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# Silver-catalyzed synthesis of disubstituted isoxazoles by cyclization of alkynyl oxime ethers

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ABSTRACT

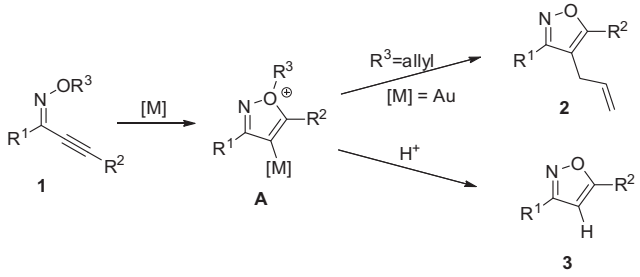
A facile and practical synthesis of 3,5-disubstituted isoxazoles via a silver-catalyzed cyclization and subsequent protonation of alkynyl oxime ethers has been developed. The methodology was successfully applied to the synthesis of a biologically active isoxazolecarboxylic acid.



## 1. Introduction

Heterocycles are well known for their wide range of biological properties.[1] Among the various bioactive heterocycles, isoxazoles attract great interest because of their wide reaching applications in the medicinal chemistry[2] and material science.[3] The vast majority of existing methodologies for the synthesis of isoxazoles[4–9] rely on either the condensation of a hydroxylamine with a 1,3-dicarbonyl compound or α,β-unsaturated carbonyl compound,[10] or the [3+2] cycloaddition reaction between an alkyne and a nitrile oxide.[11] These methods usually require harsh conditions and result in poor chemo- and regioselectivities. For this reason, research into novel and efficient methods for the synthesis of isoxazoles is continuously being pursued.[12]

The transition metal-catalyzed intramolecular addition of a heteroatom to an alkyne is one of the most powerful strategies for the synthesis of heterocyclic compounds.[13] This area has, however, been less explored for isoxazoles.[14–16] Recently, we have developed a methodology for the synthesis of trisubstituted isoxazoles **2** through a gold-catalyzed domino reaction of an alkynyl oxime ether, involving a 5-*endo*-*dig* cyclization and a subsequent Claisen-type [3,3]-sigmatropic rearrangement (Scheme 1).[17] We anticipated that the reaction in the presence of Brønsted acid would suppress the migration of substituent $R^3$ and produce the 3,5-disubstituted isoxazoles **3**, via protonation of the vinyl metal intermediate **A**. Therefore, a switchable divergent synthesis of tri- and disubstituted isoxazoles can be accomplished by tuning the reaction conditions. Herein, we report an efficient and versatile methodology for the synthesis of 3,5-disubstituted isoxazoles, through the transition metal-catalyzed cyclization of alkynyl oxime ethers in connection with our recent explorations of the chemistry of conjugated imines.[18]




**Scheme 1.** Transition metal-catalyzed synthesis of isoxazoles.

## 2. Results and discussion

Our studies commenced with a screening of catalysts (Table 1). (*Z*)-*O*-Benzyl alkynyl oxime ether **1a**, which was easily prepared by the condensation of 1,3-diphenylprop-2-yn-1-one with *O*-benzylhydroxylamine hydrochloride, was selected as a model substrate, since the benzyl group would act as a good leaving group.[19,20] The

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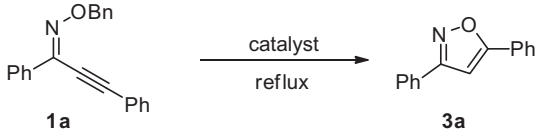
**Table 1**
Optimization of the cyclization reaction[a]




