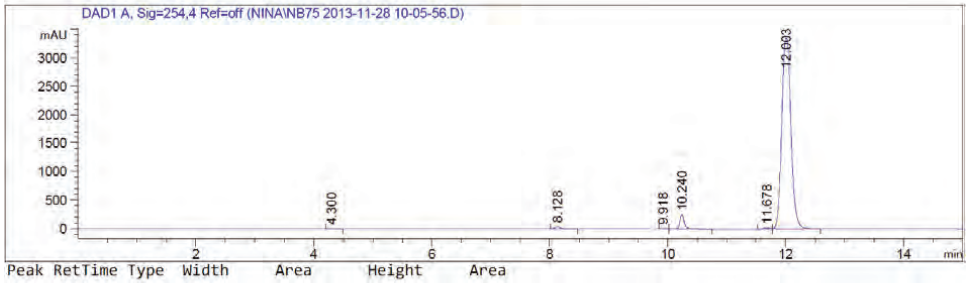
Fig. S-27. HPLC elution profiles for compound **34**, upper method A and lower method B.



35



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.345	BB	0.0900	1.47841e4	2396.31665	99.9182
2	10.548	BB	0.0798	12.10475	2.17994	0.0818



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.300	BB	0.0694	12.09601	2.45778	0.0320
2	8.128	BB	0.0751	189.58134	37.76797	0.5013
3	9.918	BB	0.0583	5.52080	1.30700	0.0146
4	10.240	BB	0.0742	1236.32520	249.91795	3.2690
5	11.678	BV	0.1044	136.08669	20.12759	0.3598
6	12.003	VB	0.1280	3.62400e4	3355.45898	95.8233

Fig. S-28. HPLC elution profiles for compound **35**, upper method A and lower method B.