Copper-catalyzed [4 + 2] oxidative annihilation of \(\alpha,\beta\)-unsaturated ketoxime acetates with ethyl trifluoropyruvate

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Experimental section

General

Unless otherwise noted, all experiments were performed under N₂ atmosphere. Commercial solvents and reagents were used without further purification. Thin-layer chromatography (TLC) was performed on silica gel plates (60F-254) using UV-light (254 nm). Flash chromatography was conducted on silica gel (200-300 mesh). NMR (400 MHz for ¹H NMR, 100 MHz for ¹³C NMR) spectra were recorded in CDCl₃ with TMS as the internal standard. Chemical shifts are reported in ppm and coupling constants are given in Hz. Data for ¹H NMR are recorded as follows: chemical shift (ppm), multiplicity (s, singlet; d, doublet; t, triplet; q, quarter; m, multiplet), coupling constant (Hz), integration. Data for ¹³C NMR are reported in terms of chemical shift (δ, ppm). High-resolution mass spectra (HRMS) were obtained on an Agilent mass spectrometer using ESI-TOF (electrospray ionization-time of flight). The α,β-unsaturated ketoamine acetates were all known compounds and synthesized according to previously reported literature procedures.¹ Ethyl trifluoropyruvate 2a was purchased and used without additional purification.

General procedure for the synthesis of 3

₁ (0.3 mmol), 2a (1.2 mmol), CuI (6 mg, 10 mol%), DDQ (102 mg, 0.45 mmol), DMAP (7 mg, 20 mol%) and NiF₂ (29 mg, 0.3 mmol) were loaded into a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N₂ was pumped into it. The solvent toluene (3 mL, 0.1 M) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C for 12 h. After completion of the reaction (detected by TLC), the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under vacuum. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to give the products 3.

General procedure for the synthesis of 4

₁ (0.3 mmol), 2a (1.2 mmol), CuI (6 mg, 10 mol%), DDQ (102 mg, 0.45 mmol), DMAP (7 mg, 20 mol%) and NiF₂ (29 mg, 0.3 mmol) were loaded into a 25 mL Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N₂ was pumped into it. The solvent toluene (3 mL, 0.1 M) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C (oil bath) for 12 h. After completion of the reaction (detected by TLC), the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under vacuum. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to give the products 4.

Scale-up synthesis of compound 3a

₁a (1.355 g, 5 mmol), ethyl trifluoropyruvate 2a (3.402 g, 20 mmol), CuI (0.952 g, 10 mol%), DDQ (1.703 g, 7.5 mmol), DMAP (0.112 g, 20 mol%) and NiF₂ (0.484 g, 5 mmol) were loaded into
a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N₂ was pumped into it. The solvent toluene (15 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product 3a 1.207 g (65% yield).

Scale-up synthesis of compound 3f

1f (1.376 g, 5 mmol), ethyl trifluoropyruvate 2a (3.402 g, 20 mmol), Cul (0.952 g, 10 mol%), DDQ (1.703 g, 7.5 mmol), DMAP (0.112 g, 20 mol%) and NiF₂ (0.484 g, 5mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N₂ was pumped into it. The solvent toluene (15 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product 3f 1.060 g (55% yield).

Control experiments

1a (78 mg, 0.3 mmol), ethyl trifluoropyruvate 2a (204 mg, 1.2 mmol), Cul (6 mg, 10 mol%), DMAP (7 mg, 20 mol%) and NiF₂ (29 mg, 0.3 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N₂ was pumped into it. The solvent toluene (3 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product 5a (84 mg, 75% yield).

1a (78 mg, 0.3 mmol), ethyl trifluoropyruvate 2a (204 mg, 1.2 mmol), Cul (6 mg, 10 mol%), DDQ (102 mg, 0.45 mmol), DMAP (7 mg, 20 mol%), NiF₂ (29 mg, 0.3 mmol) and radical scavenger (0.3–1.2 mmol) were loaded into a Schlenk tube equipped with a Teflon-coated magnetic stir bar. The Schlenk tube was placed under vacuum for 1 min and then N₂ was pumped into it. The solvent toluene (3 mL) was added into the Schlenk tube by syringe. The reaction mixture was stirred at 120 °C (oil bath) for 12 h. Then the reaction tube was allowed to cool to room temperature and the reaction solution was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel (Petroleum Ether/EtOAc= 10:1) to give the product 3a or 5a.
Compounds characterization

**Diethyl 4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3a)**

84 mg, 75% yield; White solid; Mp 78–79 °C; $^1$H NMR (400 MHz, Chloroform-d) δ 7.94 (d, $J = 7.1$ Hz, 2H), 7.54 (t, $J = 7.3$ Hz, 1H), 7.47 (t, $J = 7.5$ Hz, 2H), 6.94 (s, 1H), 4.42–4.27 (m, 4H), 1.39 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.5, 162.9, 160.4, 150.2, 134.4, 132.4, 128.9, 127.4, 121.0 (q, $J = 284.9$ Hz), 102.1, 92.2 (q, $J = 32.0$ Hz), 63.5, 62.7, 14.2, 14.0 ppm; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C$_{17}$H$_{16}$F$_3$NO$_3$ [M+H]$^+$ 372.1053, found 372.1053.

