Organic chemistry of enyne sulfones: convenient one-pot synthesis of 2-ethoxy-3-ethynyl-4-methylene-2-perfluoroalkyl-3-(phenylsulfonyl)tetrahydrofurans

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One-pot cycloaddition of the enyne sulfones **1**–**3** and **5** with propargylic alkoxides stereoselectively proceeds in DMF and exclusively gives the 2-ethoxy-3-ethynyl-4-methylene-2-perfluoroalkyl-3-(phenylsulfonyl)tetrahydrofurans **6a**–**e**, **7a**,**b**, **8a**,**b** and **9a**,**b**.

Highly functionalized tetrahydrofurans are of current interest in organic syntheses in view of their occurrence in many classes of bioactive natural products.[1] There are many synthetic procedures for highly functionalized tetrahydrofurans, such as 2,5-disubstituted or more highly substituted compounds.[2] However, methods for the synthesis of 3- or 4-methylenetetrahydrofurans are quite limited because it is difficult to construct the methylene group in the preparations of furanoids.[3] A 3-methylene group in the precursor of the furanoids is a prerequisite before construction of the tetrahydrofuran ring.[4] As a recent novel methodology, Balme and co-workers reported the Michael addition of propargyl (prop-2-ynyl) alcohols to α,β-unsaturated carbonyl compounds and the successive 5-*exo*-*dig* cyclization catalyzed by a palladium(0) complex.[5]

Recently, we have reported the regioselective addition reactions of 2-sulfonylbut-1-en-3-ynes (enyne sulfones) with alkoxides.[6] We next turned our attention to synthetic applications of alkoxide-addition reactions to the enyne sulfones. Our previous results have provided exclusive formation of the allenic sulfones *via* a resonance structure **I**↔**I′** (Fig. 1). When the addition reaction of our enyne sulfones with the prop-2-ynyl alkoxide could be performed, a β-(prop-2-ynyloxy)-propargylic anion forms. If the 5-*exo*-*dig* mode of cyclization of the anion proceeds without the intermediacy of transition metals, this novel method will be both practical and convenient for the construction of the 3-methylenetetrahydrofurans. This paper describes the regio- and stereoselective cyclization of propargyl alkoxides to the enyne sulfones: an exclusive formation of highly functionalized 3-methylenetetrahydrofurans.

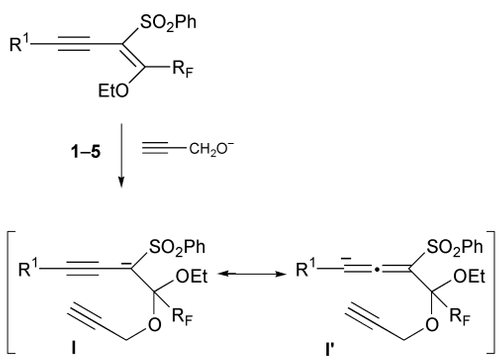
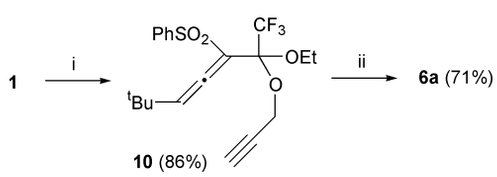


Fig. 1

Results and discussion

The enyne sulfones were prepared according to our previous report.[6] First, we performed the addition reaction of the enyne sulfone **1** (R^1 = *t*-Bu) with propargyl alcohol ($R^2 = R^3 = R^4$ = H) in the presence of NaH in DMF. The one-pot cycloaddition proceeded successfully to give 3-(3,3-dimethylbut-1-ynyl)-2-ethoxy-4-methylene-3-(phenylsulfonyl)tetrahydrofuran **6a** in 50% yield (Entry 1, Table 1). The structure of **6a** was determined by IR, ^{1}H, ^{13}C and ^{19}F NMR, MS, and elemental analysis. The IR spectrum showed the acetylenic absorption at ν 2230 cm^{-1}, and the ^{1}H NMR spectrum showed the characteristic *exo*-methylene protons at δ 5.10 (t, *J* 1 Hz) and 5.31 (t, *J* 1 Hz), and the 5-methylene protons at δ 4.64 (dd, *J* 12 and 1 Hz) and 5.12 (dd, *J* 12 and 1 Hz), respectively. The ^{19}F NMR spectrum showed a single stereoisomer at δ_F −0.83. The mass spectrum and the elemental analysis gave the molecular formula ($C_{20}H_{23}F_3O_4S$). The stereostructure of **6a** was determined by NOE experiments. Irradiation of the *t*-Bu protons at δ 1.23 increased the intensity of the methylene protons of the ethoxy group. The result shows that the stereoisomer is (2*R**,3*R**). We next performed reactions of **1** with other propargylic alkoxides and the results are shown in Table 1. The reaction of the enyne **4** (R^1 = H) gave a complex mixture (Entry 10); however, *n*-Bu- **2** and Ph-substituted **3** gave the corresponding cyclized products in moderate to good yields.

