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STEREOSELECTIVE PREPARATION AND COPE REARRANGEMENT of 2-CF_3-*CIS*-2,3-BIS(ALKENYL)OXIRANES: A FACILE ROUTE TO 2-CF_3-SUBSTITUTED OXACYCLES

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This paper is dedicated to Professor Ryoji Noyori in celebration of his 70th birthday.

Abstract – We describe here a facile route to 2-trifluoromethyl-substituted 4,5-dihydrooxepins, which involves stereoselective preparation and Cope rearrangement of 2-trifluoromethyl-*cis*-2,3-bis(alkenyl)oxiranes. Treatment of 1,1-dichloro-2-hydroxy-2-trifluoromethylalk-3-enes with alkenyllithium and then lithium 2,2,6,6-tetramethylpiperidide generated *cis*-2,3-bis(alkenyl)-2-lithio-3-trifluoromethyloxiranes, which reacted with a variety of electrophiles to give the corresponding tri- and tetrasubstituted oxiranes stereoselectively. Cope rearrangement of the *cis*-oxiranes proceeded upon heating, giving rise to 2-trifluoromethyl-substituted 4,5-dihydrooxepins in high to excellent yields. The Cope rearrangement is found remarkably accelerated by the presence of such metal substituents as boryl, silyl, and stannyl groups at 7-position, that can act as versatile functionalities for further elaboration of the ring-enlarged products. Subsequent reduction and oxidation of the rearranged products gave 2-trifluoromethylated oxepanes and oxepins in good yields.

INTRODUCTION

Since incorporation of fluorine atoms into biologically active substances can often enhances or changes physical, chemical, and biological activities of parent compounds, organofluorine compounds are of great

importance in pharmaceuticals and agrochemicals.[1] For example, the presence of a CF_3 group enhances thermal and metabolic stabilities as well as lipophilic property of organic molecules. Meanwhile, such seven-membered oxacycles as oxepanes and oxepines have gained much attention due to their occurrence in biologically active natural products, especially marine natural products.[2] For example, dictyoxepin, antibiotic extract from the brown algae *Dictyota acutiloba*, contains 4,5-dihydrooxepin skeleton (Figure 1).[3] Benzooxepin framework is found in tenucarb isolated from *Asphodeline tenuior*,[4] while isolaurepinnacin, one of *Laurencia* acetogenins, consists of 2,7-*cis*-disubstituted 4,5-dehydrooxepane.[5] However, examples of fluorinated seven-memberd oxacycles are quite limited probably due to the lack of their synthetic methods.[6] In this context, development of synthetic methods for fluorinated oxepanes and oxepines is of particular interest for exploration of potent drugs and pesticides based on seven-membered oxacycles.

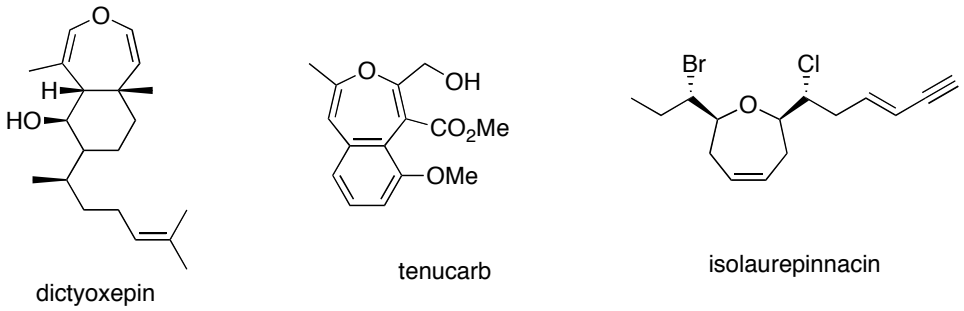
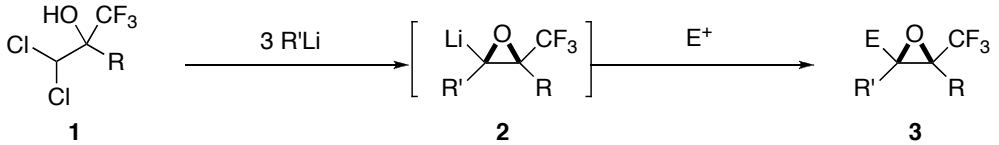


Figure 1. Examples of biologically active seven-membered oxacycles

We have recently found that CF_3-containing dichlorohydrins **1**, readily prepared from commercially available 1,1-dichloro-3,3,3-trifluoropropan-2-one, react with 3 molar amounts of R′Li at –98 °C to generate *cis*-2,3-disubstituted 2-lithio-3-trifluoromethyloxiranes **2**, which are trapped with various electrophiles to give CF_3-containing tri- and tetrasubstituted oxiranes **3** stereoselectively (Scheme 1).[7]

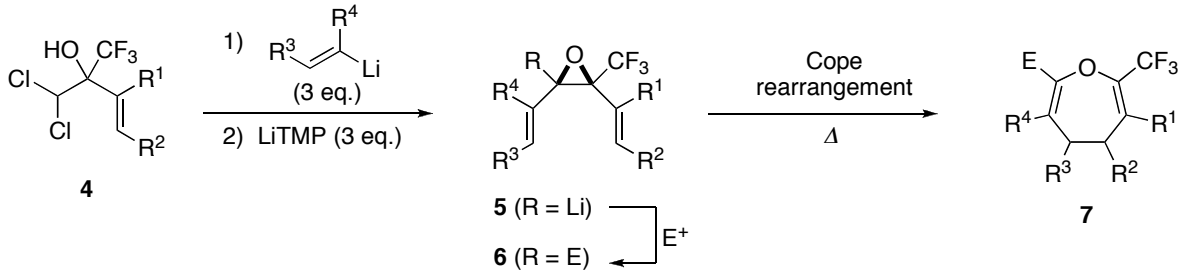
Scheme 1. Stereoselective preparation of CF_3-containing tri- and tetrasubstituted oxiranes **3**



Since Cope rearrangement of *cis*-2,3-bis(alkenyl)oxiranes is one of efficient methods for construction of seven-membered oxacycle frameworks,[8] we envisioned that 2-CF_3-substituted 4,5-dihydrooxepins could be synthesized if the protocol was applicable to stereoselective preparation of *cis*-bis(alkenyl)oxiranes **6** (Scheme 2). On the contrary to our expectation, the protocol was found not effective for preparation of **6**. After many experiments, we were delighted to find that the addition of lithium 2,2,6,6-tetramethylpiperidide (LiTMP) to a mixture of 1,1-dichloro-2-hydroxy-2-trifluoro- methylalk-3-enes **4**

and alkenyllithiums in THF led to the efficient generation of lithio-oxiranes **5**. We describe herein stereoselective preparation by the modified protocol and Cope rearrangement of **6** leading to 4,5-dihydrooxepins **7**.[9] Further transformations of the rearranged products (**7**), such as cross-coupling reaction, oxidation, and reduction, are also presented.

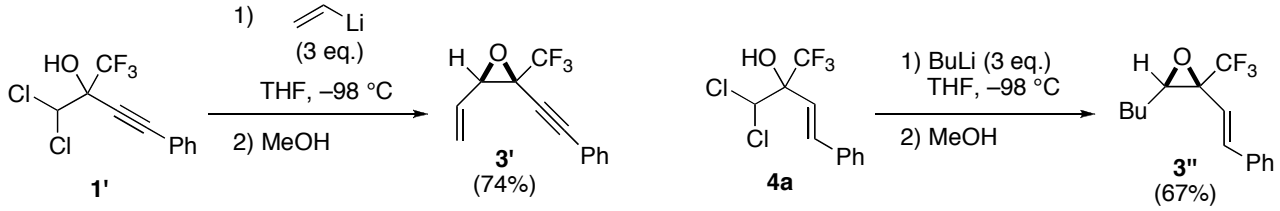
Scheme 2. Synthesis of 2-CF_3-4,5-dihydrooxepins **7**



RESULTS AND DISCUSSION

As shown in Scheme 1, we have recently developed stereoselective synthesis of CF_3-containing tri- and tetrasubstituted oxiranes **3** from readily available dichlorohydrins **1**.[7a,b] For example, treatment of phenylethynyl-substituted dichlorohydrin **1′** with vinyllithium followed by quenching with methanol gave **3′** as a single diastereomer in 74% yield, while the reaction of **4a** containing a styryl group with BuLi proceeded smoothly at –98 °C, giving rise to **3″** in 67% yield (Scheme 3).[7a,b]

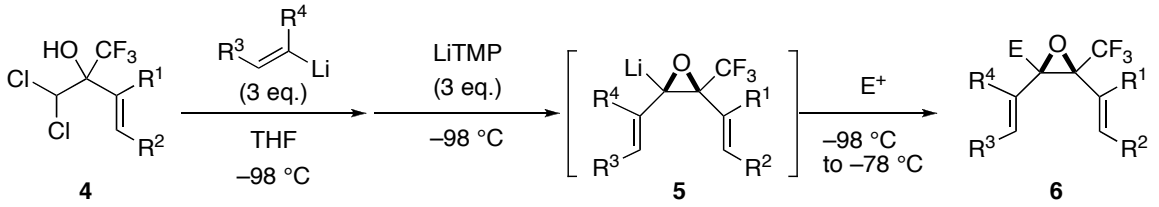
Scheme 3. Stereoselective formation of CF_3-substituted oxiranes **3**



Accordingly, we applied the sequence of operations to styryl derivative **4a** with vinyllithium (3 molar amounts) in THF at –98 °C followed by quenching with MeOH. Both conversion of **4a** and yield of **6a**, however, were less than 10%; most of **4a** was recovered unchanged. Based on our hypothetical mechanism in which oxirane-formation is assumed to be triggered by deprotonation of the methine proton in **1**,[7a,b] and the success of oxirane formation shown in Scheme 3, we considered that the failure was ascribed to both lower basicity of vinyllithium and/or lower acidity of the methine proton in **4a**. Then, we examined such an additive as HMPA, TMEDA, or DME to the THF solution in order to enhance the basicity of vinyllithium. The addition of HMPA gave complex mixture, while **6a** formed in around 60% yield along with unidentified byproducts when TMEDA or DME was employed as an additive. Finally, the addition of lithium 2,2,6,6-tetramethylpiperidide (LiTMP, 3 molar amounts) was found highly effective to generate the corresponding oxiranyllithiums **5** which could be trapped with a variety of

electrophiles (E^+).[10] The lithium amide base could deprotonate the methine proton and vinyllithium could behave as a nucleophile.[11,12] The modified procedure was applied to synthesis of various CF_3-substituted *cis*-bis(alkenyl)oxiranes **6** as summarized in Table 1. Generally, *cis*-**6** was isolated as a single stereoisomer except for **6e**, **6i**, **6p**, **6r**, and **6s**.[13]

Table 1. Preparation of 2-CF_3-*cis*-2,3-bis(alkenyl)oxiranes **6**[a]

