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Diastereoselective Synthesis of CF_3- and CF_2H-Substituted Spiroethers from Aryl-Fused Cycloalkenylalkanols by Photoredox Catalysis

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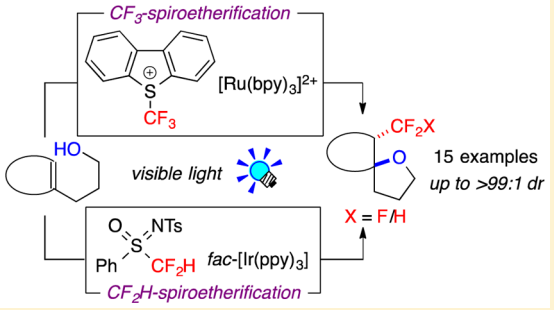
Supporting Information

ABSTRACT: Simple synthesis of CF_3- and CF_2H-spiroethers from aryl-fused cycloalkenylalkanols by photoredox catalysis has been developed. Modification of the fluoromethylating reagents and the photoredox catalysts leads to both CF_3- and CF_2H-spiroetherification. The present photocatalytic system allows us to access a variety of new *anti*-fluoromethylated spiroethers in a highly selective manner.

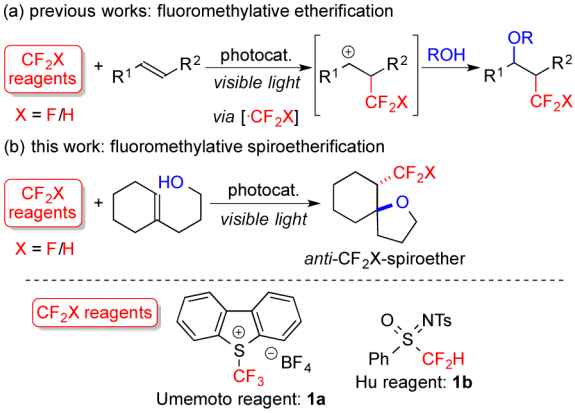


INTRODUCTION

Spiroether scaffolds are frequently found in biologically active natural products.[1] Thus, spiroether derivatives are considered to be latent important structural motifs as drugs.[2] On the other hand, fluoromethyl groups such as trifluoromethyl (CF_3) and difluoromethyl (CF_2H) groups have attracted much attention especially in the fields of pharmaceuticals and agrochemicals because of improvement of ADME.[3] To the best of our knowledge, a simple synthetic method for spiroethers containing CF_3 and CF_2H groups has been undeveloped so far.

For the past several years, photoredox catalysis with $[Ru(bpy)_3]^{2+}$ and *fac*-$[Ir(ppy)_3]$ has become a useful synthetic tool for radical reactions.[4] In particular, photocatalytic radical fluoromethylation is regarded as a versatile strategy for synthesis of fluoromethylated organic molecules.[5−7] We have been developing photoredox-catalyzed fluoromethylative difunctionalization of olefins through efficient generation of fluoromethyl radicals ($^{\bullet}CF_2X$) from appropriate fluoromethylating (CF_2X) reagents **1**.[8] We reported that photocatalytic reaction of olefins with appropriate CF_2X reagents such as Umemoto reagent **1a**[9] and Hu reagent **1b**[10] in the presence of alcohols efficiently affords the corresponding fluoromethylated ethers. Formation of an α-fluoromethylated carbocationic intermediate via photoredox single-electron-transfer (SET) processes is supposed to be a key process in the present reaction system, and subsequent nucleophilic attack of alcohols produces the fluoromethylative difunctionalized products (Scheme 1a). These results prompted us to design the olefinic substrate for a unique organic skeleton. Herein we will report on novel synthesis of a variety of spiroethers containing CF_3 and CF_2H groups from cycloalkenylalkanols via fluoromethylative spiroetherification (Scheme 1b). In addition, the present photocatalytic system turns out to be a highly diastereoselective reaction. This strategy allows us to access new CF_3- and CF_2H-substituted spiroethers, where the fluoromethyl group and the oxygen functionality are positioned in an *anti*-fashion.

Scheme 1. Fluoromethylative Etherification of Olefins by Photoredox Catalysis



RESULTS AND DISCUSSION

We commenced to examine the photocatalytic reaction of 3-(3,4-dihydro-1-naphthyl)propanol (**2a**) with 1.1 equiv of Umemoto reagent **1a** in the presence of 5 mol % of $[Ru(bpy)_3](PF_6)_2$ and 1.1 equiv of 2,6-lutidine at room

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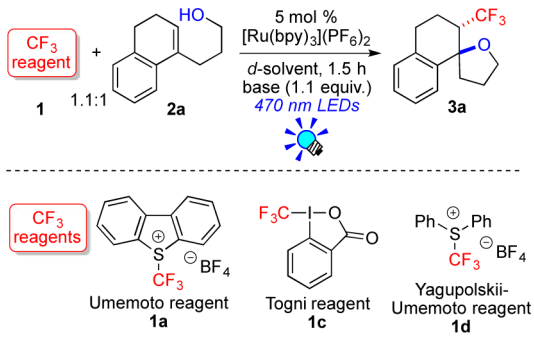
temperature under visible light irradiation (470 nm) on an NMR scale. As a result, the desired CF_3-spiroether, 6,7-benzo-10-trifluoromethyl-1-oxaspiro[4,5]decane (**3a**), was obtained, but choice of the solvent, reaction temperature, and base turned out to be crucial for the yields and diastereoselectivity (entries 1−8 in Table 1).

Table 1. Optimization of the Photocatalytic CF_3-Spiroetherification of 2a[a]



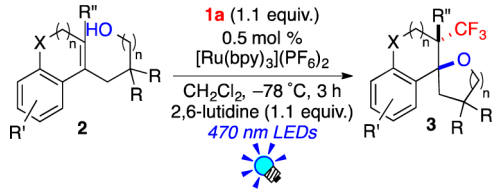
entry	CF_3-reagent	*d*-solvent	temp	base	% yield of 3a[b]	dr[c]
1	**1a**	CD_2Cl_2	rt	2,6-lutidine	71	93:7
2	**1a**	acetone-d_6	rt	2,6-lutidine	67	97:3
3	**1a**	CD_3CN	rt	2,6-lutidine	70	95:5
4	**1a**	DMSO-d_6	rt	2,6-lutidine	44	75:25
5	***1a***	CD_2Cl_2	−78 °C	2,6-*lutidine*	92	98:2
6	***1a***	*acetone-d_6*	−78 °C	2,6-*lutidine*	89	97:3
7	**1a**	CD_2Cl_2	−78 °C	K_2CO_3	51	42:58
8	**1a**	CD_2Cl_2	−78 °C	none	34	43:57
9	**1c**	CD_2Cl_2	−78 °C	2,6-lutidine	0	
10	**1d**	CD_2Cl_2	−78 °C	2,6-lutidine	0	
11[d]	**1a**	CD_2Cl_2	−78 °C	2,6-lutidine	0	
12[e]	**1a**	CD_2Cl_2	−78 °C	2,6-lutidine	0	

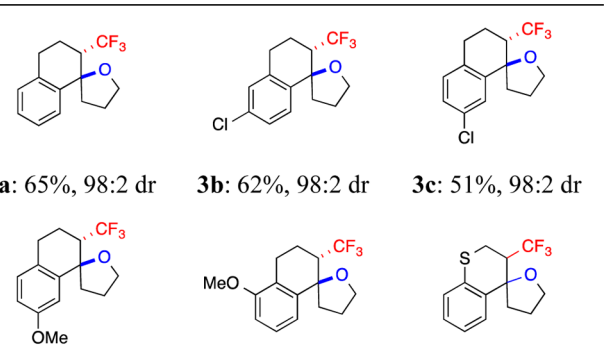
[a]For reaction conditions, see the Experimental Section. Optimal conditions are highlighted in italic. [b]Yields were determined by ^1H NMR spectroscopy using $SiEt_4$ as an internal standard. [c]Diastereomeric ratios (dr) were determined by ^{19}F NMR spectroscopy. [d]In the dark. [e]No catalyst.

