Supplementary Material (ESI) for Chemical Communications

Supporting Information

An improved synthesis of 1,2-benzisoxazoles: TBAF mediated 1,3-dipolar cycloaddition of nitrile oxides and benzyne

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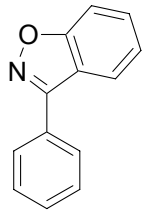
General Information

Melting points were recorded using a Stuart Scientific SMP3 melting point apparatus and are uncorrected. High Resolution Mass Spectra were recorded on VG micron Autospec or Bruker microTOF. Fourier Transform Infrared Spectroscopy (FT-IR) spectra were obtained on Perkin Elmer 1600 series or Bruker Tensor 27 spectrometer. ^{1}H and ^{13}C-NMR spectra were recorded on a Bruker AV(III) 400, Bruker AV 400, Bruker DPX 400 (400MHz (^{1}H) and 100 MHz (^{13}C)) spectrometers. Coupling constant are given in hertz (Hz) and the following notations indicate the multiplicity of the signals: s (singlet), d (doublet), brd (broad doublet), t (triplet), q (quartet), sept (septet), m (multiplet). Column chromatography was performed using Merck silica gel 60 (230-400 mesh). All solvents and reagents were used as received from commercial suppliers.

Experimental Section

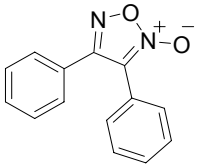
General procedure for the synthesis of 1,2-benzisoxazoles – synthesis of 3-(phenyl)-1,2-benzisoxazole (3) [1]**:**



A mixture of phenylhydroximoyl chloride **5** (50.0 mg, 0.32 mmol) and *o*-(trimethylsilyl)phenyl triflate **4** (147.0 mg, 0.12 mL, 0.48 mmol) was stirred in THF (0.40 mL) at room temperature for 5 min followed by addition of a solution of TBAF in THF (1M, 0.67 mL, 0.77 mmol) in single portion. The volatile components were removed under reduced pressure on a rotatory evaporator at 40 ^{o}C. The crude mixture was purified by flash column chromatography on silica gel using 1% ethyl acetate in petroleum ether 40-60 ^{o}C as eluting solvent, giving 3-(phenyl)-1,2-benzisoxazole **3** as an off-white solid (47.0 mg, 0.24 mmol, 75 %).

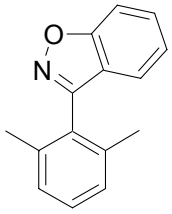
Off-white solid; mp 80–83 ^{o}C (lit.[2] 80–82 ^{o}C); IR (υ[cm^{-1}]) 1613; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04-7.97 (m, 2H), 7.94 (d, *J* = 8.0 Hz, 1H), 7.66-7.52 (m, 5H), 7.39 (t, *J* = 7.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.7, 157.2, 130.1, 129.7, 129.1 (2C), 128.8, 127.9 (2C), 123.8, 122.1, 120.4, 110.0; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{13}H_{10}NO$, 196.0757; found 196.0762.

3,4-Diphenylfuraxon (6)[4]



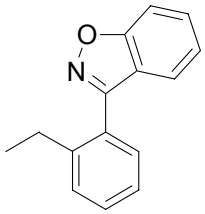
Obtained as a by-product from benzonitrile oxide, synthesized from phenylhydroximoyl chloride using general procedure and also obtained on treating phenylhydroximoyl chloride with 1 equiv of TBAF in THF, obtained in the range of 30-50 %; white solid; IR (υ[cm^{-1}]) 1592, 1507, 1423, 1115, 655; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.51 (m, 5H), 7.49-7.43 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 131.0, 130.6, 129.1, 129.0, 128.7, 128.3, 126.7, 122.9; HRMS (ESI) (*m/z*): $[M+Na]^+$ calcd for $C_{14}H_{10}N_2NaO_2$, 261.0634; found 261.0626.

3-(2,6-Dimethylphenyl)-1,2-benzisoxazole (7)



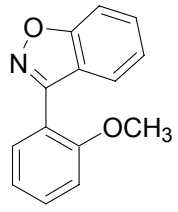
Synthesized from 2,6-dimethylphenylhydroximoyl chloride using general procedure, 71 mg, 0.32 mmol, 99 %; yellow solid; mp 85–86 °C (lit.[5] 83–84 °C); IR (υ[cm^{-1}]) 3011, 1610; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (td, *J* = 8.5, 0.8 Hz, 1H), 7.61 (ddd, *J* = 8.2, 6.9, 1.2 Hz, 1H), 7.41 (bd, *J* = 7.7 Hz, 1H), 7.35-7.29 (m, 2H), 7.20 (brd, *J* = 7.5 Hz, 2H), 2.15 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.1, 157.7, 137.7, 129.8, 129.4, 127.6 (2C), 127.1, 123.6, 121.9 (2C), 121.8, 110.0, 20.1 (2C); HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{15}H_{14}NO$, 224.1070; found 224.1075.