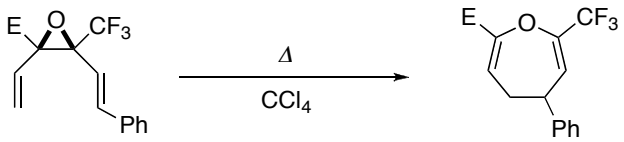


entry	**4**	R^1	R^2	R^3	R^4	E^+	**6**	E	yield (%)[b]
1	**4a**	H	Ph	H	H	MeOH	**6a**	H	77
2	**4a**	H	Ph	H	H	MeI	**6b**	Me	72
3	**4a**	H	Ph	H	H	Me_3SnCl	**6c**	Me_3Sn	64
4	**4a**	H	Ph	H	H	Me_3SiCl	**6d**	Me_3Si	77
5	**4a**	H	Ph	H	H	CO_2, then Me_3SiCHN_2	**6e**	MeO_2C	70[c]
6	**4a**	H	Ph	H	H	$(Me_2CO)_2B(O^iPr)$	**6f**	$(Me_2CO)_2B$	72
7	**4a**	H	Ph	H	H	Ph_2CO	**6g**	$Ph_2C(OH)$	62
8	**4a**	H	Ph	H	H	*t*-$BuMe_2SiCl$	**6h**	*t*-$BuMe_2Si$	–[d]
9	**4a**	H	Ph	H	Ph	MeOH	**6i**	H	86[e]
10	**4a**	H	Ph	H	Ph	Me_3SiCl	**6j**	Me_3Si	75
11	**4b**	H	H	H	Ph	Me_3SiCl	**6k**	Me_3Si	71
12	**4c**	Ph	H	H	H	MeOH	**6l**	H	80
13	**4b**	H	H	H	H	$PhCH_2Br$	**6m**	$PhCH_2$	60
14	**4b**	H	H	H	H	Me_3SnCl	**6n**	Me_3Sn	56
15	**4b**	H	H	H	H	*t*-$BuMe_2SiCl$	**6o**	*t*-$BuMe_2Si$	46
16	**4a**	H	Ph	H	OEt	MeOH	**6p**	H	67[f]
17	**4a**	H	Ph	–$(CH_2)_3O$–		MeOH	**6q**	H	25
18	**4d**	–$O(CH_2)_3$–		H	H	MeOH	**6r**	H	61[g]
19	**4d**	–$O(CH_2)_3$–		H	H	Me_3SiCl	**6s**	Me_3Si	69[h]

[a] **4** (1.0 mmol), alkenyllithium (3.0 mmol), LiTMP (3.0 mmol), THF (5 mL), –98 °C, 3~6 h; E^+ (1.5 mmol), –98 °C to –78 °C. [b] Isolated yield. [c] *cis*/*trans* = 92:8. [d] Oxirane **6h** rearranged even at room temperature. [e] *cis*/*trans* = 89:11. [f] *cis*/*trans* = 79:21. [g] *cis*/*trans* = 70:30. [h] *cis*/*trans* = 78:22.

With *cis*-bis(alkenyl)oxiranes **6** in hand, we next studied the Cope rearrangement. At first, (*E*)-2-phenylethenyl- and 3-vinyl-substituted oxiranes **6a**–**6h** were selected as a typical model and heated in CCl_4. The rearrangement of **6a** and **6b** reached to completion upon heating at 100 °C in 12 h and 8 h, respectively (Table 2, entries 1 and 2). Bis(alkenyl)oxiranes **6c**–**6e** substituted by a Me_3Sn, Me_3Si, or MeO_2C group reacted at lower temperatures in shorter times (entries 3-5). In case of **6e**, *trans*-isomer did not undergo the rearrangement at all under the conditions and was recovered quantitatively. Furthermore, the reaction was markedly accelerated by a bulky group like (pinacolato)boryl or hydroxydiphenylmethyl (entries 6 and 7). Noteworthy is that *tert*-butyldimethylsilyl (TBS)-substituted oxirane **6h** rearranged even at room temperature to prevent the isolation. Thus, bulkier substituent E appears to force two terminal sp^2 carbons locate closer each other (the Thorpe-Ingold effect) and to accelerate the Cope rearrangement.

Table 2. Cope rearrangement of **6a**–**6h**[a]



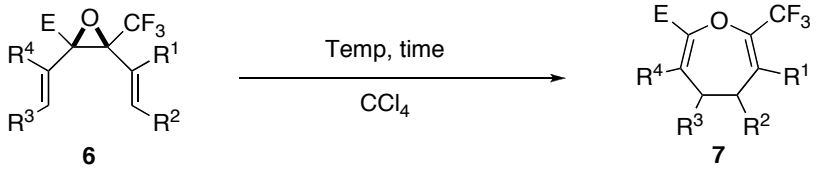
6 **7**

entry	**6**	E	T (°C) / t (h)	**7**	yield (%)[b]	entry	**6**	E	T (°C) / t (h)	**7**	yield (%)[b]
1	**6a**	H	100/12	**7a**	93	5	**6e**	MeO_2C	80/2	**7e**	96[c]
2	**6b**	Me	100/8	**7b**	85	6	**6f**	$(Me_2CO)_2B$	60/3	**7f**	99
3	**6c**	Me_3Sn	80/4	**7c**	88	7	**6g**	$Ph_2C(OH)$	60/2	**7g**	95
4	**6d**	Me_3Si	80/2	**7d**	92	8	**6h**	*t*-$BuMe_2Si$	60/2	**7h**	55[d]

[a] A solution of oxirane **6** (0.5 mmol) in CCl_4 (3 mL) was heated in a sealed tube. The reaction was monitored by ^{19}F NMR. [b] Isolated yield. [c] Isolated yield based on *cis*-diastereomer of **6e**. [d] Isolated yield based on dichlorohydrin **4h**.

The scope of this approach to **7** is summarized in Table 3. The isolated yields of **7** were generally high. Rate-enhancement of the rearrangement by incorporation of a silyl or stannyl group was again observed (entries 2, 3, 6, and 7). An enol moiety also could participate in the rearrangement (entries 8–11). Bicyclic oxepins **7q**–**7s** were isolated with enol moieties being intact in high yields after purification by silica gel column chromatography, while **7p** was obtained as a ketone probably due to hydrolysis during column chromatography on silica gel.

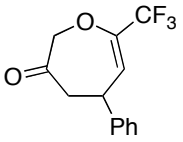
Table 3. Synthesis of 2-CF_3-4,5-dihydrooxepines **6i–6s**.[a]



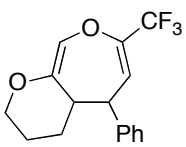
6 **7**

entry	**6**	T (°C) / t (h)	**7**	yield (%)[b]	entry	**6**	T (°C) / t (h)	**7**	yield (%)[b]
1	**6i**	120/4	**7i**	89[c]	7	**6o**	60/3	**7o**	94
2	**6j**	85/2	**7j**	92	8	**6p**	140/10	**7p**	63[c]
3	**6k**	85/2	**7k**	95	9	**6q**	140/ 6	**7q**[d]	90
4	**6l**	100/48	**7l**	93	10	**6r**	140/24	**7r**	89[c]
5	**6m**	80/5	**7m**	>99	11	**6s**	100/18	**7s**	86[c]
6	**6n**	80/3	**7n**	89					

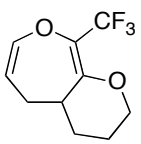
[a] A solution of oxirane **6** (0.5 mmol) in CCl_4 (3 mL) was heated in a sealed tube. The reaction was monitored by ^{19}F NMR. [b] Isolated yield. [c] Isolated yield based on *cis*-diastereomer of **6**. [d] The relative stereochemistry at 4,5-positions was not determined.



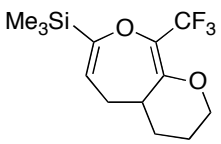
7p



7q



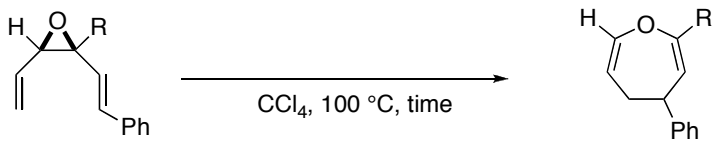
7r



7s

To estimate the CF_3 effect on the rearrangement, we carried out Cope rearrangement of *cis*-2-[(*E*)-2-phenylethenyl]-3-ethenyloxirane (**8a**) and 2-isopropyl-*cis*-2-[(*E*)-2-phenylethenyl]-3-ethenyl-oxirane (**8b**) at 100 °C (Scheme 4). The reactions of those went to completion over 11 h and 4 h in 87% and 83% yields, respectively, indicating that the presence of a sterically demanding isopropyl group accelerated the rearrangement. On the other hand, the fact that **6a** bearing a CF_3 group, whose steric size is comparable with an isopropyl group on the basis of A values (*i*-Pr: 2.21; CF_3: 2.4–2.5 kcal/mol),[14] rearranged to **7a** with longer time than **8b**, suggested that a CF_3 group sterically accelerated but electronically retarded the Cope rearrangement.

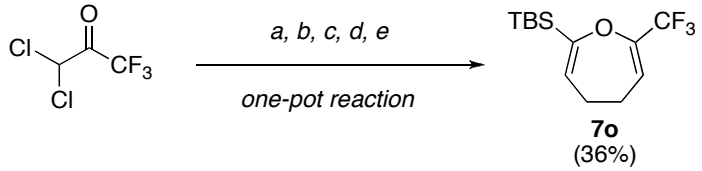
Scheme 4. CF_3 effect on the Cope rearrangement



8a (R = H) 11 h **9a** (87% yield)
8b (R = *i*-Pr) 4 h **9b** (83% yield)
6a (R = CF_3) 12 h **7a** (93% yield)

Versatility of the present approach is demonstrated by one-pot synthesis of **7o** from 1,1-dichloro-3,3,3-trifluoropropan-2-one. Thus, treatment of the ketone with 4 molar equivalents of vinyllithium and then LiTMP in THF at –98 °C followed by the addition of TBSOTf generated the corresponding divinyloxirane in situ. Quenching of excess TBSOTf with MeOH and heating the resulting mixture at 60 °C gave **7o** in 36% yield as shown in Scheme 5.

Scheme 5. One-pot synthesis of **7o** from 1,1-dichloro-3,3,3-trifluoropropan-2-one



7o
(36%)

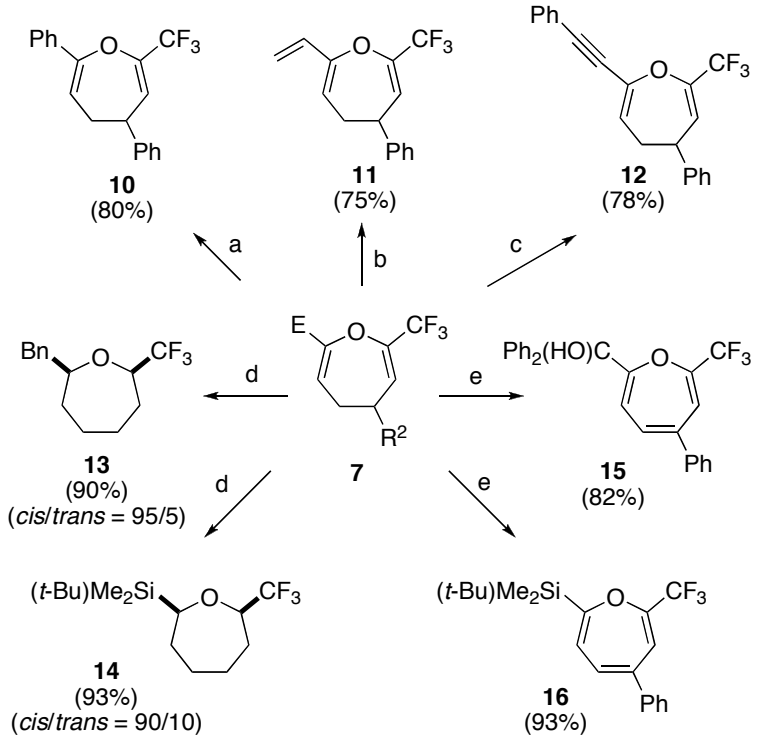
Reagents and conditions: (a) vinyllithium (4 eq.), THF, –98 °C; (b) LiTMP (3 eq.), –98 °C; (c) *t*-BuMe$_2$SiOTf (3 eq.), –98 °C to –78 °C; (d) MeOH, –78 °C; (e) 60 °C.