It should be noted that the reactions in dichloromethane (71% NMR yield, 93:7 dr), acetone (67%, 97:3), and acetonitrile (70%, 95:5) furnished the product **3a** in a good diastereoselective manner compared with that in DMSO (44%, 75:25) (entries 1−4). Lower reaction temperature (−78 °C in a dry ice−methanol bath) significantly improved the yield (dichloromethane 92% and acetone 89%) (entries 5 and 6). Use of an inorganic base, K_2CO_3, and the reaction in the absence of a base caused a harmful effect on the yield and selectivity (entries 7 and 8). In addition, other CF_3 sources such as Togni reagent **1c** and Yagupolskii−Umemoto reagent **1d** did not provide the product **3a** at all under the present conditions (entries 9 and 10). Furthermore, both the photocatalyst and visible light irradiation are essential for the present reaction (entries 11 and 12).

With the optimal reaction conditions in hand, we investigated the scope of the present photocatalytic CF_3-spiroetherification. It is noteworthy that catalyst loading can be reduced to 0.5 mol % (Table 2). The reaction of **2a** afforded

Table 2. Scope of the Present Photocatalytic CF_3-Spiroetherification of Aryl-Fused Cycloalkenylalkanols (2)[b]





3a: 65%, 98:2 dr **3b**: 62%, 98:2 dr **3c**: 51%, 98:2 dr

3d: 41%, 93:7 dr **3e**: 67%, 98:2 dr [a]**3f**: 18%, 92:8 dr

3g: 46%, 70:30 dr **3h**: 76%, 83:17 dr **3i**: 63%, 96:4 dr

3j: 82%, >99:1 dr **3k**: 79%, >99:1 dr [a]**3l**: 87%, 85:15 dr

[a]Acetone was used as a solvent. [b]For reaction conditions, see the Experimental Section. Diastereomeric ratios (dr) were determined by ^{19}F NMR spectra of crude reaction mixtures.

the CF_3-spiroether **3a** as a single diastereomer in a 65% isolated yield after silica-gel column chromatography. Single-crystal X-ray crystallography confirmed the *anti*-isomer, (2*R**,2′*S**)-**3a**, was formed as a major isomer (98:2 dr).[11] Even if Cl (**2b**, **2c**) and MeO (**2d**, **2e**) groups are located at various positions, the yields and selectivity were not influenced. The corresponding *anti*-CF_3-spiroethers (**3b**−**e**) were obtained in 41−67% yields with 93:7−98:2 dr. The thiacyclic derivative (**2f**), seven-membered cycloalkene (**2g**), and five-membered cycloalkene (**2h**) were also applied to the present reaction, but yields and diastereoselectivity were sluggish (**3f**, 18%, 92:8 dr; **3g**, 46%, 70:30 dr; **3h**, 76%, 83:17 dr). It should be noted that the structure of the tether moiety significantly affects the diastereoselectivity. The pendant alcohol elongated with a

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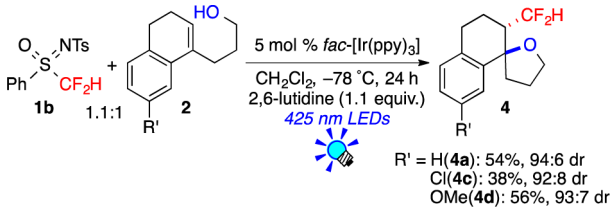
single methylene unit (**2i**) has a beneficial effect on the diastereoselectivity (**3i**, 63%, 96:4 dr). Remarkably, the existence of two geminal methyl groups (**2j**,**k**) on the tether virtually caused formation of a single *anti*-diastereomer (**3j**, 82%, >99:1 dr; **3k**, 79%, >99:1). Furthermore, the reaction of the alcohol with the tetrasubstituted olefin moiety (**2l**) smoothly produced the CF_3-spiroether with the quaternary carbon atom adjacent to the spirocarbon atom (**3l**) in good yield with moderate diastereoselectivity (87%, 85:15 dr). These results suggest that the present photocatalytic system is amenable to highly diastereoselective synthesis of CF_3-spiroethers from aryl-fused cycloalkenylalkanols.[12] Diastereoselectivity is considerably dependent on the structure of the cyclic alkene and pendant alcohol moieties.

These results encouraged us to extend the reaction to synthesis of CF_2H-spiroether through photoredox-catalyzed difluoromethylation. Recently, we reported on photocatalytic oxydifluoromethylation of olefins mediated by *fac*-[Ir(ppy)$_3$] using *N*-tosyl-*S*-difluoromethyl-*S*-phenylsulfoximine (Hu reagent, **1b**) as a difluoromethyl source.[8h] Thus, we conducted the reaction of cycloalkenylalkanol using **1b** and *fac*-[Ir(ppy)$_3$] in place of **1a** and $[Ru(bpy)_3]^{2+}$, respectively, under visible light irradiation (425 nm), otherwise under the optimized reaction conditions (Scheme 2). The reaction of **2a** required longer

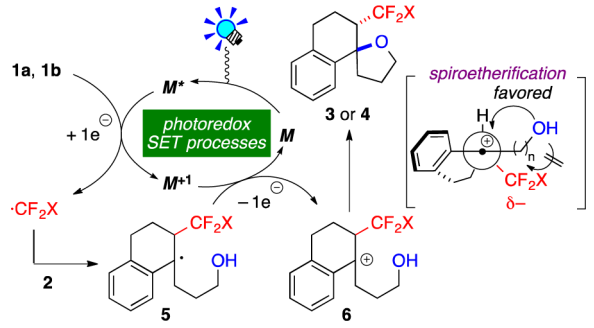
Scheme 2. Photocatalytic CF_2H-Spiroetherification of Cycloalkenylalkanols (2)



reaction time (24 h) but produced the corresponding CF_2H-spiroether **4a** in a 54% isolated yield. The present photocatalytic CF_2H-spiroetherification could be also applied to **2c** and **2d**, leading to the CF_2H-spiroethers in a good diastereoselective manner (**4c**, 38%, 92:8 dr; **4d**, 56%, 93:7 dr). Single-crystal X-ray analysis for the major diastereomer of **4a** revealed that the present CF_2H-spiroetherification also proceeded in an *anti*-fashion.[11] These results suggest that the present photocatalytic system is useful synthetic protocol for a variety of not only *anti*-CF_3- but also *anti*-CF_2H-spiroethers from aryl-fused cycloalkenylalkanols by modification of the fluoromethylating reagents and photocatalysts.

A plausible reaction mechanism is shown in Scheme 3. First, the excited Ru or Ir photocatalyst (***M****) undergoes SET to Umemoto reagent **1a** or Hu reagent **1b**, leading to generation of fluoromethyl radical ($^{\bullet}CF_2X$) and the highly oxidized species Ru^{III}/Ir^{IV} (***M**$^{+1}$*). The generated fluoromethyl radical ($^{\bullet}CF_2X$) adds to cycloalkenylalkanol **2** in a regioselective manner to give the radical intermediate **5**. Subsequently, the highly oxidized species ***M**$^{+1}$* oxidized **5** to afford the α-fluoromethyl substituted carbocationic intermediate **6** and the photocatalyst ***M*** of the ground state. The key intermediate **6** undergoes intramolecular nucleophilic attack of the dangling alcohol in an *anti*-fashion presumably because the nucleophilic attack favors the opposite side of the electronegative fluoromethyl group,[8g,13] leading to the predominant formation of the *anti*-fluoromethylated spiroethers **3** or **4**.

Scheme 3. Plausible Reaction Mechanism



CONCLUSION

In conclusion, we have developed a versatile synthesis of both CF_3- and CF_2H-containing spiroethers from aryl-fused cycloalkenylalkanols through photoredox-catalyzed fluoromethylative spiroetherification. Under similar reaction conditions, simple modification of the fluoromethylating reagent and photocatalyst induces formation of both CF_3- and CF_2H-spiroetherification. This is the first example of an access to *anti*-fluoromethylated spiroethers with excellent diastereoselectivity. Further studies on stereoselective fluoromethylation are underway in our laboratory.

