Reactions of β-alkoxyvinyl trifluoromethyl ketones with terminal alkynes — Reagent-controlled regioselectivity addition reactions

Shizheng Zhu, Guifang Jin, and Huiling Jiang

Abstract: Reactions of β-alkoxyvinyl trifluoromethyl ketones ROCH=CHCOCF$_3$ (**1**, R = Et, Me$_2$CHCH$_2$), and their cyclic analogues 4-trifluoroacetyl-2,3-dihydrofuran (**2a**) and 5-trifluoroacetyl-3,4-dihydro-2*H*-pyran (**2b**), with terminal alkynes R-C≡CH (**3**, R = Ph, PhCH$_2$, HOCH$_2$, C$_5$H$_{11}$) mainly gave the 1,2-addition products (carbonyl alkynylation) in the presence of *n*-BuLi. However, promoted by ZnCl$_2$–Et$_3$N, the reaction of **1** or **2** with equivalent alkyne predominately provided 1,4-addition products.

Key words: β-alkoxyvinyl trifluoromethyl ketones, alkynes, 1,2-addition, 1,4-addition, catalysts.

Résumé : En présence de butyl lithium, les réactions des β-alcoxyvinyl trifluorométhyl cétones de formule générale ROCH=CHCOCF$_3$ (**1**; R = Et, Me$_2$CHCH$_2$) et de leurs analogues cycliques, tels le 4-trifluoroacétyl-2,3-dihydrofurane (**2a**) et le 5-trifluoroacétyl-3,4-dihydro-2*H*-pyrane (**2b**) avec des alcynes vrais de formule générale R-C≡CH (**3**; R = Ph, PhCH$_2$, HOCH$_2$, C$_5$H$_{11}$) conduisent principalement à des produits d'additions 1,2 (alcynylation du carbonyle). Toutefois, lorsque la réaction est catalysée par du ZnCl$_2$ en présence de Et$_3$N, les réactions des composés **1** et **2** avec un équivalent d'alcyne conduisent principalement aux produits d'additions 1,4.

Mots clés : β-alcoxyvinyl trifluorométhyl cétones, alcynes, addition 1,2, addition 1,4, catalyseurs.

[Traduit par la Rédaction]

Introduction

The present strongly developed interest in organofluorine chemistry has led to considerable studies of trifluoromethyl ketones (1) and, in particular, α,β-unsaturated trifluoromethyl ketones (2). Such ketones have been used as intermediates in heterocyclic synthesis (3) and have also been viewed as synthetic targets owing to their possible pharmacological interest (4). β-Alkoxylvinyl trifluoromethyl ketones (ROCH=CHCOCF$_3$, **1**) are potential fluorinated 1,3-dicarbonyl compounds. Since they were first prepared in 1967 (5), their preparations and chemical transformations have been extensively investigated (6). Our group and others have studied the reactions of acyclic β-alkylvinyl trifluoromethyl ketones with Grignard reagents derivated from alkyl and aryl halides. Generally, acyclic β-alkoxyvinyl trifluoromethyl ketones and the cyclic analogues **2a** and **2b** reacted with Grignard reagents gave the corresponding α,β-unsaturated trifluoromethyl ketone as the sole product, which arose from 1,4-addition on the β-position of the double bond and was followed by β-elimination of alkoxyl group (7). In contrast, the organic zinc compounds prepared in situ reacted with β-alkoxyvinyl trifluoromethyl ketones giving only the 1,2-addition products (Scheme 1) (6*d*, 8).

The factors determining the selectivity between 1,2- and 1,4-additions to a wide range of α,β-unsaturated carbonyl compounds have received much attention and, in particular, asymmetric conjugate additions have been developed (9). The hard acid – soft base concepts have been used to permit the generalizations that among organometallic reagents, organolithiums, which are hard nucleophiles, react by 1,2-addition, and organocopper reagents, which are softer ones, react by 1,4-addition (10). Grignard reagents were seen to lie somewhere between them. Since then there have been major advances in explaining the selectivity of these additions. In reactions that proceed by kinetic control with organometallic reagents having a highly localized negative charge, a charge-controlled 1,2-addition can be expected. In contrast, in additions of nucleophiles having charge dislocalization where the reaction is frontier orbital controlled, a 1,4-addition is expected. However, other factors, notably steric and solvent effects and the nature of the nucleophile, disturb these simple generalizations.

