Stereoselective tandem synthesis of thiazolo fused naphthyridines and thienopyridines from \( o \)-alkynylaldehydes via Au(III)-catalyzed regioselective \( 6\)-endo-\( dig \) ring closure

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General Method: $^1$H NMR (300 MHz, 400 MHz) and $^{13}$C NMR (75 MHz, 100 MHz) spectra were recorded in CDCl$_3$. Chemical shifts for carbons are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Data are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, dd = doublet of doublet), coupling constants in Hertz, and integration. High-resolution mass spectra were recorded on electrospray mass spectrometer. Crystal structure analysis was accomplished on single crystal X-ray diffractometer. TLC analysis was performed on commercially prepared 60 F$_{254}$ silica gel plates and visualized by either UV irradiation or by staining with I$_2$. All purchased chemicals were used as received. All melting points are uncorrected. The specific rotations were measured with Rudolph autopol II automatic polarimeter using light of 546 nm wavelength.

General Procedure for the Synthesis of $\omega$-Alkanylaldehyde $1a$–$o$, $2$, $3a$–$e$. The $\omega$-alkanyl aldehyde $1a$–$o$, $2a$–$e$ was readily prepared by coupling reaction of corresponding $\omega$-halo aldehyde with terminal alkynes using reported procedures.\textsuperscript{1} The structure and purity of known starting materials were confirmed by comparison of their physical and spectral data ($^1$H NMR, $^{13}$C NMR, and HRMS) with those reported in literature.

2-(Phenylethynyl)quinoline-3-carbaldehyde ($1a$).\textsuperscript{1a} The product was obtained as a white solid; $^1$H NMR (300 MHz, CDCl$_3$) $\delta$: 10.8 (s, 1H), 8.75 (s, 1H), 8.81 (d, $J$ = 8.4 Hz, 1H), 7.97 (d, $J$ = 8.1 Hz, 1H), 7.87 (td, $J$ = 1.5 Hz, 1H), 7.72–7.61 (m, 3H), 7.48–7.42 (m, 3H); $^{13}$C NMR (CDCl$_3$) $\delta$: 190.81, 150.18, 143.91, 137.17, 133.07, 132.33, 129.88, 129.68, 129.34, 128.84, 128.62, 128.26, 126.44, 121.35, 95.55, 85.55. HRMS Calcd for C$_{18}$H$_{11}$NO (M+H$^+$): 257.0841, found: 257.0852.
**2-(p-Tolylethynyl)quinoline-3-carbaldehyde (1b).**

The product was obtained as a white solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 10.78 (s, 1H), 8.71 (s, 1H), 8.15 (d, \(J = 8.7\) Hz, 1H), 7.91 (d, \(J = 8.1\) Hz, 1H), 7.85–7.79 (d, \(J = 8.4\) Hz, 1H), 7.60–7.53 (m, 3H), 7.19–7.15 (m, 2H), 2.34 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 190.9, 150.2, 144.1, 140.4, 137.1, 133.0, 132.3, 129.7, 129.4, 129.3, 128.8, 128.1, 126.4, 118.3, 96.0, 85.1, 21.7. HRMS Calcd for C\(_{19}\)H\(_{13}\)NO (M+H\(^+\)): 271.0997, found: 271.0979.

**2-((4-Ethylphenyl)ethynyl)quinoline-3-carbaldehyde (1c).**

This compound was obtained as a light brown solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 10.78 (s, 1H), 8.71 (s, 1H), 8.14 (d, \(J = 8.7\) Hz, 1H), 7.93 (d, \(J = 8.0\) Hz, 1H), 7.83 (t, \(J = 7.3\) Hz, 1H), 7.61–7.57 (m, 3H), 7.25–7.21 (m, 2H), 2.67 (q, \(J = 7.3\) Hz, 2H), 1.24 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 190.9, 150.1, 146.5, 144.1, 137.0, 132.9, 129.6, 129.2, 128.7, 128.1, 128.1, 126.3, 118.4, 96.0, 85.0, 28.9, 15.2. HRMS Calcd for C\(_{20}\)H\(_{15}\)NO (M+H\(^+\)): 285.1154, found: 285.1154.

**2-((4-Methoxyphenyl)ethynyl)quinoline-3-carbaldehyde (1d).**

The product was obtained as a orange solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 10.80 (s, 1H), 8.73 (s, 1H), 8.16 (d, \(J = 8.4\)Hz, 1H), 7.96–7.83 (m, 2H), 7.66–7.59 (m, 3H), 6.95–6.83 (m, 2H), 3.86 (s, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 190.9, 160.9, 150.2, 144.2, 137.0, 134.0, 132.9, 129.6, 129.2, 128.7, 128.0, 126.3, 114.3, 113.3, 96.1, 84.2, 55.4. HRMS Calcd for C\(_{19}\)H\(_{13}\)NO\(_2\) (M+H\(^+\)): 287.0946, found: 287.0951.
2-(Thiophen-3-ylethynyl)quinoline-3-carbaldehyde (1e).\textsuperscript{1a} The product was obtained as a white solid; $^1$H NMR (300 MHz, CDCl$_3$) δ: 10.78 (s, 1H), 7.97 (d, $J = 8.4$ Hz, 1H), 7.88 (t, $J = 1.5$ Hz, 1H), 7.79–7.78 (m, 1H), 7.63 (t, $J = 0.9$ Hz, 1H), 7.39–7.33 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 190.8, 150.2, 143.9, 137.2, 133.1, 131.6, 130.0, 129.7, 129.3, 128.8, 128.2, 126.4, 126.0, 120.5, 90.8, 85.4. HRMS Calcd for C$_{16}$H$_9$NOS (M+H$^+$): 263.0405, found: 263.0450.

2-((m-Tolylethynyl)quinoline-3-carbaldehyde (1f).\textsuperscript{1a} The product was obtained as an orange solid; $^1$H NMR (300 MHz, CDCl$_3$) δ: 10.81 (s, 1H), 8.74 (s, 1H), 8.17 (d, $J = 7.8$ Hz, 1H), 7.96 (d, $J = 8.1$ Hz, 1H), 7.87 (t, $J = 7.2$ Hz, 1H), 7.63 (t, $J = 7.2$ Hz, 1H), 7.51 (d, $J = 7.8$ Hz, 2H), 7.33–7.24 (m, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 190.9, 150.2, 144.0, 138.4, 137.1, 133.0, 132.9, 130.8, 129.7, 129.4, 129.3, 128.8, 128.5, 128.2, 126.4, 121.1, 95.9, 85.2, 21.2. HRMS Calcd for C$_{19}$H$_{13}$NO (M+H$^+$): 271.0997, found: 271.0970.

