Supporting Information:

Direct construction of 5-methyl-2-phenylisoxazol-3(2H)-ones via hypervalent iodine mediated oxidative tandem cyclization of 3-oxo-N-phenylbutanamides catalyzed by zinc oxide (ZnO)

Wei-Bing Liu*[a], Peng Zhou[a], Cui Chen [a], Qing Zhang[a], Zhi-Bo Zhu*[b]

Address:

*[a] School of Chemistry and Life Science, Guangdong University of Petrochemical Technology, 2 Guangdu Road, Maoming 525000, China

*[b] School of Pharmaceutical Sciences, Southern Medical University, Guangzhou 510515, China

Email: lwb409@yahoo.com.cn

* Wei-Bing Liu

Email:zzb24@yahoo.com.cn

* Zhi-Bo Zhu

General method. All the reactions were carried out at 100 °C for 5 h in a Schlenk tube equipped with magnetic stir bar. Solvents and all reagents were used as received. ^{1}H NMR spectra were recorded in $CDCl_3$ at 400 MHz and ^{13}C NMR spectra were recorded in $CDCl_3$ at 100 MHz. GC–MS was obtained using electron ionization (EI). Thin layer chromatography was performed using 600 mesh silica gel plates, and visualization was effected with short wavelength UV light (254 nm). All melting points are uncorrected. All the other chemicals were purchased from Aldrich Chemicals or J & K Scientific Ltd.

Typical procedure for the synthesis of 5-methyl-2-phenylisoxazol-3(2H)-one (2a). A mixture of 3-oxo-N-phenylbutanamid (**1a**) (177 mg, 1.0 mmol), ZnO (16 mg, 0.2 mmol), iodobenzene diacetate (DIB) (418 mg, 1.3 mmol) and dioxane (2.0 mL) was added successively in Schlenk tube. After stirring for 5 h at 100 °C, the solution was

directly subjected to isolation by PTLC (GF_{254}), eluted with a 10:5 petroleum ether / ethyl acetate mixture to afford the desired product **2a** (142 mg, 81%).

Characterization data for all prepared compounds:

5-methyl-2-phenylisoxazol-3(2H)-one (2a) (Known compound, see: Perronnet, J.; Girault, P.; Demoute, J. P. *J. Heterocyclic Chem.* **1980**, *17*, 727-731)

^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.43 (t, *J* = 8.4 Hz, 2H), 7.26 (t, *J* = 8.4 Hz, 1H), 6.58 (s, 1H), 2.17 (s, 3H).

5-methyl-2-*o*-tolylisoxazol-3(2H)-one (2b)

Pale viscous oil; IR νmax (KBr): 2973, 2885, 1746, 1686, 1457, 1380, 1325, 1210, 1088, 1049, 881, 668 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.28-7.26 (m, 2H), 7.24-7.21 (m, 2H), 6.25 (s, 1H), 2.26 (s, 3H), 2.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 161.2, 156.5, 137.6, 133.8, 131.4, 128.8, 126.9, 126.6, 112.0, 17.9, 16.0; MS (EI) m/z (%): 118.10 (100.00), 189.12 (67.36); Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40; Found: C, 69.88; H, 6.02; N, 7.59

5-methyl-2-*p*-tolylisoxazol-3(2H)-one (2c)

Pale viscous oil; IR νmax (KBr): 1747, 1678, 1627, 1517, 1454, 1409, 1291, 1207, 1117, 1042, 963, 740, 690 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.38 (d, *J* = 8.0 Hz, 2H), 7.19 (d, *J* = 8.0 Hz, 2H), 6.51 (s, 1H), 2.33 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 160.8, 137.6, 136.0, 134.8, 129.8, 120.7, 109.6, 20.9, 11.5; MS (EI) m/z (%): 118.13 (100.00), 189.10 (89.98); Anal. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40; Found: C, 69.69; H, 5.91; N, 7.44

2-(2-chlorophenyl)-5-methylisoxazol-3(2H)-one (2d)

Pale viscous oil; IR νmax (KBr): 2973, 2885, 1733, 1678, 1453, 1380, 1271, 1089, 1049, 881, 669 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.91 (d, *J* = 7.6 Hz, 1H), 7.39-7.31 (m, 3H), 6.84 (s, 1H), 2.18 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 158.1, 152.6, 133.4, 129.3, 129.1, 128.8, 128.7, 128.6, 117.7, 20.7; MS (EI) m/z (%): 138.05 (100.00), 209.33 (64.35); Anal. Calcd for $C_{10}H_8ClNO_2$: C, 57.30; H, 3.85; N, 6.68; Found: C, 57.11; H, 4.03; N, 6.76

2-(4-chlorophenyl)-5-methylisoxazol-3(2H)-one (2e) (Known compound, see:

Perronnet, J.; Girault, P.; Demoute, J. P. *J. Heterocyclic Chem.* **1980**, *17*, 727-731)

^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.48 (d, *J* = 8.8 Hz, 2H), 7.36 (d, *J* = 8.8 Hz, 2H), 6.53 (s, 1H), 2.14 (s, 3H).

