Electronic Supplementary Material (ESI) for ChemComm.

Supplementary Information

Silver-Mediated Radical Cyclization: Construction of Δ^2-Isoxazolines from α-Halo Ketoximes and 1,3-Dicarbonyl Compounds

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(A) General Experimental Procedure

(a) Materias

Substrates **1a-1k** were prepared according to literature procedures.[1]

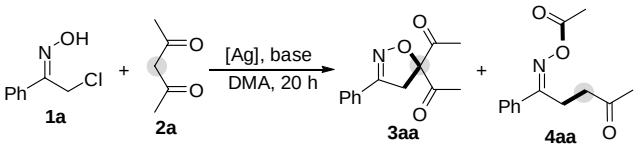
(b) General Procedures for Silver-Mediated Synthesis of Isoxazolines 3:

Conditions A: To a Schlenk tube were added α-halo ketoxime **1** (0.3 mmol), 1,3-dicarbonyl compound **2** (**2a-2e**) (0.6 mmol), Ag_2CO_3 (0.6 mmol), K_2CO_3 (0.3 mmol) and DMA (3 mL). Then the tube was charged with argon, and was stirred at 50 ^oC for about 20 h until complete consumption of starting material as monitored by TLC and/or GC-MS analysis. After the reaction was finished, the reaction mixture was washed with brine. The aqueous phase was re-extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4, concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20:1) to afford the desired product **3**.

Conditions B: To a Schlenk tube were added α-halo ketoxime **1** (0.3 mmol), 1,3-dicarbonyl compound **2** (**2f-2q**) (0.6 mmol), Ag_2CO_3 (0.6 mmol), Cs_2CO_3 (0.3 mmol) and DMA (3 mL). Then the tube was charged with argon, and was stirred at 50 ^oC for about 20 h until complete consumption of starting material as monitored by TLC and/or GC-MS analysis. After the reaction was finished, the reaction mixture was washed with brine. The aqueous phase was re-extracted with ethyl acetate. The combined organic extracts were dried over Na_2SO_4, concentrated in vacuum, and the resulting residue was purified by silica gel column chromatography (hexane/ethyl acetate = 20:1) to afford the desired product **3**.

(c) Table S1. Screening Optimizing Reaction Conditions

Table S1. Screening Optimal Conditions[a]

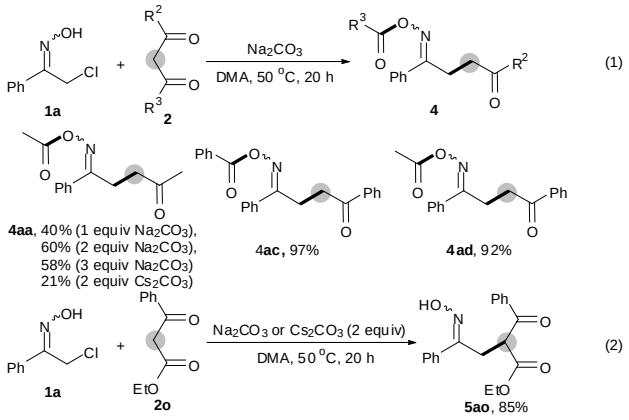


Entry	[M] [equiv]	Base [equiv]	Solvent	Isolated Yield [%]	
				3aa	**4aa**
1	Ag_2CO_3 (0.1)	K_2CO_3 (1)	DMA	9	trace
2	Ag_2CO_3 (1)	K_2CO_3 (1)	DMA	63	trace
3	Ag_2CO_3 (2)	K_2CO_3 (1)	DMA	80	trace
4	Ag_2CO_3 (2.5)	K_2CO_3 (1)	DMA	79	trace
5	—	K_2CO_3 (1)	DMA	0	15
6	Ag_2CO_3 (2)	K_2CO_3 (2)	DMA	50	trace
7	Ag_2CO_3 (2)	—	DMA	trace	0
8	Ag_2CO_3 (2)	Cs_2CO_3 (1)	DMA	16	trace
9	Ag_2CO_3 (2)	Na_2CO_3 (1)	DMA	16	trace
10	Ag_2CO_3 (2)	KOAc (1)	DMA	44	trace
11	Ag_2CO_3 (2)	Et_3N (1)	DMA	15	trace
12	Ag_2CO_3 (2)	DABCO (1)	DMA	76	trace
13	Ag_2CO_3 (2)	K_2CO_3 (1)	DMF	41	trace
14	Ag_2CO_3 (2)	Cs_2CO_3 (1)	DMSO	30	trace
15	Ag_2CO_3 (2)	Cs_2CO_3 (1)	toluene	trace	trace
16	$AgNO_3$ (2)	K_2CO_3 (1)	DMA	6	trace
17	AgOAc (2)	K_2CO_3 (1)	DMA	16	trace
18	Ag_2O (2)	K_2CO_3 (1)	DMA	19	trace
19[b]	Ag_2CO_3 (2)	K_2CO_3 (1)	DMA	75	trace
20	$Cu(OAc)_2$ (2)	K_2CO_3 (1)	DMA	trace	15
21	$PhI(OAc)_2$ (2)	K_2CO_3 (1)	DMA	trace	trace

[a] Reaction conditions: **1a** (0.3 mmol), **2a** (2 equiv), [M], base, and DMA (*N,N*-diethylacetamide, 3 mL) at room temperature under argon. [b] At 50 ^oC.

(d) Scheme S1 Base-Mediated the Reaction of 2-Chloro-1-phenylethanone Oxime (1a) with 1,3-Dicarbonyl compounds (2)

As shown in Scheme S1, the reaction of 2-chloro-1-phenylethanone oxime (**1a**) with 1,3-dicarbonyl compounds **2** in the presence of bases alone were performed to increasing the length of the carbon chain. The results in Table 1 indicated that only 15% yield of 5-(acetoxyimino)-5-phenylpentan-2-one (**4aa**) was isolated from 2-chloro-1-phenylethanone oxime (**1a**) and pentane-2,4-dione (**2a**) in the presence of 1 equiv K_2CO_3 (entry 5; Table 1). Thus, the effect of bases was screened, and the results demonstrated that Na_2CO_3 was a preferred base in view of the yield, and the amount of Na_2CO_3 was found to affect the yield (Eq 1): While the reaction afforded the desired product **4aa** in 40% yield at a loading of 1 equiv Na_2CO_3, the yield was increased from 40% to 60% at 2 equiv Na_2CO_3 and to 58% using 3 equiv Na_2CO_3. 1,3-Diketones **2c** and **2d**, containing a or two phenyl groups adjacent to the carbonyl group, provided the corresponding products **4ac** and **4ad** in excellent yields. Using 3-keto ester **2o**, however, only nucleophilic replacement product **5ao** was obtained in the presence of Na_2CO_3 or Cs_2CO_3 (Eq 2).

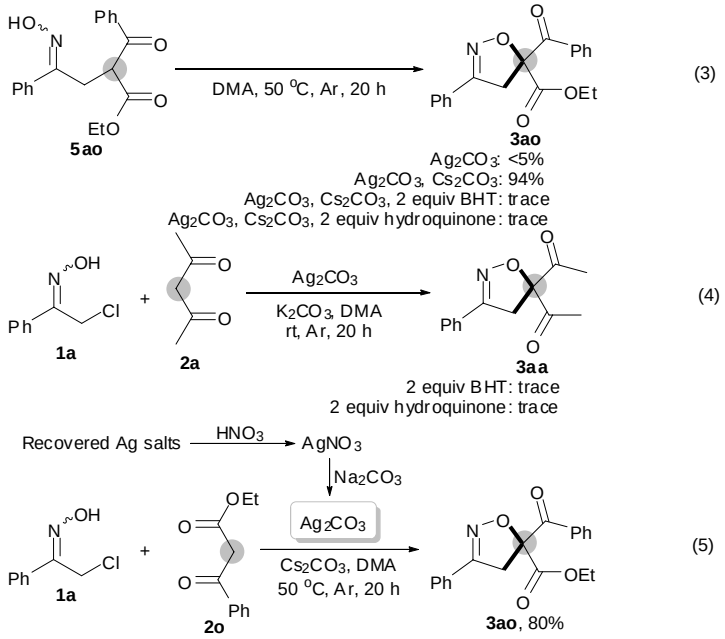


Scheme S1 Base-Mediated the Reaction of 2-Chloro-1-phenylethanone Oxime (**1a**) with 1,3-Dicarbonyl compounds (**2**).

(e) Scheme S2 Control Experiments

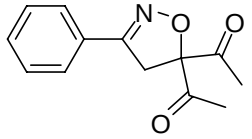
To elucidate the mechanism, some control experiments were carried out (Scheme S2). The results in Eq 3 showed that the reactivity of substrate **5ao** was rather lower using Ag_2CO_3 alone. To our delight, substrate **5ao** could be readily converted to isoxazoline **3aa** in the presence of both Ag_2CO_3 and K_2CO_3 (94% yield). These suggest that substrate **5ao** may be an intermediate for this Ag-mediated transformation. Subsequently, two radical inhibitors, BHT (2,6-di-*tert*-butyl-4-methylphenol) and hydroquinone, were added to this Ag-mediated reaction (Eq 3): a stoichiometric amount of BHT (2 equiv) or hydroquinone (2 equiv) resulted in no conversion of substrate **5ao**. Identical results were observed from the reaction substrate **1a** and diketone **2a** in the presence of either BHT or hydroquinone (Eq 4). These results imply that this Ag-mediated transformation includes a radical process, and the generation of a radical at the 2 position of 1,3-dicarbonyl compounds can be triggered by Ag_2CO_3.[8]

Notably, the silver salts were recovered and reused among this current reaction (Eq 5).[8e] Excess Ag_2CO_3 and all silver species were filtrated after the reaction and in turn treated with nitric acid and Na_2CO_3 to recover fresh Ag_2CO_3. Interestingly, the fresh Ag_2CO_3 was also efficient for this current reaction without loss of activity (Eq 5).



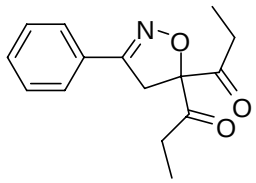
Scheme S2 Control Experiments.

(B) Analytical data for 3-5



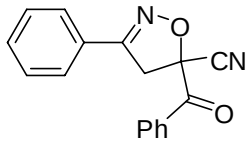
1,1'-(3-phenyl-4,5-dihydroisoxazole-5,5-diyl)diethanone (3aa):

White solid, mp 78.3-79.6 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67-7.64 (m, 2H), 7.47-7.39 (m, 3H), 3.78 (s, 2H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.4, 156.6, 131.0, 128.9, 127.7, 126.9, 97.5, 40.1, 25.9; IR (KBr, cm^{-1}): 1719, 1689; LRMS (EI, 70 eV) *m/z* (%): 231 (M^+, 4), 189 (100), 160 (21), 118 (85); HRMS *m/z* (ESI) calcd for $C_{13}H_{14}NO_3$ $(M+H)^+$ 232.0968, found 232.0964.



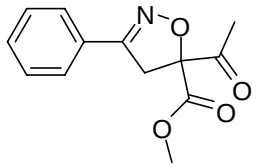
1,1'-(3-phenyl-4,5-dihydroisoxazole-5,5-diyl)dipropan-1-one (3ab):

White solid, mp 89.0-89.9 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67-7.64 (m, 2H), 7.46-7.38 (m, 3H), 3.78 (s, 2H), 2.84-2.64 (m, 4H), 1.09 (t, *J* = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.4, 156.6, 130.9, 128.9, 127.9, 126.9, 97.7, 40.7, 31.7, 7.3; IR (KBr, cm^{-1}): 1720, 1693; LRMS (EI, 70 eV) *m/z* (%): 259 (M^+, 1), 203 (20), 146 (18), 57 (100); HRMS *m/z* (ESI) calcd for $C_{15}H_{18}NO_3$ $(M+H)^+$ 260.1281, found 260.1282.



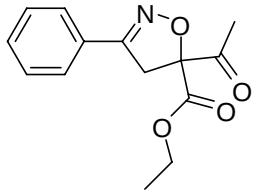
5-benzoyl-3-phenyl-4,5-dihydroisoxazole-5-carbonitrile (3ae):

White solid, mp 102.2-103.5 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.28-8.26 (m, 2H), 7.71-7.68 (m, 3H), 7.56 (t, *J* = 8.0 Hz, 2H), 7.52-7.43 (m, 3H), 4.65 (d, *J* = 17.2 Hz, 1H), 3.92 (d, *J* = 17.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 185.2, 156.8, 135.1, 131.4, 130.7, 128.9, 127.2, 126.9, 116.9, 81.5, 43.7; IR (KBr, cm^{-1}): 1691; LRMS (EI, 70 eV) *m/z* (%): 276 (M^+, 1), 249 (2), 221 (2), 105 (100); HRMS *m/z* (ESI) calcd for $C_{17}H_{13}N_2O_2$ $(M+H)^+$ 277.0972, found 277.0983.



5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid methyl ester (3af):

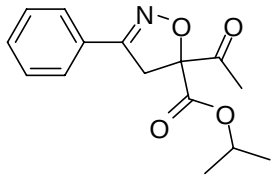
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67-7.64 (m, 2H), 7.46-7.38 (m, 3H), 3.94-3.83 (m, 5H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.4, 167.9, 156.5, 130.8, 128.8, 127.8, 126.9, 92.6, 53.6, 40.9, 25.8; IR (KBr, cm^{-1}): 1751, 1695; LRMS (EI, 70 eV) *m/z* (%): 247 (M^+, 4), 188 (46), 177 (36), 144 (100); HRMS *m/z* (ESI) calcd for $C_{13}H_{14}NO_4$ $(M+H)^+$ 248.0917, found 248.0909.



5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (3ag):

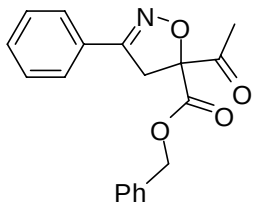
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67-7.64 (m, 2H), 7.45-7.38 (m, 3H), 4.32-4.27 (m, 2H), 3.94-3.81 (m, 2H), 2.42 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.5, 167.3, 156.5, 130.8, 128.8, 127.9, 126.9, 92.7, 62.9, 40.8, 25.8, 13.9; IR (KBr, cm^{-1}): 1749, 1698; LRMS (EI, 70 eV) *m/z* (%): 261

(M^+, 3), 176 (7), 162 (14), 144 (100); HRMS *m/z* (ESI) calcd for $C_{14}H_{16}NO_4$ $(M+H)^+$ 262.1074, found 262.1083.



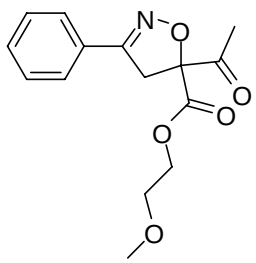
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid isopropyl ester (3ah):

Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.66-7.64 (m, 2H), 7.44-7.37 (m, 3H), 5.15-5.08 (m, 1H), 3.93-3.77 (m, 2H), 2.41 (s, 3H), 1.29 (t, *J* = 6.0 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.4, 166.8, 156.4, 130.7, 128.8, 128.0, 126.9, 92.8, 71.0, 40.6, 25.7, 21.4 (2C); IR (KBr, cm^{-1}): 1754, 1693; LRMS (EI, 70 eV) *m/z* (%): 275 (M^+, 3), 188 (50), 160 (18), 144 (100); HRMS *m/z* (ESI) calcd for $C_{15}H_{18}NO_4$ $(M+H)^+$ 276.1230, found 276.1243.



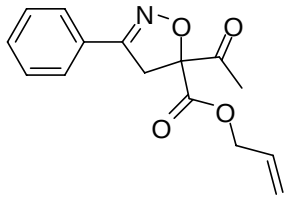
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid benzyl ester (3ai):

Colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ: 7.67-7.64 (m, 2H), 7.44-7.34 (m, 8H), 5.27 (s, 2H), 3.96-3.82 (m, 2H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.2, 167.2, 156.5, 134.5, 130.8, 128.8, 128.6 (2C), 128.3, 128.2, 126.9, 92.7, 68.3, 40.8, 25.8; IR (KBr, cm^{-1}): 1746, 1688; LRMS (EI, 70 eV) *m/z* (%): 323 (M^+, 1), 236 (8), 188 (15), 91 (100); HRMS *m/z* (ESI) calcd for $C_{19}H_{18}NO_4$ $(M+H)^+$ 324.1230, found 324.1256.



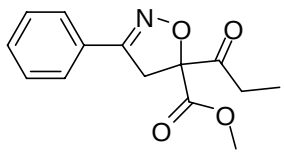
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid 2-methoxyethyl ester (3aj):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65-7.63 (m, 2H), 7.44-7.36 (m, 3H), 4.38-4.36 (m, 2H), 3.97-3.78 (m, 2H), 3.60-3.58 (m, 2H), 3.33 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.6, 167.4, 156.4, 130.8, 128.8, 127.9, 126.9, 92.5, 69.7, 65.4, 58.8, 40.6, 25.6; IR (KBr, cm^{-1}): 1756, 1696; LRMS (EI, 70 eV) *m/z* (%): 291 (M^+, 1), 221 (5), 188 (64), 144 (100); HRMS *m/z* (ESI) calcd for $C_{15}H_{18}NO_5$ $(M+H)^+$ 292.1179, found 292.1190.



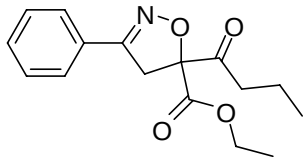
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid allyl ester (3ak):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.66-7.64 (m, 2H), 7.45-7.37 (m, 3H), 5.95-5.85 (m, 1H), 5.37-5.26 (m, 2H), 4.72 (d, *J* = 5.6 Hz, 2H), 3.94-3.83 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.4, 167.0, 156.5, 130.8, 130.6, 128.8, 127.9, 126.9, 119.6, 92.7, 67.1, 40.8, 25.8.; IR (KBr, cm^{-1}): 1749, 1690; LRMS (EI, 70 eV) *m/z* (%): 273 (M^+, 3), 202(6), 188 (50), 144 (100); HRMS *m/z* (ESI) calcd for $C_{15}H_{16}NO_4$ $(M+H)^+$ 274.1074, found 274.1082.



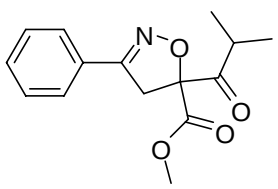
3-phenyl-5-propionyl-4,5-dihydroisoxazole-5-carboxylic acid methyl ester (3al):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.65-7.64 (m, 2H), 7.45-7.37 (m, 3H), 3.89 (s, 2H), 3.83 (s, 3H), 2.85-2.80 (m, 2H), 1.09 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 205.4, 168.0, 156.5, 130.8, 128.8, 127.9, 126.9, 92.6, 53.6, 41.3, 31.5, 7.2; IR (KBr, cm^{-1}): 1756, 1694; LRMS (EI, 70 eV) *m/z* (%): 261 (M^+, 1), 202 (10), 144 (16), 57 (100); HRMS *m/z* (ESI) calcd for $C_{14}H_{16}NO_4$ $(M+H)^+$ 262.1074, found 262.1083.



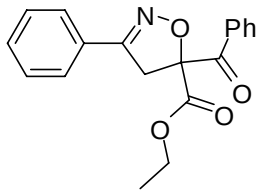
5-butyryl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (3am):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67-7.65 (m, 2H), 7.45-7.38 (m, 3H), 4.31-4.26 (m, 2H), 3.93-3.82 (m, 2H), 2.77 (t, *J* = 7.2 Hz, 2H), 1.67-1.61 (m, 2H), 1.30 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 204.8, 167.5, 156.5, 130.8, 128.8, 128.0, 126.9, 92.8, 62.9, 41.0, 39.9, 16.6, 13.9, 13.4; IR (KBr, cm^{-1}): 1750, 1689; LRMS (EI, 70 eV) *m/z* (%): 289 (M^+, 1), 216 (12), 144 (16), 71 (100); HRMS *m/z* (ESI) calcd for $C_{16}H_{20}NO_4$ $(M+H)^+$ 290.1387, found 290.1396.



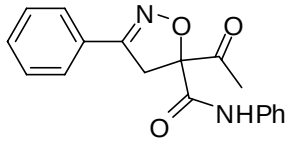
5-isobutyryl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid methyl ester (3an):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.68-7.65 (m, 2H), 7.46-7.38 (m, 3H), 3.89 (s, 2H), 3.83 (s, 3H), 3.32-3.25 (m, 1H), 1.18 (d, *J* = 6.8 Hz, 3H), 1.11 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 208.9, 168.2, 156.5, 130.8, 128.8, 127.9, 127.0, 92.7, 53.5, 41.8, 36.8, 18.9, 18.7; IR (KBr, cm^{-1}): 1752, 1697; LRMS (EI, 70 eV) *m/z* (%):275 (M^+, 1), 232 (42), 172 (70), 71 (100); HRMS *m/z* (ESI) calcd for $C_{15}H_{18}NO_4$ $(M+H)^+$ 276.1230, found 276.1242.



