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Stereoselective Synthesis of 1-Fluoro-*exo*,*exo*-2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes: Synthesis of (±)-1-Fluoromembrine

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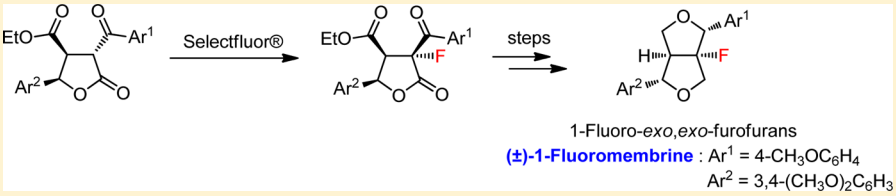
Supporting Information



ABSTRACT: Stereoselective synthesis of 1-fluoro-*exo*,*exo*-2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes is described. The synthetic strategy involves stereoselective fluorination of 3,4-*trans*-4,5-*cis*-3-aroyl-5-arylparaconic esters using Selectfluor to afford the corresponding fluorinated paraconic esters in good yields as a single isomer, which are subjected to reduction employing $LiAlH_4$ or DIBALH followed by furofuran formation under acidic or Lewis acid conditions to afford a series of 1-fluoro-*exo*,*exo*-furofurans in moderate yields. The synthetic protocol also provides an access to (±)-1-fluoromembrine.

INTRODUCTION

The diverse range of biological properties, e.g., antitumor, antihypertensive, anti-inflammatory, insecticidal, and platelet-activating factor antagonist activities, of furofuran lignans containing the 2,6-diaryl-3,7-dioxabicyclo[3.3.0]octane skeleton has inspired organic chemists to develop their syntheses.[1] Examples of bioactive furofuran lignans possessing the 2,6-diaryl groups on either the *exo*- or the *endo*-face of the 3,7-dioxabicyclo[3.3.0]octane unit are membrine,[2] xanthoxylol,[3] phillygenin,[4] and diyangambin[5] (Figure 1). Although considerable efforts devoted to the development of synthetic methodologies for the synthesis of this class of bioactive compounds have been reported,[6] works related to structural modification to improve their chemical and pharmaceutical profiles are rare.[7]

Over the past decade, organofluorine compounds have received particular attention as highlighted in their applications in various fields, including pharmaceuticals, agrochemicals, and material sciences.[8] The presence of the fluorine atom(s) in organic molecules can lead to the improvement of their physical and chemical properties as well as their metabolic stability in comparison to those of the parent nonfluorinated molecules. The enhancement is attributed to the high bonding energy of the C−F bond, the size of the fluorine atom, and the extraordinary inductive and resonance effects caused by the fluorine atom.[9] To the best of our knowledge, the synthesis of furofurans bearing a fluorine atom in the 3,7-dioxabicyclo[3.3.0]octane structural unit has never been explored. It is therefore anticipated that the development of the synthetic strategies to access 2,6-diaryl-substituted furofurans possessing a fluorine atom on the bicyclic core skeleton should offer an expedient access to the synthesis of the diverse array of fluorinated furofuran natural products which may be found of particular interest in pharmaceutical research.

We have previously reported a general and efficient synthetic strategy for the stereoselective synthesis of 1-substituted *exo*,*endo*-2,6-diarylfurofurans, including (±)-gmelinol and analogues (Scheme 1), starting from 3,4-*trans*-4,5-*cis*-α-aroylparaconic esters **1** (*TC*-**1**), which were readily obtained by reacting the vicinal dianions of α-aroylsuccinic esters with aromatic aldehydes in the presence of $ZnCl_2$.[6g] We report herein a synthetic strategy to access 1-fluorinated analogues of 2,6-diarylfurofurans in a stereoselective manner. It is envisioned that 1-fluoro-2,6-diaryl-3,7-dioxabicyclo[3.3.0]octanes **3**, including 1-fluoromembrine (**3jA**), should be obtained by stereoselective fluorination of the readily available *TC*-**1** followed by reduction and furofuran formation as shown in Scheme 1.

RESULTS AND DISCUSSION

Stereoselective Fluorination of *TC*-1 to Fluorinated Paraconic Esters 2. The key compound *TC*-**1a** was readily prepared according to our previously reported work.[6g] Primarily, stereoselective fluorination of *TC*-**1a** employing Selectfluor as a fluorinating agent was carefully investigated.[10] Thus, treatment of *TC*-**1a** with Selectfluor (1.5 equiv) in CH_3CN at room temperature overnight (16 h) afforded the corresponding fluorinated paraconic ester **2a**, after aqueous workup followed by crystallization (EtOAc/hexanes), in 74% yield as a single isomer. It is worth mentioning that **2a** must be handled with care since it readily decomposed during acidic

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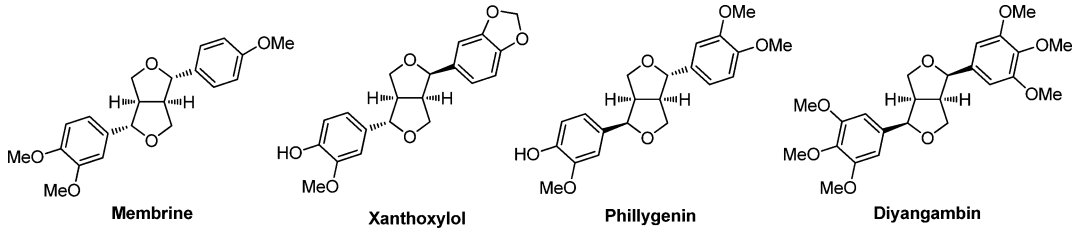
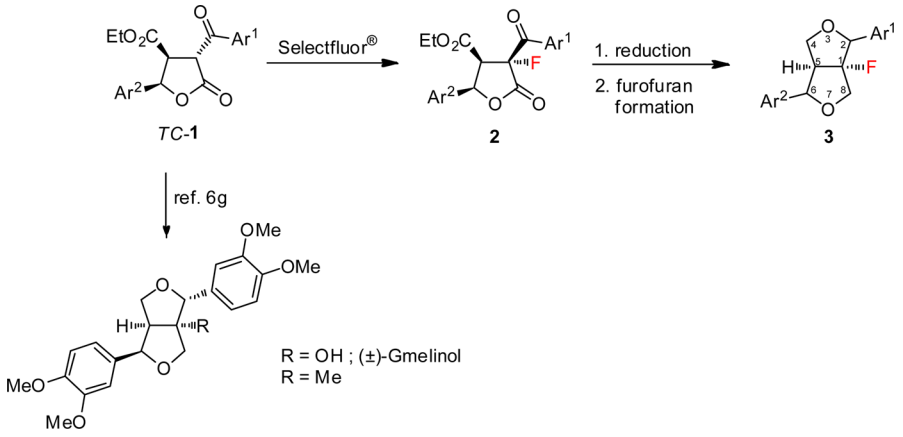


Figure 1. Selected examples of *exo,endo-*, *endo,endo-*, and *exo,exo*-furofurans.

Scheme 1. Proposed Synthetic Strategy to 1-Fluorinated Furofurans 3



workup and/or chromatography on silica gel (SiO_2). A better yield of **2a** (89% yield) was achieved when the reaction was carried out in CH_3CN/H_2O (4:1, v/v) using Selectfluor (2 equiv) at room temperature for 4 h (Table 1, entry 1).[11] Under the optimized reaction conditions (Table 1, entry 1), the scope of substrates was examined, and the results are summarized in Table 1. The electrophilic fluorination of *TC*-**1b–d** proceeded with high stereoselectivity to provide the corresponding products **2b–d** in good to high yields (74–91%, Table 1, entries 2–4) as a single isomer after crystallization (EtOAc/hexanes). The electronic nature of substituents on the aromatic substrates was found to have a considerable effect on the stability of the desired products (Table 1, entries 5 and 6). Under the standard reaction conditions, compounds *TC*-**1e** and *TC*-**1f** possessing strong electron-donating substituents (dimethoxy and methylenedioxy) on both aromatic rings yielded the corresponding products as revealed by their ^{1}H NMR (400 MHz) spectra. Unfortunately, the crude mixtures rapidly decomposed during purification by crystallization from EtOAc/hexanes. It is anticipated that excessive electron density made by the methoxy and the methylenedioxy groups would facilitate the ease of γ-butyrolactone ring-opening, which then causes the decomposition of **2e** and **2f**. Hence, in an effort to expand the substrate scope, the fluorination reactions of *TC*-**1g–i** possessing moderate electron-donating group were examined. The experimental results confirmed our hypothesis in that the corresponding products **2g–i** were obtained in good to high yields (71–92% yields), each as a single isomer, (Table 1, entries 7–9). Even though the relative stereochemistry of compounds **2** could not be assigned at this stage, it is believed that their relative stereochemistries are as indicated in Table 1. We reasoned that Selectfluor should access from the less hindered face of the enol form of *TC*-**1** (opposite side compared to the carboethoxy group at the C-4 position and the aryl group at C-5), leading to the relative stereochemistry assigned. The relative stereochemistry of **2a** was later confirmed after conversion of **2a** to its corresponding bislactone **5a** (Scheme 2). Thus, chemoselective reduction[12] of the keto group of **2a** employing DIBALH (1 equiv) in THF at −78 °C for 1 h quantitatively yielded **4a**, whose relative stereochemistry as indicated in Scheme 2 could be confirmed in the later step. The observed stereochemical outcomes of **4a** can be explained by the fact that the hydride preferentially approached the keto group of the initially formed Al-chelated intermediate **A** from the face opposite the carboethoxy group and the aryl group at the C-4 and C-5 positions, respectively, to avoid the steric repulsion (Scheme 2). While a catalytic amount of *p*-TsOH failed to promote the lactonization of **4a**, the reaction smoothly took place when **4a** was exposed to $Ti(OiPr)_4$ (1 equiv) in refluxing toluene to yield the corresponding bislactone **5a** in quantitative yield as a single isomer.[13] The relative stereochemistry of **5a** was established by the NOE experiments (see the Supporting Information). At this stage, the relative stereochemistries of **2a** and **4a** could be confirmed as depicted in Table 1 and Scheme 2. The relative stereochemistries of **2b–d** and **2g–i** were then assigned on the same basis as that of **2a** (Table 1).

Synthesis of 1-Fluorinated *exo,exo*-Furofurans 3A from Fluorinated Paraconic Esters 2. Having compounds **2** in hand, we next focused our attention on their conversions to 1-fluorinated furofurans **3**. It is envisaged that the desired 1-fluorinated furofuran **3a** should be derived from acid-catalyzed cyclization of the tetrol **6a**, which in turn can be prepared by reduction of **2a** (Scheme 3).[14] Indeed, treatment of **2a** employing $LiAlH_4$ (LAH, 10 equiv) in refluxing THF for 2 h yielded the expected tetrol **6a** in 67% yield as a 1:1.5 mixture of two diastereoisomers (^{1}H NMR analysis). Disappointingly, treatment of **6a** (1:1.5 dr) with methanesulfonyl chloride in pyridine at room temperature overnight[6h,15] failed to provide the desired 1-fluorinated furofuran **3a**; the corresponding