1a 3a

| Entry | Catalyst | Proton source | Solvent | Time (h) | Yield (%)[b] |
|---|---|---|---|---|---|
| 1 | $AuCl_3$ | PhOH | THF | 24 | 23 |
| 2 | $AuCl(PPh_3)$ | PhOH | THF | 24 | 9 |
| 3 | $AgBF_4$ | PhOH | THF | 6 | 80 |
| 4 | $AgSbF_6$ | PhOH | THF | 24 | 32 |
| 5 | $Cu(OTf)_2$ | PhOH | THF | 24 | 59 |
| 6 | $AgBF_4$ | MeOH | THF | 6 | 48 (50)[c] |
| 7 | $AgBF_4$ | AcOH | THF | 2 | 71 |
| 8 | $AgBF_4$ | PhOH | benzene | 6 | 14 |
| 9 | $AgBF_4$ | PhOH | toluene | 1 | 39 |
| 10 | $AgBF_4$ | none | THF | 6 | NR[d] |
| 11 | none | PhOH | THF | 6 | NR[d] |

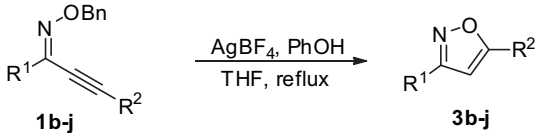
[a] Reaction conditions: **1a** (0.16 mmol), 20 mol % of catalyst, 2.0 equiv of proton source, solvent (5 mL).
[b] Yield of isolated product after chromatography.
[c] Yield in parentheses is for the recovered starting material **1a**.
[d] NR: no reaction.

screening of various metal catalysts (20 mol %), in the presence of phenol as a proton source, in THF at reflux, revealed $AgBF_4$ to be optimal both for reaction time and yield (80%) (entries 1–5). We then examined different proton sources. MeOH led to low conversions into the corresponding 3,5-disubstituted isoxazole **3a** (48% yield) (entry 6). Although acetic acid could accelerate the silver-catalyzed cyclization reaction, the yield was lower, due to the formation of a decomposition product (entry 7). These results suggest that weakly acidic conditions are required. The reaction was strongly influenced by the choice of solvent, with benzene and toluene leading to decreased chemical yields of **3a** (entries 8 and 9). A control reaction, in the absence catalyst or proton source, did not lead to any conversion, confirming that these results are attributed predominantly to the silver-catalyzed and phenol-promoted reaction.

On the basis of the above results, a proposed mechanism is shown in Scheme 2. The addition of an oxygen atom to the Ag(I)-activated C–C triple bond, in 5-*endo*-*dig* fashion, generates an oxonium intermediate **C**. The protonation of **C** by phenol, and subsequent elimination of the benzyl cation produces **D**. The benzyl cation would undergo polymerization, since the formation of any benzyl phenyl ether was not observed in the reaction mixture. Finally, the aromatization of **D** affords isoxazole **3a** and liberates the catalytic silver species.

To examine the scope of the reaction, we treated various alkynyl oxime ethers **1b–j** with $AgBF_4$ and phenol, in refluxing THF, and obtained the corresponding disubstituted isoxazoles **3b–j** in moderate to good yield (Table 2). The cyclization reaction of **1b**, which had alkyl group on the triple bond terminus, proceeded to give **3b** in good yield (entry 1). Interestingly, substrates **1c–e**, bearing an oxygen functionality at the propargylic position ($R^2$) efficiently underwent the cyclization within 1 h to yield **3c–e** (entry 2–4). We propose that the chelation of the oxygen atom enhances the reactivity of catalyst. It is noteworthy that the unprotected hydroxyl group did not inhibit the course of the reaction (entry 4). Variation of the substituent at $R^1$ was then examined using a substrate bearing the acetoxy group at the propargylic position. Both electron-rich and electron-poor aryl groups, and a hydrogen atom were readily accommodated, producing the expected disubstituted isoxazoles **3f–h** and monosubstituted isoxazole **3i** in good yield, respectively (entries 5–8). A notably high chemical yield was observed in the reaction of **1g**, which has a *p*-trifluoromethylphenyl group at $R^1$. An imino ester **1j** was also employed in this reaction, affording isoxazole carboxylate **3j** in high yield (entry 9).