These cycloadditions strongly depend on the solvent. The addition of **1** with propargyl alkoxide in THF gave the allenic sulfone **10** exclusively (Scheme 1).[6] Successive treatment of **10**



Scheme 1 *Reagents and conditions*: i, ≡–CH_2OH, NaH, THF, 0 °C; ii, *t*-BuOK, *t*-BuOH, reflux, 10 min.

with *t*-BuOK/*t*-BuOH also afforded (2*R**,3*R**)-**6a** in good yield. We could not ascertain the details of the solvent dependence of these reactions; however, DMF would act as a good solvent to increase the nucleophilicity of the propargyl anion. The interconversion of allenic and propargylic sulfones proceeds easily,[7] so that the allenic sulfone **10** also reacts under the basic reaction conditions to give the allenic anion **I′** and undergo the cyclization. The high stereoselectivity of these cycloadditions can be explained as follows. The cycloaddition is thought to proceed *via* a cyclic transition state **11A** and **11B** as shown in Fig. 2. The

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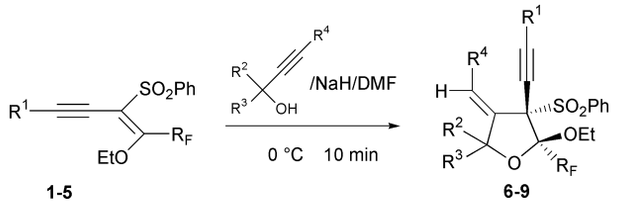


Table 1 One-pot synthesis of 3-alkynyl-2-ethoxy-4-methylene-2-perfluoroalkyl-3-(phenylsulfonyl)tetrahydrofurans from enyne sulfones

	Enyne sulfone			Propargyl alcohol			
Entry		R^1	R_F	R^2	R^3	R^4	Product (% yield)
1	**1**	Bu^t	CF_3	H	H	H	**6a** (50)
2	**1**	Bu^t	CF_3	H	H	Ph	**6b** (39)
3	**1**	Bu^t	CF_3	Me	Me	H	**6c** (60)
4	**1**	Bu^t	CF_3	$(CH_2)_{11}$		H	**6d** (43)
5	**1**	Bu^t	CF_3	$(CH_2)_4$		Ph	**6e** (43)
6	**2**	Bu	CF_3	Me	Me	H	**7a** (48)
7	**2**	Bu	CF_3	$(CH_2)_5$		H	**7b** (39)
8	**3**	Ph	CF_3	Me	Me	H	**8a** (53)
9	**3**	Ph	CF_3	$(CH_2)_5$		H	**8b** (47)
10	**4**	H	CF_3	Me	Me	H	
11	**5**	Ph	CF_3CF_2	Me	Me	H	**9a** (57)
12	**5**	Ph	CF_3CF_2	$(CH_2)_5$		H	**9b** (quant.)

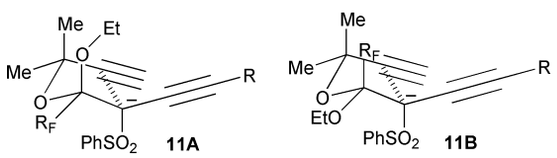
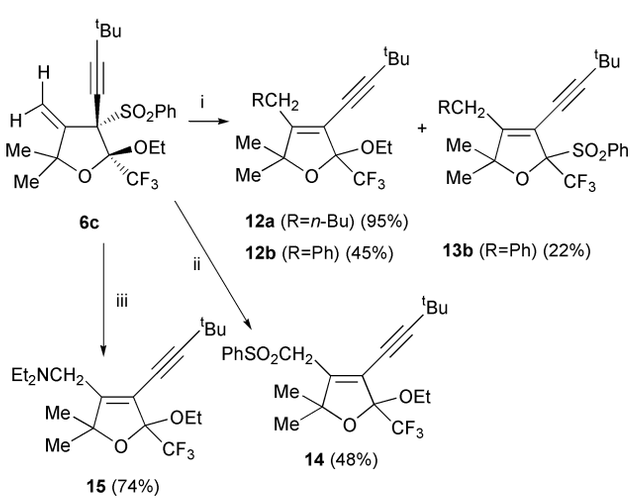


Fig. 2

ethoxy group would occupy the axial position due to stereoelectronic effects.[8] The conformer **11A** gives (2*R**,3*R**)-tetrahydrofurans.

3(4)-Methylenetetrahydrofurans are potentially versatile intermediates. We next examined the additional transformation of these tetrahydrofurans by desulfonylation.[9] The reaction of **6c** with *n*-BuLi afforded the 3(4)-pentyl-2,5-dihydrofuran **12a** in 95% yield (Scheme 2). The reaction with PhLi also gave



Scheme 2 *Reagents and conditions*: i, *n*-BuLi or PhLi, THF, −78 °C; ii, $CH_2(CO_2Et)_2$, NaH, DMF, reflux; iii, Et_2NLi, THF, 0 °C.

addition to the *exo*-methylene carbon to give the dihydrofurans **12b** and **13b**; however, ethyl malonate did not participate in the addition reaction. The product in this case was the 2,5-dihydrofuran **14**, formed by 1,3-migration of the phenylsulfonyl group. Lithium diethylamide afforded the diethylaminomethyl derivative **15** in high yield.

Experimental

Mps were determined on a Yanagimoto micro-melting-point apparatus and are uncorrected. Elemental analyses were performed at the Microanalytical Laboratory of Gifu Pharmaceutical University. ^{1}H, ^{13}C and ^{19}F NMR spectra were determined with a Varian Inova 400 (400 MHz) spectrometer at the Center of Instrumentation of Gifu University. Chemical shifts are expressed in parts per million (ppm) with respect to tetramethylsilane as internal standard. The ^{19}F NMR (376.4 MHz) spectra were obtained in $CDCl_3$ with trifluoroacetic acid as external standard. Splitting patterns are designated as follows: s, singlet; d, doublet; t, triplet; q, quartet. *J*-Values are given in Hz. IR spectra of solids (KBr) and liquids (film) were recorded on a JASCO IR A-100 infrared spectrometer. EI Mass spectra (MS) were obtained using a JMS-SX102A spectrometer with a direct-insertion probe at an ionization voltage of 70 eV. Preparations of the enyne sulfones **2**–**5** were performed according to our previous report.[6]