During our continuous study on the fluorinated push–pull

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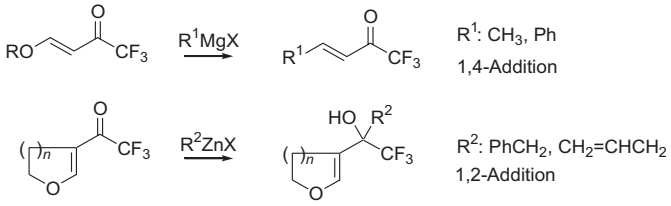
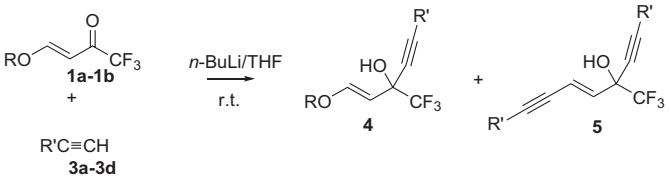
Scheme 1.



Scheme 2.



R: C_2H_5 (a); $CH_2CH(CH_3)_2$ (b); R': Ph (a); $PhCH_2$ (b); $HOCH_2$ (c); C_5H_{11} (d)

ethylene compounds (11), we investigated the alkynylation of β-substituted unsaturated trifluoromethyl ketones **1** and **2** with terminal alkynes in detail. We found that the reaction products mainly depend on the promoted reagents. *n*-Butyl lithium promoted addition reactions gave 1,2-addition products, a process favored by charge control. $ZnCl_2$–Et_3N promoted addition reactions provided 1,4-addition products, a process favored by orbital control. Herein we report these results.

Results and discussion

Reaction of β-alkoxyvinyl trifluoromethyl ketone **1a** with PhC≡CH **3a** proceeded smoothly at room temperature in the presence of 1 equiv. of *n*-BuLi in THF and finished in 2 h (monitored by TLC). Flash chromatographic purification on silica gel (*n*-hexane – ethyl acetate) gave two products, 1-ethoxy-5-phenyl-3-trifluoromethyl-1penten-4-yne-3-ol (**4a**, 41%) and 1,7-diphenyl-3-trifluoromethyl-4-heptene-1,6-diyn-3-ol (**5a**, 20%), which is an over addition product. When 2 equiv. of *n*-BuLi and **3a** were used, the yield of **5a** increased to 52% (See Scheme 2, Table 1).

The proton NMR spectra of **4a** and **5a** showed that both of them are *trans*-alkenes. The coupling constants between the two alkene's protons were 13 Hz in **4a** and 15 Hz in **5a**, and the chemical shifts of the two alkene's protons in **4a** were 7.12 and 5.00 ppm owing to the presence of the ethoxyl group on the double bond; while in compound **5a** they were 6.56 and 6.31 ppm. Under the same reaction conditions, the reaction of β-isobutoxyvinyl trifluoromethyl ketone (**1b**) with **3a** gave the same results as **1a**.

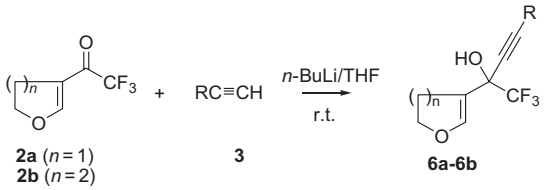
Interestingly, terminal alkynes **3b**–**3d** reacted with **1** affording only 1,2-addition products. No further addition products were detected or isolated even when excessive equivalents of alkynes **3** and *n*-BuLi were used or by prolonging the reaction time to 24 h. When reacted with ketones **1a** and **1b**, the terminal alkynes **3** have excellent regioselectivity except for **3a**. The selectivity could be explained by the structures of the nucleophiles. The phenylacetylene ion is charge delocalized owing to its conjugation structure, therefore, it gave both 1,2-addition and 1,4-addition products. The alkynes **3b**–**3d** only gave 1,2-addition products because their ions have highly localized negative charges without conjugation structures.

Table 1. Reactions of β-alkoxyvinyl trifluoromethyl ketone with alkynes promoted by *n*-BuLi.