**Diethyl 4-(4-fluorophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3b)**

55 mg, 47% yield; Brown solid; Mp 63–65 °C; $^1$H NMR (400 MHz, Chloroform-d) δ 7.97–7.94 (m, 2H), 7.15 (t, $J = 8.6$ Hz, 2H), 6.89 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.2$ Hz, 3H) ppm; $^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.5 (d, $J = 253.7$ Hz), 163.5, 161.8, 160.4, 150.2, 130.7 (d, $J = 2.9$ Hz), 129.9, 129.8, 121.0 (q, $J = 284.9$ Hz), 116.2, 116.0, 101.8, 92.2 (q, $J = 32.0$ Hz), 63.6, 62.8, 14.2, 14.0; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -79.4, -106.6 ppm; HRMS (ESI-TOF): m/z calcd for C$_{17}$H$_{16}$F$_3$NO$_3$ [M+H]$^+$ 390.0959, found 390.1010.

**Diethyl 4-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3c)**

61 mg, 50% yield; White oil; $^1$H NMR (400 MHz, Chloroform-d) δ 7.88 (d, $J = 8.6$ Hz, 2H), 7.44 (d, $J = 8.7$ Hz, 2H), 6.88 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.4, 161.9, 160.3, 150.3, 138.9, 132.8, 129.2, 128.8, 121.0 (q, $J = 284.8$ Hz), 101.6, 92.2 (q, $J = 32.1$ Hz), 63.6, 62.8, 14.2, 14.0 ppm; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C$_{17}$H$_{16}$ClF$_3$NO$_3$ [M+H]$^+$ 406.0644, found 406.0658.

**Diethyl 4-(4-bromophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3d)**

62 mg, 46% yield; White oil; $^1$H NMR (400 MHz, Chloroform-d) δ 7.80 (d, $J = 8.6$ Hz, 2H), 7.60 (d, $J = 8.5$ Hz, 2H), 6.87 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.3, 162.1, 160.3, 150.3, 133.3, 132.2, 129.0, 127.4, 120.9 (q, $J = 284.9$ Hz), 101.6, 92.2 (q, $J = 32.1$ Hz), 63.6, 62.9, 14.2, 14.0 ppm; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C$_{17}$H$_{16}$BrF$_3$NO$_3$ [M+H]$^+$ 450.0158, found 450.0152.

**Diethyl 4-(4-cyanophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3e)**

48 mg, 40% yield; Yellow oil; $^1$H NMR (400 MHz, Chloroform-d) δ 8.04 (d, $J = 8.5$ Hz, 2H), 7.77 (d, $J = 8.4$ Hz, 2H), 6.88 (s, 1H), 4.42–4.27 (m, 4H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H) ppm; $^{13}$C NMR (100 MHz, CDCl$_3$) δ 163.1, 161.9, 160.0, 150.8, 138.2, 132.7, 128.0, 120.8 (q, $J = 285.8$ Hz), 118.1, 115.8, 101.3, 92.2 (q, $J = 32.5$ Hz), 63.8, 63.0, 14.2, 14.0 ppm; $^{19}$F NMR (376 MHz, CDCl$_3$) δ -79.2 ppm; HRMS (ESI-TOF): m/z calcd for C$_{18}$H$_{18}$F$_3$N$_2$O$_3$ [M+H]$^+$ 397.1006, found 397.1003.
Diethyl 4-(p-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3f)

70 mg, 60% yield; Purple oil; 1H NMR (400 MHz, Chloroform-δ) δ 7.76 (d, J = 8.1 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H), 6.84 (s, 1H), 4.34 – 4.18 (m, 4H), 2.33 (s, 3H), 1.31 (t, J = 7.1 Hz, 3H), 1.22 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.6, 162.5, 160.5, 149.9, 143.2, 131.7, 129.6, 127.4, 121.1 (q, J = 284.8 Hz), 102.1, 92.3 (q, J = 31.9 Hz), 63.4, 62.7, 21.7, 14.2, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for C13H19F3NO5 [M+H]+ 386.1210, found 386.1211.