EXPERIMENTAL SECTION

General Experimental Methods. $[Ru(bpy)_3](PF_6)_2$[14] and substrates[15] were prepared according to the reported literature. All chemicals for synthesis of the substrates were commercially available, and Umemoto reagent was purchased from Aldrich. All the reactions were conducted using standard Schlenk tube techniques. Acetone was treated with molecular sieves 3 Å, distilled, and stored under N_2 atmosphere. CH_2Cl_2 was purified through columns containing alumina and alumina−Cu catalyst and stored under N_2. Purification of the substrates and the products was performed by flash column chromatography on silica gel or aluminum oxide. Visible light irradiation was performed with a Relyon LED lamp (3 W × 2; λ = 470 or 425 ± 15 nm). ^1H, ^{13}C, and ^{19}F NMR spectra were acquired on a 400 MHz or a 500 MHz NMR spectrometer. ^1H chemical shifts were referenced to residual protio impurities in the deuterated solvents, and trifluoroacetic acid (−76.55 ppm) was used as an external standard of ^{19}F NMR spectra. All the NMR signals of new compounds were assigned by 2D NMR measurements ($^1H-^1H$ COSY and HSQC). The crystallographic data were deposited at the Cambridge Crystallographic Data Centre: (2*R**,2′*S**)-**3a** (CCDC 1474812), (2*R**,2′*R**)-**3a** (CCDC 1476100), **3b** (CCDC 1474813), **3j** (CCDC 1474815), **3k** (CCDC 1474814), and **4a** (CCDC 1474816).

Synthesis of Alkenyl Bromides. To synthesize cycloalkenylalkanols **2**, alkenyl bromides (4-bromo-1,2-dihydronaphthalene, 4-bromo-7-chloro-1,2-dihydronaphthalene, 4-bromo-6-methoxy-1,2-dihydronaphthalene, 4-bromo-8-methoxy-1,2-dihydronaphthalene, and 9-bromo-6,7-dihydro-5*H*-benzo[7]annulene) were prepared with the procedures reported by Alexakis et al.[15c]

Spectral data for new alkenyl bromides are shown below.

4-Bromo-6-chloro-1,2-dihydronaphthalene. Pale yellow oil (2.90 g, 59%). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.55−7.02 (3H; Ar), 6.49 (t, J = 4.8 Hz, 1H; CBr=C*H*CH$_2$), 2.80 (t, J = 8.0 Hz, 2H; ArCH$_2$C*H*$_2$), 2.40−2.34 (m, 2H; ArC*H*$_2$CH$_2$).

4-Bromo-2H-thiochromene. Pale yellow oil (2.25 g, 49%). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.66−7.14 (4H; Ar), 6.44 (t, J = 6.0 Hz, 1H; CBr=C*H*CH$_2$), 3.40 (d, J = 6.0 Hz, 2H; SC*H*$_2$CH).

General Procedures for Synthesis of Cycloalkenylalkanols 2a, 2b, and 2k. Cycloalkenylalkanols were prepared with the modified procedures reported by List et al.[15b] and Alexakis et al.[15c] To a Et_2O (2.0 mL) solution of the corresponding alkenyl bromide (5.00 mmol) in a 50 mL two-neck flask cooled at −78 °C under N_2

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atmosphere was slowly added ^{t}BuLi (10.0 mmol, in pentane). The mixture was stirred for 30 min at −78 °C and then diluted with Et_2O (3.0 mL). After addition of oxetane or 3,3-dimethyloxetane (10.0 mmol) to the mixture, $BF_3{\cdot}OEt_2$ (10.0 mmol) was added slowly. After being stirred for 15 min at −78 °C, Et_3N (4.0 mL) was added dropwise, and the mixture was warmed to room temperature. The resulting mixture was filtered through an aluminum oxide plug and eluted with Et_2O/MeOH (95:5), and the volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel, and the volatiles were removed under high vacuum to afford the desired product.

Note that 3-bromo-1-propanol or 3-bromo-2,2-dimethyl-1-propanol was formed as a byproduct and it was hard to separate from the cycloalkenylalkanol by column chromatography. The best way to remove them was high vacuum evaporation.

*3-(3,4-Dihydronaphthalen-1-yl)propanol (**2a**).* Purification by flash column chromatography (hexane/AcOEt = 2:1) afforded **2a** as a white solid (0.580 g, 59%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.27−7.13 (4H; *Ar*), 5.89 (t, J = 4.4 Hz, 1H; C=C*H*CH$_2$), 3.71 (t, J = 6.4 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 2.74 (t, J = 8.0 Hz, 2H; ArC*H*$_2$CH$_2$), 2.55 (t, J = 7.6 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.28−2.22 (m, 2H; ArCH$_2$C*H*$_2$), 1.85−1.78 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.27 (brs, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 137.0, 136.0, 134.8, 127.8, 126.8, 126.5, 125.4, 122.8, 62.8, 31.5, 29.1, 28.6, 23.3. HRMS (ESI-TOF) exact mass for $[C_{13}H_{16}O + Na]^+$ calcd m/z 211.1093, found 211.1090.

*3-(6-Chloro-3,4-dihydronaphthalen-1-yl)propanol (**2b**).* Purification by flash column chromatography (hexane/AcOEt = 2:1) afforded **2b** as a yellow oil (0.540 g, 53%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.16−7.12 (3H; *Ar*), 5.89 (t, J = 4.4 Hz, 1H; C=C*H*CH$_2$), 3.71 (dt, J = 6.4 Hz, 5.2 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 2.71 (t, J = 8.0 Hz, 2H; ArC*H*$_2$CH$_2$), 2.52 (t, J = 7.2 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.27−2.24 (m, 2H; ArCH$_2$C*H*$_2$), 1.82−1.75 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.27 (t, J = 5.2 Hz, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): 138.8, 135.4, 133.3, 132.1, 127.8, 126.4, 125.6, 124.0, 62.7, 31.3, 29.0, 28.4, 23.0. HRMS (ESI-TOF) exact mass for $[C_{13}H_{15}ClO + Na]^+$ calcd m/z 245.0704, found 245.0708.

*3-(3,4-Dihydronaphthalen-1-yl)-2,2-dimethylpropanol (**2k**).* Purification by flash column chromatography (hexane/AcOEt = 2:1) afforded **2k** as a pale yellow solid (0.626 g, 56%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.38−7.11 (4H; *Ar*), 5.88 (t, J = 4.4 Hz, 1H; C=C*H*CH$_2$), 3.30 (s, 2H; OHC*H*$_2$CMe$_2$CH$_2$), 2.72 (t, J = 8.0 Hz, 2H; ArC*H*$_2$CH$_2$), 2.48 (s, 2H; OHCH$_2$CMe$_2$C*H*$_2$), 2.25−2.20 (m, 2H; ArCH$_2$C*H*$_2$), 1.38 (brs, 1H; O*H*), 0.86 (s, 6H; OHCH$_2$C*Me*$_2$CH$_2$). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 136.7, 136.1, 134.3, 129.2, 127.7, 126.6, 126.2, 123.3, 71.7, 40.0, 36.6, 29.0, 25.0, 23.5. HRMS (ESI-TOF) exact mass for $[C_{15}H_{20}O + Na]^+$ calcd m/z 239.1406, found 239.1411.

General Procedures for Synthesis of Cycloalkenylalkanols 2c−2g. Cycloalkenylalkanols were prepared with the modified procedures reported by List et al.[15b] and Alexakis et al.[15c] To a Et_2O (2.0 mL) solution of the corresponding alkenyl bromide (5.00 mmol) in a 50 mL two-neck flask cooled at −78 °C under N_2 atmosphere was slowly added ^{n}BuLi (5.00 mmol, in hexane). The mixture was stirred for 1 h at −78 °C and then diluted with Et_2O (3.0 mL). After addition of oxetane (10.0 mmol) to the mixture, $BF_3{\cdot}OEt_2$ (5.00 mmol) was added slowly. After being stirred for 15 min at −78 °C, H_2O (2.0 mL) was added dropwise, and the mixture was warmed to room temperature. The resulting mixture was washed with H_2O and extracted with Et_2O. The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford the desired product.

