Tetrahedron 65 (2009) 1988–1994

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Lewis acid-promoted reactions of ethenetricarboxylates with γ-CF_3-substituted propargyl alcohols

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ARTICLE INFO

Article history:
Received 12 September 2008
Received in revised form 25 December 2008
Accepted 6 January 2009
Available online 14 January 2009

ABSTRACT

The Lewis acid-promoted reaction of an ethenetricarboxylate derivative (**1**) with CF_3-substituted propargyl alcohols has been examined. Reaction of γ-CF_3 propargyl alcohols in the presence of zinc bromide gave five-membered CF_3-containing tetrahydrofurans in 66–85% yield. The CF_3 group activates alkyne as an electron-withdrawing group. On the other hand, reaction of γ-trifluoromethyl-α-aryl propargyl alcohols **2** with **1** in the presence of 1 equiv of $SnCl_4$ gave cyclobutane derivatives **6** in 29–49% yield. Formation of cyclobutane **6a** arises from the [2+2] cycloaddition between ethenetricarboxylate **1** and chloroallene **8**, which is produced by the reaction of propargyl alcohol **2a** and $SnCl_4$.

1. Introduction

Fluorine-containing molecules are interesting because of their biological activities.[1] Introduction of fluorine atoms into biologically important skeletons such as heterocycles and carbocycles is expected to lead to various activities. Recently, the synthesis of methylenetetrahydrofurans by one-pot formal [3+2] cycloadditions involving propargylic alcohols with electrophilic alkenes has been developed.[2] The synthetic methods provide powerful tools to prepare highly functionalized tetrahydrofuran rings. The reactions can be effectively promoted by base, base/transition metals, and Lewis acids, depending on the substrates.

Efficient preparation of CF_3-substituted propargylic alcohols has been reported recently.[3] The CF_3 substituent is known as an efficient electron-withdrawing group due to the inductive effect of fluorine atoms.[4] We have reported zinc and indium-promoted formal [3+2] cycloadditions of ethenetricarboxylates with propargyl alcohol to afford tetrahydrofurans.[2f] The highly electrophilic reactivity of ethenetricarboxylates led to an efficient one-pot reaction. We have also reported a Lewis acid-catalyzed cyclization of ethenetricarboxylate derivative **1** with γ-ester and silicon substituted propargyl alcohols to give methylenetetrahydrofurans stereoselectively.[2g]

In this study, during examination of the applicability of Lewis acid-catalyzed cyclization of the ethenetricarboxylate derivative **1** with γ-CF_3-substituted propargylic alcohols, it was found that reaction of γ-CF_3 propargyl alcohols with **1** in the presence of $SnCl_4$ gave cyclobutane derivatives, via a chloroallene intermediate.

2. Results and discussion

The reaction of triethyl ethenetricarboxylate (**1**) and γ-CF_3-substituted propargyl alcohols **2a–e**[3,5] in the presence of $ZnBr_2$ (0.2 equiv) was examined at first. Reaction of **1** and **2a–e** in the presence of $ZnBr_2$ (0.2 equiv) at 110 °C in toluene overnight gave **3a–e** in 66–85% yield, as diastereomer mixtures in a 1:1 to 1:1.3 ratio, respectively (Eq. 1). The result is in accord with the reported reaction of propargyl alcohols.[2f,g] For the geometry of the alkene moiety, *Z*-CF_3-substituted methylenetetrahydrofurans were obtained selectively.[6] Although the low 2,5-substituent diastereoselectivity is a general problem of tetrahydrofuran formation using α-substituted propargyl alcohols,[2] the diastereomers of certain derivatives (**3c–e**) could be separated by column chromatography. The reaction of **1** and 1-(3,3,3-trifluoroprop-1-ynyl)cyclohexanol **4** with $ZnBr_2$ (0.2 equiv) gave **5** in 32% yield (Eq. 2). The lower yield may arise from steric hindrance in the initial addition step.

The reaction of diethyl benzylidenemalonate with **2a** in the presence of $ZnBr_2$ was also examined. The reaction gave the starting material, diethyl benzylidenemalonate and a complex mixture and the possible cycloadducts could not be isolated. Thus, the high reactivity of **1** compared to benzylidenemalonate was shown by this efficient cyclization reaction.

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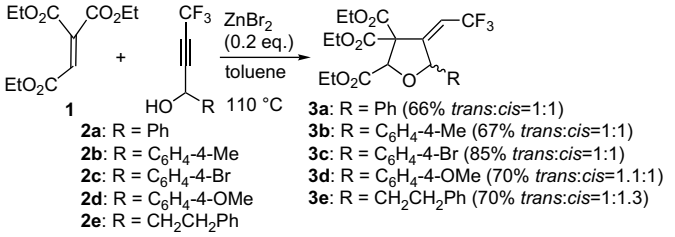
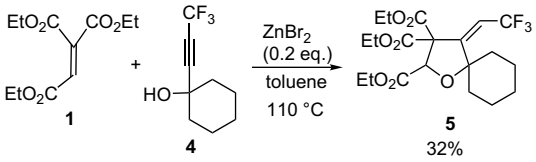
doi:10.1016/j.tet.2009.01.024

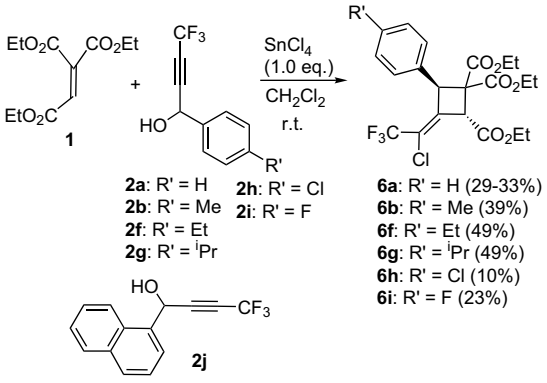


(1)



(2)

Various Lewis acids such as $AlCl_3$, $InBr_3$, $FeCl_3$, and $TiCl_4$–Et_3N[7] were examined, however, they gave complex mixtures. $SnCl_4$ was expected to have different reactivity, and reaction of **1** with ester-substituted propargyl alcohol gave the *E*-isomer tetrahydrofuran, which is a different stereoisomer from that obtained with the other Lewis acids, zinc, aluminum, and indium halides.[2g] Interestingly, reaction of 4,4,4-trifluoro-1-phenylbut-2-yn-1-ol (**2a**) with **1** in the presence of 1 equiv of $SnCl_4$ gave a product **6a** containing chlorine in 29–33% yield (Eq. 3).[8] The cyclobutane structure of **6a** was determined by X-ray analysis (Fig. 1).[9] The reaction of **2b**,**f**,**g** and **1** with $SnCl_4$ gave **6b**,**f**,**g** in 39–49% yield.[10] The reaction of 4-Cl and 4-F substituted substrates **2h**,**i** with **1** gave cyclobutanes **6h**,**i** in low yields, along with complex mixtures. The reaction of **2c**,**d** (R′=Br and OMe) and **2j** and **1** gave complex mixtures.[11] The reaction of an aliphatic derivative **2e** and **1** gave a complex mixture along with recovered **2e** and the reaction of **4** and **1** did not proceed under similar reaction conditions.



(3)

Formation of **6a** is speculated to arise from the [2+2] cycloaddition between **1** and chloroallene **8**.[12] Chloroallene **8** is postulated to be produced by the reaction of **2a** and $SnCl_4$.[7,13] The reaction of **2a** in the presence of $SnCl_4$ without **1** was thus performed. The reaction gave propargyl chloride **7**, chloroallene **8**, and ether derivative **9** in 10–14%, 10–16%, and 30–48% (dr 1:1) yields, respectively (Eq. 4). Chloroallene **8** was found to be unstable and decomposed in a concentrated state. Propargyl chloride **7** and chloroallene **8** are formed by nucleophilic substitution reactions of propargylic substrate **2a** with $SnCl_4$. Ether derivative **9** may be formed by nucleophilic substitution reaction between **2a** and $SnCl_4$-activated propargyl alcohol **2a**. The α-phenyl group of **2a** may facilitate these substitution reactions.