5-benzoyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (3ao):[2]

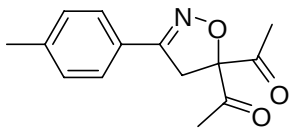
Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14-8.12 (m, 2H), 7.71-7.69 (m, 2H), 7.61-7.57 (m, 1H), 7.49-7.38 (m, 5H), 4.56 (d, *J* = 17.6 Hz, 1H), 4.26-4.21 (m, 2H), 3.72 (d, *J* = 17.6 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 189.9, 169.0, 156.1, 133.9, 133.3, 130.7, 130.0, 128.7, 128.6, 128.0, 127.0, 91.9, 62.7, 42.1, 13.7; LRMS (EI, 70 eV) *m/z* (%): 323 (M^+, 1), 250 (88), 190 (18), 105 (100).



5-acetyl-*N*,3-diphenyl-4,5-dihydroisoxazole-5-carboxamide (3ap):

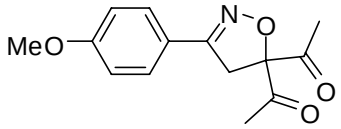
Pale yellow solid, mp 149.2-150.7 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.76 (s, 1H), 7.67-.7.60 (m, 4H), 7.48-7.34 (m, 5H), 7.17 (t, *J* = 7.6 Hz, 1H), 4.29 (d, *J* = 17.6 Hz, 1H), 3.72 (d, *J* = 18 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.6, 166.3, 158.0, 136.4, 131.2, 129.1, 128.9, 127.1, 125.3, 119.9, 93.1,

40.8, 25.3; IR (KBr, cm^{-1}): 1730, 1681; LRMS (EI, 70 eV) *m/z* (%): 308 (M^+, 1), 207 (18), 188 (89), 146 (100); HRMS *m/z* (ESI) calcd for $C_{18}H_{17}N_2O_3$ $(M+H)^+$ 309.1234, found 309.1230.



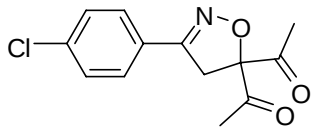
1,1'-(3-*p*-tolyl-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ca):

White solid, mp 74.6-75.9 ^oC (uncorrected); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.54 (d, *J* = 6.4 Hz, 2H), 7.21 (d, *J* = 6.8 Hz, 2H), 3.75 (s, 2H), 2.37 (s, 3H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.5, 156.5, 141.3, 129.5, 126.9, 124.9, 97.4, 40.2, 25.7, 21.4; IR (KBr, cm^{-1}): 1720, 1687; LRMS (EI, 70 eV) *m/z* (%): 245 (M^+, 12), 203 (75), 160 (52), 132 (100); HRMS *m/z* (ESI) calcd for $C_{14}H_{16}NO_3$ $(M+H)^+$ 246.1125, found 246.1142.



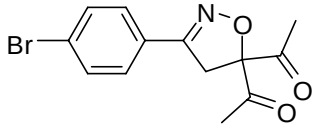
1,1'-(3-(4-methoxyphenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3da):

White solid, mp 88.9-90.1 ^oC (uncorrected); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.60-7.56 (m, 2H), 6.93-6.89 (m, 2H), 3.82 (s, 3H), 3.73 (s, 2H), 2.34 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.6, 161.6, 156.1, 128.6, 120.2, 114.2, 97.3, 55.3, 40.3, 25.8; IR (KBr, cm^{-1}): 1717, 1690; LRMS (EI, 70 eV) *m/z* (%): 261 (M^+, 29), 219 (42), 176 (49), 148 (100); HRMS *m/z* (ESI) calcd for $C_{14}H_{16}NO_4$ $(M+H)^+$ 262.1074, found 262.1083.



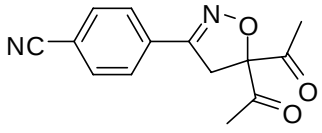
1,1'-(3-(4-chlorophenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ea):

White solid, mp 78.4-79.6 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.58 (d, *J* = 8.4 Hz, 2H), 7.38 (d, *J* = 8.4 Hz, 2H), 3.73 (s, 2H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.1, 155.7, 137.0, 129.2, 128.2, 126.3, 97.8, 39.8, 25.8; IR (KBr, cm^{-1}): 1719, 1688; LRMS (EI, 70 eV) *m/z* (%): 267 (M^++2, 3), 265 (M^+, 9), 222 (100), 180 (63); HRMS *m/z* (ESI) calcd for $C_{13}H_{13}ClNO_3$ $(M+H)^+$ 266.0578, found 266.0586.



1,1'-(3-(4-bromophenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3fa):

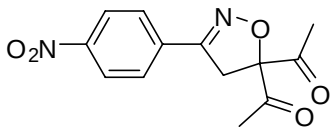
White solid, mp 97.1-98.1 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.62-7.47 (m, 4H), 3.73 (s, 2H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.1, 155.8, 132.1, 128.3, 126.7, 125.3, 97.8, 39.8, 25.8; IR (KBr, cm^{-1}): 1718, 1688; LRMS (EI, 70 eV) *m/z* (%): 311 (M^++2, 10), 309 (M^+, 11), 267 (100), 226 (47); HRMS *m/z* (ESI) calcd for $C_{13}H_{13}BrNO_3$ $(M+H)^+$ 310.0073, found 310.0076.



4-(5,5-diacetyl-4,5-dihydroisoxazol-3-yl)benzonitrile (3ga):

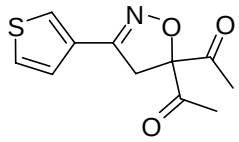
White solid, mp 128.5-129.5 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77-7.69 (m, 4H), 3.76 (s, 2H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.6,

155.4, 132.6, 132.0, 127.4, 117.9, 114.2, 98.3, 39.3, 25.8; IR (KBr, cm^{-1}): 1721, 1689; LRMS (EI, 70 eV) *m/z* (%): 256 (M^+, 1), 214 (100), 186 (45), 171 (63); HRMS *m/z* (ESI) calcd for $C_{14}H_{13}N_2O_3$ $(M+H)^+$ 257.0921, found 257.0921.



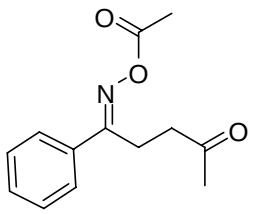
1,1'-(3-(4-nitrophenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ha):

White solid; mp 138.0-139.7 ^oC (uncorrected); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.24 (d, *J* = 8.8 Hz, 2H), 7.83 (d, *J* = 8.8 Hz, 2H), 3.80 (s, 2H), 2.36 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 201.5, 155.1, 148.8, 133.8, 127.8, 124.0, 98.4, 39.4, 25.8; IR (KBr, cm^{-1}): 1722, 1687; LRMS (EI, 70 eV) *m/z* (%): 276 (M^+, 1), 234 (100), 206 (43), 191 (44); HRMS *m/z* (ESI) calcd for $C_{13}H_{13}N_2O_5$ $(M+H)^+$ 277.0819, found 277.0823.



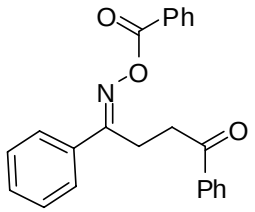
1,1'-(3-(thiophen-3-yl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ia):

White solid; mp 109.6-110.4 ^oC (uncorrected); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.53-7.52 (m, 1H), 7.46-7.44 (m, 1H), 7.39-7.37 (m, 1H), 3.74 (s, 2H), 2.35 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 202.3, 152.6, 129.4, 127.3, 127.0, 125.4, 97.2, 40.7, 25.8; IR (KBr, cm^{-1}): 1717, 1686; LRMS (EI, 70 eV) *m/z* (%): 237 (M^+, 10), 195 (100), 166 (16), 152 (55); HRMS *m/z* (ESI) calcd for $C_{11}H_{12}NO_3S$ $(M+H)^+$ 238.0532, found 238.0538.



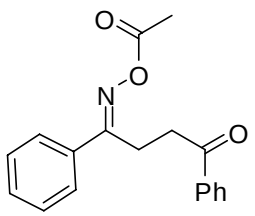
(*E*)-5-(acetoxyimino)-5-phenylpentan-2-one (4aa):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (d, *J* = 7.2 Hz, 2H), 7.44-7.38 (m, 3H), 3.09 (t, *J* = 8.0 Hz, 2H), 2.68 (t, *J* = 8.0 Hz, 2H), 2.25 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 206.1, 168.9, 165.3, 133.3, 130.7, 128.7, 127.2, 39.7, 29.8, 22.1, 19.8; IR (KBr, cm^{-1}): 1763, 1698; HRMS *m/z* (ESI) calcd for $C_{13}H_{16}NO_3$ $(M+H)^+$ 234.1125, found 234.1127.



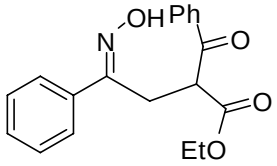
(*E*)-4-(benzoyloxyimino)-1,4-diphenylbutan-1-one (4ac):

White solid, mp 92.3-93.4 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09-8.07 (m, 2H), 7.94-7.91 (m, 2H), 7.85-7.83 (m, 2H), 7.61-7.54 (m, 2H), 7.50-7.41 (m, 7H), 3.46-3.42 (m, 2H), 3.34-3.30 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.6, 166.5, 163.7, 136.1, 133.5, 133.4, 130.9, 129.6, 128.8 (2C), 128.7, 128.6, 128.0, 127.3, 35.2, 22.9; IR (KBr, cm^{-1}): 1727, 1677; HRMS *m/z* (ESI) calcd for $C_{23}H_{20}NO_3$ $(M+H)^+$ 358.1438, found 358.1434.



(*E*)-4-(acetoxyimino)-1,4-diphenylbutan-1-one (4ad):

White solid, mp 80.4-81.6 ^{o}C (uncorrected); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.92 (d, *J* = 7.6 Hz, 2H), 7.75 (d, *J* = 6.8 Hz, 2H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.46-7.38 (m, 5H), 3.30-3.20 (m, 4H), 2.23 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 197.5, 168.7, 165.4, 136.2, 133.4, 133.3, 130.7, 128.7, 128.6, 127.9, 127.2, 35.1, 22.7, 19.7; IR (KBr, cm^{-1}): 1758, 1681; HRMS *m/z* (ESI) calcd for $C_{18}H_{18}NO_3$ $(M+H)^+$ 296.1281, found 296.1273.



(*E*)-ethyl 2-benzoyl-4-(hydroxyimino)-4-phenylbutanoate (5ao):

Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 9.63 (s, 1H), 7.94 (d, *J* = 7.6 Hz, 2H), 7.59-7.52 (m, 3H), 7.43-7.32 (m, 5H), 4.96 (t, *J* = 7.6 Hz, 1H), 3.98-3.92 (m, 2H), 3.51-3.40 (m, 2H), 1.01 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 194.6, 169.3, 157.0, 135.8, 135.2, 133.6, 129.4, 128.6 (2C), 128.5, 126.6, 61.6, 50.5, 26.4, 13.6.

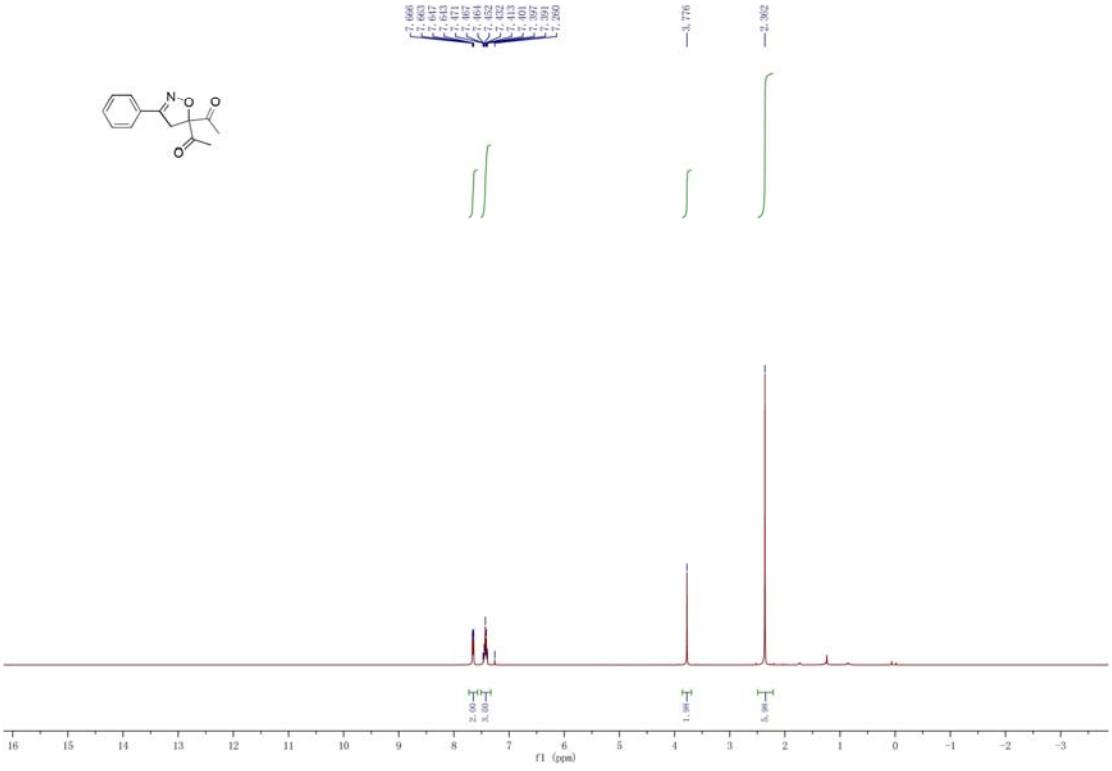
(C) Reference

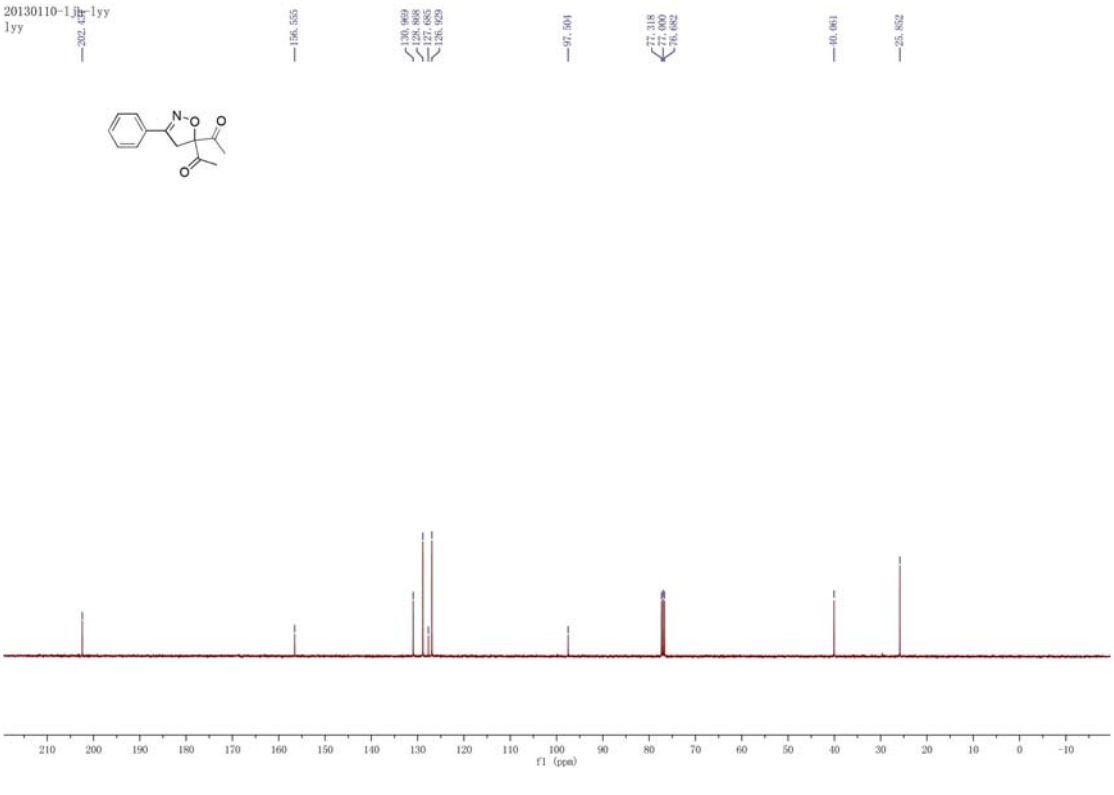
1 *(a)* J. M. Hatcher, M. C. Kohler and D. M. Coltart, *Org. Lett.*, 2011, **13**, 3810; *(b)* T. C. Wabnitz, S. Saaby and K. A. Jørgensen, *Org. Biomol. Chem.*, 2004, **2**, 828; *(c)* V. Pavlishchuk, F. Birkelbach, T. Weyhermuller, K.Wieghardt and P. Chaudhuri, *Inorg. Chem.*, 2002, **41**, 4405; *(d)* S. K. Boyer, R. A. Pfund, R. E. Portmann, G. H. Sedelmeier and H. F. Wetter, *Helv. Chim. Acta.*, 1988, **71**, 337.

2 M. Yamauchi, *J. Heterocyclic Chem*., 2002, **39**, 1013.

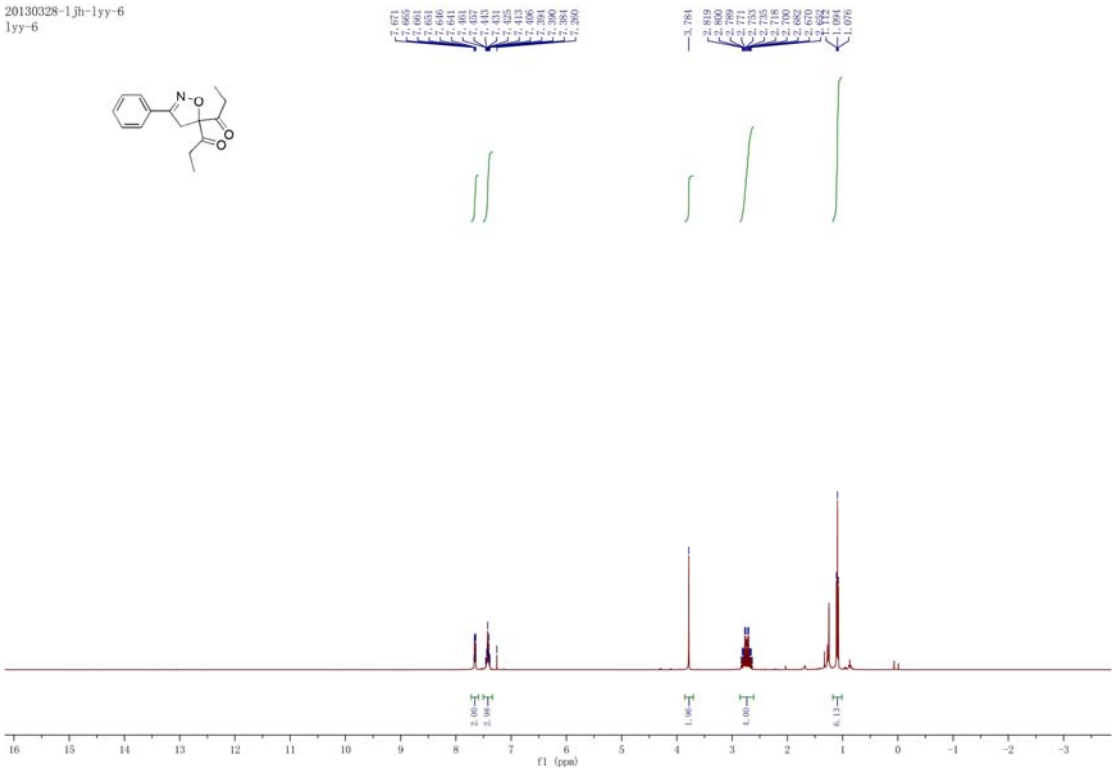
(D) Spectra

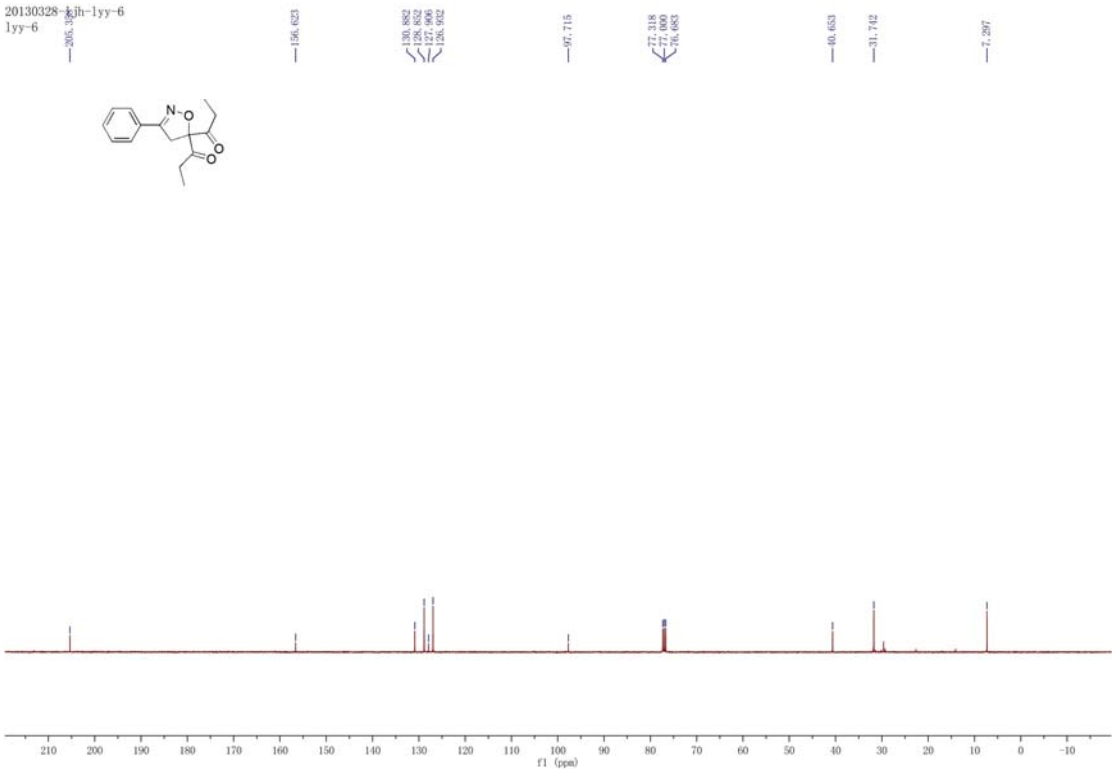
1,1'-(3-phenyl-4,5-dihydroisoxazole-5,5-diyl)diethanone (3aa):



