SUPPORTING INFORMATION

**TRIFLIC ANHYDRIDE—A MILD REAGENT FOR HIGHLY EFFICIENT
SYNTHESIS OF 1,2-BENZISOXAZOLES, ISOXAZOLO AND ISOTHIAZOLO
QUINOLINES WITHOUT ADDITIVE OR BASE**

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EXPERIMENTAL (GENERAL)

The reagents employed were of high purity commercial samples which were used as received (Fischer, Merck and Sigma Aldrich). Reactions were carried out in oven-dried RB flask. Column chromatography was performed on silica gel (200-400 mesh). TLC was performed on alumina silica gel 60F₂₅₄ (Fischer) detected by UV light (254 nm) and iodine vapors. The melting points were determined by open capillaries on a Buchi apparatus and are uncorrected. The IR spectra were recorded on a Nicolet-Impact-410 FT-IR spectrometer, using KBr pellets. ¹H NMR and ¹³C NMR spectra were recorded on a Bruker AC-300F, 300 MHz, spectrometer in DMSO-*d*₆ using TMS as an internal standard with ¹H resonance frequency of 300 MHz, ¹³C resonance frequency of 75 MHz. GC analyses were performed on Nucon 5700 series Gas chromatograph. GC-MS analyses were performed on Shimadzu 2010 series mass selective detector instrument. Elemental analysis was carried out by using Heraeus CHN rapid analyzer. All the compounds gave C, H and N analysis within $\pm 0.4\%$ of the theoretical values. Dry DCM and EDC were obtained from commercial source by the standard procedure.^[27]

Typical procedure for the synthesis of 1,2-benzisoxazole using triflic anhydride

The desired 2-hydroxyaryl aldoxime or ketoxime (2.0 mmol) in 5 mL dry DCM was taken in an oven-dried RB flask. To the reaction mixture was added drop wise triflic anhydride (2.0 mmol) in DCM under nitrogen for 15 minutes. The reaction mixture was stirred at RT and the progress of the reaction was monitored by TLC and GC-MS (Table 1). After completion of reaction, the contents were poured to crushed ice (100 mL) and neutralized with 10% NaHCO₃ solution (20 mL) and extracted with DCM (30-40 mL). The pure products were obtained by column chromatography with hexane-ethyl acetate mixture (80:20). All the 1,2-benzisoxazole derivatives were characterized by GC-MS, ¹H, ¹³C NMR and by elemental analysis and the results are compared with authentic samples.

Characterization data of various substituted 1,2-benzisoxazole derivatives

1,2-Benzisoxazole (1)^{1, 3, 4}

Yield: 230 mg (96%); colorless liquid. IR (KBr): 3045, 2919, 1620, 1513, 1463, 1407, 1246, 1028, 822, 712 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO-}d_6$): δ = 7.19 (m, 4H), 8.43 (s, 1H). ^{13}C NMR (75MHz, $\text{DMSO-}d_6$): δ = 161.0, 143.8, 135.2, 123.9, 121.0, 120.2, 110.4. GC-MS: m/z 119 $[\text{M}]^+$. Anal. Calc. For $\text{C}_7\text{H}_5\text{NO}$: C, 70.58; H, 4.23; N, 11.76% found: C, 70.52; H, 4.21; N, 11.70 %.

6-Hydroxy-1,2-benzisoxazole (2)¹

Yield: 260 mg (93%); colorless liquid. IR (KBr): 3250, 3062, 2957, 2930, 1628, 1604, 1576, 1541, 1308, 1141, 696 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO-}d_6$): δ = 4.65 (s, 1H, OH), 6.80 (m, 2H), 7.20 (m, 1H), 8.44 (s, 1H). ^{13}C NMR (75MHz, $\text{DMSO-}d_6$): δ = 156.1, 152.1, 148.8, 135.3, 128.1, 125.7, 118.4. GC-MS: m/z 135 $[\text{M}]^+$. Anal. Calc. For $\text{C}_7\text{H}_5\text{NO}_2$: C, 62.22; H, 3.73; N, 10.37% found: C, 62.26; H, 3.70; N, 10.32 %.

7-Methoxy-1,2-benzisoxazole (3)^{1, 2}

Yield: 288 mg (90%); yellow liquid. IR (KBr): 3051, 3031, 1626, 1582, 1530, 1474, 1411, 1285, 1229, 794 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO-}d_6$): δ = 3.78 (s, 3H, OCH_3), 6.75 (m, 2H), 7.15 (m, 1H), 8.47 (s, 1H). ^{13}C NMR (75MHz, $\text{DMSO-}d_6$): δ = 152.1, 148.8, 145.3, 134.6, 128.1, 124.9, 117.1, 58.9. GC-MS: m/z 149 $[\text{M}]^+$. Anal. Calc. For $\text{C}_8\text{H}_7\text{NO}_2$: C, 64.42; H, 4.73; N, 9.39% found: C, 64.38; H, 4.70; N, 9.35 %.