(*E*)-2-Ethoxy-1,1,1-trifluoro-3-(phenylsulfonyl)non-2-en-4-yne 2

IR (film; cm^{-1}) ν_{max} 2220 (acetylene), 1380–1290, 1260–1100 (SO_2); ^{1}H NMR δ 0.90 (3H, t, *J* 7, Me), 1.33–1.46 (2H, m, CH_2), 1.41 (3H, t, *J* 7, Me), 1.49–1.53 (2H, m, CH_2), 2.39 (2H, t, *J* 7, CH_2), 4.13 (2H, q, *J* 7 Hz, OCH_2), 7.53–7.57 (2H, m, ArH), 7.63–7.67 (1H, m, ArH), 7.95–7.98 (2H, m, ArH); ^{13}C NMR δ 13.67 (q), 15.19 (q), 19.94 (t), 22.00 (t), 30.10 (t), 68.91 (s), 72.65 (t), 108.78 (q, *J* 2), 119.83 (q, *J* 282, CF_3), 119.96 (s), 128.51 (2d), 129.02 (2d), 134.05 (d), 140.42 (s), 152.78 (q, *J* 34); ^{19}F NMR δ −8.76 (3F, s, CF_3); MS *m*/*z* 360 (M^+) (Calc. for $C_{17}H_{19}F_3O_3S$: C, 56.66; H, 5.31. Found: C, 56.55; H, 5.22%).

(*E*)-4-Ethoxy-5,5,5-trifluoro-1-phenyl-3-(phenylsulfonyl)pent-3-en-1-yne 3

Yellow needles, mp 54–55 °C; IR (film; cm^{-1}) ν_{max} 2190 (acetylene), 1380–1240, 1220–1050 (SO_2); ^{1}H NMR δ 1.46 (3H, t, *J* 7, Me), 4.21 (2H, t, *J* 7, OCH_2), 7.30–7.39 (5H, m, ArH), 7.55–7.65 (2H, m, ArH), 7.66–7.69 (1H, m, ArH), 8.01–8.03 (2H, m, ArH); ^{13}C NMR δ 15.25 (q), 72.88 (t), 77.42 (s), 105.62 (s), 119.77 (q, *J* 282, CF_3), 121.74 (s), 122.75 (s), 128.60 (2d), 128.68 (3d), 129.15 (2d), 129.85 (d), 131.82 (d), 134.25 (d), 140.21 (s), 152.92 (q, *J* 33); ^{19}F NMR δ −9.03 (3F, s, CF_3); MS

m/*z* 380 (M^+) (Calc. for $C_{19}H_{15}F_3O_3S$: C, 59.99; H, 3.97. Found: C, 60.05; H, 3.96%).

(*E*)-4-Ethoxy-5,5,5-trifluoro-3-(phenylsulfonyl)pent-3-en-1-yne 4

IR (film; cm^{-1}) ν_{max} 3250, 2100 (acetylene), 1310, 1220–1080 (SO_2); ^1H NMR δ 1.42 (3H, t, *J* 7, Me), 3.82 (1H, q, *J* 1, acetylenic H), 4.15–4.20 (2H, m, OCH_2), 7.54–7.70 (3H, m, ArH), 7.97–8.01 (2H, m, ArH); ^{13}C NMR δ 15.12 (q), 66.60 (s), 71.36 (d), 72.81 (t), 93.74 (q, *J* 2), 119.28 (q, *J* 283, CF_3), 128.44 (2d), 129.15 (2d), 134.37 (d), 140.17 (s), 155.38 (q, *J* 34); ^{19}F NMR δ −9.00 (3F, s, CF_3); MS *m*/*z* 304 (small M^+) (Calc. for $C_{13}H_{11}F_3O_3S$: C, 51.31; H, 3.64. Found: C, 50.89; H, 3.64%).

(*E*)-4-Ethoxy-5,5,6,6,6-pentafluoro-1-phenyl-3-(phenylsulfonyl)-hex-3-en-1-yne 5

Colorless prisms, mp 86–87 °C; IR (film; cm^{-1}) ν_{max} 2200 (acetylene), 1380–1250, 1240–1020 (SO_2); ^1H NMR δ 1.46 (3H, t, *J* 7, Me), 4.31 (2H, q, *J* 7, OCH_2), 7.26–7.38 (5H, m, ArH), 7.54–7.58 (2H, m, ArH), 7.65–7.69 (1H, m, ArH), 8.00–8.03 (2H, m, ArH); ^{13}C NMR δ 15.40 (q), 74.95 (t), 77.80 (s), 106.28 (s), 110.90 (q, *J* 40, CF_2), 118.79 (q, *J* 325 and 37, CF_3), 121.67 (s), 126.51 (s), 128.60 (2d), 128.61 (2d), 129.12 (2d), 129.95 (d), 131.79 (2d), 134.29 (d), 140.01 (s), 152.93 (s); ^{19}F NMR δ −33.20 (2F, br d, *J* 2, CF_2), −0.80 (3F, t, *J* 2, CF_3); MS *m*/*z* 430 (M^+) (Calc. for $C_{20}H_{15}F_5O_3S$: C, 55.81; H, 3.51. Found: C, 55.75; H, 3.58%).