Entry	Reactants	Mol. ratio	Time (h)	Products and yields (%)[a]
1	**1a**, **3a**	1:1	2	**4a** (41), **5a** (20)
2	**1a**, **3a**	1:2	2	**4a** (18), **5a** (52)
3	**1b**, **3a**	1:1	2	**4b** (39), **5a** (28)
4	**1b**, **3a**	1:2	2	**4b** (23), **5a** (59)
5	**1a**, **3b**	1:1	4	**4c** (68)
6	**1b**, **3b**	1:1	4	**4d** (65)
7	**1a**, **3c**	1:1	24	**4e** (64)
8	**1b**, **3c**	1:1	24	**4f** (61)
9	**1b**, **3d**	1:1	24	**4g** (67)
10	**2a**, **3a**	1:1	4	**6a** (81)
11	**2a**, **3a**	1:2	4	**6a** (84)
12	**2b**, **3a**	1:1	4	**6b** (81)

[a]The yields are calculated on the ketones.

Scheme 3.



R: Ph (a); $PhCH_2$ (b); $HOCH_2$ (c); C_5H_{11} (d)

In contrast, the cyclic analogues, 4-trifluoroacetyl-2,3-dihydrofuran (**2a**) and 5-trifluoro-3,4-dihydro-2*H*-pyran (**2b**) are less reactive. In the presence of *n*-BuLi, the reactions between **2** and **3a** needed a longer time period (typical 4 h) and only 1,2-addition products **6a** and **6b** were obtained in good yields (Scheme 3). With 2 equiv. of **3a** and *n*-BuLi, no further reaction product was observed. These results indicated the considerable difference between the phenylacetylene lithium reagent and the Grignard reagents that gave exclusively the 1,4-addition products, carbon–carbon double bond attacking products (7, 8).

Recently, considerable progress has been developed in the alkynylation of carbonyl compounds using Lewis acids in combination with bases (12). For example, Jiang and Si (13) prepared a series of propargylic alcohols by treatment of the aromatic aldehydes with terminal alkynes promoted by zinc chloride and triethyl amine. In the subsequent studies on the alkynylation of the β-substituted unsaturated trifluoromethyl ketones **1** and **2**, we also used the $ZnCl_2$–Et_3N system as the promotor. Thus, a mixture of **3a** (1.5 mmol), anhydr. $ZnCl_2$ (2.25 mmol), and Et_3N (2.25 mmol) in toluene was stirred at room temperature for 1 h, then **1a** (1.5 mmol) in 10 mL THF was added. After it was stirred overnight, TLC analysis showed that the reaction was finished, and chromatography purification gave the ketone **7a** (14) in 81% yield. When 2 equiv. of **3a** was used, this reaction gave two products, **7a** (58%) and the double-alkylated product **5a** (25%) (Scheme 4).

Under the same reaction conditions, the reaction of equivalent **3a** to **2a** afforded product **8a** (53%) (Table 2). How-

Scheme 4.

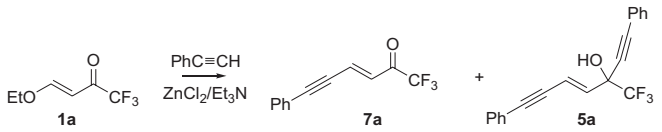


Table 2. Reactions of β-alkoxyvinyl trifluoromethyl ketone with alkynes promoted by $ZnCl_2$–Et_3N.

Entry	Reactants	Mol. ratio	Time (h)	Products and yields (%)[a]
1	**1a**, **3a**	1:1	24	**7a** (81)
2	**1a**, **3a**	1:2	24	**7a** (58), **5a** (25)
3	**2a**, **3a**	1:1	24[b]	**8a** (53), **9a** (7)
4	**2a**, **3b**	1:1	24[b]	No reaction
5	**2b**, **3a**	1:1	36	**8b** (44)

[a]The yields are calculated on the ketones.
[b]The reactions were carried out at 80 °C, the other reactions were at room temperature.

