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Study on the 1,3-dipolar cycloaddition reaction of 4-ethoxy-1,1,1-trifluoro-3-buten-2-one with nitrile oxides

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Abstract—1,3-Dipolar cycloaddition (1,3-DC) reaction of 4-ethoxy-1,1,1-trifluoro-3-buten-2-one **1** with nitrile oxides was studied. It was found that besides its C=C participating in the formation of isoxazole rings, trifluoromethyl activated C=O also underwent 1,3-DC reaction with nitrile oxides to afford 1,4,2-dioxazole rings. Single crystal diffraction analysis also evidenced the diheterocyclic configuration.

1. Introduction

Heterocycles are an important class of compounds, not only because of their natural abundance, but also because of their chemical, biological, and technical significances. Above all the heterocycles, isoxazole is one of the most useful compounds, which was found as an important unit in many biologically active compounds.[1] Most of them are important as drugs or biocides, including the human neurokinin NK-1 receptors sulfonamide sulfamethoxazole,[2] the *Xenopus laevis* oocytes,[3] the guinea pig tracheal strips,[4] and so on. Furthermore, isoxazoles have a considerable synthetic potential as masked 1,3-dicarbonyl systems due to their ring-opening reactions,[5] and have attracted increasing attention. The development of isoxazole chemistry has recently advanced to the discovery of new synthetic methods. Most of these are based on the capacity of the substance containing the highly reactive group $-C\equiv\overset{+}{N}-\overset{-}{O}$, which is found in nitrile oxides[6] and fulminic acid,[7] to react with aliphatic triple and double bonds to afford the isoxazole and isoxazoline rings, respectively. Fluorine, due to its unique electronic property and its similar atom radius as hydrogen, quite often imparts specific beneficial properties to organic molecules.[8] As a consequence of these characteristics, a group containing fluorine could be utilized to substitute a non-fluorinated one in a biologically active molecule, which might dramatically change the activity of the compound. Thus development of efficient methodology for the synthesis of fluorine-containing heterocycles is an active area of research.

2. Results and discussion

Trifluoromethyl-containing α,β-unsaturated ketone 4-ethoxy-1,1,1-trifluoro-3-buten-2-one **1** is very robust and can react easily with several kinds of nucleophiles, electrophiles, and dipoles. Many literatures have reported the chemical transformation of compound **1** and a large number of trifluoromethylated heterocyclic molecules have been obtained.[9] Our group has described several cycloaddition reactions of compound **1**, such as DA reaction with vinyl ether affording six-membered heterocycles,[9b] and 1,3-dipolar reaction with pyridinium *N*-ylide[10] and *C*-arylnitrones[9b] giving the fluorine-containing five-membered heterocycles. As a continuation of our research interest in chemical transformation of fluorinated α,β-unsaturated ketones, we investigated the 1,3-dipolar cycloaddition (1,3-DC) reaction of compound **1** with nitrile oxides. It was found that the reaction afforded bicycloaddition products, in which isoxazole and 1,4,2-dioxazole rings were formed simultaneously.

Due to the circumstance that dimerization always occurs in the isoxazole synthesis from the nitrile oxide, hydroxamyl chloride is usually utilized to prepare nitrile oxide in situ to avoid its dimerization.[11] It is well known that hydroxamyl chlorides are easily converted into nitrile oxides in the presence of base, usually using triethylamine (TEA). To our disappointment, in the presence of TEA only dimer **4a** was isolated from the reaction mixture, though materials **1** and **2a** were consumed completely (Table 1, entry 1). Other inorganic bases were examined and it was found that sodium hydrogen carbonate, sodium carbonate, and potassium carbonate could successfully promote the reaction and the expected product **3a** was obtained though in low yields (Table 1, entries 2, 5, and 6). Solvent optimization indicated that this reaction proceeded most readily in benzene and no