2-((3,5-Dimethoxyphenyl)ethynyl)quinoline-3-carbaldehyde (1g).\textsuperscript{1b} The product was obtained as an orange solid; $^1$H NMR (300 MHz, CDCl$_3$) δ: 10.8 (s, 1H), 8.76 (s, 1H), 8.18 (d, $J = 7.8$ Hz, 1H), 7.99–7.86 (m, 2H), 7.64 (t, $J = 7.3$ Hz, 1H), 6.85 (s, 2H), 6.56 (s, 1H), 3.83 (s, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$) δ: 190.9, 160.8, 150.3, 143.9, 137.3, 133.2, 129.8, 129.4, 128.9, 128.4, 126.6, 122.6, 110.1, 103.6, 95.6, 85.1, 55.7. HRMS (ESI) Calcd for C$_{20}$H$_{18}$NO$_3$ (M+H$^+$) 317.1052, found 317.1060.
2-(Cyclohexylethynyl)quinoline-3-carbaldehyde (1h). The product was obtained as a white solid; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 10.70 (s, 1H), 8.69 (s, 1H), 8.12 (d, \(J = 8.7\) Hz, 1H), 7.93 (d, \(J = 8.1\) Hz, 1H), 7.86–7.80 (m, 1H), 7.58 (td, \(J = 0.9\) and 7.9 Hz, 1H), 2.80–2.75 (m, 1H), 2.02–1.97 (m, 2H), 1.82–1.55 (m, 5H), 1.47–1.36 (m, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 191.4, 150.1, 144.6, 136.8, 132.8, 129.6, 129.2, 128.8, 127.9, 126.2, 102.0, 77.5, 32.1, 29.9, 25.7, 24.9. HRMS (ESI) Calcd for C\(_{18}\)H\(_{17}\)NO (M+H\(^+\)) 263.1310, found 263.1311.

2-(Cyclopropylethynyl)quinoline-3-carbaldehyde (1i). The product was obtained as a white solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 10.65 (s, 1H), 8.67 (s, 1H), 8.10 (s, 1H), 7.92–7.73 (m, 2H), 7.59 (s, 1H), 1.63–1.62 (m, 1H), 1.14–1.02 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 191.2, 150.1, 144.4, 136.8, 132.8, 129.6, 129.1, 128.8, 127.8, 126.2, 101.4, 72.8, 9.2, 0.4. HRMS (ESI) Calcd for C\(_{15}\)H\(_{11}\)NO (M+H\(^+\)) 221.0841, found 221.0842.

2-(Hex-1-yn-1-yl)quinoline-3-carbaldehyde (1j). The product was obtained as a yellow oil; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 10.68 (s, 1H), 8.68 (s, 1H), 8.11 (d, \(J = 8.4\) Hz, 1H), 7.93–7.80 (m, 2H), 7.61–7.56 (m, 2H), 2.59 (t, \(J = 7.2\) Hz, 2H), 1.73–1.66 (m, 2H), 1.57–1.47 (m, 2H), 0.97 (t, \(J = 7.2\) Hz, 3H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 191.0, 150.1, 144.5, 136.8, 131.8, 129.6, 129.2, 128.7, 127.9, 126.2, 98.1, 87.8, 30.2, 22.2, 19.4, 13.6. HRMS (ESI) Calcd for C\(_{16}\)H\(_{15}\)NO (M+H\(^+\)) 237.1154, found 237.1162.
2-((4-Nitrophenyl)ethynyl)quinoline-3-carbaldehyde (1k). The product was obtained as a yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) δ: 10.71 (s, 1H), 8.76 (s, 1H), 8.26 (d, $J = 8.8$ Hz, 2H), 8.17 (d, $J = 8.8$ Hz, 1H), 7.98 (d, $J = 8.0$ Hz, 1H), 7.91–7.87 (m, 1H), 7.83 (d, $J = 8.0$ Hz, 2H), 7.66 (t, $J = 8.0$ Hz, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 189.9, 150.0, 147.9, 142.4, 137.9, 133.4, 133.1, 132.6, 129.6, 129.4, 128.9, 128.8, 128.1, 126.6, 123.8, 92.3, 89.8. HRMS (ESI) Calcd for C$_{18}$H$_{10}$N$_2$O$_3$ (M+H$^+$) 302.0691, found 302.0692.

6-Methoxy-2-(phenylethynyl)quinoline-3-carbaldehyde (1l). The product was obtained as a yellow solid; $^1$H NMR (300 MHz, CDCl$_3$) δ: 10.78 (s, 1H), 8.61 (s, 1H), 8.06 (d, $J = 9.3$ Hz, 1H), 7.70–7.67 (m, 2H), 7.52–7.41 (m, 4H), 7.17 (d, $J = 2.7$ Hz, 1H), 3.96 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): 191.0, 159.0, 146.6, 141.5, 135.3, 132.2, 130.8, 129.7, 129.1, 128.6, 127.7, 126.3, 121.6, 106.2, 94.7, 85.6, 55.8. HRMS (ESI) Calcd for C$_{19}$H$_{13}$NO$_2$ (M+H$^+$) 287.0946, found 287.0947.

6-Methoxy-2-(m-tolylethynyl)quinoline-3-carbaldehyde (1m). This compound was obtained as a yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) δ: 10.78 (s, 1H), 8.61 (s, 1H), 8.07 (d, $J = 9.5$ Hz, 1H), 7.51–7.47 (m, 3H), 7.30–7.24 (m, 2H), 7.16 (d, $J = 2.2$ Hz, 1H), 3.95 (s, 3H), 2.37 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 191.0, 159.5, 146.4, 141.5, 138.3, 135.4, 132.8, 130.6, 129.3, 128.4, 127.8, 126.4, 121.1, 106.2, 85.1, 55.8, 21.2. HRMS (ESI) Calcd for C$_{20}$H$_{15}$NO$_2$ (M+H$^+$) 301.1103, found: 301.1103.
2-(Cyclopropylethynyl)-6-methoxyquinoline-3-carbaldehyde (1n).

The product was obtained as a yellow needles (DCM/Ether), mp: 181–182 °C: $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 10.6 (s, 1H), 8.45 (s, 1H), 7.91 (d, $J = 9.16$ Hz, 1H), 7.39 (d, $J = 8.24$ Hz, 1H), 7.04 (s, 1H), 3.88 (s, 3H), 1.57–1.53 (m, 1H), 0.95–0.93 (m, 4H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 191.3, 158.5, 146.3, 141.8, 134.9, 130.4, 128.8, 127.2, 126.0, 106.0, 100.2, 55.6, 9.0, 0.2. HRMS Calcd for C$_{16}$H$_{13}$NO$_2$ (M+H$^+$): 251.0946, found 251.0947.

6-Methyl-2-(phenylethynyl)quinoline-3-carbaldehyde (1o). $^{1d}$ The product was obtained as a yellow solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 10.80 (s, 1H), 8.65 (s, 1H), 8.07 (d, $J = 8.8$ Hz, 1H), 7.71–7.70 (m, 4H), 7.51–7.41 (m, 4H), 7.37–7.24 (m, 3H), 2.57 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 190.9, 148.9, 143.0, 138.6, 136.3, 135.5, 132.3, 129.7, 129.0, 128.9, 128.6, 128.3, 126.5, 121.5, 95.1, 85.6, 21.7. HRMS Calcd for C$_{19}$H$_{13}$NO (M+H$^+$): 271.0997, found 271.0998.