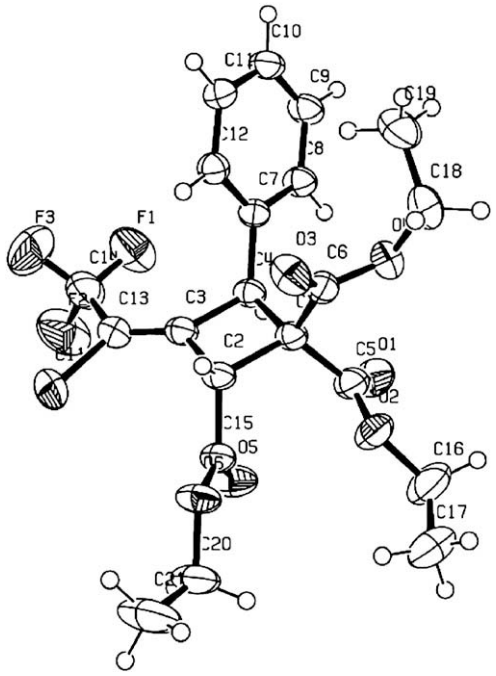
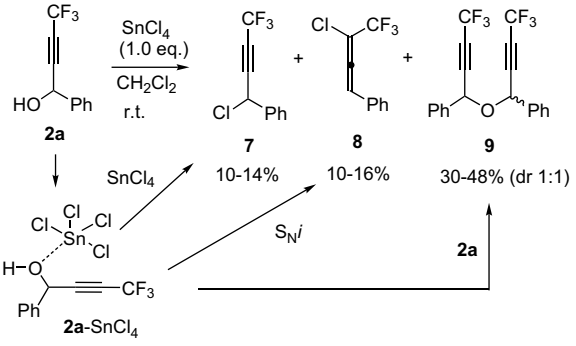
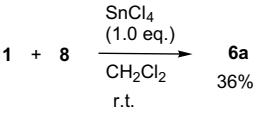


Figure 1. ORTEP drawing of the cyclobutane **6a** (thermal ellipsoids are drawn at 50% probability).

The reaction of the unstable allene **8** with **1** without $SnCl_4$ did not proceed. The reaction with $SnCl_4$ gave cyclobutane **6a** in 36% yield (Eq. 5). Although the yields are not very good probably because of the instability of the intermediate allene **8** under the reaction conditions, a novel reaction involving the formation of chloroallene and subsequent [2+2] cycloaddition by $SnCl_4$ was found.

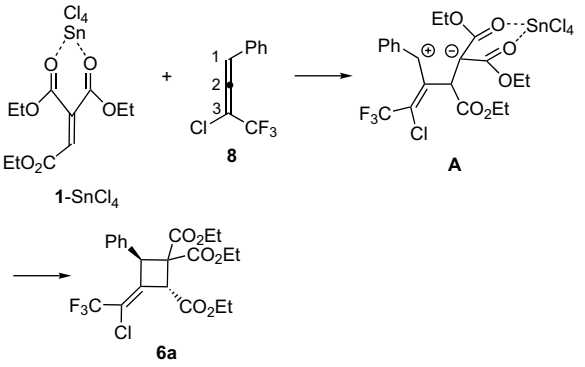


(4)



(5)

The regioselectivity of the [2+2] cycloaddition may be explained by larger HOMO of C2 (HOMO coefficients: C2, −0.41; C1, −0.27; C3, +0.04) in 3-chloro-4,4,4-trifluoro-1-phenylbuta-1,2-diene **8** in the reaction with highly electrophilic olefin **1** coordinated with $SnCl_4$ (Scheme 1).[14] The possible zwitter-ion intermediates **A** may be also stabilized by the Ph group. One stereoisomer of the cyclobutane was isolated and its structure confirmed by X-ray analysis (Fig. 1). Since the obtained yields were low, the preference for the obtained stereochemistry in **6a** is not clear.



Scheme 1.

In summary, a new reaction of γ-CF_3 α-aryl propargyl alcohols **2** with **1** in the presence of $SnCl_4$ to give cyclobutane derivatives **6** was found. Reaction of γ-CF_3 propargyl alcohols in the presence of zinc bromide also gave five-membered CF_3-containing tetrahydrofurans. CF_3 moieties in both products would attract much attention, because of the difficulty in preparation of CF_3-containing skeletons. Further improvement of the selectivity and elucidation of the effects of the CF_3 group in these reactions are under investigation.

3. Experimental section

3.1. General methods

Melting points are uncorrected. IR spectra were recorded in the FT-mode. ^{1}H NMR spectra were recorded at 400 MHz. ^{13}C NMR spectra were recorded at 100.6 MHz. ^{19}F NMR spectra were recorded at 376 MHz. ^{1}H chemical shifts are reported in parts per million relative to Me_4Si. ^{13}C chemical shifts are reported in parts per million relative to $CDCl_3$ (77.1 ppm). ^{19}F chemical shifts are reported in parts per million relative to $CFCl_3$. ^{13}C multiplicities were determined by DEPT and HSQC. Mass spectra were recorded at an ionizing voltage of 70 eV by EI or FAB. All reactions were carried out under a nitrogen atmosphere.

γ-CF_3-substituted propargyl alcohols **2a**,**c**,**e**,**j** and **4** were prepared according to Refs. 3 and 5 and **2b**,**f**–**i** were prepared according to the reported procedure.[3]

3.1.1. Compound *2b*

R_f=0.6 (hexane–ether=1:1); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.37 (s, 3H), 2.53 (br s, 1H), 5.49 (qd, *J*=2.7, 2.7 Hz, 1H), 7.22 (d, *J*=8.1 Hz, 2H), 7.37 (d-like, *J*=8.1 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 21.26 (CH_3), 63.94 (CH, q, J_{FC}=1.5 Hz), 73.31 (C, q, J_{FC}=53 Hz), 86.77 (C, q, J_{FC}=7 Hz), 114.16 (C, q, J_{FC}=258 Hz), 126.67 (CH), 129.76 (CH), 135.20 (C), 139.38 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −50.98 (d, J_{FH}=3.1 Hz); IR (neat) 3348, 2928, 2277, 1276, 1143 cm^{-1}; MS (EI) *m*/*z* 214 (M^+, 70), 199 (100%); HRMS M^+ 214.0602 (calcd for $C_{11}H_9F_3O$ 214.0605).

3.1.2. Compound *2f*

R_f=0.7 (hexane–ether=2:1); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.24 (t, *J*=7.6 Hz, 3H), 2.66 (q, *J*=7.6 Hz, 2H), 2.76 (br s, 1H), 5.46 (br s, 1H), 7.23 (d-like, *J*=8.2 Hz, 2H), 7.38 (d-like, *J*=8.2 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 15.53 (CH_3), 28.66 (CH_2), 63.90 (CH, q, J_{FC}=1.5 Hz), 73.28 (C, q, J_{FC}=53 Hz), 86.74 (C, q, J_{FC}=7 Hz), 114.16 (C, q, J_{FC}=258 Hz), 126.78 (CH), 128.59 (CH), 135.35 (C), 145.71 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −50.96 (d, J_{FH}=3.1 Hz); IR (neat) 3324, 2970, 2277, 1277, 1146 cm^{-1}; MS (EI) *m*/*z* 228 (M^+); HRMS M^+ 228.0765 (calcd for $C_{12}H_{11}F_3O$ 228.0762). Anal. Calcd for $C_{12}H_{11}F_3O$: C, 63.16; H, 4.86. Found: C, 63.53; H, 4.84.