2-(4-methoxyphenyl)-5-methylisoxazol-3(2H)-one (2f)

Pale viscous oil; IR νmax (KBr): 2915, 2837, 1740, 1683, 1515, 1490, 1399, 1249, 1121, 1033, 880, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.39 (d, *J* = 8.4 Hz, 2H), 6.91 (d, *J* = 8.4 Hz, 2H), 6.46 (s, 1H), 3.79 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 157.8, 154.7, 137.4, 128.8, 122.6, 114.5, 110.0, 55.5, 11.4; MS (EI) m/z (%): 205.05 (100.00); Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83; Found: C,64.44; H, 5.52; N, 6.99

2-(4-ethoxyphenyl)-5-methylisoxazol-3(2H)-one (2g)

Colorless crystals; mp: 85.7-86.5 ^{o}C; IR νmax (KBr): 2955, 2870, 1741, 1675, 1510, 1398, 1249, 1114, 1047, 823, 728 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.37 (d, *J* = 8.8 Hz, 2H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.51 (s, 1H), 4.01 (q, *J* = 7.2 Hz, 2H), 2.18 (s, 3H), 1.39 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 157.2, 154.6, 137.4, 128.6, 122.6, 115.1, 110.1, 63.7, 14.7, 11.5; MS (EI) m/z (%): 219.05 (100.00); Anal. Calcd for $C_{12}H_{13}NO_3$: C, 65.74; H, 5.98; N, 6.39; Found: C, 65.77; H, 5.88; N, 6.54

2-(2,4-dimethoxyphenyl)-5-methylisoxazol-3(2H)-one (2h)

Pale viscous oil; IR νmax (KBr): 2911, 2834, 1748, 1672, 1605, 1522, 1456, 1409, 1291, 1209, 1154, 1033, 828 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.28 (d, *J* = 8.0 Hz, 1H), 6.50 (s, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 6.29 (s, 1H), 3.79 (s, 6H), 2.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 160.5, 155.0, 154.8, 136.3, 128.1, 117.1, 112.6, 104.5, 99.7, 55.8, 55.6, 11.5; MS (EI) m/z (%): 88.10 (100.00), 235.18 (36.65); Anal. Calcd for $C_{12}H_{13}NO_4$: C, 61.27; H, 5.57; N, 5.95; Found: C, 61.45; H, 6.66; N, 6.08

2-(4-chloro-2,5-dimethoxyphenyl)-5-methylisoxazol-3(2H)-one (2i)

Colorless crystals; mp: 96.5-97.2 ^{o}C; IR νmax (KBr): 2966, 2824, 1689, 1613, 1594, 1511, 1450, 1400, 1211, 1179, 1034, 851, 812, 725 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.13 (s, 1H), 7.00 (s, 1H), 6.76 (s, 1H), 3.78 (s, 6H), 2.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 164.0, 149.3, 142.4, 136.6, 114.7, 113.0, 112.1, 111.1, 100.8, 56.8, 56.7, 11.5; MS (EI) m/z (%): 269.35 (100.00); Anal. Calcd for $C_{12}H_{12}ClNO_4$: C, 53.44; H,

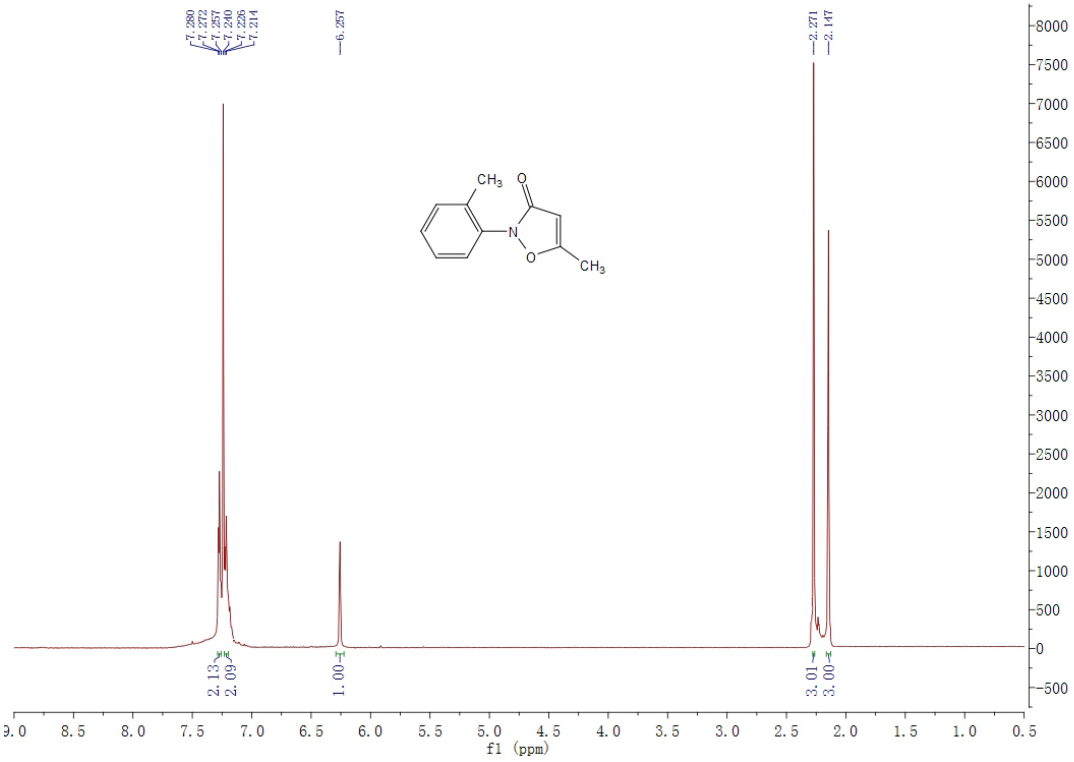
4.49; N, 5.19; Found: C, 53.38; H, 4.61; N, 5.38