Diethyl 4-(4-methoxyphenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3g)

77 mg, 64% yield; Purple oil; 1H NMR (400 MHz, Chloroform-δ) δ 7.90 (d, J = 8.9 Hz, 2H), 6.96–6.91 (m, 3H), 4.40–4.28 (m, 4H), 3.85 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H), 1.28 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.7, 163.2, 161.7, 160.5, 149.7, 129.3, 126.9, 121.1 (q, J = 284.9 Hz), 114.2, 102.2, 92.2 (q, J = 31.9 Hz), 63.4, 62.6, 55.5, 14.1, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for C13H19F3NO5 [M+H]+ 402.1159, found 402.1155.

Diethyl 4-(3-methoxyphenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3h)

65 mg, 54% yield; Purple oil; 1H NMR (400 MHz, Chloroform-δ) δ 7.48–7.46 (m, 2H), 7.37 (t, J = 7.9 Hz, 1H), 7.09–7.06 (m, 1H), 6.90 (s, 1H), 4.41–4.24 (m, 4H), 3.85 (s, 3H), 1.38 (t, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.5, 162.8, 160.4, 160.1, 145.0, 135.8, 130.0, 121.0 (q, J = 286.8 Hz), 120.0, 118.4, 112.3, 102.2, 92.2 (q, J = 32.0 Hz), 63.5, 62.7, 55.5, 14.1, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C13H19F3NO5 [M+H]+ 402.1159, found 402.1156.

Diethyl 4-(3-bromophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3i)

54 mg, 40% yield; Yellow solid; Mp 72–73 °C; 1H NMR (400 MHz, Chloroform-δ) δ 8.08 (s, 1H), 7.83 (d, J = 7.9 Hz, 1H), 7.67 (d, J = 9.9 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 6.86 (s, 1H), 4.43–4.28 (m, 4H), 1.39 (t, J = 7.1 Hz, 3H), 1.31 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.3, 161.9, 160.2, 150.4, 136.4, 135.4, 130.42, 130.40, 126.1, 123.3, 120.9 (q, J = 285.9 Hz), 101.7, 92.2 (q, J = 32.6 Hz), 63.7, 62.9, 14.2, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C17H16BrF3NO5 [M+H]+ 450.0158, found 450.0147.

Diethyl 4-(2-methoxyphenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3j)

84 mg, 70% yield; Purple oil; 1H NMR (400 MHz, Chloroform-δ) δ 7.70 (d, J = 7.7 Hz, 1H), 7.44 (t, J = 7.0 Hz, 1H), 7.05–6.90 (m, 3H), 4.38–4.31 (m, 4H), 3.86 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 164.8, 163.7, 160.7, 158.5, 147.6, 133.1, 130.4, 124.8, 121.2, 121.0 (q, J = 285.8 Hz), 111.5, 107.0, 91.6 (q, J = 32.0 Hz), 63.4, 62.4, 55.7, 14.1, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C15H18F3NO5 [M+H]+ 402.1159, found 402.1157.
Diethyl 4-(2-fluorophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3k)

49 mg, 42% yield; Yellow oil; 1H NMR (400 MHz, Chloroform-d) δ 7.90 (t, J = 8.6 Hz, 1H), 7.53–7.48 (m, 1H), 7.25 (t, J = 7.7 Hz, 1H), 7.17–7.12 (m, 1H), 6.92 (d, J = 2.9 Hz, 1H), 4.41–4.30 (m, 4H), 1.38 (t, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.4, 161.9, 161.7 (d, J = 254.5 Hz), 160.2, 149.2 (d, J = 1.8 Hz), 133.9 (d, J = 8.8 Hz), 130.5 (d, J = 2.5 Hz), 124.9 (d, J = 3.5 Hz), 123.3 (d, J = 10.8 Hz), 120.9 (q, J = 285.8 Hz), 116.6 (d, J = 22.3 Hz), 105.4 (d, J = 10.1 Hz), 91.6 (q, J = 32.2 Hz), 63.6, 62.7, 14.2, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.3, -112.7 ppm; HRMS (ESI-TOF): m/z calcd for C17H13F4NO5 [M+H]+ 390.0959, found 390.0957.

