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Synthesis of novel 2-trifluoromethyl-1-methylene-3-phenylindene derivatives via carbocyclization reaction of 2-trifluoromethyl-1,1-diphenyl-1,3-enynes

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ABSTRACT

Trifluoromethylated enynyl sulfones **3** were reacted with PhLi at −78 °C for 2–4 h to give 2-trifluoromethyl-1,1-diphenyl-1,3-enynes **6** in good yields. Carbocyclization reaction of **6** with 10 mol% of $Pd(OAc)_2$ in cosolvent of CF_3COOH and MC (4:1) at room temperature for 1 h afforded 2-trifluoromethyl-1-methylene-3-phenylindene derivatives **7** in good yields.

1. Introduction

The indene ring system has been found as an important framework in many drug candidates possessing interesting biological activities [1–5]. Numerous methods for the synthesis of this family of compounds have been well documented in the previous literatures [6–11], but methods are mostly related to the synthesis of nonfluorinated indene derivatives. However, there have been quite limited methodologies for the preparation of trifluoromethylated indenes. Since the introduction of a trifluoromethyl group into the organic molecules has often increased the biological properties [12,13], many efforts have been devoted to the development of synthetic methodologies for the preparation of trifluoromethylated indenes. 1-Trifluoromethylindene was prepared from the reaction of 2,2,3-trifluoro-3-(trifluoromethyl)indanone with zinc in the presence of HCl, in which 2,2,3-trifluoro-3-(trifluoromethyl)indanone was synthesized by the radical-addition reaction of benzaldehyde to hexafluoropropene [14]. Gassman also prepared a series of trifluoromethylated indenes through the photoinduced addition of trifluoromethyl iodide to indene followed by dehydroiodination, the addition of (trifluoromethyl)-trimethylsilane to 1-indanone followed by dehydration or the sigmatropic cyclization of the appropriate phenylvinyl carbocation [15]. 1,3-Disubstituted 2-trifluoromethylated indenes were synthesized by reduction of α-trifluoromethyl-β-phenylated enones, followed by cyclization reaction in the presence of $AlCl_3$ [16,17]. One-pot synthesis of 2-trifluoromethyl indene was established by the reaction of the di-Grignard reagent of α,α′-dichloro-*o*-xylene with trifluoroacetate, followed by dehydration [18]. Recently, 1,1-disubstituted 3-trifluoromethylated indenes were synthesized through the cyclization of 1-trifluoromethyl-1-phenylallyl amine derivatives by TMSOTf [19]. However, the most of these methods focused on the preparation of trifluoromethylated indenes. In spite of importance of 1-methylene indene derivatives such as Sulindac in recent years [3,4], to our knowledge, the methods for the preparation of trifluoromethylated 1-methylene indenes have not been reported in the previous literatures. Herein, we wish to report a novel and general approach to 2-trifluoromethyl-1-methylene-3-phenylindenes via the carbocyclization reaction of 2-trifluoromethyl-1,1-diphenyl-1,3-enynes.

2. Results and discussion

Trifluoromethylated enynyl sulfones **3a**–**h** (E/Z = 9/91) as precursors to 2-trifluoromethyl-1,1-diphenyl-1,3-enynes were prepared in 84–99% yields from the oxidation of trifluoromethylated enynyl sulfides **2a**–**h** (E/Z = 9/91) which were synthesized in 78–98% yields from the reaction of pentafluoroethyl phenyl dithioketal **1** with aryl or alkyl substituted ethynyllithium reagents (2.5 equiv.) (Scheme 1) [20]. The assignment of E and Z isomers of

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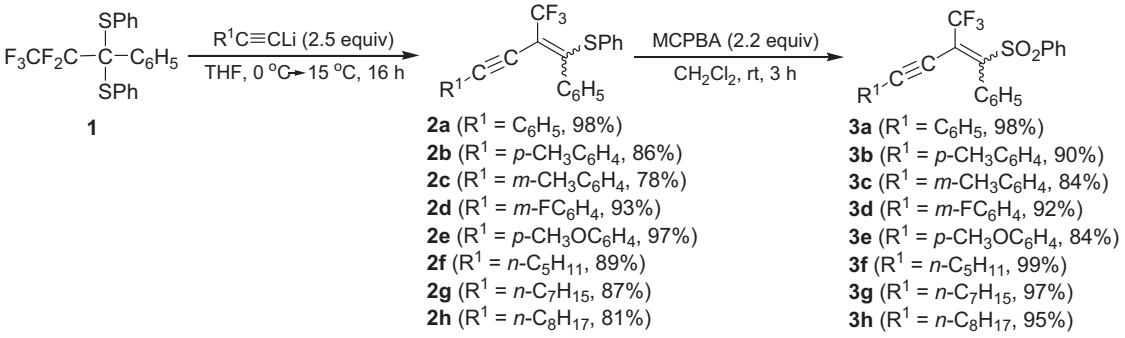