**Table 2**
Silver-catalyzed synthesis of disubstituted isoxazoles[a]

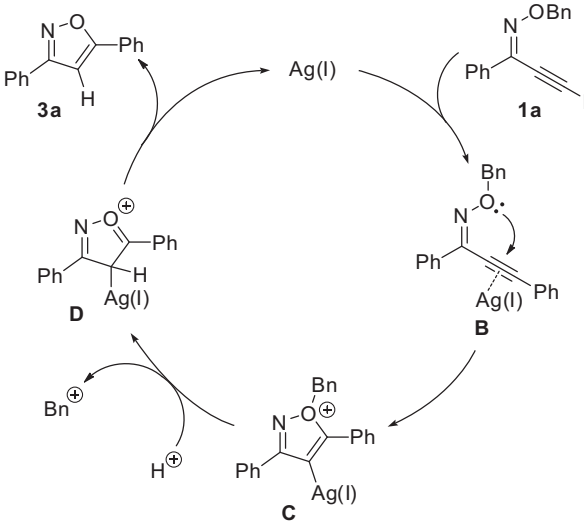



1b-j 3b-j

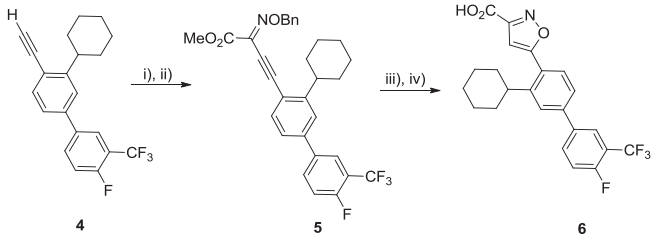
| Entry | Substrate | $R^1$ | $R^2$ | Time (h) | Product | Yield (%)[b] |
|---|---|---|---|---|---|---|
| 1 | **1b** | Ph | *n*-Bu | 6 | **3b** | 70 |
| 2 | **1c** | Ph | $CH_2OMe$ | 1 | **3c** | 71 |
| 3 | **1d** | Ph | $CH_2OAc$ | 1 | **3d** | 80 |
| 4 | **1e** | Ph | $CH_2OH$ | 1 | **3e** | 65 |
| 5 | **1f** | 4-$MeOC_6H_4$ | $CH_2OAc$ | 1 | **3f** | 60 |
| 6 | **1g** | 4-$CF_3C_6H_4$ | $CH_2OAc$ | 1 | **3g** | 86 |
| 7 | **1h** | 2-Furyl | $CH_2OAc$ | 1 | **3h** | 64 |
| 8 | **1i** | H | $CO_2Et$ | 7 | **3i** | 59 |
| 9 | **1j** | $CO_2Me$ | Ph | 12 | **3j** | 81 |

[a] Reaction conditions: **1** (0.16 mmol), 20 mol % of catalyst, 2.0 equiv of phenol, THF (5 mL).
[b] Yield of isolated product after chromatography.

To illustrate the potential utility of this reaction, we have examined its application to synthesis of the biologically active isoxazolecarboxylic acid **6**, which was synthesized by Ellman's group and found to be a strong *Mycobacterium tuberculosis* phosphatase PtpB inhibitor (Scheme 3).[21] Unfortunately, their synthetic strategy for the synthesis of isoxazole ring, involving [3+2] cycloaddition reaction, was inefficient and resulted in a low yield. In contrast, our method was highly effective, as shown in Scheme 3. The cyclization




**Scheme 2.** Proposed reaction pathway.




i) $MeO_2CCOCl$, CuI, $Et_3N$, THF, 61%. ii) $BnONH_2 \cdot HCl$, Pyridine, $Na_2SO_4$, MeOH, 60%
iii) $AgBF_4$, Phenol, 1,4-dioxane, 75%. iv) 1M NaOH, THF, quant.