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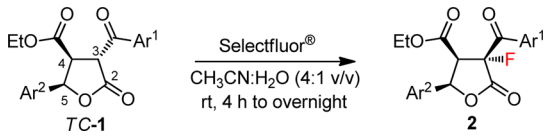
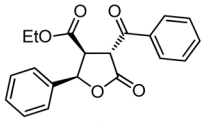
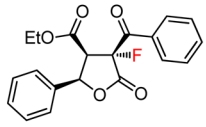
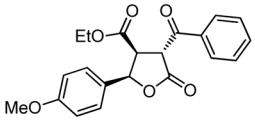
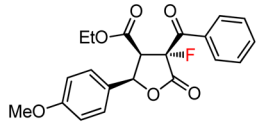
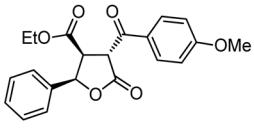
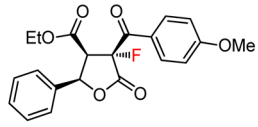
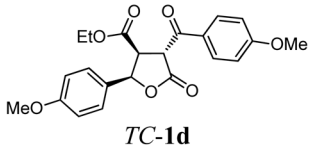
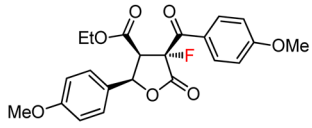
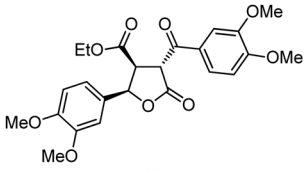
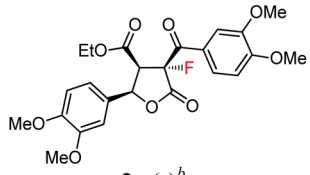
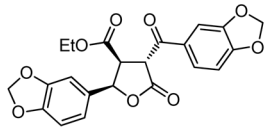
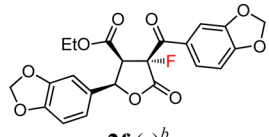
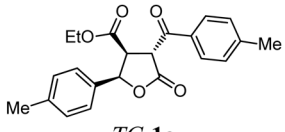
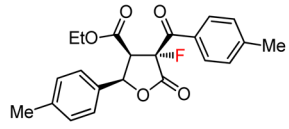
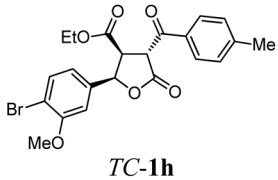
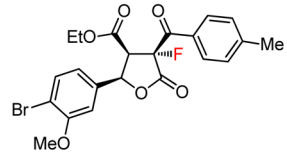
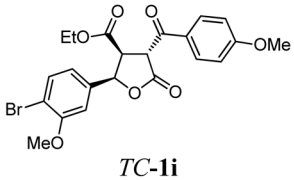
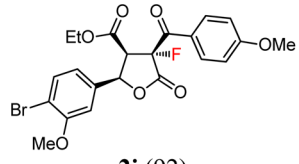
Table 1. Synthesis of Compounds 2 by Stereoselective Fluorination of *TC*-1



TC-**1** **2**

entry	*TC*-**1**	reaction time (h)	compounds **2** (%)[a]
1	 *TC*-**1a**	4 h	 **2a** (89)
2	 *TC*-**1b**	6 h	 **2b** (79)
3	 *TC*-**1c**	7 h	 **2c** (91)
4	 *TC*-**1d**	6 h	 **2d** (74)
5	 *TC*-**1e**	4 h	 **2e** (-)[b]
6	 *TC*-**1f**	4 h	 **2f** (-)[b]
7	 *TC*-**1g**	4 h	 **2g** (90)
8	 *TC*-**1h**	overnight (16 h)	 **2h** (71)
9	 *TC*-**1i**	overnight (16 h)	 **2i** (92)

[a]Isolated yields after crystallization from EtOAc/hexanes. [b]The crude mixture rapidly decomposes during crystallization (EtOAc/hexanes) and/or chromatography on silica gel (SiO_2) (see the text).

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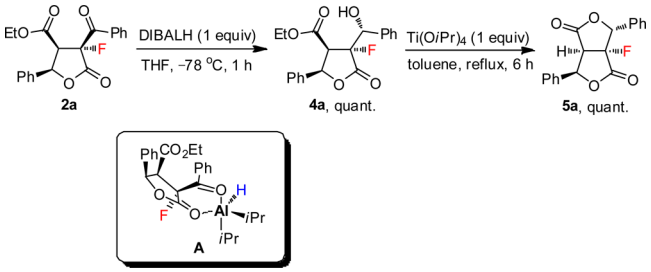
Scheme 2. Assignment of the Relative Stereochemistry of 2a



mesylated derivatives and a trace amount of partially cyclized products were observed (see the Supporting Information). To our delight, cyclization of **6a** smoothly proceeded employing *p*-TsOH (cat.) in refluxing toluene.[16] The cyclized products isolated were 1-fluorinated *exo,exo*-furofuran **3aA** (66% yield) and *endo,exo*-furofuran **3aB** (7% yield). The relative stereochemistries of *exo,exo*-furofuran **3aA** and *endo,exo*-furofuran **3aB** were confirmed by the NOE and NOESY experiments (see the Supporting Information). The formation of 1-fluorinated *exo,exo*-furofuran **3aA** and *endo,exo*-furofuran **3aB** from the diastereomeric mixture of **6a** could be rationalized as that the cyclization proceeded via the S_N1 fashion through the benzylic carbonium ion followed by cyclization to form the thermodynamically more stable 1-fluorinated *exo,exo*-furofuran **3aA** as the major product as shown in Scheme 3. By following a similar synthetic strategy, compounds **2b–d** and **2g–i** were subjected to reduction [LAH (10 equiv), refluxing THF, 2 h] to furnish tetrols **6b–d** and **6g–i** in 62–73% yields, each as inseparable diastereomeric mixtures of two diastereomers (^{1}H NMR analysis). Subsequent treatment of **6b–d** and **6g–i**, with a catalytic amount of *p*-TsOH, yielded the corresponding 1-fluorinated *exo,exo*-furofurans **3A** and 1-fluorinated *endo,exo*-furofurans **3B** in moderate to good yields. The results are summarized in Table 2.

Synthesis of 1-Fluorinated *exo,exo*-Furofurans 3A from 1-Fluorobislactols 7. Having accomplished an access to a variety of 1-fluorinated *exo,exo*-furofurans **3A** and 1-fluorinated *endo,exo*-furofurans **3B** through reduction of **2**, leading to tetrols **6**, followed by acid-catalyzed cyclization of tetrols **6** (Scheme 3 and Table 2), we anticipated that bislactols of type **7**, which could be derived from the reduction of **2** using DIBALH, should provide 1-fluoro-*exo,endo*-furofurans of type **3C** upon reduction using $Et_3SiH/BF_3{\cdot}OEt_2$. Thus, treatment of **2a** with DIBALH (6 equiv) at −78 °C for 3 h and then 0 °C for 2 h provided the expected 1-fluorobislactol **7a** in 51% yield as a mixture of diastereomers (Table 3). Next, reduction of **7a** using Et_3SiH was investigated. Treatment of **7a** with $BF_3{\cdot}OEt_2$ (10 equiv) and Et_3SiH (10 equiv) in dichloromethane at −78 °C for 5 h gave compound **8a** in 92% yield without the observation of 1-fluorinated *exo,endo*-furofuran **3aC** (Table 3, entry 1). The formation of **8a** resulted from partial reduction of a more stable oxonium ion intermediate generated at the C-4 position by Et_3SiH. This implied that oxonium ion formation at C-8 was less favorable than that at C-4. When the reaction was carried out at higher temperature (−20 °C for 5 h), **8a** and *exo,exo*-furofuran **3aA** were obtained, after simple chromatographic purification, in 62% and 18% yields, respectively (Table 3, entry 2). Increasing the reaction temperature led to higher ratios of *exo,exo*-furofuran **3aA** to **8a** (Table 3, entry 3). Finally, the reaction carried out at 0 °C for 4 h yielded 1-fluorinated *exo,exo*-furofuran **3aA** and 1-fluorinated *endo,exo*-furofuran **3aB** in 74% and 8% yields, respectively (Table 3, entry 4). The formation of **8a**, **3aA**, and **3aB** from **7** could be explained as summarized in Scheme 4. Upon treatment of **7a** with $BF_3{\cdot}OEt_2$ in dichloromethane at low temperature, an initially formed intermediate **D**, was trapped by a hydride ion from Et_3SiH to give **8a**, which was the key compound for further transformation to **3aA** and **3aB**. At higher temperature, **8a** further reacted with $BF_3{\cdot}OEt_2$, generating an intermediate **E**, which then further reacted with Et_3SiH to afford a thermodynamically less stable 1-fluorinated *exo,endo*-furofuran, **3aC**. It was assumed that, under the reaction conditions, **3aC** underwent $BF_3{\cdot}OEt_2$-catalyzed ring opening[17] of the furofuran unit to produce the benzylic carbonium ion intermediates **F** and **G**, respectively. Cyclization of the intermediates **F** and **G** gave a thermodynamically more stable 1-fluoro-*exo,exo*-furofuran, **3aA**, as a major product. On the other hand, the formation of a less stable 1-fluorinated *endo,exo*-furofuran, **3aB**, as a minor product was assumed as a result of the cyclization of the intermediate **G**.

Due to a tedious chromatographic separation of a mixture of **3aA** and **3aB**, we chose the reaction conditions as indicated in Table 3, entry 3, as our standard reaction conditions for the preparation of additional derivatives of 1-fluorinated *exo,exo*-furofurans **3A**. Table 4 summarizes the results obtained from the reactions of **2b–d** and **2g–i** with DIBALH to provide the corresponding 1-fluorobislactols **7b–d** and **7g–i**, each as a mixture of diastereomers, in moderate yields (42–58% yields) (Table 4, entries 1–7). Reductive deoxygenation of 1-fluorobislactols **7b–d** and **7g–i** (each as a mixture of diastereomers) furnished the corresponding mixtures of 1-fluorinated *exo,exo*-furofurans **3bA–3dA** and **3gA–3iA** and **8b–8d** and **8g–8i**. Each pair of **3A** and **8** can be easily

Scheme 3. Preparation of 1-Fluorofurofurans 3aA and 3aB

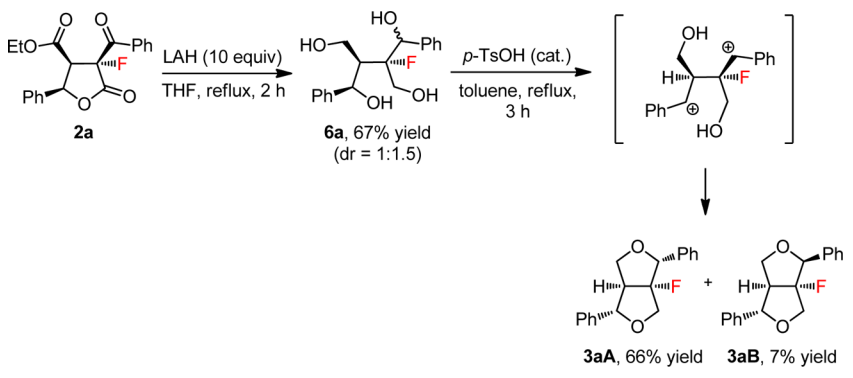


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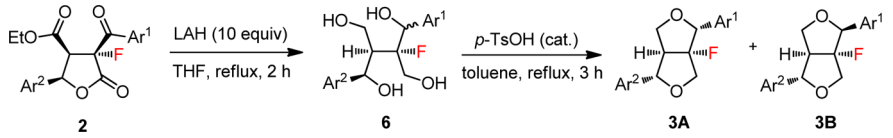
Table 2. Preparation of Tetrols 6, 1-Fluorinated *exo,exo*-Furofurans 3A, and 1-Fluorinated *endo,exo*-Furofurans 3B

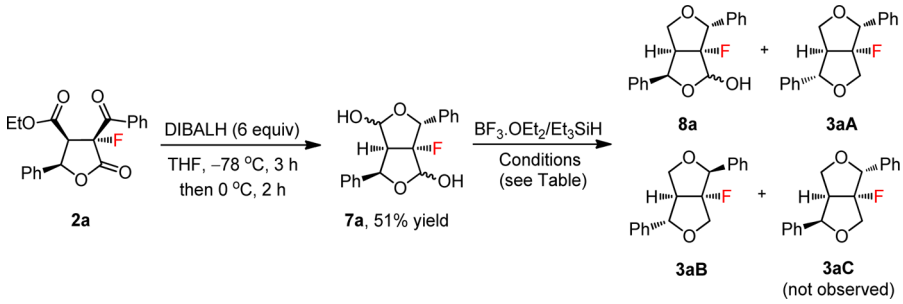


2 6 3A 3B

entry	2	Ar^1	Ar^2	6 (yield, %; dr)[a,b]	3A (yield, %)[a]	3B (yield, %)[a]
1	**2a**	C_6H_5	C_6H_5	**6a** (66, 1:1.5)	**3aA** (66)	**3aB** (7)
2	**2b**	C_6H_5	4-$MeOC_6H_4$	**6b** (66, 1:2.3)	**3bA** (57)	**3bB** (7)
3	**2c**	4-$MeOC_6H_4$	C_6H_5	**6c** (62, 1:4)	**3cA** (67)	**3cB** (5)
4	**2d**	4-$MeOC_6H_4$	4-$MeOC_6H_4$	**6d** (70, 1:2.9)	**3dA** (61)	**3dB** (18)
5	**2g**	4-MeC_6H_4	4-MeC_6H_4	**6g** (73, 1:3.1)	**3gA** (64)	**3gB** (12)
6	**2h**	4-Br-3-$MeOC_6H_3$	4-MeC_6H_4	**6h** (68, 1:1.9)	**3hA** (71)	**3hB** (trace)[c]
7	**2i**	4-Br-3-$MeOC_6H_3$	4-$MeOC_6H_4$	**6i** (65, 1:3.3)	**3iA** (70)	**3iB** (trace)[c]

[a]Isolated yields. [b]Ratios were determined by ^{1}H NMR analysis. [c]Observed by ^{19}F NMR analysis.