2-((4-tert-Butylphenyl)ethynyl)benzaldehyde (2). $^{1e}$ This compound was obtained as a off white solid; $^1$H NMR (400 MHz, CDCl$_3$) $\delta$: 10.65 (s, 1H), 7.93 (d, $J = 6.84$ Hz, 1H), 7.63–7.61 (m, 1H), 7.55 (t, $J = 6.88$ Hz, 1H), 7.51–7.49 (m, 2H), 7.43–7.38 (m, 3H), 1.33 (s, 9H); $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$: 191.6, 152.4, 135.7, 133.7, 133.1, 128.3, 127.1, 127.0, 125.5, 119.2, 96.6, 84.2, 34.8, 31.0. HRMS Calcd for C$_{19}$H$_{18}$O (M+H$^+$): 262.1358, found: 262.1359.
3-(Phenylethynyl)benzo[\(b\)]thiophene-2-carbaldehyde (3a).\(^{1a}\) This compound was obtained as a yellow brown solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 10.40 (s, 1H), 8.10–8.08 (m, 1H), 7.82 (d, \(J = 7.3\) Hz, 1H), 7.59–7.56 (m, 2H), 7.51–7.43 (m, 2H), 7.37–7.33 (m, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 180.9, 139.9, 137.5, 135.8, 128.4, 126.0, 125.3, 125.1, 124.2, 122.1, 121.5, 119.8, 118.3, 95.5, 77.0. HRMS Calcd for C\(_{17}\)H\(_{10}\)O (M+H\(^+\)): 262.0452, found: 262.0451

3-(\(p\)-Tolylethynyl)benzo[\(b\)]thiophene-2-carbaldehyde (3b). The product was obtained as a yellow needles (DCM/Ether), mp: 177–179 °C : \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 10.4 (s, 1H), 8.14 (d, \(J = 7.8\) Hz, 1H), 7.87–7.85 (m, 1H), 7.56–7.48 (m, 4H), 7.23 (d, \(J = 8.24\) Hz, 2H), 2.41 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 184.6, 143.0, 140.7, 139.6, 139.2, 131.8, 129.3, 128.8, 125.5, 125.1, 123.2, 118.7, 99.4, 80.0, 21.5. HRMS Calcd for C\(_{18}\)H\(_{12}\)O (M+H\(^+\)): 276.0609, found 276.0608.

3-((4-Methoxyphenyl)ethynyl)benzo[\(b\)]thiophene-2-carbaldehyde (3c):\(^{1f}\)

The product was obtained as a yellow solid; \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 10.43 (s, 1H), 8.12 (dd, \(J = 2.2, 8.1\) Hz, 1H), 7.85 (d, \(J = 7.3\) Hz, 1H), 7.57–7.49 (m, 4H), 6.93–6.91 (m, 2H), 3.84 (s, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 184.6, 160.6, 142.7, 141.1, 139.4, 133.5,
128.8, 128.3, 125.5, 125.1, 123.3, 114.3, 113.8, 99.4, 79.6, 55.4. HRMS Calcd for C_{18}H_{12}O_{2}SNa (M+Na\(^{+}\)): 315.0456, found: 315.0457.

3-(Thiophen-3-ylethynyl)benzo[b]thiophene-2-carbaldehyde (3d).\(^{1a}\) This compound was obtained as yellow solid; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)): \(\delta\) 10.41 (s, 1H), 8.12–8.10 (m, 1H), 7.86–7.84 (m, 1H), 7.69–7.67 (m, 1H), 7.53–7.48 (m, 2H), 7.37–7.35 (m, 1H), 7.28–7.27 (m, 1H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta\) 183.6, 143.0, 140.5, 138.9, 130.2, 129.3, 128.3, 127.0, 125.6, 125.1, 124.5, 122.8, 120.5, 93.6, 79.7. HRMS Calcd for C_{15}H_{8}OS (M+H\(^{+}\)): 268.0017, found 268.0017.

3-((4-(Trifluoromethyl)phenyl)ethynyl)benzo[b]thiophene-2-carbaldehyde (3e).\(^{1a}\) This compound was obtained as a dark brown solid; \(^{1}\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 10.40 (s, 1H), 8.09–8.07 (m, 1H), 7.84 (d, \(J = 7.3\) Hz, 1H), 7.69 (d, \(J = 8.0\) Hz, 2H), 7.62 (d, \(J = 8.8\) Hz, 2H), 7.53–7.45 (m, 2H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 184.1, 144.2, 141.0, 139.2, 132.2, 129.0, 126.6, 125.8, 125.60, 125.57, 124.9, 123.4, 97.1, 82.6. HRMS Calcd for C_{18}H_{9}F_{3}OS (M+H\(^{+}\)): 330.0326, found 330.0326.

**General procedure for the synthesis of Benzo[b] thiazolo[2,3-f][1,6]naphthyridine 5a–o.**

An oven-dried Schlenk tube with a Teflon screw valve was charged with 1.1 equiv of \(L(-)\) Cysteine methyl ester hydrochloride 4, EDC (2.0 mL), 0.5 mmol of the 2-alkynylaldehyde 1a–o, 2, 3a–e, and AuCl\(_3\) (10 mol %). The reaction mixture was heated to 80 °C until 2-alkynylaldehyde 1a–o, 2, 3a–e had been completely consumed (as determined by TLC) and was allowed to cool to room temperature. The reaction mixture was diluted with ethyl acetate.
(10 mL) and water (15 mL). Organic layer was concentrated under reduced pressure. The crude material so obtained was purified by column chromatography on silica gel.

(3S,12bR)-methyl 5-phenyl-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5a). The product was obtained as a yellow needles (DCM/Ether), mp: 177–179 °C; [α]D27.5 = -357.0 (c 0.1, MeOH). 1H NMR (400 MHz, CDCl3) δ: 8.23 (s, 1H), 8.08 (d, J = 8.8 Hz, 1H), 7.77 (d, J = 8.0 Hz, 1H), 7.74–7.71 (m, 2H), 7.67 (t, J = 8.0 Hz, 1H), 7.51 (t, J = 8.0 Hz, 1H), 7.39–7.37 (m, 4H), 6.39 (s, 1H), 4.29–4.27 (m, 1H), 3.82 (s, 3H), 3.36–3.32 (m, 1H), 3.12–3.08 (m, 1H); 13C NMR (100 MHz, CDCl3) δ: 172.0, 147.1, 142.5, 137.8, 132.2, 131.1, 129.8, 129.3, 128.9, 128.4, 127.7, 127.3, 126.9, 121.9, 96.4, 87.4, 67.4, 64.9, 52.7, 37.7. HRMS Calcd for C22H18N2O2S (M+H+): 374.1089, found 374.1088.