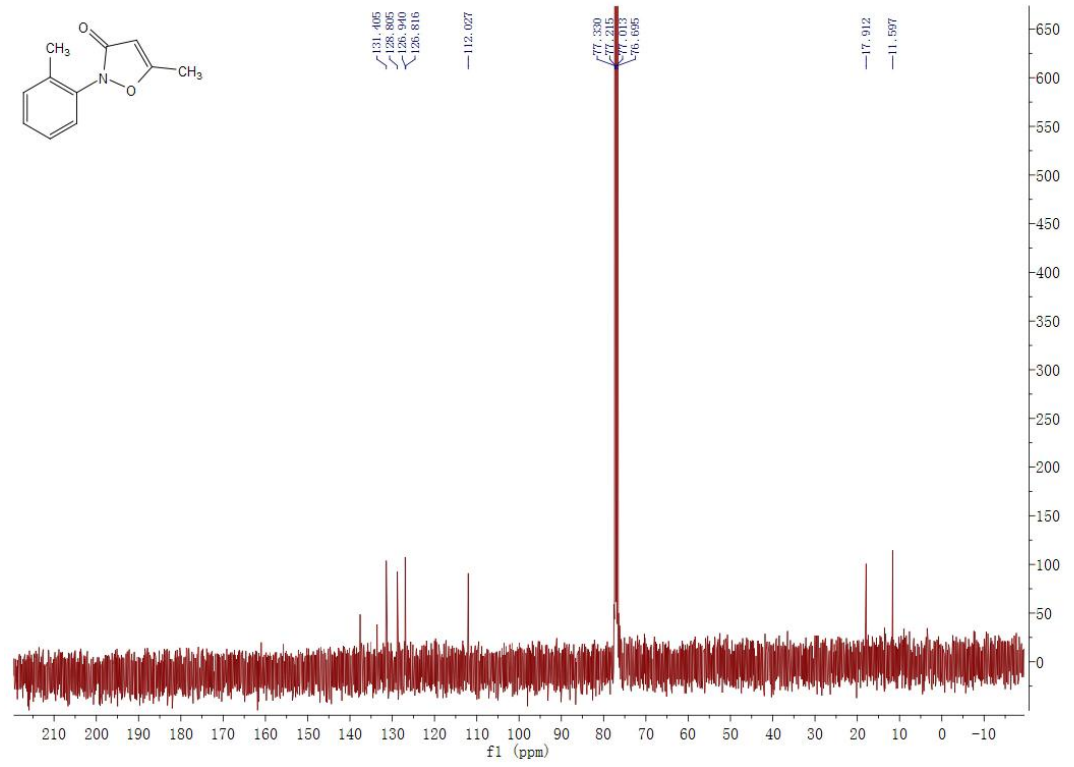
5-methyl-2-(2,4-dimethylphenyl)isoxazol-3(2H)-one (2j)

Pale viscous oil; IR νmax (KBr): 2969, 2924, 1747, 1699, 1597, 1512, 1449, 1383, 1202, 1109, 1045, 970, 814, 739, 654 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 Hz) δ 7.07 (s, 1H), 7.01 (t, *J* = 7.2 Hz, 2H), 6.22 (s, 1H), 2.31 (s, 3H), 2.21 (s, 3H), 2.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 Hz) δ 166.6, 154.1, 138.8, 137.4, 131.9, 127.6, 126.8, 122.2, 112.5, 21.0, 17.7, 11.5; MS (EI) m/z (%): 132.10 (100.00), 203.17 (72.45); Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89; Found: C, 70.03; H, 6.62; N, 6.99