Diethyl 4-[[1,1'-biphenyl]-4-yl]-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3l)

89 mg, 66% yield; Purple oil; 1H NMR (400 MHz, Chloroform-d) δ 8.03 (d, J = 8.2 Hz, 2H), 7.70 (d, J = 8.4 Hz, 2H), 7.63 (d, J = 7.4 Hz, 2H), 7.50–7.46 (m, 2H), 7.42–7.39 (m, 1H), 6.99 (s, 1H), 4.44–4.30 (m, 4H), 1.41 (t, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.6, 162.4, 160.5, 150.0, 145.2, 134.0, 133.2, 129.1, 128.3, 128.0, 127.5, 127.3, 121.1 (q, J = 285.0 Hz), 102.0, 92.3 (q, J = 32.0 Hz), 63.5, 62.8, 14.2, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C23H17F4NO5 [M+H]+ 448.1366, found 448.1360.

Diethyl 4-(naphthalen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3m)

57 mg, 45% yield; White solid; Mp 77–78 °C; 1H NMR (400 MHz, Chloroform-d) δ 8.35 (s, 1H), 8.13–8.11 (m, 1H), 7.97–7.87 (m, 3H), 7.61–7.53 (m, 2H), 7.11 (s, 1H), 4.46–4.30 (m, 4H), 1.42 (t, J = 7.1 Hz, 3H), 1.32 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.6, 162.7, 160.6, 150.0, 135.3, 132.8, 131.8, 129.3, 128.9, 128.6, 128.3, 127.9, 127.0, 121.1 (q, J = 285.8 Hz), 123.6, 102.1, 92.4 (q, J = 32.0 Hz), 63.6, 62.8, 14.3, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.2 ppm; HRMS (ESI-TOF): m/z calcd for C26H15F4NO5 [M+H]+ 422.1210, found 422.1202.

Diethyl 4-((thiophen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3n)

52 mg, 46% yield; Purple oil; 1H NMR (400 MHz, Chloroform-d) δ 7.63 (d, J = 3.8 Hz, 1H), 7.59 (d, J = 5.0 Hz, 1H), 7.14–7.12 (m, 1H), 6.81 (s, 1H), 4.42–4.27 (m, 4H), 1.39 (t, J = 7.1 Hz, 3H), 1.30 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.5, 160.4, 157.3, 149.6, 140.4, 132.7, 130.8, 128.2, 121.0 (q, J = 285.1 Hz), 101.8, 91.8 (q, J = 32.1 Hz), 63.5, 62.8, 14.2, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for C18H15F4NO5S [M+H]+ 378.0618, found 378.0614.

2-Ethyl 6-methyl 4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3o)

68 mg, 63% yield; White solid; Mp 91–93 °C; 1H NMR (400 MHz, Chloroform-d) δ 7.94 (d, J = 7.3 Hz, 2H), 7.54 (t, J = 7.4 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 6.96 (s, 1H), 4.39–4.27 (m, 2H), 3.93 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H) ppm; 13C NMR (100 MHz, CDCl3) δ 163.5, 162.8, 160.9, 149.7, 134.3, 132.5, 128.9, 127.4, 121.0 (q, J = 284.9 Hz), 102.3, 92.3 (q, J = 32.1 Hz), 63.6, 53.3, 14.0 ppm; 19F NMR (376 MHz, CDCl3) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C16H13F4NO5 [M+H]+ 358.0897, found 358.0893.
2-Ethyl 6-isopropyl 4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3p)  

58 mg, 50% yield; Yellow oil; ³¹H NMR (400 MHz, Chloroform-d) δ 7.93 (d, J = 7.2 Hz, 2H), 7.56–7.45 (m, 3H), 6.90 (s, 1H), 5.26–5.20 (m, 1H), 4.38–4.27 (m, 2H), 1.38–1.36 (m, 6H), 1.30 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 163.6, 163.0, 159.9, 150.3, 134.5, 132.4, 128.9, 127.4, 121.1 (q, J = 284.9 Hz), 101.9, 92.2 (q, J = 32.0 Hz), 70.9, 63.4, 21.8, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₁₇H₁₂F₃NO₅ [M+H]+ 386.1210, found 386.1204.

Ethyl 4,6-diphenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4a)  

90 mg, 80% yield; White solid; Mp 74–76 °C; ³¹H NMR (400 MHz, Chloroform-d) δ 8.01 (d, J = 7.1 Hz, 2H), 7.92 (d, J = 7.0 Hz, 2H), 7.56–7.47 (m, 6H), 6.63 (s, 1H), 4.37–4.27 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 165.0, 164.5, 160.7, 135.8, 132.0, 131.7, 131.2, 128.9, 128.8, 127.4, 127.0, 121.6 (q, J = 284.2 Hz), 95.1, 91.7 (q, J = 31.7 Hz), 63.3, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₂₀H₁₇F₂NO₃ [M+H]+ 376.1155, found 376.1152.