Table 3. Optimization for the Reductive Dehydroxylation Using BF_3·OEt_2 and Et_3SiH

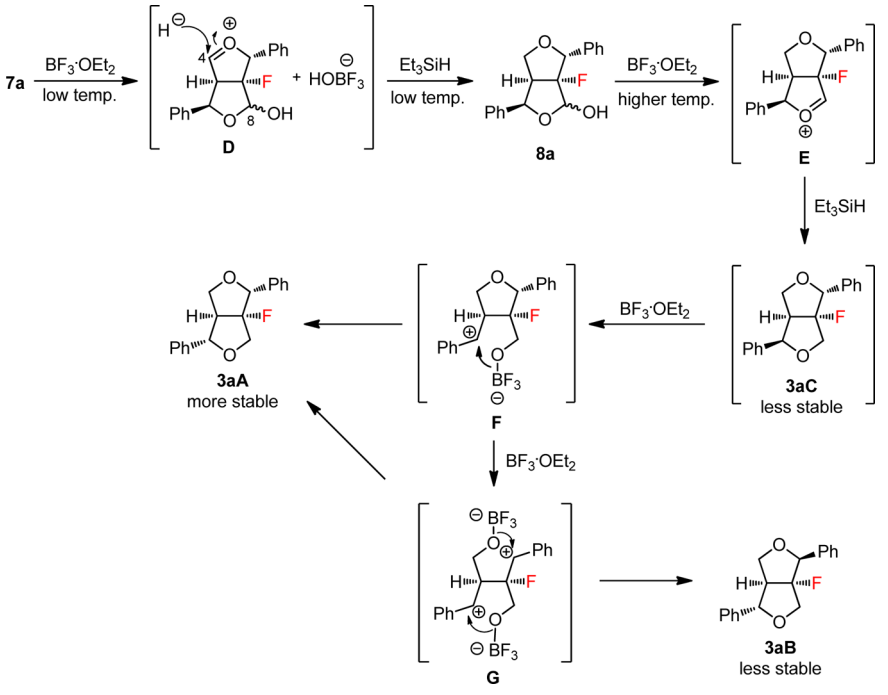


2a **7a**, 51% yield **8a** **3aA** **3aB** **3aC** (not observed)

entry	conditions[a]	yield[b] (%) 8a	3aA	3aB
1	−78 °C, 5 h	92		
2	−20 °C, 5 h	62	18	
3	−20 to 0 °C, 1.5 h	33	51	
4	0 °C, 4 h		74	8

[a]Reactions were performed on a 0.1 mmol scale using 10 equiv of both BF_3·OEt_2 and Et_3SiH in CH_2Cl_2 (2 mL). [b]Isolated yields.

Scheme 4. Proposed Mechanism for the Formation of 8a, 3aA, and 3aB by Treatment of 7a with Et_3SiH/BF_3·OEt_2



D 8a E F G

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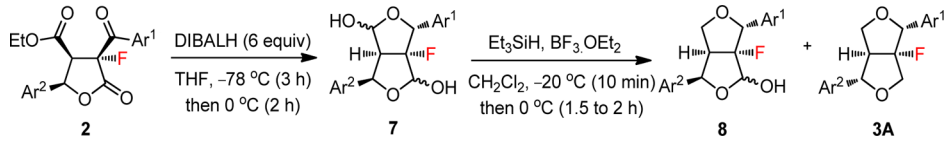
Table 4. Preparation of Bislactols 7, 1-Fluoro-8-hydroxyfurofurans 8, and 1-Fluoro-*exo,exo*-furofurans 3A



2 7 8 3A

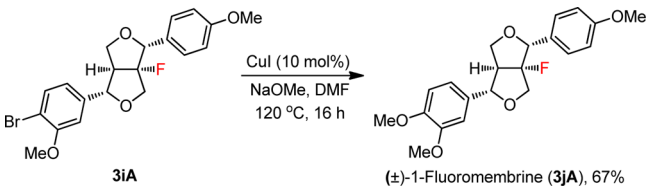
entry	2	Ar^1	Ar^2	7 (yield, %)[a,b]	8 (yield, %)[a,b]	3A (yield, %)[a]
1	**2a**	C_6H_5	C_6H_5	**7a** (51)	**8a** (33)	**3aA** (51)
2	**2b**	C_6H_5	4-$MeOC_6H_4$	**7b** (47)	**8b** (25)	**3bA** (47)
3	**2c**	4-$MeOC_6H_4$	C_6H_5	**7c** (43)	**8c** (36)	**3cA** (42)
4	**2d**	4-$MeOC_6H_4$	4-$MeOC_6H_4$	**7d** (48)	**8d** (29)	**3dA** (52)
5	**2g**	4-MeC_6H_4	4-MeC_6H_4	**7g** (58)	**8g** (18)	**3gA** (64)
6	**2h**	4-Br-3-$MeOC_6H_3$	4-MeC_6H_4	**7h** (43)	**8h** (21)	**3hA** (54)
7	**2i**	4-Br-3-$MeOC_6H_3$	4-$MeOC_6H_4$	**7i** (42)	**8i** (18)	**3iA** (61)

[a]Isolated yields. [b]The ratio of isomers could not be determined.

separated by means of chromatographic purification, providing 1-fluorinated *exo,exo*-furofurans **3bA**−**3dA** and **3gA**−**3iA** in moderate yields (42−64% yields) as shown in Table 4.

Synthesis of (±)-1-Fluoromembrine (3jA). (±)-Membrine was isolated in 1993 from the grains of *Rollinia membranacea* in the area of Antioquia in Colombia (Figure 1).[2a] In this study, we further demonstrated the synthetic application of the developed protocol for the synthesis of (±)-1-fluoromembrine. Due to the limitation on the electrophilic fluorination of paraconic esters **1** possessing strong electron-donating substituents on aromatic rings (Table 1, entries 5 and 6), the direct preparation of (±)-1-fluoromembrine (**3jA**) from its corresponding paraconic ester of type **1** is not possible. Therefore, an indirect synthesis was considered. To our delight, it was found that (±)-1-fluoromembrine can be prepared in 67% yield from the reaction of 1-fluoro-*exo,exo*-furofuran **3iA** with NaOMe in the presence of CuI (10 mol %) in DMF at 120 °C for 16 h (Scheme 5).[18]

Scheme 5. Synthesis of (±)-1-Fluoromembrine (3jA) by Cu(I)-Catalyzed Coupling Reaction of 3iA with NaOMe in DMF



3iA (±)-1-Fluoromembrine (**3jA**), 67%

CONCLUSION

In summary, we have demonstrated a general entry for the synthesis of 1-fluoro-*exo,exo*-furofurans **3A**. The key fluorinated paraconic esters **2** were obtained by the electrophilic fluorination of 3,4-*trans*-4,5-*cis*-α-aroylparaconic esters **1** employing Selectfluor. Reduction of **2** with LAH to give the corresponding tetrols **6** followed by acid-catalyzed (*p*-TsOH) furofuran formation afforded 1-fluoro-*exo,exo*-furofurans **3A** as the major products together with 1-fluoro-*endo,exo*-furofurans **3B** as the minor products. Alternatively, reduction of **2** with DIBALH to give 1-fluorobislactols **7** followed by reductive deoxygenation using a combination of $BF_3{\cdot}OEt_2/Et_3SiH$ gave the corresponding 1-fluoro-*exo,exo*-furofurans **3A** in moderate yields and *exo,endo*-1-fluoro-8-hydroxyfurofurans **8** as the minor products. The synthesis of (±)-1-fluoromembrine (**3jA**) could be achieved by Cu(I)-catalyzed cross-coupling reaction of **3iA** with NaOMe in DMF. The developed method could be applied to the synthesis of other 1-fluorinated *exo,exo*-furofuran lignan natural product analogues. Finally, it should be noted that, except for the easily decomposable fluorinated compounds **2**, other fluorinated analogues reported in this work are relatively stable in comparison to the parent compounds.

EXPERIMENTAL SECTION

General Information. ^1H NMR spectra were recorded on 400 and 500 MHz spectrometers and are reported in parts per million. Proton-decoupled ^{13}C NMR spectra were recorded on 100 and 125 MHz spectrometers and are reported in parts per million. ^{19}F NMR spectra were recorded on 376 and 470 MHz spectrometers and are reported in parts per million. Reactions were monitored by thin-layer chromatography and visualized by UV and a solution of $KMnO_4$. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Dichloromethane (CH_2Cl_2) was distilled over calcium hydride and stored over activated molecular sieves (4 Å). All glassware and syringes were oven-dried and kept in a desiccator before use. Silica gel was used for column chromatography. Other common solvents [CH_2Cl_2, hexanes, ethyl acetate (EtOAc), methanol (MeOH), and acetone] were distilled before use.

Synthesis of Compounds 2. *Ethyl (2R*,3S*,4R*)-4-Benzoyl-4-fluoro-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (**2a**): General Procedure A.* To a solution of *TC*-**1a** (0.5 mmol, 170 mg) in a CH_3CN/H_2O mixture (4:1, v/v; 2 mL) was added Selectfluor [1.0 mmol (356 mg), 0.25 mmol (89 mg) every 30 min] at room temperature. After the reaction was completed, as monitored by TLC, it was quenched with water. The reaction mixture was extracted with EtOAc (10 mL × 3). The combined organic phase was washed with water (10 mL × 2) and brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation at room temperature gave a crude product which was subjected to purification by recrystallization (EtOAc/hexanes) to give a single isomer of **2a** (159 mg, 89%) as a white solid: mp 119−122 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.16−8.11 (m, 2H), 7.70−7.64 (m, 1H), 7.57−7.50 (m, 2H), 7.47−7.35 (m, 5H), 6.13 (d, *J* = 6.2 Hz, 1H), 4.05 (dd, *J* = 18.2, 6.2 Hz, 1H), 3.89−3.78 (m, 2H), 0.91 (t, *J* = 7.1 Hz, 3H); ^{19}F NMR (470 MHz, $CDCl_3$) δ −153.5 (d, *J* = 17.9 Hz, 1F); ^{13}C NMR (125 MHz, $CDCl_3$) δ 189.8 (d, *J* = 25.3 Hz, C), 166.7 (d, *J* = 21.9 Hz, C), 165.5 (d, *J* = 12.5 Hz, C), 134.4 (CH), 133.4 (d, *J* = 3.5 Hz, C), 133.3 (C), 130.7 (CH), 130.6 (CH), 129.0 (CH), 128.4 (4 × CH), 125.8 (2 × CH), 98.8 (d, *J* = 194.6 Hz, CF), 79.3 (CH), 61.6 (CH_2), 56.4 (d, *J* = 21.6 Hz, CH), 13.3 (CH_3); IR ($CHCl_3$) ν_{max} 1801s, 1748s, 1689s, 1449m, 1176s, 1031m, 900m, 697m cm^{-1}; MS *m*/*z* (rel intens, %) 356 (M^+, 1), 290 (43), 289 (83), 105 (100), 103 (49), 77(77); HRMS (ESI-TOF) calcd for $C_{20}H_{17}FO_5Na$ $[M + Na]^+$ 379.0958, found 379.0954.