3.1.3. Compound *2g*

R_f=0.4 (hexane–ether=4:1); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25 (d, *J*=7.0 Hz, 6H), 2.90 (br s, 1H), 2.92 (septet, *J*=7.0 Hz, 1H), 5.41 (br q, *J*=2.7 Hz, 1H), 7.26 (d, *J*=8.1 Hz, 2H), 7.38 (d-like, *J*=8.1 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 23.92 (CH_3), 33.98 (CH), 63.85 (CH), 73.28 (C, q, J_{FC}=53 Hz), 86.68 (C, q, J_{FC}=7 Hz), 114.16 (C, q, J_{FC}=258 Hz), 126.82 (CH), 127.17 (CH), 135.38 (C), 150.33 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −50.95 (d, J_{FH}=3.1 Hz); IR (neat) 3303, 2965, 2277, 1277, 1146 cm^{-1}; MS (EI) *m*/*z* 242 (M^+, 27), 227 (56), 199 (100%); HRMS M^+ 242.0914 (calcd for $C_{13}H_{13}F_3O$ 242.0918). Anal. Calcd for $C_{13}H_{13}F_3O$: C, 64.46; H, 5.41. Found: C, 64.18; H, 5.40.

3.1.4. Compound *2h*

R_f=0.3 (hexane–ether=4:1); brown crystals, mp 46–47 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.83 (br s, 1H), 5.52 (br s, 1H), 7.38 (d-like, *J*=8.6 Hz, 2H), 7.42 (d-like, *J*=8.6 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 63.32 (CH), 73.71 (C, q, J_{FC}=53 Hz), 86.01 (C, q, J_{FC}=6 Hz), 114.03 (C, q, J_{FC}=258 Hz), 128.02 (CH), 129.25 (CH), 135.28 (C), 136.39 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −51.13 (d, J_{FH}=2.7 Hz); IR (neat) 3336, 2279, 1598, 1490, 1276, 1146 cm^{-1}; MS (EI) *m*/*z* 234, 236 (M^+); HRMS M^+ 234.0052 (calcd for $C_{10}H_6{}^{35}ClF_3O$ 234.0059), 236.0030 (calcd for $C_{10}H_6{}^{37}ClF_3O$ 236.0030).

3.1.5. Compound *2i*

R_f=0.7 (hexane–ether=2:1); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 2.70 (br d, *J*=4.9 Hz, 1H), 5.55 (br s, 1H), 7.10 (dd-like, *J*=8.7, 8.6 Hz, 2H), 7.48 (dd-like, *J*=8.6, 5.2 Hz, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 63.35 (CH), 73.64 (C, q, J_{FC}=53 Hz), 86.30 (C, q, J_{FC}=7 Hz), 114.08 (C, q, J_{FC}=258 Hz), 116.05 (CH, d, J_{FC}=22 Hz), 128.63 (CH, d, J_{FC}=8 Hz), 133.91 (C, d, J_{FC}=3 Hz), 163.19 (C, J_{FC}=249 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −112.59 (m, 1×F), −51.10 (d, J_{FH}=3.1 Hz, 3×F); IR (neat) 3324, 2279, 1608, 1511, 1279, 1146 cm^{-1}; MS (EI) *m*/*z* 218 (M^+, 38), 217 (71), 201 (91), 151 (100%); HRMS M^+ 218.0354 (calcd for $C_{10}H_6F_4O$ 218.0355).

3.2. Typical experimental procedure (Eq. 1)

To a solution of **1** (122 mg, 0.5 mmol) in toluene (0.9 mL) was added 1-(4-bromophenyl)-4,4,4-trifluorobut-2-yn-1-ol (**2c**) (140 mg, 0.5 mmol) and $ZnBr_2$ (22 mg, 0.1 mmol). The mixture was heated at 110 °C and stirred for 16 h. The reaction mixture was cooled to room temperature and quenched by water (1.5 mL) and then saturated aqueous $NaHCO_3$. The mixture was extracted with dichloromethane and the organic phase was washed with water, dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by column chromatography over silica gel with hexane–ether as eluent to give *trans*-**3c** (108 mg, 41%) and *cis*-**3c** (115 mg, 44%).

3.2.1. *trans*-*3c*

R_f=0.4 (hexane–ether=2:1); colorless crystals, mp 104.5–105.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.288 (t, *J*=7.1 Hz, 3H), 1.289 (t, *J*=7.1 Hz, 3H), 1.37 (t, *J*=7.1 Hz, 3H), 4.15–4.40 (m, 6H), 5.20 (s, 1H), 6.06 (qd, *J*=2.6, 2.6 Hz, 1H), 6.29 (qd, *J*=8.6, 2.4 Hz, 1H), 7.17 (d-like, *J*=8.5 Hz, 2H), 7.47 (d-like, *J*=8.5 Hz, 2H). Selected NOEs are between δ 7.17 (*o*-*H* of C_6H_4-*p*-Br) and 5.20 (*CH*CO_2Et), 6.06 (O*CH*C_6H_4-*p*-Br). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.83 (CH_3), 13.98 (CH_3), 14.05 (CH_3), 61.84 (CH_2), 63.09 (CH_2), 63.50 (CH_2), 67.81 (C), 79.98 (CH), 82.00 (CH), 118.74 (CH, q, J_{FC}=36 Hz), 122.15 (C, q, J_{FC}=272 Hz), 123.21 (C), 129.97 (CH), 131.74 (CH), 136.38 (C), 147.66 (C, q, J_{FC}=5 Hz), 165.31 (C), 165.97 (C), 168.14 (C). Selected HMBC correlations are between δ 5.20 (*CH*CO_2Et) and δ 147.66 (*C*=CHCF$_3$) and between δ 6.06 (O*CH*C_6H_4-*p*-Br) and 79.98 (*CH*CO_2Et). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −60.13 (dd, J_{FH}=9.2, 3.1 Hz); IR (KBr) 2983, 1758, 1734, 1254, 1219, 1095 cm^{-1}; MS (EI) *m*/*z* 524 (M^+, 9.9),

522 (M^+, 9.2), 451 (100), 449 (99%); HRMS M^+ 522.0505 (calcd for $C_{21}H_{22}{}^{79}BrF_3O_7$ 522.0501), 524.0484 (calcd for $C_{21}H_{22}{}^{81}BrF_3O_7$ 524.0481). Anal. Calcd for $C_{21}H_{22}BrF_3O_7$: C, 48.20; H, 4.24. Found: C, 48.18; H, 4.26.

*3.2.2. cis-**3c***

R_f=0.3 (hexane–ether=2:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.21 (t, J=7.1 Hz, 3H), 1.28 (t, J=7.1 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 4.09–4.42 (m, 6H), 5.07 (s, 1H), 5.74 (qd, J=2.7, 2.7 Hz, 1H), 6.07 (qd, J=8.7, 2.7 Hz, 1H), 7.24 (d-like, J=8.5 Hz, 2H), 7.46 (d-like, J=8.5 Hz, 2H). Selected NOEs are between δ 5.74 (OC*H*C$_6$H$_4$-*p*-Br) and 5.07 (*CH*CO$_2$Et), 7.24 (*o-H* of C$_6$H$_4$-*p*-Br). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.79 (CH_3), 13.90 (CH_3), 13.95 (CH_3), 61.65 (CH_2), 63.07 (CH_2), 63.31 (CH_2), 68.38 (C), 80.58 (CH), 82.13 (CH), 118.14 (CH, q, J_{FC}=37 Hz), 121.92 (C, q, J_{FC}=272 Hz), 123.24 (C), 130.55 (CH), 131.49 (CH), 135.87 (C), 149.71 (C, q, J_{FC}=5 Hz), 165.26 (C), 166.39 (C), 167.04 (C). Selected HMBC correlations are between δ 5.07 (*CH*CO$_2$Et) and δ 149.71 (*C*=CHCF$_3$) and between δ 6.07 (C=*CH*CF$_3$) and 68.38 (*C*(CO$_2$Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −59.70 (dd, J_{FH}=7.6, 3.1 Hz); IR (neat) 2984, 1740, 1490, 1259, 1215, 1120 cm^{-1}; MS (EI) m/z 524 (M^+, 9.9), 522 (M^+, 9.9), 451 (99), 449 (100%); HRMS M^+ 522.0494 (calcd for $C_{21}H_{22}{}^{79}BrF_3O_7$ 522.0501), 524.0479 (calcd for $C_{21}H_{22}{}^{81}BrF_3O_7$ 524.0481). Anal. Calcd for $C_{21}H_{22}BrF_3O_7$: C, 48.20; H, 4.24. Found: C, 48.03; H, 4.31.