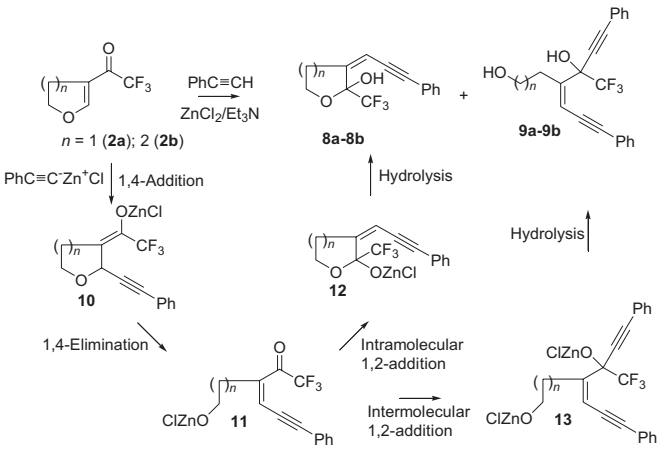
ever, for the reaction of **2b** with **3a**, the alkynylation only occurred at the double bond carbon atom giving the product **8b**. The final product was obtained from a rearrangement of 1,4-addition intermediate **10**, followed by an 1,4-elimination of the alkoxyl group to produce intermediate **11**, then an intramolecular 1,2-addition occurred and gave the final stable product (Scheme 5). The driving force for the rearrangement might be the conjugation of the double bond with the triple bond. Since the intermediate **11** has a ketone functional group, the intermolecular 1,2-addition gave the double addition intermediate **13**, which was hydrolyzed and produced product **9**. It is noteworthy that five-membered **2a** produced two addition products **8a** and **9a**, while six-membered ketone **2b** only afforded **8b**. This difference is aroused from the intermediate **11**. When n = 1 (**2a**), the ethoxyl **11a** is not as flexible as the propoxyl chain **11b** (n = 2, **2b**). Therefore, **11b** can occur through an intramolecular 1,2-addition reaction exclusively, and **11a** can proceed to both intra- and inter-molecular 1,2-addition reactions. Unfortunately, the ketones did not react with 3-phenylpropyne (**3b**) under several different reaction conditions, even at high temperature. The possible reason is that 3-phenylpropyne is not as active as phenylacetylene and $ZnCl_2$–Et_3N could not promote the addition reaction.

In summary, we have studied the reaction and regioselectivity of terminal alkyne addition to β-alkoxyvinyl trifluoromethyl ketone, which is very sensitive to the promoted reagents and ketone structure. Promoted by n-BuLi, the addition of terminal alkynes gave 1,2-addition products in high yields, in marked contrast to the 1,4-additions promoted by $ZnCl_2$–Et_3N. The high regioselectivity and its tenability of the terminal alkynes to enones and the accessibility of fluorine-contained adducts may be useful in the application of these reactive compounds for the effective synthesis of bioactive fluorine-containing substances.

Experimental

Solvents were purified and dried before use. Melting points were determined on a Mel-Temp apparatus and are

Scheme 5.



uncorrected. ^{1}H NMR and ^{19}F NMR spectra were recorded on Varian-360 or Bruker AM-300 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as internal and external standards, respectively; NMR spectra were recorded in chloroform-*d* unless otherwise stated. IR spectra were obtained with a PerkinElmer 983G spectrophotometer using KBr disks of the compound. Low- and high-resolution mass spectra were obtained on HP 5989a and Finnigan MAT instruments, respectively. This institute performed the elemental analyses.

General procedure for the reaction of the alkyne with ketone in the presence of *n*-BuLi

A solution of n-butyl lithium – THF (3 mL, 4.8 mmol) and 10 mL THF was added dropwise to a 50 mL three-necked flask containing phenylacetylene (0.49 g, 4.8 mmol) in 15 mL THF, after stirring at room temperature for 15 min, β-alkoxylvinyl trifluoromethyl ketone (**1a**) (0.806 g, 4.8 mmol) in 10 mL THF was added. The solution was stirred for 2 h and TLC analysis showed the reaction was completed, and then 40 mL of a satd. NH_4Cl solution was added and extracted with ether (3 × 20 mL). The organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated in vacuum. The residue was purified by flash chromatography by using n-hexane–EtOAc as eluent to give two products, **4a** (26%) and **5a** (51%).

1-Ethoxy-5-phenyl-3-trifluoromethyl-1-penten-4-yn-3-ol (4a)

Yield: 41%. FT-IR (KBr, cm^{-1}) ν: 3423 (s), 2984 (w), 2239 (s), 1655 (s), 1491 (s), 1189 (vs). ^{1}H NMR ($CDCl_3$) δ: 7.43 (m, 5H, Ph), 7.12 (d, 1H, J = 12.6 Hz, CH), 5.00 (d, 1H, J = 12.6 Hz, CH), 3.84 (q, J = 7.5 Hz, 2H, OCH_2), 2.90 (s, 1H, OH), 1.32 (t, J = 7.5 Hz, 3H, CH_3). ^{19}F NMR ($CDCl_3$): –81.73 (s, CF_3). MS (70 eV) m/z (%): 270 (M^+, 7.13), 241 (M^+ – Et, 14.11), 225 (M^+ – OEt, 2.72), 201 (M^+ – CF_3, 100.00), 173 (M^+ – CF_3CO, 37.16), 102 (PhC≡CH, 8.40), 77 (Ph^+, 14.85). HR-MS (EI) M^+ calcd. for $C_{14}H_{13}F_3O_2$: 270.0893; found: 270.0865.