(3S,12bR)-methyl5-(p-tolyl)-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5b). The product was obtained as a yellow needles (DCM/Ether), mp: 173–175 °C; [α]D27 = -317.1 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 8.69 (s, 1H), 8.13 (d, J = 8.8 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.80 (td, J = 6.6 and 1.5 Hz, 1H), 7.57 (t, J = 8.0 Hz, 1H), 6.88–6.83 (m, 4H), 6.51 (s, 1H), 5.84 (s, 1H), 5.55 (td, J = 5.1 and 1.5 Hz, 1H), 3.69 (s, 3H), 3.54–3.49 (m, 1H), 3.32–3.27 (m, 1H), 2.17 (s, 3H); 13C NMR (100 MHz, CDCl3) δ: 193.3, 162.8, 161.9, 149.8, 136.5, 135.3, 134.8, 132.4, 131.7, 129.9, 129.8, 129.3, 129.2, 128.9, 127.8, 127.3, 127.2, 70.0, 52.6, 37.3, 21.0. HRMS Calcd for C23H20N2O2S (M+H+): 388.1245, found 388.1244.
(3S,12bR)-Methyl-5-(4-ethylphenyl)-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5c). The product was obtained as a yellow needles (DCM/Ether), mp: 155–157 °C; \([\alpha]_D^{27} = -289.6\) (c 0.1, MeOH): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.23 (s, 1H), 8.11–8.09 (m, 1H), 7.81–7.76 (m, 1H), 7.72–7.68 (m, 1H), 7.66–7.63 (m, 2H), 7.58 (d, \(J = 7.8\) Hz, 1H), 7.55–7.48 (m, 1H), 7.21–7.18 (m, 2H), 6.37 (s, 1H), 4.27 (t, \(J = 6.9\) Hz, 1H), 3.81 (s, 3H), 3.33–3.31 (m, 1H), 3.11–3.07 (m, 1H), 2.66 (q, \(J = 6.9\) Hz, 2H), 1.22 (t, \(J = 7.3\) Hz, 3H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 172.0, 146.1, 146.0, 137.8, 134.0, 132.2, 131.2, 130.4, 129.8, 128.8, 128.7, 127.5, 128.0, 127.7, 127.3, 126.9, 119.0, 67.4, 64.9, 52.7, 37.8, 28.9, 15.2. HRMS Calcd for C\(_{24}\)H\(_{22}\)N\(_2\)O\(_2\)S (M+H\(^+\)): 402.1402, found 402.1403.

(3S,12bR)-Methyl-5-(4-methoxyphenyl)-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5d). The product was obtained as a yellow needles (DCM/Ether), mp: 171–172 °C; \([\alpha]_D^{27} = -319.4\) (c 0.1, MeOH): \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\): 8.75 (s, 1H), 8.20 (d, \(J = 8.4\) Hz, 1H), 8.02 (d, \(J = 8.1\) Hz, 1H), 7.87 (t, \(J = 7.2\) Hz, 1H), 7.64 (t, \(J = 7.5\) Hz, 1H), 6.93 (d, \(J = 8.4\) Hz, 2H), 6.68–6.60 (m, 3H), 5.93 (s, 1H), 5.60 (t, \(J = 5.4\) Hz, 1H), 3.77 (s, 3H), 3.72 (s, 3H), 3.58–3.52 (m, 1H), 3.40–3.33 (m, 1H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\): 193.3, 162.8, 161.9, 158.5, 149.8, 135.4, 134.7, 131.7, 130.5, 130.0, 129.8, 129.2, 127.9, 127.4, 127.1, 113.6, 70.0, 55.1, 52.6, 36.8. HRMS Calcd for C\(_{23}\)H\(_{20}\)N\(_2\)O\(_3\)S (M+H\(^+\)): 404.1195, found 404.1195.
(3S,12bR)-Methyl-5-(thiophen-3-yl)-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5e). The product was obtained as a yellow needles (DCM/Ether), mp: 159–161 °C; [α]D = -276.7 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl₃) δ: 8.22 (d, J = 3.2 Hz, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.77–7.74 (m, 2H), 7.66–7.63 (m, 1H), 7.51–7.48 (m, 1H), 7.36–7.34 (m, 1H), 7.31–7.28 (m, 1H), 6.36–6.33 (m, 1H), 4.27–4.25 (m, 1H), 3.79 (s, 3H), 3.34–3.30 (m, 1H), 3.24–3.22 (m, 1H), 3.11–3.05 (m, 1H); 13C NMR (100 MHz, CDCl₃) δ: 172.0, 147.1, 142.6, 137.6, 131.2, 129.9, 129.8, 128.8, 127.6, 127.3, 126.9, 125.5, 121.1, 91.8, 87.1, 67.4, 64.8, 52.7, 37.7. HRMS Calcd for C₂₀H₁₆N₂O₂S₂ (M+H⁺): 380.0653, found 380.0654.

(3S,12bR)-Methyl-5-(m-tolyl)-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5f). The product was obtained as a yellow needles (DCM/Ether), mp: 172–174 °C; [α]D = -319.1 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl₃) δ: 8.24 (s, 1H), 8.10 (d, J = 7.68 Hz, 1H), 7.83–7.78 (m, 1H), 7.73–7.67 (m, 1H), 7.56–7.49 (m, 4H), 7.30–7.26 (m, 1H), 7.22–7.20 (m, 1H), 6.41 (s, 1H), 4.30 (t, J = 6.2 Hz, 1H), 3.84 (s, 3H), 3.38–3.34 (m, 1H), 3.14–3.09 (m, 1H), 2.37 (s, 3H); 13C NMR (100 MHz, CDCl₃) δ: 172.2, 147.1, 142.6, 138.1, 137.8, 134.0, 132.6, 131.1, 130.3, 129.7, 129.3, 128.8, 128.2, 127.6, 127.3, 126.9, 121.7, 96.7, 87.1, 67.4, 64.9, 52.7, 37.8, 21.0. HRMS Calcd for C₂₃H₂₀N₂O₂S (M+H⁺): 388.1245, found 388.1247.
(3S,12bR)-Methyl-3-(3,5-dimethoxyphenyl)-3,12-b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5g). The product was obtained as a yellow needles (DCM/Ether), mp: 179–182 °C; [α]D^27 = -325.1 (c 0.1, MeOH); 1H NMR (400 MHz, CDCl_3) δ: 8.16 (s, 1H), 7.99–7.97 (m, 1H), 7.68–7.66 (m, 1H), 7.59–7.55 (m, 1H), 7.44–7.40 (m, 2H), 6.80 (t, J = 2.28Hz, 1H), 6.74 (t, J = 2.28Hz, 1H), 6.40 (d, J = 2.28Hz, 1H), 6.28 (s, 1H), 4.19 (t, J = 5.96 Hz, 1H), 3.68 (s, 9H), 3.27–3.23 (m, 1H), 3.09–2.99 (m, 1H); 13C NMR (100 MHz, CDCl_3) δ: 168.0, 156.49, 156.46, 143.1, 133.7, 127.3, 125.8, 124.7, 123.6, 123.4, 123.0, 119.1, 105.9, 98.2, 92.3, 82.9, 63.4, 60.8, 51.4, 48.6, 33.7, 25.6. HRMS Calcd for C_{24}H_{22}N_{2}O_{4}S (M+H^+): 434.1300, found 434.1302.