*3.2.3. Compound **3a***

R_f=0.4 (hexane–AcOEt=3:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) 1:1 diastereomer mixture, δ (ppm) 1.19–1.37 (m, 9H), 4.07–4.40 (m, 6H), 5.07 (s, 1×0.5H), 5.22 (d, J=0.5 Hz, 1×0.5H), 5.78 (dq, J=2.8, 2.8 Hz, 1×0.5H), 6.05 (dq, J=8.8, 2.7 Hz, 1×0.5H), 6.11 (dq, J=2.6, 2.6 Hz, 1×0.5H), 6.28 (dq, J=8.8, 2.4 Hz, 1×0.5H), 7.27–7.34 (m, 5H). Selected NOEs are between δ 5.07 (*cis CH*CO$_2$Et) and 5.78 (*cis* OC*H*Ph) and between δ 5.22 (*trans CH*CO$_2$Et) and 7.27–7.34 (*trans o*-H of Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.83 (CH_3), 13.95 (CH_3), 13.97 (CH_3), 14.00 (CH_3), 14.06 (CH_3), 61.60 (CH_2), 61.76 (CH_2), 63.00 (CH_2), 63.25 (CH_2), 63.37 (CH_2), 67.91 (C), 68.57 (C), 79.81 (CH), 80.57 (CH), 82.66 (CH), 82.96 (CH), 117.95 (CH, q, J_{FC}=37 Hz), 118.47 (CH, q, J_{FC}=37 Hz), 122.03 (C, q, J_{FC}=272 Hz), 122.23 (C, q, J_{FC}=272 Hz), 128.21 (CH), 128.30 (CH), 128.55 (CH), 128.87 (CH), 128.93 (CH), 129.00 (CH), 136.79 (C), 137.25 (C), 148.09 (C, q, J_{FC}=5 Hz), 150.24 (C, q, J_{FC}=5 Hz), 165.31 (C), 165.54 (C), 166.01 (C), 166.66 (C), 167.23 (C), 168.23 (C). Selected HMBC correlations are between δ 5.07 (*cis CH*CO$_2$Et) and 150.24 (*cis C*=CHCF$_3$) and δ 5.22 (*trans CH*CO$_2$Et) and 148.09 (*trans C*=CHCF$_3$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −59.79 (dd, J_{FH}=7.5, 3.0 Hz), −60.28 (dd, J_{FH}=9.2, 3.2 Hz); IR (neat) 2986, 1774–1732, 1457, 1368, 1246, 1121 cm^{-1}; MS (EI) m/z 444 (M^+, 8), 371 (100%); HRMS M^+ 444.1393 (calcd for $C_{21}H_{23}F_3O_7$ 444.1396).

*3.2.4. Compound **3b***

R_f=0.6 (hexane–ether=4:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) 1:1 diastereomer mixture, δ (ppm) 1.20 (t, J=7.1 Hz, 3×0.5H), 1.279 (t, J=7.1 Hz, 3×0.5H), 1.286 (t, J=7.1 Hz, 3×0.5H), 1.294 (t, J=7.1 Hz, 3×0.5H), 1.33 (t, J=7.1 Hz, 3×0.5H), 1.34 (t, J=7.1 Hz, 3×0.5H), 2.32 (s, 3×0.5H), 2.33 (s, 3×0.5H), 4.07–4.40 (m, 6H), 5.05 (s, 1×0.5H), 5.20 (d, J=0.7 Hz, 1×0.5H), 5.75 (dq, J=2.8, 2.8 Hz, 1×0.5H), 6.03 (dq, J=8.8, 2.7 Hz, 1×0.5H), 6.09 (dq, J=2.6, 2.6 Hz, 1×0.5H), 6.26 (dq, J=8.7, 2.4 Hz, 1×0.5H), 7.10–7.22 (m, 4H). Selected NOEs are between δ 5.05 (*cis CH*CO$_2$Et) and 5.75 (*cis* OC*H*Ar) and between δ 5.20 (*trans CH*CO$_2$Et) and 7.10–7.22 (*trans o*-H of Ar). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.73 (CH_3), 13.84 (CH_3), 13.88 (CH_3), 13.89 (CH_3), 13.96 (CH_3), 21.13 (CH_3), 21.16 (CH_3), 61.48 (CH_2), 61.63 (CH_2), 62.90 (CH_2), 63.14 (CH_2), 63.25 (CH_2), 67.87 (C), 68.56 (C), 79.62 (CH), 80.42 (CH), 82.41 (CH), 82.75 (CH), 117.56 (CH, q, J_{FC}=37 Hz), 118.18 (CH, q, J_{FC}=37 Hz), 122.01 (C, q, J_{FC}=272 Hz), 122.22 (C, q, J_{FC}=272 Hz), 128.03 (CH), 128.69 (CH), 128.90 (CH), 129.16 (CH), 133.85 (C), 134.30 (C), 138.71 (C), 138.74 (C), 148.24 (C, q, J_{FC}=5 Hz), 150.45 (C, q, J_{FC}=5 Hz), 165.25 (C), 165.52 (C), 165.95 (C), 166.63 (C), 167.20 (C), 168.20 (C). Selected HMBC correlations are between δ 5.05 (*cis CH*CO$_2$Et) and 150.45 (*cis C*=CHCF$_3$) and δ 5.20 (*trans CH*CO$_2$Et) and 148.24 (*trans C*=CHCF$_3$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −59.75 (dd, J_{FH}=9.0, 2.3 Hz), −60.32 (dd, J_{FH}=8.4, 2.8 Hz); IR (neat) 2985, 1742, 1254, 1213, 1129, 1024 cm^{-1}; MS (EI) m/z 458 (M^+); HRMS M^+ 458.1554 (calcd for $C_{22}H_{25}F_3O_7$ 458.1552). Anal. Calcd for $C_{22}H_{25}F_3O_7$: C, 57.64; H, 5.50. Found: C, 57.22; H, 5.50.