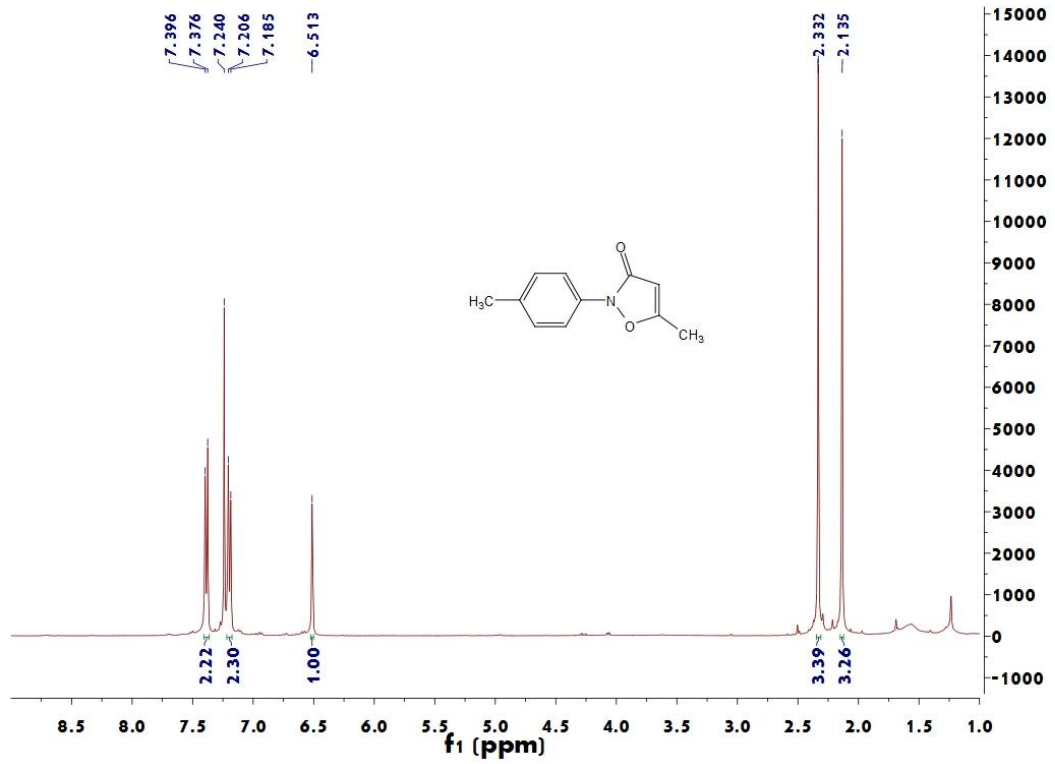
NMR spectra

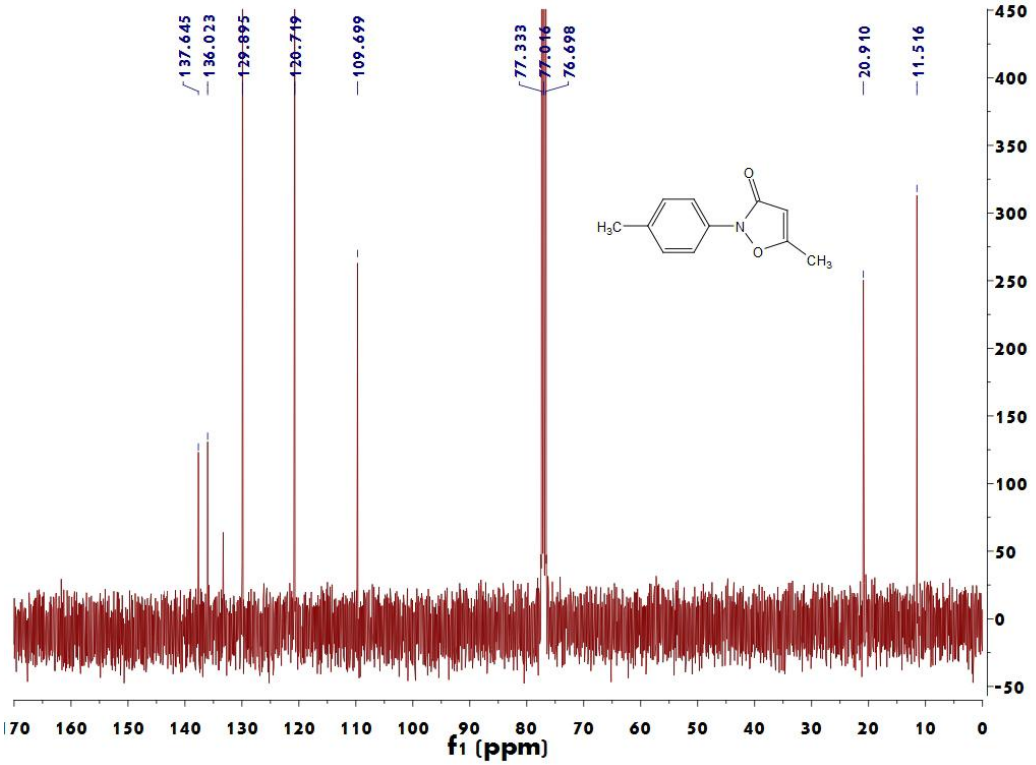
5-methyl-2-*o*-tolylisoxazol-3(2H)-one (2b)