Reactions of enyne sulfones 1–5 with alkynyl alkoxides. General procedure

A DMF (1.00 ml) solution of sodium propargyl oxide [prepared from propargyl alcohol (0.05 g, 0.83 mmol) and NaH (0.05 g, 1.25 mmol)] was added dropwise to a DMF (2.00 ml) solution of (*E*)-2-ethoxy-1,1,1-trifluoro-7,7-dimethyl-3-(phenylsulfonyl)hept-2-en-4-yne **1** (0.15 g, 0.42 mmol) at 0 °C. The reaction mixture was stirred for 10 min and poured into water (150 ml). The organic layer was separated and the aqueous layer was extracted with diethyl ether. The organic layer and the extracts were combined, and dried over $MgSO_4$. The solvent was removed under reduced pressure. The residue was purified by preparative TLC on silica gel with AcOEt–*n*-hexane 1 : 10 as eluent, to give (2*R**,3*R**)-3-(3,3-dimethylbut-1-ynyl)-2-ethoxy-4-methylene-3-phenylsulfonyl-2-(trifluoromethyl)tetrahydrofuran **6a** (0.09 g, 50%) as a colorless oil, IR (film; cm^{-1}) ν_{max} 2230 (acetylene), 1320, 1200–1130 (SO_2); ^1H NMR (400 MHz; $CDCl_3$) δ 1.23 (9H, s, Me × 3), 1.28 (3H, t, *J* 7, Me), 3.89–3.97 (1H, m, OCH_2), 4.10–4.16 (1H, m, OCH_2), 4.64 (1H, dd, *J* 12 and 1, 5-H), 5.10 (1H, t, *J* 1, olefinic H), 5.12 (1H, dd, *J* 12 and 1, 5-H), 5.31 (1H, t, *J* 1, olefinic H), 7.42–7.54 (2H, m, ArH), 7.62–7.68 (1H, m, ArH), 7.93–8.02 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.51 (q), 28.06 (s), 30.30 (3q), 62.55 (t), 69.85 (s), 72.81 (t), 76.02 (s), 101.41 (s), 107.33 (q, $J_{C\text{-}F}$ 37, 2-C), 116.62 (t), 122.03 (q, *J* 294, CF_3), 127.70 (2d), 132.04 (2d), 134.06 (d), 136.47 (s), 141.42 (s); ^{19}F NMR δ −0.83 (3F, s, CF_3); MS *m*/*z* 416 (M^+) (Calc. for $C_{20}H_{23}F_3O_4S$: C, 57.71; H, 5.57. Found: C, 57.55; H, 5.51%). The stereochemistry of **6a** was determined by NOE experiments. Irradiation of *t*-Bu protons at δ 1.23 increased the intensity of the methylene protons of the EtO group (6%). *ortho*-Aromatic protons at δ 7.93–8.02 also were irradiated; however, the intensity of the methylene protons of the ethoxy group was unaffected.

(2*R,3*R**)-(*Z*)-4-Benzylidene-3-(3,3-dimethylbut-1-ynyl)-2-ethoxy-3-phenylsulfonyl-2-(trifluoromethyl)tetrahydrofuran 6b.** A colorless oil; IR (KBr; cm^{-1}) ν_{max} 2250 (acetylene), 1230–1100 (SO_2); ^1H NMR (400 MHz; $CDCl_3$) δ 1.19 (3H, t, *J* 7, Me), 1.27 (9H, s, Me × 3), 3.29–3.43 (2H, m, OCH_2), 4.63 (1H, d, *J* 15, 5-H), 4.77 (1H, d, *J* 15, 5-H), 6.30 (1H, s, olefinic H), 7.21–7.44 (5H, m, ArH), 7.49–7.56 (3H, m, ArH), 7.67–7.70 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.30 (q), 28.57 (s), 30.72 (3q), 58.94 (t), 68.89 (s), 74.19 (t), 74.44 (d), 109.72 (s), 110.87 (q, *J* 33), 116.01 (s), 122.02 (q, *J* 287, CF_3), 125.20 (2d), 126.08 (2d), 128.88 (2d), 129.31 (2d), 132.76 (d), 137.38 (s), 144.83 (s), 149.66 (s); ^{19}F NMR δ −4.08 (3F, s, CF_3); MS *m*/*z* 492 (M^+) (Calc. for $C_{26}H_{27}F_3O_4S$: C, 63.40; H, 5.53. Found: C, 63.22; H, 5.60%). The stereochemistry of the benzylidene group of **6b** was determined to be *Z* by NOE experiments. Irradiation of the olefinic proton at δ 6.30 increased the intensity of 5-H (3%).

(2*R,3*R**)-2-Ethoxy-3-(3,3-dimethylbut-1-ynyl)-5,5-dimethyl-4-methylene-3-phenylsulfonyl-2-(trifluoromethyl)tetrahydrofuran 6c.** Mp 117–119 °C, colorless prisms; IR (KBr; cm^{-1}) ν_{max} 2230 (acetylene), 1310, 1200–1100 (SO_2); ^1H NMR (400 MHz; $CDCl_3$) δ 1.20 (9H, s, Me × 3), 1.30 (3H, t, *J* 7, Me), 1.49 (3H, s, Me), 1.75 (3H, s, Me), 3.87–3.90 (1H, m, OCH_2), 4.06–4.12 (1H, m, OCH_2), 5.17 (1H, s, olefinic H), 5.27 (1H, d, *J* 1, olefinic H), 7.47–7.49 (2H, m, ArH), 7.61–7.64 (1H, m, ArH), 8.03–8.04 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.99 (q), 28.46 (q), 29.80 (q), 30.68 (3q), 30.94 (s), 62.42 (t), 72.98 (s), 78.61 (s), 88.43 (s), 100.57 (s), 106.50 (q, *J* 30), 117.62 (t), 122.51 (q, *J* 293, CF_3), 128.51 (2d), 128.67 (2d), 133.11 (d), 137.51 (s), 150.85 (s); ^{19}F NMR δ 0.81 (3F, s, CF_3); MS *m*/*z* 444 (M^+) (Calc. for $C_{22}H_{27}F_3O_4S$: C, 59.45; H, 6.12. Found: C, 59.45; H, 6.16%). The stereochemistry of **6c** was determined by NOE experiments. Irradiation of *t*-Bu protons increased the intensity of the methylene protons of the ethoxy group (7%); however, irradiation of *ortho*-aromatic protons at δ 8.03–8.04 did not increase the intensity of the ethoxy group signals.