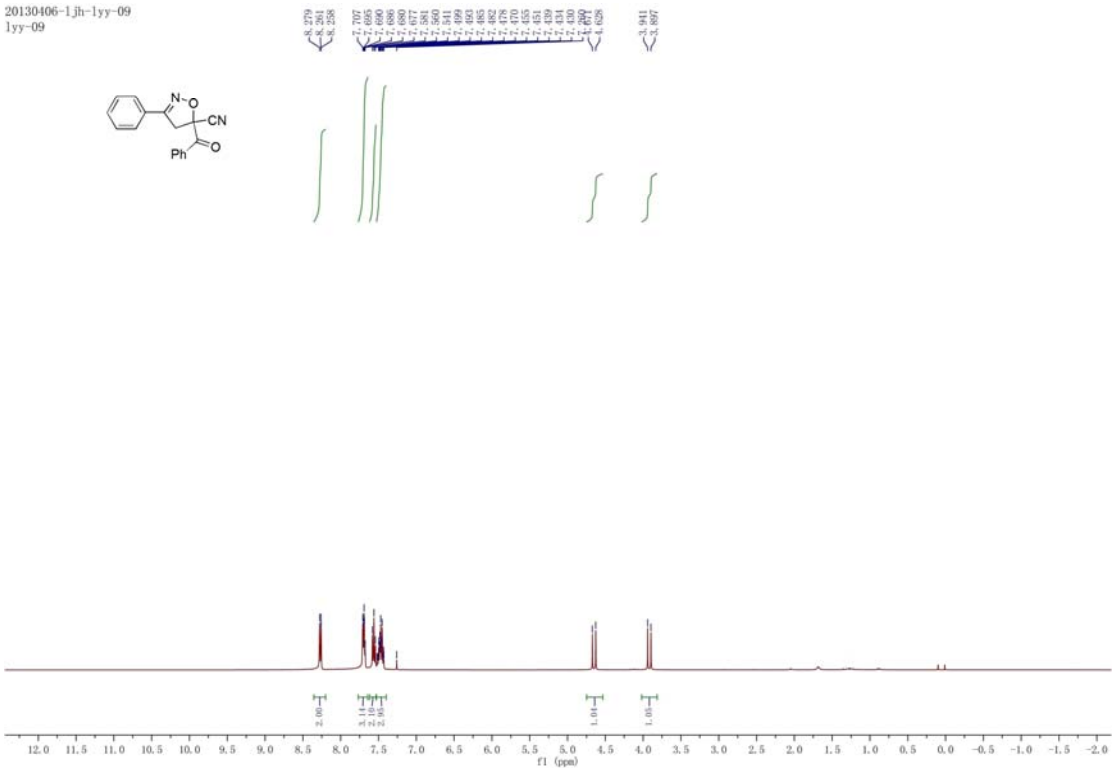


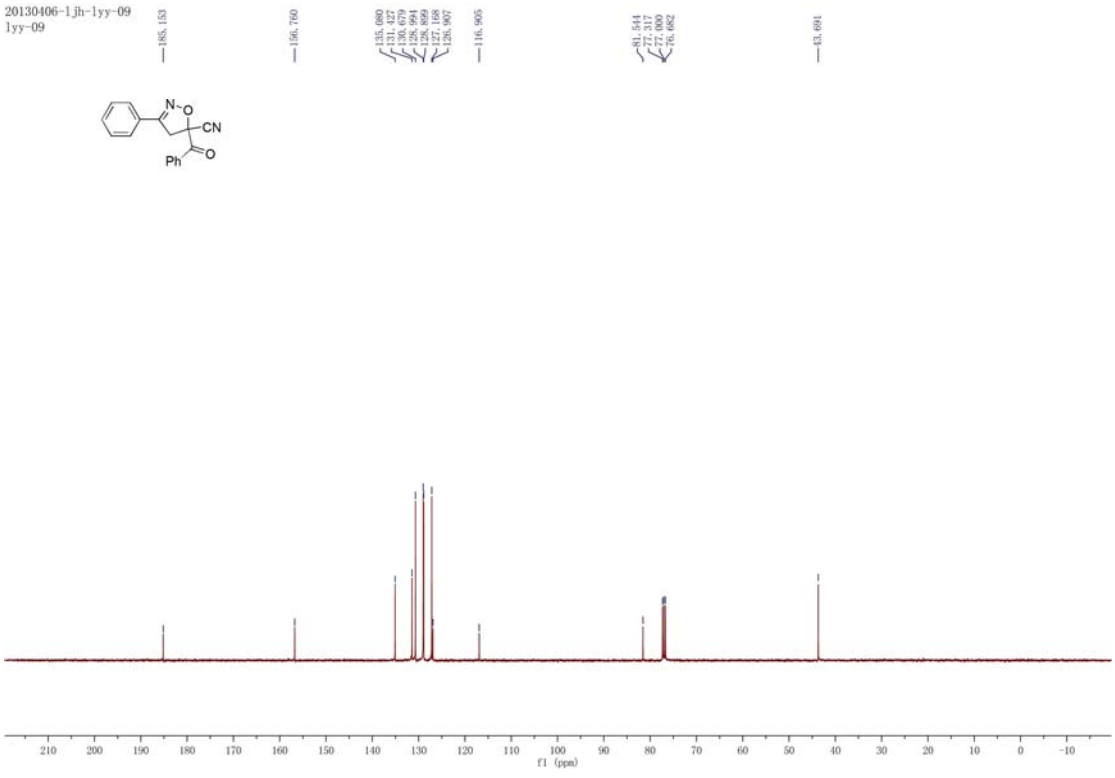
1,1'-(3-phenyl-4,5-dihydroisoxazole-5,5-diyl)dipropan-1-one (3ab):



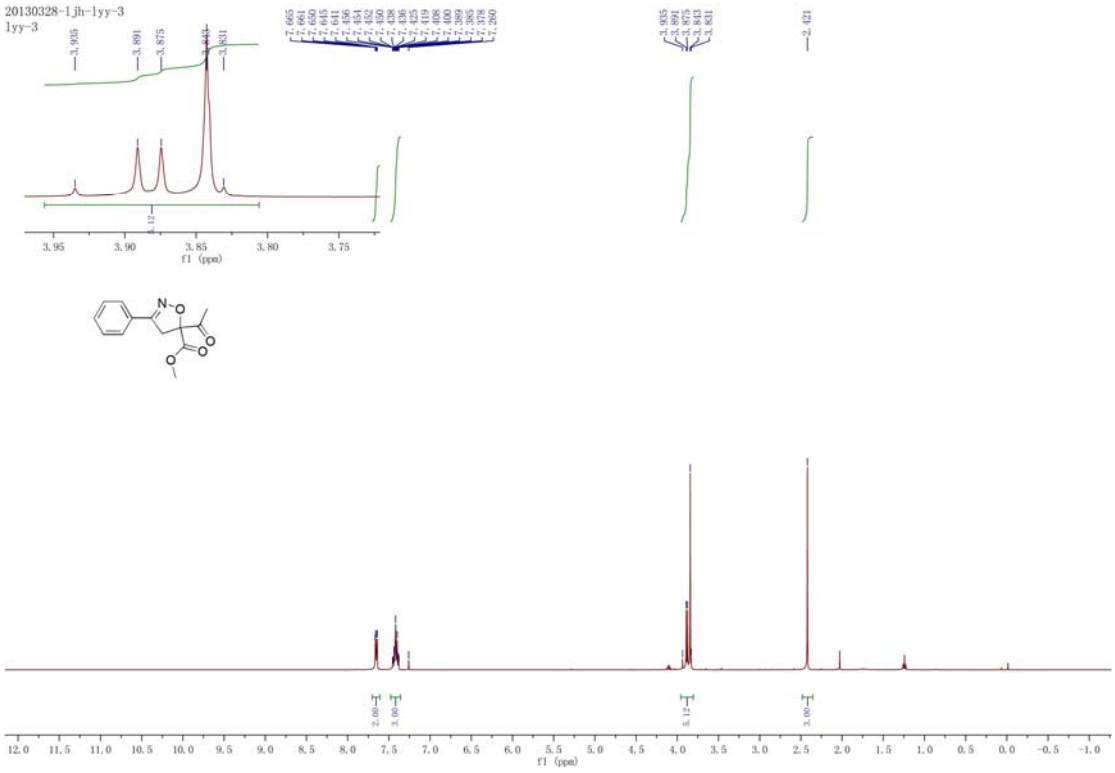


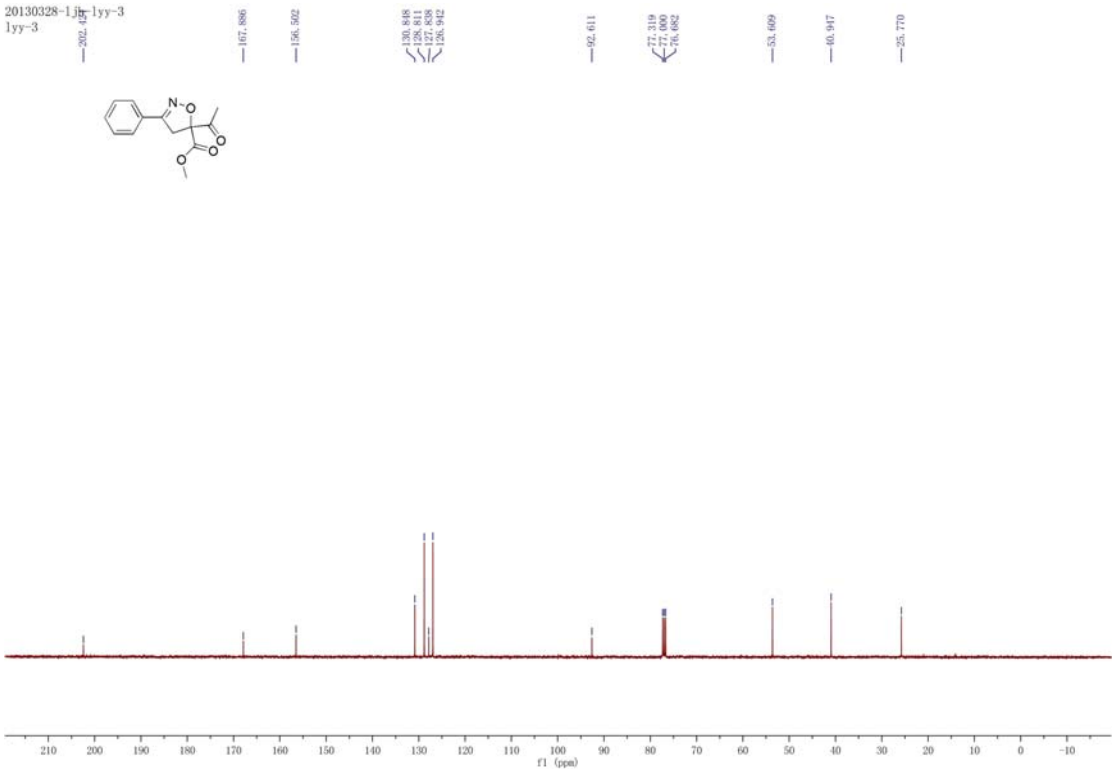
5-benzoyl-3-phenyl-4,5-dihydroisoxazole-5-carbonitrile (3ae):



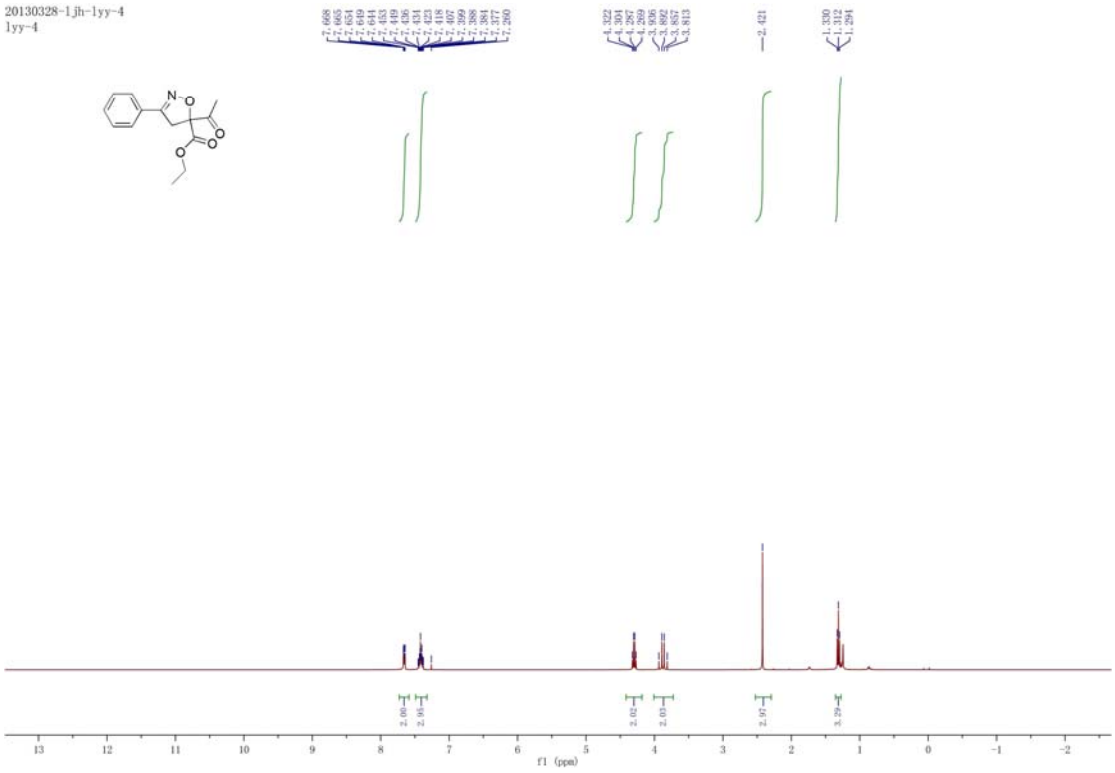


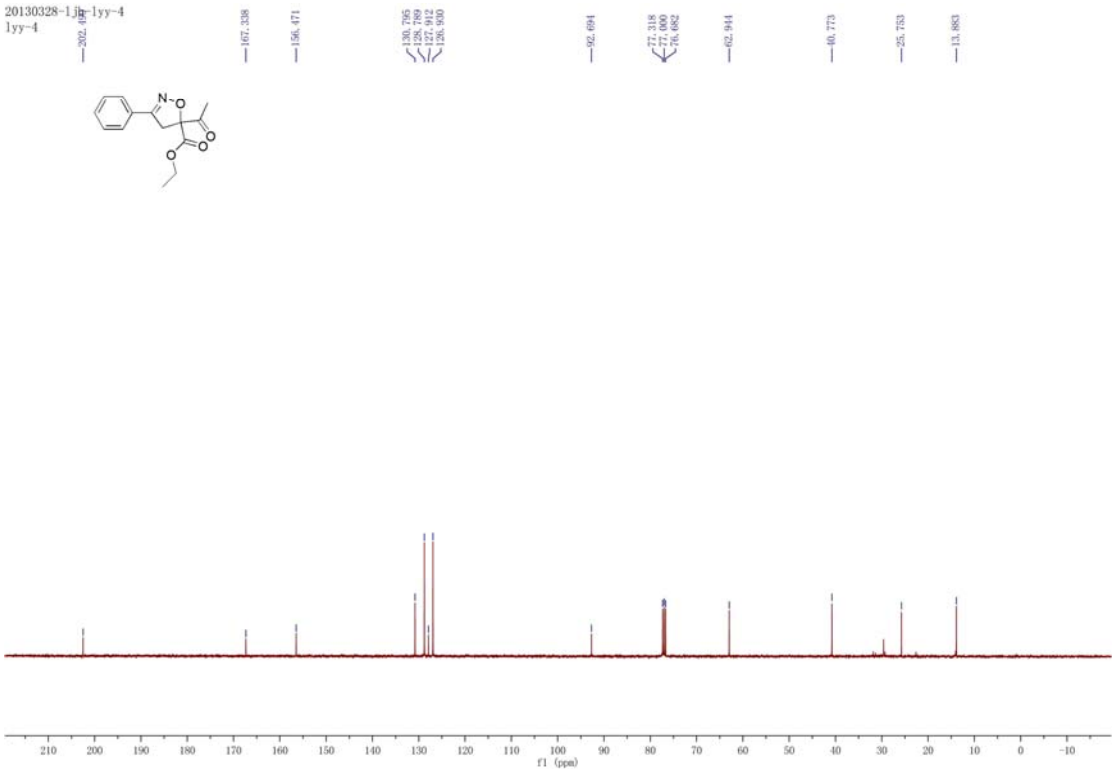
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid methyl ester (3af):