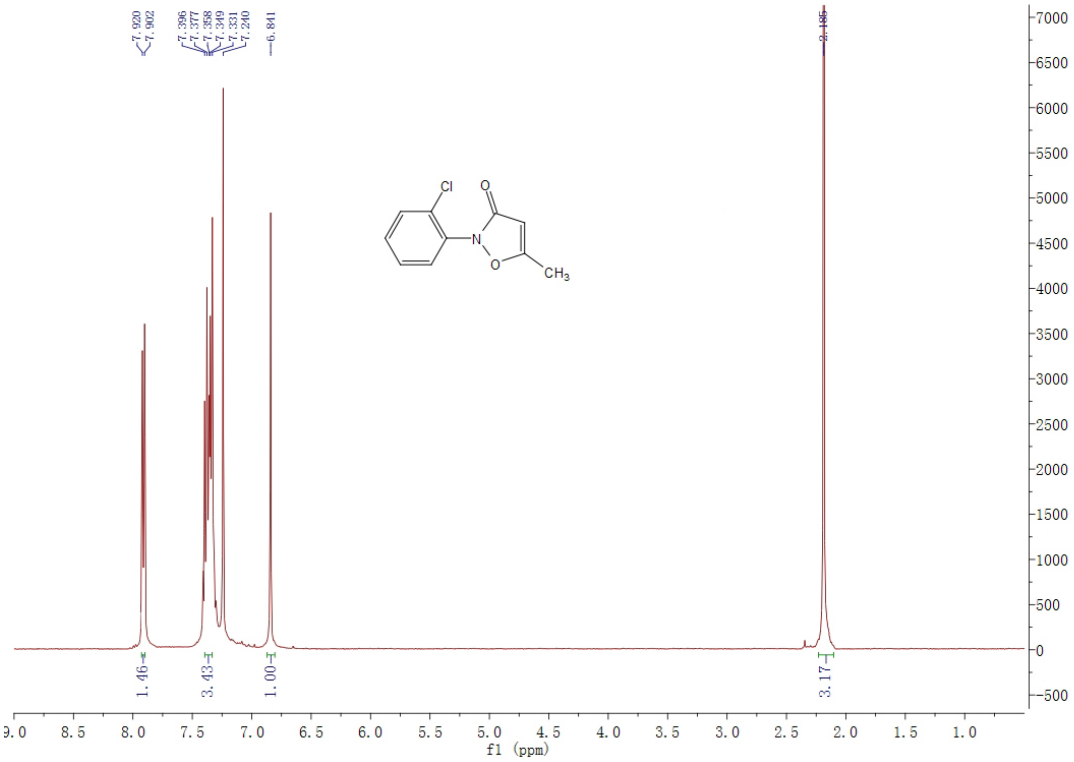


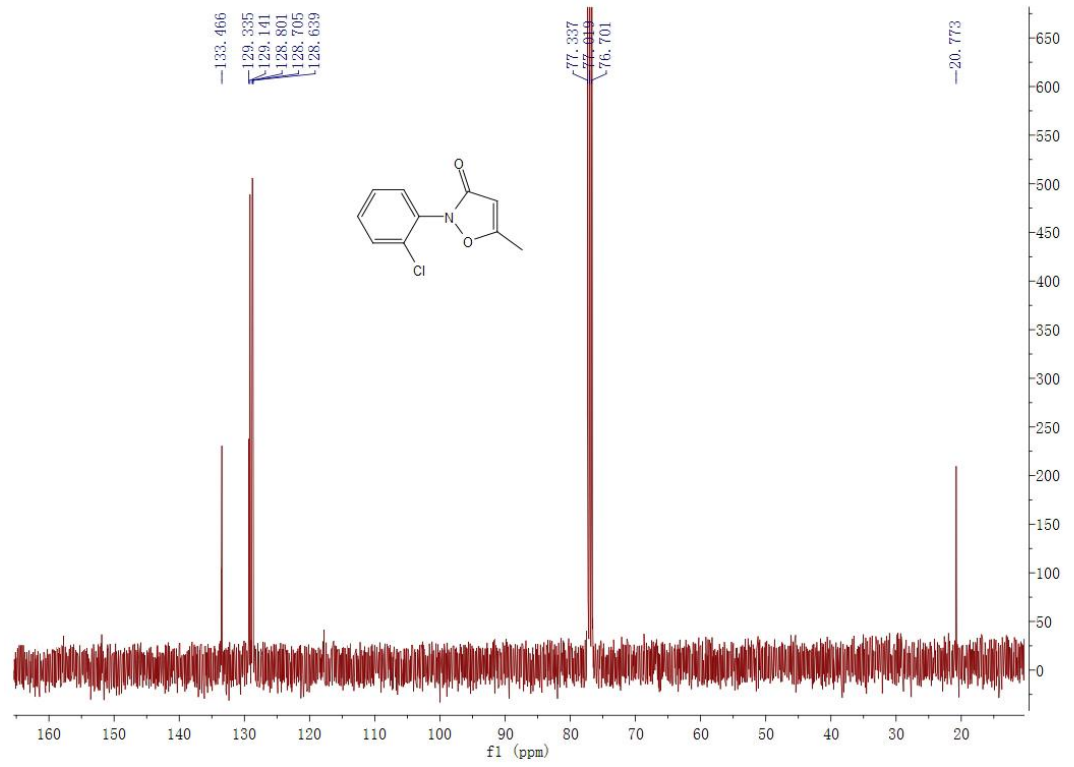
5-methyl-2-*p*-tolylisoxazol-3(2H)-one (2c)



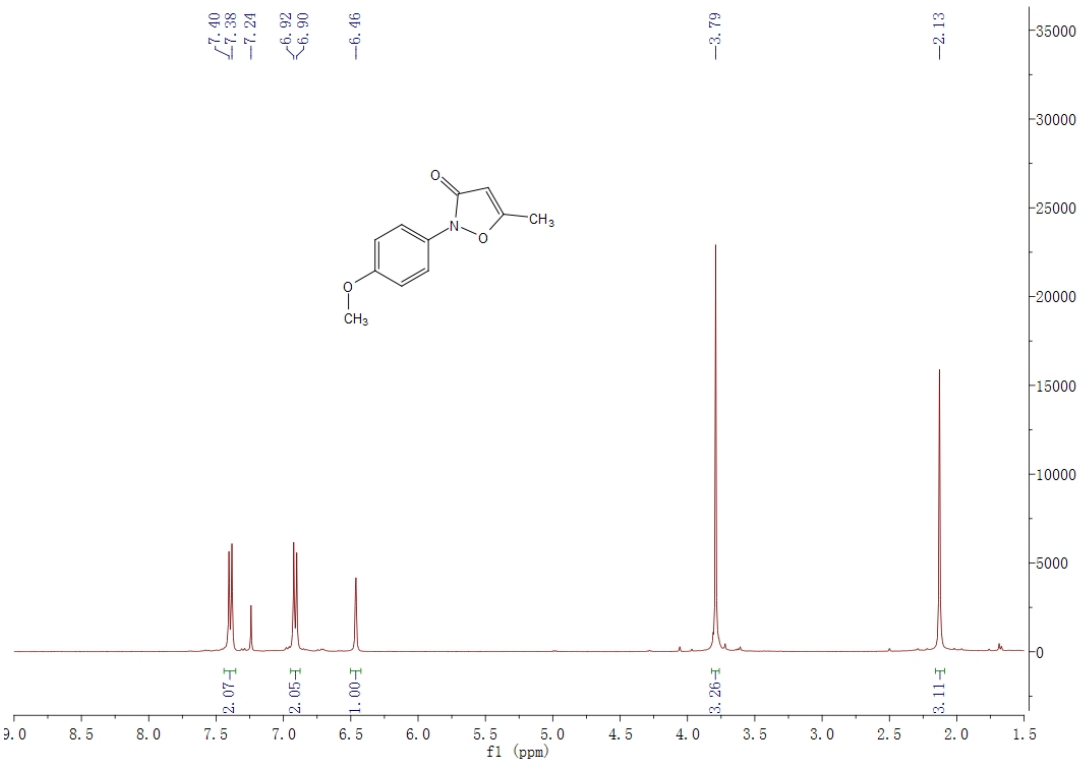


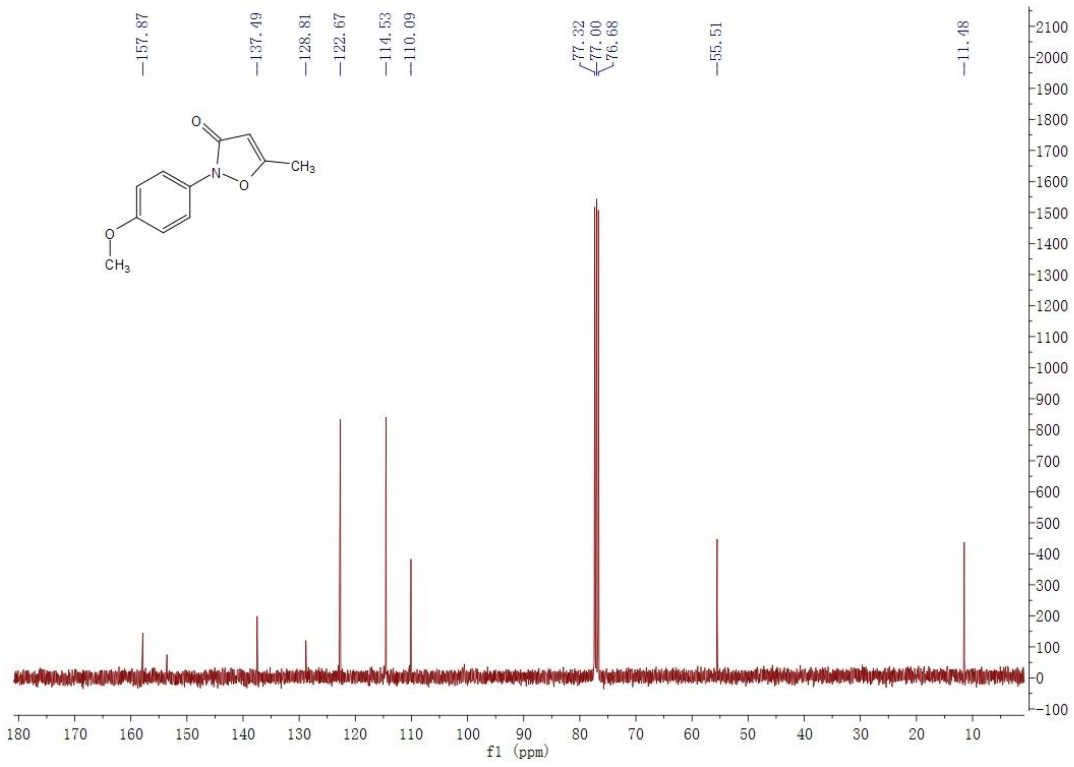
2-(2-chlorophenyl)-5-methylisoxazol-3(2H)-one (2d)