Demonstrated in Scheme 6 are synthetic transformations of the rearranged products (**7**), involving cross-coupling reaction with the aid of a metal moiety introduced as substituent E, reduction to oxepanes, and oxidation to oxepines. Cross-coupling reaction of stannane **7c** and boronate **7f** with aryl, alkenyl, and alkynyl halides underwent smoothly in the presence of a Pd catalyst to produce **10**-**12** in good yields.[15] Hydrogenation of **7m** and **7o** with Pd/C under H_2 (1 atm) proceeded stereoselectively to give **13** and **14**, respectively, with high *cis* selectivity,[16] while **7g** and **7h** were dehydrogenated efficiently to afford **15** and **16** in good yields when DDQ was employed as an oxidant in toluene.

CONCLUSION

In summary, we have developed a facile synthetic route to 2-CF_3-substituted seven-membered oxacycles, which involves *cis*-selective preparation of 2,3-bis(alkenyl)oxiranes substituted by a CF_3 group and an arbitrarily incorporated substituent E, and their Cope rearrangement. The present methodology allows us to synthesize conveniently diverse 2-trifluoromethylated oxepanes and oxepins, which may contribute to exploration and development of potent pharmaceuticals and agrochemicals.

Scheme 6. Synthetic transformation of **7**



Reagents and conditions: (a) iodobenzene, $Pd_2(dba)_3$ (2.5 mol%)/P(*t*-Bu)$_3$ (10 mol%), CsF, dioxane, 100 °C; (b) vinyl bromide, $Pd_2(dba)_3$ (2.5 mol%)/P(*t*-Bu)$_3$ (10 mol%), KOH, THF, rt; (c) bromo(phenyl)acetylene, $Pd_2(dba)_3$ (2.5 mol%)/P(*t*-Bu)$_3$ (10 mol%), KOH, THF, rt; (d) H_2 (1 atm), Pd/C, MeOH, rt; (e) DDQ, toluene, 100 °C.

EXPERIMENTAL

General information. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on Varian Mercury 200 (^{1}H, 200 MHz; ^{13}C, 50 MHz; ^{19}F, 188 MHz), JEOL EX-270 (^{1}H, 270 MHz; ^{13}C, 67.5 MHz), and JEOL JNM-EPC 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) spectrometers in $CDCl_3$ with chemical shifts referenced to internal standards Me_4Si (0 ppm, ^{1}H), $CDCl_3$ (7.26 ppm, ^{1}H; 77.0 ppm, ^{13}C), $CFCl_3$ (0 ppm, ^{19}F). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; brs, broad singlet for ^{1}H and ^{19}F NMR data. Infrared spectra were recorded on a Shimadzu FTIR-8100 spectrometer. Mass spectra were performed on JEOL JMS-700 spectrometer. Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University. Melting points were determined using a Yanagimoto Micro Melting Point Apparatus. TLC analyses were performed by means of Merck Kieselgel 60 F_{254} and column chromatography was carried out using Merck Kieselgel 60 (230-400 mesh). Preparative HPLC was carried out with a Japan Analytical Industry Co., Ltd, LC-908 chromatograph using a JAIGEL–1H and –2H GPC columns.

Preparation of **4**: dichlorohydrins **4** were prepared according to the procedure described in the previous publication (Ref. 7a and 7b). Data of **4a** is reported in ref. 7b.

1,1-Dichloro-2-trifluoromethylbut-3-en-2-ol (4b): 80% yield, a colorless oil. Bp 52 ºC/2.2 kPa. R_f 0.30 (pentane/Et_2O 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 3.41 (brs, 1H), 5.71 (d, *J* = 10.8 Hz, 1H), 5.83 (d, *J* = 17.0 Hz, 1H), 5.93 (s, 1H), 6.14 (dd, *J* = 17.0, 10.8 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 72.3, 79.0 (q, *J* = 27.7 Hz), 122.6, 126.1 (q, *J* = 285.0 Hz), 128.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –75.5. IR (neat): 3568, 3103, 3007, 1415, 1352, 1273, 1225, 1190, 1151, 1099, 1051, 988, 951, 812, 779 cm^{-1}. EIMS (70 eV) *m*/*z*: 212 (0.04, M^++4), 210 (0.3, M^++2), 208 (0.4, M^+), 125 (100). Anal. Calcd for $C_5H_5Cl_2F_3O$: C, 28.73; H, 2.41. Found: C, 28.77; H, 2.47.

1,1-Dichloro-3-phenyl-2-trifluoromethylbut-3-en-2-ol (4c): 20% yield, a pale yellow oil. R_f 0.40 (hexane/Et_2O 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 3.10 (brs, 1H), 5.51 (s, 1H), 5.83 (s, 1H), 6.13 (s, 1H), 7.34–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 73.9, 80.6 (q, *J* = 28.6 Hz), 121.3, 123.4 (q, *J* = 287.8 Hz), 128.3, 128.5, 129.4, 137.0, 144.0. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.4. IR (neat): 3545, 3086, 3057, 2959, 2858, 1625, 1598, 1493, 1443, 1360, 1190, 1144, 1103, 1089, 1076, 1030, 1003, 966, 936, 822, 777, 754 cm^{-1}. EIMS (70 eV) *m*/*z*: 288 (2, M^++4), 286 (13, M^++2), 285 (3, M^++1), 284 (21, M^+), 201 (100). Anal. Calcd for $C_{11}H_9Cl_2F_3O$: C, 46.34; H, 3.18. Found: C, 46.10; H, 3.36.

3,3-Dichloro-2-(5,6-dihydro-4*H*-pyran-2-yl)-1,1,1-trifluoropropan-2-ol (4d): 55% yield, a colorless oil. R_f 0.30 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.82 (m, 1H), 2.12 (m, 1H), 3.35 (s, 1H), 4.04 (dd, *J* = 4.6, 5.8 Hz, 2H), 5.34 (t, *J* = 3.9 Hz, 1H), 6.20 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 19.7, 21.7, 67.0, 72.6, 79.2 (q, *J* = 28.6 Hz), 101.2, 124.1 (q, *J* = 287.2 Hz), 146.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –73.4. IR (neat): 3535, 3026, 2935, 2881 2852, 1676, 1465, 1350, 1271, 1188, 1159, 1058, 918, 848, 707 cm^{-1}. EIMS (70 eV) *m*/*z*: 268 (2, M^++4), 266 (8, M^++2), 264 (12, M^+), 181 (100). Anal. Calcd for $C_8H_9Cl_2F_3O_2$: C, 36.25; H, 3.42. Found: C, 36.52; H, 3.43.

General procedure for the preparation of *cis*-bis(alkenyl)oxiranes 6: To a solution of an alkenyllithium (3.0 mmol) in THF (5 mL) was added dichlorohydrin **4** (1.0 mmol) at –98 °C and then freshly prepared LiTMP (3.0 mmol, 0.67 M in THF) at –98 °C. The resulting solution was stirred at –98 °C for 3~6 h and then treated with an electrophile (1.5~3 mmol) at –98 °C. The solution was warmed gradually to –78 °C and quenched with saturated aq. NH_4Cl solution at –78 °C. The aqueous layer was extracted with Et_2O three times. The combined organic layer was washed with saturated aq. NaCl solution and dried over anhydrous $MgSO_4$. Removal of the organic solvent under reduced pressure followed by column chromatography on silica gel gave **6**.

(*E*)-(*3S*,4R)-3,4-Epoxy-1-phenyl-3-trifluoromethylhexa-1,5-diene (6a):** 77% yield, a colorless oil. R_f 0.48 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 3.90 (d, *J* = 6.2 Hz, 1H), 5.43-5.78 (m, 3H), 6.28 (d, *J* = 16.0 Hz, 1H), 6.89 (d, *J* = 16.0 Hz, 1H), 7.24–7.53 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 61.9, 62.4 (q, *J* = 36.5 Hz), 115.1, 123.1 (q, *J* = 279.0 Hz), 124.2, 126.9, 128.7, 128.8, 129.7, 135.1, 137.0. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –76.0. IR (neat): 3086, 3063, 1655, 1579, 1497, 1450,

1377, 1344, 1302, 1261, 1151, 1074, 982, 930, 883, 839, 748 cm^{-1}. Anal. Calcd for $C_{13}H_{11}F_3O$: C, 65.00; H, 4.62. Found: C, 65.21; H, 4.74.

(*E*)-(*3S*,4R)-3,4-Epoxy-4-methyl-1-phenyl-3-trifluoromethylhexa-1,5-diene (6b):** 72% yield, a colorless oil. R_f 0.48 (hexane/EtOAc 10:1). ^1H NMR (200 MHz, $CDCl_3$, δ): 1.71 (s, 3H), 5.31 (dd, *J* = 10.8, 1.2 Hz, 1H), 5.39 (dd, *J* = 16.0, 1.2 Hz, 1H), 5.72 (dd, *J* = 16.0, 10.8 Hz, 1H), 6.20 (d, *J* = 16.0 Hz, 1H), 6.75 (d, *J* = 16.0 Hz, 1H), 7.22–7.49 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 15.9, 65.6, 66.5 (q, *J* = 35.5 Hz), 117.8, 119.8, 123.8 (q, *J* = 281.2 Hz), 126.8, 128.6, 128.8, 135.3, 135.9, 136.0. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –66.9. IR (neat): 3030, 2943, 1653, 1497, 1451, 1417, 1387, 1313, 1294, 1263, 1184, 1130, 1072, 1020, 988, 972, 935, 891 cm^{-1}. Anal. Calcd for $C_{14}H_{13}F_3O$: C, 66.14; H, 5.15. Found: C, 66.23; H, 5.09.

(*E*)-(*3S*,4S)-3,4-Epoxy-1-phenyl-3-trifluoromethyl-4-trimethylstannylhexa-1,5-diene (6c):** 64% yield, a pale yellow oil. R_f 0.56 (hexane/EtOAc 10:1). ^1H NMR (200 MHz, $CDCl_3$, δ): 0.26 (s, 9H), 5.00-5.13 (m, 2H), 5.60–5.74 (m, 1H), 6.14 (d, *J* = 16.0 Hz, 1H), 6.70 (d, *J* = 16.0 Hz, 1H), 7.16–7.44 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): –8.16, 64.6 (q, *J* = 34.8 Hz), 70.0, 115.0, 117.2, 124.3 (q, *J* = 277.7 Hz), 126.7, 128.3, 128.6, 135.6, 136.2, 136.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.1. IR (neat): 3086, 3061, 3028, 2984, 2918, 1652, 1601, 1497, 1450, 1406, 1360, 1292, 1261, 1174, 1153, 1111, 1061, 968, 914, 895, 773, 756 cm^{-1}. Anal. Calcd for $C_{16}H_{19}F_3OSn$: C, 47.68: H, 4.75. Found: C, 47.86; H, 5.05.