(3S,12bR)-Methyl-5-cyclohexyl-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5h). The product was obtained as a yellow needles, mp: 161–163 °C; [α]D^27 = -301.3 (c 0.1, MeOH); 1H NMR (400 MHz, CDCl_3) δ: 8.37 (s, 0.5H)(minor), 8.13 (s, 1H)(major), 8.05–8.00 (m, 1.7H)(major + minor), 7.77–7.72 (m, 1.7H) (major + minor), 7.67–7.60 (m, 1.7H)(major + minor), 7.50–7.44 (m, 1.8H)(major + minor), 6.26 (s, 1H)(major), 6.08 (s, 0.5H)(minor), 4.27–4.23 (m, 1H)(major), 4.04–4.02 (m, 0.5H)(minor), 3.81 (s, 3H)(major), 3.79 (s, 1.5H)(minor), 3.48–3.43 (m, 0.5H)(minor), 3.31–3.27 (m, 1H)(major), 3.15–3.10 (m, 0.6H)(minor), 3.08–3.05 (m, 1H)(major), 2.74–2.69 (m, 1.6H)(major + minor), 1.98–1.92 (m, 3H)(major + minor), 1.79–1.76 (m, 3H)(major + minor), 1.67–1.62 (m, 3H)(major + minor); 13C NMR (100 MHz, CDCl_3) δ: 172.1, 171.5, 147.5, 146.9, 143.2, 143.1, 137.6, 133.8, 133.2, 133.2, 130.8, 130.1, 129.5, 128.8, 128.7, 127.6, 127.1, 126.9, 126.7, 102.7.
100.7, 79.1, 78.7, 68.6, 67.5, 65.7, 64.8, 52.7, 52.6, 38.7, 37.5, 32.0, 30.0, 29.9, 25.7, 25.0, 24.9. HRMS Calcd for C_{22}H_{24}N_{2}O_{2}S (M+H\(^{+}\)) : 380.1558, found 380.1559.

\[(3S,12bR)-\text{Methyl-5-cyclopropyl-3,12b-dihydro-2H-benzo[b] thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5i).}\]

The product was obtained as a yellow needles (DCM/Ether), mp: 162–165 °C; \([\alpha]_{D}^{27.5} = -275.0\) (c 0.1, MeOH): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.17 (s, 1H), 8.02 (d, \(J = 8.76\) Hz, 1H), 7.75 (d, \(J = 8.04\) Hz, 1H), 7.67–7.63 (m, 1H), 7.51–7.47 (m, 1H), 6.25 (s, 1H), 4.27 (t, \(J = 6.62\) Hz, 1H), 3.84 (s, 3H), 3.33–3.30 (m, 1H), 3.10–3.06 (m, 1H), 1.60–1.58 (m, 1H), 1.04–0.96 (m, 4H); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\): 172.0, 171.4, 147.5, 146.8, 142.9, 137.4, 134.0, 133.0, 132.9, 130.9, 130.2, 129.5, 128.6, 128.57, 127.6, 127.55, 127.1, 126.9, 126.6, 102.1, 100.2, 74.4, 74.0, 68.7, 67.4, 65.7, 64.8, 52.6, 52.57, 38.8, 37.6, 9.15, 9.1, 9.0, 8.8, 8.7, 0.4. HRMS Calcd for C\(_{19}\)H\(_{18}\)N\(_{2}\)O\(_{2}\)S (M+H\(^{+}\)) : 338.1089, found 388.1089.

\[(3S,12bR)-\text{Methyl-5-butyl-3,12b-dihydro-2H-benzo[b] thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (dr=67:33 (5j).}\]

The product was obtained as a yellow needles, mp: 161–163 °C; \([\alpha]_{D}^{27} = -301.3\) (c 0.1, MeOH): \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\): 8.29 (s, 0.5H)(minor), 8.08 (s, 1H)(major), 7.98–7.93 (m, 1.5H)(major + minor), 7.83–7.79 (d, \(J = 12.84\) Hz, 0.3H)(minor), 7.69–7.63 (m, 1.9H)(major + minor), 7.59–7.53 (m, 1.9H)(major + minor), 7.51–7.45 (m, 0.5H)(minor), 7.41–7.35 (m, 1.5H)(major + minor), 7.26–7.21 (m, 0.5H)(minor) 6.18 (s, 1H)(major), 5.97 (s, 0.4H)(minor), 4.19–4.16 (m, 1H)(major), 3.98–3.95 (m, 0.6H)(minor), 3.72–3.70 (m, 4.6H)(major + minor), 3.41–3.31 (m, 1H)(major), 3.24–3.19 (m, 1H)(major), 3.08–2.96 (m, 2H)(major + minor), 2.47–2.42 (q, \(J = 14.2\) Hz, 7.32 Hz 2.8H)(major + minor) 1.61–1.53(m, 2.42H)(major + minor).
1.45–1.34 (m, 2.5H) (major + minor), 0.87–0.84 (m, 4H) (major + minor); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 171.9, 171.3, 147.3, 146.7, 142.8, 137.4, 134.0, 132.8, 132.4, 130.9, 130.1, 129.4, 128.4, 127.4, 127.0, 126.8, 126.5, 124.8, 102.6, 98.8, 97.0, 78.9, 76.6, 67.2, 65.6, 64.6, 52.8, 52.5, 52.4, 38.7, 37.4, 30.0, 21.8, 19.3, 13.7, 13.4, 0.8.

HRMS Calcd for C$_{20}$H$_{22}$N$_2$O$_2$S (M+H$^+$): 354.1402, found 354.1401.

(3S,12bR)-Methyl-5-(4-nitrophenyl)-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-$f$][1,6]naphthyridine-3-carboxylate (5k). The product was obtained as a yellow needles (DCM/Ether), mp: 178–180 °C; $[\alpha]_D^{27.5}$ = -345.0 (c 0.1, MeOH); $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.16–8.11 (m, 4H), 7.84 (d, $J = 8.04$ Hz, 1H), 7.75–7.69 (m, 3H), 7.55 (t, $J = 7.32$ Hz, 1H), 6.91 (s, 1H), 6.38 (s, 1H), 4.83 (d, $J = 5.88$ Hz, 1H), 3.86 (s, 3H), 3.29–3.26 (m, 1H), 2.98–2.94 (m, 1H); $^{13}$C NMR (100 MHz, CDCl$_3$) δ: 170.2, 154.0, 149.1, 147.0, 145.2, 143.3, 132.1, 130.6, 130.5, 130.3, 129.5, 128.8, 128.2, 127.2, 99.9, 70.3, 68.1, 53.1, 37.2, 35.9. HRMS Calcd for C$_{22}$H$_{17}$N$_3$O$_4$S (M+H$^+$): 419.0940, found 419.0943.