*3-(7-Chloro-3,4-dihydronaphthalen-1-yl)propanol (**2c**).* Purification by flash column chromatography (CH_2Cl_2) afforded **2c** as a pale yellow oil (0.391 g, 35%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.22−7.05 (3H; *Ar*), 5.94 (t, J = 4.4 Hz, 1H; C=C*H*CH$_2$), 3.73−3.69 (m, 2H; OHC*H*$_2$CH$_2$CH$_2$), 2.69 (t, J = 8.0 Hz, 2H; ArC*H*$_2$CH$_2$), 2.51 (t, J = 7.6 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.27−2.22 (m, 2H; ArCH$_2$C*H*$_2$), 1.84−1.77 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.27 (brs, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 136.6, 135.3, 135.2, 132.2, 128.9, 126.6, 126.5, 122.9, 62.7, 31.2, 28.8, 27.9, 23.1. HRMS (ESI-TOF) exact mass for $[C_{13}H_{15}OCl + Na]^+$ calcd m/z 245.0704, found 245.0700.

*3-(7-Methoxy-3,4-dihydronaphthalen-1-yl)propanol (**2d**).* Purification by flash column chromatography (CH_2Cl_2/AcOEt = 20:1) afforded **2d** as a pale yellow oil (0.498 g, 46%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.07−6.68 (3H; *Ar*), 5.91 (t, J = 4.4 Hz, 1H; C=C*H*CH$_2$), 3.80 (s, 3H; O*Me*), 3.70 (t, J = 6.4 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 2.67 (t, J = 8.0 Hz, 2H; ArC*H*$_2$CH$_2$), 2.52 (t, J = 8.0 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.25−2.20 (m, 2H; ArCH$_2$C*H*$_2$), 1.85−1.78 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.27 (brs, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 158.5, 135.9 (2C), 129.1, 128.3, 126.1, 110.9, 109.8, 62.8, 55.5, 31.4, 29.1, 27.6, 23.6. HRMS (ESI-TOF) exact mass for $[C_{14}H_{18}O_2 + Na]^+$ calcd m/z 241.1199, found 241.1202.

*3-(5-Methoxy-3,4-dihydronaphthalen-1-yl)propanol (**2e**).* Purification by flash column chromatography (CH_2Cl_2/AcOEt = 20:1) afforded **2e** as a yellow oil (0.359 g, 34%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.18−6.78 (3H; *Ar*), 5.90 (t, J = 4.4 Hz, 1H; C=C*H*CH$_2$), 3.84 (s, 3H; O*Me*), 3.71 (dt, J = 6.4 Hz, 5.6 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 2.74 (t, J = 8.0 Hz, 2H; ArC*H*$_2$CH$_2$), 2.54 (t, J = 7.6 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.24−2.19 (m, 2H; ArCH$_2$C*H*$_2$), 1.83−1.76 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.26 (t, J = 5.6 Hz, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 156.3, 135.90, 135.86, 126.5, 125.6, 124.8, 115.9, 109.7, 62.8, 55.7, 31.6, 29.5, 22.6, 20.1. HRMS (ESI-TOF) exact mass for $[C_{14}H_{18}O_2 + Na]^+$ calcd m/z 241.1199, found 241.1204.

*3-(2H-Thiochromen-4-yl)propanol (**2f**).* Purification by flash column chromatography (CH_2Cl_2/AcOEt = 20:1) afforded **2f** as a yellow oil (0.340 g, 33%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.34−7.10 (4H; *Ar*), 5.92 (t, J = 5.6 Hz, 1H; C=C*H*CH$_2$), 3.68 (dt, J = 6.0 Hz, 5.6 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 3.30 (d, J = 5.6 Hz, 2H; SC*H*$_2$CH), 2.59 (t, J = 7.2 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 1.78−1.71 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.27 (t, J = 5.6 Hz, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 138.1, 133.7, 133.6, 127.9, 127.5, 125.7, 125.0, 119.4, 62.5, 31.4, 30.4, 25.0. HRMS (ESI-TOF) exact mass for $[C_{12}H_{14}OS + Na]^+$ calcd m/z 229.0658, found 229.0660.

*3-(6,7-Dihydro-5H-benzo[7]annulen-9-yl)propanol (**2g**).* Purification by flash column chromatography (CH_2Cl_2/AcOEt = 20:1) afforded **2g** as a pale yellow oil (0.418 g, 39%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.27−7.15 (4H; *Ar*), 5.99 (t, J = 7.2 Hz, 1H; C=C*H*CH$_2$), 3.62 (t, J = 6.4 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 2.57 (t, J = 8.0 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.55 (t, J = 7.2 Hz, 2H; ArC*H*$_2$CH$_2$), 2.12−2.05 (m, 2H; C*H*$_2$CH$_2$CH), 1.83−1.78 (dt, J = 7.2 Hz, 6.8 Hz, 2H; CH$_2$C*H*$_2$CH), 1.67−1.60 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.18 (brs, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 141.6, 141.2, 140.7, 129.0, 126.7, 126.3, 126.1, 126.0, 62.8, 34.8, 32.8, 32.5, 32.0, 24.6. HRMS (ESI-TOF) exact mass for $[C_{14}H_{18}O + Na]^+$ calcd m/z 225.1250, found 225.1247.

General Procedures for Synthesis of Indenyl Alcohols 2h and 2j. Indenyl alcohols were prepared with the modified procedures reported by Taylor et al.[15a] and List et al.[15b] To a Et_2O (2.0 mL) solution of indene (5.00 mmol) in a 50 mL two-neck flask cooled at 0 °C under N_2 atmosphere was added dropwise ^{n}BuLi (5.00 mmol). After being stirred for 1 h at 0 °C, the mixture was cooled to −78 °C and Et_2O (3.0 mL) was added. After addition of oxetane or 3,3-dimethyloxetane (10.0 mmol) to the mixture, $BF_3{\cdot}OEt_2$ (5.00 mmol) was added slowly. After being stirred for 1 h at −78 °C, Et_3N (2.0 mL) was added dropwise, and the mixture was allowed to warm to room temperature. The resulting mixture was filtered through an aluminum oxide plug eluted with Et_2O/MeOH (95:5), and volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford the desired product.

*3-(1H-Inden-3-yl)propanol (**2h**).* Purification by flash column chromatography (hexane/AcOEt = 2:1) afforded **2h** as a pale yellow oil (0.380 g, 43%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.47−7.19 (4H; *Ar*), 6.24 (t, J = 1.6 Hz, 1H; C=C*H*CH$_2$), 3.76 (dt, J = 6.4 Hz, 5.2 Hz, 2H; OHC*H*$_2$CH$_2$CH$_2$), 3.34 (d, J = 2.0 Hz, 2H; ArC*H*$_2$CH), 2.66 (t, J = 7.2 Hz, 2H; OHCH$_2$CH$_2$C*H*$_2$), 2.01−1.94 (m, 2H; OHCH$_2$C*H*$_2$CH$_2$), 1.31 (t, J = 5.2 Hz, 1H; O*H*). ^{13}C NMR (100

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MHz, $CDCl_3$, rt): δ 145.4, 144.7, 144.0, 128.2, 126.2, 124.7, 123.9, 119.1, 62.8, 37.9, 31.1, 24.1. HRMS (ESI-TOF) exact mass for $[C_{12}H_{14}O + Na]^+$ calcd m/z 197.0937, found 197.0935.

*3-(1H-Inden-3-yl)-2,2-dimethylpropanol (**2j**).* Purification by flash column chromatography (hexane/AcOEt = 2:1) afforded **2j** as a pale yellow oil (0.658 g, 61%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.46–7.17 (4H; *Ar*), 6.26 (s, 1H; C=C*H*CH_2), 3.40 (d, J = 4.0 Hz, 2H; OHC*H*$_2$CMe_2CH_2), 3.37 (s, 2H; ArC*H*$_2$CH), 2.57 (s, 2H; OHCCH_2Me$_2$C*H*$_2$), 1.40 (brs, 1H; O*H*), 0.96 (s, 6H; OHCH_2C*Me*$_2$CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 146.7, 144.3, 141.6, 131.9, 126.1, 124.4, 123.8, 119.8, 71.9, 38.0, 36.6, 35.8, 24.7. HRMS (ESI-TOF) exact mass for $[C_{14}H_{18}O + Na]^+$ calcd m/z 225.1250, found 225.1247.