**Scheme 3.** Synthesis of phosphatase PtpB inhibitor.

of alkynyl oxime ether **5**, which was readily prepared from alkyne **4**, afforded desired isoxazolecarboxylate in 75% yield. We finally succeeded in the total synthesis of phosphatase PtpB inhibitor **6**, by hydrolyzing the ester with 1 M NaOH.

## 3. Conclusion

We have successfully developed a novel method for the synthesis of disubstituted isoxazoles from alkynyl oxime ethers via a silver-catalyzed cyclization and subsequent protonation with phenol. This protocol was successfully applied to the synthesis of a biologically active compound. The reaction is straightforward, and allows for the efficient construction of substituted isoxazoles.

## 4. Experimental section

### 4.1. General

NMR spectra were recorded at 300 MHz/75 MHz ($^1$H NMR/$^{13}$C NMR) or 500 MHz/125 MHz ($^1$H NMR/$^{13}$C NMR) using Varian Gemini-300 (300 MHz), Varian MERCURY plus 300 (300 MHz), or Varian NMR system AS 500 (500 MHz) spectrometers. Chemical shifts ($\delta$) are reported as follows: chemical shift, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, quint=quintet, sext=sextet, m=multiplet, br=broad), coupling constants, and integration. IR spectra were obtained on a Perkin–Elmer SpectrumOne A spectrometer. Mass spectra were obtained by EI, CI or ESI methods on a Hitachi M-4100 and Thermo Fisher Scientific Exactive. Preparative TLC separations (PTLC) were carried out on pre-coated silica gel plates (E. Merck 60F$_{254}$). THF was freshly distilled from benzophenone ketyl radical anion prior to use.

### 4.2. General procedure for the silver-catalyzed synthesis of disubstituted isoxazole 3

To a solution of alkynyl oxime ether **1** (0.15 mmol) in THF (5 mL) were added phenol (28 mg, 0.3 mmol) and $AgBF_4$ (5.8 mg, 0.03 mmol), with a drying tube filled with silica gel at room temperature. After being stirred at reflux for 1–12 h (TLC monitoring), the reaction mixture was concentrated under reduced pressure. The residue was purified by preparative TLC (hexane/AcOEt=3–10:1) to afford isoxazole **3**. The physical and spectroscopic data of **3a**[5] and **3j**[12h] were in accord with those reported in the literature.

*4.2.1. 5-Butyl-3-phenylisoxazole (**3b**).* A colorless oil. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.81–7.78 (2H, m), 7.46–7.41 (3H, m), 6.28 (1H, d, $J$=0.5 Hz), 2.85 (2H, t, $J$=7.5 Hz), 1.73 (2H, quint, $J$=7.5 Hz), 1.43 (2H, sext, $J$=7.5 Hz), 0.96 (3H, t, $J$=7.5 Hz). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$: 174.3, 162.3, 129.7, 129.4, 128.8, 126.7, 98.7, 29.6, 26.5, 22.2, 13.7. HRMS $m/z$: calcd for $C_{13}H_{15}NO$ ($M^+$) 201.1153. Found: 201.1156.

*4.2.2. 5-(Methoxymethyl)-3-phenylisoxazole (**3c**).* A colorless oil. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.83–7.79 (2H, m), 7.47–7.44 (3H, m), 6.58 (1H, t, $J$=0.5 Hz), 4.60 (2H, s), 3.48 (3H, s). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$: 169.8, 162.4, 130.0, 128.9, 126.80, 126.76, 100.9, 65.4, 58.9. HRMS $m/z$: calcd for $C_{11}H_{11}NO_2$ ($M^+$) 189.0790. Found: 189.0802.

*4.2.3. Acetic acid (3-phenyl-5-isoxazolyl)methyl ester (**3d**).* A colorless oil. IR (NaCl) cm$^{-1}$: 1750. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.82–7.79 (2H, m), 7.47–7.45 (3H, m), 6.63 (1H, d, $J$=0.5 Hz), 5.23 (2H, d, $J$=0.5 Hz), 2.15 (3H, s). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$: 170.1, 167.1, 162.5, 130.1, 128.9, 128.6, 126.7, 102.1, 56.3, 20.5. HRMS $m/z$: calcd for $C_{12}H_{11}NO_3$ ($M^+$) 217.0738. Found: 217.0752.