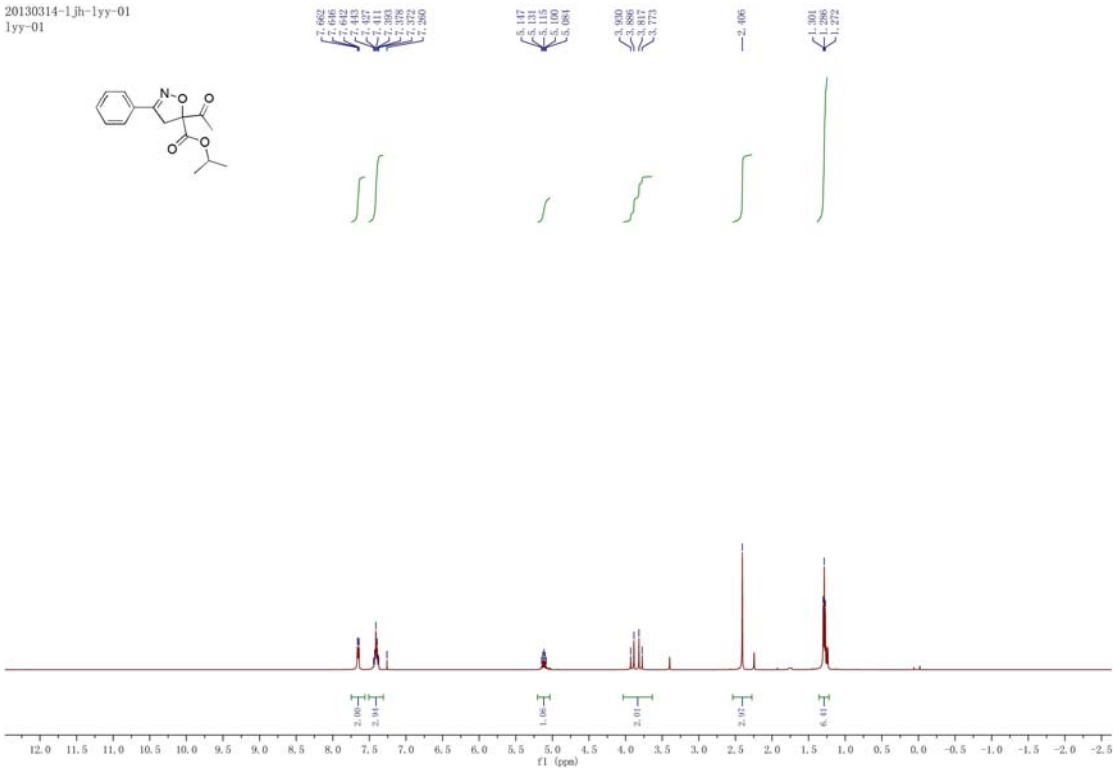


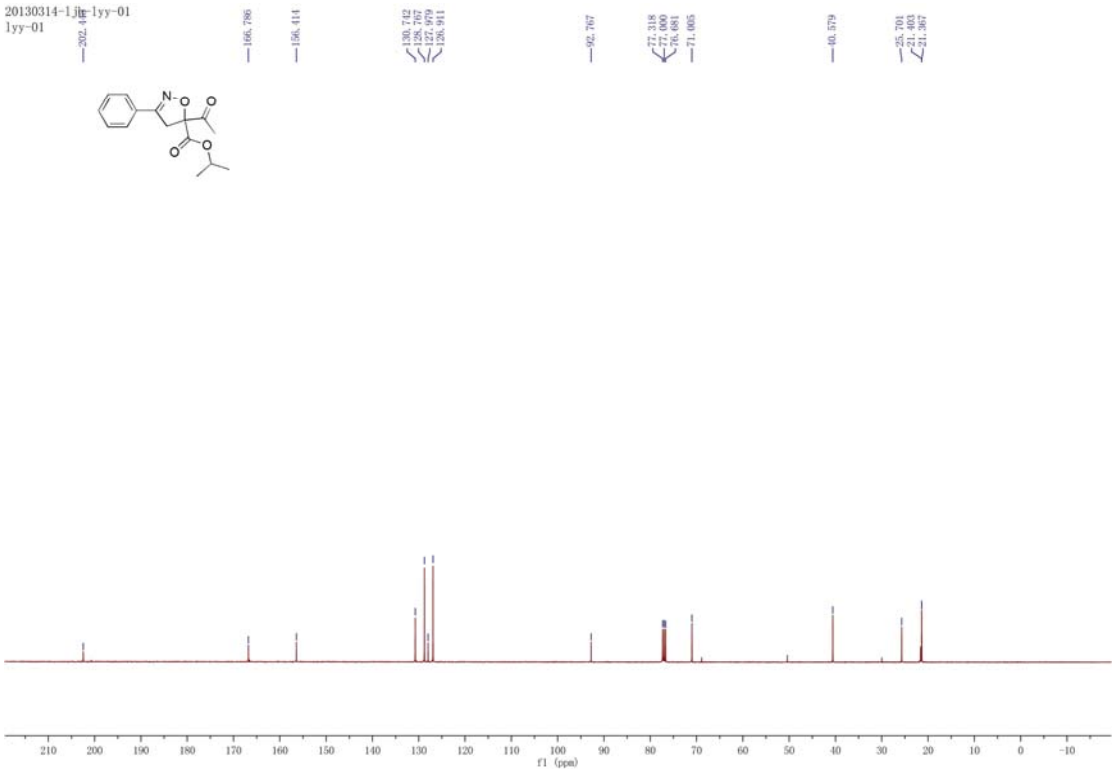
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (3ag):



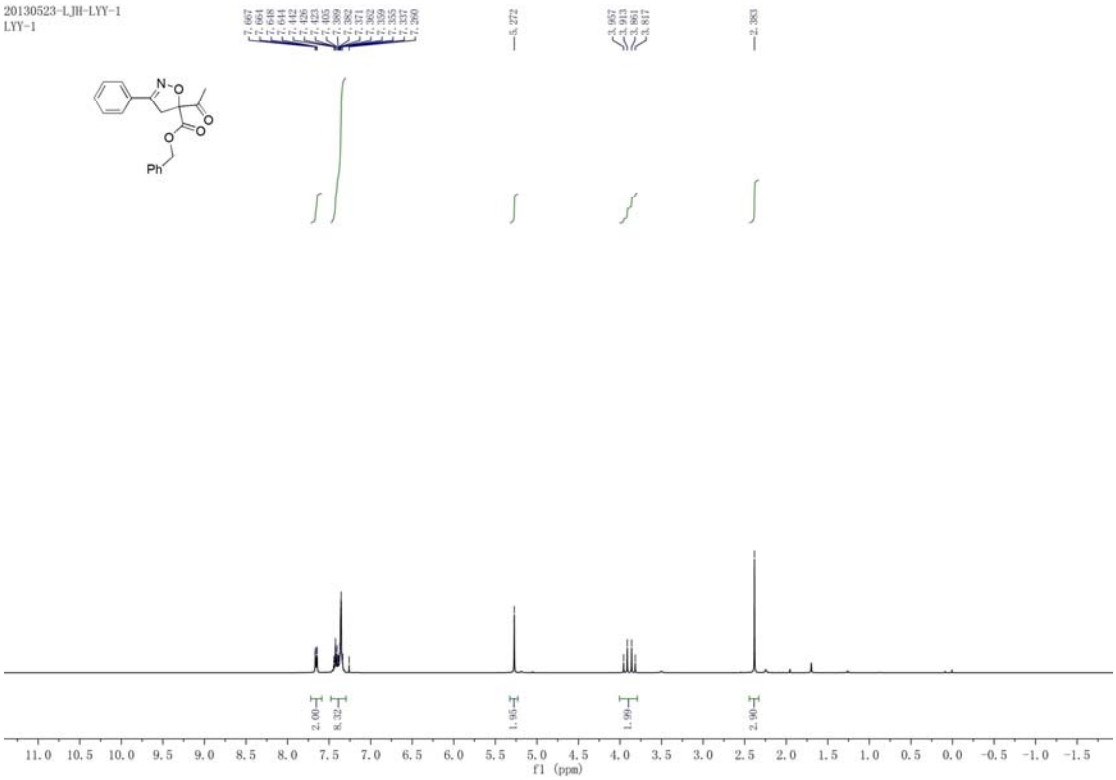


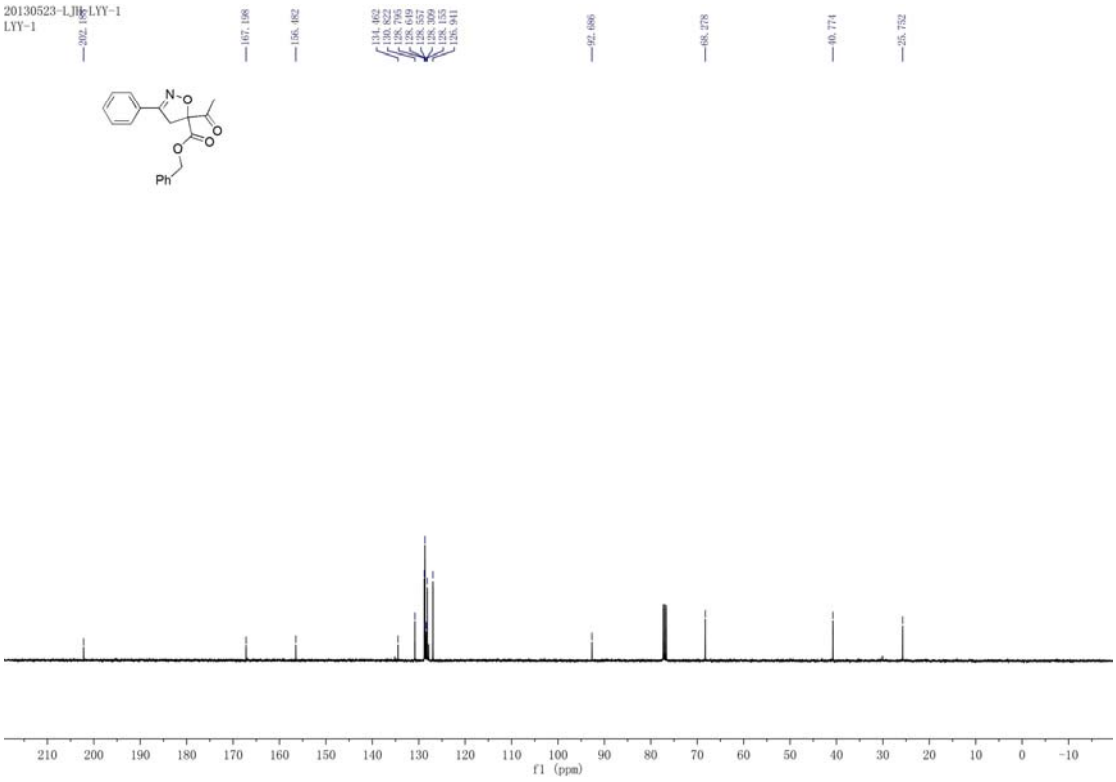
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid isopropyl ester (3ah):





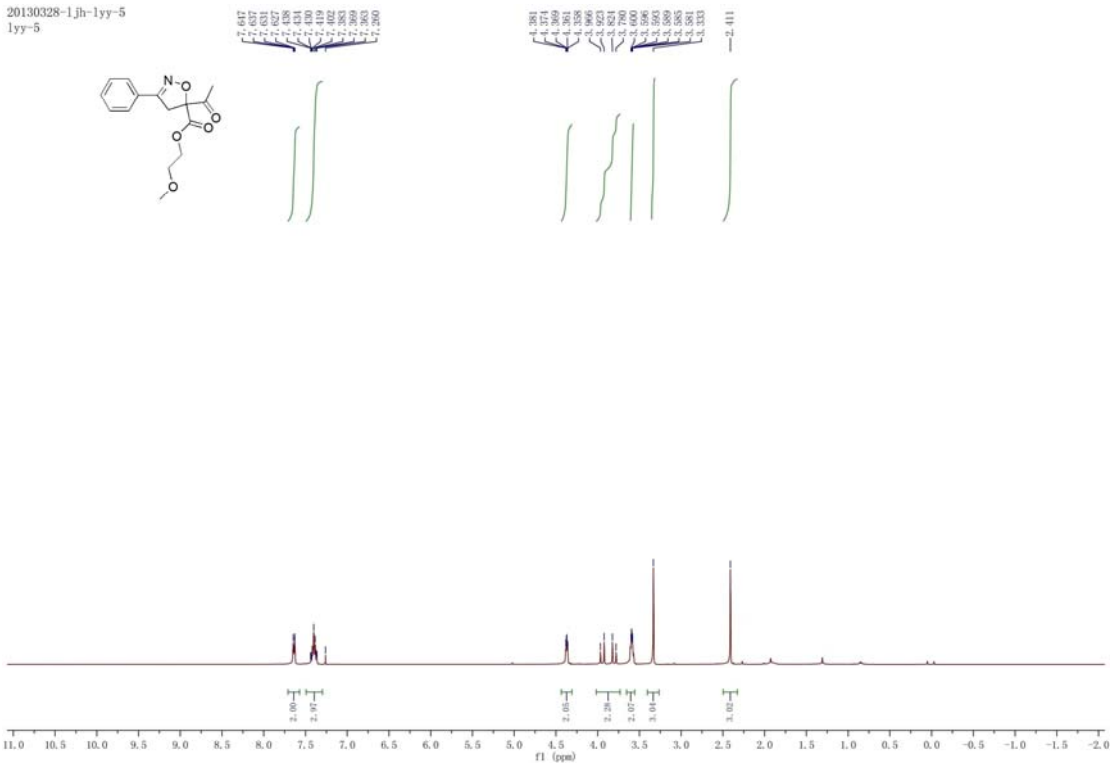
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid benzyl ester (3ai):

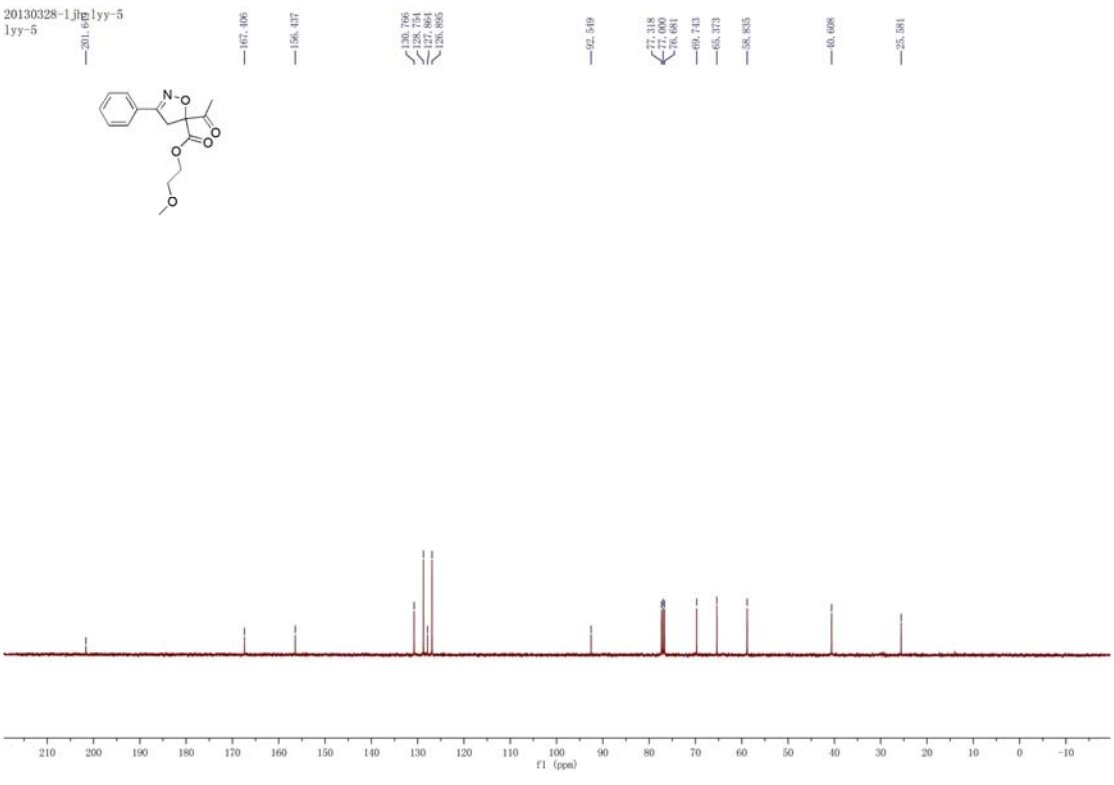




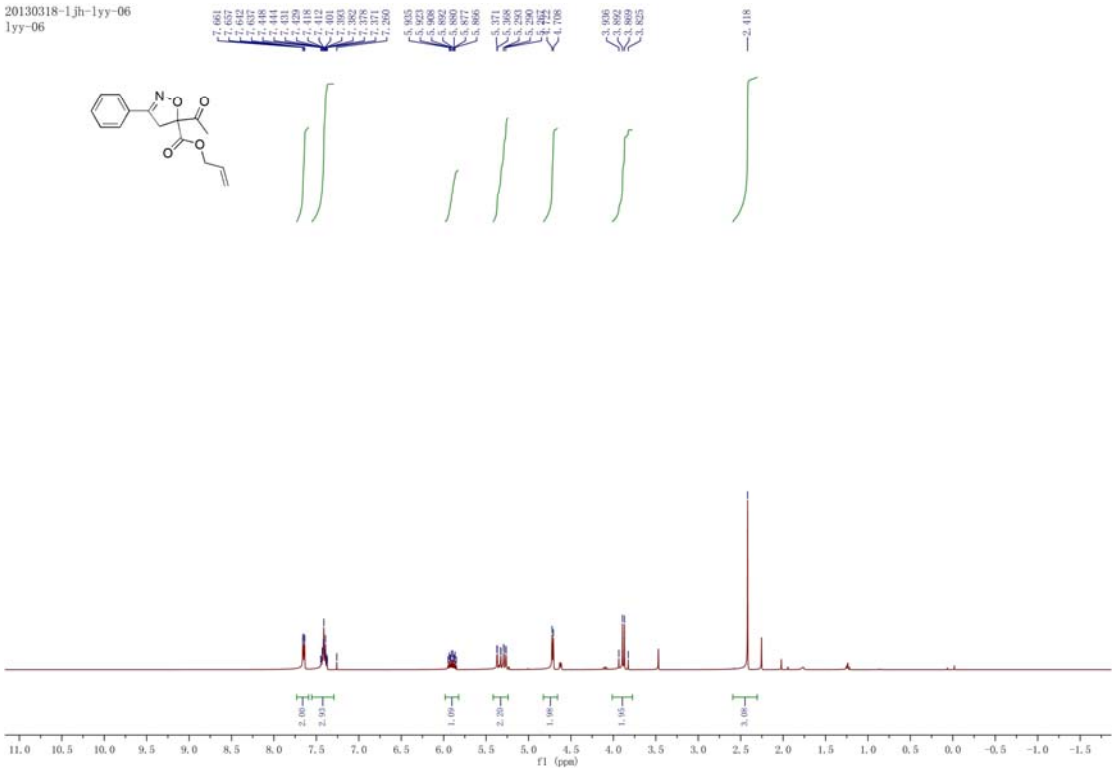
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid 2-methoxyethyl ester

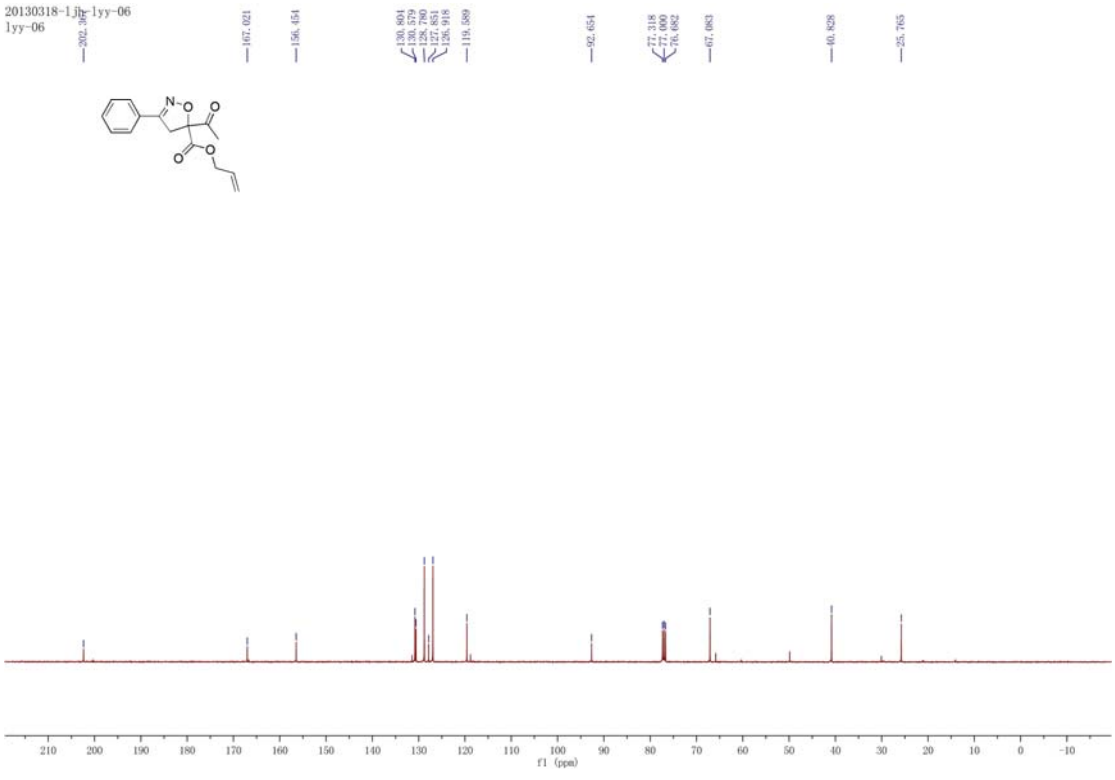
(3aj):