*3.2.5. trans-**3d***

R_f=0.4 (hexane–ether=1:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.28 (t, J=7.1 Hz, 3H), 1.29 (t, J=7.1 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 3.79 (s, 3H), 4.15–4.29 (m, 4H), 4.31–4.42 (m, 2H), 5.21 (d, J=0.7 Hz, 1H), 6.08 (qd, J=2.7, 2.7 Hz, 1H), 6.25 (qd, J=8.6, 2.4 Hz, 1H), 6.86 (d-like, J=8.8 Hz, 2H), 7.21 (d-like, J=8.8 Hz, 2H). Selected NOEs are between δ 7.21 (*o-H* of C$_6$H$_4$-*p*-OMe) and 5.21 (*CH*CO$_2$Et), 6.08 (OC*H*C$_6$H$_4$-*p*-OMe). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.82 (CH_3), 13.98 (CH_3), 14.05 (CH_3), 55.28 (CH_3), 61.71 (CH_2), 62.97 (CH_2), 63.34 (CH_2), 67.91 (C), 79.65 (CH), 82.29 (CH), 113.86 (CH), 118.27 (CH, q, J_{FC}=36 Hz), 122.25 (C, q, J_{FC}=271 Hz), 129.51 (C), 129.59 (CH), 148.47 (C, q, J_{FC}=5 Hz), 159.98 (C), 165.56 (C), 166.09 (C), 168.30 (C). Selected HMBC correlations are between δ 5.21 (*CH*CO$_2$Et) and δ 148.47 (*C*=CHCF$_3$) and between δ 6.08 (OC*H*C$_6$H$_4$-*p*-OMe) and 79.65 (*CH*CO$_2$Et). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −60.22 (dd, J_{FH}=9.2, 3.1 Hz); IR (neat) 2985, 1742, 1612, 1516, 1249, 1213, 1129, 1033 cm^{-1}; MS (EI) m/z 474 (M^+, 5.0), 401 (84), 135 (100%); HRMS (FAB) $(M+Na)^+$ 479.1392 (calcd for $C_{22}H_{25}F_3O_8Na$ 497.1399). Anal. Calcd for $C_{22}H_{25}F_3O_8$: C, 55.70; H, 5.31. Found: C, 55.35; H, 5.09.

*3.2.6. cis-**3d** (including a small amount of impurity)*

R_f=0.3 (hexane–ether=1:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.22 (t, J=7.1 Hz, 3H), 1.30 (t, J=7.1 Hz, 3H), 1.34 (t, J=7.1 Hz, 3H), 3.79 (s, 3H), 4.09–4.41 (m, 6H), 5.04 (s, 1H), 5.73 (qd, J=2.7, 2.7 Hz, 1H), 6.03 (qd, J=8.8, 2.7 Hz, 1H), 6.83 (d-like, J=8.6 Hz, 2H), 7.26 (d, J=8.6 Hz, 2H). Selected NOEs are between δ 5.04 (OC*H*C$_6$H$_4$-*p*-OMe) and 5.73 (*CH*CO$_2$Et), 7.26 (*o-H* of C$_6$H$_4$-*p*-OMe). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.84 (CH_3), 13.95 (CH_3), 13.98 (CH_3), 55.27 (CH_3), 61.57 (CH_2), 62.97 (CH_2), 63.20 (CH_2), 68.58 (C), 80.38 (CH), 82.61 (CH), 113.62 (CH), 117.74 (CH, q, J_{FC}=37 Hz), 122.05 (C, q, J_{FC}=272 Hz), 129.06 (C), 130.27 (CH), 150.69 (C, q, J_{FC}=5 Hz), 160.08 (C), 165.39 (C), 166.67 (C), 167.28 (C). Selected HMBC correlations are between δ 5.04 (*CH*CO$_2$Et) and δ 150.69 (*C*=CHCF$_3$) and between δ 6.03 (C=*CH*CF$_3$) and 68.58 (*C*(CO$_2$Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −59.68 (dd, J_{FH}=9.2, 3.1 Hz); IR (neat) 2985, 1739, 1613, 1517, 1252, 1114, 1031 cm^{-1}; MS (EI) m/z 474 (M^+, 30), 401 (98), 327 (50), 281 (59), 213 (75), 135 (100%); HRMS (FAB) $(M+Na)^+$ 497.1397 (calcd for $C_{22}H_{25}F_3O_8Na$ 497.1399).

*3.2.7. trans-**3e***

R_f=0.3 (hexane–ether=4:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.26 (t, J=7.1 Hz, 3H), 1.275 (t, J=7.1 Hz, 3H), 1.281 (t, J=7.1 Hz, 3H), 1.83–2.07 (m, 2H), 2.63–2.82 (m, 2H), 4.13–4.31 (m, 6H), 5.15–5.20 (m, 1H), 5.30 (d, J=0.7 Hz, 1H), 6.13 (qd, J=8.9, 2.4 Hz, 1H), 7.17–7.21 (m, 3H), 7.27–7.30 (m, 2H). Selected NOEs are between δ 1.83–2.07 (OCH*CH*$_2$CH$_2$) and 5.15–5.20 (OC*H*CH$_2$CH$_2$), 5.30 (OC*H*CO$_2$Et). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.81 (CH_3), 13.91 (CH_3), 14.02 (CH_3), 31.81 (CH_2), 36.22 (CH_2, q, J=1.5 Hz), 61.71 (CH_2), 62.84 (CH_2), 63.28 (CH_2), 67.34 (C), 80.20 (CH), 116.31 (CH, q, J_{FC}=36 Hz), 122.74 (C, q, J_{FC}=271 Hz),

126.07 (CH), 128.46 (CH), 128.56 (CH), 141.06 (C), 149.48 (C, q, J_{FC}=5 Hz), 165.33 (C), 166.00 (C), 168.68 (C). Selected HMBC correlations are between δ 5.30 (*CH*CO_2Et) and δ 149.48 (*C*=CHCF$_3$) and between δ 6.13 (C=*CH*CF$_3$) and 67.34 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −59.79 (dd, J_{FH}=9.2, 3.1 Hz); IR (neat) 2985, 1744, 1369, 1254, 1213, 1123 cm^{-1}; MS (EI) *m*/*z* 472 (M$^+$, 30), 399 (100), 279 (68%); HRMS M$^+$ 472.1705 (calcd for $C_{23}H_{27}F_3O_7$ 472.1709). Anal. Calcd for $C_{23}H_{27}F_3O_7$: C, 58.47; H, 5.76. Found: C, 58.34; H, 5.73.

3.2.8. *cis*-**3e**

R_f=0.2 (hexane–ether=4:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.26 (t, *J*=7.1 Hz, 3H), 1.29 (t, *J*=7.1 Hz, 3H), 1.31 (t, *J*=7.1 Hz, 3H), 1.99–2.15 (m, 2H), 2.68–2.87 (m, 2H), 4.19–4.36 (m, 6H), 4.86–4.91 (m, 1H), 4.96 (s, 1H), 5.84 (qd, *J*=8.8, 2.6 Hz, 1H), 7.16–7.21 (m, 3H), 7.26–7.30 (m, 2H). Selected NOEs are between δ 4.86–4.91 (OC*H*CH_2CH_2) and 4.96 (OC*H*CO_2Et), 1.99–2.15 (OCHC*H*$_2$$CH_2$). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.83 (CH_3), 13.97 (CH_3), 14.05 (CH_3), 31.69 (CH_2), 35.96 (CH_2, q, *J*=1.5 Hz), 61.56 (CH_2), 62.91 (CH_2), 63.10 (CH_2), 68.30 (C), 79.86 (CH), 80.73 (CH), 115.50 (CH, q, J_{FC}=36 Hz), 122.54 (C, q, J_{FC}=271 Hz), 126.03 (CH), 128.43 (CH), 128.64 (CH), 141.05 (C), 151.95 (C, q, J_{FC}=5 Hz), 165.42 (C), 166.55 (C), 167.70 (C). Selected HMBC correlations are between δ 4.96 (*CH*CO_2Et) and δ 151.95 (*C*=CHCF$_3$), 79.86 (OCHC$H_2$$CH_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −59.52 (dd, J_{FH}=9.2, 3.1 Hz); IR (neat) 2984, 1741, 1368, 1261, 1214, 1124 cm^{-1}; MS (EI) *m*/*z* 472 (M$^+$, 30), 399 (100) 327 (42%); HRMS M$^+$ 472.1707 (calcd for $C_{23}H_{27}F_3O_7$ 472.1709).