Procedures for Synthesis of the Other Indenyl Alcohols. *4-(1H-Inden-3-yl)butanol (**2i**).* The cycloalkenylalkanol was prepared with the modified procedures reported by Taylor et al.[15a] and List et al.[15b] To a THF (2.0 mL) solution of indene (0.594 g, 5.11 mmol) in a 50 mL two-neck flask cooled at 0 °C under N_2 atmosphere was added dropwise ^{n}BuLi (1.95 mL, 5.07 mmol, 2.6 M in hexane). After being stirred for 1 h at 0 °C, the mixture was diluted with THF (2.0 mL), and *tert*-butyl(4-iodobutoxy)dimethylsilane (1.89 g, 6.02 mmol) was added. The resulting mixture was stirred for 1.5 h at 50 °C and then cooled to room temperature. The resulting mixture was filtered through a Celite pad followed by an aluminum oxide plug and eluted with Et_2O, and volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 2:1) to afford **2i** as a pale yellow oil (0.471 g, 49%). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.47–7.18 (4H; *Ar*), 6.22 (s, 1H; C=C*H*CH_2), 3.70 (t, J = 6.4 Hz, 2H; OHC*H*$_2$CH_2), 3.33 (s, 2H; ArC*H*$_2$CH), 2.60 (t, J = 7.6 Hz, 2H; CC*H*$_2$CH_2), 1.80–1.75 (m, 2H; CCH$_2$C*H*$_2$), 1.73–1.67 (m, 2H; OHCH$_2$C*H*$_2$), 1.23 (brs, 1H; O*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 145.6, 144.7, 144.3, 128.1, 126.1, 124.6, 123.9, 119.0, 63.0, 37.8, 32.8, 27.6, 24.3. HRMS (ESI-TOF) exact mass for $[C_{13}H_{16}O + Na]^+$ calcd m/z 211.1093, found 211.1091.

*2,2-Dimethyl-3-(2-methyl-1H-inden-3-yl)propanol (**2l**).* The cycloalkenylalkanol was prepared with the modified procedures reported by Taylor et al.[15a] and List et al.[15b] To a Et_2O (2.0 mL) solution of 2-methylindene (0.667 g, 5.12 mmol) in a 50 mL two-neck flask cooled at 0 °C under N_2 atmosphere was added dropwise ^{n}BuLi (1.95 mL, 2.6 M in hexane, 5.07 mmol). After being stirred for 1 h at 0 °C, the mixture was cooled to −78 °C, and Et_2O (3.0 mL) was added. After addition of 3,3-dimethyloxetane (0.891 g, 10.3 mmol) to the mixture, $BF_3{\cdot}OEt_2$ (0.650 mL, 5.20 mmol) was added slowly. After the mixture was stirred for 1 h at −78 °C, Et_3N (2.0 mL) was added dropwise, and the mixture was allowed to warm to room temperature. The resulting mixture was filtered through an aluminum oxide plug and eluted with Et_2O/MeOH (95:5), and volatiles were evaporated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (hexane/AcOEt = 4:1) to afford the mixture of two isomers. To promote isomerization, Et_3N was added to the mixture, and the mixture was stirred for 2 h at 50 °C. Then, Et_3N was evaporated under vacuum to afford pure **2l** (0.521 g, 47%) as a pale yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.36–7.08 (4H; *Ar*), 3.41 (d, J = 6.0 Hz, 2H; OHCH_2CMe_2CH_2), 3.31 (s, 2H; ArCH_2CH), 2.51 (s, 2H; OHCCH_2Me$_2$CH_2), 2.09 (s, 3H, C=C*Me*), 1.40 (t, J = 6.0 Hz, 1H; O*H*), 0.96 (s, 6H; OHCH_2C*Me*$_2$CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 148.2, 142.5, 141.7, 134.9, 126.0, 123.6, 123.1, 119.3, 72.4, 43.1, 38.5, 33.6, 25.0, 15.4. HRMS (ESI-TOF) exact mass for $[C_{15}H_{20}O + Na]^+$ calcd m/z 239.1406, found 239.1408.

Typical Procedures of NMR Experiments. An NMR tube was charged with **2a** (4.7 mg, 0.0250 mmol), Umemoto reagent **1a** (9.4 mg, 0.0276 mmol), $[Ru(bpy)_3](PF_6)_2$ (1.1 mg, 1.28 μmol), 2,6-lutidine (3.0 mg, 0.0280 mmol), tetraethylsilane as an internal standard, and CD_2Cl_2 (0.40 mL) under N_2 atmosphere. The mixture was degassed by three freeze–pump–thaw cycles. The reaction was carried out at −78 °C (dry ice–MeOH bath) under visible light irradiation (placed at a distance of 2–3 cm from blue LED lamp, λ = 470 ± 15 nm). The spectra are shown in the Supporting Information.

Note that yields were determined by ^{1}H NMR spectra, and diastereomeric ratios were determined by ^{19}F NMR spectra.

General Procedures for Synthesis of CF_3-Containing Spiroethers by Photoredox Catalysis. A 20 mL Schlenk tube was charged with **2** (0.250 mmol), Umemoto reagent **1a** (0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (0.00125 mmol), 2,6-lutidine (0.275 mmol), and CH_2Cl_2 (4.0 mL) under N_2 atmosphere. The mixture was degassed by three freeze–pump–thaw cycles. The Schlenk tube was placed 2–3 cm away from blue LED lamps (λ = 470 ± 15 nm). The mixture was stirred for 3 h at −78 °C (dry ice-methanol bath) under visible light irradiation. The resulting mixture was warmed to room temperature, washed with water (10 mL), and extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica-gel to afford the product **3**.

Note that diastereomeric ratios (dr) were determined by ^{19}F NMR spectra of the crude products, **3h** and **3l** were obtained as a mixture of two diastereomers, while in the case of the other spiroethers, only the major isomer was obtained by flash column chromatography, and acetone was used as a solvent instead of CH_2Cl_2 when **3f** and **3l** were used as the substrates.

(2R,2′S*)-2′-(Trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene] ((2R*,2′S*)-**3a**).* Purification of the crude products (dr 98:2) by flash column chromatography (hexane/Et_2O = 20:1) afforded (2*R**,2′*S**)-**3a** as a white solid (41.7 mg, 65%, a single isomer). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.38–7.05 (4H; *Ar*), 4.25–4.12 (m, 2H; OCH_2CH$_2$), 2.93–2.90 (m, 2H; ArCH_2CH$_2$), 2.74–2.63 (m, 1H; CF_3C*H*CH$_2$), 2.57–2.50 (m, 1H; CC*H*HCH$_2$), 2.30–2.23 (m, 1H; CF_3CHC*H*H), 2.16–2.06 (m, 2H; CCH$_2$C*H*$_2$), 2.02–1.92 (2H; CCH*H*CH$_2$, CF_3CHCH*H*). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 144.6, 134.6, 128.3, 127.5 (q, J = 281.3 Hz), 127.2, 126.5, 125.3, 84.0, 69.9, 47.4 (q, J = 23.9 Hz), 35.8, 27.6, 25.9, 21.5. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.7 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{14}H_{15}F_3O + Na]^+$ calcd m/z 279.0967, found 279.0967. Mp 45 °C.

(2R,2′S*)-6′-Chloro-2′-(trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene] (**3b**).* Purification of the crude products (dr 98:2) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3b** as a white solid (45.1 mg, 62%, a single isomer). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.30–7.06 (3H; *Ar*), 4.21–4.10 (m, 2H; OCH_2CH$_2$), 2.90–2.87 (m, 2H; ArCH_2CH$_2$), 2.69–2.62 (m, 1H; CF_3C*H*CH$_2$), 2.55–2.48 (m, 1H; CC*H*HCH$_2$), 2.30–2.23 (m, 1H; CF_3CHC*H*H), 2.13–2.06 (m, 2H; CCH$_2$C*H*$_2$), 2.01–1.88 (2H; CCH*H*CH$_2$, CF_3CHCH*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 143.0, 136.6, 133.0, 128.8, 127.4 (q, J = 281.1 Hz), 126.9, 126.7, 83.6, 69.8, 47.3 (q, J = 24.1 Hz), 35.7, 27.4, 25.9, 21.2. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.6 (d, J = 9.4 Hz). HRMS (ESI-TOF) exact mass for $[C_{14}H_{14}ClF_3O + Na]^+$ calcd m/z 313.0577, found 313.0582. EA calcd for $C_{14}H_{14}ClF_3O$: C, 57.84; H, 4.85. Found: C, 57.59; H, 4.70. Mp 45 °C.