Keywords: 1,3-Dipolar cycloaddition reaction; Fluorine-containing alkene; Isoxazole; Dioxazole; Nitrile oxide.
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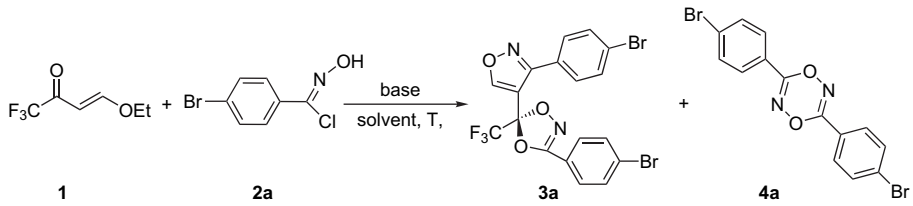
Table 1. Optimization of conditions for the reaction between compounds **1** and **2a**



1 **2a** **3a** **4a**

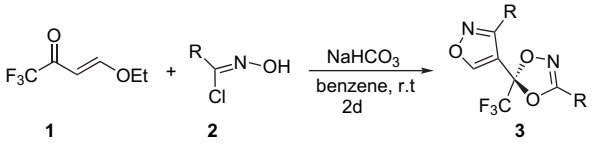
Entry	Material (**1**:**2a**)	Base	Solvent	**3a** (%)[a]	**4a** (%)[a]
1	1:2	Et_3N	CH_2Cl_2	—	40
2	1:2	$NaHCO_3$	Benzene	23	17
3	1:2	$NaHCO_3$	THF	—	42
4	1:2	$NaHCO_3$	DMF	—	37
5	1:2	Na_2CO_3	Benzene	12	22
6	1:2	K_2CO_3	Benzene	18	27
7	*1:4*	*$NaHCO_3$*	*Benzene*	*61*	*21*

[a] Isolated yield.

product was discovered when using THF and DMF as solvents (Table 1, entries 3 and 4). Interestingly, the yield was increased obviously with addition of hydroxamyl chloride **2a** (Table 1, entry 7), which resulted in more intermediate nitrile oxide participating in the expected 1,3-DC reaction. The optimized conditions (Table 1, entry 7) were applied to the 1,3-DC addition reaction of other hydroxamyl chlorides (**2b–i**) and the results are summarized in Table 2.

Just like **2a**, other substituted-phenyl hydroxamyl chlorides underwent 1,3-DC reaction smoothly with compound **1** in the presence of sodium hydrogen carbonate to give corresponding diheterocycles **3b–i** in moderate to good yields (Table 2, entries 2–8). From our early studies, we found that it was difficult for nitrile oxides containing strong electron-withdrawing group to react with fluorine-containing optically active imines.[12] Differently, hydroxamyl chlorides **2b** and **2f** substituted by nitro group could react with compound **1** on the occasion and afford the isoxazole derivatives **3b** and **3f** although with low yield down to 27% (Table 1, entry 2). Furthermore, aliphatic hydroxamyl chloride **2i** could also afford the diheterocycle in a considerable yield (Table 2, entry 9). Unfortunately, it was a failure synthesizing corresponding aliphatic diheterocycles when employing other aliphatic materials under the same reaction conditions.

Table 2. $NaHCO_3$-mediated 1,3-DC addition reaction of compound **1**[a]



1 **2** **3**

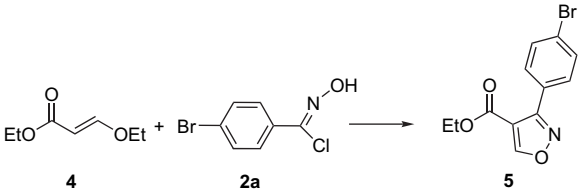
1 : 4

Entry	Nitrile oxide (R=)	**3**[b] (%)
1	**2a** (*p*-BrC_6H_4)	**3a** (61)
2	**2b** (*p*-$NO_2C_6H_4$)	**3b** (27)
3	**2c** (*p*-FC_6H_4)	**3c** (45)
4	**2d** (*p*-MeC_6H_4)	**3d** (46)
5	**2e** (*o*-FC_6H_4)	**3e** (43)
6	**2f** (*m*-$NO_2C_6H_4$)	**3f** (32)
7	**2g** (*o*-ClC_6H_4)	**3g** (79)
8	**2h** (C_6H_5)	**3h** (71)
9	**2i** ($CH{=}CHC_6H_5$)	**3i** (42)

[a] Corresponding by-products were isolated in each case.
[b] Isolated yield.