1-Isobutoxy-5-phenyl-3-trifluoromethyl-1-penten-4-yn-3-ol (4b)

Yield: 39%. FT-IR (KBr, cm^{-1}) ν: 3423 (s), 2961 (s), 2235 (s), 1651 (w), 1491 (m), 1191 (vs). ^{1}H NMR ($CDCl_3$) δ: 7.51 (m, 5H, Ph), 7.18 (d, 1H, J = 12.6 Hz, CH), 5.01 (d,

1H, J = 12.6 Hz, CH), 3.55 (d, J = 6.6 Hz, 2H, OCH_2), 2.82 (s, 1H, OH), 2.04 (m, 1H, $CH(CH_3)_2$), 0.98 (d, J = 6.9 Hz, 6H, $2CH_3$). ^{19}F NMR ($CDCl_3$): –81.99 (s, CF_3). MS (70 eV) *m/z* (%): 299 (M^+H, 0.41), 298 (M^+, 2.11), 229 ($M^+ - CF_3$, 45.04), 173 ($M^+ - CF_3 - {}^+CHCH(CH_3)_2$), 100.00), 102 (Ph≡CH, 12.11), 77 (Ph^+, 7.08). HRMS (EI) M^+ calcd. for $C_{16}H_{17}F_3O_2$: 298.1186; found: 298.1181.

1-Ethoxy-6-phenyl-3-trifluoromethyl-1-hexen-4-yn-3-ol (4c)

Yield: 68%. FT-IR (KBr, cm^{-1}) ν: 3423 (s), 2983 (s), 2237 (m), 1656 (s), 1183 (vs). ^1H NMR ($CDCl_3$) δ: 7.35 (m, 5H, Ph), 7.03 (d, 1H, J = 12.6 Hz, CH), 4.96 (d, 1H, J = 12.6 Hz, CH), 3.81 (q, J = 6.9 Hz, 2H, OCH_2), 3.78 (s, 2H, Ph*C*H_2), 2.81 (s, 1H, OH), 1.31 (t, J = 6.9 Hz, 3H, CH_3). ^{19}F NMR ($CDCl_3$): –82.21 (s, CF_3). MS (70 eV) *m/z* (%): 284 (M^+, 0.97), 267 ($M^+H - H_2O$, 22.38), 215 ($M^+ - CF_3$, 100.00), 187 ($M^+ - CF_3CO$, 10.43), 115 ($PhCH_2C{\equiv}C^+$, 24.41), 91 ($PhCH_2^+$, 16.55), 77 (Ph^+, 5.62). Anal. calcd. for $C_{15}H_{15}O_2F_3$ (%): C 63.38, H 5.28; found: C 63.63, H 5.55.

1-Isobutoxy-6-phenyl-3-trifluoromethyl-1-hexen-4-yn-3-ol (4d)

Yield: 65%. FT-IR (KBr, cm^{-1}) ν: 3427 (s), 2962 (s), 2240 (m), 1672 (s), 1655 (vs), 1181 (vs). ^1H NMR ($CDCl_3$) δ: 7.36 (m, 5H, Ph), 7.07 (d, 1H, J = 12.6 Hz, CH), 4.95 (d, 1H, J = 12.6 Hz, CH), 3.73 (s, 2H, $PhCH_2$), 3.51 (d, J = 6.6 Hz, 2H, OCH_2), 2.75 (s, 1H, OH), 1.96 (m, 1H, $CH(CH_3)_2$), 0.96 (d, J = 7.2 Hz, 6H, $2CH_3$). ^{19}F NMR ($CDCl_3$): –82.20 (s, CF_3). MS (70 eV) *m/z* (%): 312 (M^+, 1.84), 243 ($M^+ - CF_3$, 100.00), 187 ($M^+ - CF_3 - {}^+CHCH(CH_3)_2$), 85.68), 115 ($PhCH_2C{\equiv}C^+$, 24.83), 91 ($PhCH_2^+$, 19.01), 77 ($Ph^+$, 5.62), 57 ($CH_2CH(CH_3)_2$, 61.2). Anal. calcd. for $C_{17}H_{19}O_2F_3$ (%): C 65.38, H 6.09; found: C 64.99, H 6.48.