(2R,2′S*)-7′-Chloro-2′-(trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene] (**3c**).* Purification of the crude products (dr 98:2) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3c** as a colorless oil (37.0 mg, 51%, a single isomer). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 7.33–6.99 (3H; *Ar*), 4.25–4.11 (m, 2H; OCH_2CH$_2$), 2.89–2.85 (m, 2H; ArCH_2CH$_2$), 2.69–2.59 (m, 1H; CF_3C*H*CH$_2$), 2.56–2.49 (m, 1H; CC*H*HCH$_2$), 2.29–2.22 (m, 1H; CF_3CHC*H*H), 2.14–2.07 (m, 2H; CCH$_2$C*H*$_2$), 2.01–1.89 (2H; CCH*H*CH$_2$, CF_3CHCH*H*). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 146.4, 133.1, 132.2, 129.8, 127.43, 127.37 (q, J = 281.1 Hz), 125.3, 83.7, 69.9, 47.2 (q, J = 24.1 Hz), 35.6, 27.0, 25.8, 21.2. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.7 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{14}H_{14}ClF_3O + Na]^+$ calcd m/z 313.0577, found 313.0576.

(2R,2′S*)-7′-Methoxy-2′-(trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene] (**3d**).* Purification of the crude products (dr 93:7) by flash column chromatography (hexane/Et_2O = 10:1) afforded **3d** as a white solid (29.5 mg, 41%, a single isomer). ^{1}H NMR (400 MHz, $CDCl_3$, rt): δ 6.99–6.73 (3H; *Ar*), 4.23–4.13 (m, 2H; OCH_2CH$_2$), 3.80 (s, 3H; O*Me*), 2.86–2.83 (m, 2H; ArCH_2CH$_2$),

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2.71−2.60 (m, 1H; CF_3CHCH_2), 2.56−2.49 (m, 1H; $CCHHCH_2$), 2.27−2.20 (m, 1H; CF_3CHCHH), 2.16−2.05 (m, 2H; CCH_2CH_2), 2.00−1.89 (2H; $CCHHCH_2$, CF_3CHCHH). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 158.3, 145.9, 129.3, 127.6 (q, J = 281.2 Hz), 126.8, 113.2, 110.4, 84.0, 70.0, 55.4, 47.4 (q, J = 23.7 Hz), 35.7, 26.8, 25.9, 21.6. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.6 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{15}H_{17}F_3O_2 + Na]^+$ calcd m/z 309.1073, found 309.1069. Mp 47 °C.

(2R,2′S*)-5′-Methoxy-2′-(trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene]* (**3e**). Purification of the crude products (dr 98:2) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3e** as a white solid (47.3 mg, 67%, a single isomer). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.21−6.71 (3H; *Ar*), 4.52−4.12 (m, 2H; OCH_2CH_2), 3.81 (s, 3H; O*Me*), 2.91−2.84 (m, 1H; $ArCHHCH_2$), 2.74−2.59 (m, 2H; $ArCHHCH_2$, CF_3CHCH_2), 2.55−2.48 (m, 1H; $CCHHCH_2$), 2.32−2.26 (m, 1H; CF_3CHCHH), 2.17−2.05 (m, 2H; CCH_2CH_2), 2.00−1.85 (2H; $CCHHCH_2$, CF_3CHCHH). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 156.5, 146.1, 127.6 (q, J = 281.1 Hz), 126.9, 123.6, 117.3, 108.1, 84.0, 70.1, 55.4, 47.1 (q, J = 23.9 Hz), 36.0, 25.9, 21.9, 21.1. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −65.7 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{15}H_{17}F_3O_2 + Na]^+$ calcd m/z 309.1073, found 309.1077. EA calculated for $C_{15}H_{17}F_3O_2$: C, 62.93; H, 5.99. Found: C, 62.76; H, 5.74. Mp 67 °C.

3′-(Trifluoromethyl)-4,5-dihydro-3H-spiro[furan-2,4′-thiochromane] (**3f**). Purification of the crude products (dr 92:8) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3f** as a colorless oil (12.6 mg, 18%, a single isomer). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.42−7.09 (4H; *Ar*), 4.31−4.26 (m, 1H; $OCHHCH_2$), 4.10−4.03 (m, 1H; $OCHHCH_2$), 3.35 (dd, J = 12.2 Hz, 5.2 Hz, 1H; $SCHHCH$), 3.19 (dd, J = 11.8 Hz, 1H; $SCHHCH$), 2.94−2.84 (m, 1H; SCH_2CH), 2.46−2.38 (m, 1H; $CCHHCH_2$), 2.13−2.08 (m, 1H; $CCHHCH_2$), 2.04−1.94 (m, 2H; CCH_2CH_2). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 142.0, 131.2, 127.9, 126.57 (q, J = 282.5 Hz), 126.56, 124.8, 124.6, 83.1, 70.0, 46.2 (q, J = 24.1 Hz), 33.3, 24.9, 23.6 (q, J = 3.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −65.3 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{13}H_{13}F_3OS + Na]^+$ calcd m/z 297.0531, found 297.0528.

6-(Trifluoromethyl)-4′,5′,6,7,8,9-hexahydro-3′H-spiro[benzo[7]annulene-5,2′-furan] (**3g**). Purification of the crude products (dr 70:30) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3g** as a colorless oil (30.9 mg, 46%, a single isomer). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.57−7.07 (4H; *Ar*), 4.18−4.13 (m, 1H; $OCHHCH_2$), 4.05−3.99 (m, 1H; $OCHHCH_2$), 3.07−3.00 (m, 1H; $ArCHHCH_2$), 2.82−2.77 (m, 1H; $ArCHHCH_2$), 2.67−2.60 (m, 1H; CF_3CHCH_2), 2.44−2.39 (m, 1H; $CCHHCH_2$), 2.28−2.03 (3H; CF_3CHCHH, $CCHHCH_2$, CF_3CHCHH), 1.93−1.82 (2H; $ArCH_2CHH$, CCH_2CHH), 1.75−1.63 (2H; CCH_2CHH, $ArCH_2CHH$). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 142.7, 137.9, 130.7, 127.4 (q, J = 283.5 Hz), 127.3, 126.5, 126.3, 86.5, 68.3, 50.5 (q, J = 22.7 Hz), 38.4, 36.7, 27.0, 25.0, 23.7. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −62.3 (brs). HRMS (ESI-TOF) exact mass for $[C_{15}H_{17}F_3O + Na]^+$ calcd m/z 293.1124, found 293.1121.

2′-(Trifluoromethyl)-2′,3′,4,5-tetrahydro-3H-spiro[furan-2,1′-indene] (**3h**). Purification of the crude products (dr 83:17) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3h** as a colorless oil (46.8 mg, 76%, a mixture of isomers, 83:17). Major isomer (2*R**,2′*S**)-**3h**. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.28−7.20 (4H; *Ar*), 4.16−4.04 (m, 2H; OCH_2CH_2), 3.10−2.94 (3H; CF_3CHCH_2, $ArCH_2CH$), 2.58−2.51 (m, 1H; $CCHHCH_2$), 2.28−2.09 (m, 2H; CCH_2CH_2), 1.97−1.90 (m, 1H; $CCHHCH_2$). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 147.5, 138.0, 128.5, 127.7, 127.3 (q, J = 278.6 Hz), 124.7, 122.8, 91.8, 68.9, 53.4 (q, J = 25.9 Hz), 33.5, 30.6 (q, J = 3.0 Hz), 26.4; ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.9 (d, J = 9.1 Hz). Minor isomer (2*R**,2′*R**)-**3h**. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.28−7.20 (4H; *Ar*), 4.16−4.04 (m, 2H; OCH_2CH_2), 3.10−2.94 (3H; CF_3CHCH_2, $ArCH_2CH$), 2.34−2.09 (4H; CCH_2CH_2, CCH_2CH_2). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 145.6, 139.4, 128.8, 127.7, 127.0 (q, J = 279.1 Hz), 124.7, 122.9, 90.7, 69.2, 51.9 (q, J = 25.1 Hz), 38.7, 31.2 (q, J = 2.8 Hz), 26.6. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −67.2 (d, J = 9.5 Hz). HRMS (ESI-TOF) exact mass for $[C_{13}H_{13}F_3O + Na]^+$ calcd m/z 265.0811, found 265.0810.