Ethyl (2R,3S*,4R*)-4-Benzoyl-4-fluoro-2-(4-methoxyphenyl)-5-oxotetrahydrofuran-3-carboxylate (**2b**).* According to general

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procedure A, the reaction of *TC*-**1b** (0.2 mmol, 74 mg) and Selectfluor (0.4 mmol, 143 mg) in a mixture of CH_3CN/H_2O (4:1, v/v; 1.2 mL) gave **2b** (61 mg, 79%) as a white solid after crystallization (EtOAc/hexanes): mp 123−125 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15−8.10 (m, 2H), 7.70−7.64 (m, 1H), 7.57−7.50 (m, 2H), 7.39−7.34 (m, 2H), 6.96−6.91 (m, 2H), 6.08 (d, J = 6.4 Hz, 1H), 4.03 (dd, J = 18.8, 6.4 Hz, 1H), 3.91−3.82 (m, 2H), 3.84 (s, 3H), 0.96 (t, J = 7.2 Hz, 3H); ^{19}F NMR (470 MHz, $CDCl_3$) δ −153.0 (d, J = 19.3 Hz, 1F); ^{13}C NMR (125 MHz, $CDCl_3$) δ 190.1 (d, J = 26.0 Hz, C), 167.0 (d, J = 22.3 Hz, C), 165.7 (d, J = 12.0 Hz, C), 160.1 (C), 134.3 (CH), 133.5 (d, J = 3.8 Hz, C), 130.6 (CH), 130.5 (CH), 128.4 (2 × CH), 127.4 (2 × CH), 125.1 (C), 113.9 (2 × CH), 98.8 (d, J = 194.6 Hz, CF), 79.3 (d, J = 1.6 Hz, CH), 61.6 (CH_2), 56.6 (d, J = 21.4 Hz, CH), 55.3 (CH), 13.4 (CH_3); IR ($CHCl_3$) ν_{max} 1793s, 1742s, 1702s, 1513m, 1320m, 1252s, 1232s, 1025s, 1005s, 814m, 740m cm^{-1}; MS m/z (rel intens, %) 356 (M^+, 3), 355 (M − 1, 12), 320 (42), 295 (45), 253 (21), 221 (53), 135 (43), 105 (100), 77(94); HRMS (ESI-TOF) calcd for $C_{21}H_{19}FO_6Na$ $[M + Na]^+$ 409.1063, found 409.1065.

Ethyl (2R,3S*,4R*)-4-Fluoro-4-(4-methoxybenzoyl)-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (**2c**).* According to general procedure A, the reaction of *TC*-**1c** (1.0 mmol, 369 mg) and Selectfluor (2.0 mmol, 710 mg) in a mixture of CH_3CN/H_2O (4:1, v/v; 4 mL) gave **2c** (352 mg, 91%) as a white solid after crystallization (EtOAc/hexanes): mp 154−157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15−8.07 (m, 2H), 7.45−7.31 (m, 5H), 7.02−6.94 (m, 2H), 6.09 (d, J = 5.8 Hz, 1H), 3.96 (dd, J = 17.4, 5.8 Hz, 1H), 3.90 (s, 3H), 3.82 (q, J = 7.2 Hz, 2H), 0.88 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −153.2 (d, J = 16.2 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.4 (d, J = 24.7 Hz, C), 167.0 (d, J = 21.8 Hz, C), 165.7 (d, J = 13.2 Hz, C), 164.6 (C), 133.4 (CH), 133.3 (CH), 133.2 (C), 128.9 (CH), 128.4 (2 × CH), 126.2 (C), 125.7 (2 × CH), 113.8 (2 × CH), 99.1 (d, J = 193.2 Hz, CF), 79.3 (CH), 61.5 (CH_2), 56.3 (d, J = 21.3 Hz, CH), 55.6 (CH_3), 13.4 (CH_3); IR (neat) ν_{max} 1800s, 1726s, 1688s, 1569s, 1509s, 1285s, 1259s, 1168s, 1094m, 899m cm^{-1}; MS m/z (rel intens, %) 386 (M^+, 9), 368 (27), 320 (38), 285 (18), 255 (21), 230 (18), 165 (22), 157 (25), 149 (31), 135 (55), 121 (37), 91 (73), 79 (79), 77(72), 67 (85), 55 (100); HRMS (ESI-TOF) calcd for $C_{21}H_{19}FO_6Na$ $[M + Na]^+$ 409.1063, found 409.1060.

Ethyl (2R,3S*,4R*)-4-Fluoro-4-(4-methoxybenzoyl)-2-(4-methoxyphenyl)-5-oxotetrahydrofuran-3-carboxylate (**2d**).* According to general procedure A, the reaction of *TC*-**1d** (0.3 mmol, 120 mg) and Selectfluor (0.6 mmol, 212 mg) in a mixture of CH_3CN/H_2O (4:1, v/v; 1.2 mL) gave **2d** (93 mg, 74%) as a white solid after crystallization (EtOAc/hexanes): mp 151 °C dec; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (dd, J = 9.0, 1.8 Hz, 2H), 7.30 (dd, J = 7.9, 7.9 Hz, 1H), 7.03−6.92 (m, 4H), 6.89 (dd, J = 8.3, 2.2 Hz, 1H), 6.06 (d, J = 5.9 Hz, 1H), 3.96 (dd, J = 17.5, 5.9 Hz, 1H), 3.90 (s, 3H), 3.85 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H), 0.91 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −153.1 (d, J = 16.2 Hz, 1F); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.7 (d, J = 24.8 Hz, C), 167.1 (d, J = 22.4 Hz, C), 165.8 (d, J = 12.6 Hz, C), 164.6 (C), 160.0 (C), 133.4 (CH), 133.3 (CH), 127.3 (2 × C), 126.3 (C), 125.2 (C), 113.9 (2 × CH), 113.8 (2 × CH), 99.2 (d, J = 193.9 Hz, CF), 79.3 (CH), 61.5 (CH_2), 56.5 (d, J = 21.4 Hz, CH), 55.6 (CH_3), 55.3 (CH_3), 13.4 (CH_3); IR ($CHCl_3$) ν_{max} 1800s, 1748s, 1677s, 1600s, 1516s, 1033s, 904s, 843m, 618m cm^{-1}; MS m/z (rel intens, %) 416 (M^+, 1), 325 (16), 251 (24), 135 (100), 77(26); HRMS (ESI-TOF) calcd for $C_{22}H_{21}FO_7Na$ $[M + Na]^+$ 439.1464, found 439.1468.

Ethyl (2R,3S*,4R*)-4-Fluoro-4-(4-methylbenzoyl)-5-oxo-2-(p-tolyl)tetrahydrofuran-3-carboxylate (**2g**).* According to general procedure A, the reaction of *TC*-**1g** (1.0 mmol, 367 mg) and Selectfluor (2.0 mmol, 711 mg) in a mixture of CH_3CN/H_2O (4:1, v/v; 4.0 mL) gave **2g** (347 mg, 90%) as a white solid after crystallization (EtOAc/hexanes): mp 135−138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (dd, J = 8.1, 1.6 Hz, 2H), 7.33 (d, J = 7.8 Hz, 2H), 7.31 (d, J = 7.8 Hz, 2H), 7.22 (d, J = 8.1 Hz, 2H), 6.09 (d, J = 6.0 Hz, 1H), 3.99 (dd, J = 18.0, 6.1 Hz, 1H), 3.86 (q, J = 7.2 Hz, 2H), 2.46 (s, 3H), 2.37 (s, 3H), 0.94 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −153.3 (d, J = 18.0 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.1 (d, J = 25.2 Hz, C), 167.0 (d, J = 22.1 Hz, C), 165.7 (d, J = 12.8 Hz, C), 145.7 (C), 138.9 (2 × C), 130.9 (CH), 130.8 (CH), 130.2 (C), 129.2 (2 × CH), 129.1 (2 × CH), 125.7 (2 × CH), 99.0 (d, J = 193.8 Hz, CF), 79.4 (CH), 61.5 (CH_2), 56.5 (d, J = 21.4 Hz, CH), 21.9 (CH_3), 21.2 (CH_3), 13.4 (CH_3); IR (neat) ν_{max} 1801s, 1725s, 1679s, 1601s, 1294m, 1166s, 979s cm^{-1}; MS m/z (rel intens, %) 384 (M^+, trace), 218 (8), 118 (100), 91(52); HRMS (ESI-TOF) calcd for $C_{22}H_{21}FO_5Na$ $[M + Na]^+$ 407.1270, found 407.1272.

Ethyl (2R,3S*,4R*)-2-(4-Bromo-3-methoxyphenyl)-4-fluoro-4-(4-methylbenzoyl)-5-oxotetrahydrofuran-3-carboxylate (**2h**).* According to general procedure A, the reaction of *TC*-**1h** (1.0 mmol, 463 mg) and Selectfluor (2.0 mmol, 712 mg) in a mixture of CH_3CN/H_2O (4:1, v/v; 4.0 mL) gave **2h** (340 mg, 71%) as a pale yellow solid after crystallization (EtOAc/hexanes): mp 113−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (dd, J = 8.2, 1.6 Hz, 2H), 7.44 (d, J = 8.8 Hz, 1H), 7.32 (d, J = 8.2 Hz, 2H), 7.13 (d, J = 3.0 Hz, 1H), 6.80 (dd, J = 8.8, 3.0 Hz, 1H), 6.22 (d, J = 5.6 Hz, 1H), 4.33 (dd, J = 17.3, 5.6 Hz, 1H), 3.90−3.78 (m, 5H), 2.44 (s, 3H), 0.92 (t, J = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.5 (d, J = 17.3 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 188.5 (d, J = 24.5 Hz, C), 166.5 (d, J = 21.9 Hz, C), 165.5 (d, J = 14.1 Hz, C), 159.0 (C), 145.9 (C), 133.6 (C), 133.3 (CH), 130.9 (CH), 130.8 (CH), 130.6 (C), 129.3 (2 × CH), 116.8 (CH), 113.6 (CH), 111.1 (C), 99.0 (d, J = 193.1 Hz, CF), 78.9 (CH), 61.6 (CH_2), 55.7 (CH_3), 54.2 (d, J = 21.8 Hz, CH), 21.9 (CH_3), 13.5 (CH_3); IR (neat) ν_{max} 1798s, 1752s, 1680s, 1603s, 1472s, 1322s, 1020s, 912s cm^{-1}; MS m/z (rel intens, %) 479 (M^+, trace), 398 (42), 379 (20), 351 (56), 333 (22), 305 (100), 280 (76), 250 (24), 203 (20), 119 (94), 91(78), 65 (45); HRMS (ESI-TOF) calcd for $C_{22}H_{20}BrFO_6Na$ $[M + Na]^+$ 501.0324, found 501.0336 and 503.0321.

Ethyl (2R,3S*,4R*)-2-(4-Bromo-3-methoxyphenyl)-4-fluoro-4-(4-methoxybenzoyl)-5-oxotetrahydrofuran-3-carboxylate (**2i**).* According to general procedure A, the reaction of *TC*-**1i** (5.0 mmol, 2.39 g) and Selectfluor (10.0 mmol, 3.54 g) in a mixture of CH_3CN/H_2O (4:1, v/v; 20.0 mL) gave **2i** (2.28 g, 92%) as a white solid after crystallization (EtOAc/hexanes): mp 124−126 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 9.0, 1.6 Hz, 2H), 7.44 (d, J = 8.8 Hz, 1H), 7.13 (d, J = 3.0 Hz, 1H), 6.99 (d, J = 9.0 Hz, 2H), 6.80 (dd, J = 8.8, 3.0 Hz, 1H), 6.21 (d, J = 5.5 Hz, 1H), 4.31 (dd, J = 17.0, 5.5 Hz, 1H), 3.95−3.76 (m, 8H), 0.92 (t, J = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −154.2 (d, J = 17.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 187.0 (d, J = 24.1 Hz, C), 166.6 (d, J = 22.6 Hz, C), 165.6 (d, J = 14.0 Hz, C), 164.7 (C), 159.0 (C), 133.6 (C), 133.5 (CH), 133.4 (CH), 133.3 (CH), 126.1 (C), 116.8 (CH), 113.9 (2 × CH), 113.6 (CH), 111.0 (C), 99.1 (d, J = 192.2 Hz, CF), 78.9 (CH), 61.5 (CH_2), 55.7 (d, J = 12.0 Hz, CH_3), 54.1 (d, J = 21.8 Hz, CH), 13.5 (CH_3); IR (neat) ν_{max} 1800s, 1746s, 1669s, 1598s, 1573s, 1297s, 1162s, 1017s, 911s, 765m cm^{-1}; MS m/z (rel intens, %) 494 (M^+, 0.6), 395 (57), 366 (41), 349 (74), 321 (54), 293 (48), 287 (52), 135 (100), 77 (40); HRMS (ESI-TOF) calcd for $C_{22}H_{20}BrFO_7Na$ $[M + Na]^+$ 517.0273, found 517.0274 and 519.0256.