Ethyl 6-(4-nitrophenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4b)  

79 mg, 63% yield; Yellow solid; Mp 137–138 °C; ³¹H NMR (400 MHz, Chloroform-d) δ 8.32 (d, J = 8.6 Hz, 2H), 8.07 (d, J = 8.6 Hz, 2H), 7.98 (d, J = 7.4 Hz, 2H), 7.57–7.47 (m, 3H), 6.73 (s, 1H), 4.39–4.27 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 164.4, 163.6, 158.0, 149.6, 137.0, 135.1, 132.1, 128.9, 127.6, 127.4, 124.0, 121.3 (q, J = 285.8 Hz), 97.2, 91.9 (q, J = 32.0 Hz), 63.6, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₂₀H₁₇F₂NO₃ [M+H]+ 421.1006, found 421.1009.

Ethyl 6-(4-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4c)  

97 mg, 80% yield; Yellow solid; Mp 105–106 °C; ³¹H NMR (400 MHz, Chloroform-d) δ 7.98 (d, J = 8.6 Hz, 2H), 7.91 (d, J = 6.9 Hz, 2H), 7.53–7.47 (m, 3H), 6.97 (d, J = 8.5 Hz, 2H), 6.60 (s, 1H), 4.35–4.25 (m, 2H), 3.86 (s, 3H), 1.27 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 165.2, 163.4, 162.6, 160.4, 131.9, 131.4, 129.2, 128.9, 128.3, 126.9, 121.6 (q, J = 284.3 Hz), 114.0, 94.9, 91.7 (q, J = 31.6 Hz), 63.2, 55.5, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for C₂₁H₁₈F₂NO₃ [M+H]+ 406.1261, found 406.1258.

Ethyl 6-(3-bromophenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4d)  

61 mg, 45% yield; Yellow solid; Mp 104–106 °C; ³¹H NMR (400 MHz, Chloroform-d) δ 8.08–7.92 (m, 3H), 7.83 (d, J = 7.9 Hz, 1H), 7.65 (d, J = 6.8 Hz, 1H), 7.56–7.47 (m, 3H), 7.36 (t, J = 7.9 Hz, 1H), 6.59 (s, 1H), 4.37–4.26 (m, 2H), 1.29 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 164.7, 164.1, 159.1, 135.5, 134.8, 133.3, 131.9, 130.5, 129.7, 128.8, 127.4, 125.5, 123.1, 121.4 (q, J = 284.8 Hz), 95.8, 91.8 (q, J = 31.9 Hz), 63.4, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₂₃H₁₅BrF₃NO₃ [M+H]+ 454.0260, found 454.0251.
Ethyl 4-phenyl-6-(m-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4e)

84 mg, 72% yield; Yellow solid; Mp 61–63 °C; \(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.93 (d, \(J = 6.4\) Hz, 2H), 7.85 (s, 1H), 7.77 (d, \(J = 7.2\) Hz, 1H), 7.54–7.49 (m, 3H), 7.40–7.34 (m, 2H), 6.63 (s, 1H), 4.38–4.27 (m, 2H), 2.45 (s, 3H), 1.29 (t, \(J = 7.1\) Hz, 3H) ppm; \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 165.0, 164.7, 160.5, 138.6, 135.7, 132.5, 132.0, 131.2, 128.9, 128.6, 127.9, 126.9, 124.6, 121.6 (q, \(J = 285.8\) Hz), 95.3, 91.7 (q, \(J = 31.7\) Hz), 63.2, 21.5, 14.0 ppm; \(^1^F\) NMR (376 MHz, CDCl\(_3\)) \(\delta\) -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C\(_{21}\)H\(_{15}\)F\(_3\)NO\(_3\) [M+H]\(^+\) 390.1312, found 390.1311.

Ethyl 6-(2-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4f)

45 mg, 37% yield; Yellow oil; \(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.08 (d, \(J = 9.6\) Hz, 1H), 7.98 (d, \(J = 6.6\) Hz, 2H), 7.52–7.46 (m, 4H), 7.16–7.06 (m, 2H), 7.00 (d, \(J = 7.4\) Hz, 1H), 4.34–4.23 (m, 2H), 3.97 (s, 3H), 1.24 (d, \(J = 7.1\) Hz, 3H) ppm; \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 165.4, 165.1, 159.1, 157.2, 135.9, 131.3, 131.8, 130.4, 130.1, 128.7, 127.8, 121.5 (q, \(J = 285.8\) Hz), 121.2, 119.5, 111.4, 100.9, 90.7 (q, \(J = 31.6\) Hz), 63.3, 56.0, 14.1 ppm; \(^1^F\) NMR (376 MHz, CDCl\(_3\)) \(\delta\) -79.2 ppm; HRMS (ESI-TOF): m/z calcd for C\(_{22}\)H\(_{16}\)F\(_2\)NO\(_3\) [M+H]\(^+\) 406.1256, found 406.1257.