(1R,2S*)-2-(Trifluoromethyl)-2,3,3′,4′,5′,6′-hexahydrospiro[indene-1,2′-pyran]* (**3i**). Purification of the crude products (dr 96:4) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3i** as a colorless oil (40.7 mg, 63%, a single isomer). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.48−7.23 (4H; *Ar*), 3.92−3.87 (m, 1H; $OCHHCH_2$), 3.76−3.70 (m, 1H; $OCHHCH_2$), 3.36 (dd, J = 16.0 Hz, 8.0 Hz, 1H; $ArCHHCH$), 3.31−3.23 (m, 1H; CF_3CHCH_2), 3.05 (dd, J = 16.0 Hz, 3.6 Hz, 1H; $ArCHHCH$), 2.11−2.08 (m, 2H; CCH_2CH_2), 1.98−1.83 (m, 2H; CCH_2CH_2), 1.75−1.66 (m, 2H; OCH_2CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, rt): δ 145.5, 141.0, 129.0, 127.5 (q, J = 279.5 Hz), 126.9, 124.9, 123.9, 84.6, 63.8, 51.5 (q, J = 25.5 Hz), 31.3, 29.7, 25.6, 19.8. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.5 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{14}H_{15}F_3O + Na]^+$ calcd m/z 279.0967, found 279.0970.

(2R,2′S*)-4,4-Dimethyl-2′-(trifluoromethyl)-2′,3′,4,5-tetrahydro-3H-spiro[furan-2,1′-indene]* (**3j**). Purification of the crude products (dr >99:1) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3j** as a white solid (55.2 mg, 82%, a single isomer). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.37−7.22 (4H; *Ar*), 3.66 (d, J = 8.4 Hz, 1H; $OCHHCMe_2$), 3.61 (d, J = 8.4 Hz, 1H; $OCHHCH_2$), 3.36 (dd, J = 16.0 Hz, 8.0 Hz, 1H; $ArCHHCH$), 3.26−3.14 (m, 1H; CF_3CHCH_2), 3.09 (dd, J = 16.2 Hz, 4.8 Hz, 1H; $ArCHHCH$), 2.53 (d, J = 14.0 Hz, 1H; $CCHHCMe_2$), 2.06 (d, J = 14.4 Hz, 1H; $CCHHCMe_2$), 1.32 (s, 3H; CCH_2CMeMe), 1.21 (s, 3H; CCH_2CMeMe). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 146.2, 139.8, 128.9, 128.3, 127.2 (q, J = 278.5 Hz), 124.7, 123.1, 92.9, 79.5, 54.5 (q, J = 25.3 Hz), 45.9, 40.8, 31.5, 27.8, 26.9. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −66.0 (d, J = 10.2 Hz). HRMS (ESI-TOF) exact mass for $[C_{15}H_{17}F_3O + Na]^+$ calcd m/z 293.1124, found 293.1125. Mp 43 °C.

(2R,2′S*)-4,4-Dimethyl-2′-(trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene]* (**3k**). Purification of the crude products (dr > 99:1) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3k** as a white solid (56.7 mg, 79%, a single isomer). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.60−7.09 (4H; *Ar*), 3.80 (d, J = 8.4 Hz, 1H; $OCHHCH_2$), 3.76 (d, J = 8.4 Hz, 1H; $OCHHCH_2$), 2.88−2.84 (m, 2H; $ArCH_2CH_2$), 2.65−2.57 (m, 1H; CF_3CHCH_2), 2.46 (d, J = 13.6 Hz, 1H; $CCHHCMe_2$), 2.32−2.23 (m, 1H; CF_3CHCHH), 2.07−1.98 (m, 1H; CF_3CHCHH), 1.94 (1H; $CCHHCMe_2$), 1.18 (s, 3H, CCH_2CMeMe), 1.16 (s, 3H, CCH_2CMeMe). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 143.7, 135.3, 128.7, 127.5 (q, J = 281.2 Hz), 127.3, 126.0, 124.2, 84.3, 80.4, 47.8 (q, J = 23.4 Hz), 47.3, 40.5, 28.2, 27.6, 26.0, 19.5. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −65.3 (d, J = 9.8 Hz). HRMS (ESI-TOF) exact mass for $[C_{16}H_{19}OF_3 + Na]^+$ calcd m/z 307.1280, found 307.1278. Mp 58 °C.

2′,4,4-Trimethyl-2′-(trifluoromethyl)-2′,3′,4,5-tetrahydro-3H-spiro[furan-2,1′-indene] (**3l**). Purification of the crude products (dr 85:15) by flash column chromatography (hexane/Et_2O = 20:1) afforded **3l** as a white solid (55.9 mg, 87%, a mixture of isomers: 85:15). Major isomer (2*R**,2′*R**)-**3l**. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.30−7.18 (4H; *Ar*), 3.57−3.50 (m, 2H; OCH_2CMe_2), 3.26 (d, J = 16.2 Hz, 1H; $ArCHHCMe$), 3.03 (d, J = 16.2 Hz, 1H; $ArCHHC$), 2.46 (d, J = 14.2 Hz, 1H; $CCHHCMe_2$), 2.07 (d, J = 14.2 Hz, 1H; $CCHHCMe_2$), 1.42 (s, 3H; CF_3CMe), 1.34 (s, 3H; CCH_2CMeMe), 1.20 (s, 3H; CCH_2CMeMe). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 146.8, 140.0, 128.8 (q, J = 283.5 Hz), 128.5, 126.8, 124.5, 122.8, 93.7, 78.6, 56.6 (q, J = 22.3 Hz), 44.6 (q, J = 2.5 Hz), 40.1, 39.8, 28.2, 27.2, 15.4. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −70.4. Minor isomer (2*R**,2′*S**)-**3l**. ^1H NMR (400 MHz, $CDCl_3$, rt): δ7.30−7.18 (4H; *Ar*), 3.64 (d, J = 15.4 Hz, 1H; $ArCHHCMe$), 3.57−3.50 (m, 2H; OCH_2CMe_2), 2.66 (d, J = 15.4 Hz, 1H; $ArCHHC$), 2.38 (d, J = 13.6 Hz, 1H; $CCHHCMe_2$), 2.09 (d, J = 13.6 Hz, 1H; $CCHHCMe_2$), 1.35 (s, 3H; CCH_2CMeMe), 1.23 (s, 3H; CCH_2CMeMe), 1.14 (s, 3H; CF_3CMe). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 145.1, 140.3, 128.8, 128.5 (q, J = 281.9 Hz), 126.9, 125.6, 123.6, 95.3, 79.1, 53.7 (q, J = 23.5 Hz), 44.7, 40.1, 39.5, 28.2, 27.4, 19.4. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −70.7. HRMS (ESI-TOF) exact mass for $[C_{16}H_{19}F_3O + Na]^+$ calcd m/z 307.1280, found 307.1283.