(3S,12bR)-Methyl-10-methoxy-5-phenyl-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-$f$][1,6]naphthyridine-3-carboxylate (dr=67:33) (5l). The product was obtained as a yellow needles (DCM/Ether), mp: 179–181 °C; $[\alpha]_D^{27.5}$ = -355.0 (c 0.1, MeOH); $^1$H NMR (400 MHz, CDCl$_3$) δ: 8.25 (s, 0.5H) (minor), 8.07 (s, 1H) (major), 7.92 (t, $J = 9.16$ Hz, 1.64H) (major + minor), 7.66–7.64 (m, 2H) (major + minor), 7.60–7.58 (m, 1.2H) (major + minor), 7.33–7.29 (m, 5H) (major + minor), 7.28–7.24 (m, 1H) (major + minor), 6.99–6.96 (m, 1.5H) (major + minor), 6.30 (s, 1H) (major), 6.07 (s, 0.4H) (minor), 4.22 (t, $J = 7.08$ Hz, 1H) (major), 4.06–4.02 (m, 0.5H) (minor), 3.84 (s, 1.5H) (minor), 3.82 (m,
3H) (major), 3.75 (s, 3H) (major), 3.72 (s, 1.4H) (minor), 3.45–3.41 (m, 1H) (major + minor), 3.45–3.41 (m, 1H) (major + minor), 3.31–3.26 (m, 1H) (major + minor), 3.11–3.00 (m, 2H) (major + minor); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta: 169.2, 168.8, 155.7, 155.70, 141.2, 140.3, 137.0, 135.4, 131.0, 130.0, 129.4, 127.6, 127.4, 126.5, 125.5, 120.6, 120.0, 119.3, 102.4, 102.2, 93.0, 84.7, 65.8, 64.7, 63.0, 62.2, 58.9, 52.8, 49.9, 36.1, 35.1. HRMS Calcd for C\(_{23}\)H\(_{20}\)N\(_2\)O\(_3\)S (M+H\(^+\)): 404.1195, found 404.1195.

(3S,12\(b\)R)-Methyl-10-methoxy-5-(\(m\)-tolyl)-3,12b-dihydro-2\(H\)-benzo[\(b\)]thiazolo[2,3-\(f\)][1,6]naphthyridine-3-carboxylate (dr=62:38) (5m). The product was obtained as a yellow needles (DCM/Ether), mp: 173–175 °C; \([\alpha]\)\(_D\)^{27.5} = -319.0 (c 0.1, MeOH); \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta: 8.31\) (s, 0.6H)(minor), 8.12 (s, 1H)(major), 7.97 (t, \(J=9.16\)Hz 2H)(major + minor), 7.52–7.44 (m, 3.8H) (major + minor), 7.32–7.21 (m, 4.1H) (major + minor), 7.18–7.16 (m, 1.8H) (major + minor), 7.03–7.02 (m, 2H) (major + minor), 6.35 (s, 0.9H) (major), 6.13 (s, 0.6H) (minor), 4.27 (t, \(J=6.62\)Hz 1H) (major), 4.09 (t, \(J=5.8\)Hz 0.8H) (minor), 3.96–3.88 (m, 5.3Hz) (major + minor), 3.81–3.78 (m, 3.1H) (major + minor), 3.51–3.46 (m, 0.7H) (major), 3.36–3.32 (m, 1H) (major), 3.17–3.06 (m, 2.2H) (major + minor) 2.35–2.34(m, 5.4H) (major + minor); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta: 171.9, 171.5, 158.5, 158.3, 143.8, 43.1, 139.84, 139.82, 138.0, 137.97, 137.95, 133.7, 132.7, 132.5, 130.3, 130.2, 130.0, 129.9, 129.1, 128.2, 128.17, 128.1, 123.3, 122.5, 121.9, 121.8, 105.1, 104.9, 95.9, 94.1, 87.1, 86.6, 68.5, 67.4, 65.6, 64.9, 55.5, 55.4, 52.6, 52.5, 38.7, 37.8, 21.1. HRMS Calcd for C\(_{24}\)H\(_{22}\)N\(_2\)O\(_3\)S (M+H\(^+\)): 418.1351, found 418.1350.

The product was obtained as a yellow needles, mp: 161–163 °C; [α]D27 = -275.3 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 8.15 (s, 0.5H)(minor), 7.97 (s, 1H)(major), 7.82 (t, J=9.52Hz 1.8H)(major + minor), 7.24–7.18 (m, 1.8H) (major + minor), 6.90 (s, 2H) (major + minor), 6.13 (s, 1H) (major) 5.91 (s, 0.5H) (minor), 4.17 (t, J=6.6Hz 1H) (major ), 3.99 (t, J=6.2Hz 0.4H) (minor), 3.78–3.73 (m, 9H) (major + minor), 3.07–2.95 (m, 2H) (major + minor), 1.16–1.08 (m, 1.5H) (major + minor), 0.94–0.78 (m, 6.2H) (major + minor); 13C NMR (100 MHz, CDCl3) δ: 171.8, 171.4, 158.1, 157.9, 143.6, 142.8, 140.1, 140.0, 137.6, 133.2, 132.6, 130.0, 129.9, 129.6, 127.6, 122.9, 122.1, 105.0, 104.7, 100.9, 99.1, 74.2, 73.8, 68.6, 67.3, 65.6, 64.7, 55.3, 55.28, 53.3, 52.5, 52.4, 38.7, 37.5, 15.0, 8.8, 8.7, 8.6, 8.4, 0.3. HRMS Calcd for C20H20N2O3S (M+H+): 368.1195, found 368.1196.

(3S,12bR)-Methyl-10-methyl-5-phenyl-3,12b-dihydro-2H-benzo[b]thiazolo[2,3-f][1,6]naphthyridine-3-carboxylate (5o). The product was obtained as a yellow needles (DCM/Ether), mp: 177–179 °C; [α]D29 = -357.0 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 8.74 (s, 1H), 8.17 (d, J = 8.72 Hz, 1H), 7.84 (s, 1H), 7.77 (dd, J=6.8 and 1.8 Hz, 1H), 7.24–7.22 (m, 3H), 7.14–7.12 (m, 2H), 6.61 (s, 1H), 5.96 (s, 1H), 5.72–5.70 (m, 1H), 3.83 (s, 3H), 3.75–3.70 (m, 1H), 3.47–3.41 (m, 1H), 2.66 (s, 3H); 13C NMR (100 MHz, CDCl3) δ: 193.6, 162.8, 161.0, 137.3, 135.7, 135.4, 134.2, 134.0, 129.4, 128.7, 128.4, 128.2, 127.9, 127.0, 126.8, 69.8, 52.6, 37.8, 29.6, 21.5. HRMS Calcd for C23H20N2O2S (M+H+): 388.1245, found 388.1244.
(3S,10bR)-Methyl-5-(4-(tert-butyl)phenyl)-3,10b-dihydro-2H-thiazolo[2,3-a]isoquinoline-3-carboxylate (dr=55:45) (6). The product was obtained as a yellow needles, mp: 161–163 °C; [α]D27 = -299.3 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 7.54–7.39 (m, 1.1H)(major + minor), 7.31–7.27 (m, 0.7H) (major + minor), 7.24–7.13 (m, 0.5H) (major + minor), 6.18 (s, 0.12H) (major), 5.96–5.92 (m, 0.2H) (major + minor), 4.20–4.17 (m, 0.18H ) (major), 3.94–3.85 (m, 0.16H ) (minor), 3.72–3.69 (m, 1H) (major), 3.42–3.35 (m, 0.4H) (major + minor), 3.28–3.24 (m, 0.24H)(minor), 3.07–2.99 (m, 0.52H) (major + minor), 1.24 (s, 2.1H) (major + minor), 1.17–1.09 (m, 0.7H) (major + minor); 13C NMR (100 MHz, CDCl3) δ: 171.1, 171.0, 170.6, 170.5, 150.8, 150.7, 143.4, 140.4, 140.6, 138.6, 136.6, 132.1, 132.0 131.4, 130.3, 130.2, 129.0, 127.9, 127.6, 127.4, 127.3, 127.2, 127.0, 126.5, 126.2, 125.9, 124.4, 124.3, 123.7, 123.0, 122.2, 121.7, 120.8, 119.1, 119.0, 96.1, 94.5, 85.6, 85.1, 69.1, 69.2, 68.5, 67.7, 64.9, 64.8, 64.5, 64.4, 64.1, 64.0,39.2, 38.2, 37.9, 36.9, 36.4, 33.8, 30.9, 30.2, 28.7, 27.3, 14.2. HRMS Calcd for C23H25NO2S (M+H+): 379.1606, found 379.1606.