2a (R^1 = C_6H_5, 98%)
2b (R^1 = *p*-$CH_3C_6H_4$, 86%)
2c (R^1 = *m*-$CH_3C_6H_4$, 78%)
2d (R^1 = *m*-FC_6H_4, 93%)
2e (R^1 = *p*-$CH_3OC_6H_4$, 97%)
2f (R^1 = *n*-C_5H_{11}, 89%)
2g (R^1 = *n*-C_7H_{15}, 87%)
2h (R^1 = *n*-C_8H_{17}, 81%)

3a (R^1 = C_6H_5, 98%)
3b (R^1 = *p*-$CH_3C_6H_4$, 90%)
3c (R^1 = *m*-$CH_3C_6H_4$, 84%)
3d (R^1 = *m*-FC_6H_4, 92%)
3e (R^1 = *p*-$CH_3OC_6H_4$, 84%)
3f (R^1 = *n*-C_5H_{11}, 99%)
3g (R^1 = *n*-C_7H_{15}, 97%)
3h (R^1 = *n*-C_8H_{17}, 95%)

Scheme 1.

3a–**h** was made by the comparison of chemical shift of authentic sample in ^{19}F NMR spectroscopy [21] and the anisotropic effect of the sulfonyl group. Therefore, the chemical shift of the CF_3 group (Z-isomer) arranged to the same side of the sulfonyl group could be deshielded. It has been established that ^{19}F NMR signal (∼−55.70 ppm) in the Z-isomer is less shielded than that (∼−59.00 ppm) in the E-isomer.

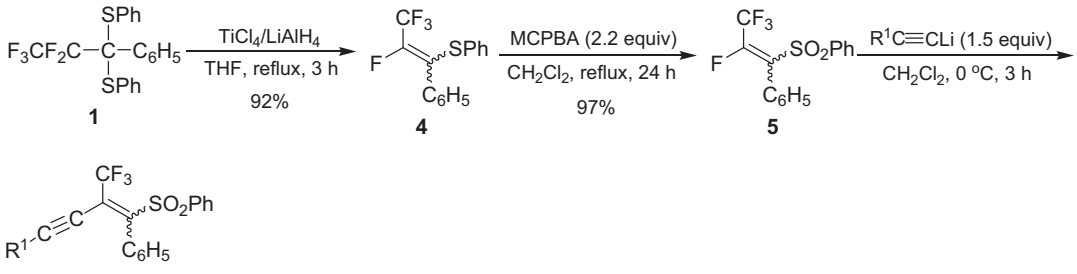
Since **1** was not reacted with trimethylsilyl or triisopropylsilyl substituted ethynyllithium reagents, enynyl sulfones **3i**–**j** (E/Z = 35/65) were prepared in 64–72% yields as a mixture of E and Z isomers from the reaction of β-fluoro-β-trifluoromethylvinyl sulfone **5**, formed by oxidation of β-fluoro-β-trifluoromethylvinyl sulfide **4** [22], with trimethylsilyl or triisopropylsilyl substituted ethynyllithium reagents in CH_2Cl_2 at 0 °C for 3 h (Scheme 2).

Vinyl sulfones **3** are very reactive species to react with organolithium reagents. Thus, further reactions of **3a**–**j** with phenyllithium reagents (2.2 equiv.) in THF at −78 °C for 2–4 h afforded the corresponding 2-trifluoromethyl-1,1-diphenyl-1,3-enynes **6a**–**j** in 63–77% yields. The use of other solvents such as hexane or ether in this reaction caused not only to retard the reaction, but also to decrease the yield of **6**. Reaction temperature in this reaction was also important to maximize the yield of **6**. The results of these reactions were summarized in Table 1. A recent study has established that this type of addition-elimination reaction of **3** with aryl, alkyl or trialkylsilyl ethynyllithium reagent provided the corresponding trifluoromethylated endiynes in good yields [23]. Advantage for the exchange of sulfonyl group in enynyl sulfones **3** to phenyl group is to utilize two phenyl rings for the Pd-catalyzed cyclization of arene-alkyne substrates via intramolecular electrophilic hydroarylation.