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Procedures for Synthesis of (2*R,2′*R**)-3a (*syn*-Isomer).** *(2R*,2′R*)-2′-(Trifluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro-[furan-2,1′-naphthalene] ((2R*,2′R*)-**3a**).* A 20 mL Schlenk tube was charged with **2a** (47.0 mg, 0.250 mmol), Umemoto reagent **1a** (93.6 mg, 0.275 mmol), $[Ru(bpy)_3](PF_6)_2$ (1.1 mg, 0.00125 mmol), and CH_2Cl_2 (4.0 mL) under N_2 atmosphere. The mixture was degassed by three freeze−pump−thaw cycles. The Schlenk tube was placed 2−3 cm away from blue LED lamps (λ = 470 ± 15 nm). The mixture was stirred for 3 h at −78 °C (dry ice−methanol bath) under visible light irradiation. The resulting mixture was warmed to room temperature, washed with water (10 mL) and extracted with CH_2Cl_2 (10 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product (dr 45:55) was purified by flash column chromatography on silica gel (hexane/Et_2O = 20:1) to afford (2*R**,2′*R**)-**3a** (9.7 mg, 15%, a single isomer) as a white solid. ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.47−7.04 (4H; *Ar*), 4.29−4.24 (m, 1H; OC*H*HCH$_2$), 4.16−4.11 (m, 1H; OCH*H*CH$_2$), 2.98−2.89 (m, 1H; ArC*H*HCH$_2$), 2.78−2.71 (m, 1H; ArCH*H*CH$_2$), 2.68−2.61 (m, 1H; CF$_3$C*H*CH$_2$), 2.32−1.97 (6H; CC*H*HCH$_2$, CF$_3$CHC*H*H, CCH$_2$C*H*$_2$, CCH*H*CH$_2$, CF$_3$CHCH*H*). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 141.3, 135.4, 128.1, 127.1 (q, J = 282.4 Hz), 127.0, 126.7, 125.9, 82.5, 69.3, 46.2 (q, J = 23.6 Hz), 43.7, 25.8, 25.2, 22.0. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −64.5 (d, J = 10.2 Hz). HRMS (ESI-TOF) exact mass for $[C_{14}H_{15}F_3O + Na]^+$ calcd m/z 279.0967 found 279.0971.

Note that diastereomeric ratio was determined by ^{19}F NMR spectrum of the crude product.

General Procedures for Synthesis of CF_2H-Containing Spiroethers by Photoredox Catalysis. A 20 mL Schlenk tube was charged with **2** (0.250 mmol), Hu reagent **1b** (0.275 mmol), *fac*-$[Ir(ppy)_3]$ (0.0125 mmol), 2,6-lutidine (0.275 mmol), and CH_2Cl_2 (4.0 mL) under N_2 atmosphere. The mixture was degassed by three freeze−pump−thaw cycles. The Schlenk tube was placed at 2−3 cm away from blue LED lamps (λ = 425 ± 15 nm). The mixture was stirred for 24 h at −78 °C (dry ice−methanol bath) under visible light irradiation. The resulting mixture was warmed to room temperature, washed with water (10 mL), and extracted with CH_2Cl_2 (10 mL × 3). The combined organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica-gel to afford the product **5**.

Note that diastereomeric ratios were determined by ^{19}F NMR spectra of crude products.

(2R,2′S*)-2′-(Difluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro-[furan-2,1′-naphthalene] (**4a**).* Purification of the crude products (dr 94:6) by flash column chromatography (hexane/Et_2O = 20:1) afforded **4a** as a white solid (31.9 mg, 54%, a mixture of isomers, 94:6). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.34−7.06 (4H; *Ar*), 6.19 (dt, J = 56.4 Hz, 1.2 Hz, 1H; CF$_2$*H*), 4.30−4.09 (m, 2H; OCH_2CH$_2$), 2.94−2.89 (m, 2H; ArCH_2CH$_2$), 2.45−2.30 (2H; CC*H*HCH$_2$, CF$_2$HC*H*CH$_2$), 2.26−2.10 (2H; CF$_2$HCHC*H*H, CCH$_2$C*H*H), 2.03−1.82 (3H; CF$_2$HCHCH*H*, CCH$_2$CH*H*, CCH*H*CH$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 145.2, 135.0, 128.6, 127.1, 126.3, 124.8, 116.6 (t, J = 239.7 Hz), 84.2, 70.6, 47.9 (t, J = 19.7 Hz), 35.7, 27.7, 26.0, 18.3. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −120.5 (ddd, J = 287.2 Hz, 54.9 Hz, 10.5 Hz, 1F), −126.4 (ddd, J = 287.6 Hz, 57.6 Hz, 26.4 Hz, 1F). HRMS (ESI-TOF) exact mass for $[C_{14}H_{16}F_2O + Na]^+$ calcd m/z 261.1061, found 261.1066. EA calcd for $C_{14}H_{16}F_2O$: C, 70.57; H, 6.77. Found: C, 70.42; H, 6.52. Mp 41 °C.

(2R,2′S*)-7′-Chloro-2′-(difluoromethyl)-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene] (**4c**).* Purification of the crude products (dr 92:8) by flash column chromatography (hexane/Et_2O = 20:1) afforded **4c** as a white solid (25.6 mg, 38%, a mixture of isomers, 92:8). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.29−6.99 (3H; *Ar*), 6.09 (dt, J = 56.2 Hz, 1.2 Hz, 1H; CF$_2$*H*), 4.30−4.08 (m, 2H; OCH_2CH$_2$), 2.90−2.83 (m, 2H; ArCH_2CH$_2$), 2.44−2.28 (2H; CC*H*HCH$_2$, CF$_2$HC*H*CH$_2$), 2.26−2.07 (2H; CF$_2$HCHC*H*H, CCH$_2$C*H*H), 2.04−1.78 (3H; CF$_2$HCHCH*H*, CCH$_2$CH*H*, CCH*H*CH$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 147.1, 133.4, 132.0, 130.0, 127.3, 124.9, 116.4 (t, J = 239.8 Hz), 83.9, 70.8, 47.6 (t, J = 19.9 Hz), 35.7, 27.2, 26.0, 18.1. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −120.6 (ddd, J = 288.4 Hz, 55.3 Hz, 10.5 Hz, 1F), −126.5 (ddd, J = 288.4 Hz, 57.6 Hz, 26.4 Hz, 1F). HRMS (ESI-TOF) exact mass for $[C_{14}H_{15}ClF_2O + Na]^+$ calcd m/z 295.0672, found 295.0675. Mp 66 °C.

(2R,2′S*)-2′-(Difluoromethyl)-7′-methoxy-3′,4,4′,5-tetrahydro-2′H,3H-spiro[furan-2,1′-naphthalene] (**4d**).* Purification of the crude products (dr 93:7) by flash column chromatography (hexane/Et_2O = 10:1) afforded **4d** as a colorless oil (37.4 mg, 56%, a mixture of isomers, 93:7). ^1H NMR (400 MHz, $CDCl_3$, rt): δ 7.00−6.73 (3H; *Ar*), 6.09 (dt, J = 56.4 Hz, 1.2 Hz, 1H; CF$_2$*H*), 4.30−4.08 (m, 2H; OCH_2CH$_2$), 3.80 (s, 3H; O*Me*), 2.86−2.81 (m, 2H; ArCH_2CH$_2$), 2.44−2.30 (2H; CC*H*HCH$_2$, CF$_2$HC*H*CH$_2$), 2.23−2.09 (2H; CF$_2$HCHC*H*H, CCH$_2$C*H*H), 2.01−1.81 (3H; CF$_2$HCHCH*H*, CCH$_2$CH*H*, CCH*H*CH$_2$). ^{13}C NMR (125 MHz, $CDCl_3$, rt): δ 158.1, 146.4, 129.6, 127.2, 116.7 (t, J = 239.6 Hz), 112.9, 110.1, 84.2, 70.7, 55.4, 47.8 (t, J = 19.7 Hz), 35.6, 26.9, 26.0, 18.5. ^{19}F NMR (376 MHz, $CDCl_3$, rt): δ −119.5 (ddd, J = 287.6 Hz, 54.6 Hz, 10.9 Hz, 1F), −125.4 (ddd, J = 288.0 Hz, 58.0 Hz, 26.7 Hz, 1F). HRMS (ESI-TOF) exact mass for $[C_{15}H_{18}F_2O_2 + Na]^+$ calcd m/z 291.1167, found 291.1166.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00953.

Full spectroscopic data for all new compounds and crystallographic data (PDF)

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Notes

The authors declare no competing financial interest.

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