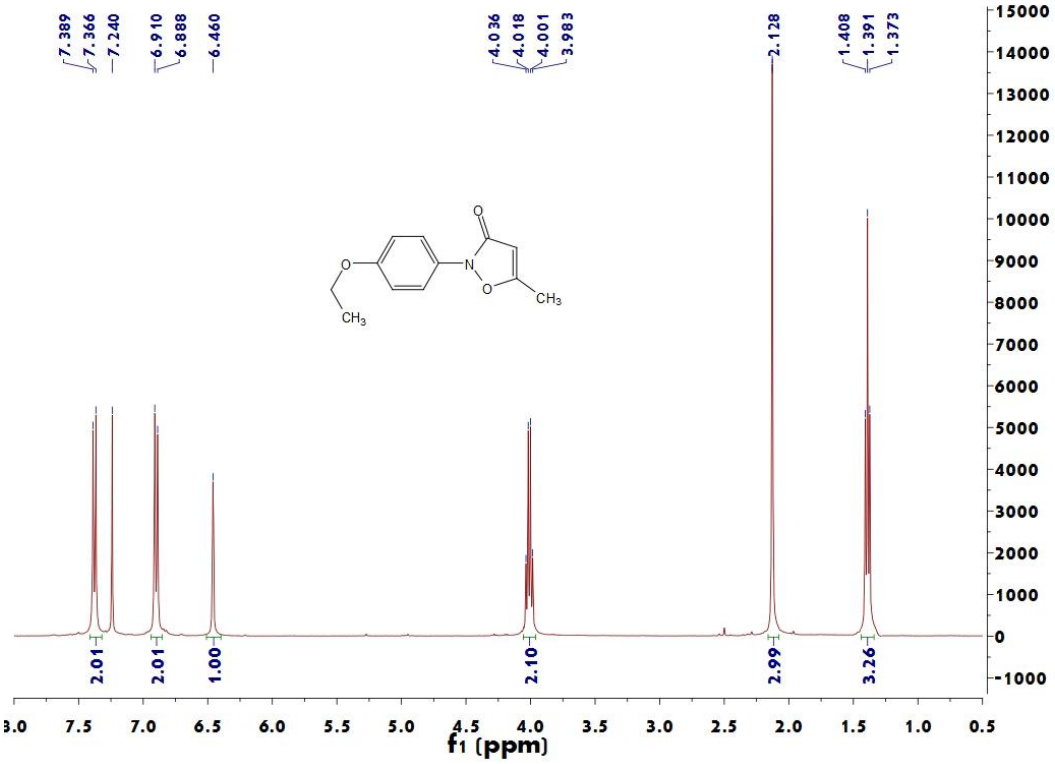


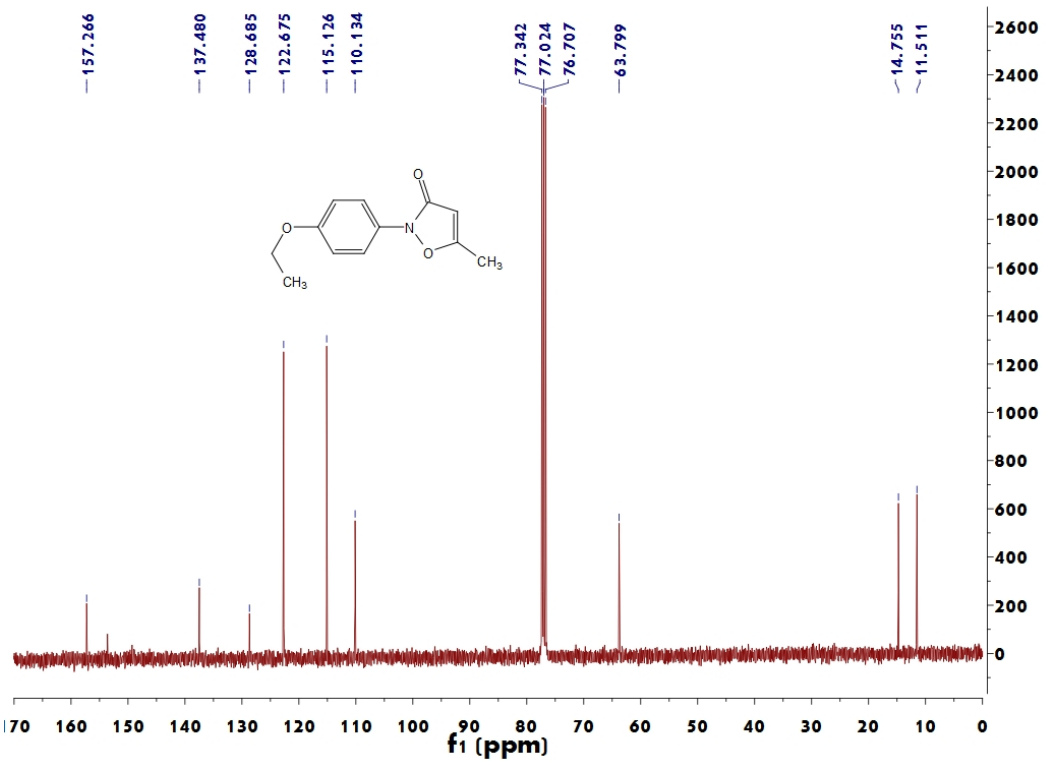
2-(4-methoxyphenyl)-5-methylisoxazol-3(2H)-one (2f)