(2*R,3*R**)-2-Ethoxy-3-(3,3-dimethylbut-1-ynyl)-4-methylene-3-phenylsulfonyl-2-trifluoromethyl-1-oxaspiro[4.11]hexadecane 6d.** Colorless prisms, mp 57–59 °C; IR (KBr; cm^{-1}) ν_{max} 2230 (acetylene), 1330, 1220–1120 (SO_2); ^1H NMR (400 MHz; $CDCl_3$) δ 1.19 (9H, s, Me × 3), 1.29 (3H, t, *J* 7, Me), 1.31–1.69 (20H, m, CH_2), 1.81–1.87 (1H, m, CH_2), 2.24–2.32 (1H, m, CH_2), 3.83–3.91 (1H, m, OCH_2), 4.02–4.15 (1H, m, OCH_2), 5.19 (1H, s, olefinic H), 5.21 (1H, s, olefinic H), 7.45–7.49 (2H, m, ArH), 7.60–7.64 (1H, m, ArH), 8.03–8.05 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.48 (q), 19.55 (t), 20.58 (t), 22.42 (t), 22.45 (t), 22.71 (t), 22.73 (t), 26.30 (t), 26.46 (t), 26.56 (t), 27.97 (s), 30.18 (3q), 32.46 (t), 35.99 (t), 61.71 (t), 72.97 (s), 78.83 (s), 92.29 (s), 100.13 (s), 105.79 (q, *J* 30, 2-C), 117.96 (t), 122.00 (q, *J* 293, CF_3), 127.60 (2d), 132.31 (2d), 133.73 (d), 137.60 (s), 149.28 (s); ^{19}F NMR δ 0.32 (3F, s, CF_3); MS *m*/*z* 568 (small M^+) (Calc. for $C_{31}H_{43}F_3O_4S$: C, 65.47; H, 7.62. Found: C, 65.12; H, 7.61%).

(2*R,3*R**)-(*Z*)-4-Benzylidene-2-ethoxy-3-(3,3-dimethylbut-1-ynyl)-3-phenylsulfonyl-2-trifluoromethyl-1-oxaspiro[4.4]nonane 6e.** IR (film; cm^{-1}) ν_{max} 2230 (acetylene), 1120–1100 (SO_2); ^1H NMR (400 MHz; $CDCl_3$) δ 1.19 (9H, s, Me × 3), 1.30 (3H, t, *J* 7, Me), 1.45–1.60 (2H, m, CH_2), 1.63–1.87 (6H, m, CH_2), 3.56–3.58 (2H, m, OCH_2), 6.02 (1H, s, olefinic H), 7.28–7.32 (5H, m, ArH), 7.49–7.54 (3H, m, ArH), 7.75–7.77 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.43 (q), 24.51 (t), 24.71 (t), 28.56 (s), 30.58 (3q), 38.17 (t), 38.82 (t), 59.20 (t), 70.48 (s), 74.54 (d), 99.43 (s), 108.20 (s), 109.57 (s), 119.09 (q, *J* 287, CF_3), 123.37 (s), 125.41 (2d), 127.51 (2d), 128.74 (2d), 128.85 (d), 129.20 (2d), 132.66 (d), 137.34 (s), 145.36 (s), 152.32 (s); ^{19}F NMR δ 3.48 (3F, s, CF_3); MS *m*/*z* 405 ($M^+ - PhSO_2H$).

(2*R,3*R**)-2-Ethoxy-3-(hex-1-ynyl)-5,5-dimethyl-4-methylene-3-phenylsulfonyl-2-(trifluoromethyl)tetrahydrofuran 7a.** IR (film; cm^{-1}) ν_{max} 2240 (acetylene), 1330, 1200–1100

(SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 0.89 (3H, t, *J* 7, Me), 1.29 (3H, t, *J* 7, Me), 1.32–1.41 (2H, m, CH_2), 1.42–1.58 (2H, m, CH_2), 1.49 (3H, s, Me), 1.74 (3H, s, Me), 2.26 (2H, t, *J* 7, CH_2), 3.85–3.89 (1H, m, OCH_2), 4.05–4.09 (1H, m, OCH_2), 5.23 (1H, s, olefinic H), 5.28 (1H, d, *J* 1, olefinic H), 7.45–7.49 (2H, m, ArH), 7.60–7.64 (1H, m, ArH), 7.99–8.02 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 13.68 (q), 15.44 (q), 18.95 (t), 22.05 (t), 29.35 (q), 30.08 (t), 30.43 (q), 61.89 (t), 73.44 (s), 87.90 (s), 93.10 (s), 117.08 (t), 122.21 (q, *J* 293), 127.72 (2d), 132.21 (2d), 137.42 (s), 133.79 (d), 150.26 (s), 155.60 (s); ^{19}F NMR δ −0.91 (3F, t, *J* 2, CF_3); MS *m*/*z* 429 ($M^+ - CH_3$) (Calc. for $C_{22}H_{27}F_3O_4S$: C, 59.45; H, 6.12. Found: C, 59.20; H, 6.20%). The stereochemistry of **7a** was determined by NOE experiments. Irradiation of one set of methylene protons of the hexynyl group at δ 2.26 increased the intensities of both the methylene protons of the ethoxy group (2%) and the *ortho*-aromatic protons (3%). However, irradiation of the *ortho*-aromatic protons at δ 7.99–8.02 did not increase the intensity of the methylene protons of the ethoxy group.