Ethyl 4-(4-chlorophenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4g)

69 mg, 56% yield; Yellow solid; Mp 134–135 °C; \(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.95–7.90 (m, 4H), 7.54–7.44 (m, 5H), 6.57 (s, 1H), 4.36–4.26 (m, 2H), 1.27 (t, \(J = 7.1\) Hz, 3H) ppm; \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 164.8, 163.4, 161.1, 137.6, 133.6, 132.2, 131.3, 129.0, 128.6, 127.0, 121.5 (q, \(J = 284.2\) Hz), 94.6, 91.7 (q, \(J = 31.9\) Hz), 63.3, 14.0 ppm; \(^1^F\) NMR (376 MHz, CDCl\(_3\)) \(\delta\) -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C\(_{20}\)H\(_{15}\)F\(_3\)NO\(_3\) [M+H]\(^+\) 410.0765, found 410.0761.

Ethyl 4-(4-nitrophenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4h)

96 mg, 76% yield; Orange solid; Mp 136–138 °C; \(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 8.31 (d, \(J = 8.6\) Hz, 2H), 8.07 (d, \(J = 8.6\) Hz, 2H), 7.98 (d, \(J = 7.3\) Hz, 2H), 7.57–7.47 (m, 3H), 6.73 (s, 1H), 4.39–4.27 (m, 2H), 1.29 (t, \(J = 7.1\) Hz, 3H) ppm; \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 164.4, 163.6, 158.0, 149.6, 137.0, 135.1, 132.1, 128.9, 127.6, 127.4, 124.0, 121.3 (q, \(J = 285.8\) Hz), 97.2, 91.9 (q, \(J = 32.0\) Hz), 63.6, 14.0 ppm; \(^1^F\) NMR (376 MHz, CDCl\(_3\)) \(\delta\) -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C\(_{20}\)H\(_{15}\)F\(_3\)N\(_2\)O\(_3\) [M+H]\(^+\) 421.1006, found 421.1001.

Ethyl 4-(4-methoxyphenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4i)

106 mg, 87% yield; Yellow solid; Mp 103–105 °C; \(^1^H\) NMR (400 MHz, Chloroform-\(d\)) \(\delta\) 7.99 (d, \(J = 6.5\) Hz, 2H), 7.87 (d, \(J = 8.8\) Hz, 2H), 7.52–7.45 (m, 3H), 6.99 (d, \(J = 8.8\) Hz, 2H), 6.52 (s, 1H), 4.35–4.25 (m, 2H), 3.87 (s, 3H), 1.27 (t, \(J = 7.1\) Hz, 3H) ppm; \(^1^C\) NMR (100 MHz, CDCl\(_3\)) \(\delta\) 165.2, 164.8, 162.8, 160.7, 136.0, 131.5, 128.9, 128.7, 127.4, 123.5, 121.6 (q, \(J = 284.8\) Hz), 114.3, 93.9, 91.6 (q, \(J = 31.7\) Hz), 63.2, 55.6, 14.0 ppm; \(^1^F\) NMR (376 MHz, CDCl\(_3\)) \(\delta\) -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C\(_{22}\)H\(_{16}\)F\(_3\)NO\(_3\) [M+H]\(^+\) 406.1261, found 406.1258.
Ethyl 6-phenyl-4-(m-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4j)

84 mg, 72% yield; Yellow solid; Mp 90–91 °C; ¹H NMR (400 MHz, Chloroform-d) δ 8.02 (d, J = 6.8 Hz, 2H), 7.73 (s, 2H), 7.54–7.47 (m, 3H), 7.41–7.34 (m, 2H), 6.62 (s, 1H), 4.38–4.27 (m, 2H), 2.45 (s, 3H), 1.29 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 165.0, 164.5, 160.9, 138.7, 135.8, 132.1, 131.1, 128.8, 128.7, 127.4, 127.4, 124.2, 121.6 (q, J = 284.8 Hz), 95.0, 91.7 (q, J = 31.7 Hz), 63.2, 21.5, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₁₉H₁₉F₃NO₅ [M+H]+ 390.1312, found 390.1311.