Compound **3b** formed a fine crystal after recrystallization from CH_2Cl_2 and ether, and then single crystal diffraction analysis was carried on it (Fig. 1). It clearly showed that isoxazole ring did not lie in the same plane with phenyl and the torsion angle is 82.29°. In the crystal, molecules were separated into two parts, which oriented in opposite directions. Furthermore, O_4 and O_5 of nitrophenyl formed intermolecular hydrogen bond with H_4 on the isoxazole ring and intermolecular halogen bond with F_3 of the trifluoromethyl in the other molecule, respectively. Therefore, every molecule was connected with each other by these intermolecular hydrogen bonds and halogen bonds and then boundless chains were formed. All these chains were also packed with each other by the hydrogen bonds that existed between two chains, and the distances were 2.646 and 2.718 Å.

In order to examine the substitution effect of fluorine atoms, non-fluorine-containing analogue compound was chosen to be employed to react with hydroxamyl chloride **2a**. Unfortunately, preparation of non-fluorine-containing α,β-unsaturated methyl ketone was unsuccessful. So (*E*)-ethyl 3-ethoxyacrylate **4** was employed instead in this case. It was found that only the double bond underwent the 1,3-DC reaction and formed the single-heterocycle product **5** in excellent yield (Scheme 1). Furthermore, the reaction could also proceed smoothly using TEA as the base. It means that without the electron-withdrawing effect of the trifluoromethyl the carbonyl was unable to react with nitrile oxide.



4 **2a** **5**

1 : 4

Scheme 1. (1) $NaHCO_3$, benzene, rt, 2 d, >99%; (2) Et_3N, CH_2Cl_2, rt, 1 d, 78%.

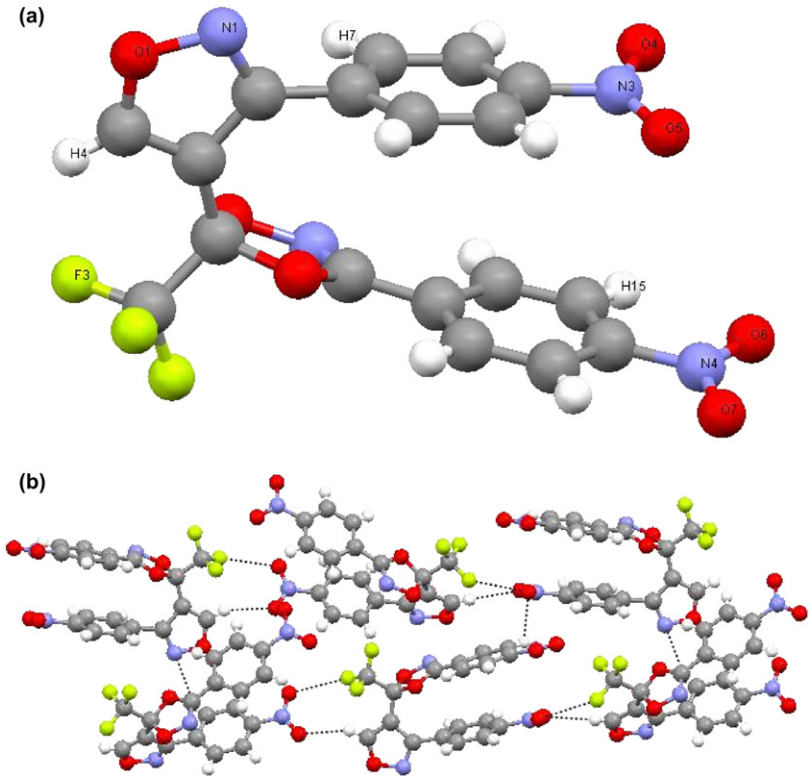


Figure 1. (a) Structure of **3b** (R=$C_6H_4NO_2$); (b) packing map.