3-(2-Ethylphenyl)-1,2-benzisoxazole (8)



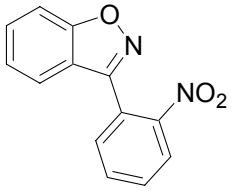
Synthesized from 2-ethylphenylhydroximoyl chloride using general procedure, 0.66 mg, 0.30 mmol, 93 %; brown oil; IR (υ[cm^{-1}]) 2972, 1609; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68-7.66 (m, 1H), 7.62-7.59 (m, 2H), 7.52-7.45 (m, 3H), 7.40-7.33 (m, 2H), 2.78 (q, *J* = 7.5 Hz, 2H), 1.18 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 158.0, 143.9, 130.2, 130.0, 129.7, 129.4, 127.1, 126.0, 123.7, 122.2 (2C), 109.9, 26.6, 15.8; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{15}H_{14}NO$, 224.1070; found 224.1069.

3-(2-Methoxyphenyl)-1,2-benzisoxazole (9)



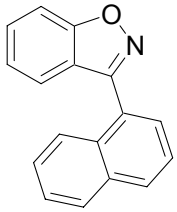
Synthesized from 2-methoxyphenylhydroximoyl chloride using general procedure, 67 mg, 0.30 mmol, 92 %; yellow brown oil; IR (υ[cm^{-1}]) 3011, 1610; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (brd, *J* = 8.0 Hz, 1H), 7.67 (dd, *J* = 7.5, 1.7 Hz, 1H), 7.63 (brd, *J* = 8.4 Hz, 1H), 7.58-7.50 (m, 2H), 7.33-7.29 (m, 1H), 7.14-7.09 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 157.4, 156.4, 131.6, 131.3, 129.4, 123.5, 123.1, 121.9, 120.9, 117.6, 111.4, 109.7, 55.5; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{12}NO_2$, 226.0823; found 226.0864.

3-(2-Nitrophenyl)-1,2-benzisoxazole (10)



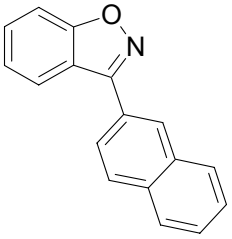
Synthesized from 2-nitrophenylhydroximoyl chloride using general procedure, 56 mg, 0.24 mmol, 75 %; yellow solid; mp 105–108 ^{o}C; IR (υ[cm^{-1}]) 1610, 1532, 1351, 852; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22-8.19 (m, 1H), 7.84-7.72 (m, 3H), 7.69-7.67 (m, 1H), 7.64-7.60 (m, 1H), 7.47 (brd, J = 8.0 Hz, 1H), 7.36-7.32 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 155.7, 148.7, 133.5, 132.2, 131.1, 130.1, 125.0, 124.1, 123.5, 120.9 (2C), 110.15; HRMS (ESI) (*m/z*): $[M+Na]^+$ calcd for $C_{13}H_8N_2NaO_3$, 263.0427; found 263.0422.

3-(1-Naphthalen)-1,2-benzisoxazole (11)[6]



Synthesized from 1-naphthalenhydroximoyl chloride using general procedure, 78 mg, 0.32 mmol 99 %; orange brown oil; IR (υ[cm^{-1}]) 1610; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, J = 8.4 Hz, 1H), 8.06 (brd, J = 8.3 Hz, 1H), 7.98 (brd, J = 7.6 Hz, 1H), 7.82 (dd, J = 1.2, 7.1 Hz, 1H), 7.74 (brd, J = 8.5 Hz, 1H), 7.66-7.51 (m, 5H), 7.35-7.31 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 157.5, 133.9, 131.3, 130.4, 129.9, 128.4, 128.3, 127.0, 126.4, 125.7, 125.5, 125.2, 123.7, 122.4, 122.3, 110.0; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{12}NO$, 246.0913; found 246.0907.

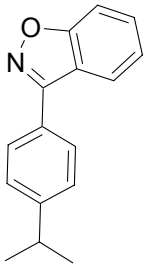
3-(2-Naphthalen)-1,2-benzisoxazole (12)



Synthesized from 2-naphthalenhydroximoyl chloride using general procedure, 67 mg, 0.28 mmol, 85 %; orange brown oil; IR (υ[cm^{-1}]) 1611; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (s, 1H), 8.12-7.93 (m, 5H), 7.71-7.69 (m, 1H), 7.65-7.58 (m, 3H), 7.45-7.41 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 157.2, 134.0, 133.2, 129.8, 129.0, 128.5, 127.9 (2C), 127.2,

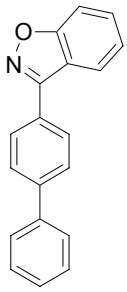
126.8, 126.4, 125.0, 123.9, 122.3, 120.6, 110.2; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{17}H_{12}NO$, 246.0913; found 246.0913.