*4.2.4. 3-Phenyl-5-isoxazolylmethanol (**3e**).* A colorless solid. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.82–7.79 (2H, m), 7.47–7.45 (3H, m), 6.58 (1H, s), 4.84 (2H, s), 2.08 (1H, s). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$: 171.9, 162.5, 130.1, 128.9, 128.8, 126.8, 100.0, 56.6, 26.4. HRMS $m/z$: calcd for $C_{10}H_9NO_2$ ($M^+$) 175.0633. Found: 175.0633.

*4.2.5. Acetic acid [3-(4-Methoxyphenyl)-5-isoxazolyl]methyl ester (**3f**).* A colorless oil. IR (NaCl) cm$^{-1}$: 1744. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.75–7.72 (2H, m), 6.99–6.96 (2H, m), 6.56 (1H, s), 5.21 (2H, s), 3.85 (3H, s), 2.14 (3H, s). $^{13}$C NMR ($CDCl_3$, 75 MHz) $\delta$: 170.2, 166.9, 162.1, 161.1, 128.2, 121.2, 114.3, 102.0, 56.4, 35.3, 20.6. HRMS $m/z$: calcd for $C_{13}H_{13}NO_4$ ($M^+$) 247.0844. Found: 247.0866.

*4.2.6. Acetic acid [3-[4-(Trifluoromethyl)phenyl]-5-isoxazolyl]methyl ester (**3g**).* A colorless oil. IR (NaCl) cm$^{-1}$: 1745. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.93 (2H, dd, $J$=8.5, 0.5 Hz), 7.73 (2H, dd, $J$=8.5, 0.5 Hz), 6.67 (1H, s), 5.25 (2H, d, $J$=0.5 Hz), 2.16 (3H, s). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 170.2, 167.9, 161.4, 132.0 (q, $J$=33 Hz), 127.1, 125.9 (q, $J$=3.6 Hz), 123.8 (q, $J$=271 Hz), 102.2, 56.3, 20.6. HRMS $m/z$: calcd for $C_{13}H_{10}F_3NO_3$ ($M^+$) 285.0612. Found: 285.0625.

*4.2.7. Acetic acid [3-(2-furanyl)-5-isoxazolyl]methyl ester (**3h**).* A colorless oil. IR (NaCl) cm$^{-1}$: 1748. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 7.56 (1H, dd, $J$=2.0, 1.0 Hz), 6.92 (1H, dd, $J$=3.5, 1.0 Hz), 6.58 (1H, s), 6.53 (1H, dd, $J$=3.5, 2.0 Hz), 5.21 (2H, s), 2.14 (3H, s). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 170.2, 167.9, 161.4, 127.1, 125.99, 125.96, 125.93, 125.90, 102.2, 56.3, 20.6. HRMS $m/z$: calcd for $C_{13}H_{10}F_3NO_3$ ($M^+$) 285.0612. Found: 285.0625.

*4.2.8. 5-Isoxazolecarboxylic acid ethyl ester (**3i**).* A colorless oil. IR (NaCl) cm$^{-1}$: 1735. $^1$H NMR ($CDCl_3$, 300 MHz) $\delta$: 8.37 (1H, d, $J$=2.0 Hz), 6.96 (1H, d, $J$=2.0 Hz), 4.45 (2H, q, $J$=7.0 Hz), 1.43 (3H, t, $J$=7.0 Hz). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 160.1, 156.7, 150.6, 108.7, 77.2, 62.3, 14.1. HRMS $m/z$: calcd for $C_6H_7NO_3$ ($M^+$) 141.0425. Found: 141.0427.