Ethyl 4-(3-bromophenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4k)

80 mg, 55% yield; Yellow solid; Mp 108–110 °C; ¹H NMR (400 MHz, Chloroform-d) δ 8.12 (t, J = 1.9 Hz, 1H), 7.97–7.82 (m, 3H), 7.65 (d, J = 7.9 Hz, 1H), 7.55–7.48 (m, 3H), 7.36 (t, J = 7.9 Hz, 1H), 6.54 (s, 1H), 4.36–4.25 (m, 2H), 1.27 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 164.7, 163.4, 161.2, 137.7, 134.6, 132.3, 130.9, 130.4, 130.3, 128.9, 127.0, 126.0, 123.0, 118.6 (q, J = 284.9 Hz), 94.7, 91.6 (q, J = 31.9 Hz), 63.4, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₂₀H₁₆BrF₃NO₅ [M+H]+ 454.0260, found 454.0251.

Ethyl 6-phenyl-4-(o-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4l)

53 mg, 45% yield; Yellow oil; ¹H NMR (400 MHz, Chloroform-d) δ 7.86 (d, J = 7.0 Hz, 2H), 7.54–7.43 (m, 4H), 7.36–7.25 (m, 3H), 6.29 (s, 1H), 4.38–4.30 (m, 2H), 2.51 (s, 3H), 1.30 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 168.1, 164.9, 159.8, 137.0, 136.6, 132.1, 131.4, 130.9, 130.0, 129.8, 128.2, 127.0, 126.1, 121.4 (q, J = 284.8 Hz), 98.5, 91.3 (q, J = 31.7 Hz), 63.3, 20.3, 14.1 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₂₁H₁₉F₃NO₅ [M+H]+ 390.1312, found 390.1307.

Ethyl 6-phenyl-4-(thiophen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4m)

86 mg, 75% yield; Yellow solid; Mp 83–84 °C; ¹H NMR (400 MHz, Chloroform-d) δ 7.89 (d, J = 7.1 Hz, 2H), 7.68 (d, J = 3.7 Hz, 1H), 7.55–7.41 (m, 4H), 7.14 (t, J = 4.4 Hz, 1H), 6.54 (s, 1H), 4.31 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 164.8, 160.4, 158.8, 141.2, 132.0, 131.4, 131.0, 129.5, 128.9, 127.9, 126.8, 121.4 (q, J = 284.4 Hz), 94.5, 91.4 (q, J = 31.8 Hz), 63.3, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.4 ppm; HRMS (ESI-TOF): m/z calcd for C₁₉H₁₉F₃NO₅S [M+H]+ 382.0719, found 382.0716.

Ethyl 4-phenyl-6-(thiophen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4n)

95 mg, 83% yield; Yellow solid; Mp 63–65 °C; ¹H NMR (400 MHz, Chloroform-d) δ 7.97 (d, J = 7.6 Hz, 2H), 7.74 (d, J = 3.7 Hz, 1H), 7.56–7.46 (m, 4H), 7.20–7.13 (m, 1H), 6.48 (s, 1H), 4.37–4.27 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ 164.7, 164.3, 155.7, 135.6, 134.7, 131.7, 130.4, 129.5, 128.7, 128.4, 127.4, 121.4 (q, J = 284.3 Hz), 93.9, 91.6 (q, J = 31.7 Hz), 63.3, 14.0 ppm; ¹⁹F NMR (376 MHz, CDCl₃) δ -79.3 ppm; HRMS (ESI-TOF): m/z calcd for C₁₉H₁₉F₃NO₅S [M+H]+ 382.0719, found 382.0714.
Ethyl (E)-4-phenyl-6-styryl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4o)

75 mg, 62% yield; Yellow oil; \( ^1 \)H NMR (400 MHz, Chloroform-d) \( \delta \) 7.95 (d, \( J = 6.8 \) Hz, 2H), 7.59–7.54 (m, 3H), 7.52–7.45 (m, 3H), 7.42–7.36 (m, 3H), 6.65 (d, \( J = 15.9 \) Hz, 1H), 6.17 (s, 1H), 4.41–4.26 (m, 2H), 1.30 (t, \( J = 7.1 \) Hz, 3H) ppm; \( ^{13} \)C NMR (100 MHz, CDCl) \( \delta \) 164.8, 164.2, 158.8, 137.5, 135.7, 135.3, 131.6, 129.8, 129.0, 128.7, 127.9, 127.3, 121.6 (q, \( J = 284.8 \) Hz), 119.3, 98.4, 91.4 (q, \( J = 31.4 \) Hz), 63.2, 14.0 ppm; \( ^{19} \)F NMR (376 MHz, CDCl) \( \delta \) -79.3 ppm; HRMS (ESI-TOF): m/z calc for C\(_{22}\)H\(_{19}\)F\(_3\)NO\(_3\) [M+H]\(^+\) 402.1312, found 402.1310.