6-Ethoxy-4-trifluoromethyl-5-hexen-2-yn-1,4-diol (4e)

Yield: 64%. FT-IR (KBr, cm^{-1}) ν: 3392 (vs), 2983 (s), 2235 (m), 1727 (s), 1186 (vs). ^1H NMR ($CDCl_3$) δ: 7.00 (d, J = 12.6 Hz, 1H, CH), 4.92 (d, J = 12.6 Hz, 1H, CH), 4.36 (s, 2H, CH_2), 3.82 (q, J = 6.9 Hz, 2H, OCH_2), 3.10 (m, 1H, OH), 2.19 (m, 1H, OH), 1.31 (t, J = 6.9 Hz, 3H, CH_3). ^{19}F NMR ($CDCl_3$): –81.82 (s, CF_3). MS (70 eV) *m/z* (%): 225 (M^+H, 1.81), 224 (M^+, 0.83), 207 ($M^+H - H_2O$, 46.76), 179 ($M^+ -$ OEt, 6.89), 155 ($M^+ - CF_3$, 100.00), 109 ($M^+ - CF_3 -$ HOEt, 49.74), 69 (CF_3^+, 17.44). Anal. calcd. for $C_9H_{11}O_3F_3$ (%): C 48.21, H 4.91; found: C 48.51, H 5.23.

6-Isobutoxy-4-trifluoromethyl-5-hexen-2-yn-1,4-diol (4f)

Yield: 61%. FT-IR (KBr, cm^{-1}) ν: 3398 (vs), 2963 (s), 2234 (m), 1727 (s), 1653 (s), 1194 (vs). ^1H NMR ($CDCl_3$) δ: 7.01 (d, J = 12.6 Hz, 1H, =*CH*), 4.93 (d, J = 12.6 Hz, 1H, =*CH*), 4.51 (d, J = 6.6 Hz, 2H, OCH_2), 4.35 (s, 2H, CH_2), 2.19 (s, 2H, 2OH), 2.01 (m, 1H, C*H*$(CH_3)_2$), 0.95 (d, J = 6.6 Hz, 6H, CH_3). ^{19}F NMR ($CDCl_3$): –82.08 (s, CF_3). MS (70 eV) *m/z* (%): 252 (M^+, 3.17), 234 ($M^+ - H_2O$, 1.75), 183 ($M^+ - CF_3$, 76.91), 127 ($M^+ - CF_3 -$ CH≡CCH_2OH, 100.00), 109 ($M^+ - CF_3 - H_2O -$ CH≡CCH_2OH, 47.73), 69 (CF_3, 12.71), 57 ($CH_2CH(CH_3)_2$, 96.42). HR-MS (EI) M^+ calcd. for $C_{11}H_{15}F_3O_3$: 252.0979; found: 252.0973.

1,7-Diphenyl-3-trifluoromethyl-4-heptene-1,6-diyn-3-ol (5a)

Yield: 20%. FT-IR (KBr, cm^{-1}) ν: 3404 (s), 2976 (m), 2236 (s), 1655 (m), 1491 (vs), 1191 (vs). ^1H NMR ($CDCl_3$) δ: 7.40 (m, 10H, 2Ph), 6.56 (d, 1H, J = 15.6 Hz, CH), 6.31 (d, 1H, J = 15.6 Hz, CH), 3.01 (s, 1H, OH). ^{13}C NMR (75.3 MHz, $CDCl_3$) δ_C: 134.7 (C-4), 132.1, 132.0, 129.7, 128.9, 128.8, 128.5 (ArC), 122.7 (q, $^1J_{C\text{-}F}$ = 280 Hz, CF_3), 122.7 (ArC-1), 120.7 (ArC-1), 116.3 (C-5), 93.7 (C-7), 89.0 (C-2), 86.0 (C-1), 81.8 (C-6), 71.9 (q, ^1J = 48 Hz, C-3). ^{19}F NMR ($CDCl_3$): –80.48 (s, CF_3). MS (70 eV) *m/z* (%): 326 (M^+, 15.73), 257 ($M^+ - CF_3$, 100.00), 226 ($M^+H -$ PhC≡C^+, 20.70), 127 (PhC≡$CCH{=}CH^+$, 14.24), 101 (PhC≡C^+, 10.57), 77 (Ph^+, 14.85). HR-MS (EI) M^+ calcd. for $C_{20}H_{13}F_3O$: 326.0895; found: 326.0919.