5-Bromo-1,2-benzisoxazole (4) ¹

Yield: 375 mg (88%); light brown liquid. IR (KBr): 3057, 1625, 1593, 1573, 1516, 1394, 1310, 1090, 821, 714 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO}-d_6$): δ = 7.32 (m, 3H), 8.50 (s, 1H). ^{13}C NMR (75MHz, $\text{DMSO}-d_6$): δ = 162.4, 142.5, 134.2, 124.6, 122.1, 122.1, 112.4. GC-MS: m/z 196 $[\text{M}]^+$, 198 $[\text{M}]^+$. Anal. Calc. For $\text{C}_7\text{H}_4\text{BrNO}$: C, 42.46; H, 2.04; N, 7.07% found: C, 42.42; H, 2.01; N, 6.98 %.

3-Methyl-1,2-benzisoxazole (5) ^{1,2}

Yield: 260 mg (96%); colorless liquid. IR (KBr): 3037, 2919, 1614, 1597, 1527, 1405, 1323, 813 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO}-d_6$): δ = 2.38 (s, 3H, CH_3), 7.29 (m, 4H). ^{13}C NMR (75MHz, $\text{DMSO}-d_6$): δ = 160.3, 152.1, 130.8, 126.1, 122.1, 121.3, 112.1, 16.5. GC-MS: m/z 133 $[\text{M}]^+$. Anal. Calc. For $\text{C}_8\text{H}_7\text{NO}$: C, 72.16; H, 5.30; N, 10.52% found: C, 72.15; H, 5.28; N, 10.49 %.

3,6-Dimethyl-1,2-benzisoxazole (6) ^{1,2}

Yield: 290 mg (90%); light yellow liquid. IR (KBr): 3046, 3018, 2958, 1622, 1542, 1421, 1315, 1250, 850, 728 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO}-d_6$): δ = 2.30 (s, 3H, CH_3), 2.48 (s, 3H, CH_3), 7.23 (m, 3H). ^{13}C NMR (75MHz, $\text{DMSO}-d_6$): δ = 160.3, 153.1, 132.8, 125.1, 121.4, 121.1, 110.2, 18.6, 16.8. GC-MS: m/z 147 $[\text{M}]^+$. Anal. Calc. For $\text{C}_9\text{H}_9\text{NO}$: C, 73.45; H, 6.16; N, 9.52% found: C, 73.42; H, 6.12; N, 9.50 %.

3-Methyl-6-hydroxy-1,2-benzisoxazole (7) ^{1, 2}

Yield: 254 mg (86%); colorless liquid. IR (KBr): 3258, 3080, 2947, 2930, 1635, 1610, 1566, 1521, 1312, 1138, 656 cm^{-1} . ^1H NMR (300MHz, $\text{DM SO-}d_6$): δ = 2.38 (s, 3H, CH_3), 4.82 (s, 1H, OH), 6.89 (m, 2H), 7.12 (m, 1H). ^{13}C NMR (75MHz, $\text{DMSO-}d_6$): δ = 159.5, 154.2, 149.7, 136.3, 129.2, 126.7, 118.4, 18.8. GC-MS: m/z 149 $[\text{M}]^+$. Anal. Calc. For $\text{C}_8\text{H}_7\text{NO}_2$: C, 64.42; H, 4.73; N, 9.39% found: C, 64.40; H, 4.71; N, 9.38 %.

6-Ethyl-3-methyl-1,2-benzisoxazole (8) ¹

Yield: 292 mg (91%); pale yellow liquid. IR (KBr): 3060, 3022, 2960, 1620, 1542, 1423, 1325, 1266, 750, 722 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO-}d_6$): δ = 1.32 (t, 3H, CH_3), 2.36 (s, 3H, CH_3), 2.52 (q, 2H, CH_2), 7.14 (m, 3H). ^{13}C NMR (75MHz, $\text{DMSO-}d_6$): δ = 162.3, 152.1, 131.8, 124.1, 122.4, 121.0, 110.2, 34.6, 16.5, 14.7. GC-MS: m/z 161 $[\text{M}]^+$. Anal. Calc. For $\text{C}_{10}\text{H}_{11}\text{NO}$: C, 74.51; H, 6.88; N, 8.69% found: C, 74.50; H, 6.86; N, 8.70 %.