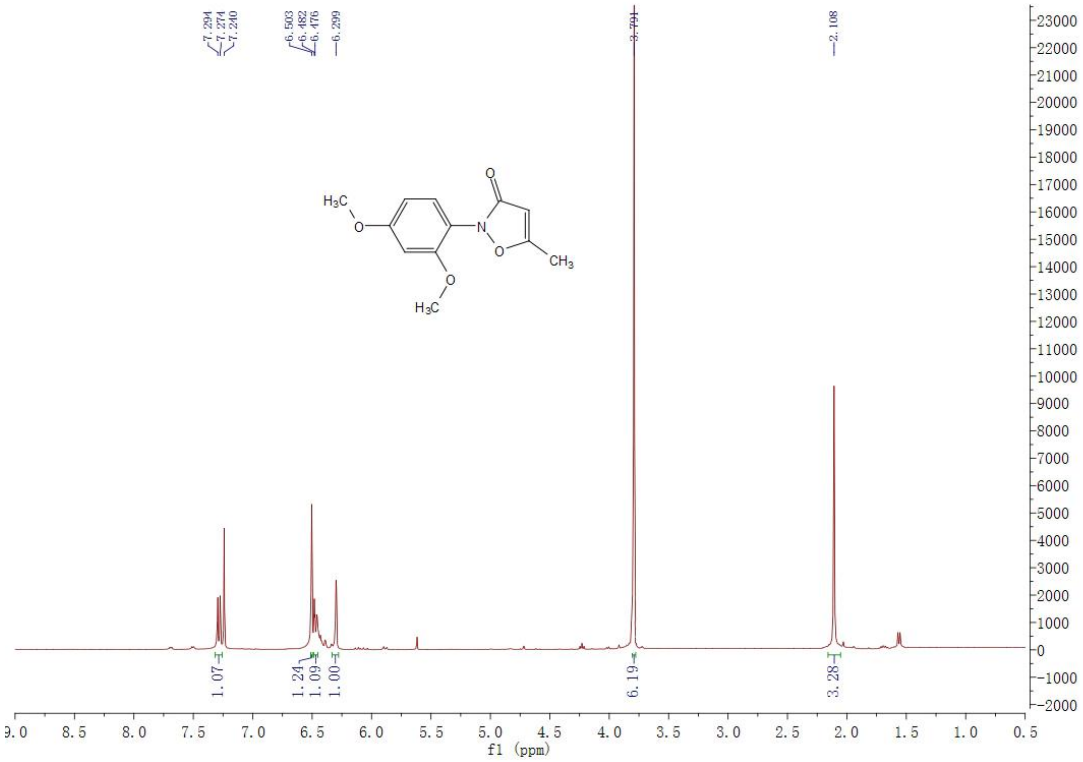


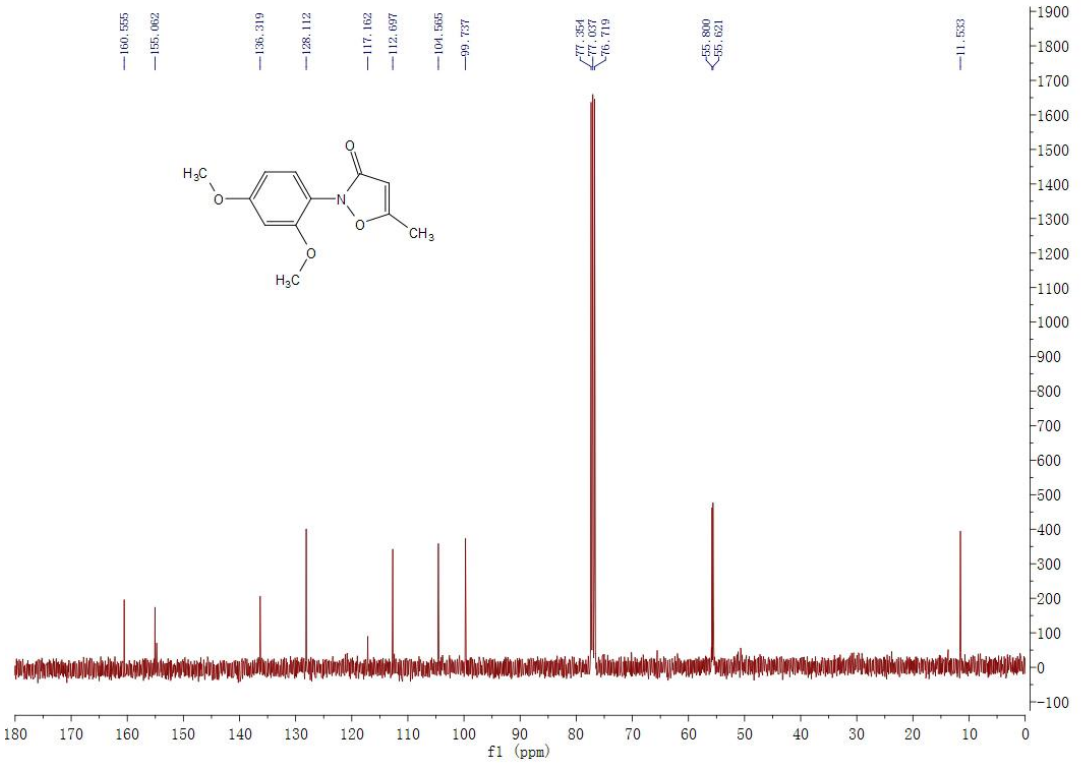
2-(4-ethoxyphenyl)-5-methylisoxazol-3(2H)-one (2g)