(*E*)-(*3S*,4S)-3,4-Epoxy-1-phenyl-3-trifluoromethyl-4-trimethylsilylhexa-1,5-diene (6d):** 77% yield, a pale yellow oil. R_f 0.55 (hexane/EtOAc 10:1). ^1H NMR (200 MHz, $CDCl_3$, δ): –0.20 (s, 9H), 5.07 (ddd, *J* = 16.4, 10.8, 1.6 Hz, 1H), 5.16 (ddd, *J* = 16.4, 10.8, 1.6 Hz, 1H), 5.65 (dd, *J* = 16.4, 10.8 Hz, 1H), 6.10 (d, *J* = 16.0 Hz, 1H), 6.65 (d, *J* = 16.0 Hz, 1H), 7.26–7.43 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): –1.15, 65.9 (q, *J* = 35.5 Hz), 67.0, 116.2, 117.8, 124.1 (q, *J* = 277.9 Hz), 126.7, 128.3, 128.6, 134.9, 135.6, 136.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): -69.8. IR (neat): 3086, 3063, 3030, 2959, 2905, 1685, 1638, 1497, 1450, 1406, 1361, 1292, 1253, 1178, 1153, 1109, 986, 968, 920, 845, 758 cm^{-1}. Anal. Calcd for $C_{16}H_{19}F_3OSi$: C, 61.51; H, 6.13. Found: C, 61.76; H, 6.18.

(*E*)-(*3S*,4S)-3,4-Epoxy-4-methoxycarbonyl-1-phenyl-3-trifluoromethylhexa-1,5-diene (6e):** 70% yield, a colorless oil. R_f 0.20 (hexane/Et_2O 10:1). ^1H NMR (200 MHz, $CDCl_3$, δ): 3.85 (s, 3H), 5.48–5.88 (m, 3H), 6.19 (d, *J* = 16.2 Hz, 1H), 6.82 (d, *J* = 16.2 Hz, 1H), 7.24–7.50 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 53.0, 66.4 (q, *J* = 36.5 Hz), 67.4, 113.9, 122.4 (q, *J* = 280.3 Hz), 123.4, 127.1, 127.7, 128.7, 129.1, 134.6, 138.6, 165.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.4. IR (neat): 3030, 2957, 2851, 1655, 1603, 1580, 1746, 1499, 1439, 1387, 1261, 1170, 1142, 1063, 970, 945, 856 cm^{-1}. Anal. Calcd for $C_{15}H_{13}F_3O_3$: C, 60.40; H, 4.39. Found: C, 60.31, H, 4.56.

(*E*)-(*3S*,4R)-3,4-Epoxy-1-phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-trifluoromethylhexa-1,5-diene (6f):** 72% yield, an off-white solid. Mp 57 ºC (dec). ^1H NMR (200 MHz,

$CDCl_3$, δ): 1.32 (s, 12H), 5.32–5.74 (m, 3H), 6.15 (d, *J* = 16.0 Hz, 1H), 6.82 (d, *J* = 16.0 Hz, 1H), 7.28–7.55 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 24.6, 65.6 (q, *J* = 33.5 Hz), 68.1, 85.0, 115.9, 121.2, 123.5 (q, *J* = 280.6 Hz), 126.8, 128.6 (2C), 132.7, 135.2, 137.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –73.1. IR (KBr): 3084, 3059, 2963, 1647, 1489, 1460, 1297, 1172, 1147, 1106, 954, 763 cm^{-1}. Anal. Calcd for $C_{19}H_{22}BF_3O_3$: C, 62.32; H, 6.06. Found: C, 62.12; H, 6.01.

(*E*)-(*3S,*4S**)-3,4-Epoxy-4-(hydroxydiphenyl)methyl-1-phenyl-3-trifluoromethylhexa-1,5-diene (6g):** 62% yield, an off-white solid. R_f 0.28 (hexane/EtOAc 10:1). Mp 90 ºC (dec). ^1H NMR (200 MHz, $CDCl_3$, δ): 3.51 (brs, 1H), 4.88–5.00 (m, 2H), 5.58 (dd, *J* = 11.8, 10.2 Hz, 1H), 6.13 (d, *J* = 16.0 Hz, 1H), 6.68 (d, *J* = 16.0 Hz, 1H), 7.17–7.63 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 67.8 (q, *J* = 36.5Hz), 76.3, 78.8, 118.6, 119.6, 122.0 (q, *J* = 279.1 Hz), 126.7, 127.3, 127.5, 127.6, 127.9, 128.1(2C), 128.6, 128.7, 132.4, 135.3, 136.9, 143.0, 145.9. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –63.2 (d, *J* = 3.4 Hz). IR (KBr): 3583, 3061, 2976, 2868, 1655, 1601, 1491, 1408, 1285, 1138, 1072, 970, 845, 750, 700 cm^{-1}. Anal. Calcd for $C_{26}H_{21}F_3O_2$: C, 73.92; H, 5.01. Found: C, 73.65; H, 5.11.

(*E*)-(*3S,*4R**)-3,4-Epoxy-1,5-diphenyl-3-trifluoromethylhexa-1,5-diene (6i):** 86% yield, a colorless oil. R_f 0.48 (hexane/EtOAc 10:1). ^1H NMR (200 MHz, $CDCl_3$, δ): 4.28 (s, 1H), 5.36 (dd, *J* = 1.2, 1.0 Hz, 1H), 5.67 (dd, *J* = 1.0, 0.8 Hz, 1H), 6.12 (d, *J* = 16.0 Hz, 1H), 6.81 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 61.7, 62.5 (q, *J* = 35.4 Hz), 113.4, 115.4, 123.3 (q, *J* = 278.1 Hz), 125.5, 126.9, 128.5, 128.6, 128.7, 128.8, 135.2, 136.7, 137.7, 137.8. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –75.0 (major), –68.7 (minor). IR (neat): 3084, 3059, 3030, 1651, 1576, 1497, 1448, 1418, 1344, 1319, 1294, 1261, 1184, 1153, 1074, 974, 935, 914, 840, 777, 748 cm^{-1}. Anal. Calcd for $C_{19}H_{15}F_3O$: C, 72.14; H, 4.78. Found: C, 72.41; H, 4.80.

(*E*)-(*3S,*4R**)-3,4-Epoxy-1,5-diphenyl-4-trimethylsilyl-3-trifluoromethylhexa-1,5-diene (6j)**: 75% yield, a pale yellow oil. R_f 0.52 (hexane/EtOAc 10:1). ^1H NMR (200 MHz, $CDCl_3$, δ): 0.16 (s, 9H), 5.30 (d, *J* = 1.0 Hz, 1H), 5.69 (d, *J* = 1.0 Hz, 1H), 6.33 (d, *J* = 15.8 Hz, 1H), 6.84 (d, *J* = 15.8 Hz, 1H), 7.27–7.51 (m, 10H). ^{13}C NMR (67.5MHz, $CDCl_3$, δ): –0.75, 66.4 (q, *J* = 35.5 Hz), 68.2, 112.5, 115.6, 122.4 (q, *J* = 278.3 Hz), 125.7, 126.7, 128.0, 128.1, 128.4, 128.5, 132.0, 135.5, 136.5, 136.9. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –69.7. IR (neat): 3059, 3028, 2956, 1292, 1253, 1180, 1153, 1031, 906, 846 cm^{-1}. Anal. Calcd for $C_{22}H_{23}F_3OSi$: C, 68.01; H, 5.97. Found: C, 68.05; H, 5.91.

(*E*)-(*3S,*4R**)-3,4-Epoxy-4-trimethylsilyl-5-phenyl-3-trifluoromethylhexa-1,5-diene (6k)**: 71% yield, a pale yellow oil. R_f 0.26 (hexane). ^1H NMR (200 MHz, $CDCl_3$, δ): 0.04 (s, 9H), 5.13 (d, *J* = 1.0 Hz, 1H), 5.31 (d, *J* = 11.0 Hz, 1H), 5.45 (d, *J* = 17.0 Hz, 1H), 5.62 (d, *J* = 1.0 Hz, 1H), 5.92 (dd, *J* = 17.0, 11.0 Hz, 1H), 7.26–7.36 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –0.78, 66.2 (q, *J* = 34.8 Hz), 67.4, 112.3, 122.2, 124.6, 125.7, 126.4 (q, *J* = 275.2 Hz), 128.4, 128.5, 136.8, 144.1. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –69.8. IR (neat): 3084, 3059, 3028, 2956, 1497, 1253, 1178, 1151, 908, 846 cm^{-1}. Anal.

Calcd for $C_{16}H_{19}F_3OSi$: C, 61.51; H, 6.13. Found: C, 61.62; H, 6.13.

(*3S, *4R**)-3,4-Epoxy-2-phenyl-3-trifluoromethylhexa-1,5-diene (6l):** 80% yield, a colorless oil. R_f 0.55 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 4.00 (d, *J* = 7.2 Hz, 1H), 5.44–5.84 (m, 2H), 5.66 (s, 1H), 5.85 (s, 1H), 7.29–7.42 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 61.1, 63.6 (q, *J* = 35.5 Hz), 120.8, 122.9 (q, *J* = 280.6 Hz), 124.2, 126.6, 128.4, 128.5, 130.5, 136.6, 137.4. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –73.7. IR (neat): 3088, 3058, 3030, 2961, 2932, 2860, 1881, 1624, 1576, 1497, 1447, 1379, 1346, 1300, 1177, 1148, 1074, 988, 932, 858, 799, 780, 742, 704 cm^{-1}. Anal. Calcd for $C_{13}H_{11}F_3O$: C, 65.00; H, 4.62. Found: C, 65.26, H, 4.64

(*E*)-(*3S,*4R**)-3,4-Epoxy-4-benzyl-3-tri-fluoromethylhexa-1,5-diene (6m)**: 60% yield, a colorless oil. R_f 0.48 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 3.30 (q, 2H), 5.16 (dd, *J* = 17.2, 1.2 Hz, 1H), 5.26 (dd, *J* = 11.0, 1.2 Hz, 1H), 5.37–5.65 (m, 3H), 5.84 (dd, *J* = 17.2, 11.0 Hz, 1H), 7.22–7.34 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 36.4 (q, *J* = 3.3 Hz), 67.0 (q, *J* = 34.8 Hz), 68.9, 120.3, 121.7 (q, *J* = 280.0 Hz), 122.0, 126.7, 128.2 (2C), 129.4, 132.7, 136.0. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –66.2. IR (neat): 3089, 3032, 1496, 1456, 1419, 1296, 1174, 1151, 1018, 933 cm^{-1}. Anal. Calcd for $C_{14}H_{13}F_3O$: C, 66.14; H, 5.15. Found: C, 66.31; H, 5.41.