2-(4,5-Dihydrofuran-3-yl)-1,1,1-trifluoro-4-phenyl-3-butyn-2-ol (6a)

Yield: 81%. FT-IR (KBr, cm^{-1}) ν: 3407 (s), 2971 (m), 2234 (s), 1656 (s), 1490 (s), 1173 (vs). ^1H NMR ($CDCl_3$) δ: 7.40 (m, 5H, Ph), 6.76 (s, 1H, CH), 4.50 (m, 2H, OCH_2), 3.35 (s, 1H, OH), 2.83 (m, 2H, C*H*$_2$). ^{19}F NMR ($CDCl_3$): –79.52 (s, CF_3). MS (70 eV) *m/z* (%): 268 (M^+, 8.56), 251 ($M^+ -$ OH, 10.52), 199 ($M^+ - CF_3$, 100.00), 97 ($M^+ - CF_3 -$ PhC≡C^+, 38.99). Anal. calcd. for $C_{14}H_{11}O_2F_3$ (%): C 62.69, H 4.10; found: C 62.92, H 4.22.

*2-(5,6-Dihydro-4**H**-pyran-3-yl)-1,1,1-trifluoro-4-phenyl-3-butyn-2-ol (6b)*

Yield: 81%. FT-IR (KBr, cm^{-1}) ν: 3412 (s), 2955 (m), 2232 (s), 1658 (s), 1491 (s), 1167 (vs). ^1H NMR ($CDCl_3$) δ: 7.41 (m, 5H, Ph), 7.08 (s, 1H, CH), 4.04 (m, 2H, OCH_2), 2.97 (s, 1H, OH), 2.27 (m, 2H, CH=C-C*H*$_2$), 1.90 (m, 2H, CH_2). ^{19}F NMR ($CDCl_3$): –79.24 (s, CF_3). MS (70 eV) *m/z* (%): 282 (M^+, 6.91), 213 ($M^+ - CF_3$, 100.00), 111 ($M^+ - CF_3 -$ PhC≡CH, 5.67), 83 ($OCH_2CH_2CH_2C{=}CH^+$, 8.40), 77 (Ph^+, 10.85). HR-MS (EI) M^+ calcd. for $C_{15}H_{13}F_3O_2$: 282.0893; found: 282.0868.

General procedure for the reaction of acetylene with ketone in the presence of $ZnCl_2$–Et_3N

Phenylacetylene (0.153 g, 1.5 mmol) was added under an argon atmosphere at room temperature to a solution of anhydr. $ZnCl_2$ (0.306 g, 2.25 mmol) and triethylamine (0.32 mL, 2.25 mmol) in dried toluene (10 mL). After stirring for 1 h, β-alkoxylvinyl trifluoromethyl ketone (0.252 g, 1.5 mmol) was added dropwise. The mixture was stirred overnight and TLC analysis confirmed that the reaction was finished, then the mixture was washed with 40 mL of a satd. NH_4Cl solution, followed by extraction with ether (3 × 20 mL). The organic layer was washed with brine (30 mL), dried over Na_2SO_4, and concentrated in vacuum to give a residue, which was purified by flash chromatography by using *n*-hexane–EtOAc as eluent to give the product.

1,1,1-Trifluoro-6-phenyl-hex-3-en-5-yn-2-one (7a)

Yellow liquid; yield: 58%–81%. FT-IR (KBr, cm^{-1}) ν: 2195 (s), 1722 (s), 1602 (s), 1582 (s), 1205 (s), 1148 (s). ^1H NMR ($CDCl_3$) δ: 7.42 (m, 5H, Ph), 7.25 (d, J = 15.3 Hz, 1H, $CF_3COCH{=}$), 6.85 (d, J = 15.0 Hz, 1H, C*H*=C). ^{19}F NMR ($CDCl_3$): –77.80 (s, CF_3). MS (70 eV) *m/z* (%): 224 (M^+, 90.95), 155 ($M^+ - CF_3$, 100.00), 127 ($M^+ - COCF_3$,

66.73), 77 (Ph^+, 14.43). Anal. calcd. for $C_{12}H_7OF_3$ (%): C 64.29, H 3.15; found: C 64.29, H 3.16.