3-(4-Isopropylbenzo)-1,2-benzisoxazole (13)



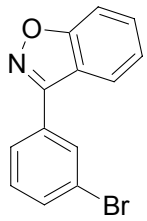
Synthesized from 4-isopropylphenylhydroximoyl chloride using general procedure, 65 mg, 0.28 mmol, 87 %; amorphous solid; mp 78–81 °C; IR (υ[cm^{-1}]) 3011, 2966, 1611; ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (td, *J* = 8.0, 0.9 Hz, 1H), 7.92 (brd, *J* = 8.3 Hz, 2H), 7.67-7.65 (m, 1H), 7.62-7.58 (m, 1H), 7.44 (brd, *J* = 8.0 Hz, 2H), 7.38 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1H), 3.02 (sept., *J* = 7.0 Hz, 1H), 1.33 (d, *J* = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 157.2, 151.3, 129.7, 128.1 (2C), 127.2 (2C), 126.4, 123.7, 122.3, 120.6, 110.1, 34.1, 23.9 (2C); HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{16}H_{16}NO$, 238.1226; found 238.1230.

3-(4-Biphenyl)-1,2-benzisoxazole (14)



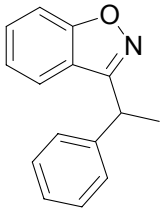
Synthesized from 4-biphenylhydroximoyl chloride using general procedure, 83 mg, 0.30 mmol, 95 %; yellow solid; m.p. 116–119 °C (lit.[7] 119–120 °C); IR (υ[cm^{-1}]) 1613; ^1H NMR (400 MHz, $CDCl_3$) δ 8.09-8.06 (m, 2H), 8.00 (td, *J* = 8.0, 0.9 Hz, 1H), 7.83-7.80 (m, 2H), 7.70-7.68 (m, 3H), 7.65-7.61 (m, 1H), 7.53-7.48 (m, 2H), 7.44-7.40 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.8, 156.8, 142.9, 140.1, 129.7, 128.9 (2C), 128.4 (2C), 127.8, 127.7 (3C), 127.1 (2C), 123.8, 122.1, 120.4, 110.1; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{19}H_{14}NO$, 272.1070; found 272.1077.

3-(3-Bromophenyl)-1,2-benzisoxazole (15)



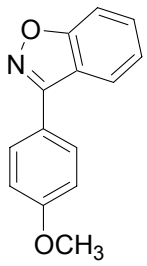
Synthesized from 3-bromophenylhydroximoyl chloride using general procedure, 68 mg, 0.24 mmol, 78 %; pale yellow solid; mp 86–89 ^{o}C (lit.[8] 93–94 ^{o}C); IR (υ[cm^{-1}]) 1612; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 1.8 Hz, 1H), 7.93 (d, *J* = 7.6 Hz, 2H), 7.71-7.63 (m, 3H), 7.49-7.42 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.9, 156.0, 133.2, 130.9 (2C), 130.6, 130.0, 126.6, 124.1, 123.1, 121.9, 120.0, 110.3; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{13}H_9{}^{79}BrNO$, 273.9862; found 273.9856.

3-(1-Phenyl-ethyl)-1,2-benzisoxazole (16)



Synthesized from 1-phenyl-ethylhydroximoyl chloride using general procedure, 36 mg, 0.16 mmol, 50 %; colourless oil; IR (υ[cm^{-1}]) 2982, 2932, 2855, 1612, ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.44 (m, 1H), 7.38 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1H), 7.28-7.22 (m, 4H), 7.20-7.14 (m, 2H), 7.05 (ddd, *J* = 8.0, 7.0, 0.9 Hz, 1H), 4.46 (q, *J* = 7.2 Hz, 1H), 1.78 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2, 161.0, 142.3, 129.5, 128.8 (2C), 127.5 (2C), 127.0, 123.0, 121.9, 121.0, 109.8, 38.0, 20.0; HRMS (ESI) (*m/z*): $[M+Na]^+$ calcd for $C_{15}H_{13}NNaO$, 246.0889; found 246.0912.

3-(4-Methoxyphenyl)-1,2-benisoxazole (17)



Synthesized from 4-methoxyphenylhydroximoyl chloride using general procedure, 66 mg, 0.29 mmol, 92 %; white solid; mp 100–102 ^{o}C (lit.[3] 100–101 ^{o}C); IR (υ[cm^{-1}]) 3011, 1613; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95-7.91 (m, 3H), 7.65-7.56 (m, 2 H), 7.37 (ddd, *J* = 8.0, 6.9, 1.1 Hz, 1H), 7.11-7.09 (m, 1H), 7.08-7.06 (m, 1H), 3.89 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)

δ 163.7, 161.2, 156.7, 129.6, 129.3 (2C), 123.6, 122.2, 121.1, 120.5, 114.5 (2C), 110.1, 55.3; HRMS (ESI) (*m/z*): $[M+H]^+$ calcd for $C_{14}H_{12}NO_2$, 226.0863; found 226.0863.

References:

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