(*3S,*4S**)-3,4-Epoxy-3-trifluoromethyl-4-trimethylstannylhexa-1,5-diene (6n):** 56% yield, a colorless oil. R_f 0.64 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.24 (m, 9H), 4.94 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.11 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.35–5.50 (m, 2H), 5.63 (dd, *J* = 17.0, 11.0 Hz, 1H), 5.79 (dd, *J* = 17.0, 11.0 Hz, 1H), ^{13}C NMR (125 MHz, $CDCl_3$, δ): –8.16, 64.5 (q, *J* = 34.5 Hz), 69.2, 114.8, 121.7, 124.2 (q. *J* = 279.3 Hz), 126.4, 136.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.2. IR (neat): 3096, 2984, 2922, 2856, 1628, 1412, 1367, 1296, 1157, 1117, 1022, 984, 916, 880, 777 cm^{-1}. Anal. Calcd for $C_{10}H_{15}F_3OSn$: C, 36.74; H, 4.62. Found: C, 37.02; H, 4.50.

(*3S,*4S**)-4-(*tert*-Butyldimethylsilyl)-3,4-epoxy-3-trifluoromethylhexa-1,5-diene (6o):** 46% yield, a colorless oil. R_f 0.40 (hexane). ^{1}H NMR (270 MHz, $CDCl_3$, δ): 0.07 (s, 6H), 0.91 (s, 9H), 4.98 (dd, *J* = 17.0, 1.6 Hz, 1H), 5.12 (dd, *J* = 11.0, 1.6 Hz, 1H), 5.29 (d, *J* = 17.0 Hz, 1H), 5.41 (d, *J* = 11.0 Hz, 1H), 5.58 (dd, *J* = 17.0, 11.0 Hz, 1H), 5.70 (dd, *J* = 17.0, 11.0 Hz, 1H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –3.40 (q, *J* = 4.1 Hz), 18.7, 26.6, 27.4, 66.2 (q, *J* = 35.6 Hz), 116.3, 122.4, 125.8 (q. *J* = 276.9 Hz), 126.8, 136.0. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –69.3. IR (neat): 3095, 2956, 2933, 2860, 1635, 1474, 1412, 1363, 1182, 1154, 1026, 939, 843 cm^{-1}. Anal. Calcd for $C_{13}H_{21}F_3OSi$: C, 56.09; H, 7.60. Found: C, 56.34; H, 7.42.

(*E*)-(*3S,*4R**)-3,4-Epoxy-5-ethoxy-1-phenyl-3-trifluoromethylhexa-1,5-diene (6p):** 67% yield, a colorless oil. R_f 0.46 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.24 (t, *J* = 7.0 Hz, 3H), 3.68 (q, *J* = 7.0 Hz, 2H), 3.90 (s, 1H), 4.15 (d, *J* = 2.4 Hz, 1H), 4.19 (d, *J* = 2.4 Hz, 1H), 6.17 (d, *J* = 16.2 Hz, 1H), 6.84 (d, *J* = 16.2 Hz, 1H), 7.22–7.48 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 14.2, 59.4, 61.6

(q, *J* = 35.5 Hz), 63.5, 85.5, 114.1, 122.9 (q, *J* = 279.3 Hz), 126.8, 128.6, 128.7, 133.7, 137.4, 153.4. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –75.3 (*cis*), –69.3 (*trans*). IR (neat): 3086, 3061, 3030, 2984, 2932, 2905, 2887, 1668, 1638, 1498, 1481, 1450, 1344, 1317, 1263, 1186, 1157, 1068, 972, 935, 866, 820, 748 cm^{-1}. Anal. Calcd for $C_{15}H_{15}F_3O_2$: C, 63.38; H, 5.32. Found: C, 63.11; H, 5.47.

1-(5,6-Dihydro-4*H*-pyran-2-yl)-1,2-epoxy-4*E*-phenyl-2-(trifluoromethyl)buta-1,3-diene (6q): 25% yield, a colorless oil. R_f 0.33 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.70 (m, 2H), 1.98 (m, 2H), 3.83 (s, 1H), 3.95 (t, *J* = 5.2 Hz, 2H), 4.88 (t, *J* = 3.9 Hz, 1H), 6.15 (d, *J* = 16.2 Hz, 1H), 6.79 (d, *J* = 16.2 Hz, 1H), 7.29–7.45 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 19.7, 21.5, 59.0, 61.6 (q, *J* = 35.3 Hz), 66.4, 101.4, 114.6, 124.1 (q, *J* = 278.0 Hz), 126.8, 128.5, 128.7, 135.0 137.0, 145.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –75.3. IR (neat): 3061, 3028, 2933 2874, 1684, 1448, 1344, 1294, 1188, 1153, 1062, 968, 933, 748, 690 cm^{-1}. Anal. Calcd for $C_{16}H_{15}F_3O_2$: C, 64.86; H, 5.10. Found: C, 65.06; H, 5.14.

1-(5,6-Dihydro-4*H*-pyran-2-yl)-1,2-epoxy-1-(trifluoromethyl)buta-1,3-diene (6r): 61% yield, a colorless oil. R_f 0.45 (hexane/EtOAc 10:1). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 1.86 (m, 2H), 2.09 (m, 2H), 3.52 (d, *J* = 7.8 Hz, 1H), 4.05 (m, 2H), 5.10 (t, *J* = 4.0 Hz, 1H), 5.47–5.87 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 19.8, 22.0, 60.1, 61.1 (q, *J* = 36.2 Hz), 66.8, 103.5, 123.7, 124.1 (q, *J* = 279.2 Hz), 130.0, 144.2. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –74.9 (*cis*), –67.2 (*trans*). IR (neat): 3099, 2935, 2880, 1676, 1448, 1390, 1352, 1306, 1172, 1149, 1097 1055, 995, 993, 733 cm^{-1}. Anal. Calcd for $C_{10}H_{11}F_3O_2$: C, 54.55; H, 5.04. Found: C, 54.83; H, 5.27.

1-(5,6-Dihydro-4*H*-pyran-2-yl)-1-(trifluoromethyl)-2-(trimethylsilyl)-buta-1,3-diene (6s): 69% yield, a pale yellow oil. R_f 0.50 (hexane/EtOAc 10:1). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.17 (s, 9H), 1.66–1.88 (m, 2H), 1.95–2.15 (m, 2H), 3.94 (m, 2H), 4.91 (t, *J* = 3.9 Hz, 1H), 5.01 (dd, *J* = 17.0, 1.8 Hz, 1H), 5.07 (dd, *J* = 11.0, 1.8 Hz, 1H), 5.76 (dd, *J* = 17.0, 11.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): –1.45, 19.6, 22.1, 64.7, 65.6 (q, *J* = 36.2 Hz), 66.5, 102.5, 114.9, 124.7 (q, *J* = 278.5 Hz), 133.9, 145.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –68.4 (*cis*), –66.1 (*trans*). IR (neat): 2953, 2934, 2851, 1684, 1301, 1288 1254, 1163, 1086, 1061, 916, 845, 762, 665 cm^{-1}. Anal. Calcd for $C_{13}H_{19}F_3O_2Si$: C, 53.40; H, 6.55. Found: C, 53.47; H, 6.71.

General procedure for the preparation of 7: A screw-capped test tube was charged with **6** (0.5 mmol) and CCl_4 (3 mL). Then the test tube was capped, sealed tightly, and heated in an oil bath. The progress of the rearrangement was monitored by ^{19}F NMR spectra of the aliquot of the reaction mixture. When **6** was thoroughly consumed, heating was stopped and the solvent was evaporated under reduced pressure to give the crude product which was purified by column chromatography on silica gel, giving rise to **7**. The isolated yields were calculated based on *cis*-bis(alkenyl)oxiranes in cases of **6e**, **6i**, **6p**, **6r**, and **6s**: *trans*-isomer of which did not undergo the rearrangement under the conditions and were easily separated

from the rearranged products with quantitative recovery by silica gel column chromatography.

4,5-Dihydro-4-phenyl-2-trifluoromethyloxepin (7a): 93% yield, a colorless oil. R_f 0.50 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.44–2.61 (m, 2H), 3.86–3.88 (m, 1H), 4.99–5.09 (m, 1H), 5.81 (d, *J* = 4.2 Hz, 1H), 6.39 (d, *J* = 7.2 Hz, 1H), 7.19–7.39 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 33.9, 42.9, 109.6, 114.2 (q, *J* = 3.4 Hz), 120.1 (q, *J* = 272.6 Hz), 127.0, 127.2, 128.8, 141.6 (q, *J* = 33.4 Hz), 142.9, 144.1. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.3 (d, *J* = 2.6 Hz). IR (neat): 3086, 3063, 3030, 2916, 2858, 1688, 1665, 1605, 1493, 1454, 1404, 1373, 1294, 1242, 1199, 1132, 1076, 1032, 995, 924, 600, 756, 735 cm^{-1}. EIMS (70 eV) *m*/*z*: 242 (0.9, M^++2), 241 (10, M^++1), 240 (72, M^+), 171 (45, M^+–CF_3), 115 (100). Anal. Calcd for $C_{13}H_{11}F_3O$: C, 65.00; H, 4.62. Found: C, 65.05; H, 4.62.

4,5-Dihydro-7-methyl-4-phenyl-2-trifluoromethyloxepin (7b): 85% yield, a colorless oil. R_f 0.51 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.88 (s, 3H), 2.40–2.55 (m, 2H), 3.69–3.74 (m, 1H), 4.99 (t, *J* = 6.6 Hz, 1H), 5.69 (d, *J* = 3.8 Hz, 1H), 7.15–7.37 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 20.5, 32.7, 42.2, 107.3, 114.3, 120.3 (q, *J* = 273.2 Hz), 126.9, 127.3, 128.6, 141.2, 141.7 (q, *J* = 33.1 Hz), 154.2. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.7 (d, *J* = 1.7 Hz). IR (neat): 3086, 3063, 3030, 2953, 2922, 2880, 2585, 1686, 1603, 1493, 1452, 1379, 1302, 1246, 1133, 1053, 1009, 972, 924, 885, 833, 758, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 256 (1, M^++2), 255 (17, M^++1), 254 (100, M^+), 157 (60). Anal. Calcd for $C_{14}H_{13}F_3O$: C, 66.14; H, 5.15. Found: C, 66.24; H, 5.15.

4,5-Dihydro-4-phenyl-2-trifluoromethyl-7-trimethylstannyloxepin (7c): 88% yield, a colorless oil. R_f 0.60 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.15 (m, 9H), 2.49 (m, 1H), 2.68 (m, 1H), 3.77–3.79 (m, 1H), 5.27 (dd, *J* = 7.8, 6.0 Hz, 1H), 5.60 (d, *J* = 3.6 Hz, 1H), 7.17–7.43 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): –9.57, 34.5, 42.9, 113.6, 120.3 (q, *J* = 274.5 Hz), 123.6, 126.8, 127.3, 128.6, 143.0 (q, *J* = 32.6 Hz), 144.3, 166.9. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.6 (d, *J* = 1.9 Hz). IR (neat): 3028, 2914, 2855, 1682, 1628, 1603, 1493, 1454, 1373, 1294, 1240, 1188, 1130, 1078, 1020, 918, 883, 756 cm^{-1}. EIMS (70 eV) *m*/*z*: 390 (6, M^+–13), 389 (39, M^+–14), 388 (15, M^+–15), 220 (100). Anal. Calcd for $C_{16}H_{19}F_3OSn$: C, 47.68; H, 4.75. Found: C, 47.90; H, 4.77.