Recently, intramolecular palladium-catalyzed hydroarylation of alkynes became a powerful tool for the construction of carbo- and heterocycles. Especially, hydroarylation of *o*-alkynyl biaryls has been studied, in which it was found that a variety of *o*-alkynyl biaryls having electron-neutral or electron-deficient group underwent 5-*exo*-*dig* carbocyclization to give 9-benzylidene-9*H*-fluorene derivatives [24]. Therefore, we examined the possibility of carbocyclization of **7** under palladium catalyzed condition. After screening the palladium catalyzed condition, it was found that the use of 10 mol% Pd(OAc) in the presence of CF_3CO_2H and CH_2Cl_2 (4:1) provided 2-trifluoromethy-1-methylene-3-phenylindenes **7** via 5-*exo*-*dig* carbocyclization exclusively. In this carbocyclization, aryl-substituted 1,3-enynes **6a**–**e** afforded 1-methylene indenes **7a**–**e** as one isomer predominately, whereas alkyl-substituted 1,3-enynes **6f**–**h** provided 1-methylene indenes **7f**–**h** in the same stereoisomer ratios of 5/4. The results of these reactions were summarized in Table 2. In the case of carbocyclization of trimethylsilyl- or triisopropylsilyl-substituted 1,3-enynes **6i**–**j**, protodesilylation product **7i** was obtained (Scheme 3). We did not observe the 6-*endo*-*dig* carbocyclization. Other palladium-catalyzed system did not provide the better results. Assignment of 5-*exo*-*dig* hydroarylation product **7** was based on ^1H NMR chemical shift. The ^1H NMR of **7f** showed that the peak of vinyl protons of E and Z isomer appeared as a triplet at δ = 6.93 and 6.78 ppm, respectively. The chemical shifts of two vinyl protons of **7i** in the ^1H NMR are 6.36 and 6.15 ppm, respectively. It was postulated that this reaction proceeds via *ortho*-palladation of **6** to give intermediate [I], which undergoes the insertion to a triple bond to give vinylpalladium species [II]. Protiodepalladation of [II] affords 1-methylene indenes **7** (Scheme 4).

3. Conclusion

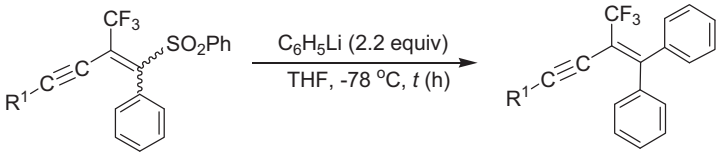
In conclusion, we synthesized 2-trifluoromethy-1-methylene-3-phenylindene derivatives **7** via 5-*exo*-*dig* carbocyclization of 2-trifluoromethyl-1,1-diphenyl-1,3-enynes **6** by the use of 10 mol% Pd(OAc) in the presence of CF_3CO_2H and CH_2Cl_2 (4:1). Aryl-substituted 1,3-enynes **6a**–**e** afforded 1-methylene indenes **7a**–**e** as one isomer predominately, whereas alkyl-substituted ones **6f**–**h**



3i (R^1 = TMS, 72%)
3j (R^1 = TIPS, 64%)

Scheme 2.

Table 1
Preparation of 2-trifluoromethyl-1,1-diphenyl-1,3-enynes **6**.



3 **6**

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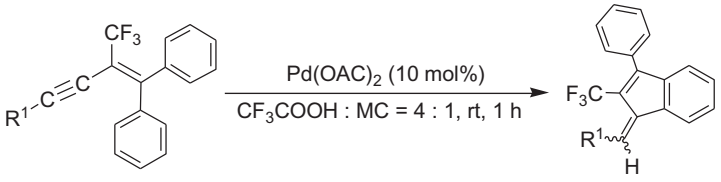
Compound no	R^1	*t* (h)	Yield (%)[a]
6a	C_6H_5	3	63
6b	*p*-$CH_3C_6H_4$	3	75
6c	*m*-$CH_3C_6H_4$	3	72
6d	*p*-$CH_3OC_6H_4$	3	77
6e	*m*-FC_6H_4	3	71
6f	*n*-C_5H_{11}	2	71
6g	*n*-C_7H_{15}	2	70
6h	*n*-C_8H_{17}	2	73
6i	$(CH_3)_3Si$	4	74
6j	$[(CH_3)_2CH]_3Si$	4	74

[a] Isolated yield.