Ethyl-5-(2-ethoxy-2-oxoethyl)-4-phenyl-2-(trifluoromethyl)-2,5-dihydrooxazole-2-carboxylate (5a)

White oil; dr 15:1; \( ^1 \)H NMR (400 MHz, Chloroform-d) \( \delta \) 7.75 (d, \( J = 7.4 \) Hz, 2H), 7.51–7.47 (m, 1H), 7.41 (t, \( J = 7.3 \) Hz, 2H), 5.96 (dd, \( J = 7.6, 3.8 \) Hz, 1H), 4.27 (q, \( J = 7.0 \) Hz, 2H), 4.10 (q, \( J = 7.0 \) Hz, 2H), 2.89–2.78 (m, 2H), 1.28 (t, \( J = 7.0 \) Hz, 3H), 1.17 (t, \( J = 7.0 \) Hz, 3H) ppm; \( ^{13} \)C NMR (100 MHz, CDCl) \( \delta \) 176.5, 169.5, 164.2, 132.9, 129.1, 128.8, 121.6 (q, \( J = 285.9 \) Hz), 106.6 (q, \( J = 30.8 \) Hz), 85.5, 63.0, 61.3, 39.1, 14.0, 13.9 ppm; \( ^{19} \)F NMR (376 MHz, Chloroform-d) \( \delta \) -78.6 ppm; HRMS (ESI-TOF): m/z calc for C\(_{17}\)H\(_{19}\)F\(_3\)NO\(_5\) [M+H]\(^+\) 374.1215, found 374.1230.

References

NMR Spectra of compounds

Diethyl 4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3a)
Diethyl 4-(4-fluorophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3b)
Diethyl 4-(4-chlorophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3c)
Diethyl 4-(4-bromophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3d)
Diethyl 4-(4-cyanophenyl)-2-((trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3e)
Diethyl 4-(p-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3f)
Diethyl 4-(4-methoxyphenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3g)
Diethyl 4-(3-methoxyphenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3h)
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\begin{align*}
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Diethyl 4-(3-bromophenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3i)
Diethyl 4-(2-methoxyphenyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3j)
Diethyl 4-(2-fluorophenyl)-2-((trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3k)
Diethyl 4-[[1,1'-biphenyl]-4-yl]-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3l)
Diethyl 4-(naphthalen-2-yl)-2-((trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3m)
Diethyl 4-(thiophen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3n)
2-Ethyl 6-methyl 4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3o)
2-Ethyl 6-isopropyl 4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2,6-dicarboxylate (3p)
Ethyl 4,6-diphenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4a)
Ethyl 6-(4-nitrophenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4b)
Ethyl 6-(4-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4c)
Ethyl 6-(3-bromophenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4d)
Ethyl 4-phenyl-6-(m-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4e)
Ethyl 6-(2-methoxyphenyl)-4-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4f)
Ethyl 4-(4-chlorophenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4g)
Ethyl 4-(4-nitrophenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4h)
Ethyl 4-(4-methoxyphenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4i)
Ethyl 6-phenyl-4-(m-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4j)
Ethyl 4-(3-bromophenyl)-6-phenyl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4k)
Ethyl 6-phenyl-4-(o-tolyl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4l)
Ethyl 6-phenyl-4-(thiophen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4m)
Ethyl 4-phenyl-6-(thiophen-2-yl)-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4n)
Ethyl (E)-4-phenyl-6-styryl-2-(trifluoromethyl)-2H-1,3-oxazine-2-carboxylate (4o)
Ethyl-5-(2-ethoxy-2-oxoethyl)-4-phenyl-2-(trifluoromethyl)-2,5-dihydrooxazole-2-carboxylate (5a)
Crystal structure and data for compound 3o
Table 1. Crystal data and structure refinement for 2105130246_0m.

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<tr>
<td>Largest diff. peak and hole</td>
<td>0.287 and -0.218 e.Å⁻³</td>
</tr>
</tbody>
</table>
HRMS (ESI-TOF) analysis of the reaction mixture

HRMS [ESI/TOF]: m/z calculated for C$_{5}$H$_{11}$O$_6$F$_y$Na$_x$ [M+Na]$^+$ 396.1029, found 396.1012.