3. Conclusion

In summary, 1,3-DC reaction of compound **1** with nitrile oxides was studied and the reaction formed a series of bicycloaddition products in moderate to good yields. Moreover, single crystal diffraction analysis of the product **3b** indicated that hydrogen bonds and halogen bonds determined the molecular configuration together. Compared to fluorine-containing compound, similar hydrocarbon without the activation of trifluoromethyl only reacted at the double bond and afforded single-heterocycle compound. At the same time, mild reaction conditions, easy manipulation, straightforward procedure, and considerable yields of useful products make this transformation potentially useful in organic synthesis.

4. Experimental

4.1. General

Melting points were measured on a Temp-Melt apparatus and are uncorrected. ^{1}H, ^{13}C, and ^{19}F NMR spectra were recorded on Bruker AM-300 or AM-400 instruments with Me_4Si and $CFCl_3$ as the internal standards, respectively. FTIR spectra were obtained with a Nicolet AV-360 spectrophotometer. Low resolution mass spectra (LRMS) or high resolution mass spectra (HRMS) were obtained on a Finnigan GC–MS 4021 or a Finnigan MAT-8430 instrument using the electron impact ionization technique (70 eV), respectively. Single crystal X-ray structure analysis was performed on a Bruker P4 instrument.

4.2. Experimental procedure

The mixture of **1** (0.3 mmol) and hydroxamyl chloride **2a** (1.2 mmol) in 2 mL of benzene was added slowly into the mixture of $NaHCO_3$ (0.6 mmol) in 1 mL benzene at 0 °C. Then the mixture was warmed to room temperature. TLC analysis was used to monitor the reaction. After one day, the reaction was complete. After general work-up, the residue was purified by column chromatography on silica gel (hexane/AcOEt=40:1) to give the product **3a** in a yield of 61%.

4.2.1. 3-(4-Bromophenyl)-5-(3-(4-bromophenyl)isoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3a. Yellow solid, mp: 81–83 °C, yield: 61%. ^{1}H NMR ($CDCl_3$): δ 8.80 (1H, s, CH═), 7.65–7.26 (8H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.21 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 160.2 (C_5), 159.6 (C_4), 158.2 (C_3), 132.4 (Ph), 131.7 (Ph), 130.6 (Ph), 129.2 (Ph), 128.2 (Ph), 127.6 (Ph), 126.4 (Ph), 124.7 (Ph), 120.7 (CF_3, $^1J_{CF}$=230 Hz), 111.5 (C_1), 106.9 (C_2). MS (*m*/*z*, %): 519 (M^+, 14.61), 450 (M^+-CF_3, 12.52), 320 (M^+-p-BrC_6H_4CNO, 12.97), 251 (M^+-p-$BrC_6H_4CNO-CF_3$, 60.37), 69 (CF_3, 41.84). IR (cm^{-1}): 1634, 1594, 1489, 1402, 1205, 1098, 1010. HRMS calcd for $C_{18}H_9Br_2F_3N_2O_3$: 515.8932; found 515.8947.

4.2.2. 3-(4-Nitrophenyl)-5-(3-(4-nitrophenyl)isoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3b. Yellow solid, mp: 110–112 °C, yield: 27%. ^{1}H NMR ($CDCl_3$): δ 8.92 (1H, s, CH═), 8.39–8.20 (4H, m, Ph), 7.84–7.72 (4H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.25 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 160.3 (C_5), 159.2 (C_4), 157.4 (C_3), 150.3 (Ph), 148.9 (Ph), 133.6 (Ph), 130.3 (Ph), 129.6 (Ph), 129.4 (Ph),

127.6 (Ph), 124.3 (Ph), 125.8 (CF_3, $^1J_{CF}$=248 Hz), 121.9 (C_1), 111.3 (C_2). MS (*m/z*, %): 450 (M^+, 6.64), 381 (M^+-CF_3, 2.45), 379 (M^+-CF_3-2H, 57.44), 284 (M^+-p-$NO_2C_6H_4CNO-2H$, 11.93), 216 (M^+-p-$NO_2C_6H_4CNO-CF_3-H$, 100), 69 (CF_3, 35.01). IR (cm^{-1}): 1596, 1525, 1348, 1198, 1098, 854. HRMS calcd for $C_{18}H_9F_3N_4O_7$: 450.0423; found 450.0422.