Table 2
Preparation of 2-trifluoromethyl-1-methylene-3-phenylindenes **7**. ‘



6 **7**

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Compound no	R^1	Yield (%)[a]
7a	C_6H_5	81
7b	*p*-$CH_3C_6H_4$	70
7c	*m*-$CH_3C_6H_4$	71
7d	*p*-$CH_3OC_6H_4$	60
7e	*m*-FC_6H_4	58
7f	*n*-C_5H_{11}	83
7g	*n*-C_7H_{15}	78
7h	*n*-C_8H_{17}	80

[a] Isolated yield.

provided **7f–h** as a mixture of E and Z isomers (5:4). In the case of carbocyclization of trimethylsilyl- or triisopropylsilyl-substituted 1,3-enynes **6i–j**, reduced product **7i** was obtained.

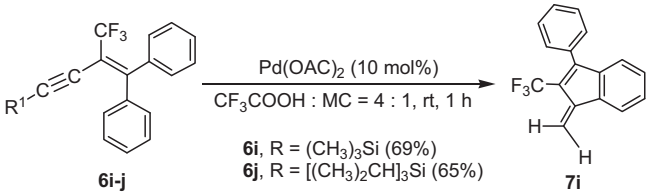
4. Experimental

^1H and ^{13}C NMR spectra were recorded on a 400 MHz Bruker AVANCEII^{++} NMR spectrometer with tetramethylsilane (TMS) as an internal standard and ^{19}F NMR spectra were also recorded on a 400 MHz Bruker AVANCEII^{++} NMR spectrometer with $CFCl_3$ as an internal standard and the upfield as negative. All chemical shifts (δ) are expressed in parts per million and coupling constant (*J*) are given in Hertz. Mass spectra were obtained by using Agilent Technologies 6890N GC/5973 Network MSD (EI, 70 eV). Elemental analysis data were obtained by using EA1110 elemental analyzer. Melting points were determined in open capillary tubes and are uncorrected.

Commercially available reagents were purchased from Aldrich, Lancaster, Tokyo Kasei and Fluorochem. All solvents were dried by general purification method. Flash chromatography was performed on 40–60 μm silica gel (230–400 mesh).

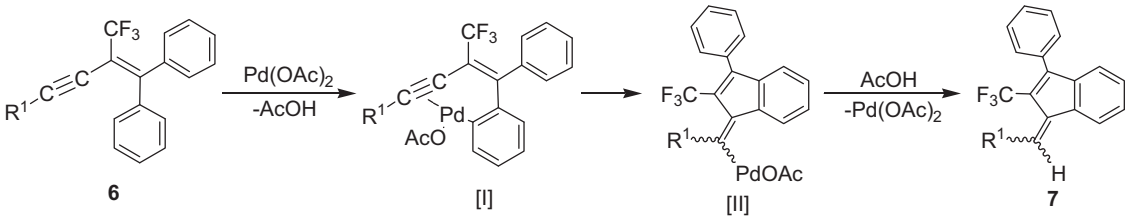
4.1. General procedure for the preparation of 2-trifluoromethyl-1-phenyl-1-phenylthio-1,3-enynes (2)

A 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with 1-alkyne (5.0 mmol) and 10 mL of THF. The reaction mixture was cooled to 0 °C and *n*-BuLi (2.5 M



6i-j **7i**

Scheme 3.



Scheme 4.

solution in hexane) 2.0 mL (5.0 mmol) was added dropwise. After the reaction mixture was stirred at 0 °C for 1 h, 1,1-bis(phenylthio)-2,2,3,3,3-pentafluoropropyl benzene (**1**) (2.0 mmol) dissolved in THF (4 mL) was added at 0 °C. The reaction mixture was warmed to 15 °C and then stirred for 16 h. The reaction mixture was extracted with ether twice, dried over anhydrous $MgSO_4$ and chromatographed on SiO_2 column. Elution with hexane provided 1,3-enynyl sulfides **2**.