Synthesis of (2R*,3S*,4R*)-Ethyl 4-Fluoro-4-[(R*)-hydroxyphenylmethyl]-5-oxo-2-phenyltetrahydrofuran-3-carboxylate (4a). To a solution of **2a** (178 mg, 0.5 mmol) in dry THF (1.5 mL) at −78 °C was added DIBALH (1 M solution in hexane, 0.5 mL, 0.5 mmol) dropwise at −78 °C over a period of 10 min. The reaction mixture was stirred at −78 °C for 1 h. It was quenched with an aqueous solution of sodium potassium tartrate at 0 °C. After being stirred at room temperature for 6 h, the reaction mixture was extracted with EtOAc (15 mL × 3). The combined organic phase was washed with water (15 mL) and brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave **4a** (178 mg, quantitative) as a colorless viscous oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.6 Hz, 2H), 7.43−7.30 (m, 8H), 5.93 (d, J = 5.5 Hz, 1H), 5.37 (d, J = 22.5 Hz, 1H), 3.81−3.68 (m, 3H), 2.59−2.42 (br s, 1H), 0.82 (t, J = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −165.9 (t, J = 18.6 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6 (d, J = 21.0 Hz, C), 167.1 (d, J = 17.0 Hz, C), 136.8 (C), 133.7 (C), 128.7 (2 × CH), 128.5 (2 × CH), 128.3 (2 × CH), 128.2 (2 × CH), 125.4 (2 × CH), 98.1 (d, J = 185.0 Hz, CF), 79.3 (CH), 72.2 (d, J = 23.0 Hz, CH), 61.3 (CH_2), 55.8 (d, J = 24.0 Hz, CH), 13.4 (CH_3); IR (neat) ν_{max} 3453br, 1777s, 1749s, 1725s, 1186s, 1040m, 750s cm^{-1}; MS m/z

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(rel intens, %) 358 (M^+, 2), 320 (18), 206 (26), 159 (29), 131 (47), 105 (52), 79 (44), 77 (100); HRMS (ESI-TOF) calcd for $C_{20}H_{19}FO_5Na$ $[M + Na]^+$ 381.1114, found 381.1106.

Synthesis of (3*R,3a*R**,6*R**,6a*S**)-3a-Fluoro-3,6-diphenyltetrahydrofuro[3,4-*c*]furan-1,4-dione (5a).** A solution of **4a** (89 mg, 0.25 mmol) in dry toluene (1.5 mL) was treated with tetraisopropyl titanate (1 M solution in toluene, 0.25 mL, 0.25 mmol). The reaction mixture was heated to reflux temperature for 6 h. It was quenched with 1 M HCl and then extracted with EtOAc (15 mL × 3). The combined organic phase was washed with water (15 mL) and brine (15 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave **5a** (78 mg, quantitative) as a light green viscous oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55−7.30 (m, 1H), 6.10 (d, J = 9.8 Hz, 1H), 5.70 (d, J = 13.1 Hz, 1H), 4.20 (dd, J = 18.8, 9.8 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −168.9 (dd, J = 18.8, 13.1 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6 (d, J = 28.0 Hz, C), 168.2 (d, J = 4.0 Hz, C), 132.7 (C), 130.3 (d, J = 4.0 Hz, C), 129.9 (CH), 129.7 (CH), 129.2 (2 × CH), 128.8 (2 × CH), 126.3 (2 × CH), 125.3 (2 × CH), 96.5 (d, J = 211.0 Hz, CF), 82.5 (d, J = 27.0 Hz, CH), 77.8 (d, J = 5.0 Hz, CH), 51.9 (d, J = 2.0 Hz, CH); IR ($CHCl_3$) ν_{max} 1796s, 1182m, 1019m, 909s cm^{-1}; MS m/z (rel intens, %) 312 (M^+, 2), 292 (100), 274 (71), 248 (66), 203 (54), 178 (98), 105 (72), 77 (55); HRMS (ESI-TOF) calcd for $C_{18}H_{13}FO_4Na$ $[M + Na]^+$ 335.0696, found 335.0687.

Synthesis of Compounds 6. *(2S*,3R*,4R*)-2-Fluoro-2,3-bis(hydroxymethyl)-1,4-diphenylbutane-1,4-diol (**6a**): General Procedure B.* To a suspension of lithium aluminum hydride (LAH) (115 mg, 3.0 mmol) in dry THF (1.5 mL) at −78 °C was added a solution of **2a** (98 mg, 0.3 mmol) in THF (1.5 mL). The reaction mixture was then refluxed for 2 h. After cooling, it was quenched with a dropwise of EtOAc at 0 °C for 15 min followed by an additional aqueous solution of sodium potassium tartrate. After being stirred at room temperature overnight, the reaction mixture was extracted with EtOAc (10 mL × 3). The combined organic phase was washed with water (10 mL) and brine (10 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation, the crude product was purified by column chromatography (SiO_2, 40−60% EtOAc in hexanes) to give a 1:1.5 diastereomeric mixture of **6a** (63 mg, 66%) as a colorless oil: ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.42−7.33 (m, 2H* and 2H), 7.27−7.00 (m, 8H and 8H*), 5.41−5.32 (m, 1H), 5.21−5.05 (m, 2H and 3H*), 4.98 (dd, J = 22.4, 6.4 Hz, 1H), 4.88 (t, J = 5.7 Hz, 1H), 4.83 (t, J = 5.6 Hz, 1H*), 4.62 (t, J = 4.8 Hz, 1H), 4.19−3.91 (m, 1H and 2H*), 3.87−3.62 (m, 3H and 4H*), 2.57−2.47 (m, 1H), 2.33−2.25 (m, 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −169.5 (s, 1F*), −172.2 to −173.6 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 145.0 (C*), 144.7 (C), 140.7 (C), 140.6 (C*), 128.6 (CH*), 128.5 (CH*), 128.4 (CH), 128.3 (CH), 127.9 (2 × CH), 127.8 (2 × CH*), 127.6 (2 × CH), 127.5 (2 × CH*), 127.4 (CH), 127.3 (CH*), 126.5 (CH), 126.4 (CH*), 125.6 (2 × CH), 125.5 (2 × CH*), 100.3 (d, J = 182.6 Hz, CF), 98.2 (d, J = 183.2 Hz, CF*), 75.3 (d, J = 23.4 Hz, CH*), 74.0 (d, J = 21.6 Hz, CH), 70.6 (d, J = 9.6 Hz, CH), 70.3 (d, J = 12.2 Hz, CH*), 62.8 (d, J = 26.3 Hz, CH_2), 61.1 (d, J = 23.9 Hz, CH_2*), 57.8 (d, J = 8.9 Hz, CH_2), 57.7 (d, J = 7.2 Hz, CH_2*), 52.4 (d, J = 19.6 Hz, CH), 50.3 (d, J = 20.2 Hz, CH*); IR (neat) ν_{max} 3354br, 1453m, 1052s, 704s cm^{-1}; MS m/z (rel intens, %) 320 (M^+, trace), 265 (18), 147 (26), 129 (24), 107 (100), 105 (61), 91 (15), 79 (78), 77 (75); HRMS (ESI-TOF) calcd for $C_{18}H_{21}FO_4Na$ $[M + Na]^+$ 343.1321, found 343.1322.

(2S,3R*,4R*)-2-Fluoro-2,3-bis(hydroxymethyl)-4-(4-methoxyphenyl)-1-phenylbutane-1,4-diol (**6b**).* According to general procedure B, the reaction of LAH (0.76 g, 20.0 mmol) and **2b** (0.76 g, 2.0 mmol) in THF (20 mL) gave a 1:2.3 diastereomeric mixture of **6b** (0.46 g, 66%) as a colorless oil after column chromatography (SiO_2, 10% acetone in CH_2Cl_2): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.42−7.31 (m, 2H* and 2H), 7.28−7.05 (m, 5H and 4H*), 6.97−6.85 (m, 2H*), 6.80−6.65 (m, 2H and 1H*), 5.41−5.30 (m, 2H), 5.20−5.02 (m, 3H and 1H*), 5.02−4.91 (m, 1H), 4.91−4.75 (m, 3H*), 4.67−4.54 (m, 1H), 4.19−3.88 (m, 4H*), 3.87−3.60 (m, 7H and 4H*), 2.53−2.43 (m, 1H), 2.30−2.20 (m, 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −169.5 to −169.4 (m, 1F*), −172.0 to −172.5 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 158.5 (C), 158.4 (C*), 140.7 (C), 140.6 (C*), 136.8 (C), 136.4 (C*), 128.5 (2 × CH*), 128.4 (2 × CH), 127.5 (2 × CH), 127.4 (2 × CH*), 127.3 (CH and CH*), 126.6 (2 × CH), 126.5 (2 × CH*), 113.3 (2 × CH), 113.2 (2 × CH*), 99.9 (d, J = 183.0 Hz, CF and CF*), 75.2 (d, J = 23.6 Hz, CH*), 74.0 (d, J = 21.5 Hz, CH), 70.3 (d, J = 9.3 Hz, CH), 70.1 (d, J = 12.0 Hz, CH*), 62.8 (d, J = 26.3 Hz, CH_2), 61.1 (d, J = 23.9 Hz, CH_2*), 57.8 (d, J = 8.8 Hz, CH_2), 57.7 (d, J = 5.8 Hz, CH_2*), 55.6 (CH_3*), 54.6 (CH_3), 52.4 (d, J = 19.6 Hz, CH*), 50.3 (d, J = 20.1 Hz, CH); IR (neat) ν_{max} 3317br, 1509m, 1242s, 1047s, 1005s, 847s, 698s cm^{-1}; MS m/z (rel intens, %) 350 (M^+, trace), 137 (100), 135 (33), 109 (55), 94 (36), 77 (48); HRMS (ESI-TOF) calcd for $C_{19}H_{23}FO_5Na$ $[M + Na]^+$ 373.1427, found 373.1425.

(2S,3R*,4R*)-2-Fluoro-2,3-bis(hydroxymethyl)-1-(4-methoxyphenyl)-1-phenylbutane-1,4-diol (**6c**).* According to general procedure B, the reaction of LAH (0.76 g, 20.0 mmol) and **2c** (0.76 g, 2.0 mmol) in THF (20 mL) gave a 1:4 diastereomeric mixture of **6c** (0.49 g, 70%) as a colorless oil after column chromatography (SiO_2, 2% MeOH in CH_2Cl_2): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.33−7.24 (m, 2H and 2H*), 7.23−7.02 (m, 5H and 5H*), 6.82−6.72 (m, 2H and 2H*), 5.43−5.36 (m, 1H*), 5.27−5.21 (m, 1H*), 5.20−5.10 (m, 2H), 5.09−4.98 (m, 2H), 4.98−4.83 (m, 1H and 4H*), 4.67−4.58 (m, 1H), 4.24−3.84 (m, 4H*), 3.84−3.55 (m, 7H and 3H*), 2.59−2.48 (m, 1H), 2.30−2.22 (m, 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −169.9 (s, 1F*), −172.5 (s, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.2 (C and C*), 145.1 (C and C*), 132.6 (C and C*), 129.6 (2 × CH*), 129.5 (2 × CH), 127.9 (2 × CH), 127.8 (2 × CH*), 126.5 (CH), 126.4 (CH*), 125.6 (2 × CH and 2 × CH*), 113.0 (2 × CH), 112.9 (2 × CH*), 100.0 (d, J = 182.4 Hz, CF and CF*), 75.0 (d, J = 23.4 Hz, CH*), 73.6 (d, J = 21.4 Hz, CH), 70.7 (d, J = 9.2 Hz, CH), 70.4 (d, J = 12.1 Hz, CH*), 62.8 (d, J = 26.3 Hz, CH_2), 61.2 (d, J = 24.5 Hz, CH_2*), 57.8 (d, J = 8.6 Hz, CH_2), 57.7 (d, J = 10.3 Hz, CH_2*), 54.6 (CH_3 and CH_3*), 52.4 (d, J = 19.4 Hz, CH*), 50.3 (d, J = 20.2 Hz, CH); IR (neat) ν_{max} 3321br, 1510m, 1247s, 1180s, 1048s, 999s cm^{-1}; MS m/z (rel intens, %) 350 (M^+, 0.3), 178 (100), 177 (90), 161 (47); HRMS (ESI-TOF) calcd for $C_{19}H_{23}FO_5Na$ $[M + Na]^+$ 373.1427, found 373.1425.