4.2.3. X-ray data of compound 3b. $C_{18}H_9F_3N_4O_7$: FW=450.29; temperature 293(2) K; monoclinic, *P*2(1)/*c*; wavelength 0.71 Å; a=23.378(3) Å, b=10.1309(13) Å, c=7.7185(10) Å, α=90.00°, β=90.00°, γ=90.00°; V=1828.1(4) Å^3; Z=4, D_c=1.636 Mg/m^3; absorption coefficient 0.147 mm^{-1}; $F(000)$=912; $1.74<\theta<27.00$; reflections collected 10,384; absorption correction empirical; transmission 1.000_{max}–0.7516_{min}. Final R indices R_1=0.0395, wR_2=0.0744. The CCDC number is 621809.

4.2.4. 3-(4-Fluorophenyl)-5-(3-(4-fluorophenyl)isoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3c. Yellow solid, mp: 107–108 °C, yield: 45%. ^{1}H NMR ($CDCl_3$): δ 8.66 (1H, s, CH=), 8.21–7.88 (4H, m, Ph), 7.22–7.15 (4H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.20 (s, CF_3), −102.3 (s, 1F), −105.1 (s, 1F). ^{13}C NMR ($CDCl_3$): δ 161.3 (C_5), 159.2 (C_4), 155.4 (C_3), 134.2 (Ph), 132.0 (Ph), 131.4 (Ph), 129.2 (Ph), 124.3 (Ph), 123.9 (Ph), 121.8 (CF_3, $^1J_{CF}$=231 Hz), 112.4 (C_1), 109.0 (C_2). MS (*m/z*, %): 396 (M^+, 0.12), 395 (M^+-H, 0.59), 259 (M^+-p-FC_6H_4CNO, 1.35), 194 (M^+-p-$FC_6H_4CNO-CF_3$, 1.48), 69 (CF_3, 4.22). IR (cm^{-1}): 1602, 1506, 1380, 1200, 837. HRMS calcd for $C_{18}H_9F_5N_2O_3$: 396.0533; found 396.0517.

4.2.5. 3-*p*-Tolyl-5-(3-*p*-tolylisoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3d. Yellow oil, yield: 46%. ^{1}H NMR ($CDCl_3$): δ 8.78 (1H, s, CH=), 7.48 (4H, dd, $^3J_{HH}$=1.8, 8.4 Hz, Ph), 7.18 (4H, dd, $^3J_{HH}$=1.8, 8.4 Hz, Ph), 2.40 (3H, s, Me), 2.30 (3H, s, Me). ^{19}F NMR ($CDCl_3$): δ −83.23 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 161.1 (C_5), 159.3 (C_4), 158.8 (C_3), 150.3 (Ph), 143.2 (Ph), 139.9 (Ph), 129.5 (Ph), 128.9 (Ph), 129.4 (Ph), 127.2 (Ph), 124.5 (Ph), 119.4 (Ph), 120.9 (CF_3, $^1J_{CF}$=288 Hz), 111.7 (C_1), 101.4 (C_2). MS (*m/z*, %): 388 (M^+, 22.60), 387 (M^+-H, 32.33), 318 (M^+-H-CF_3, 22.19), 255 (M^+-p-MeC_6H_4CNO, 1.49), 202 (CF_3+M^+-p-MeC_6H_4CNO, 3.86), 186 (M^+-p-$MeC_6H_4CNO-CF_3$, 100), 69 (CF_3, 11.91). IR (cm^{-1}): 1611, 1591, 1520, 1438, 1257, 835. HRMS calcd for $C_{20}H_{15}F_3N_2O_3$: 388.1035; found 388.1034.