3.2.9. Compound **5**

R_f=0.6 (hexane–ether=1:2); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 1.25 (t, *J*=7.1 Hz, 3H), 1.28 (t, *J*=7.1 Hz, 3H), 1.31 (t, *J*=7.1 Hz, 3H), 1.24–1.33 (m, 1H), 1.54–1.95 (m, 9H), 4.14–4.37 (m, 6H), 5.06 (s, 1H), 5.87 (q, *J*=9.7 Hz, 1H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.82 (CH_3), 13.97 (CH_3), 14.07 (CH_3), 21.87 (CH_2), 22.11 (CH_2), 24.76 (CH_2), 32.56 (CH_2, q, J_{FC}=3 Hz), 34.22 (CH_2, q, J_{FC}=3 Hz), 61.41 (CH_2), 62.75 (CH_2), 62.94 (CH_2), 69.11 (C), 78.20 (CH), 85.95 (C), 115.60 (CH, q, J_{FC}=37 Hz), 122.46 (C, q, J_{FC}=271 Hz), 155.12 (C, q, J_{FC}=6 Hz), 165.99 (C), 166.84 (C), 168.27 (C). Selected HMBC correlations are between δ 5.06 (*CH*CO_2Et) and δ 155.12 (*C*=CHCF$_3$), 85.95 (OC(CH$_2$)$_5$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −55.64 (d, J_{FH}=9.2 Hz); IR (neat) 2937, 1742, 1256, 1119 cm^{-1}; MS (EI) *m*/*z* 436 (M$^+$, 15), 363 (100%); HRMS M$^+$ 436.1715 (calcd for $C_{20}H_{27}F_3O_7$ 436.1709). Anal. Calcd for $C_{20}H_{27}F_3O_7$: C, 55.04; H, 6.24; F, 13.06. Found: C, 55.22; H, 6.39; F, 12.73.

3.3. Reaction of 1 and 2a in the presence of $SnCl_4$ (Eq. 3)

To a solution of **1** (122 mg, 0.5 mmol) in CH_2Cl_2 (0.9 mL) was added 4,4,4-trifluoro-1-phenylbut-2-yn-1-ol (**2a**) (100 mg, 0.5 mmol) and $SnCl_4$ (130 mg, 0.06 mL, 0.5 mmol). The mixture was stirred at room temperature for 19 h. The reaction mixture was quenched by water and then saturated aqueous $NaHCO_3$. The mixture was extracted with dichloromethane and the organic phase was dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by column chromatography over silica gel with hexane–ether as eluent to give **6a** (77 mg, 33%) as an isolable product.

3.3.1. Compound **6a**

R_f=0.5 (hexane–ether=1:1); pale yellow crystals, mp 76–78 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.733 (t, *J*=7.1 Hz, 3H), 1.25 (t, *J*=7.1 Hz, 3H), 1.31 (t, *J*=7.1 Hz, 3H), 3.49–3.57 (m, 1H), 3.68–3.76 (m, 1H), 4.13–4.33 (m, 4H), 4.83 (dq, *J*=3.8, 2.2 Hz, 1H), 5.43 (dq, *J*=3.4, 2.7 Hz, 1H), 7.17–7.20 (m, 2H), 7.23–7.31 (m, 3H). Selected NOEs are between δ 7.17–7.20 (*o*-H of Ph) and 4.83 (*CH*CO_2Et), 5.43 (*CH*Ph). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.39 (CH_3), 13.95 (CH_3), 14.11 (CH_3), 50.80 (CH), 54.04 (CH), 58.71 (C), 61.90 (CH_2), 62.32 (CH_2), 62.42 (CH_2), 118.12 (C, q, J_{FC}=41 Hz), 119.84 (C, q, J_{FC}=273 Hz), 128.11 (CH), 128.13 (CH), 128.38 (CH), 135.44 (C, q, J_{FC}=2 Hz), 142.31 (C, q, J_{FC}=3 Hz), 166.48 (C), 167.39 (C), 167.42 (C). Selected HMBC correlations are between δ 4.82 (*CH*CO_2Et), 5.43 (*CH*Ph) and δ 142.31 (*C*=CClCF$_3$) and between δ 4.82 (*CH*CO_2Et), 5.43 (*CH*Ph) and δ 58.71 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −65.82 (dd, J_{FH}=2.3, 2.3 Hz); IR (KBr) 2992, 1733, 1274, 1188, 1136 cm^{-1}; MS (EI) *m*/*z* 464 (M$^+$, 9), 462 (M$^+$, 26), 416 (49), 388 (43), 343 (43), 315 (100%); HRMS M$^+$ 462.1053 (calcd for $C_{21}H_{22}{}^{35}ClF_3O_6$ 462.1057), 464.1032 (calcd for $C_{21}H_{22}{}^{37}ClF_3O_6$ 464.1028). Anal. Calcd for $C_{21}H_{22}ClF_3O_6$: C, 54.49; H, 4.79; Cl, 7.66; F, 12.31. Found: C, 54.55; H, 4.86; Cl, 7.59; F, 12.02.

3.3.2. Compound **6b**

R_f=0.3 (hexane–ether=4:1); yellow crystals, mp 73–74 °C (hexane–AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.756 (t, *J*=7.1 Hz, 3H), 1.25 (t, *J*=7.1 Hz, 3H), 1.31 (t, *J*=7.1 Hz, 3H), 2.30 (s, 3H), 3.52–3.61 (m, 1H), 3.70–3.78 (m, 1H), 4.12–4.32 (m, 4H), 4.82 (dq, *J*=3.8, 2.2 Hz, 1H), 5.38 (dq, *J*=3.5, 2.7 Hz, 1H), 7.05–7.10 (m, 4H). Selected NOEs are between δ 7.07–7.10 (Ar) and 4.82 (*CH*CO_2Et), 5.38 (*CH*C_6H_4-4-Me). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.39 (CH_3), 13.98 (CH_3), 14.12 (CH_3), 21.17 (CH_3), 50.77 (CH), 53.82 (CH), 58.76 (C), 61.88 (CH_2), 62.28 (CH_2), 62.38 (CH_2), 117.96 (C, q, J_{FC}=41 Hz), 119.88 (C, q, J_{FC}=273 Hz), 128.02 (CH), 129.03 (CH), 132.42 (C, q, J_{FC}=1.5 Hz), 137.83 (C), 142.66 (C, q, J_{FC}=2 Hz), 166.57 (C), 167.44 (C), 167.50 (C). Selected HMBC correlations are between δ 4.82 (*CH*CO_2Et), 5.38 (*CH*C_6H_4-4-Me) and δ 142.66 (*C*=CClCF$_3$) and between δ 4.82 (*CH*CO_2Et), 5.38 (*CH*C_6H_4-4-Me) and δ 58.76 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −65.78 (dd, J_{FH}=2.3, 2.3 Hz); IR (KBr) 2989, 1757, 1735, 1273, 1192, 1132, 1023 cm^{-1}; MS (EI) *m*/*z* 478 (M$^+$, 11), 476 (M$^+$, 28), 432 (66), 430 (86), 402 (95), 329 (100%); HRMS M$^+$ 476.1213 (calcd for $C_{22}H_{24}{}^{35}ClF_3O_6$ 476.1214), 478.1210 (calcd for $C_{22}H_{24}{}^{37}ClF_3O_6$ 478.1184). Anal. Calcd for $C_{22}H_{24}ClF_3O_6$: C, 55.41; H, 5.07. Found: C, 55.39; H, 5.05.