(2S,3R*,4R*)-2-Fluoro-2,3-bis(hydroxymethyl)-1,4-bis(4-methoxyphenyl)butane-1,4-diol (**6d**).* According to general procedure B, the reaction of LAH (0.76 g, 20.0 mmol) and **2d** (0.83 g, 2.0 mmol) in THF (20 mL) gave a 1:2.9 diastereomeric mixture of **6d** (0.47 g, 62%) as a colorless oil after column chromatography (SiO_2, 5% acetone in CH_2Cl_2): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.31−7.23 (m, 2H and 2H*), 7.14−7.05 (m, 2H and 2H*), 6.81−6.70 (m, 4H and 4H*), 5.33 (d, J = 4.0 Hz, 1H*), 5.24 (d, J = 4.1 Hz, 1H*), 5.14−4.98 (m, 2H and 3H*), 4.91 (dd, J = 23.1 and 6.1 Hz, 1H), 4.85−4.75 (m, 1H), 4.59 (t, J = 4.9 Hz, 1H), 4.17−3.90 (m, 4H*), 3.88−3.60 (m, 11H and 7H*), 2.54−2.44 (m, 1H), 2.25−2.17 (m, 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −169.6 (s, 1F*), −172.6 to −172.9 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.2 (C and C*), 158.5 (C and C*), 136.8 (C), 136.6 (C*), 132.6 (C), 132.5 (C*), 129.5 (2 × CH*), 129.4 (2 × CH), 126.6 (2 × CH), 126.5 (2 × CH*), 113.0 (2 × CH), 113.2 (2 × CH*), 112.9 (2 × CH), 112.8 (2 × CH*), 100.0 (d, J = 182.4 Hz, CF and CF*), 74.9 (d, J = 20.8 Hz, CH*), 73.6 (d, J = 21.3 Hz, CH), 70.4 (d, J = 8.8 Hz, CH), 70.2 (d, J = 12.2 Hz, CH*), 62.8 (d, J = 26.7 Hz, CH_2), 61.2 (d, J = 29.3 Hz, CH_2*), 57.9 (d, J = 8.7 Hz, CH_2), 57.8 (d, J = 6.4 Hz, CH_2*), 54.6 (2 × CH_3 and 2 × CH_3*), 52.4 (d, J = 19.8 Hz, CH*), 50.3 (d, J = 20.5 Hz, CH); IR (neat) ν_{max} 3315br, 1512m, 1247m, 1031s, 732s cm^{-1}; MS m/z (rel intens, %) 381 [$(M + 1)^+$, 0.2], 380 (M^+, 0.3), 196 (44), 189 (29), 178 (96), 163 (50), 148 (66), 139 (100), 138 (81), 136 (94), 110 (75), 95 (68), 77 (80); HRMS (ESI-TOF) calcd for $C_{20}H_{25}FO_6Na$ $[M + Na]^+$ 403.1532, found 403.1539.

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(2S,3R*,4R*)-2-Fluoro-2,3-bis(hydroxymethyl)-1,4-di-p-tolylbutane-1,4-diol (**6g**).* According to general procedure B, the reaction of LAH (0.76 g, 20.0 mmol) and **2g** (0.77 g, 2.0 mmol) in THF (20 mL) gave a 1:3.1 diastereomeric mixture of **6g** (0.51 g, 73%) as a colorless oil after column chromatography (SiO_2, 5% acetone in CH_2Cl_2): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.40−7.32 (m, 2H and 2H*), 7.22−7.06 (m, 6H and 6H*), 5.45 (d, J = 3.3 Hz, 1H*), 5.41 (d, J = 4.1 Hz, 1H*), 5.31−5.12 (m, 2H and 4H*), 5.06 (dd, J = 22.8 and 6.3 Hz, 1H), 4.95 (t, J = 5.8 Hz, 1H), 4.88 (t, J = 5.6 Hz, 1H*), 4.70 (t, J = 4.9 Hz, 1H), 4.30−4.13 (m, 1H), 4.12−4.02 (m, 1H*), 3.99−3.72 (m, 4H and 2H*), 2.67−2.59 (m, 1H), 2.42−2.27 (m, 6H and 7H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −169.2 (s, 1F*), −172.1 to −172.7 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 143.4 (C), 143.0 (C*), 139.1 (C), 139.0 (C*), 138.1 (C and C*), 137.2 (C), 137.1 (C*), 129.9 (2 × CH), 129.8 (4 × CH*), 129.7 (2 × CH), 129.6 (2 × CH), 129.5 (2 × CH*), 126.9 (2 × CH and 2 × CH*), 101.3 (d, J = 182.5 Hz, CF and CF*), 76.5 (d, J = 23.7 Hz, CH*), 75.2 (d, J = 21.3 Hz, CH), 72.0 (d, J = 9.1 Hz, CH), 71.8 (d, J = 12.0 Hz, CH*), 64.2 (d, J = 26.4 Hz, CH_2), 62.5 (d, J = 24.0 Hz, CH_2*), 59.3 (d, J = 8.7 Hz, CH_2), 59.2 (d, J = 7.8 Hz, CH_2*), 53.8 (d, J = 19.5 Hz, CH*), 51.7 (d, J = 20.2 Hz, CH), 21.6 (CH_3 and CH_3*), 21.5 (CH_3 and CH_3*); IR (neat) ν_{max} 3286br, 1513m, 1253m, 1043s, 769s cm^{-1}; MS m/z (rel intens, %) 348 (M^+, trace), 261 (25), 233 (26), 147 (52), 146 (55), 128 (44), 119 (70), 91 (100), 77 (30); HRMS (ESI-TOF) calcd for $C_{20}H_{25}FO_4Na$ $[M + Na]^+$ 371.1634, found 371.1633.

(2S,3R*,4R*)-4-(4-Bromo-3-methoxyphenyl)-2-fluoro-2,3-bis(hydroxymethyl)-1-(p-tolyl)butane-1,4-diol (**6h**).* According to general procedure B, the reaction of LAH (0.76 g, 20.0 mmol) and **2h** (0.96 g, 2.0 mmol) in THF (20 mL) gave a 1:1.9 diastereomeric mixture of **6h** (0.63 g, 71%) as a colorless oil after column chromatography (SiO_2, 5% acetone in CH_2Cl_2): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.27−7.10 (m, 4H and 4H*), 7.03−6.92 (m, 2H and 2H*), 6.67−6.56 (m, 1H and 1H*), 5.67−5.51 (br, 1H*), 5.46−5.31 (m, 1H), 5.30−5.13 (m, 2H and 2H*), 5.06−4.85 (m, 2H and 2H*), 4.71−4.55 (br, 1H), 4.32−3.55 (m, 7H and 8H*), 2.60−2.51 (m, 1H), 2.34−2.26 (m, 1H*), 2.18 (s, 3H), 2.17 (s, 3H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −171.7 to −172.0 (m, 1F), −176.4 to −176.9 (m, 1F*); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.0 (C and C*), 144.2 (C), 144.0 (C*), 137.7 (C*), 137.6 (C), 136.8 (C*), 136.6 (C), 133.3 (CH), 133.2 (CH*), 129.1 (CH*), 128.4 (CH), 128.2 (3 × CH and 3 × CH*), 114.9 (CH and CH*), 114.1 (CH and CH*), 111.3 (C and C*), 99.9 (d, J = 183.6 Hz, CF and CF*), 76.4 (d, J = 21.2 Hz, CH*), 74.3 (d, J = 24.3 Hz, CH), 70.1 (d, J = 10.9 Hz, CH), 69.6 (d, J = 13.3 Hz, CH*), 63.1 (d, J = 24.7 Hz, CH_2), 61.4 (d, J = 24.7 Hz, CH_2*), 57.9 (CH_2), 57.8 (CH_2*), 54.9 (CH_3 and CH_3*), 49.3 (d, J = 18.8 Hz, CH*), 46.5 (d, J = 19.8 Hz, CH), 20.3 (CH_3 and CH_3*); IR (neat) ν_{max} 3182br, 1466m, 1283m, 1047s, 1011s, 800s cm^{-1}; MS m/z (rel intens, %) 443 [$(M + 1)^+$, 0.1], 442 (M^+, 0.1), 215 (100), 128 (28), 105 (25), 91 (24), 77 (23); HRMS (ESI-TOF) calcd for $C_{20}H_{24}BrFO_5Na$ $[M + Na]^+$ 465.0688, found 465.0684 and 467.0661.

(2S,3R*,4R*)-4-(4-Bromo-3-methoxyphenyl)-2-fluoro-2,3-bis(hydroxymethyl)-1-(4-methoxyphenyl)butane-1,4-diol (**6i**).* According to general procedure B, the reaction of LAH (1.14 g, 20.0 mmol) and **2i** (1.44 g, 3.0 mmol) in THF (30 mL) gave a 1:3.3 diastereomeric mixture of **6i** (0.96 g, 70%) as a colorless oil after column chromatography (SiO_2, 5% acetone in CH_2Cl_2): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.32−7.19 (m, 3H and 3H*), 7.19−7.13 (m, 1H), 7.12−7.05 (m, 1H*), 6.82−6.68 (m, 2H and 2H*), 6.67−6.58 (m, 1H and 1H*), 5.40 (d, J = 3.3 Hz, 1H), 5.26−5.17 (m, 2H), 5.15−5.10 (m, 2H*), 5.09−5.04 (m, 1H*), 4.99 (t, J = 5.7 Hz, 1H), 4.96−4.91 (m, 2H*), 4.91−4.84 (m, 1H), 4.68−4.57 (m, 1H and 1H*), 4.02−3.85 (m, 2H and 2H*), 3.85−3.60 (m, 8H and 8H*), 2.60−2.47 (m, 1H and 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −171.5 to −172.0 (m, 1F and 1F*); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.2 (C and C*), 159.0 (C and C*), 146.8 (C*), 144.2 (C), 133.3 (CH), 132.3 (C*), 136.6 (C), 133.3 (CH), 132.3 (C), 130.3 (C*), 129.5 (2 × CH), 129.4 (2 × CH*), 128.9 (CH*), 117.8 (CH*), 114.9 (CH), 114.0 (CH), 113.4 (C*), 113.0 (2 × CH and CH*), 112.0 (CH*), 111.3 (C), 111.1 (CH*), 99.9 (d, J = 182.9 Hz, CF and CF*), 74.1 (d, J = 24.5 Hz, CH), 73.7 (d, J = 21.8 Hz, CH*), 70.5 (d, J = 9.9 Hz, CH*), 70.1 (d, J = 11.0 Hz, CH), 63.1 (d, J = 24.5 Hz, CH_2), 62.9 (d, J = 23.2 Hz, CH_2*), 57.9 (CH_2*), 57.8 (CH_2), 54.9 (CH_3), 54.6 (CH_3 and CH_3*), 54.5 (CH_3*), 50.2 (d, J = 20.3 Hz, CH*), 46.5 (d, J = 19.8 Hz, CH); IR (neat) ν_{max} 3183br, 1511m, 1462m, 1250s, 1019s cm^{-1}; MS m/z (rel intens, %) 459 [$(M + 1)^+$, 0.3], 458 (M^+, 0.3), 277 (18), 265 (28), 216 (76), 214 (84), 207 (100), 137 (54), 109 (69), 108 (60), 77 (56); HRMS (ESI-TOF) calcd for $C_{20}H_{24}BrFO_6Na$ $[M + Na]^+$ 481.0637, found 481.0637 and 483.0626.