4.2.6. 3-(2-Fluorophenyl)-5-(3-(2-fluorophenyl)isoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3e. Yellow oil, yield: 43%. ^{1}H NMR ($CDCl_3$): δ 8.78 (1H, s, CH=), 7.47–7.24 (4H, m, Ph), 7.13–6.91 (4H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.55 (s, CF_3), −105.45 (s, 1F), −112.5 (s, 1F). ^{13}C NMR ($CDCl_3$): δ 160.2 (C_5), 159.6 (C_4), 158.1 (C_3), 132.4 (Ph), 131.7 (Ph), 130.6 (Ph), 128.2 (Ph), 127.6 (Ph), 126.3 (Ph), 124.7 (Ph), 119.2 (Ph), 120.7 (CF_3, $^1J_{CF}$=231 Hz), 111.5 (C_1), 106.1 (C_2). MS (*m/z*, %): 396 (M^+, 9.16), 326 (M^+-H-CF_3, 40.48), 259 (M^+-o-FC_6H_4CNO, 5.14), 194 (M^+-o-$FC_6H_4CNO-CF_3$, 80.76), 69 (CF_3, 30.21). IR (cm^{-1}): 1630, 1594, 1499, 759. HRMS calcd for $C_{18}H_9F_5N_2O_3$: 396.0533; found 396.0533.

4.2.7. 3-(3-Nitrophenyl)-5-(3-(3-nitrophenyl)isoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3f. Yellow solid, mp: 88–90 °C, yield: 32%. ^{1}H NMR ($CDCl_3$): δ 8.93 (1H, s, CH=), 8.44–7.97 (4H, m, Ph), 7.74–7.66 (4H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.27 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 160.5 (C_5), 158.9 (C_4), 157.3 (C_3), 135.0 (Ph), 132.7 (Ph), 132.4 (Ph), 130.5 (Ph), 130.2 (Ph), 129.8 (Ph), 127.4 (Ph), 127.3 (Ph), 125.0 (Ph), 124.1 (Ph), 122.4 (Ph), 121.8 (Ph), 128.4 (CF_3, $^1J_{CF}$=286 Hz), 111.3 (C_1), 106.0 (C_2). MS (*m/z*, %): 450 (M^+, ESI). IR (cm^{-1}): 1655, 1541, 1535, 1087, 805. HRMS calcd for $C_{18}H_9F_3N_4O_7$+Na^+: 473.0316; found 473.0325.

4.2.8. 3-(2-Chlorophenyl)-5-(3-(2-chlorophenyl)isoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3g. Yellow oil, yield: 79%. ^{1}H NMR ($CDCl_3$): δ 8.83 (1H, s, CH=), 7.60–7.31 (8H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.27 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 159.8 (C_5), 157.7 (C_4), 154.7 (C_3), 135.3 (Ph), 134.4 (Ph), 132.6 (Ph), 131.3 (Ph), 130.9 (Ph), 130.4 (Ph), 129.7 (Ph), 129.1 (Ph), 128.4 (Ph), 128.0 (Ph), 126.8 (Ph), 123.3 (CF_3, $^1J_{CF}$=274 Hz), 111.4 (C_1), 97.5 (C_2). MS (*m/z*, %): 429 (M^+, 2.06), 360 (M^+-CF_3, 2.52), 276 (M^+-m-ClC_6H_4CNO, 0.57), 205 (M^+-m-$ClC_6H_4CNO-CF_3$, 14.63), 152 (m-ClC_6H_4CNO, 15.22), 69 (CF_3, 22.23). IR (cm^{-1}): 1634, 1602, 1492, 682. HRMS calcd for $C_{18}H_9F_3Cl_2N_2O_3$: (M^++H) 429.0015; found 429.0024.

4.2.9. 3-Phenyl-5-(3-phenylisoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3h. White oil, yield: 71%. ^{1}H NMR ($CDCl_3$): δ 8.72 (1H, s, CH=), 7.47–7.44 (5H, m, Ph), 7.31–7.25 (5H, m, Ph). ^{19}F NMR ($CDCl_3$): δ −83.14 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 161.1 (C_5), 159.4 (C_4), 158.7 (C_3), 132.5 (Ph), 129.9 (Ph), 129.1 (Ph), 128.8 (Ph), 128.3 (Ph), 127.0 (Ph), 126.9 (Ph), 120.6 (CF_3, $^1J_{CF}$=289 Hz), 111.6 (C_1), 97.7 (C_2). MS (*m/z*, %): 360 (M^+, 7.58), 359 (M^+-H, 15.27), 291 (M^+-CF_3, 28.30), 242 ($M^+-C_6H_5CNO$, 1.25), 173 ($M^+-H-C_6H_5CNO-CF_3$, 6.40), 69 (CF_3, 15.63). IR (cm^{-1}): 1635, 1577, 1450, 1017. HRMS calcd for $C_{18}H_{11}F_3N_2O_3$: 360.0722; found 360.0725.