(2*R,3*R**)-2-Ethoxy-3-(hex-1-ynyl)-4-methylene-3-phenylsulfonyl-2-trifluoromethyl-1-oxaspiro[4.5]decane 7b.** Colorless prisms, mp 95–97 °C; IR (KBr; cm^{-1}) ν_{max} 2240 (acetylene), 1230–1150 (SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 0.88 (3H, t, *J* 7, Me), 1.30 (3H, t, *J* 7, Me), 1.21–1.51 (8H, m, CH_2), 1.65–1.72 (4H, m, CH_2), 1.85 (1H, br d, *J* 7, CH_2), 2.26 (2H, t, *J* 7, CH_2), 2.75 (1H, br d, *J* 13, CH_2), 3.91–3.95 (1H, m, OCH_2), 4.07–4.10 (1H, m, OCH_2), 5.18 (1H, s, olefinic H), 5.25 (1H, s, olefinic H), 7.44–7.48 (2H, m, ArH), 7.59–7.63 (1H, m, ArH), 7.98–8.00 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 13.71 (q), 15.50 (q), 18.96 (t), 22.06 (t), 22.69 (t), 22.75 (t), 25.36 (t), 30.09 (t), 37.52 (t), 38.50 (t), 61.93 (t), 73.45 (s), 89.17 (s), 92.99 (s), 117.08 (t), 122.02 (q, *J* 293, CF_3), 127.69 (2d), 129.11 (s), 132.26 (2d), 133.77 (d), 137.26 (s), 150.33 (s); ^{19}F NMR δ −0.45 (3F, s, CF_3); MS *m*/*z* 484 (M^+) (Calc. for $C_{25}H_{31}F_3O_4S$: C, 61.97; H, 6.45. Found: C, 61.52; H, 6.34%).

(2*R,3*R**)-2-Ethoxy-5,5-dimethyl-4-methylene-3-phenylethynyl-3-phenylsulfonyl-2-(trifluoromethyl)tetrahydrofuran 8a.** Colorless needles, mp 95–97 °C; IR (KBr; cm^{-1}) ν_{max} 2230 (acetylene), 1330, 1220–1100 (SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.34 (3H, t, *J* 7, Me), 1.52 (3H, s, Me), 1.78 (3H, s, Me), 3.89–3.94 (1H, m, OCH_2), 4.09–4.13 (1H, m, OCH_2), 5.35 (2H, s, olefinic H), 7.25–7.47 (7H, m, ArH), 7.59–7.63 (1H, m, ArH), 8.04–8.07 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.51 (q), 29.42 (q), 30.42 (q), 62.07 (t), 82.56 (s), 88.23 (s), 91.35 (s), 106.74 (s), 117.45 (t), 121.38 (q, *J* 293, CF_3), 121.90 (s), 127.92 (2d), 128.65 (2d), 129.47 (d), 130.04 (s), 131.89 (2d), 132.30 (2d), 134.06 (d), 137.23 (s), 149.83 (s); ^{19}F NMR δ −0.72 (3F, s, CF_3); MS *m*/*z* 464 (M^+) (Calc. for $C_{24}H_{23}F_3O_4S$: C, 62.06; H, 4.99. Found: C, 61.79; H, 4.96%). The stereochemistry of **8a** was determined by NOE experiments. Irradiation of the *ortho*-aromatic protons at δ 8.04–8.07 did not increase the intensity of the methylene protons of the ethoxy group.

(2*R,3*R**)-2-Ethoxy-4-methylene-3-phenylethynyl-3-phenylsulfonyl-2-trifluoromethyl-1-oxaspiro[4.5]decane 8b.** IR (film; cm^{-1}) ν_{max} 2230 (acetylene), 1330, 1200–1100 (SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.23–1.29 (2H, m, CH_2), 1.33 (3H, t, *J* 7, Me), 1.37–1.54 (2H, m, CH_2), 1.61–1.72 (4H, m, CH_2), 1.87–1.90 (1H, br d, *J* 13, CH_2), 2.77–2.80 (1H, br d, *J* 13, CH_2), 3.96–4.00 (1H, m, OCH_2), 4.10–4.16 (1H, m, OCH_2), 5.32 (1H, s, olefinic H), 5.33 (1H, s, olefinic H), 7.22–7.47 (7H, m, ArH), 7.58–7.74 (1H, m, ArH), 8.03–8.07 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.53 (q), 22.72 (t), 22.77 (t), 25.34 (t), 37.59 (t), 38.52 (t), 62.08 (t), 82.63 (s), 88.21 (s), 89.52 (s), 91.23 (s), 105.91 (s, 2-C), 117.41 (t), 121.92 (s), 122.06 (q, *J* 293, CF_3), 127.86 (2d), 128.61 (2d), 129.42 (d), 131.86 (2d), 132.32 (2d), 134.01 (d), 137.12 (s), 149.90 (s); ^{19}F NMR δ −0.48 (3F, s, CF_3); MS *m*/*z* 504 (M^+) (Calc. for $C_{27}H_{27}F_3O_4S$: C, 64.27; H, 5.39. Found: C, 64.02; H, 5.41%).

(2*R,3*R**)-2-Ethoxy-5,5-dimethyl-4-methylene-2-pentafluoroethyl-3-phenylethynyl-3-(phenylsulfonyl)tetrahydrofuran 9a.** IR (film; cm^{-1}) ν_{max} 2230 (acetylene), 1320, 1220–1100 (SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.32 (3H, t, *J* 7, Me), 1.51 (3H, s, Me), 1.82 (3H, s, Me), 3.86–3.90 (1H, m, OCH_2), 4.19–4.23 (1H, m, OCH_2), 5.03 (1H, s, olefinic H), 5.27 (1H, d, *J* 1, olefinic H), 7.30–7.39 (5H, m, ArH), 7.44–7.48 (2H, m, ArH), 7.61–7.65 (1H, m, ArH), 8.00–8.03 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.90 (q), 29.12 (q), 30.57 (q), 60.60 (s), 62.19 (t), 79.39 (s), 82.67 (s), 89.13 (s), 91.82 (s), 117.00 (t), 118.93 (q, $J_{C\text{-}F}$ 289, CF_3), 121.95 (s), 127.89 (2d), 128.63 (2d), 129.42 (d), 131.79 (2d), 132.49 (2d), 134.24 (d), 135.79 (s), 150.10 (s); ^{19}F NMR δ −45.48 (1F, d, *J* 275, CF_2), −39.45 (1F, d, *J* 275, CF_2), −38.78 (1F, d, *J* 275, CF_2), −37.45 (1F, d, *J* 275, CF_2), 3.27 (3F, s, CF_3), 3.78 (3F, s, CF_3); MS *m*/*z* 499 ($M^+ - Me$).