Synthesis of 1-Fluorinated *exo,exo*-Furofurans 3A and *endo,exo*-Furofurans 3B: General Procedure C. The reaction mixture of **6** (0.25 mmol) and a catalytic amount of *p*-TsOH in toluene (5 mL) was equipped with a Dean−Stark trap and heated at 130 °C for 3 h. After removal of the solvent, the crude product was purified by column chromatography (SiO_2) to afford **3A** as a major product and **3B** as a minor product.

*Preparation of **3aA** and **3aB**.* According to general procedure C, the reaction of **6a** (80 mg, 0.25 mmol) and a catalytic amount of *p*-TsOH in toluene (5 mL) afforded **3aA** (47 mg, 66%) as a pale yellow oil and **3aB** (5 mg, 7%) as a yellow oil after chromatography (SiO_2, 5−10% EtOAc in hexanes).

Data for (1S,2R*,5R*,6S*)-1-fluoro-2,6-diphenyl-3,7-dioxabicyclo[3.3.0]octane (**3aA**):* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.18 (m, 10H), 4.82 (d, J = 5.4 Hz, 1H), 4.77 (d, J = 19.3 Hz, 1H), 4.49 (dd, J = 9.1, 9.1 Hz, 1H), 4.10 (dd, J = 12.0, 10.3 Hz, 1H), 4.07 (dd, J = 20.7, 10.3 Hz, 1H), 3.77 (ddd, J = 9.1, 6.7, 0.7 Hz, 1H), 3.33−3.25 (m, 1H); ^{19}F NMR (470 MHz, $CDCl_3$) δ −162.5 to −162.8 (m, 1F); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6 (C), 134.6 (d, J = 3.0 Hz, C), 128.7 (2 × CH), 128.4 (CH), 128.2 (2 × CH), 128.1 (CH), 127.3 (2 × CH), 126.1 (2 × CH), 112.0 (d, J = 204.8 Hz, CF), 86.4 (d, J = 23.9 Hz, CH), 85.6 (d, J = 5.0 Hz, CH), 73.0 (d, J = 30.9 Hz, CH_2), 70.9 (d, J = 1.9 Hz, CH_2), 59.5 (d, J = 20.5 Hz, CH); IR (neat) ν_{max} 1496m, 1455m, 1058s cm^{-1}; MS m/z (rel intens, %) 285 [$(M + 1)^+$, 3], 284 (M^+, 11), 253 (56), 117 (49), 105 (100), 77 (38); HRMS (ESI-TOF) calcd for $C_{18}H_{17}FO_2Na$ $[M + Na]^+$ 307.1110, found 307.1112.

Data for (1S,2S*,5R*,6S*)-1-fluoro-2,6-diphenyl-3,7-dioxabicyclo[3.3.0]octane (**3aB**):* ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40−7.24 (m, 10H), 4.94 (d, J = 16.3 Hz, 1H), 4.46 (d, J = 8.4 Hz, 1H), 4.11 (dd, J = 9.8, 6.3 Hz, 1H), 4.03 (d, J = 9.8 Hz, 1H), 3.89 (dd, J = 20.3, 11.5 Hz, 1H), 3.34 (dd, J = 33.3, 11.5 Hz, 1H), 2.97−2.89 (m, 1H); ^{19}F NMR (470 MHz, $CDCl_3$) δ −155.5 to −155.8 (m, 1F); ^{13}C NMR (125 MHz, $CDCl_3$) δ 139.6 (C), 134.6 (C), 128.7 (2 × CH), 128.5 (2 × CH), 128.4 (CH), 128.0 (CH), 126.3 (2 × CH), 125.1 (2 × CH), 113.8 (d, J = 199.6 Hz, CF), 88.1 (d, J = 2.0 Hz, CH), 83.5 (d, J = 31.0 Hz, CH), 74.2 (d, J = 28.6 Hz, CH_2), 69.1 (d, J = 5.9 Hz, CH_2), 60.4 (d, J = 19.4 Hz, CH); IR (neat) ν_{max} 1497m, 1452m, 1058s, 1029s cm^{-1}; MS m/z (rel intens, %) 285 [$(M + 1)^+$, 7], 284 (M^+, 14), 253 (61), 117 (47), 105 (100), 77 (38); HRMS (ESI-TOF) calcd for $C_{18}H_{17}FO_2Na$ $[M + Na]^+$ 307.1110, found 307.1113.

*Preparation of **3bA** and **3bB**.* According to general procedure C, the reaction of **6b** (88 mg, 0.25 mmol) and a catalytic amount of *p*-TsOH in toluene (5 mL) afforded **3bA** (45 mg, 57%) as a yellow oil and **3bB** (6 mg, 7%) as a pale yellow oil after chromatography (SiO_2, 5−10% EtOAc in hexanes).

Data for (1S,2R*,5R*,6S*)-1-fluoro-6-(4-methoxyphenyl)-2-phenyl-3,7-dioxabicyclo[3.3.0]octane (**3bA**):* ^{1}H NMR (400 MHz, CDC_3) δ 7.44−7.30 (m, 7H), 6.29 (d, J = 8.7 Hz, 2H), 4.86 (d, J = 5.4 Hz, 1H), 4.85 (d, J = 19.2 Hz, 1H), 4.56 (dd, J = 8.8, 8.8 Hz, 1H), 4.17 (dd, J = 20.9, 10.2 Hz, 1H), 4.13 (dd, J = 19.4, 10.2 Hz, 1H), 3.87−3.73 (m, 4H), 3.44−3.27 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −162.4 to −162.9 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (C), 134.8 (C), 131.6 (C), 128.4 (CH), 128.2 (2 × CH), 127.7 (2 × CH), 127.3 (2 × CH), 114.2 (2 × CH), 112.1 (d, J = 206.0 Hz, CF), 86.5 (d, J = 24.0 Hz, CH), 85.5 (d, J = 5.0 Hz, CH), 73.0 (d, J =

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31.0 Hz, CH_2), 70.9 (CH_2), 59.4 (d, J = 21.0 Hz, CH), 55.3 (CH_3); IR (neat) ν_{max} 1513s, 1420s, 1303m, 1245s, 1079m, 1056s, 1038s, 959s, 835s, 804s, 727s cm^{-1}; MS m/z (rel intens, %) 314 (M^+, 3), 145 (66), 135 (100), 105 (56), 91 (26), 77 (52); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_3Na$ $[M + Na]^+$ 337.1215, found 337.1219.

Data for (1S,2S*,5R*,6S*)-1-fluoro-6-(4-methoxyphenyl)-2-phenyl-3,7-dioxabicyclo[3.3.0]octane (**3bB**):* ^1H NMR (500 MHz, $CDCl_3$) δ 7.37−7.25 (m, 7H), 6.87−6.85 (m, 2H), 4.88 (d, J = 16.5 Hz, 1H), 4.46 (d, J = 8.4 Hz, 1H), 4.09 (dd, J = 9.8, 6.3 Hz, 1H), 4.01 (d, J = 9.8 Hz, 1H), 3.88 (dd, J = 20.4, 11.5 Hz, 1H), 3.75 (s, CH_3), 3.37 (dd, J = 33.1, 11.5 Hz, 1H), 2.98−2.86 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.5 to −156.5 (m, 1F); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4 (C), 139.7 (C), 128.7 (2 × CH), 128.3 (CH), 128.0 (C), 126.4 (2 × CH), 126.3 (2 × CH), 113.9 (2 × CH), 113.8 (d, J = 198.9 Hz, CF), 88.2 (d, J = 1.9 Hz, CH), 83.4 (d, J = 31.5 Hz, CH), 74.2 (d, J = 28.6 Hz, CH_2), 69.1 (d, J = 5.8 Hz, CH_2), 60.4 (d, J = 19.4 Hz, CH), 55.3 (CH_3); IR (neat) ν_{max} 1513m, 1248s, 1173m, 1029s, 833m, 735s, 698s cm^{-1}; MS m/z (rel intens, %) 314 (M^+, 6), 297 (21), 236 (21), 121 (23), 111 (26), 97 (39), 95 (55), 83 (52), 81 (63), 79 (56), 67 (100), 55 (84); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_3Na$ $[M + Na]^+$ 337.1215, found 337.1219.

*Preparation of **3cA** and **3cB**.* According to general procedure C, the reaction of **6c** (88 mg, 0.25 mmol) and a catalytic amount of p-TsOH in toluene (5 mL) afforded **3cA** (53 mg, 67%) as a white solid and **3cB** (4 mg, 5%) as a yellow oil after chromatography (SiO_2, 5−10% EtOAc in hexanes).

Data for (1S,2R*,5R*,6S*)-1-fluoro-2-(4-methoxyphenyl)-6-phenyl-3,7-dioxabicyclo[3.3.0]octane (**3cA**):* mp 120−122 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43−7.36 (m, 4H), 7.36−7.30 (m, 3H), 6.95−6.88 (m, 2H), 4.91 (d, J = 5.4 Hz, 1H), 4.79 (d, J = 19.5 Hz, 1H), 4.56 (dd, J = 9.1, 9.1 Hz, 1H), 4.43−4.22 (m, 2H), 3.83 (dd, J = 9.1, 6.8 Hz, 4H), 3.82 (s, 3H), 3.44−3.30 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −162.8 to −163.0 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8 (C), 139.7 (C), 128.9 (2 × CH), 128.8 (2 × CH), 128.2 (CH), 126.6 (d, J = 2.8 Hz, C), 126.2 (2 × CH), 113.7 (2 × CH), 111.9 (d, J = 203.9 Hz, CF), 86.3 (d, J = 23.5 Hz, CH), 85.7 (d, J = 4.9 Hz, CH), 73.0 (d, J = 30.9 Hz, CH_2), 70.9 (d, J = 2.0 Hz, CH_2), 59.4 (d, J = 20.6 Hz, CH), 55.3 (CH_3); IR (neat) ν_{max} 1513s, 1245s, 1111m, 1055s, 744s cm^{-1}; MS m/z (rel intens, %) 314 (M^+, 1), 135 (100), 117 (29), 115 (28), 105 (35), 77 (37); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_3Na$ $[M + Na]^+$ 337.1215, found 337.1220.

Data for (1S,2S*,5R*,6S*)-1-fluoro-6-(4-methoxyphenyl)-2-phenyl-3,7-dioxabicyclo[3.3.0]octane (**3cB**):* ^1H NMR (400 MHz, $CDCl_3$) δ 7.40−7.17 (m, 7H), 6.84 (d, J = 8.8 Hz, 2H), 4.87 (d, J = 16.5 Hz, 1H), 4.45 (d, J = 8.4 Hz, 1H), 4.07 (dd, J = 9.8, 6.2 Hz, 1H), 3.99 (d, J = 19.1 Hz, 1H), 3.87 (dd, J = 20.4, 11.6 Hz, 1H), 3.74 (s, CH_3), 3.36 (dd, J = 33.2, 11.6 Hz, 1H), 2.98−2.83 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.8 to −156.3 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (C), 139.6 (C), 128.7 (2 × CH), 128.4 (2 × CH), 128.0 (C), 126.4 (2 × CH), 126.3 (2 × CH), 113.9 (2 × CH), 113.8 (d, J = 199.1 Hz, CF), 88.2 (d, J = 1.8 Hz, CH), 83.4 (d, J = 31.4 Hz, CH), 74.2 (d, J = 28.7 Hz, CH_2), 69.1 (d, J = 5.8 Hz, CH_2), 60.4 (d, J = 19.5 Hz, CH), 55.3 (CH_3); IR (neat) ν_{max} 1512s, 1247s, 1172m, 1104m, 1029s, 832m, 735s, 698s cm^{-1}; MS m/z (rel intens, %) 314 (M^+, 3), 262 (17), 156 (13), 134 (100), 115 (32), 105 (23), 77 (28); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_3Na$ $[M + Na]^+$ 337.1215, found 337.1219.