### 4.3. Synthesis of isoxazolecarboxylic acid 6

*4.3.1. 4-[3-Cyclohexyl-4′-fluoro-3′-(trifluoromethyl)[1,1′-biphenyl]-4-yl]-2-oxo-3-butynoic acid methyl ester.* To a solution of CuI (14 mg, 0.072 mmol) in THF (5 mL) were added $Et_3N$ (0.4 mL, 2.89 mmol), a solution of alkyne **4**[21a] (100 mg, 1.44 mmol) in THF (2 mL) and methyl chloroglyoxalate (0.27 mL, 2.89 mmol), under an Ar atmosphere at room temperature. After being stirred at the same temperature for 15 h, the reaction mixture was diluted with $H_2O$ and extracted with $Et_2O$. The organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by PTLC (hexane/AcOEt=8:1) afforded ketoester (76 mg, 61%) as a colorless solid. IR (NaCl) cm$^{-1}$: 2191, 1744, 1674. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 7.81–7.72 (3H, m), 7.48 (1H, d, $J$=2.0 Hz), 7.41 (1H, dd, $J$=8.0, 2.0 Hz), 7.31 (1H, t, $J$=9.0 Hz), 3.99 (3H, s), 3.26–3.21 (1H, m), 1.97–1.81 (4H, m), 1.57–1.47 (4H, m), 1.33–1.25 (2H, m). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 168.9, 160.8, 159.7, 158.7, 154.1, 142.5, 136.73, 136.70, 135.7, 132.7, 132.6, 126.0, 124.8, 124.7, 117.73, 117.68, 117.5, 97.0, 91.7, 53.7, 42.4, 33.8, 26.7, 26.0. HRMS $m/z$: calcd for $C_{24}H_{20}O_3F_4$ ($M^+$) 432.1347. Found: 432.1371.

*4.3.2. 4-[3-Cyclohexyl-4′-fluoro-3′-(trifluoromethyl)[1,1′-biphenyl]-4-yl]-2-[(phenylmethoxy)imino]-3-butynoic acid methyl ester (**5**).* To a solution of alkynyl ketone (47 mg, 0.11 mmol) in MeOH (2 mL) were added *O*-benzylhydroxylamine hydrochloride (35 mg, 0.22 mmol), $Na_2SO_4$ (31 mg, 0.22 mmol), and pyridine (0.2 mL), under an $N_2$ atmosphere at room temperature. After being stirred at the same temperature for 2 h, the reaction mixture was diluted with $H_2O$ and extracted with $Et_2O$. The organic phase was washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure. Purification by PTLC (benzene) afforded **5** (42 mg 71%) as a colorless solid. IR (NaCl) cm$^{-1}$: 2202, 1736, 1622. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 7.78–7.72 (2H, m), 7.61 (1H, d, $J$=8.0 Hz), 7.45–7.28

(3H, m,), 5.47 (2H, s), 3.95 (3H, s), 3.15 (1H, tt, $J$=12.0, 3.0 Hz), 1.92–1.89 (2H, m), 1.80–1.77 (2H, m), 1.71–1.69 (1H, m), 1.47–1.39 (2H, m), 1.35–1.20 (3H, m). $^{13}$C NMR ($CDCl_3$, 125 MHz) $\delta$: 161.6, 160.5, 158.4, 151.8, 140.5, 137.15, 137.12, 136.1, 134.1, 133.9, 132.52, 132.45, 128.6, 128.43, 128.40, 125.81, 125.79, 124.4, 124.3, 120.2, 117.5, 117.3, 101.6, 82.5, 79.0, 53.2, 42.1, 33.6, 26.7, 26.1. HRMS $m/z$: calcd for $C_{31}H_{27}NO_3F_4$ ($M^+$) 537.1925. Found: 537.1941.