*4.1.1. 2-Trifluoromethyl-4-methoxyphenyl-1-phenyl-1-phenylthio-1-buten-3-yne (**2e**)*

2e (E/Z = 91/9) was prepared in 97% yield (0.796 g) according to the general procedure. **2e**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.55–6.82 (m, 14H, E-isomer), 7.40–6.73 (m, 14H, Z-isomer), 3.84 (s, 3H, E-isomer), 3.76 (s, 3H, Z-isomer); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −56.34 (s, 3F, E-isomer), 58.72 (s, 3F, Z-isomer); MS, *m*/*z* (relative intensity) 410 (M^+, 100), 395 (18), 326 (11), 298 (19), 289 (11), 217 (13), 189 (19), 121 (8), 77 (7). Anal. calcd for $C_{24}H_{17}F_3SO$: C, 70.23; H, 4.17. Found: C, 70.12; H, 4.15.

*4.1.2. 2-Trifluoromethyl-1-phenyl-1-phenylthio-1-nonen-3-yne (**2f**)*

2f (E/Z = 91/9) was prepared in 89% yield (0.666 g) according to the general procedure. **2f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.36–6.96 (m, 20H), 2.50 (t, *J* = 6.8 Hz, 2H, E-isomer), 2.13 (t, *J* = 6.8 Hz, 2H, Z-isomer), 1.68–1.31 (m, 6H, E-isomer), 1.31–1.06 (m, 6H, Z-isomer), 0.92 (t, *J* = 7.2 Hz, 3H, E-isomer), 0.80 (t, *J* = 7.2 Hz, 3H, Z-isomer); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −56.69 (s, 3F, E-isomer), 58.82 (s, 3F, Z-isomer); MS, *m*/*z* (relative intensity) 374 (M^+, 10), 318 (26), 297 (20), 265 (15), 241 (100), 209 (28), 183 (13), 165 (10), 139 (14), 121 (12), 91 (7), 77 (9). Anal. calcd for $C_{22}H_{21}F_3S$: C, 70.56; H, 5.65. Found: C, 70.42; H, 5.59.

*4.2. General procedure for the preparation of 2-trifluoromethyl-1-phenyl-1-phenylsulfonyl-1,3-enynes (**3**)*

A 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with 1,3-enynylsulfides **2** (1.5 mmol) and 15 mL of CH_2Cl_2. The reaction mixture was cooled to 0 °C and MCPBA (3.2 mmol) dissolved in 5 mL of CH_2Cl_2 was added at 0 °C, followed by stirring at room temperature for 3 h. A mixture of $NaHCO_3$ and 10% $NaHSO_3$ solution was added into the reaction mixture which was extracted with CH_2Cl_2 twice, dried over anhydrous K_2CO_3 and chromatographed on SiO_2 column. Elution with a mixture of hexane and ethyl acetate (4:1) provided 1,3-enynyl sulfones **3**.

*4.2.1. 2-Trifluoromethyl-4-methoxyphenyl-1-phenyl-1-phenylsulfonyl-1-buten-3-yne (**3e**)*

3e (E/Z = 91/9) was prepared in 84% yield (0.557 g) according to the general procedure. **3e**: mp = 84–86 °C; ^{1}H NMR ($CDCl_3$) δ 7.74–6.91 (m, 14H, E-isomer), 7.62–6.69 (m, 14H, Z-isomer), 3.83 (s, 3H, E-isomer), 3.72 (s, 3H, Z-isomer); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −55.66 (s, 3F, Z-isomer), 58.93 (s, 3F, E-isomer); MS, *m*/*z* (relative intensity) 442 (M^+, 3), 378 (48), 289 (10), 232 (18), 217 (25), 208 (100), 189 (34), 77 (15). Anal. calcd for $C_{24}H_{17}F_3SO_3$: C, 65.15; H, 3.87. Found: C, 64.93; H, 3.83.