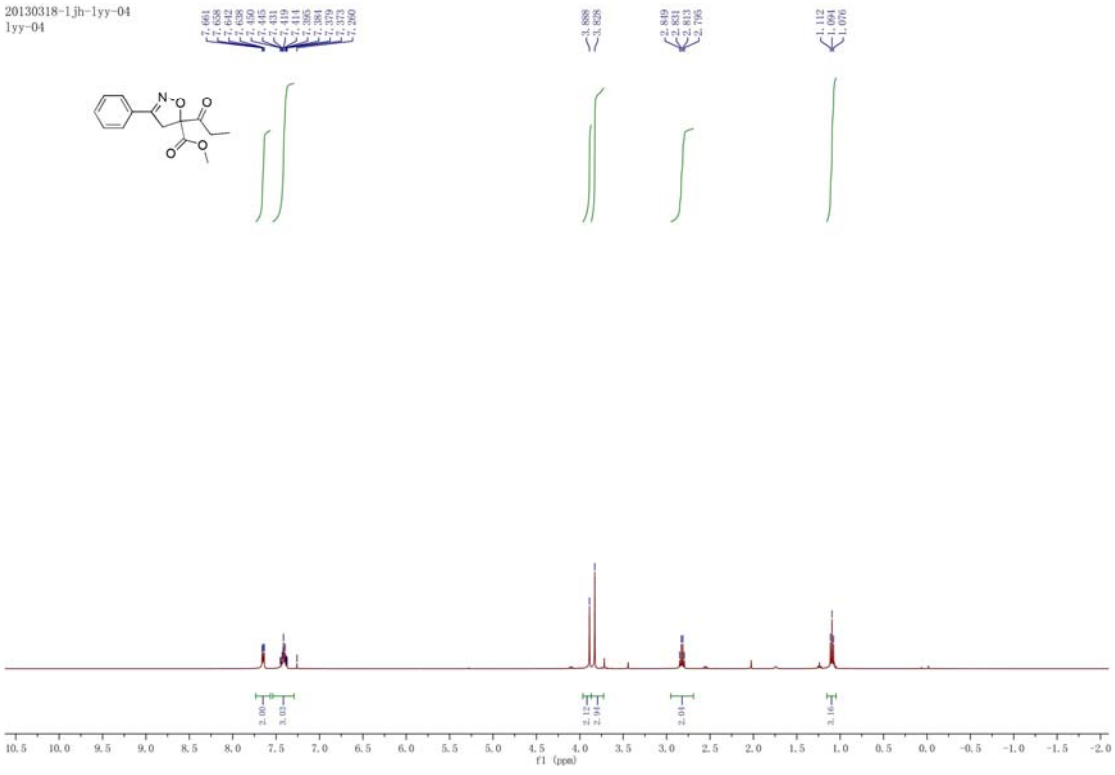


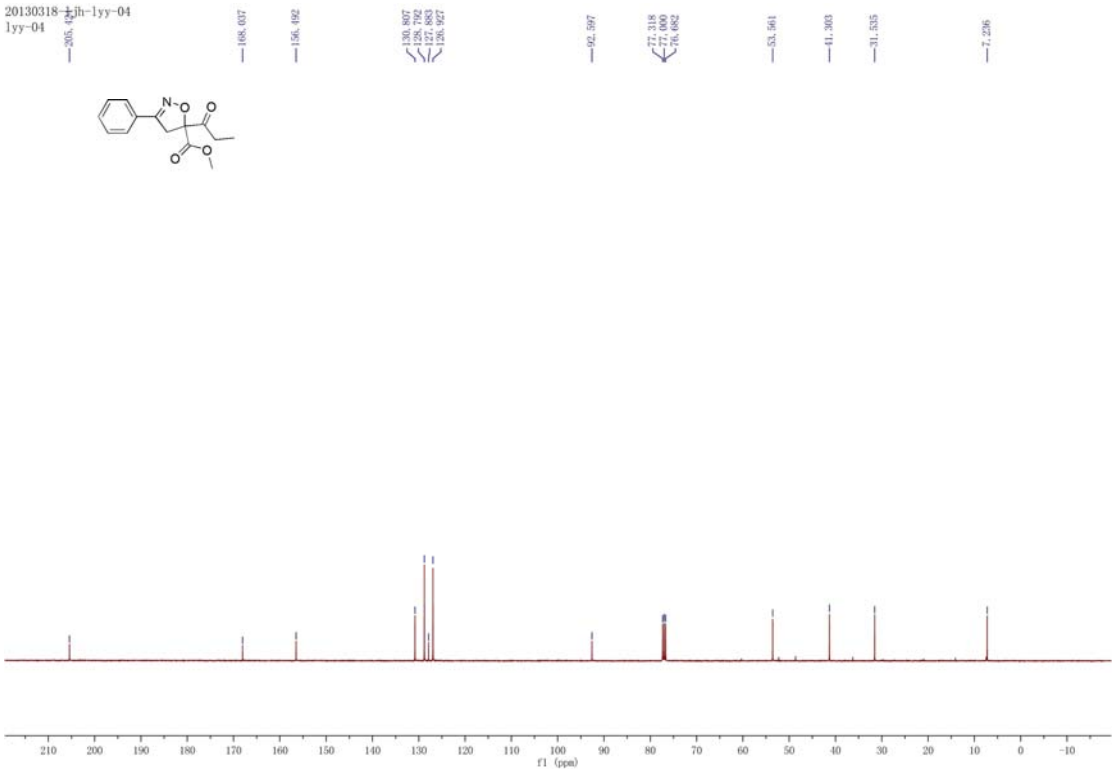
5-acetyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid allyl ester (3ak):



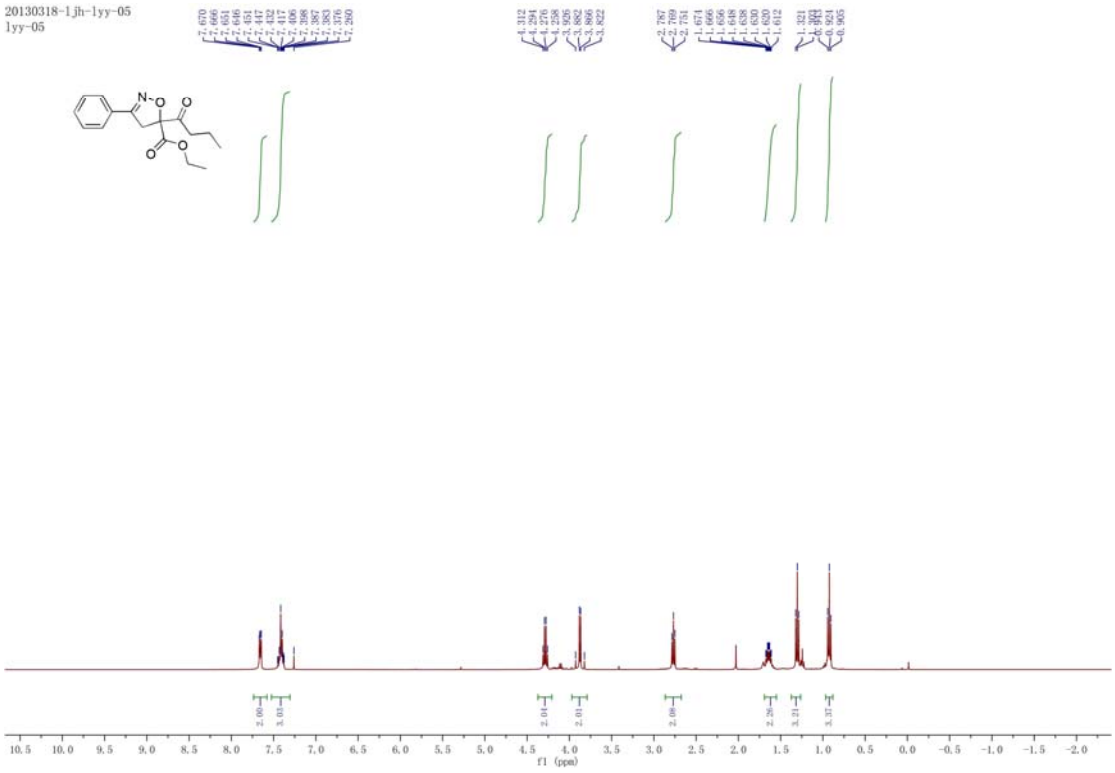


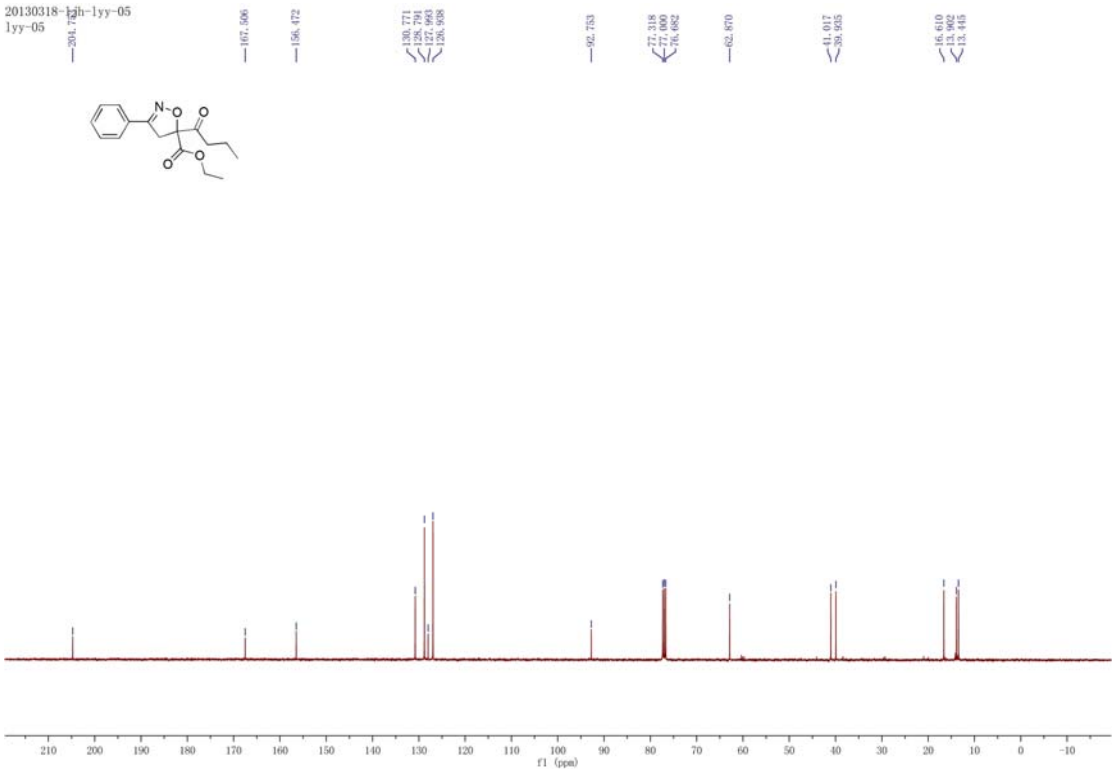
3-phenyl-5-propionyl-4,5-dihydroisoxazole-5-carboxylic acid methyl ester (3al):



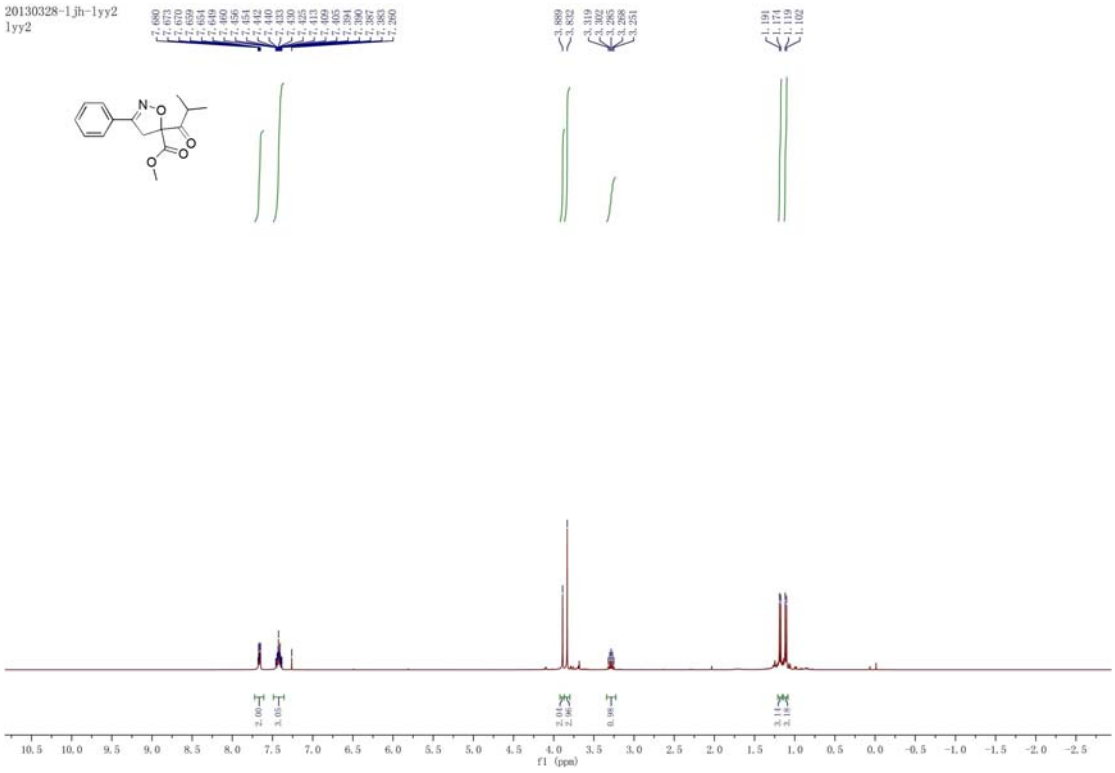


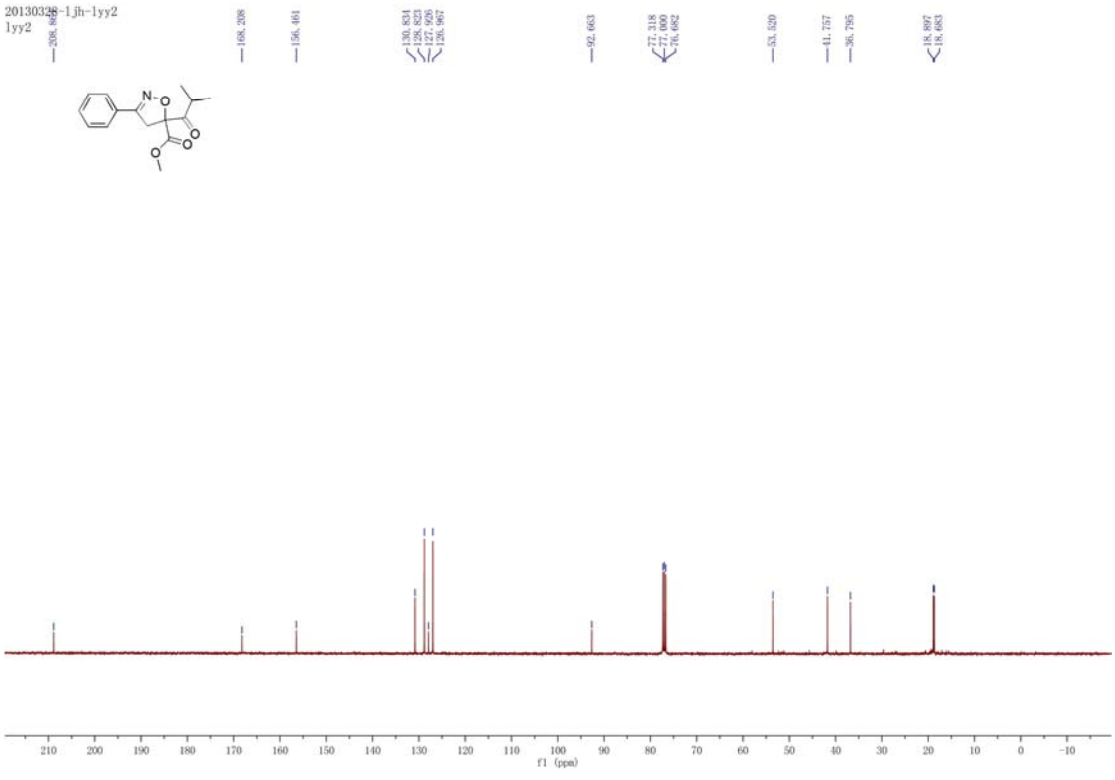
5-butyryl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (3am):



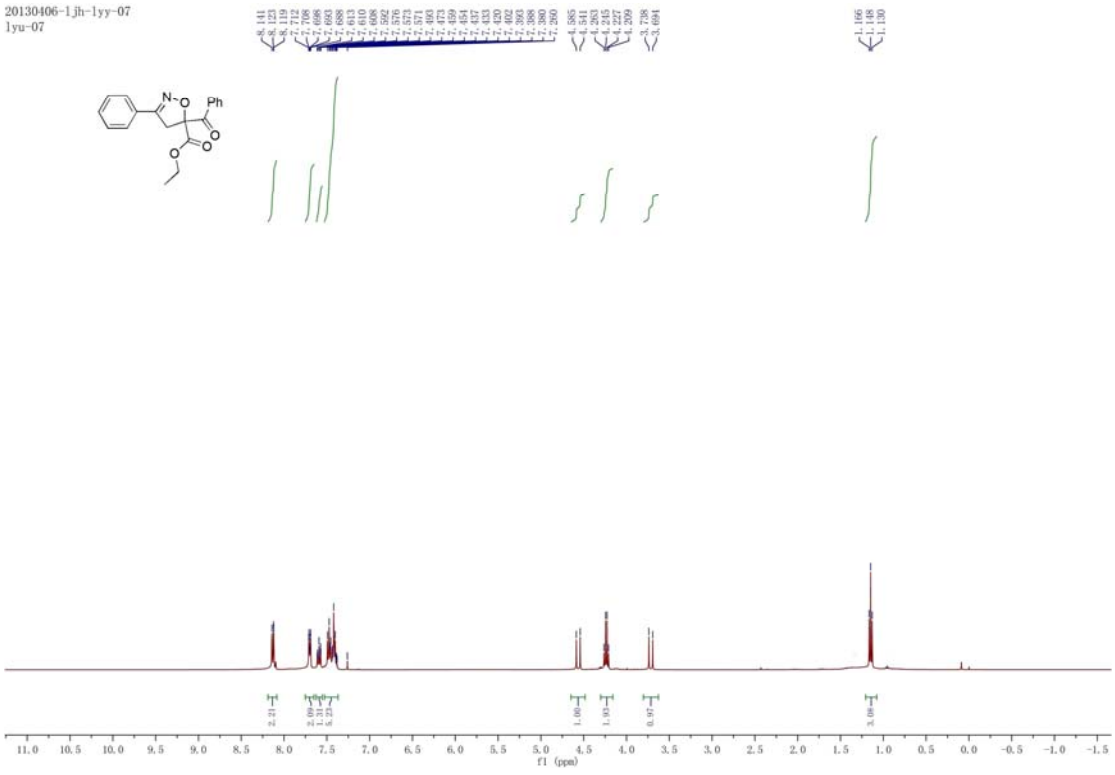


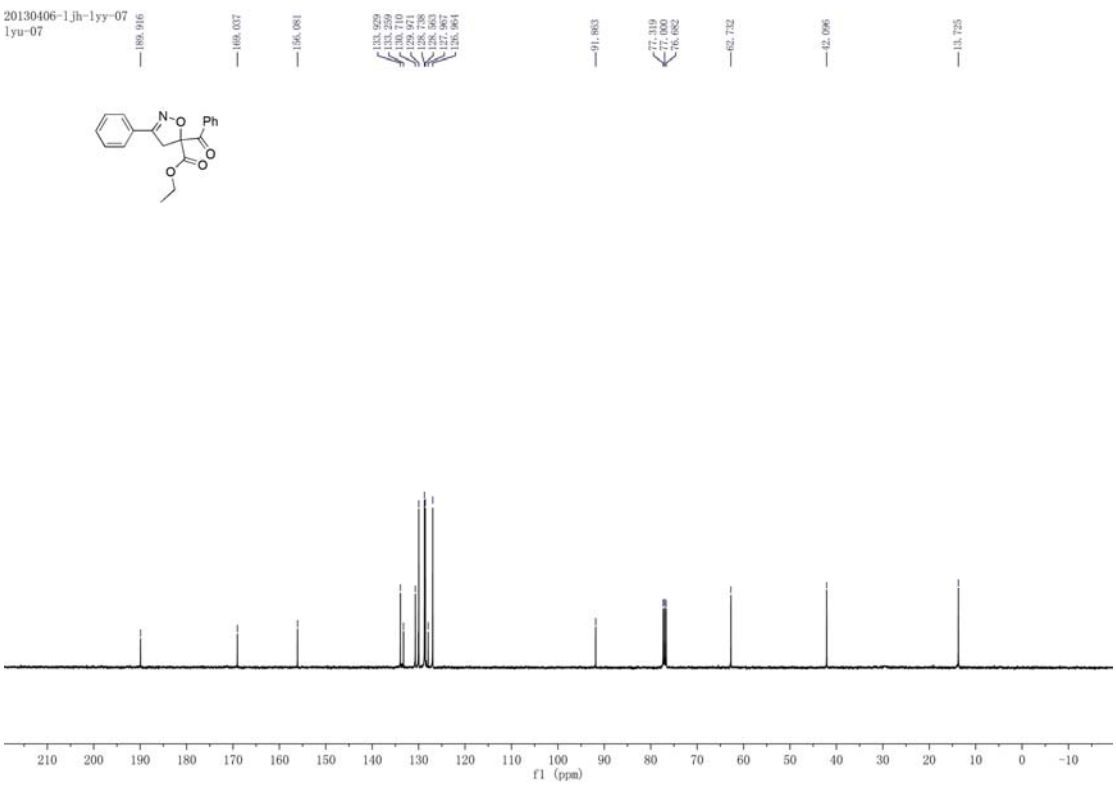
5-isobutyryl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid methyl ester (3an):