4,5-Dihydro-4-phenyl-2-tri-fluoromethyl-7-trimethylsilyloxepin (7d): 92% yield, a pale yellow oil. R_f 0.60 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.15 (s, 9H), 2.53–2.66 (m, 2H), 3.73–3.79 (m, 1H), 5.47 (t, *J* = 6.0 Hz, 1H), 5.65 (d, *J* = 3.8 Hz, 1H), 7.17–7.38 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): –2.59, 34.2, 42.7, 113.1, 120.5 (q, *J* = 273.6 Hz), 121.9, 126.9, 127.3, 128.6, 142.0 (q, *J* = 41.0 Hz), 144.3, 164.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.3 (d, *J* = 2.6 Hz). IR (neat): 3065, 3030, 2959, 2858, 1682, 1602, 1493, 1454, 1375, 1315, 1250, 1190, 1132, 1096 1032, 991, 889, 843, 752, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 314 (1, M^++2), 313 (6, M^++1), 312 (22, M^+), 73 (100). Anal. Calcd for $C_{16}H_{19}F_3O$: C, 61.51; H, 6.13. Found: C, 61.79; H, 6.13.

4,5-Dihydro-7-methoxylcarbonyl-4-phenyl-2-trifluoromethyloxepin (7e): 96% yield, a colorless oil.

R_f 0.20 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.49–2.74 (m, 2H), 3.63–3.81 (m, 1H), 3.72 (s, 3H), 5.78 (d, *J* = 4.0 Hz, 1H), 6.50 (dd, *J* = 7.2, 6.0 Hz, 1H), 7.08–7.30 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 32.8, 41.0, 52.5, 115.6, 119.8 (q, *J* = 273.0 Hz), 121.7, 127.1, 127.3, 128.9, 141.7 (q, *J* = 34.6 Hz), 142.9, 145.9, 162.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.3 (d, *J* = 2.6 Hz). IR (neat): 3065, 3030, 2955, 2912, 1742, 1686, 1664, 1602, 1493, 1439, 1350, 1319, 1275, 1196, 1138, 1061, 1032, 999, 968, 789, 756, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 300 (0.2, M^++2), 299 (3, M^++1), 298 (13, M^+), 115 (100). Anal. Calcd for $C_{15}H_{13}F_3O_3$: C, 60.40; H, 4.39. Found: C, 60.48; H, 4.58.

4,5-Dihydro-4-phenyl-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-trifluoromethyloxepin (7f): 99% yield, an off-white solid. R_f 0.36 (hexane/EtOAc 10:1). Mp 73–74 ºC. ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.24 (s, 12H), 2.43 (m, 1H), 2.64 (m, 1H), 3.71–3.77 (m, 1H), 5.67 (d, *J* = 3.6 Hz, 1H), 5.94 (dd, *J* = 7.8, 5.0 Hz, 1H), 7.09–7.30 (m, 5H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 24.7, 34.7, 42.1, 84.3, 114.4, 120.2 (q, *J* = 273.6 Hz), 125.9, 126.9, 127.1, 128.8, 140.0, 142.3 (q, *J* = 33.6 Hz), 152.4. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.3 (d, *J* = 2.6 Hz). IR (KBr): 3086, 3063, 3030, 2980, 2934, 1689, 1659, 1603, 1493, 1454, 1415, 1371, 1294, 1242, 1111, 1030, 995, 961, 923, 910, 897, 856, 839, 758, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 368 (0.2, M^++2), 367 (1, M^++1), 366 (5, M^+), 365 (2, M^+–1), 84 (100). Anal. Calcd for $C_{19}H_{22}BF_3O_3$: C, 62.32; H, 6.06. Found: C, 62.16; H, 6.06.

4,5-Dihydro-7-(hydroxydiphenyl)methyl-4-phenyl-2-trifluoromethyloxepin (7g): 95% yield, an off-white solid. R_f 0.28 (hexane/EtOAc 10:1). Mp 101–102 ºC. ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.39–2.67 (m, 2H), 3.07 (brs, 1H), 3.62–3.76 (m, 1H), 5.00 (dd, *J* = 7.8, 6.0 Hz, 1H), 5.69 (d, *J* = 3.9 Hz, 1H), 7.09–7.41 (m, 15H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 32.2, 42.1, 81.3, 112.8, 114.5, 120.1 (q, *J* = 273.6 Hz), 127.1, 127.3, 127.61, 127.66, 127.7, 127.90 (2C), 127.91, 128.7, 141.5 (q, *J* = 33.6 Hz), 143.3, 143.4, 143.6, 159.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –71.8 (d, *J* = 1.3 Hz). IR (neat): 3595, 3462, 3086, 3061, 3028, 2959, 2920, 2860, 1682, 1601, 1493, 1448, 1377, 1344, 1317, 1300, 1244, 1196, 1136, 1032, 1016, 908, 851, 826, 799, 752, 735, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 424 (0.1, M^++2), 423 (1, M^++1), 422 (4, M^+), 222 (100). Anal. Calcd for $C_{26}H_{21}F_3O_2$: C, 73.92; H, 5.01. Found: C, 73.68; H, 5.17.

7-(*tert*-Butyldimethyl)silyl-4,5-dihydro-4-phenyl-2-trifluoromethyloxepin (7h): 55% yield, a colorless oil. R_f 0.60 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.10 (s, 6H), 0.93 (s, 9H), 2.48–2.73 (m, 2H), 3.70–3.77 (m, 1H), 5.41 (dd, *J* = 7.6, 5.8 Hz, 1H), 5.63 (d, *J* = 3.8 Hz, 1H), 7.16–7.44 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): –6.71, 16.6, 27.3, 34.7, 43.0, 112.5, 120.5 (q, *J* = 272.2 Hz), 123.0, 126.8, 127.3, 128.6, 142.7 (q, *J* = 32.6 Hz), 144.4, 162.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –71.9 (d, *J* = 2.6 Hz). IR (neat): 3080, 2956, 2930, 2858, 1682, 1636, 1492, 1472, 1377, 1315, 1294, 1251, 1190, 1136, 1097, 1031, 908, 837, 826, 810, 775 cm^{-1}. EIMS (70 eV) *m*/*z*: 356 (0.5, M^++2), 355 (2, M^++1), 354 (84, M^+), 77 (100). Anal. Calcd for $C_{19}H_{25}F_3OSi$: C, 64.38; H, 7.11. Found: C, 64.45; H, 7.23.

4,5-Dihydro-4,6-diphenyl-2-trifluoromethyloxepin (7i): 89% yield, a colorless oil. R_f 0.50 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.94 (ddd, *J* = 14.2, 3.6, 1.0 Hz, 1H), 3.08 (ddd, *J* = 14.2, 9.0, 1.0 Hz, 1H), 3.78–3.90 (m, 1H), 5.79 (d, *J* = 4.0 Hz, 1H), 6.79 (s, 1H), 7.09–7.43 (m, 10H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 38.1, 42.0, 113.9, 120.2 (q. *J* = 272.0 Hz), 126.2, 127.09, 127.14, 127.3 (2C), 128.5, 128.8, 138.9, 141.5 (q, *J* = 33.8 Hz), 142.9, 143.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.6 (d, *J* = 2.6 Hz). IR (neat): 3082, 3028, 2961, 2922, 2872, 1688, 1645, 1454, 1385, 1292, 1198, 1134, 1076, 922, 864 cm^{-1}. EIMS (70 eV) *m*/*z*: 318 (2, M^++2), 317 (18, M^++1), 316 (87, M^+), 115 (100). Anal. Calcd for $C_{19}H_{15}F_3O$: C, 72.14; H, 4.78. Found: C, 72.27; H, 5.00.

4,5-Dihydro-4,6-diphenyl-2-trifluoromethyl-7-trimethylsilyloxepin (7j): 92% yield, a colorless solid. R_f 0.54 (hexane/EtOAc 10:1). Mp 70–71 ºC. ^{1}H NMR (200 MHz, $CDCl_3$, δ): –0.11 (s, 9H), 2.71 (dq, *J* = 12.4, 1.6 Hz, 1H), 3.33 (dd, *J* = 12.4, 10.4 Hz, 1H), 3.69 (dd, *J* = 10.4, 1.6 Hz, 1H), 5.67 (m, 1H), 7.03–7.50 (m, 10H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –1.26, 41.3, 41.6, 113.8, 122.6 (q. *J* = 272.0 Hz), 126.9, 127.3, 127.6, 128.0, 128.5, 128.8, 140,0, 141,9, 143.7, 144.5 (q, *J* = 31.6 Hz), 163.1. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.4 (d, *J* = 2.4 Hz). IR (KBr): 3057, 2959, 2862, 1676, 1620, 1491, 1367, 1294, 1188, 1126, 1086, 1022, 847, 762 cm^{-1}. EIMS (70 eV) *m*/*z*: 390 (3, M^++2), 389 (12, M^++1), 388 (40, M^+), 73 (100). Anal. Calcd for $C_{22}H_{23}F_3OSi$: C, 68.01; H, 5.97. Found: C, 68.13; H, 6.09.

4,5-Dihydro-3-phenyl-7-trifluoromethyl-2-trimethylsilyloxepin (7k): 95% yield, a colorless solid. R_f 0.60 (hexane/EtOAc 10:1). Mp 67–68 ºC. ^{1}H NMR (200 MHz, $CDCl_3$, δ): –0.12 (s, 9H), 2.32 (m, 2H), 2,85 (t, *J* = 5.8 Hz, 2H), 5.67 (t, *J* = 4.3 Hz, 2H), 7.17–7.22 (m, 2H), 7.29–7.37 (m, 3H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –1.23, 24.7, 32.9, 111.3 (q, *J* = 3.3 Hz), 118.4 (q, *J* = 271.0 Hz), 127.5, 128.1, 128.8, 140.2, 143.6 (q, *J* = 32.3 Hz), 144.2, 162.9. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.7 (d, *J* = 2.4 Hz). IR (KBr): 3089, 2964, 2849, 1686, 1441, 1300, 1250, 1188, 1109, 1040, 1005, 843, 772 cm^{-1}. EIMS (70 eV) *m*/*z*: 314 (0.4, M^++2), 313 (2, M^++1), 312 (7, M^+), 73 (100). Anal. Calcd for $C_{16}H_{19}F_3OSi$: C, 61.51; H, 6.13. Found: C, 61.47; H, 6.10.

4,5-Dihydro-3-phenyl-2-trifluoromethyloxepin (7l): 93% yield, a colorless oil. R_f 0.55 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.24–2.33 (m, 2H), 2.78–2.86 (m, 2H), 4.96 (dt, *J* = 7.4, 4.4 Hz, 1H), 6.43 (dt, *J* = 7.2, 2.0 Hz, 1H), 7.15–7.20 (m, 2H), 7.29–7.40 (m, 3H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 24.1, 34.3, 111.2, 120.4 (q, *J* = 274.5 Hz), 127.6, 127.9, 128.4, 135.0, 138.2, 142.1 (q, *J* = 33.6 Hz), 144.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –65.7. IR (neat): 3057, 3026, 2961, 2851, 1655, 1608, 1493, 1443, 1445, 1364, 1329, 1282, 1265, 1229, 1190, 1124, 1082, 1024, 988, 876, 767, 745, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 242 (2, M^++2), 241 (22, M^++1), 240 (100, M^+), 171 (27, M^+–CF_3). Anal. Calcd for $C_{13}H_{11}F_3O$: C, 65.00; H, 4.62. Found: C, 64.91; H, 4.74.