*4.2.2. 2-Trifluoromethyl-1-phenyl-1-phenylsulfonyl-1-nonen-3-yne (**3f**)*

3f (E/Z = 91/9) was prepared in 99% yield (0.603 g) according to the general procedure. **3f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.75–7.02 (m, 20H), 2.53 (t, *J* = 6.8 Hz, 2H, E-isomer), 2.09 (t, *J* = 6.8 Hz, 2H, Z-isomer), 1.70–1.31 (m, 6H, E-isomer), 1.31–0.87 (m, 6H, Z-isomer), 0.87 (m, 3H, E-isomer), 0.78 (t, *J* = 7.2 Hz, 3H, Z-isomer); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −55.96 (s, 3F, Z-isomer), 59.39 (s, 3F, E-isomer); MS, *m*/*z* (relative intensity) 406 (M^+, 1), 285 (15), 265 (10), 225 (26), 209 (92), 183 (46), 165 (20), 152 (18), 139 (41), 125 (31), 111 (89), 83 (100), 77 (50), 55 (21). Anal. calcd for $C_{22}H_{21}F_3SO_2$: C, 65.01; H, 5.21. Found: C, 64.87; H, 5.15.

*4.2.3. 2-Trifluoromethyl-1-phenyl-1-phenylsulfonyl-4-trimethylsilyl-1-buten-3-yne (**3i**)*

A 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with trimethylsilylacetylene (0.294 g, 3.0 mmol) and 8 mL of ether. The reaction mixture was cooled to 0 °C and MeLi (1.6 M solution in ether) 1.87 mL (3.0 mmol) was added dropwise. Another 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with **5**[17] (0.660 g, 2.0 mmol) and 15 mL of CH_2Cl_2. After the reaction mixture was stirred at 0 °C, trimethylsilylethynyllithium prepared from above was added dropwise at 0 °C, followed by strring for 3 h. The reaction mixture was extracted with CH_2Cl_2 twice, dried over anhydrous Na_2CO_3 and chromatographed on SiO_2 column. Elution with a mixture of hexane and ethyl acetate (20:1) provided **3i** (E/Z = 36/64) in 72% yield (0.588 g). **3i**: mp 72–73 °C; ^{1}H NMR ($CDCl_3$) δ 7.79–6.99 (m, 20H), 0.33 (s, 9H, E-isomer), −0.11 (s, 9H, Z-isomer); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −55.75 (s, 3F, Z-isomer), 59.09 (s, 3F, E-isomer); MS, *m*/*z* (relative intensity) 408 (M^+, 5), 344 (13), 233 (10), 183 (10), 171 (31), 170 (35), 151 (59), 135 (17), 127 (27), 125 (39), 105 (28), 97 (13), 77 (100), 51 (33). Anal. calcd for $C_{20}H_{19}F_3SO_2Si$: C,58.80; H, 4.69. Found: C, 58.65; H, 4.66.

*4.3. General procedure for the preparation of 2-trifluoromethyl-1,1-diphenyl-1,3-enynes (**6**)*

A 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with 1,3-enynyl sulfone **3** (1.0 mmol) and 5 mL of THF. The reaction mixture was cooled to −78 °C and phenyllithium (2.0 M solution in di-*n*-butyl ether) 1.1 mL (2.2 mmol) was added dropwise. After the reaction mixture was stirred at 0 °C for 2–4 h, the reaction mixture was quenched with NaCl solution. The reaction mixture was extracted with ether twice, dried over anhydrous $MgSO_4$ and chromatographed on SiO_2 column. Elution with hexane provided 1,1-diphenyl-1,3-enynes **6**.

4.3.1. 2-Trifluoromethyl-4-methoxyphenyl-1,1-diphenyl-1-buten-3-yne (6d)

6d was prepared in 77% yield (0.291 g) according to the general procedure. **6d**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.48–6.79 (m, 14H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 160.2, 155.0, 140.9, 139.4, 133.2, 130.2, 129.3, 129.2, 128.7, 128.2, 128.0, 122.5 (q, J = 274.7 Hz), 114.9, 114.2, 112.8 (q, J = 33.2 Hz), 95.4, 83.9, 55.5; ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −57.08 (s, 3F); MS, m/z (relative intensity) 378 (M^+, 100), 357 (13), 309 (18), 294 (23), 265 (30), 239 (8), 208 (8), 165 (11), 147 (8), 132 (8), 77 (7). Anal. calcd for $C_{24}H_{17}F_3O$: C, 76.18; H, 4.53. Found: C, 75.92; H, 4.48.