3-(3-Phenylprop-2-ynylidene)-2-hydroxy-2-(trifluoromethyl)tetrahydrofuran (8a)

White solid; mp 72–74 °C; yield: 53%. FT-IR (KBr, cm^{-1}) ν: 3361 (s), 2913 (s), 2200 (m), 1650 (s), 1193 (vs). ^1H NMR ($CDCl_3$) δ: 7.40 (m, 5H, Ph), 6.18 (s, 1H, CH), 4.19 (m, 2H, OCH_2), 3.07 (m, 2H, CH_2), 2.95 (m, 1H, OH). ^{13}C NMR (75.3 MHz, $CDCl_3$) δ_C: 132.2 (*C*=CH), 131.6 (ArC-4), 128.9 (ArC-3, ArC-5), 128.2 (ArC-2), 122.3 (ArC-1), 122.6 (q, $^1J_{C\text{-}F}$ = 280 Hz, CF_3), 109.4 (C=*C*H), 100.7 (*C*-CF_3), 97.1 (C=CH-*C*≡C), 88.3(C=CH-C≡*C*), 68.3 (OCH_2), 31.3 (CH_2). ^{19}F NMR ($CDCl_3$): –83.53 (s, CF_3). MS (70 eV) *m*/*z* (%): 268 (M^+, 27.41), 251 (M^+ – OH, 3.01), 199 (M^+ – CF_3, 100.00), 181 (M^+ – CF_3 – H_2O, 3.03), 91 (PhC≡C^+, 5.45), 77 (Ph^+, 19.36). HR-MS (EI) M^+ calcd. for $C_{14}H_{11}F_3O_2$: 268.0692; found: 268.0711.

3-(3-Phenylprop-2-ynylidene)-2-hydroxyl-2-(trifluoromethyl)tetrahydropyran (8b)

White solid; mp: 56–58 °C; yield: 44%. FT-IR (KBr, cm^{-1}) ν: 3397 (s), 2999 (m), 2204 (m), 1658 (m), 1443 (s), 1185 (vs). ^1H NMR ($CDCl_3$) δ: 7.48 (m, 5H, Ph), 6.24 (s, 1H, CH), 3.98 (dd, *J* = 4.8, 7.5 Hz, 2H, OCH_2), 3.14 (s, 1H, OH), 3.04 (m, 1H, CH_2), 2.60 (m, 1H, CH_2), 2.03 (m, 1H, CH_2), 1.85 (m, 1H, CH_2). ^{19}F NMR ($CDCl_3$): –82.43 (s, CF_3). MS (70 eV) *m*/*z* (%): 282 (M^+, 19.72), 213 (M^+ – CF_3, 100.00), 195 (M^+ – CF_3 – OH, 3.10), 185 (M^+ – $COCF_3$, 30.70), 77 (Ph^+, 10.47). Anal. calcd. for $C_{15}H_{13}O_2F_3$ (%): C 63.83, H 4.61; found: C 64.09, H 4.67.

4-(2-Hydroxyethyl)-1,8-diphenyl-3-trifluoromethyl-4-heptene-1,6-diyn-3-ol (9)

Yield: 7%. FT-IR (KBr, cm^{-1}) ν: 3317 (s), 2233 (m), 1640 (m), 1491 (s), 1444 (m), 1186 (vs). ^1H NMR ($CDCl_3$) δ: 7.52–7.31 (m, 10H, 2Ph), 7.30 (m, 1H, CH), 5.18 (d, *J* = 6 Hz, 1H, CH), 4.07 (m, 2H, OCH_2), 3.32 (s, 1H, OH), 3.09 (d-q, *J* = 6.3, 8.4 Hz, 1H, OH), 2.25 (m, 2H, CH_2). ^{13}C NMR (75.3 MHz, $CDCl_3$) δ_C: 132.1 (C-4), 131.9, 129.7, 128.5, 128.2, 128.2, 125.7 (ArC), 125.1 (q, $^1J_{C\text{-}F}$ = 280 Hz, CF_3), 123.2 (C-5), 88.9 (C-7), 88.4 (C-1), 85.5 (C-6), 81.6 (C-2), 73.9 (C-3), 70.3 (*C*H_2OH), 51.6 (CH_2). ^{19}F NMR ($CDCl_3$): –79.34 (s, CF_3). MS (70 eV) *m*/*z* (%): 370 (M^+, 19.72), 301 (M^+ – CF_3, 100.00), 284 (M^+ – CF_3 – OH, 3.10), 269 (M^+ – PhC≡C^+, 30.70), 77 (Ph^+, 10.47). Anal. calcd. for $C_{22}H_{17}O_2F_3$ (%): C 71.35, H 4.59; found: C 71.21, H 4.69.

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