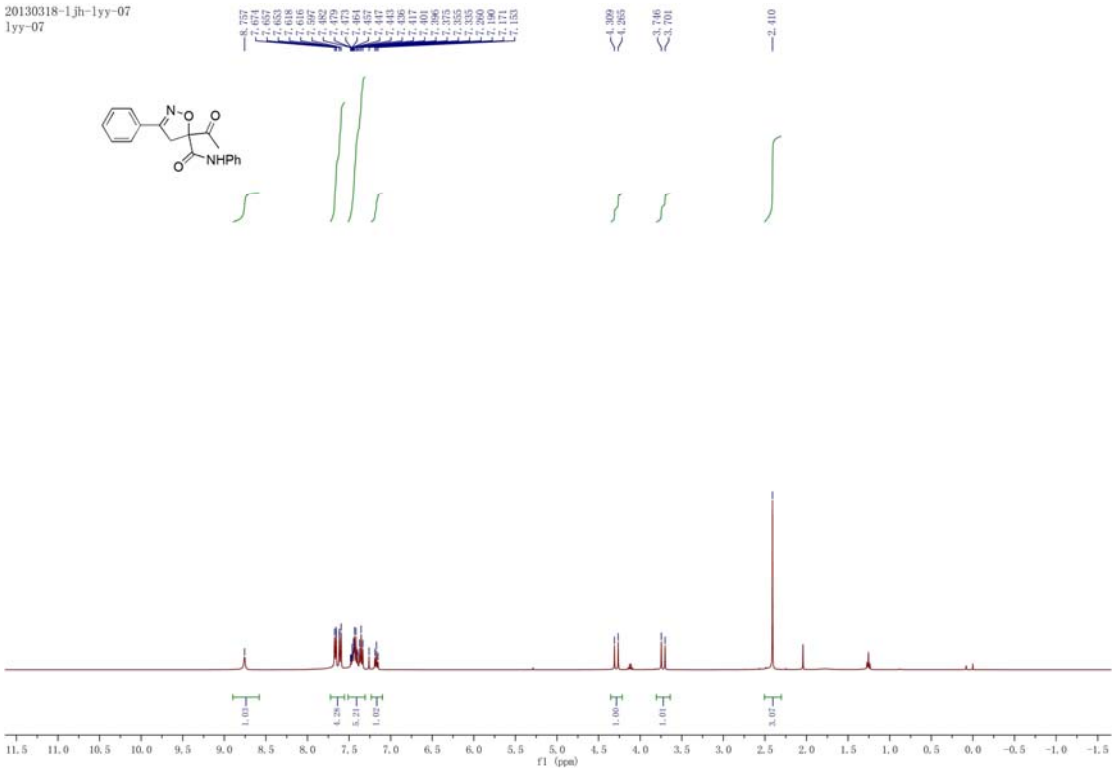


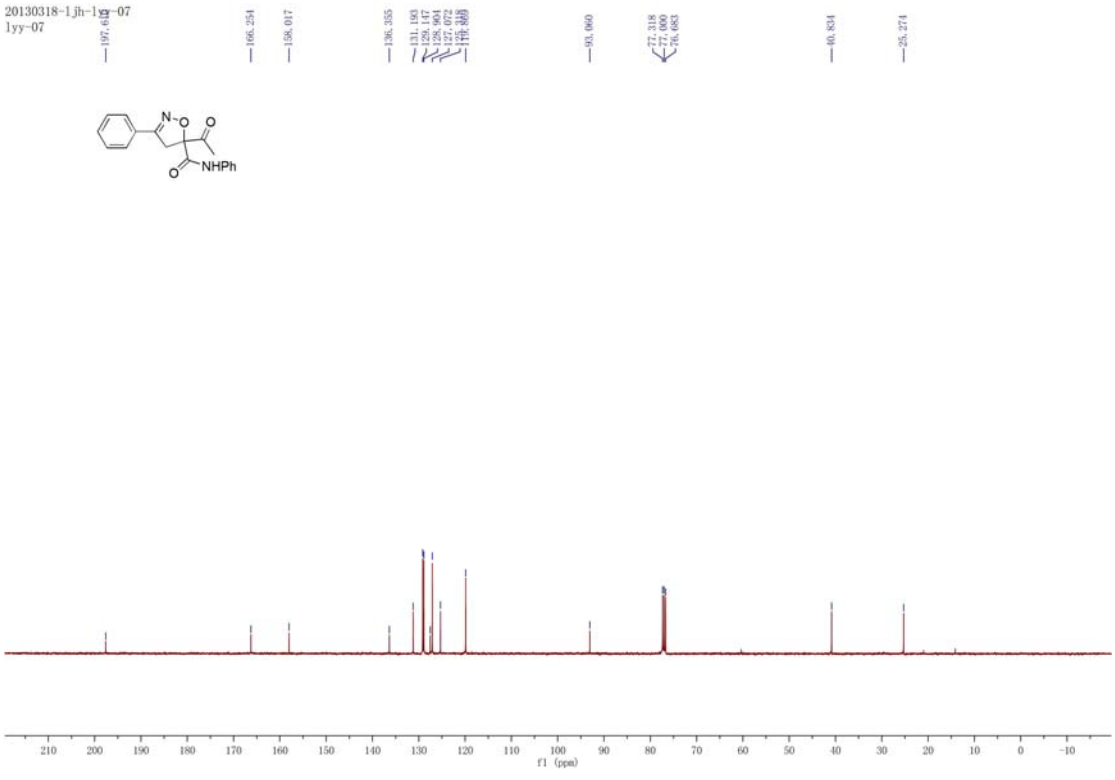
5-benzoyl-3-phenyl-4,5-dihydroisoxazole-5-carboxylic acid ethyl ester (3ao):



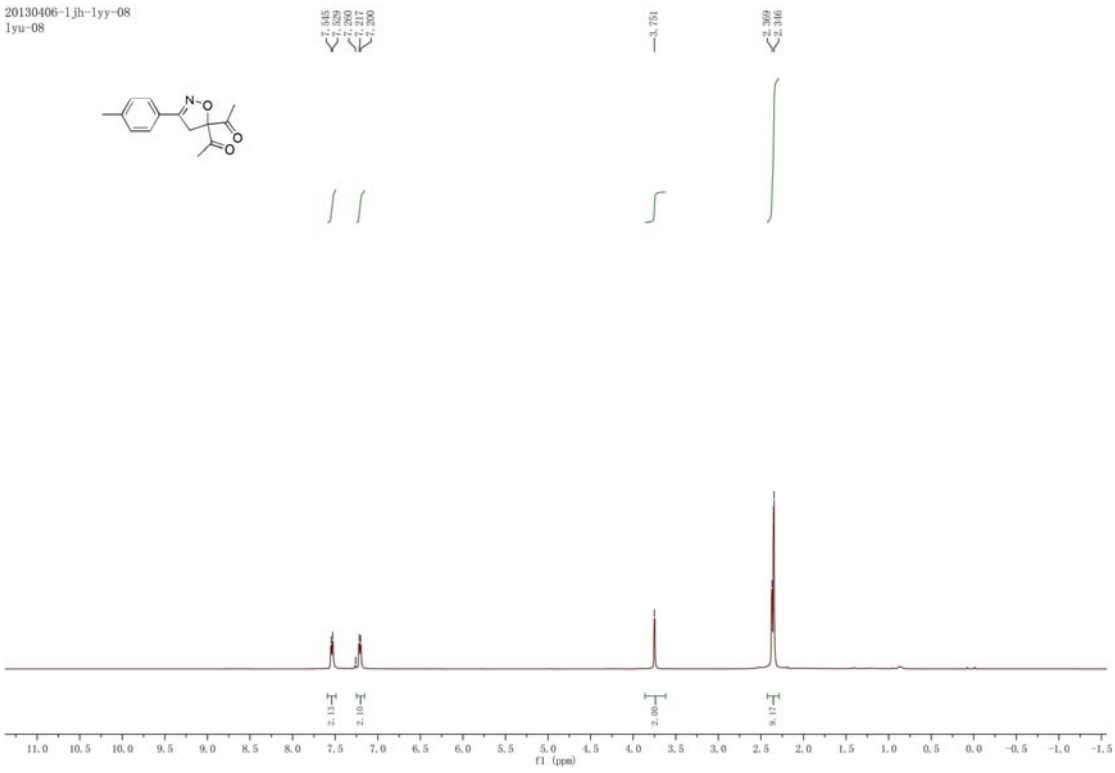


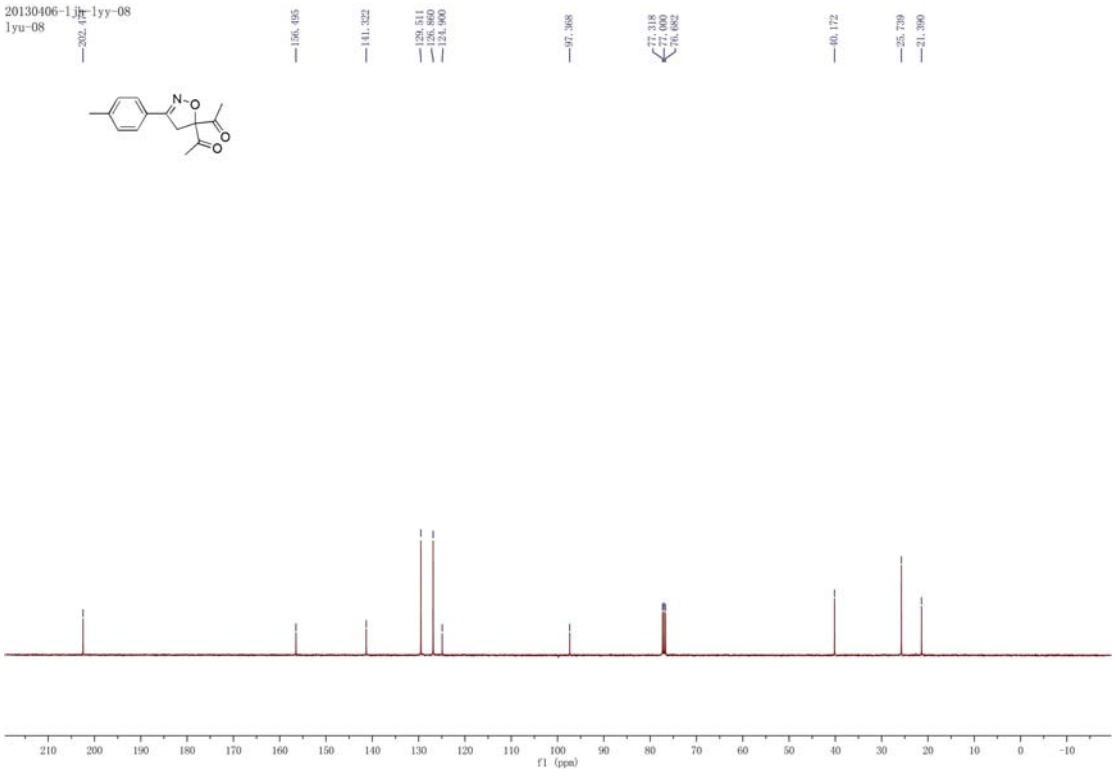
5-acetyl-*N*,3-diphenyl-4,5-dihydroisoxazole-5-carboxamide (3ap):



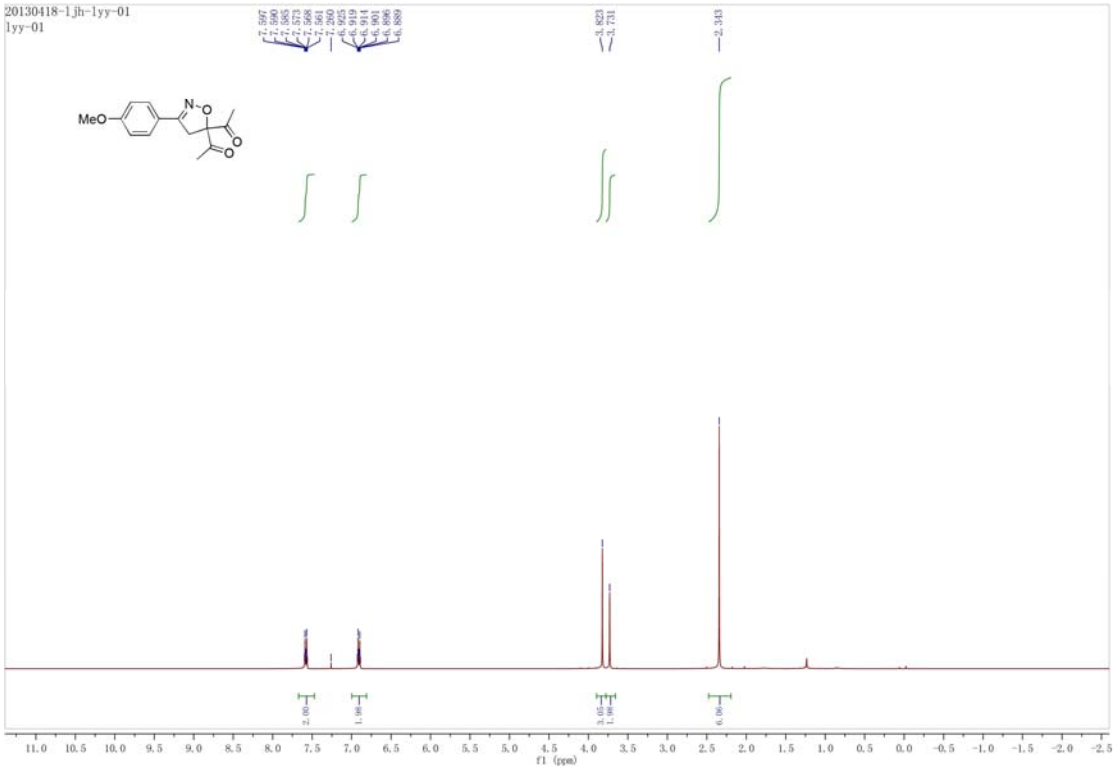


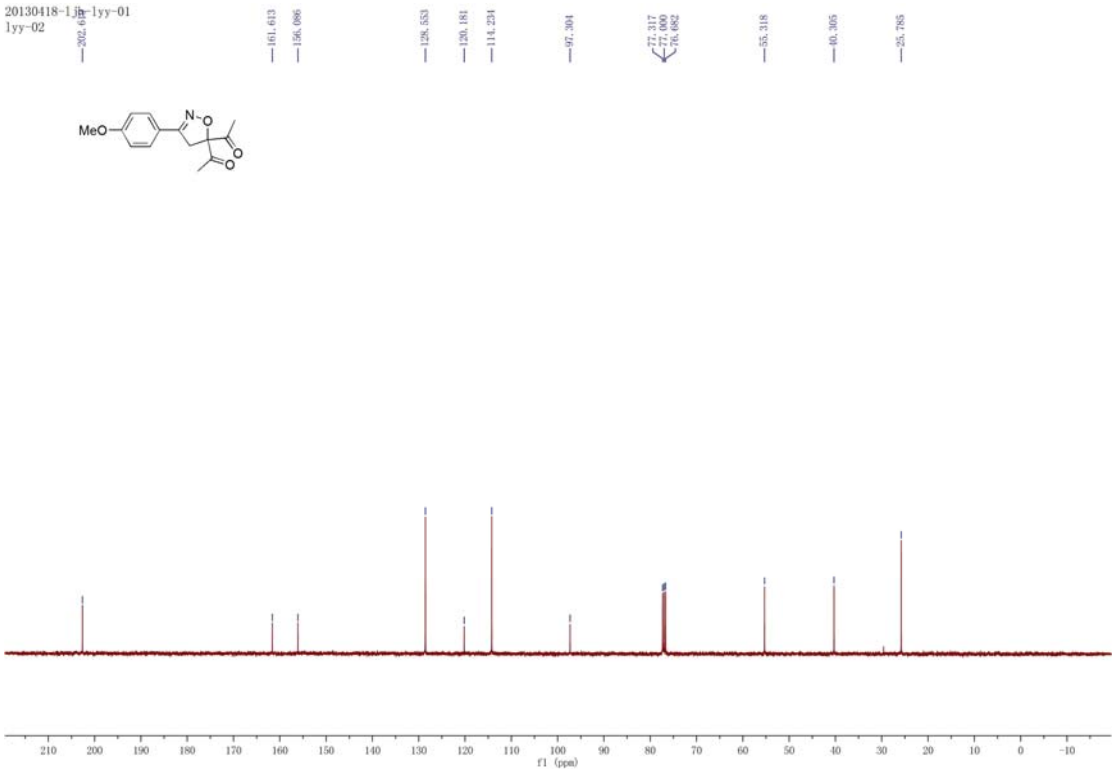
1,1'-(3-*p*-tolyl-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ca):