4.3.2. 2-Trifluoromethyl-1,1-diphenyl-1-nonen-3-yne (6f)

6f was prepared in 71% yield (0.243 g) according to the general procedure. **6f**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.60–7.16 (m, 10H), 2.25 (t, J = 6.8 Hz, 2H), 1.44–1.21 (m, 6H), 0.86 (t, J = 6.8 Hz, 3H); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −57.50 (s, 3F); MS, m/z (relative intensity) 342 (M^+, 39), 285 (80), 260 (30), 244 (23), 233 (25), 215 (100), 202 (43), 189 (20), 165 (20), 115 (12), 91 (16), 83 (21), 77 (7), 55 (15). Anal. calcd for $C_{22}H_{21}F_3$: C, 77.17; H, 6.18. Found: C, 76.88; H, 6.19.

4.3.3. 2-Trifluoromethyl-4-trimethylsilyl-1,1-diphenyl-1-buten-3-yne (6i)

6i was prepared in 74% yield (0.255 g) according to the general procedure. **6i**: colorless oil; ^{1}H NMR ($CDCl_3$) δ 7.38–7.34 (m, 10H), 0.33 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 156.5, 141.3, 140.5, 139.0, 129.8, 128.9, 127.9, 127.2, 122.1 (q, J = 274.7 Hz), 112.3 (q, J = 33.2 Hz), 100.8, 98.9, 11.0; ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −57.11 (s, 3F); MS, m/z (relative intensity) 344 (M^+, 35), 329 (9), 247 (19), 226 (10), 213 (10), 77 (16). Anal. calcd for $C_{20}H_{19}F_3Si$: C, 69.74; H, 5.56. Found: C, 69.55; H, 5.60.

4.4. General procedure for the preparation of 2-trifluoromethyl-1-methylene-3-phenylindenes (7)

A 25 mL two-neck round bottom flask equipped with a magnetic stirrer bar, a septum and nitrogen tee connected to an argon source was charged with **6** (1.0 mmol), 1 mL of CH_2Cl_2 and 4 mL of CF_3CO_2H. $Pd(OAc)_2$ was added into the reaction mixture and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was extracted with ether twice, dried over anhydrous $MgSO_4$ and chromatographed on SiO_2 column. Elution with hexane provided 2-trifluoromethyl-1-methylene-3-phenylindenes **7**.

4.4.1. 2-Trifluoromethyl-1-(4-methoxyphenyl)methylene-3-phenyl-1H-indene (7d)

7d was prepared in 60% yield (0.227 g) according to the general procedure. **7d**: mp 157–159 °C; ^{1}H NMR ($CDCl_3$) δ 8.01–7.07 (m, 14H), 3.92 (s, 3H); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −56.74 (s, 3F); MS, m/z (relative intensity) 378 (M^+, 100), 363 (11), 309 (9), 294 (12), 265 (15), 239 (7), 189 (8), 147 (5), 132 (5). Anal. calcd for $C_{24}H_{17}F_3O$: C, 76.18; H, 4.53. Found: C, 75.94; H, 4.48.

4.4.2. 2-Trifluoromethyl-1,1-diphenyl-1-nonen-3-yne (7f)

7f (E and Z isomer ratio = 5:4) was prepared in 83% yield (0.284 g) according to the general procedure. **7f**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.84–7.09 (m, 18H), 6.93 (t, J = 7.6 Hz, 1H, one isomer), 6.78 (t, J = 7.6 Hz, 1H, other isomer), 2.88 (dt, J = 7.6, 7.2 Hz, 2H, one isomer), 2.70 (dt, J = 7.6, 7.2 Hz, 2H, other isomer), 1.74–1.59 (m, 6H, one isomer), 1.43–1.26 (m, 6H, other isomer), 0.95 (t, J = 7.2 Hz, 6H); ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −52.78 (s, 3F, one isomer), −53.07 (s, 3F, other isomer); MS, m/z (relative intensity) 342 (M^+, 25), 285 (8), 272 (100), 265 (8), 251 (12), 239 (10), 215 (12), 202 (8). Anal. calcd for $C_{22}H_{21}F_3$: C, 77.17; H, 6.18. Found: C, 76.93; H, 6.15.