*4.3.3. 5-[3-Cyclohexyl-4′-fluoro-3′-(trifluoromethyl)[1,1′-biphenyl]-4-yl]-3-isoxazolecarboxylic acid methyl ester.* To a solution of alkynyl oxime ether **5** (42 mg, 0.078 mmol) in 1,4-dioxane (5 mL) were added phenol (15 mg, 0.16 mmol) and $AgBF_4$ (15 mg, 0.078 mmol), with a drying tube filled with silica gel at room temperature. After being stirred at reflux for 7 days, the reaction mixture was filtered with $SiO_2$ and concentrated under reduced pressure. Purification by PTLC (benzene) afforded isoxazole carboxylate (27 mg, 75%) as a colorless solid. IR (NaCl) $cm^{-1}$: 1741. $^1$H NMR ($CDCl_3$, 500 MHz) $\delta$: 7.82–7.76 (2H, m), 7.64 (1H, d, $J$=8.0 Hz), 7.57 (1H, d, $J$=2.0 Hz), 7.46 (1H, dd, $J$=8.0, 2.0 Hz), 7.31 (1H, t, $J$=9.0 Hz), 6.80 (1H, s), 4.04 (3H, s), 2.90 (1H, tt, $J$=11.5, 3.0 Hz), 1.92–1.77 (5H, m), 1.58–1.26 (5H, m). $^{13}$C NMR (125 MHz) $\delta$: 172.0, 160.5, 156.4, 147.6, 141.3, 136.97, 136.94, 132.6, 132.5, 130.4, 125.91, 125.88, 125.7, 125.2, 124.8, 117.6, 103.6, 53.0, 40.8, 34.4, 26.7, 26.0. HRMS $m/z$: calcd for $C_{24}H_{21}NO_3F_4$ ($M^+$) 447.1467. Found: 447.1475.

*4.3.4. 5-[3-Cyclohexyl-4′-fluoro-3′-(trifluoromethyl)[1,1′-biphenyl]-4-yl]-3-isoxazolecarboxylic acid (**6**).* To a solution of isoxazole carboxylate (27 mg, 0.06 mmol) in THF (1 mL) was added 1 M NaOH (1 mL), under $N_2$ at room temperature. After being stirred at the same temperature for 1 h, the reaction mixture was concentrated under reduced pressure, diluted with 2 M HCl and extracted with AcOEt. The organic layer was washed with 2 M HCl, washed with brine, dried over $MgSO_4$, and concentrated under reduced pressure to give **1** (26 mg, quant) as a colorless solid. IR (NaCl) $cm^{-1}$: 1719. $^1$H NMR ($CDCl_3$/$CD_3OD$ (1:1), 500 MHz) $\delta$: 7.83–7.80 (2H, m), 7.66 (1H, d, $J$=8.0 Hz), 7.59 (1H, s), 7.49 (1H, dd, $J$=8.0, 1.5 Hz), 7.34 (1H, t, $J$=9.0 Hz), 6.82 (1H, s), 2.94–2.89 (1H, m), 1.89 (3H, t, $J$=14.5 Hz), 1.79 (1H, d, $J$=12.0 Hz), 1.56 (2H, q, $J$=12.0 Hz), 1.45–1.25 (4H, m). $^{13}$C NMR ($CDCl_3$/$CD_3OD$ (1:1), 125 MHz) $\delta$: 171.6, 161.4, 157.1, 147.3, 141.0, 136.78, 136.75, 132.5, 132.4, 130.1, 125.6, 125.4, 125.1, 124.5, 117.3, 117.2, 103.6, 40.6, 34.1, 26.4, 25.7. HRMS $m/z$: calcd for $C_{23}H_{20}NO_3F_4$ ($M^+$) 434.1378. Found: 434.1387. The spectroscopic data are consistent with those reported in the literature.[21a]

## Acknowledgements

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## Supplementary data

These data include experimental procedures for the synthesis of alkynyl oxime ethers **1a**–**h** and **1j**. Supplementary data related to this article can be found online at doi:10.1016/j.tet.2011.04.083.

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