3-(4-(tert-Butyl)phenyl)isoquinoline (7). This compound was obtained as a off white solid; 1H NMR (300 MHz, CDCl3) δ: 9.25 (s, 1H), 8.00–7.97 (m, 3H), 7.90 (d, J = 8.10 Hz, 1H), 7.79 (d, J = 8.4 Hz, 1H), 7.60 ( t, J = 7.2 Hz, 1H), 7.52–7.45 (m, 3H), 1.31 (s, 9H); 13C NMR (75 MHz, CDCl3) δ: 151.3, 150.6, 150.3, 135.8, 135.7, 129.4, 126.6, 126.5, 125.8 (2C), 125.6, 124.7, 115.0, 33.6, 30.3. HRMS Calcd for C19H19N (M+H+): 261.1517, found: 261.1519.
(3S,11bR)-Methyl-5-phenyl-3,11b-dihydro-2H-benzo[4,5]thieno[2,3-c]thiazolo[3,2-a]pyridine-3-carboxylate (66:34) (8a). The product was obtained as a yellow needles, mp: 161–163 °C; [α]D31 = -301.3 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 7.89–7.84 (m, 1.8H)(major + minor), 7.71–7.66 (m, 1.8H) (major + minor), 7.56–7.53 (m, 4.0H) (major + minor), 7.36–7.24 (m, 9.2H) (major + minor), 6.32 (s, 1H) (major), 6.12 (s, 0.6H) (minor), 4.29 (t, J=6.64Hz, 1H ) (major), 3.97 (t, J=3.64Hz, 0.5H ) (minor), 3.71–3.70 (m 5.04H) (major + minor), 3.43–3.39 (m, 1.1H) (major + minor), 3.16–3.06 (m, 2.03H) (major + minor); 13C NMR (100 MHz, CDCl3) δ: 171.7, 170.8, 152.7, 146.0, 139.9, 139.4, 137.5, 137.2, 131.5, 131.4, 128.5, 128.4, 128.2, 125.5, 124.9, 124.6, 123.1, 122.9, 122.7, 122.4, 122.3, 117.1, 114.6, 97.2, 96.8, 81.8, 81.2, 66.0, 65.6, 64.5, 64.3, 52.54, 52.50, 39.0, 37.5. HRMS Calcd for C21H17NO2S2 (M+H+): 379.0701, found 379.0703.

(3S,11bR)-Methyl-5-(p-tolyl)-3,11b-dihydro-2H-benzo[4,5]thieno[2,3-c]thiazolo[3,2-a]pyridine-3-carboxylate (dr=59:41) (8b). The product was obtained as a yellow needles, mp: 162–164 °C; [α]D31 = -312.3 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 8.03–7.98 (m, 1.9H)(major + minor), 7.84–7.79 (m, 1.9H) (major + minor), 7.60–7.57 (m, 3.9H) (major + minor), 7.49–7.38 (m, 3.8H) (major + minor), 7.23 (d, J = 7.32 Hz, 4H) (major + minor), 6.46 (s, 1H) (major), 6.26 (s, 0.7H) (minor), 4.42 (t, J=6.6Hz, 1H ) (major), 4.09 (t, J=8.04Hz 0.7H ) (minor), 3.82 (s, 5.8H ) (major + minor), 3.54–3.52 (m, 1.44H) (major + minor), 3.27–3.19 (m, 1.8H) (major + minor), 2.41 (s, 5.4H) (major + minor); 13C NMR (100 MHz, CDCl3) δ: 171.6, 170.8, 152.2, 145.6, 139.8, 138.5, 138.4, 519
137.4, 137.1, 131.3, 131.2, 128.9, 125.4, 124.7, 122.9, 122.5, 122.3, 122.1, 119.7, 119.5, 117.1, 114.7, 80.5, 65.9, 65.5, 64.4, 64.2, 52.3, 38.8, 37.4, 21.2, 20.7.

HRMS Calcd for C22H19NO2S2 (M+H+): 393.0857, found 393.0855.

(3S,11bR)-Methyl-5-(4-methoxyphenyl)-3,11b-dihydro-2H-benzo[4,5]thieno[2,3-c]thiazolo[3,2-a]pyridine-3-carboxylate (dr=60:40) (8c). The product was obtained as a yellow needles, mp: 167–169 °C; [α]D27 = -311.3 (c 0.1, MeOH):

1H NMR (400 MHz, CDCl3) δ: 7.96–7.90 (m, 1H)(major + minor), 7.81–7.74 (m, 1.1H) (major + minor), 7.57–7.53 (m, 1.9H) (major + minor), 7.46–7.26 (m, 2.2H) (major + minor), 6.93–6.90 (m, 2H) (major + minor), 6.40 (s, 0.5H) (major), 6.19 (s, 0.34H) (minor), 4.41–4.37 (m, 0.5H ) (major + minor), 4.08–4.03 (m, 0.56H ) (major + minor) 3.84–3.81 (m, 5.95H ) (major + minor), 3.53–3.44 (m, 1.2H) (major + minor), 3.24–3.14 (m, 1.1H) (major + minor) ; 13C NMR (100 MHz, CDCl3) δ: 171.9, 171.0, 159.9, 159.8, 151.9, 145.3, 140.0, 139.6, 137.7, 137.4, 133.2, 133.1, 125.6, 125.0, 124.95, 124.7, 123.3, 122.9, 122.6, 122.4, 117.7, 115.2, 115.0, 114.1, 97.4, 97.0, 85.6, 80.1, 66.3, 65.9, 64.7, 64.6, 55.3, 52.7, 52.6, 39.2, 37.7 . HRMS Calcd for C22H19NO3S2 (M+H+): 409.0806, found 409.0806.