2-Benzyl-4,5-dihydro-7-trifluoromethyloxepin (7m): >99% yield, a colorless oil. R_f 0.60 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.28 (m, 4H), 3.39 (s, 2H), 4.97 (t, *J* = 5.6 Hz,

2H), 5.66 (t, *J* = 5.4 Hz, 2H), 7.17–7.33 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 24.1, 25.2, 41.5, 109.1, 111.6 (q, *J* = 3.5 Hz), 122.0 (q, *J* = 271.3 Hz), 126.3, 128.2, 128.9, 137.5, 142.4 (q, *J* = 32.3 Hz), 155.4. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.6. IR (neat): 3089, 3030, 2946, 2858, 1688, 1497, 1383, 1302, 1192, 1134, 1084, 993, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 255 (17, M^++1), 254 (97, M^+), 91 (100). Anal. Calcd for $C_{14}H_{13}F_3O$: C, 66.14; H, 5.15. Found: C, 66.42; H, 5.19.

4,5-Dihydro-2-trifluoromethyl-7-trimethylstannyloxepin (7n): 89% yield, a colorless oil. R_f 0.53 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.20 (m, 9H), 2.37–2.41 (m, 4H), 5.24 (t, *J* = 6.0 Hz, 1H), 5.67 (t, *J* = 5.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): –9.59, 25.8, 25.9, 111.2, 120.3 (q, *J* = 32.6 Hz), 143.9 (q, *J* = 32.6 Hz), 165.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.7. IR (neat): 2984, 2918, 2856, 1692, 1626, 1441, 1377, 1325, 1300, 1238, 1186, 1132, 1109, 1074, 1032, 988, 941, 874, 839, 773, 719 cm^{-1}. EIMS (70 eV) *m*/*z*: 328 (3, M^++2), 327 (28, M^++1), 326 (10, M^+), 312 (100). Anal. Calcd for for $C_{10}H_{15}F_3OSn$: C, 36.74; H, 4.62. Found: C, 37.03; H, 4.57.

2-(*tert*-Butyldimethyl)silyl-4,5-dihydro-7-trifluoromethyloxepin (7o): 94% yield, a colorless oil. R_f 0.60 (pentane). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 0.07 (s, 6H), 0.91 (s, 9H), 2.38 (m, 4H), 5.43 (t, *J* = 6.0 Hz, 1H), 5.62 (t, *J* = 5.2 Hz, 1H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –6.59, 16.6, 26.0, 26.3, 26.6, 110.0 (q, *J* = 3.7 Hz), 118.3 (q, *J* = 274.2 Hz), 123.6, 143.4 (q, *J* = 32.3 Hz), 161.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.7 (*J* = 1.7 Hz). IR (neat): 2952, 2858, 1685, 1635, 1471, 1381, 1300, 1188, 1134, 1082, 837 cm^{-1}. EIMS (70 eV) *m*/*z*: 280 (2, M^++2), 279 (8, M^++1), 278 (38, M^+), 76 (100). Anal. Calcd for $C_{13}H_{21}F_3OSi$: C, 56.09; H, 7.60. Found: C, 56.35; H, 7.45.

5-Phenyl-2,3,4,5-tetrahydro-7-trifluoromethyloxepin-3-one (7p): 63% yield, a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.96 (ddd, *J* = 10.8, 3.6, 1.2 Hz, 1H), 3.48 (dd, *J* = 12.2, 10.8 Hz, 1H), 3.79-3.91 (m, 1H), 4.52 (d, *J* = 2.6 Hz, 2H), 5.82 (d, *J* = 3.6 Hz, 1H), 7.18–7.42 (m, 5H). ^{13}C NMR (50 MHz, $CDCl_3$, δ): 40.2, 47.2, 80.2, 116.9, 120.1 (q, *J* = 272.0 Hz), 127.2, 128.3, 129.2, 141.1, 145.9 (q, *J* = 34.2 Hz), 207.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –73.3 (d, *J* = 2.6 Hz). IR (neat): 3065, 3032, 2924, 1728, 1688, 1603, 1495, 1454, 1421, 1371, 1305, 1248, 1192, 1132, 1014, 991, 962, 878, 756, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 258 (2, M^++2), 257 (16, M^++1, 15.), 256 (96, M^+), 187 (62, M^+–CF_3), 145 (100). Anal. Calcd for $C_{13}H_{11}F_3O_2$: C, 60.79; H, 4.52. Found: C, 60.94; H, 4.33.

5-Phenyl-7-trifluoromethyl-3,4,4a,5-tetrahydro-2*H*-1,8-dioxabenzocycloheptene (7q): 90% yield, a pale yellow oil. R_f 0.38 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.25–2.01 (m, 4H), 2.96 (m, 1H), 3.51 (dt, *J* = 10.4, 3.8 Hz, 1H), 3.92 (m, 1H), 4.09 (m,1H), 6.05 (d, *J* = 6.6 Hz, 1H), 6.78 (d, *J* = 1.8 Hz, 1H), 7.25–7.45 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 24.6, 25.9, 43.8, 46.4, 70.8, 111.0 (q, *J* = 3.4 Hz), 121.7 (q, *J* = 271.2 Hz), 128.5, 128.6, 128.8, 133.8, 139.2, 145.9 (q, *J* = 34.4 Hz), 147.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –73.0 (d, *J* = 1.8 Hz). IR (neat): 3062, 3030, 2960, 2877, 1726, 1691, 1492, 1452, 1296, 1261, 1188, 1132, 1080, 804, 702 cm^{-1}. EIMS (70 eV) *m*/*z*: 297 (2, M^++1), 296 (15,

M^+), 295 (2, M^+–1), 198 (100). Anal. Calcd for $C_{16}H_{15}F_3O_2$: C, 64.86; H, 5.10. Found: C, 65.08; H, 5.29.

9-Trifluoromethyl-3,4,4a,5-tetrahydro-2*H*-1,8-dioxabenzocycloheptene (7r): 89% yield, a colorless solid. R_f 0.35 (hexane/EtOAc 10:1). Mp 40–41 ºC. ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.51–1.61(m, 1H), 1.72–2.10 (m, 4H), 2.34–2.49 (m, 1H), 2.86–2.99 (m, 1H), 3.84–4.06 (m, 2H), 5.08 (dt, *J* = 7.9, 3.9 Hz, 1H), 6.45–6.50 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 22.7, 28.0, 28.9, 34.8, 69.0, 112.2, 122.6 (q, *J* = 272.2 Hz), 131.6 (q, *J* = 33.4 Hz), 146.5, 151.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –66.2 (d, *J* = 1.7 Hz). IR (neat): 3051, 2952, 2906, 2875, 1679, 1658, 1475, 1454, 1400, 1265, 1242, 1190, 1064, 920, 761, 704 cm^{-1}. EIMS (70 eV) *m*/*z*: 221 (9, M^++1), 220 (34, M^+), 136 (100). Anal. Calcd for $C_{10}H_{11}F_3O_2$: C, 54.55; H, 5.04. Found: C, 54.25; H, 5.00.

9-Trifluoromethyl-2-trimethylsilyl-3,4,4a,5-tetrahydro-2*H*-1,8-dioxabenzocycloheptene (7s): 86% yield, a pale yellow oil. R_f 0.38 (hexane/EtOAc 10:1). ^{1}H NMR (500 MHz, $CDCl_3$, δ): 0.11 (s, 9H), 1.50 (m, 1H), 1.70 (m, 1H), 1.84 (m, 2H), 2.02 (m, 1H), 2.47 (m, 1H), 2.61 (m, 1H), 3.69 (dt, *J* = 11.9, 3.2 Hz, 1H), 4.07 (m, 1H), 5.61 (dd, *J* = 7.4, 5.1 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): –2.67, 24.2, 28.6, 30.0, 36.4, 69.9, 120.7 (q, *J* = 273.1 Hz), 125.3, 133.5 (q, *J* = 32.4 Hz), 150.2, 168.5. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –65.3 (d, *J* = 1.9 Hz). IR (neat): 2953, 2867, 1670, 1638, 1452, 1383, 1313, 1250, 1230, 1190, 1163, 1086, 1059, 939, 842, 758 cm^{-1}. EIMS (70 eV) *m*/*z*: 294 (0.7, M^++2), 293 (5, M^++1), 292 (18, M^+), 72 (100). Anal. Calcd for $C_{10}H_{11}F_3O_2Si$: C, 53.40; H, 6.55. Found: C, 53.35; H, 6.71.

2-Isopropyl-2-[(*E*)-2-phenylethenyl]-3-ethenyloxirane (8b): To a suspension of anhydrous zinc chloride (1.36 g, 10 mmol) in dry THF (150 mL) at –78 ºC was added allyl chloride (0.57 g, 7.5 mmol). Then the solution was cooled to –98 ºC, and the preformed LDA (10 mmol in 15 mL of THF) was added via a cannula over 20 min. The reaction mixture was further stirred at –98 ~ –95 ºC for 15 min and (*E*)-4-methyl-1-phenylpent-1-en-3-one (0.52 g, 3.0 mmol) was added to the solution. The reaction mixture was allowed to warm to –78 ºC and was stirred at –78 °C for 2 h before quenching with saturated aq. NH_4Cl solution. Usual workup followed by silica gel column chromatography gave **8b** (0.34 g, 38% yield) as a colorless oil with diastereomeric ratio 10:1. R_f 0.50 (hexane/EtOAc 10:1). ^{1}H NMR (270 MHz, $CDCl_3$, δ): 1.03 (d, *J* = 6.5 Hz, 3H), 1.11 (d, *J* = 6.5 Hz, 3H), 1.68 (m, 3H), 3.41 (d, *J* = 8.1 Hz, 1H), 5.26–5.78 (m, 3H), 6.31 (d, *J* = 15.7 Hz, 1H), 6.70 (d, *J* = 15.7 Hz, 1H), 7.22–7.42 (m, 3H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 18.1, 18.8, 35.2, 65.2, 69.2, 120.5, 122.5, 126.4, 127.6, 128.5, 133.0, 133.6, 135.7. IR (neat): 3082, 3026, 2962, 2874, 1718, 1599, 1494, 1448, 1384, 989, 970, 925, 752 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.31; H, 8.73.

4,5-Dihydro-4-phenyloxepin (9a): 87% yield, a colorless oil. R_f 0.62 (hexane/EtOAc 10:1). ^{1}H NMR (270 MHz, $CDCl_3$, δ): 2.51 (dt, *J* = 4.6, 1.2 Hz, 2H), 3.76 (m, 1H), 4.86 (m, 2H), 6.27 (m, 2H), 7.18–7.33 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 35.6, 44.2, 107.5, 111.4, 126.4, 127.3, 128.4, 141.8, 143.4,

145.8. EIMS (70 eV) *m*/*z*: 174 (1, M^++2), 173 (12, M^++1), 172 (81, M^+), 115 (M^+–Ph, 100). Anal. Calcd for $C_{12}H_{12}O$: C, 83.69; H, 7.02. Found: C, 83.54; H, 7.18.