3.3.3. Compound **6f**

R_f=0.3 (hexane–ether=4:1); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.712 (t, *J*=7.1 Hz, 3H), 1.79 (t, *J*=7.6 Hz, 3H), 1.25 (t, *J*=7.1 Hz, 3H), 1.31 (t, *J*=7.1 Hz, 3H), 2.60 (q, *J*=7.6 Hz, 2H), 3.52–3.61 (m, 1H), 3.67–3.75 (m, 1H), 4.12–4.32 (m, 4H), 4.82 (dq, *J*=3.8, 2.2 Hz, 1H), 5.40 (dq, *J*=3.6, 2.7 Hz, 1H), 7.08–7.12 (m, 4H). Selected NOEs are between δ 7.08–7.12 (Ar) and 4.82 (*CH*CO_2Et), 5.40 (*CH*C_6H_4-4-Et). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.32 (CH_3), 13.92 (CH_3), 14.07 (CH_3), 15.63 (CH_3), 28.57 (CH_2), 50.72 (CH), 53.82 (CH), 58.72 (C), 61.84 (CH_2), 62.25 (CH_2), 62.34 (CH_2), 117.91 (C, q, J_{FC}=40 Hz), 119.85 (C, q, J_{FC}=273 Hz), 127.81 (CH), 128.03 (CH), 132.61 (C, q, J_{FC}=1.5 Hz), 142.66 (C, q, J_{FC}=2 Hz), 144.23 (C), 166.53 (C), 167.41 (C), 167.45 (C). Selected HMBC correlations are between δ 4.82 (*CH*CO_2Et), 5.40 (*CH*C_6H_4-4-Et) and δ 142.66 (*C*=CClCF$_3$) and between δ 4.82 (*CH*CO_2Et), 5.40 (*CH*C_6H_4-4-Et) and δ 58.72 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −65.77 (dd, J_{FH}=2.5, 2.5 Hz). ^{19}F/^{1}H HOESY correlations are between δ −65.77 (*CF*$_3$) and δ 5.40 (*CH*C_6H_4-4-Et) and 7.08–7.12 (Ar–*H*). IR (neat) 2982, 1739, 1514, 1369, 1264, 1191, 1145 cm^{-1}; MS (EI) *m*/*z* 492 (M$^+$, 3.4), 490 (M$^+$, 6.6), 444 (27), 416 (42), 371 (49), 343 (100%); HRMS M$^+$ 490.1366 (calcd for $C_{23}H_{26}{}^{35}ClF_3O_6$ 490.1370), 492.1351 (calcd for $C_{23}H_{26}{}^{37}ClF_3O_6$ 492.1341). Anal. Calcd for $C_{23}H_{26}ClF_3O_6$: C, 56.27; H, 5.34. Found: C, 56.32; H, 5.14.

3.3.4. Compound **6g**

R_f=0.2 (hexane–ether=4:1); pale yellow crystals, mp 56–58 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.680 (t, *J*=7.1 Hz, 3H), 1.196 (d, *J*=7.0 Hz, 3H), 1.199 (d, *J*=6.8 Hz, 3H), 1.24 (t, *J*=7.1 Hz,

3H), 1.31 (t, J=7.1 Hz, 3H), 2.86 (septet, J=6.9 Hz, 1H), 3.51–3.59 (m, 1H), 3.64–3.73 (m, 1H), 4.12–4.32 (m, 4H), 4.82 (dq, J=3.7, 2.2 Hz, 1H), 5.39 (dq, J=3.5, 2.7 Hz, 1H), 7.08–7.14 (m, 4H). Selected NOEs are between δ 7.08–7.14 (Ar) and 4.82 (C*H*CO_2Et), 5.39 (C*H*C_6H_4-4-^{i}Pr). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.36 (CH_3), 13.97 (CH_3), 14.12 (CH_3), 23.96 (CH_3), 33.85 (CH), 50.75 (CH), 53.87 (CH), 58.77 (C), 61.87 (CH_2), 62.28 (CH_2), 62.37 (CH_2), 117.98 (C, q, J_{FC}=41 Hz), 119.88 (C, q, J_{FC}=273 Hz), 126.37 (CH), 128.04 (CH), 132.73 (C), 142.62 (C, q, J_{FC}=3 Hz), 148.83 (C), 166.58 (C), 167.47 (C), 167.49 (C). Selected HMBC correlations are between δ 4.82 (C*H*CO_2Et), 5.39 (C*H*C_6H_4-4-^{i}Pr) and δ 142.62 (*C*=CClCF_3) and between δ 4.82 (C*H*CO_2Et), 5.39 (C*H*C_6H_4-4-^{i}Pr) and δ 58.77 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −65.76 (dd, J_{FH}=2.4, 2.4 Hz). ^{19}F/^{1}H HOESY correlations are between δ −65.76 (C*F*$_3$) and δ 5.39 (C*H*C_6H_4-4-^{i}Pr) and 7.08–7.14 (Ar–*H*). IR (KBr) 2964, 1735, 1300, 1261, 1187, 1146 cm^{-1}; MS (EI) m/z 506 (M^+, 20), 504 (M^+, 41), 458 (87), 430 (98), 385 (91), 357 (100%); HRMS M^+ 504.1526 (calcd for $C_{24}H_{28}{}^{35}ClF_3O_6$ 504.1527), 506.1505 (calcd for $C_{24}H_{28}{}^{37}ClF_3O_6$ 506.1497). Anal. Calcd for $C_{24}H_{28}ClF_3O_6$: C, 57.09; H, 5.59. Found: C, 57.14; H, 5.45.

3.3.5. Compound **6h** (including a small amount of impurity)

R_f=0.5 (hexane–ether=1:1); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.799 (t, J=7.1 Hz, 3H), 1.25 (t, J=7.1 Hz, 3H), 1.31 (t, J=7.1 Hz, 3H), 3.57–3.65 (m, 1H), 3.74–3.82 (m, 1H), 4.13–4.32 (m, 4H), 4.80 (dq, J=3.8, 2.2 Hz, 1H), 5.40 (dq, J=3.1, 2.8 Hz, 1H), 7.14 (d-like, J=8.5 Hz, 2H), 7.28 (d-like, J=8.5 Hz, 2H). Selected NOEs are between δ 7.14 (Ar) and 4.80 (C*H*CO_2Et), 5.40 (C*H*C_6H_4-4-Cl). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.48 (CH_3), 13.98 (CH_3), 14.13 (CH_3), 50.78 (CH), 53.33 (CH), 58.62 (C), 62.03 (CH_2), 62.52 (CH_2), 62.55 (CH_2), 118.53 (C, q, J_{FC}=41 Hz), 119.78 (C, q, J_{FC}=273 Hz), 128.62 (CH), 129.53 (CH), 133.96 (C), 134.10 (C), 141.74 (C, q, J=2 Hz), 166.37 (C), 167.29 (2×C). Selected HMBC correlations are between δ 4.80 (C*H*CO_2Et), 5.40 (C*H*C_6H_4-4-Cl) and δ 141.74 (*C*=CClCF_3) and between δ 4.80 (C*H*CO_2Et), 5.40 (C*H*C_6H_4-4-Cl) and δ 58.62 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −65.71 (dd, J_{FH}=2.4, 2.4 Hz). ^{19}F/^{1}H HOESY correlations are between δ −65.71 (C*F*$_3$) and δ 5.40 (C*H*C_6H_4-4-Cl) and 7.14 (Ar–*H*). IR (neat) 2985, 1736, 1493, 1369, 1268, 1192, 1146 cm^{-1}; MS (EI) m/z 498 (M^+, 4), 496 (M^+, 6), 450 (33), 422 (51), 351 (68), 349 (100%); HRMS M^+ 496.0660 (calcd for $C_{21}H_{21}{}^{35}Cl_2F_3O_6$ 496.0667), 498.0629 (calcd for $C_{21}H_{21}{}^{35}Cl^{37}ClF_3O_6$ 498.0638).