6-Methyl-3-phenyl-1,2-benzisoxazole (9) ¹

Yield: 365 mg (82%); low melting colorless solid. IR (KBr): 3060, 3029, 2953, 2926, 2864, 2805, 1628, 1601, 1577, 1549, 1489, 1417, 1260, 985, 695 cm^{-1} . ^1H NMR (300MHz, $\text{DMSO-}d_6$): δ = 2.40 (s, 3H, CH_3), 7.10 (m, 2H), 7.20 (m, 1H), 7.30 (m, 2H), 7.36 (m, 1H), 7.52 (m, 2H). ^{13}C NMR (75MHz, $\text{DMSO-}d_6$): δ = 162.3, 154.2, 142.3, 135.4, 129.3, 127.4, 127.2, 125.8, 124.6, 124.1, 122.1, 118.2, 112.7, 18.8. GC-MS: m/z 209 $[\text{M}]^+$. Anal. Calc. For $\text{C}_{14}\text{H}_{11}\text{NO}$: C, 80.36; H, 5.30; N, 6.69% found: C, 80.32; H, 5.25; N, 6.67 %.

6-Hydroxy-3-phenyl-1,2-benzisoxazole (10) ¹

Yield: 372 mg (85%); low melting colorless solid. IR (KBr): 3158, 3027, 2950, 2935, 2860, 2815, 1618, 1622, 1560, 1552, 1482, 1411, 1260, 945, 688 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 4.86 (s, 1H, OH), 6.78 (m, 2H), 7.24 (m, 2H), 7.38 (m, 2H), 7.56 (m, 2H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 160.3, 152.2, 140.4, 135.6, 129.0, 128.5, 127.2, 125.8, 124.6, 122.1, 122.0, 118.4, 112.1. GC-MS: m/z 211 [M]⁺. Anal. Calc. For C₁₃H₉NO₂: C, 73.92; H, 4.29; N, 6.63% found: C, 73.91; H, 4.29; N, 6.62 %.

3-(2'-Hydroxy) phenyl-1,2-benzisoxazole (11) ¹

Yield: 360 mg (83%); colorless solid. IR (KBr): 3220, 3022, 2968, 2948, 2860, 2814, 1618, 1622, 1537, 1512, 1487, 1422, 1260, 688 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 5.12 (s, 1H, OH), 6.89 (m, 2H), 7.22 (m, 2H), 7.44 (m, 4H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 161.5, 151.2, 142.4, 136.3, 129.4, 128.1, 127.4, 126.8, 125.3, 122.1, 121.7, 118.3, 112.0. GC-MS: m/z 211 [M]⁺. Anal. Calc. For C₁₃H₉NO₂: C, 73.92; H, 4.29; N, 6.63% found: C, 73.90; H, 4.28; N, 6.61 %.

3-Methylnaphtho[1,2-*d*]isoxazole (12) ^{1,3}

Yield: 350 mg (94%); colorless solid. IR (KBr): 3066, 3028, 2958, 1620, 1542, 1421, 1315, 1250, 850, 728 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 2.35 (s, 3H, CH₃), 7.18 (m, 2H), 7.34 (m, 2H), 7.40 (m, 2H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 162.0, 153.3, 141.4, 135.4, 129.3, 128.3, 128.1, 124.1, 121.8, 118.4, 112.5, 18.3. GC-MS: m/z 183 [M]⁺. Anal. Calc. For C₁₂H₉NO: C, 78.67; H, 4.95; N, 7.65% found: C, 78.64; H, 4.90; N, 7.62 %.

Characterization data of various substituted isoxazolo and isothiazolo quinoline derivatives

Isoxazolo(5,4-*b*)quinoline (13)^{5, 6, 7}

Yield: 320 mg (82%); colorless solid; mp 188-190 °C. IR (KBr): 3043, 2954, 1630, 1600, 1551, 1490, 1442, 1406, 1324, 1266, 1177, 846, 747, 689 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 6.28 (s, 1H), 7.30 (m, 1H), 7.49 (m, 1H), 7.72 (m, 1H), 8.06 (s, 1H), 8.18 (m, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 151.2, 148.5, 143.3, 139.1, 129.3, 128.9, 128.1, 127.7, 122.4, 120.4. GC-MS: m/z 170 [M]⁺. Anal. Calc. For C₁₀H₆N₂O: C, 70.58; H, 3.55; N, 16.46% found: C, 70.55; H, 3.51; N, 16.42 %.

4-Methyl-isoxazolo(5,4-*b*)quinoline (14)^{5, 6, 7}

Yield: 368 mg (92%); pale yellow solid; mp 198-199 °C. IR (KBr): 3148, 3022, 2950, 2919, 1620, 1533, 1453, 1417, 1260, 1216, 1028, 822, 689 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 2.38 (s, 3H, Me), 6.52 (s, 1H), 7.38 (m, 1H), 7.64 (m, 1H), 7.80 (m, 1H), 8.46 (m, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 155.4, 148.3, 141.6, 141.2, 129.4, 129.6, 128.2, 125.4, 122.4, 121.1, 17.6. GC-MS: m/z 184 [M]⁺. Anal. Calc. For C₁₁H₈N₂O: C, 71.73; H, 4.38; N, 15.21% found: C, 71.71; H, 4.36; N, 15.20 %.