4.2.10. 3-(*E*)-Styryl-5-(3-(*E*)-styrylisoxazol-4-yl)-5-(trifluoromethyl)-1,4,2-dioxazole 3i. Yellow oil, yield: 42%. ^{1}H NMR ($CDCl_3$): δ 8.80 (1H, s, CH=), 7.74 (1H, d, $^3J_{HH}$=16 Hz, CH=), 7.69–7.50 (10H, m, Ph), 7.44 (1H, d, $^3J_{HH}$=16 Hz, CH=), 7.10 (1H, d, $^3J_{HH}$=17 Hz, CH=), 6.80 (1H, d, $^3J_{HH}$=16 Hz, CH=). ^{19}F NMR ($CDCl_3$): δ −83.69 (s, CF_3). ^{13}C NMR ($CDCl_3$): δ 159.0 (C_5), 158.7 (C_4), 157.7 (C_3), 141.0 (Ph), 139.9 (Ph), 137.4 (Ph), 135.6 (Ph), 130.5 (Ph), 130.1 (Ph), 129.2 (Ph), 129.0 (CH), 128.8 (CH), 127.7 (CH), 127.3 (CH), 120.9 (CF_3, $^1J_{CF}$=288 Hz), 106.9 (C_1), 97.7 (C_2). MS (*m/z*, %): 412 (M^+, 9.18), 267 ($M^+-C_6H_5CHCHCNO$, 1.64), 103 ($C_6H_5CHCHCNO$, 100), 69 (CF_3, 62.31). IR (cm^{-1}): 1643, 1292, 1021. HRMS calcd for $C_{22}H_{15}F_3N_2O_3$: 412.1035; found 412.1032.

The mixture of **4** (0.3 mmol) and hydroxamyl chloride **2a** (1.2 mmol) in 2 mL of benzene was added slowly into the mixture of $NaHCO_3$ (0.6 mmol) in 1 mL benzene at 0 °C. Then the mixture was warmed to room temperature. TLC analysis was used to monitor the reaction. After one day, the reaction was over completely. After general work-up, the residue was purified by column chromatography

(hexane/AcOEt=40:1) on silica gel to give the product **5** in an excellent yield of >99%.

4.2.11. Ethyl 3-(4-bromophenyl) isoxazole-4-carboxylate. White solid, mp: 54–56 °C, yield: >99%. ^{1}H NMR ($CDCl_3$): δ 9.00 (1H, s, CH═), 7.68 (2H, d, $^3J_{HH}$=8 Hz, Ph), 7.60 (2H, d, $^3J_{HH}$=8 Hz, Ph), 4.30 (2H, dd, $^3J_{HH}$=6, 13 Hz, CH_2), 1.34 (3H, t, $^3J_{HH}$=6 Hz, CH_3). ^{13}C NMR ($CDCl_3$): δ 164.0 (C═O), 160.5 (C═N), 160.1 (C–O), 131.2 (Ph), 130.8 (Ph), 121.6 (Ph), 124.6 (Ph), 112.7 (C═C), 61.0 (CH_2), 13.9 (CH_3). MS (*m*/*z*, %): 296 or 294 (M^+, 62.37 or 67.11), 224 or 222 (M^+-CF_3, 66.15 or 64.9), 251 or 249 ($M^+-C_2H_5$, 22.42 or 13.25), 69 (CF_3, 45.46). IR (cm^{-1}): 3076, 1728, 1305, 1143. HRMS calcd for $C_{12}H_{10}BrNO_3$: 294.9844; found 294.9855.

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