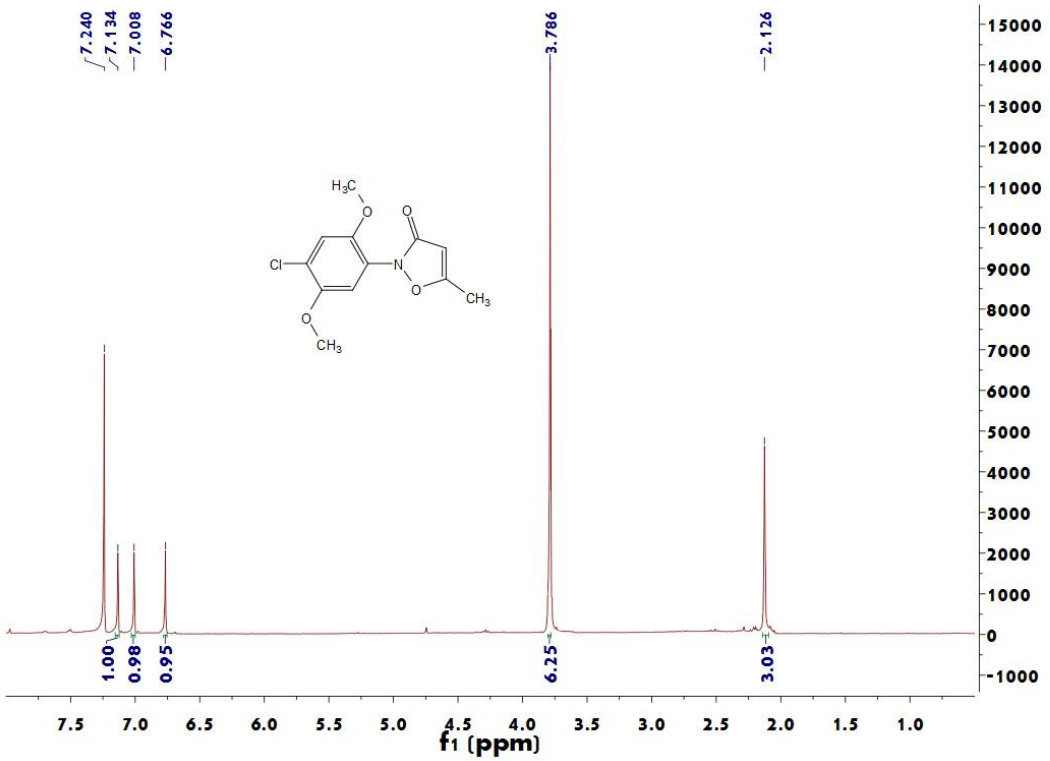


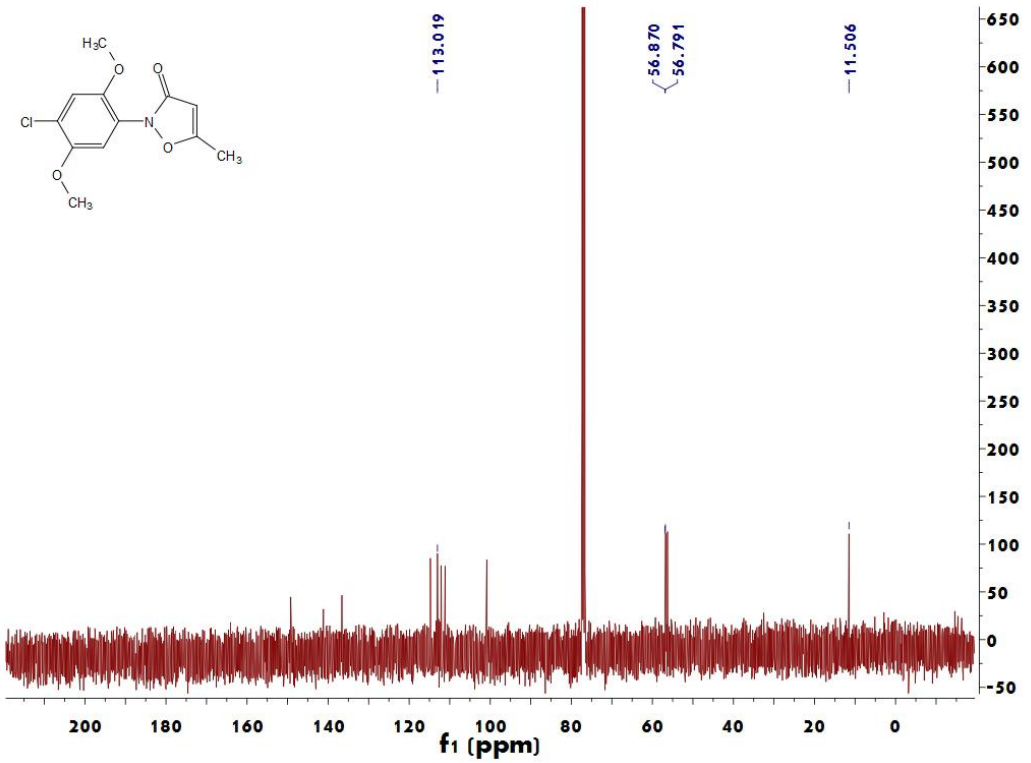
2-(2,4-dimethoxyphenyl)-5-methylisoxazol-3(2H)-one (2h)





2-(4-chloro-2,5-dimethoxyphenyl)-5-methylisoxazol-3(2H)-one (2i)





5-methyl-2-(2,4-dimethylphenyl)isoxazol-3(2H)-one (2j)