7-Methoxy-isoxazolo(5,4-*b*)quinoline (15)^{5, 6, 7}

Yield: 370 mg (82%). colorless solid; mp 190-192 °C. IR (KBr): 3083, 3029, 2953, 2926, 2864, 2805, 1637, 1577, 1549, 1489, 1417, 1260, 985, 695 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 3.86 (s, 3H, OCH₃), 6.30 (s, 1H), 7.30 (m, 1H), 7.52 (m, 1H), 7.70 (m, 1H), 8.28 (m, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 152.2, 148.2, 142.3, 140.1, 129.3, 128.9, 128.1, 127.1, 122.3, 121.1, 56.3. GC-MS: m/z 200 [M]⁺. Anal. Calc. For C₁₁H₈N₂O₂: C, 66.00; H, 4.03; N, 13.99% found: C, 65.97; H, 4.00; N, 13.96 %.

7-Methyl-isoxazolo(5,4-*b*)quinoline (16)^{5,6}

Yield: 340 mg (78%); yellow solid; mp 193-195 °C. IR (KBr): 3045, 3012, 2970, 2959, 1618, 1513, 1463, 1407, 1266, 1246, 1028, 822, 712 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 2.42 (s, 3H, Me), 6.48 (s, 1H), 7.33 (m, 1H), 7.58 (m, 1H), 7.82 (m, 1H), 8.40 (m, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 156.1, 149.3, 141.3, 141.1, 129.3, 128.7, 128.2, 126.4, 121.4, 121.1, 18.2. GC-MS: m/z 184 [M]⁺. Anal. Calc. For C₁₁H₈N₂O: C, 71.73; H, 4.38; N, 15.21% found: C, 71.72; H, 4.34; N, 15.18 %.

Isothiazolo (5,4-*b*)quinoline (17)^{6,7}

Yield: 350 mg (90%); yellow solid; mp 168-170 °C. IR (KBr): 3062, 2957, 2930, 2868, 1632, 1604, 1576, 1541, 1489, 1308, 1141, 696 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 7.70 (m, 1H), 7.84 (m, 2H), 7.98 (m, 1H), 8.26 (s, 1H), 8.57 (s, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 160.4, 151.2, 146.6, 136.6, 129.9, 128.1, 128.0, 127.3, 126.1, 119.3. GC-MS: m/z 186 [M]⁺. Anal. Calc. For C₁₀H₆N₂S: C, 64.49; H, 3.25; N, 15.04% found: C, 64.40; H, 3.22; N, 14.98%.

7-Methoxy-isothiazolo(5,4-*b*)quinoline (18)^{6,7}

Yield: 390 mg (85%); yellow solid; mp 222-224 °C. IR (KBr): 3043, 2954, 1620, 1551, 1490, 1442, 1406, 1324, 1266, 1177, 846, 747, 689 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 3.90 (s, 3H, OCH₃), 7.41 (s, 1H), 7.64 (d, 1H, *J* = 9.0Hz), 7.85 (d, 1H, *J* = 9.0Hz), 8.56 (s, 1H), 8.87 (s, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 162.4, 159.1, 150.7, 146.6, 141.8, 135.1, 128.3, 127.4, 126.4, 125.2, 119.3, 55.6. GC-MS: m/z 216 [M]⁺. Anal. Calc. For C₁₁H₈N₂OS: C, 61.09; H, 3.73; N, 12.95% found: C, 61.04; H, 3.71; N, 12.90%.

7-Methyl-isothiazolo(5,4-*b*)quinoline (19)⁷

Yield: 388 mg (90%); light brown solid; mp 188-190 °C; IR (KBr): 3068, 3017, 2958, 2931, 2871, 1628, 1547, 1490, 1308, 846, 749 cm⁻¹. ¹H NMR (300MHz, DMSO-*d*₆): δ = 2.58 (s, 3H, C7-CH₃), 7.51 (s, 1H), 7.68 (d, 1H, *J* = 9.0Hz), 7.94 (d, 1H, *J* = 9.0Hz), 8.72 (s, 1H), 8.98 (s, 1H). ¹³C NMR (75MHz, DMSO-*d*₆): δ = 161.5, 158.8, 149.7, 146.6, 140.0, 136.9, 128.3, 128.1, 127.1, 126.6, 118.4, 18.4. GC-MS: *m/z* 200 [M]⁺. Anal. Calc. For C₁₁H₈N₂S: C, 65.98; H, 4.03; N, 13.99% found: C, 65.92; H, 3.98; N, 13.96 %.

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