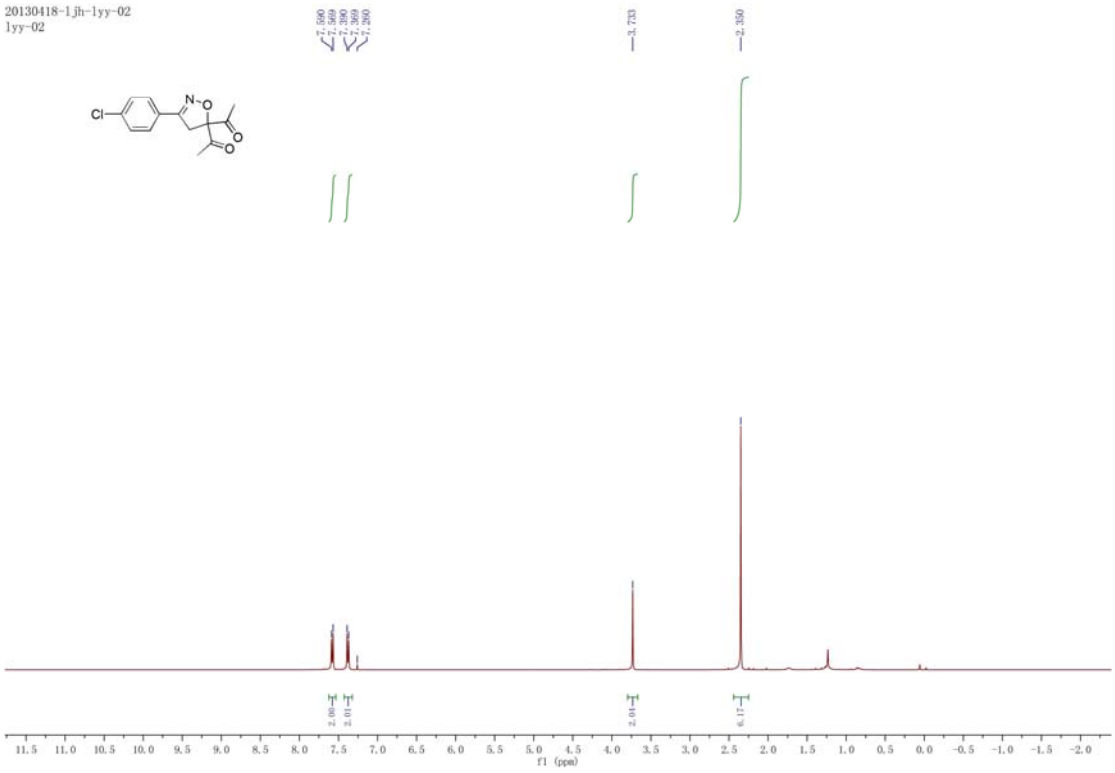


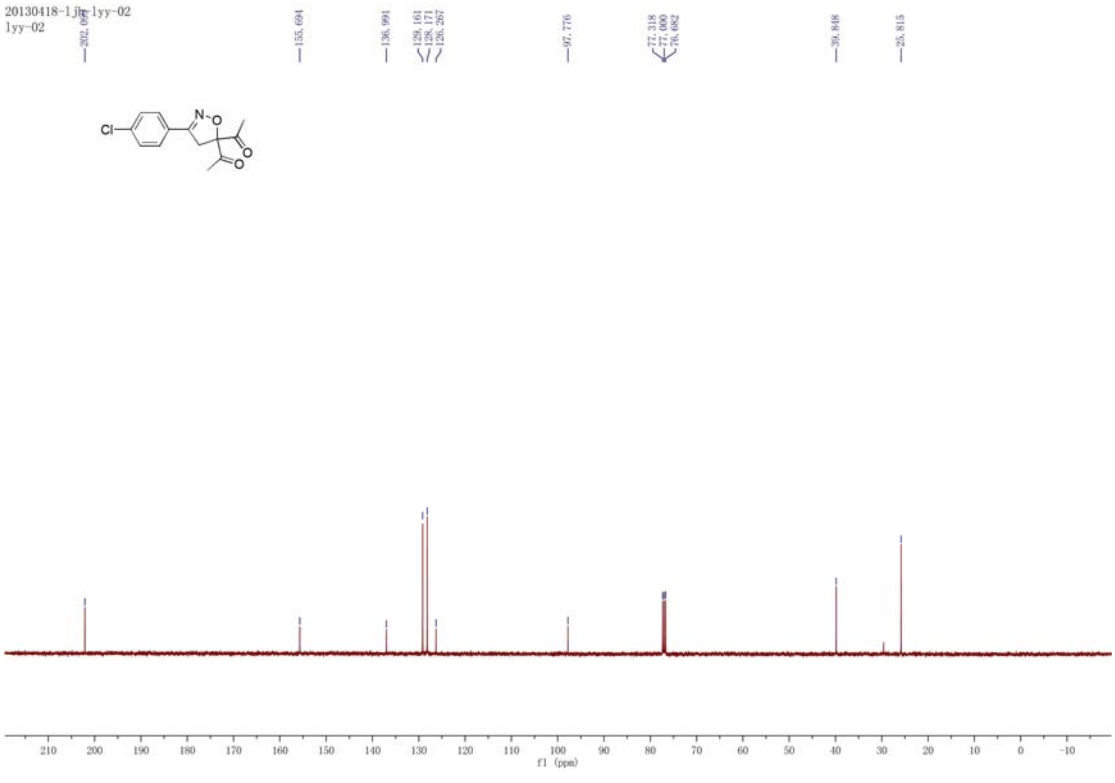
1,1'-(3-(4-methoxyphenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3da):



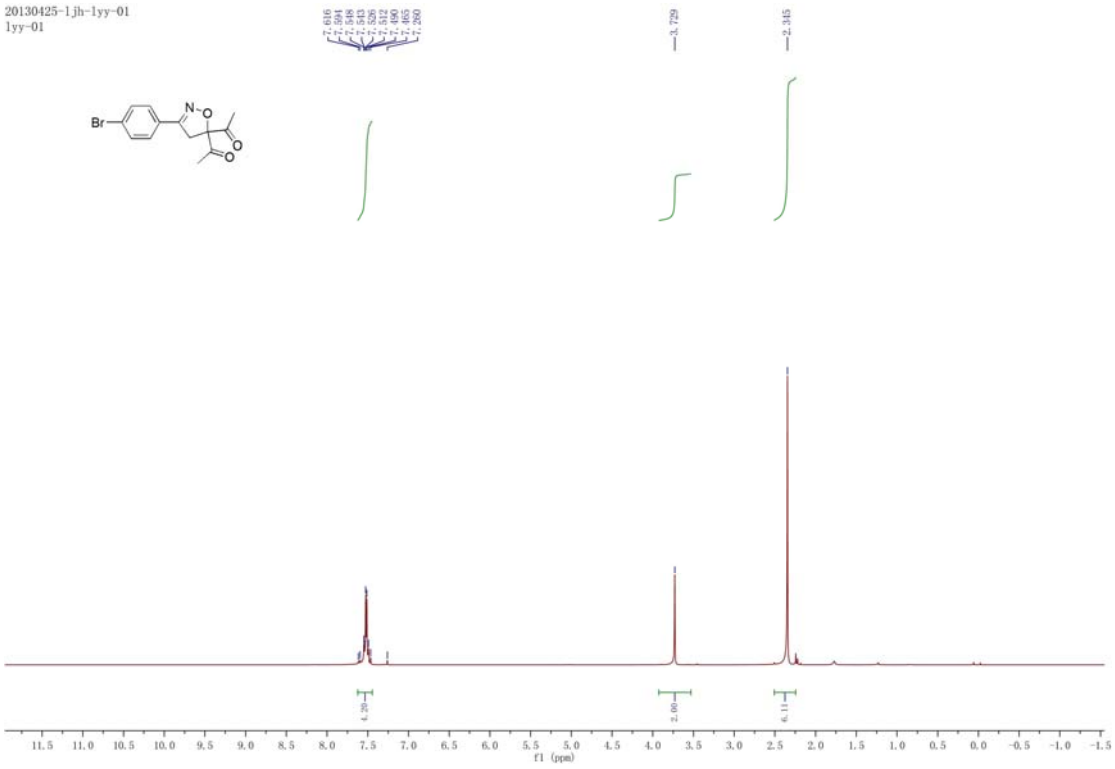


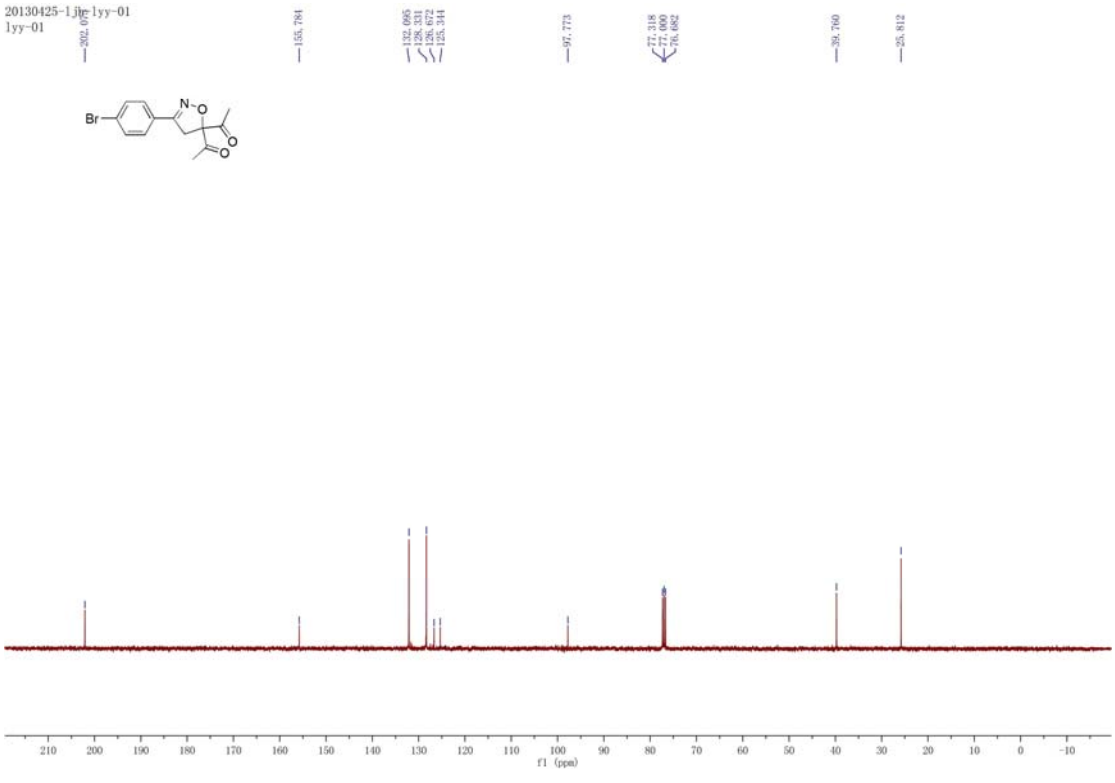
1,1'-(3-(4-chlorophenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ea):



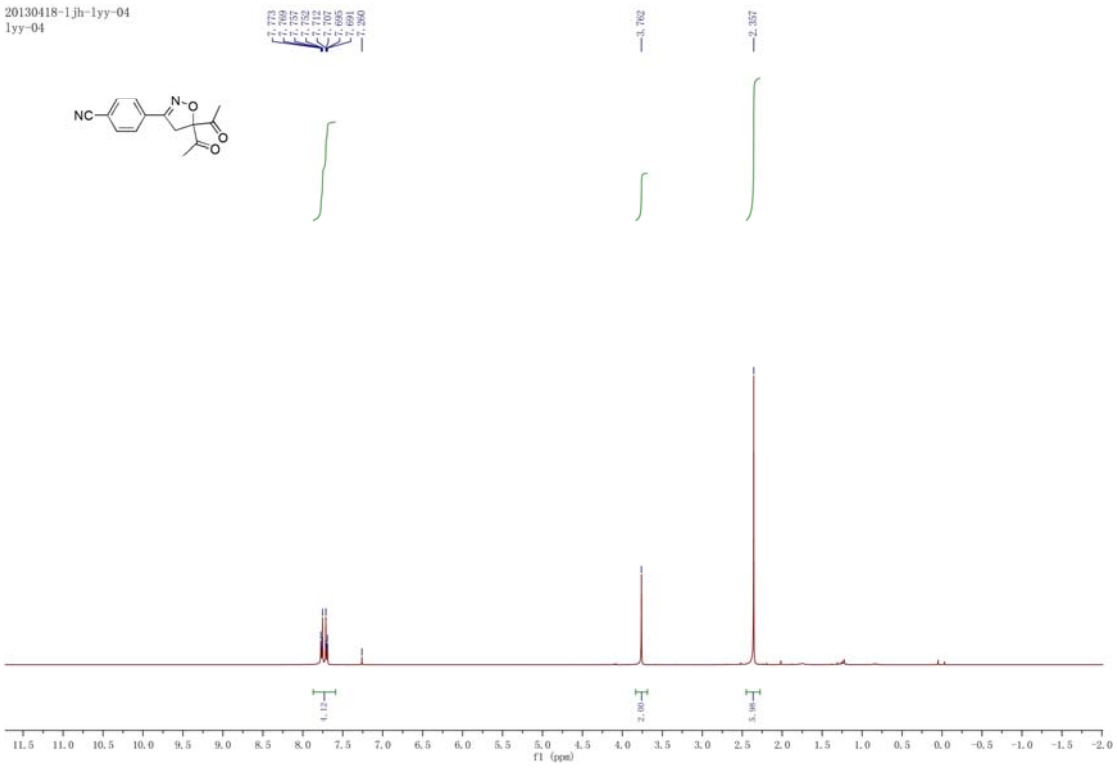


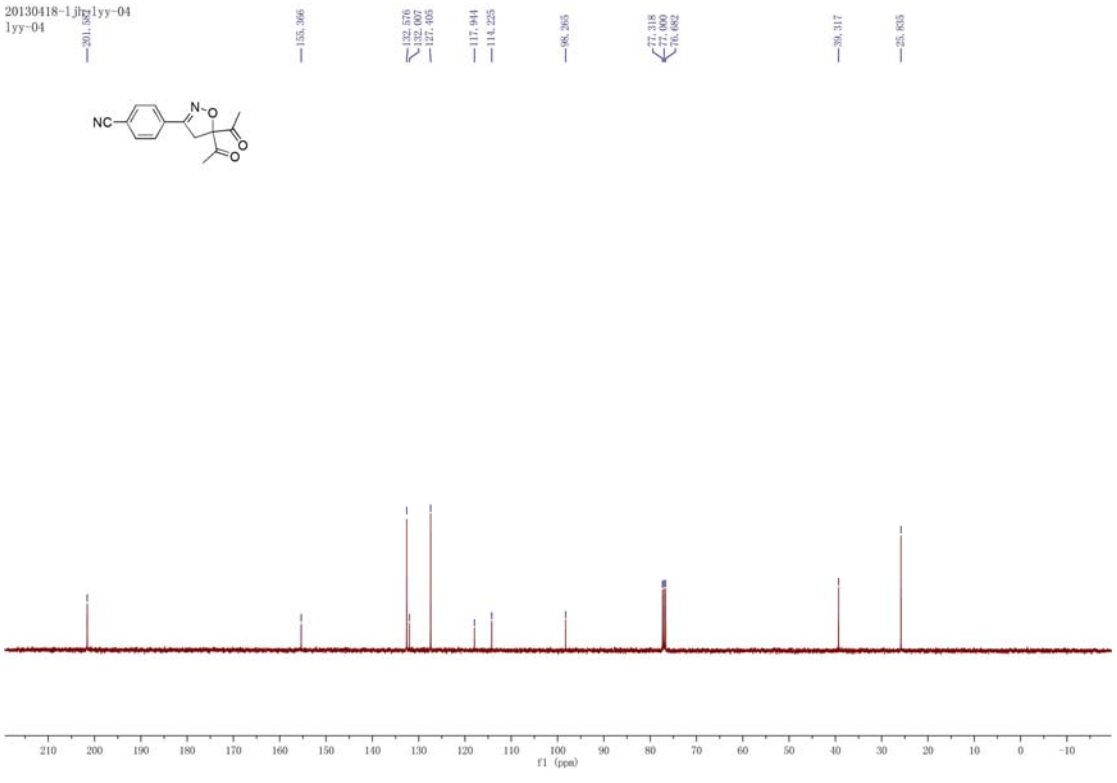
1,1'-(3-(4-bromophenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3fa):



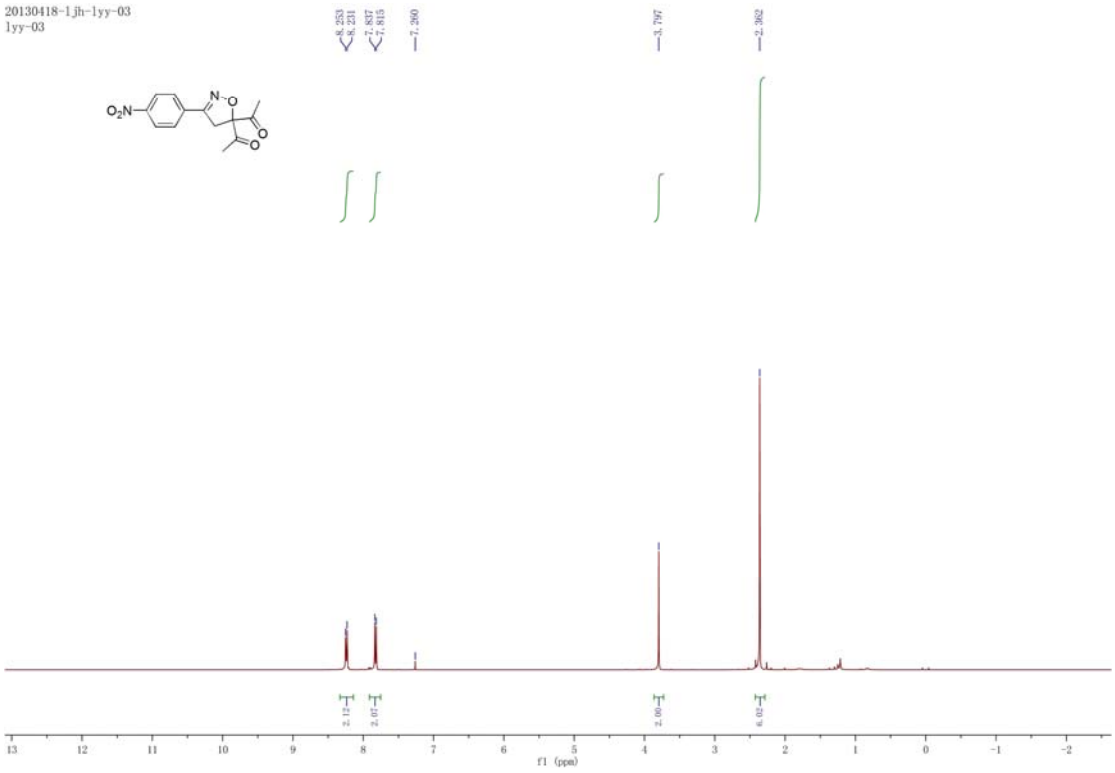


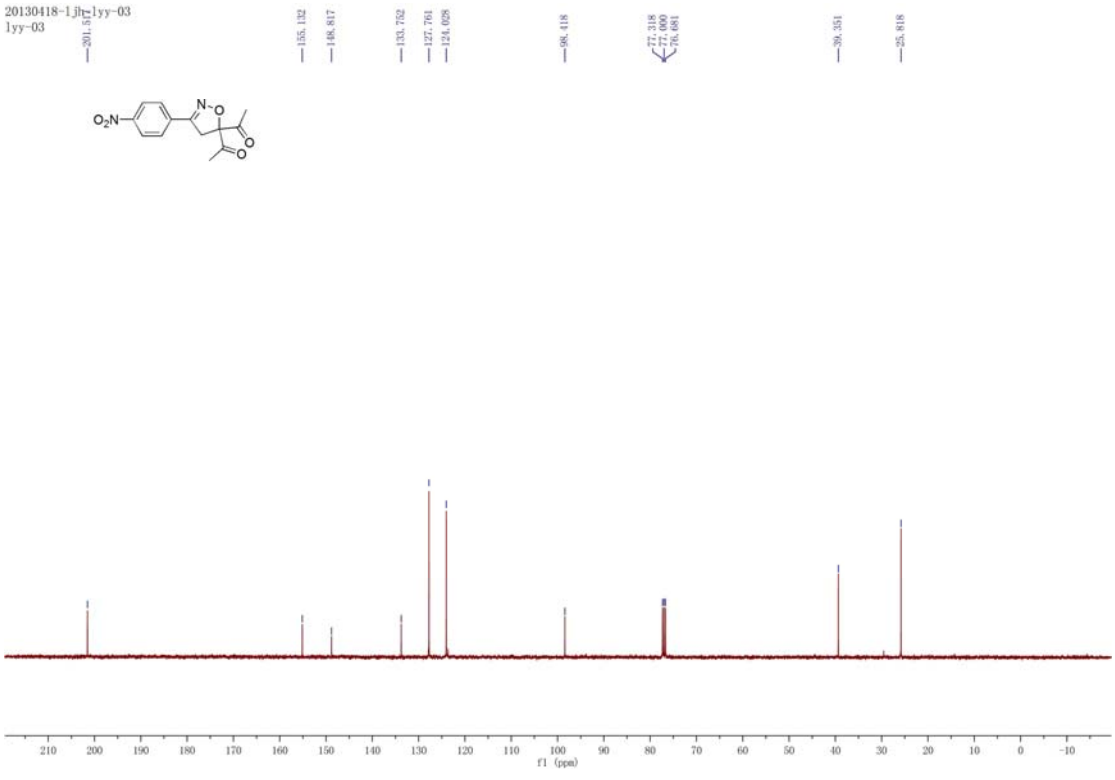
4-(5,5-diacetyl-4,5-dihydroisoxazol-3-yl)benzonitrile (3ga):