(2*R,3*R**)-2-Ethoxy-4-methylene-2-pentafluoroethyl-3-phenylethynyl-3-phenylsulfonyl-1-oxaspiro[4.5]decane 9b.** Colorless prisms, mp 108–109 °C; IR (film; cm^{-1}) ν_{max} 2230 (acetylene), 1320, 1240–1100 (SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.34 (3H, t, *J* 7, Me), 1.41–1.52 (2H, m, CH_2), 1.65–1.75 (6H, m, $CH_2 \times 3$), 1.87 (1H, br d, *J* 13, CH_2), 2.86 (1H, br d, *J* 13, CH_2), 3.89–3.97 (1H, m, OCH_2), 4.17–4.24 (1H, m, OCH_2), 4.99 (1H, s, olefinic H), 5.24 (1H, d, *J* 1, olefinic H), 7.25–7.38 (5H, m, ArH), 7.43–7.47 (2H, m, ArH), 7.61–7.64 (1H, m, ArH), 7.99–8.01 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.89 (q), 22.58 (t), 22.69 (t), 25.30 (t), 37.41 (t), 38.70 (t), 62.13 (t), 79.60 (s), 82.90 (s), 90.63 (s), 91.85 (s), 116.99 (t), 119.02 (q, *J* 289, CF_3), 122.00 (s), 127.83 (2d), 128.59 (2d), 129.34 (d), 131.75 (2d), 132.52 (2d), 134.15 (d), 150.04 (s); ^{19}F NMR δ −45.64 (1F, d, *J* 275, CF_2), −44.43 (1F, d, *J* 275, CF_2), −43.41 (1F, d, *J* 276, CF_2), −41.43 (1F, d, *J* 276, CF_2), −1.17 (3F, s, CF_3), −0.72 (3F, s, CF_3); MS *m*/*z* 554 (M^+) (Calc. for $C_{28}H_{27}F_3O_4S$: C, 60.64; H, 4.91. Found: C, 60.19; H, 4.86%).

2-Ethoxy-1,1,1-trifluoro-6,6-dimethyl-3-phenylsulfonyl-2-(prop-2-ynyloxy)hepta-3,4-diene 10. IR (film; cm^{-1}) ν_{max} 1960 (allene), 1320, 1240–1100 (SO_2); ^{1}H NMR δ 1.15 (s, Me), 1.16 (s, Me), 1.19 (t, *J* 7, Me), 2.46 (t, *J* 2, acetylenic H), 2.49 (t, *J* 2, acetylenic H), 3.61–3.79 (m, OCH_2), 4.17–4.41 (m, OCH_2), 6.05 (d, *J* 2, allenic H), 7.47–7.52 (m, ArH), 7.56–7.59 (m, ArH), 7.90–7.95 (m, ArH); ^{13}C NMR δ 14.60 (q), 29.26 (q), 29.28 (q), 34.10 (s), 34.13 (s), 51.68 (t), 60.43 (t), 74.75 (d), 77.93 (s), 78.18 (s), 98.59 (s, *J* 37), 111.21 (s), 114.31 (d), 114.60 (d), 121.47 (q, *J* 291, CF_3), 121.52 (q, *J* 291, CF_3), 128.35 (d), 128.43 (d), 128.64 (d), 133.00 (d), 141.56 (s), 141.59 (s), 206.06 (s), 206.16 (s); ^{19}F NMR δ −0.46 (3F, s, CF_3); MS *m*/*z* 416 (small M^+) (Calc. for $C_{20}H_{23}F_3O_4S$: C, 57.68; H, 5.57. Found: C, 57.24; H, 5.46%).

Reactions of (2*R**,3*R**)-2-ethoxy-3-(3,3-dimethylbut-1-ynyl)-5,5-dimethyl-4-methylene-3-phenylsulfonyl-2-(trifluoromethyl)-tetrahydrofuran 6c and organolithiums. Typical procedure

n-BuLi (0.30 ml, 0.44 mmol) was added dropwise to a THF (3.00 ml) solution of **6c** (0.10 g, 0.22 mmol) at −78 °C under an Ar atmosphere. The work-up procedure afforded 2-ethoxy-5,5-dimethyl-3-(3,3-dimethylbut-1-ynyl)-4-pentyl-2-(trifluoromethyl)-2,5-dihydrofuran **12a** (0.75 g, 95%) as a pale yellow oil, IR (film; cm^{-1}) ν_{max} 2230 (acetylene); ^{1}H NMR (400 MHz; $CDCl_3$) δ 0.92 (3H, t, *J* 7, Me), 1.24 (9H, s, Me × 3), 1.26 (3H, t, *J* 7, Me), 1.36 (3H, s, Me), 1.39 (3H, s, Me), 1.34–1.42 (4H, m, CH_2), 1.59–1.68 (2H, m, CH_2), 2.19–2.22 (2H, m, CH_2), 3.45–3.58 (2H, m, OCH_2); ^{13}C NMR (100 MHz; $CDCl_3$) δ 14.18 (q),

15.41 (q), 22.50 (t), 26.63 (q), 26.68 (q), 27.03 (t), 27.69 (t), 28.43 (s), 30.92 (3q), 32.24 (t), 58.67 (t), 70.34 (s), 89.74 (s), 106.24 (s), 108.31 (s, 2-C), 112.05 (s), 122.11 (q, *J* 290, CF_3), 159.12 (s); ^{19}F NMR δ −3.82 (3F, s, CF_3); MS *m*/*z* 291 ($M^+ - CF_3$), 345 ($M^+ - Me$) (Calc. for $C_{20}H_{31}F_3O_2$: C, 66.64; H, 8.67. Found: C, 66.49; H, 8.54%).