4.4.3. 2-Trifluoromethyl-1-methylene-3-phenyl-1H-indene (7i)

7i was prepared in 69% yield (0.188 g) according to the general procedure. **7i**: yellow oil; ^{1}H NMR ($CDCl_3$) δ 7.73–7.15 (m, 9H), 6.37 (s, 1H), 6.15 (s, 1H); ^{13}C NMR ($CDCl_3$) 149.1, 142.4, 141.2, 135.8, 132.7, 128.7, 128.6, 128.5, 127.9, 127.2, 124.5, 123.5 (q, J = 32.2 Hz), 122.1, 119.8, 115.6; ^{19}F NMR ($CDCl_3$, internal standard $CFCl_3$) δ −54.13 (s, 3F); MS, m/z (relative intensity) 272 (M^+, 100), 251 (29), 239 (31), 220 (8), 203 (13), 202 (26). Anal. calcd for $C_{17}H_{11}F_3$: C, 74.99; H, 4.07. Found: C, 74.80; H, 4.04.

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References

[1] D.J. Collins, J.J. Hobbs, C.W. Emmens, J. Med. Chem. 14 (1971) 952–957.
[2] M.R. Schneider, H. Ball, J. Med. Chem. 29 (1986) 75–79.
[3] I.M. Karaguni, K.H. Glusenkamp, A. Langerak, C. Geisen, V. Ullrich, G. Winde, T. Moroy, O. Muller, Bioorg. Med. Chem. Lett. 12 (2002) 709–713.
[4] A. Korte, J. Legros, C. Bolm, Synlett 13 (2004) 2397–2399.
[5] N.J. Clegg, S. Paruthiyil, D.C. Leitman, T.S. Scanlan, J. Med. Chem. 48 (2005) 5989–6003.
[6] E. Yoshikawa, K.V. Radhakrishnan, Y. Yamamoto, J. Am. Chem. Soc. 122 (2000) 7280–7286.
[7] Z. Xi, R. Guo, S. Mito, H. Yan, K. Kanno, K. Nakajima, T. Takahashi, J. Org. Chem. 68 (2003) 1252–1257.
[8] D. Zhang, E.K. Yum, R.C. Larock, Org. Lett. 7 (2005) 4963–4966.
[9] Y. Kuninobu, Y. Tokunaga, A. Kawata, K. Takai, J. Am. Chem. Soc. 128 (2006) 202–209.
[10] D. Zhang, Z. Liu, E.K. Yum, R.C. Larock, J. Org. Chem. 72 (2007) 251–262.
[11] S. Ye, K. Gao, H. Zhou, X. Yang, J. Wu, Chem. Commun. (2009) 5406–5408.
[12] J.T. Welch, S. Eswarakrishnan, Fluorine in Bioorganic Chemistry, John Wiley & Sons, New York, 1991.
[13] K. Uneyama, Organofluorine Chemistry, Blackwell, Oxford, 2006.
[14] H. Kimoto, H. Muramatsu, K. Inukai, Bull. Chem. Soc. Jpn. 49 (1976) 1642–1649.
[15] P.G. Gassman, J.A. Ray, P.G. Wenthold, J.W. Mickelson, J. Org. Chem. 56 (1991) 5143–5146.
[16] I.H. Jeong, Y.S. Park, M.S. Kim, S.T. Oh, Bull. Korean Chem. Soc. 22 (2001) 1173–1174.
[17] I.H. Jeong, Y.S. Park, M.S. Kim, Y.S. Song, J. Fluorine Chem. 120 (2003) 195–209.
[18] A.C. Moller, R. Blom, R.H. Heyn, O. Swang, J. Kopf, T. Seraidaris, J. Chem. Soc. Dalton Trans. (2006) 2098–2105.
[19] S.L. Jeon, J.K. Kim, J.B. Son, B.T. Kim, I.H. Jeong, Tetrahedron Lett. 47 (2006) 9107–9111.
[20] I.H. Jeong, Y.K. Min, Y.S. Kim, K.Y. Cho, K.J. Kim, Bull. Korean Chem. Soc. 14 (1993) 309–311.
[21] Y. Shen, Y. Xiang, W. Qiu, J. Chem. Soc. Perkin Trans. 1 (2001) 519–526.
[22] I.H. Jeong, Y.K. Min, Y.S. Kim, B.T. Kim, K.Y. Cho, Tetrahedron Lett. 35 (1994) 7783–7784.
[23] H.H. Jeon, J.B. Son, J.H. Choi, I.H. Jeong, Tetrahedron Lett. 48 (2007) 627–631.
[24] N. Chernyak, V. Gevorgyan, J. Am. Chem. Soc. 130 (2008) 5636–5637.