3.3.6. Compound **6i**

R_f=0.2 (hexane–ether=3:1); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 0.798 (t, J=7.1 Hz, 3H), 1.25 (t, J=7.1 Hz, 3H), 1.31 (t, J=7.1 Hz, 3H), 3.56–3.64 (m, 1H), 3.74–3.82 (m, 1H), 4.13–4.33 (m, 4H), 4.80 (dq, J=3.8, 2.2 Hz, 1H), 5.41 (dq, J=3.1, 2.6 Hz, 1H), 6.99 (t-like, J=8.8 Hz, 2H), 7.18 (dd-like, J=8.3, 5.2 Hz, 2H). Selected NOEs are between δ 7.18 (Ar) and 4.80 (C*H*CO_2Et), 5.41 (C*H*C_6H_4-4-F). ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 13.51 (CH_3), 13.97 (CH_3), 14.12 (CH_3), 50.74 (CH), 53.27 (CH), 58.68 (C, q, J=1.5 Hz), 61.99 (CH_2), 62.44 (CH_2), 62.50 (CH_2), 115.35 (CH, d, J=21 Hz), 118.43 (C, q, J_{FC}=41 Hz), 119.79 (C, q, J_{FC}=273 Hz), 129.91 (CH, d, J=8 Hz), 131.32 (C, d, J=1.5 Hz), 142.17 (C, q, J=3 Hz), 162.50 (C, d, J=247 Hz), 166.46 (C), 167.35 (2×C). Selected HMBC correlations are between δ 4.80 (C*H*CO_2Et), 5.41 (C*H*C_6H_4-4-F) and δ 142.17 (*C*=CClCF_3) and between δ 4.80 (C*H*CO_2Et), 5.41 (C*H*C_6H_4-4-F) and δ 58.68 (*C*(CO_2Et)$_2$). ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −114.12 (tt, J_{FH}=8.5, 5.2 Hz, 3×F), −65.72 (dd, J_{FH}=2.3, 2.3 Hz, 1×F). ^{19}F/^{1}H HOESY correlations are between δ −65.72 (C*F*$_3$) and δ 5.41 (C*H*C_6H_4-4-F) and 7.18 (Ar) and between δ −114.12 (C*F*$_3$) and δ 6.99 (Ar–*H*). IR (neat) 2985, 1737, 1607, 1511, 1270, 1192, 1146 cm^{-1}; MS (EI) m/z 482 (M^+, 3), 480 (M^+, 6), 434 (34), 406 (45), 361 (35), 333 (100%); HRMS M^+ 480.0961 (calcd for $C_{21}H_{21}{}^{35}ClF_4O_6$ 480.0963), 482.0973 (calcd for $C_{21}H_{21}{}^{37}ClF_4O_6$ 482.0933).

3.4. Reaction of 2a in the presence of $SnCl_4$ (Eq. 4)

To a solution of 4,4,4-trifluoro-1-phenylbut-2-yn-1-ol (**2a**) (300 mg, 1.5 mmol) in CH_2Cl_2 (2.8 mL) was added $SnCl_4$ (391 mg, 0.18 mL, 1.5 mmol). The mixture was stirred at room temperature for 17 h. The reaction mixture was quenched by water and then saturated aqueous $NaHCO_3$. The mixture was extracted with dichloromethane and the organic phase was dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by column chromatography over silica gel with hexane–ether as eluent to give **7** (44 mg, 14%), **8** (49 mg, 15%), and **9** (120 mg, 42%).

3.4.1. Compound **7**

R_f=0.4 (hexane–ether=2:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 5.66 (q, J=3.0 Hz, 1H), 7.40–7.46 (m, 3H), 7.50–7.53 (m, 2H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 47.15 (CH), 77.51 (C, q, J_{FC}=53 Hz), 83.62 (C, q, J_{FC}=6 Hz), 114.01 (C, q, J_{FC}=258 Hz), 127.62 (CH), 129.31 (CH), 129.91 (CH), 135.91 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −51.28 (d, J_{FH}=3.1 Hz); IR (neat) 2265, 1457, 1284, 1264 cm^{-1}; MS (EI) m/z 220 (M^+, 9), 218 (M^+, 27), 183 (100%); HRMS M^+ 218.0102 (calcd for $C_{10}H_6{}^{35}ClF_3$ 218.0110), 220.0056 (calcd for $C_{10}H_6{}^{37}ClF_3$ 220.0082).

3.4.2. Compound **8**

R_f=0.3 (hexane–ether=2:1); pale yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 6.93 (q, J=2.7 Hz, 1H), 7.34–7.43 (m, 5H); ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 97.98 (C, q, J_{FC}=45 Hz), 108.54 (CH), 120.25 (C, q, J_{FC}=273 Hz), 128.62 (CH), 129.26 (CH), 129.83 (C), 130.06 (CH), 201.73 (C, q, J_{FC}=2.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −66.68 (d, J_{FH}=3.1 Hz); IR (neat) 1963, 1460, 1400, 1270, 1131 cm^{-1}; MS (EI) m/z 220 (M^+, 13), 218 (M^+, 53), 183 (100%); HRMS M^+ 218.0108 (calcd for $C_{10}H_6{}^{35}ClF_3$ 218.0110), 220.0085 (calcd for $C_{10}H_6{}^{37}ClF_3$ 220.0082).

3.4.3. Compound **9**

R_f=0.2 (hexane–ether=2:1); colorless crystals, mp 52–55 °C (hexane); ^{1}H NMR (400 MHz, $CDCl_3$) obtained as 1:1 diastereomer mixture, δ (ppm) 5.31 (q, J=2.9 Hz, 1×0.5H), 5.54 (q, J=2.7 Hz, 1×0.5H), 7.39–7.49 (m, 5H). Recrystallization from hexane changed the diastereomer ratio from 1:1 to 1.5:1. ^{13}C NMR (100.6 MHz, $CDCl_3$) δ (ppm) 69.10 (CH), 69.42 (CH), 75.01 (C, q, J_{FC}=53 Hz), 75.31 (C, q, J_{FC}=53 Hz), 83.97 (C, q, J_{FC}=6 Hz), 84.07 (C, q, J_{FC}=6 Hz), 113.97 (C, q, J_{FC}=258 Hz), 127.69 (CH), 127.83 (CH), 129.09 (CH), 129.23 (CH), 129.73 (CH), 129.92 (CH), 134.94 (C), 135.04 (C); ^{19}F NMR (376 MHz, $CDCl_3$) δ (ppm) −51.02 (d, J_{FH}=3.1 Hz), −51.11 (d, J_{FH}=3.1 Hz); IR (KBr) 2265, 1282, 1144 cm^{-1}; MS (EI) m/z 382 (M^+, 2), 304 (5), 183 (100%); HRMS M^+ 382.0793 (calcd for $C_{20}H_{12}F_6O$ 382.0792). Anal. Calcd for $C_{20}H_{12}F_6O$: C, 62.83; H, 3.16. Found: C, 62.71; H, 3.24.

Acknowledgements

This work was supported by the Ministry of Education, Culture, Sports, Science, and Technology of the Japanese Government. We thank Mr. T. Matsuda and Mr. Y. Fukushima (Nara University of Education) for experimental help. We thank Nara Institute of Science and Technology (NAIST) and Prof. K. Kakiuchi (NAIST) for mass spectra. We also thank to Prof. S. Umetani (Kyoto University) for elemental analyses.

Supplementary data

Crystallographic data and ^{1}H and ^{13}C NMR data. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2009.01.024.

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9. Crystallographic data for **6a** have been deposited with the Cambridge Crystallographic Data Centre (no. CCDC 698776). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).
10. The stereochemistry of **6b**, **6f–i** was assigned by NOESY and $^{19}F/^{1}H$ HOESY (for **6f–i**) spectra, along with similarity to **6a** in the NMR spectra.
11. The alkyl groups (R′=Me, Et, ^{i}Pr) in **2b**,**f**,**g** may stabilize the cationic intermediate **A** (in Scheme 1) for the [2+2] cycloaddition as electron-donating groups. On the other hand, $SnCl_4$ possibly coordinates to OMe and Br groups (**2d**, **2c**) and causes side reactions. However, at this stage it is difficult to discuss on the electronic effects of substituents. Study on the detailed reaction mechanism is under investigation.
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