3-Benzyl-4-(3,3-dimethylbut-1-ynyl)-5-ethoxy-2,2-dimethyl-5-trifluoromethyl-2,5-dihydrofuran 12b. IR (film; cm^{-1}) ν_{max} 2230 (acetylene); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.20 (3H, s, Me), 1.24 (9H, s, Me × 3), 1.25 (3H, s, Me), 1.28 (3H, t, *J* 7, Me), 3.51–3.57 (2H, m, CH_2), 3.63 (2H, s, CH_2), 7.21–7.31 (5H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 15.44 (q), 15.45 (q), 27.12 (q), 28.44 (s), 30.92 (3q), 33.31 (t), 58.85 (t), 89.79 (s), 93.42 (s), 106.27 (s), 108.21 (q, *J* 33, 5-C), 113.92 (s), 122.06 (q, *J* 287, CF_3), 126.93 (d), 128.79 (2d), 128.92 (2d), 137.93 (s), 157.05 (s); ^{19}F NMR δ −0.80 (3F, s, CF_3); MS *m*/*z* 380 (M^+) (Calc. for $C_{22}H_{27}F_3O_2$: C, 69.45; H, 7.15. Found: C, 69.10; H, 7.06%).

3-Benzyl-4-(3,3-dimethylbut-1-ynyl)-2,2-dimethyl-5-phenylsulfonyl-5-(trifluoromethyl)-2,5-dihydrofuran 13b. IR (film; cm^{-1}) ν_{max} 2230 (acetylene), 1380, 1240–1140 (SO_2); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.20 (3H, s, Me), 1.27 (3H, s, Me), 1.29 (9H, s, Me × 3), 3.50 (1H, d, *J* 15, CH_2), 3.68 (1H, d, *J* 15, CH_2), 7.17–7.28 (5H, m, ArH), 7.34–7.39 (3H, m, ArH), 7.92–7.93 (2H, m, ArH); ^{13}C NMR (100 MHz; $CDCl_3$) δ 27.35 (q), 28.39 (q), 28.61 (s), 30.86 (3q), 33.25 (t), 72.39 (s), 73.77 (s), 91.33 (s), 106.40 (s), 116.73 (s), 123.24 (s), 126.70 (d), 126.73 (2d), 128.06 (2d), 128.57 (d), 128.69 (2d), 128.80 (2d), 137.76 (s), 138.19 (s), 153.36 (s); ^{19}F NMR δ −3.73 (3F, s, CF_3); MS *m*/*z* 407 (M^+) (Calc. for $C_{26}H_{27}F_3O_3S$: C, 65.53; H, 5.71. Found. C, 65.38; H, 5.70%).

3-(3,3-Dimethylbut-1-ynyl)-2-ethoxy-5,5-dimethyl-4-phenylsulfonylmethyl-2-trifluoromethyl-2,5-dihydrofuran 14. IR (film; cm^{-1}) ν_{max} 2240 (acetylene), 1340, 1220–1150 (SO_2); ^{1}H NMR δ 1.20 (9H, s, Me × 3), 1.21 (3H, t, *J* 7, Me), 1.50 (3H, s, Me), 1.56 (3H, s, Me), 3.28–3.36 (1H, m, OCH_2), 3.37–3.56 (1H, m, OCH_2), 4.08 (1H, d, *J* 13, SO_2CH_2), 4.20 (1H, d, *J* 13, SO_2CH_2), 7.56–7.60 (2H, m, ArH), 7.68–7.72 (1H, m, ArH), 7.88–7.96 (2H, m, ArH); ^{13}C NMR δ 15.27 (q), 26.93 (q), 27.00 (q), 28.45 (s), 30.69 (3q), 55.84 (t), 59.20 (t), 69.29 (s), 89.55 (s), 109.55 (s), 121.60 (q, *J* 287), 122.04 (s), 128.71 (2d), 129.52 (2q), 134.33 (d), 139.25 (s), 144.26 (s); ^{19}F NMR δ −0.84 (3F, s, CF_3); high-resolution mass: Calc. for $C_{22}H_{27}F_3O_4S$: *M*, 444.1582. Found: M^+, 444.1578.

Reaction of 6c with lithium diethylamide

A THF (1.00 ml) solution of lithium diethylamide (0.50 ml, 0.50 mmol) was added to a THF (2.00 ml) solution of **6c** (52 mg, 0.12 mmol) at 0 °C under an Ar atmosphere. The reaction mixture was poured into water (100 ml) and the work-up procedure afforded 3-diethylaminomethyl-4-(3,3-dimethylbut-1-ynyl)-5-ethoxy-2,2-dimethyl-5-trifluoromethyl-2,5-dihydrofuran **15** (30 mg, 74%) as a colorless oil, IR (film; cm^{-1}) ν_{max} 2230 (acetylene); ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.02 (6H, t, *J* 7, Me × 2), 1.26 (9H, s, Me × 3), 1.26 (3H, t, *J* 7, Me), 1.46 (3H, s, Me), 1.48 (3H, s, Me), 2.42–2.49 (4H, m, CH_2), 3.21 (1H, d, *J* 13, NCH_2), 3.24 (1H, d, *J* 13, NCH_2), 3.42–3.60 (2H, m, OCH_2); ^{13}C NMR (100 MHz; $CDCl_3$) δ 11.78 (2q), 15.44 (q), 27.26 (q), 27.33 (q), 28.44 (s), 30.92 (3q), 47.16 (2t), 49.49 (t), 58.76 (t), 69.84 (s), 90.14 (s), 101.62 (s), 106.58 (s), 108.08 (s), 115.45 (s), 122.02 (q, *J* 287, CF_3), 156.34 (s); ^{19}F NMR δ −3.72 (3F, s, CF_3); MS *m*/*z* 375 (M^+) (Calc. for $C_{20}H_{32}F_3NO_2$: C, 63.98; H, 8.59; N, 3.73. Found: C, 63.87; H, 8.48; N, 3.68%).

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