4,5-Dihydro-2-isopropyl-4-phenyloxepin (9b): 83% yield, a colorless oil. R_f 0.63 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 1.09 (d, *J* = 6.8 Hz, 6H), 2,24–2.57 (m, 3H), 3.83 (m, 1H), 4.78 (dt, *J* = 7.0, 4.6 Hz, 1H), 4.92 (d, *J* = 4.6 Hz, 1H), 6.31 (dq, *J* = 7.4, 1.0 Hz, 1H), 7.15–7.35 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 20.89, 20.92, 34.6, 35.3, 43.3, 107.3, 126.1, 127.2, 128.3 (2C), 143.2, 146.3, 159.5. IR (neat): 3082, 3028, 2964, 2871, 1674, 1602, 1492, 1305, 1118, 700 cm^{-1}. EIMS (70 eV) *m*/*z*: 216 (2, M^++2), 215 (15, M^++1), 214 (86, M^+), 142 (100). Anal. Calcd for for $C_{15}H_{18}O$: C, 84.07; H, 8.47. Found: C, 84.01; H, 8.56.

Cross-coupling reaction of 7 with organic halides: coupling of **7c** with iodobenzene leading to **10** was performed according to the reported procedure (ref. 15).

4,5-Dihydro-2,5-diphenyl-7-trifluoromethyloxepin (10): 80% yield, a pale yellow oil. R_f 0.50 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.70–2.79 (m, 2H), 3.79–3.88 (m, 1H), 5.84 (t, *J* = 3.8 Hz, 1H), 5.91 (d, *J* = 7.4 Hz, 1H), 7.19–7.64 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 32.7, 42.3, 108.6, 114.5, 120.5 (q, *J* = 273.9 Hz), 124.9, 127.0, 127.4, 128.4, 128.6, 128.7, 134.6, 142.0 (q, *J* = 33.3 Hz), 143.8, 155.7. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –71.6 (d, *J* = 2.4 Hz). IR (neat): 3028, 2858, 1686, 1663, 1604, 1493, 1448, 1375, 1317, 1292, 1194, 1130, 1099, 1030, 999, 907, 829, 756 cm^{-1}. EIMS (70 eV) *m*/*z*: 318 (0.7, M^++2), 317 (4, M^++1), 316 (20, M^+), 115 (100). Anal. Calcd for $C_{19}H_{15}F_3O$: C, 72.14; H, 4.78. Found: C, 72.04; H, 4.89. Coupling reactions of **7f** with vinyl bromide and phenylethynyl bromide were performed as follows: an oven-dried Schlenk tube was charged with **7f** (73 mg, 0.20 mmol), $Pd_2(dba)_3$ (9.2 mg, 0.010 mmol), P(*t*-Bu)$_3$ (4.1 mg, 0.020 mmol), and a halide (0.30 mmol), followed by THF (0.5 mL) and 3.0 M aq. KOH solution (0.60 mmol, 200 μL). The reaction mixture was stirred at rt. The reaction was monitored by TLC analysis. After completion of the reaction, the reaction mixture was cooled to rt, quenched with saturated aq. NH_4Cl solution (1 mL), and diluted with Et_2O (1 mL). The aqueous layer was extracted with diethyl ether (2 mL x 3) and the combined organic solvents was dried over anhydrous $MgSO_4$ and concentrated by rotary evaporator. Purification of the crude product by column chromatography on silica gel and GPC afforded **11** or **12**, respectively.

4,5-Dihydro-4-phenyl-2-trifluoromethyl-7-vinyloxepin (11): 75% yield, a pale yellow oil. R_f 0.52 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.52–2.74 (m, 2H), 3.71–3.79 (m, 1H), 5.14 (d, *J* = 11.0 Hz, 1H), 5.30 (t, *J* = 7.0 Hz, 1H), 5.52 (d, *J* = 17.0 Hz, 1H), 5.75 (d, *J* = 3.6 Hz, 1H), 6.11 (dt, *J* = 17.0, 11.0 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 32.7, 42.2, 113.1, 114.35, 114.39, 120.3 (q, *J* = 274.0 Hz), 127.0, 127.3, 128.7, 131.0, 141.8 (q, *J* = 33.5 Hz), 143.7, 154.8. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –71.9 (d, *J* = 2.8 Hz). IR (neat): 3030, 2858, 1686, 1664, 1605, 1493, 1454, 1377, 1294, 1194, 1132, 1078, 1032, 982, 920, 837 cm^{-1}. EIMS (70 eV) *m*/*z*: 268 (2, M^++2), 267 (16, M^++1), 266 (97, M^+), 55

(100). HRMS-EI (*m*/*z*): Calcd for $C_{15}H_{13}F_3O$ (M^+), 266.0918; Found, 266.0935.

4,5-Dihydro-4-phenyl-7-phenylethynyl-2-trifluoromethyloxepin (12): 78% yield, a pale yellow oil. R_f 0.45 (hexane/EtOAc 10:1). ^{1}H NMR (200 MHz, $CDCl_3$, δ): 2.45–2.74 (m, 2H), 3.65–3.74 (m, 1H), 5.69–5.77 (m, 2H), 7.12–7.43 (m, 10H). ^{13}C NMR (125 MHz, $CDCl_3$, δ): 33.2, 41.9, 83.4, 89.1, 115.0, 119.6, 120.8 (q, *J* = 273.6 Hz), 121.9, 127.2, 127.3, 128.3, 128.83, 128.89, 131.7, 140.4, 142.2 (q, *J* = 34.1 Hz), 143.3. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –72.6 (d, *J* = 1.7 Hz). IR (neat): 3030, 2856, 2221, 1744, 1686, 1653, 1601, 1491, 1442, 1375, 1298, 1194, 1136, 1070, 1030, 997, 893, 846, 756 cm^{-1}. EIMS (70 eV) *m*/*z*: 342 (0.9, M^++2), 341 (6, M^++1), 340 (25, M^+), 263 (48, M^+–Ph), 140 (100). HRMS-EI (*m*/*z*): Calcd for $C_{21}H_{15}F_3O$ (M^+), 340.1075; Found, 340.1069.

General procedure for catalytic hydrogenation of 7: An oven-dried Schlenk flask was charged with 10 wt% palladium on activated carbon (11 mg, 0.010 mmol) and was filled with 1 atm of hydrogen gas. Then, **7m** or **7o** (0.10 mmol) and EtOH (2 mL) were added to the flask in this order. The reaction mixture was stirred at rt for 12~15 h. The resulting mixture was diluted with EtOAc (5 mL) and was filtered through a pad of Celite. The combined filtrate was concentrated *in vacuo* to give analytically pure **13** or **14**, respectively.

2-Benzyl-7-trifluoromethyloxepane (13): 90% yield, a pale yellow oil, diastereomeric ratio 95 : 5. ^{1}H NMR (270 MHz, $CDCl_3$, δ): 1.32–1.97 (m, 8H), 2.67 (dd, *J* = 13.5, 8.1 Hz, 1H), 2.91 (dd, *J* = 13.5, 7.0 Hz, 1H), 3.71 (m, 1H), 7.19–7.30 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 24.5, 24.8, 28.9, 35.5, 42.9, 76.8 (q, *J* = 30.0 Hz), 83.0, 122.6 (q, *J* = 279.1 Hz), 126.1, 128.0, 129.4, 138.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): (*cis*) –78.8 (d, *J* = 6.8 Hz), (*trans*) –78.2 (d, *J* = 6.9 Hz). EIMS (70 eV) *m*/*z*: 259 (0.8, M^++1), 258 (5, M^+), 167 (100). HRMS-EI (*m*/*z*): Calcd for $C_{14}H_{17}F_3O$ (M^+), 258.1232; Found, 258.1241.

2-(*tert*-Butyldimethyl)silyl-7-trifluoromethyloxepane (14): Isolated as 90 : 10 *cis*/*trans* mixture in 93% yield, a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$, δ): –0.06 (s, 3H), 0.01 (s, 3H), 0.92 (s, 9H), 1.53–1.90 (m, 8H), 3.34 (t, *J* = 7.0 Hz, 1H), 3.71 (m, 1H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –8.19, –7.18, 16.8, 24.7, 27.0, 27.4, 28.7, 32.7, 75.5, 80.7 (q, *J* = 28.9 Hz), 126.9 (q, *J* = 279.2 Hz). ^{19}F NMR (188 MHz, $CDCl_3$, δ): (*cis*) –78.4 (d, *J* = 7.7 Hz); (*trans*) –78.6 (d, *J* = 6.0 Hz). EIMS (70 eV) *m*/*z*: 282 (0.8, M^+), 227 (10), 73 (100). HRMS-EI (*m*/*z*): Calcd for $C_{13}H_{25}F_3OSi$ (M^+), 282.1627; Found, 282.1621. The relative stereochemistry of CF_3 and TBS group in the major isomer of **14** was assigned *cis* by ^{1}H NMR NOE experiments of methine protons adjacent to ethereal oxygen (11% and 6%) in comparison with the literature.[16]

Typical procedure for the dehydrogenation of 7: An oven-dried screw-capped test tube was charged with **7** (0.10 mmol), DDQ (68 mg, 0.30 mmol), and toluene (1.5 mL). The test tube was heated at 100 ºC for 12 h. The reaction mixture was allowed to cool to rt and diluted with 5 mL of Et_2O for **15** or hexane for **16**. The resulting mixture was filtered through a short pad of neutral alumina and the residue

was washed with 3 portions of hexane or Et_2O, respectively. The combined filtrate was concentrated *in vacuo* to give **15** or **16**, respectively. Oxepin **15** was purified by GPC.

7-(Hydroxydiphenyl)methyl-4-phenyl-2-trifluoromethyloxepin (15): 82% yield, a pale yellow solid. Mp 102–103 ºC**.** ^{1}H NMR (270 MHz, $CDCl_3$, δ): 5.26 (d, *J* = 7.0 Hz, 1H), 6.36 (d, *J* = 7.0 Hz, 1H), 6.41 (s, 1H), 7.25–7.50 (m, 15H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): 81.0, 114.8, 118.6, 120.6 (q, *J* = 272.0 Hz), 125.6, 127.6 (2C), 127.9, 128.0 (2C), 128.2, 128.6, 138.0, 139.0, 142.9 (q, *J* = 33.3 Hz), 143.2, 159.2, 162.6. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –69.4. EIMS (70 eV) *m*/*z*: 422 (2, M^++2), 421 (12, M^++1), 420 (36, M^+), 105 (100). HRMS-EI (*m*/*z*): Calcd for $C_{26}H_{19}F_3O_2$ (M^+), 420.1337; Found, 420.1337.

7-(*tert*-Butyldimethyl)silyl-4-phenyl-2-trifluoromethyloxepin (16): 93% yield, a pale yellow oil. ^{1}H NMR (270 MHz, $CDCl_3$, δ): 0.09 (s, 6H), 0.91 (s, 9H), 5.82 (d, *J* = 6.5 Hz, 2H), 6.33 (s, 1H), 6.44 (d, *J* = 6.5 Hz, 1H), 7.27 (m, 5H). ^{13}C NMR (67.5 MHz, $CDCl_3$, δ): –5.82, 1.13, 26.7, 116.8 (q, *J* = 272.1 Hz), 118.1 (q, *J* = 4.6 Hz), 124.9, 126.7, 128.1, 129.4, 139.4, 139.6, 141.5 (q, *J* = 33.3 Hz), 169.9. ^{19}F NMR (188 MHz, $CDCl_3$, δ): –68.6. EIMS (70 eV) *m*/*z*: 354 (12, M^++2), 353 (37, M^++1), 352 (100, M^+), 73 (96). HRMS-EI (*m*/*z*): Calcd for $C_{19}H_{23}F_3OSi$ (M^+), 352.1470; Found, 352.1467.

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