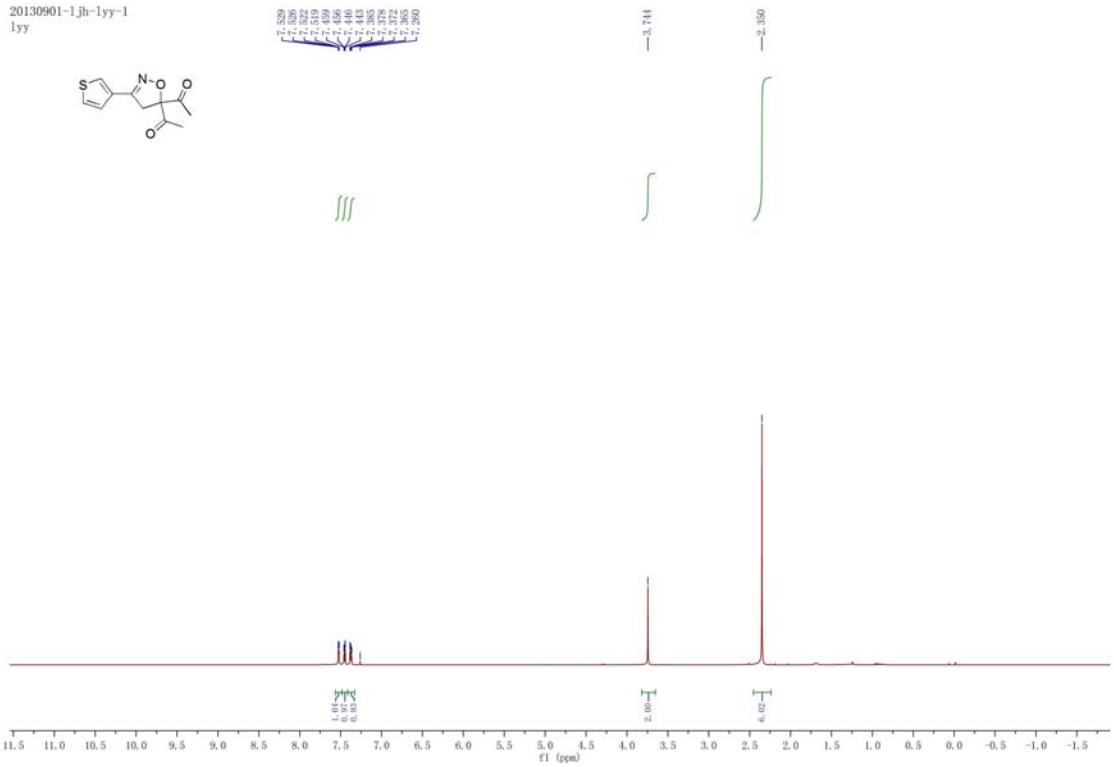


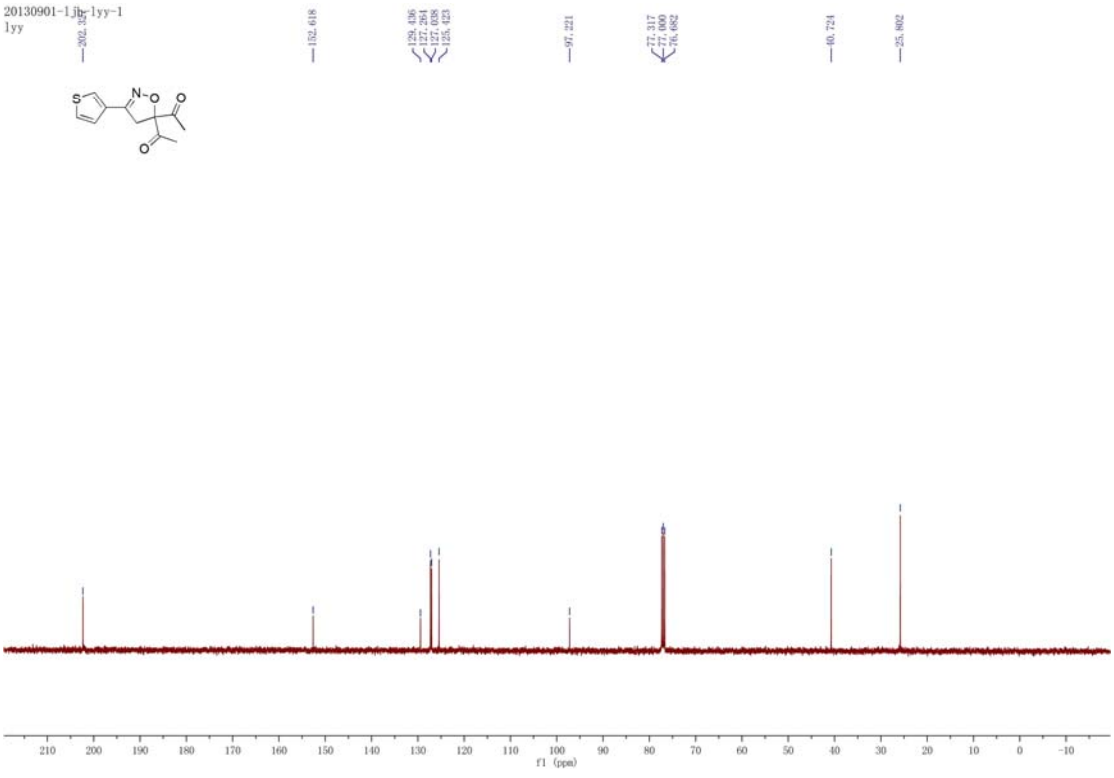
1,1'-(3-(4-nitrophenyl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ha):



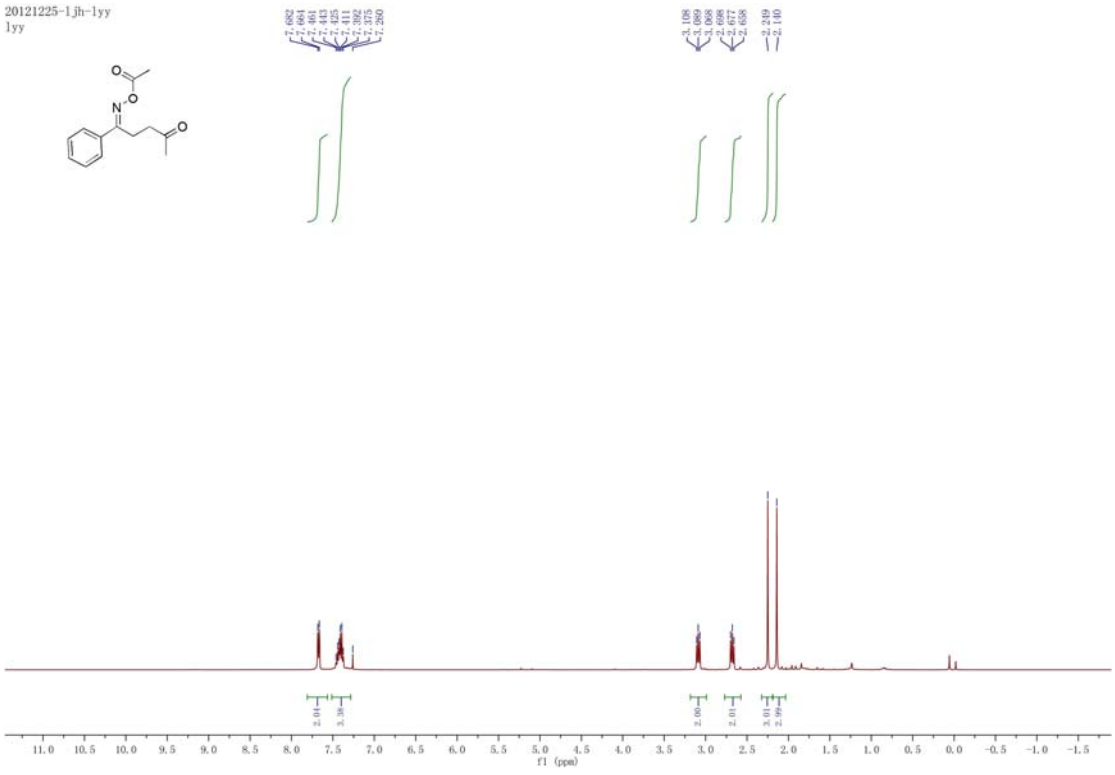


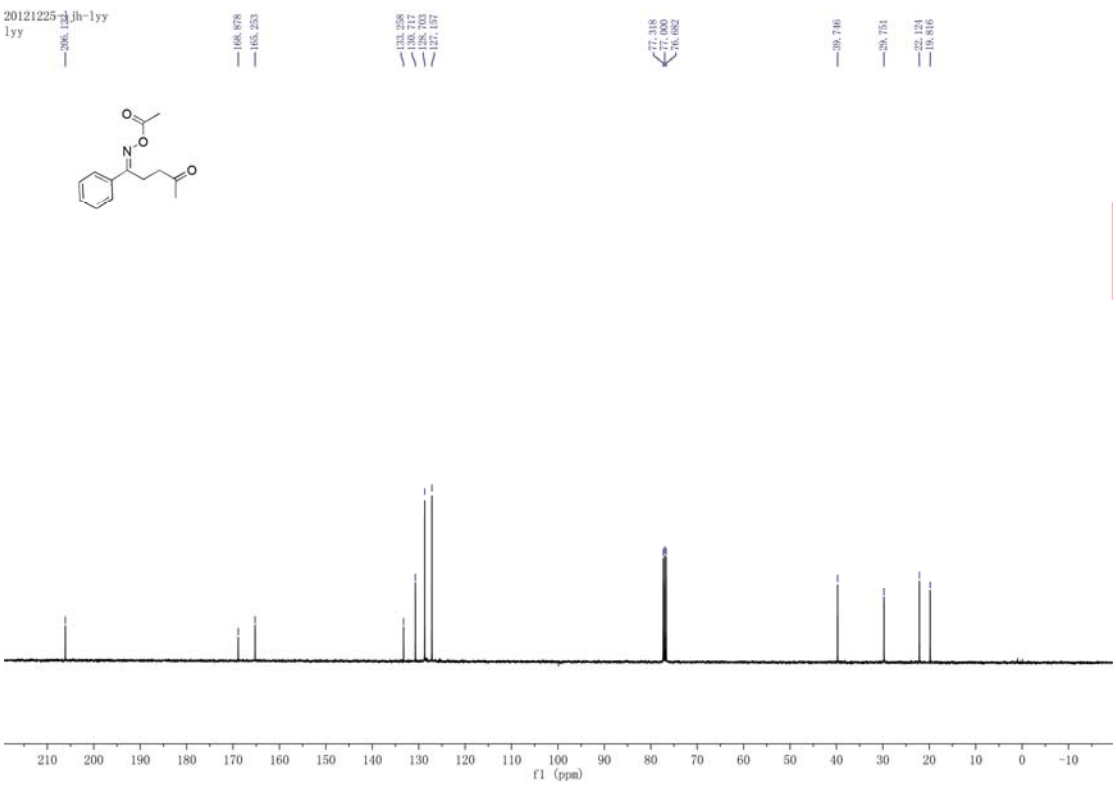
1,1'-(3-(thiophen-3-yl)-4,5-dihydroisoxazole-5,5-diyl)diethanone (3ia):



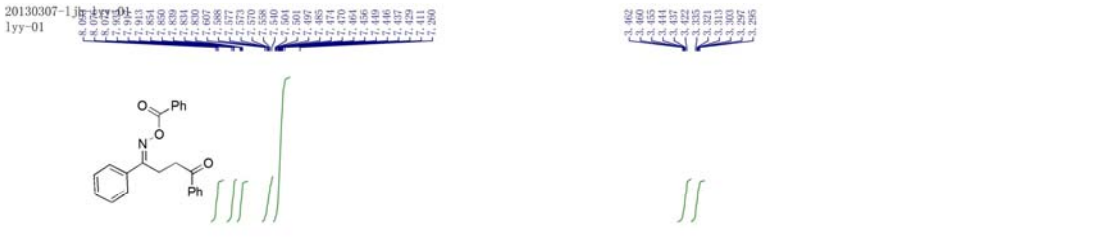


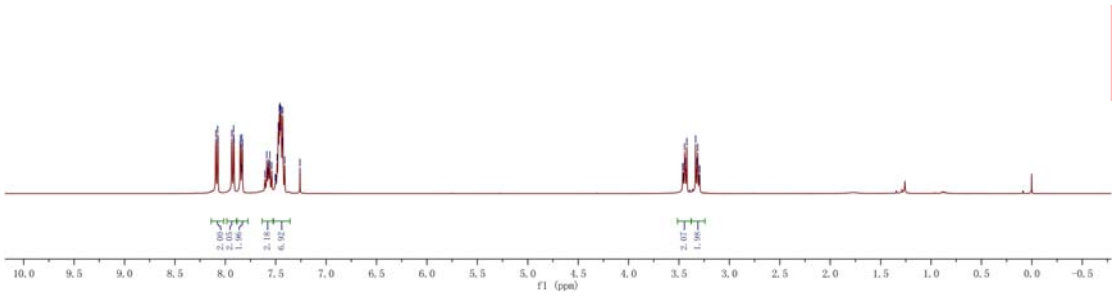
(*E*)-5-(acetoxyimino)-5-phenylpentan-2-one (4aa):

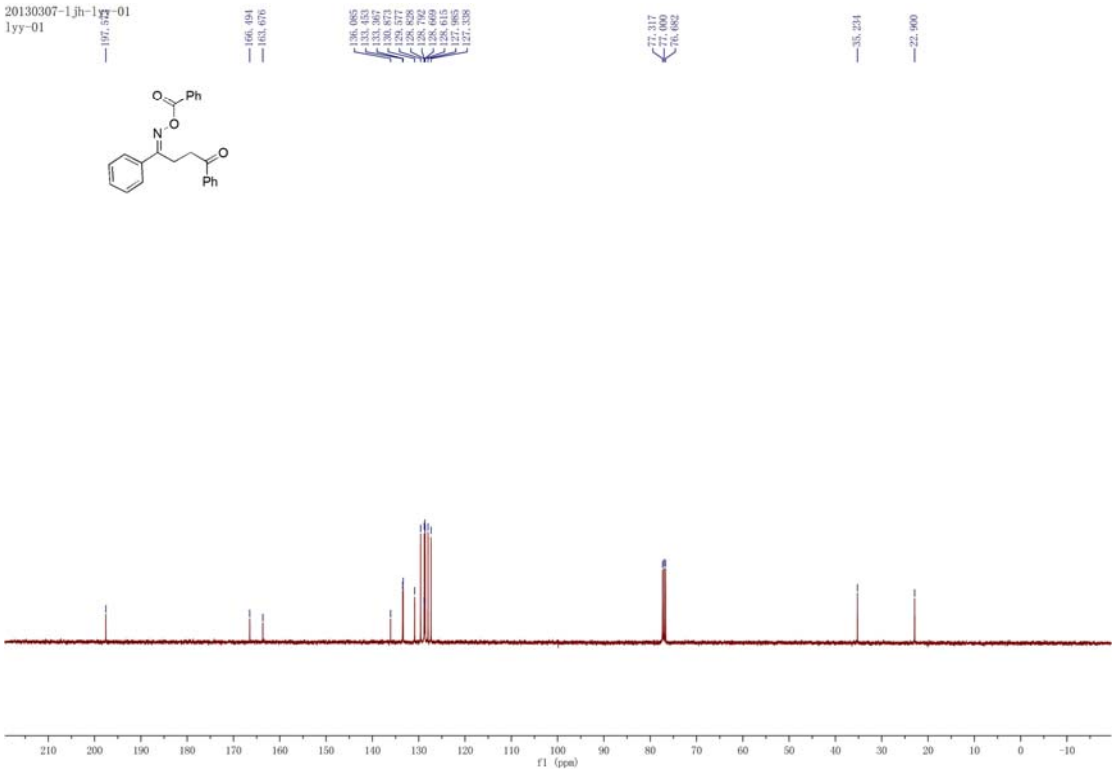




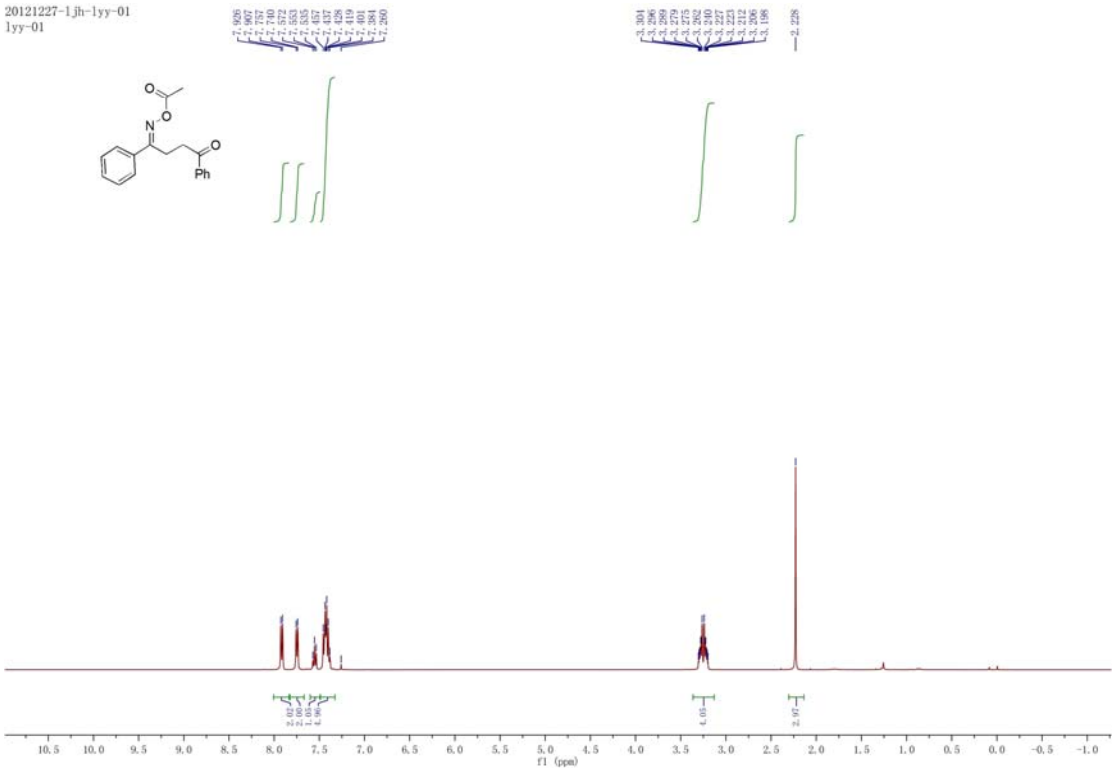
(*E*)-4-(benzoyloxyimino)-1,4-diphenylbutan-1-one (4ac):

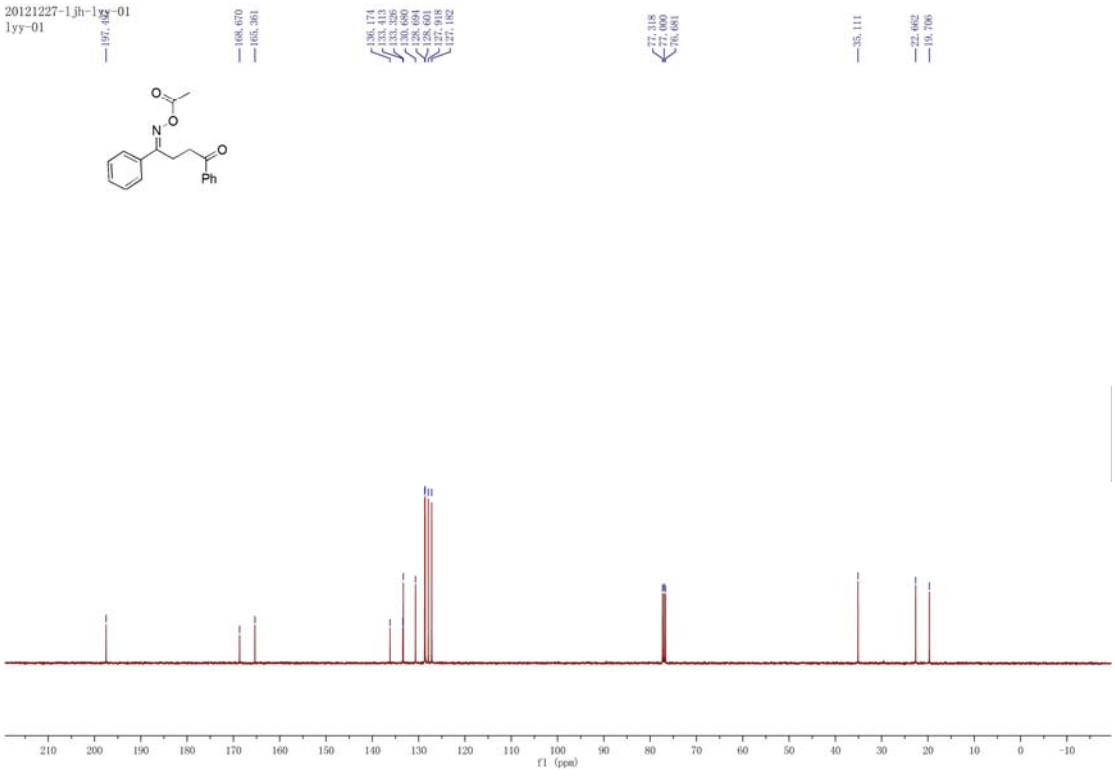






(*E*)-4-(acetoxyimino)-1,4-diphenylbutan-1-one (4ad):





(*E*)-ethyl 2-benzoyl-4-(hydroxyimino)-4-phenylbutanoate (5ao):