1H NMR (400 MHz, CDCl3) δ: 7.95–7.89 (m, 1.9H)(major + minor), 7.78–7.74 (m, 2H) (major + minor),
7.43–7.40 (m, 4H) (major + minor), 7.34–7.31 (m, 1H) (major + minor), 7.27–7.24 (m, 1H) (major + minor), 7.16 (d, J=5.84 Hz, 1H) (major + minor), 6.38 (s, 1H) (major), 6.17 (s, 0.35H) (minor), 4.38–4.36 (m, 1H) (major + minor), 4.06–4.02 (m, 0.4H) (major + minor), 3.80–3.79 (m, 4.2H) (major + minor), 3.50–3.47 (m, 1H) (major + minor), 3.16 (d, J=5.84 Hz, 1H) (major + minor), 2.92 (t, J=5.92 Hz, 1H) (major + minor), 2.36 (t, J=7.8 Hz, 0.5H) (minor), 2.17 (m, 4.5H) (major + minor), 1.96 (m, 1.2H) (major + minor), 1.71–1.07 (m, 1.9H) (major + minor); 13C NMR (100 MHz, CDCl3) δ: 171.9, 171.1, 152.5, 145.9, 140.0, 139.6, 139.2, 138.1, 137.7, 137.4, 132.5, 132.2, 132.1, 130.5, 129.5, 129.4, 129.0, 128.8, 128.7, 128.5, 128.3, 125.6, 125.0, 124.8, 123.3, 122.9, 122.8, 122.6, 122.4, 117.3, 114.8, 114.0, 97.5, 97.1, 81.5, 81.0, 66.2, 65.8, 64.6, 64.5, 52.7, 52.6, 39.2, 37.7. HRMS Calcd for C19H15NO2S3 (M+H+): 385.0265, found 385.0266.

(3S,11bR)-Methyl-5-(4-(trifluoromethyl)phenyl)-3,11b-dihydro-2H-benzo[4,5]thieno[2,3-c]thiazolo[3,2-a]pyridine-3-carboxylate (dr=50:50) (8e). The product was obtained as a yellow needles, mp: 161–163 °C; [α]D 27 = -301.3 (c 0.1, MeOH): 1H NMR (400 MHz, CDCl3) δ: 7.86–7.81 (m, 1.9H) (major + minor), 7.71–7.66 (m, 1.9H) (major + minor), 7.63–7.61 (m, 3H) (major + minor), 7.55–7.53 (m, 3H) (major + minor), 7.38–7.24 (m, 4H) (major + minor), 6.31 (s, 1H) (major), 6.11 (s, 0.5H) (minor), 4.29 (t, J=5.92 Hz, 1H) (major + minor), 3.99 (t, J=7.8 Hz, 0.5H) (minor), 3.72 (m, 4.5H) (major + minor), 3.42–3.41 (m, 1.2H) (major + minor), 3.17–3.07 (m, 1.9H) (major + minor); 13C NMR (100 MHz, CDCl3) δ: 171.8, 170.9, 154.2, 147.4, 139.7, 139.2, 137.5, 137.2, 131.7, 131.6, 126.8, 126.4, 125.6, 125.2, 125.1, 125.0, 124.8, 122.9, 122.52, 122.50, 122.3, 116.3, 113.9, 95.8, 95.3, 84.3, 83.7, 66.0, 65.7, 64.5, 64.2, 52.5, 39.0, 37.5. HRMS Calcd for C22H16F3NO2S2 (M+H+): 447.0575, found 447.0574.
Results: The relative configuration of the new stereogenic center at H\textsubscript{b} in product 5a was determined by NOESY experiments.\textsuperscript{1}H NMR spectra of 5a show that H\textsubscript{b} appears at 6.39 as a singlet and H\textsubscript{a} at 4.29–4.27 as multiplet. No distinct NOE effect was observed between H\textsubscript{b} and H\textsubscript{a} in compound 5a. This suggested that H\textsubscript{b} and H\textsubscript{a} are located in \textit{trans}-orientation.
References:


Copies of $^{1}H$ NMR, $^{13}C$ NMR

$^{1}H$ NMR

$^{13}C$ NMR
$^{13}$C NMR

![Carbon NMR spectrum of compound 1a]

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
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$^1$H NMR

![NMR spectrum](image)

1c
$^{13}$C NMR

![NMR spectrum of 1c](image-url)
\[ ^1H \text{NMR} \]

![NMR spectrum diagram](image)

**1d**
$^{13}$C NMR

![Chemical Structure](image)

**1d**

![NMR Spectrum](image)
\(^1\text{H NMR}\)

![NMR Spectrum](image)

S32
$^{13}$C NMR

![Carbon-13 NMR spectrum](image)
$^{1}$H NMR

If

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$^{13}$C NMR
\(^1\text{H NMR}\)

![NMR Spectrum](image)

\(1g\)
$^{13}$C NMR

![Carbon NMR Spectrum](image)

$^{13}$C NMR spectrum of compound 1g.
$^1$H NMR

![Chemical structure](image)

$1h$
$^{13}$C NMR

1h
$^1H$ NMR

![NMR Spectrum](image)

$lj$
$^{13}\text{C NMR}$

![Carbon NMR spectrum](image)
\(^1\text{H NMR}\)

![NMR spectrum image]

**1k**
$^{13}$C NMR

1k
\(^1\)H NMR

![NMR Spectrum](image)

**II**
$^{13}$C NMR

MeO

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$^1$H NMR

MeO

O

1m

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\(^{13}\text{C}\) NMR

1m
$^1$H NMR

1n

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**$^{13}$C NMR**

![Carbon NMR Spectrum](image)

**1n**
$^1$H NMR
$^{13}$C NMR

![13C NMR spectrum](image-url)
$^1$H NMR

![NMR Spectrum]

The spectrum shows distinct peaks at various chemical shifts, indicating the presence of different functional groups and protons in the compound. The specific shifts and integrals are essential for structural elucidation.
$^{13}$C NMR

[Chemical structure image]

2
$^1$H NMR

3a
$^{13}$C NMR

3a
$^{1}H$ NMR

3b
$^{13}\text{C NMR}$

![13C NMR spectra](image)

3b
$^1$H NMR

![](image)
$^{13}$C NMR

![Chemical Structure](image)

3c
$^1$H NMR

3d
$^{13}$C NMR

![Chemical structure diagram]

3d
$^1$H NMR

3e
$^{13}$C NMR
$^1$H NMR

5a
$^{13}$C NMR

5a
**$^{13}$C NMR**

![Carbon-13 NMR spectrum of compound 5b](Image of the NMR spectrum)
\[ ^1H \text{NMR} \]

\[ \text{5c} \]
$^{13}$C NMR

5c
\(^1\text{H NMR}\)

5d
$^{13}$C NMR

5d
$^1$H NMR

5e
$^{13}$C NMR

5e
$^1$H NMR

5f
$^1$H NMR

5g
$^{13}$C NMR

5g
$^1$H NMR
$^1$H NMR

5i
$^{13}$C NMR

5i

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$^1$H NMR
$^{13}$C NMR

![NMR spectrum image]

5j
$^1$H NMR

5k

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$^{13}$C NMR

5k
$^1$H NMR
$^1$H NMR
$^{13}$C NMR

5m
$^1$H NMR

5n
$^1$H NMR

5o
$^1$H NMR
$^{13}$C NMR

![Carbon-13 NMR Spectrum](image)
$^1$H NMR

8a
$^{13}$C NMR

8a
\(^1\text{H NMR}\)

8b

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$^1$H NMR

![NMR Spectrum](image_url)

8c
$^{13}$C NMR

8c
\(^1\)H NMR

8d
$^{13}$C NMR

8d
$^1$H NMR

8e
$^{13}$C NMR

8e
NOESY

5a (S, R isomer)

5a (expanded form)
(Full View of NOESY Spectra of Compound 5a)