*Preparation of **3dA** and **3dB**.* According to general procedure C, the reaction of **6d** (95 mg, 0.25 mmol) and a catalytic amount of p-TsOH in toluene (5 mL) afforded **3dA** (55 mg, 67%) as a pale yellow solid and **3dB** (10 mg, 12%) as a pale yellow oil after chromatography (SiO_2, 10% EtOAc in hexanes).

Data for (1S,2R*,5R*,6S*)-1-fluoro-2,6-bis(4-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octane (**3dA**):* mp 96−100 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27 (d, J = 8.5 Hz, 4H), 6.85 (d, J = 8.5 Hz, 4H), 4.78 (d, J = 5.3 Hz, 1H), 4.71 (d, J = 19.5 Hz, 1H), 4.46 (dd, J = 8.8, 8.8 Hz, 1H), 4.10−3.94 (m, 2H), 3.78−3.65 (m, 7H), 3.37−3.20 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −162.6 to −163.1 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (C), 159.5 (C), 131.6 (C), 128.8 (2 × CH), 127.7 (2 × CH), 126.6 (C), 114.4 (2 × CH), 113.9 (C), 113.7 (2 × CH), 111.8 (d, J = 204.0 Hz, CF), 86.4 (d, J = 23.0 Hz, CH), 85.4 (d, J = 5.0 Hz, CH), 72.8 (d, J = 31.0 Hz, CH_2), 70.8 (d, J = 4.0 Hz, CH_2), 55.3 (CH_3), 55.3 (CH_3); IR (neat) ν_{max} 1510m, 1243s, 1081s cm^{-1}; MS m/z (rel intens, %) 344 (M^+, 1), 135 (100), 91 (11), 71 (19); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_4Na$ $[M + Na]^+$ 367.1321, found 367.1326.

Data for (1S,2S*,5R*,6S*)-1-fluoro-2,6-bis(4-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octane (**3dB**):* ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 8.8 Hz, 2H), 7.33 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.6 Hz, 2H), 6.91 (d, J = 8.6 Hz, 2H), 4.95 (d, J = 16.5 Hz, 1H), 4.47 (d, J = 8.4 Hz, 1H), 4.14 (dd, J = 9.8, 6.3 Hz, 1H), 4.03 (d, J = 9.8 Hz, 1H), 3.90 (dd, J = 20.5, 11.5 Hz, 1H), 3.83 (s, CH_3), 3.83 (s, 3H), 3.41 (dd, J = 33.3, 11.5 Hz, 1H), 3.35−2.90 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.7 to −156.1 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (C), 159.3 (C), 131.5 (C), 128.0 (C), 127.7 (2 × CH), 126.3 (2 × CH), 114.1 (2 × CH), 113.9 (2 × CH), 113.8 (d, J = 198.9 Hz, CF), 87.9 (d, J = 1.5 Hz, CH), 83.4 (d, J = 31.4 Hz, CH), 74.0 (d, J = 28.6 Hz, CH_2), 69.0 (d, J = 5.7 Hz, CH_2), 60.2 (d, J = 19.3 Hz, CH), 55.3 (CH_3), 55.2 (CH_3); IR (neat) ν_{max} 1511s, 1304m, 1244m, 1172m, 1029s, 827m, 734s cm^{-1}; MS m/z (rel intens, %) 344 (M^+, 4), 172 (12), 147 (12), 135 (100), 121 (10), 91 (12), 77 (23); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_4Na$ $[M + Na]^+$ 367.1321, found 367.1324.

*Preparation of **3gA** and **3gB**.* According to general procedure C, the reaction of **6g** (95 mg, 0.25 mmol) and a catalytic amount of p-TsOH in toluene (5 mL) afforded **3gA** (55 mg, 67%) as a white solid and **3gB** (10 mg, 12%) as a pale yellow oil after chromatography (SiO_2, 5−10% EtOAc in hexanes).

Data for (1S,2R*,5R*,6S*)-1-fluoro-2,6-di-p-tolyl-3,7-dioxabicyclo[3.3.0]octane (**3gA**):* mp 95−97 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.0 Hz, 4H), 7.19 (d, J = 8.0 Hz, 4H), 4.86 (d, J = 5.4 Hz, 1H), 4.81 (d, J = 19.5 Hz, 1H), 4.54 (dd, J = 8.8, 8.8 Hz, 1H), 4.20−4.05 (m, 2H), 3.82 (dd, J = 8.8, 6.9 Hz, 1H), 3.43−3.26 (m, 1H), 2.36 (s, 6H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −162.7 to −163.0 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2 (C), 138.0 (C), 136.6 (C), 131.6 (d, J = 2.9 Hz, C), 129.4 (2 × CH), 128.9 (2 × CH), 127.3 (2 × CH), 126.2 (2 × CH), 111.9 (d, J = 204.2 Hz, CF), 86.4 (d, J = 23.8 Hz, CH), 85.6 (d, J = 4.8 Hz, CH), 72.9 (d, J = 30.8 Hz, CH_2), 70.9 (d, J = 1.8 Hz, CH_2), 59.4 (d, J = 20.5 Hz, CH), 21.2 (CH_3), 21.1 (CH_3); IR (neat) ν_{max} 1023s, 1009m, 904m, 807s, 775s cm^{-1}; MS m/z (rel intens, %) 313 $[(M + 1)^+,0.5]$, 312 (M^+, 0.3), 280 (21), 261 (26), 131 (50), 128 (42), 119 (100), 118 (93), 115 (55), 91 (85), 65 (30); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_4Na$ $[M + Na]^+$ 367.1321, found 367.1326.

Data for (1S,2S*,5R*,6S*)-1-fluoro-2,6-di-p-tolyl-3,7-dioxabicyclo[3.3.0]octane (**3gB**):* ^1H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, J = 7.9 Hz, 4H), 7.11 (d, J = 7.9 Hz, 4H), 4.89 (d, J = 16.5 Hz, 1H), 4.41 (d, J = 8.4 Hz, 1H), 4.07 (dd, J = 9.8, 6.3 Hz, 1H), 3.98 (d, J = 9.8 Hz, 1H), 3.86 (dd, J = 20.4, 11.6 Hz, 1H), 3.33 (dd, J = 33.4, 11.6 Hz, 1H), 2.98−2.82 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −155.5 to −156.0 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.2 (C), 137.6 (C), 136.5 (C), 132.9 (C), 129.4 (2 × CH), 129.1 (2 × CH), 126.3 (2 × CH), 125.0 (2 × CH), 113.8 (d, J = 199.2 Hz, CF), 88.0 (d, J = 1.5 Hz, CH), 83.4 (d, J = 31.4 Hz, CH), 74.2 (d, J = 28.6 Hz, CH_2), 69.0 (d, J = 5.8 Hz, CH_2), 60.4 (d, J = 19.4 Hz, CH), 21.2 (126.3 (2 × CH_3); IR (neat) ν_{max} 1514m, 1104m, 1049s, 809s, 735s cm^{-1}; MS m/z (rel intens, %) 312 (M^+, 4), 280 (37), 161 (46), 131 (50), 129 (64), 128 (73), 119 (100), 91 (78); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_4Na$ $[M + Na]^+$ 367.1321, found 367.1324.

Preparation of (1S,2R*,5R*,6S*)-6-(4-Bromo-3-methoxyphenyl)-1-fluoro-2-(p-tolyl)-3,7-dioxabicyclo[3.3.0]octane (**3hA**).* According to general procedure C, the reaction of **6h** (111 mg, 0.25 mmol) and a catalytic amount of p-TsOH in toluene (5 mL) afforded **3hA** (71 mg, 70%) as a color less oil after column chromatography (SiO_2, 7.5% EtOAc in hexanes): ^1H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.7 Hz, 1H), 7.30 (d, J = 7.9 Hz, 2H), 7.19 (d, J = 7.9 Hz, 2H), 7.13 (d, J = 3.0 Hz, 1H), 6.73 (dd, J = 8.7, 3.0 Hz, 1H), 5.13 (d, J = 4.1 Hz, 1H), 4.76 (d, J = 19.9 Hz, 1H), 4.74 (dd, J = 8.8, 8.8 Hz, 1H), 4.30−4.18 (m, 2H), 4.01 (dd, J = 8.8, 8.8 Hz, 1H), 3.80 (s, 3H), 3.32−3.26 (m, 1H), 2.36 (m, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.7 to −164.1

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(m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (C), 141.1 (C), 138.3 (C), 133.7 (CH), 131.5 (C), 129.0 (2 × CH), 127.4 (2 × CH), 114.8 (CH), 112.3 (CH), 111.7 (C), 111.2 (d, J = 203.5 Hz, CF), 86.1 (d, J = 23.7 Hz, CH), 84.9 (d, J = 4.8 Hz, CH), 73.0 (d, J = 31.1 Hz, CH_2), 72.9 (CH_2), 59.4 (d, J = 20.6 Hz, CH), 55.6 (CH_3), 21.2 (CH_3); IR (neat) ν_{max} 1572m, 1461m, 1266m, 1065s, 1008m, 770s cm^{-1}; MS m/z (rel intens, %) 407 [$(M + 1)^+$,13], 406 (M^+, 19), 289 (31), 215 (85), 214 (82), 146 (100), 145 (85), 119 (54), 91 (33); HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrFO_3Na$ [M + Na]$^+$ 429.0477, found 429.0476 and 431.0465.

Preparation of (1S,2R*,5R*,6S*)-6-(4-Bromo-3-methoxyphenyl)-1-fluoro-2-(4-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octane (**3iA**).* According to general procedure C, the reaction of **6i** (0.46 g, 1.0 mmol) and a catalytic amount of *p*-TsOH in toluene (20 mL) afforded **3iA** (0.30 g, 71%) as a white solid after column chromatography (SiO_2, 10% EtOAc in hexanes): mp 131−134 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, J = 8.7 Hz, 1H), 7.27 (d, J = 8.5 Hz, 2H), 7.06 (d, J = 3.0 Hz, 1H), 6.84 (d, J = 8.5 Hz, 2H), 6.65 (dd, J = 8.7, 3.0 Hz, 1H), 5.05 (d, J = 4.1 Hz, 1H), 4.70−4.60 (m, 2H), 4.21−4.07 (m, 2H), 3.92 (dd, J = 8.4, 8.4 Hz, 1H), 3.74 (s, 3H), 3.73 (m, 3H), 3.26−3.08 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.8 to −164.2 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.8 (C), 159.4 (C), 141.1 (C), 133.7 (CH), 128.9 (2 × CH), 126.5 (C), 114.7 (CH), 113.7 (2 × CH), 112.3 (CH), 111.7 (C), 111.0 (d, J = 203.5 Hz, CF), 86.0 (d, J = 23.5 Hz, CH), 84.9 (d, J = 5.0 Hz, CH), 72.9 (d, J = 31.1 Hz, CH_2), 72.8 (d, J = 1.9 Hz, CH_2), 59.4 (d, J = 20.5 Hz, CH), 55.6 (CH_3), 55.3 (CH_3); IR (neat) ν_{max} 1572m, 1513s, 1460s, 1248s, 1172s, 1012s, 781s cm^{-1}; MS m/z (rel intens, %) 424 [$(M + 2)^+$,18], 422 (M^+, 20), 343 (18), 305 (21), 213 (44), 146 (60), 136 (100), 77 (25); HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrFO_4Na$ [M + Na]$^+$ 445.0426, found 445.0425 and 447.0412.

Synthesis of 1-Fluorobislactols 7. *(3R*,3aR*,6R*,6aS*)-3a-Fluoro-3,6-diphenylhexahydrofuro[3,4-c]furan-1,4-diol (**7a**): General Procedure D.* To the solution of **2a** (0.36 g, 1.0 mmol) in THF (1 mL) was added DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) dropwise at −78 °C over a period of 30 min. The reaction mixture was stirred at −78 °C for 3 h and then at 0 °C for 2 h. It was quenched with an aqueous solution of sodium potassium tartrate at 0 °C. After being stirred at room temperature for 6 h, the reaction mixture was extracted with EtOAc (25 mL × 3). The combined organic phase was washed with water (25 mL) and brine (25 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave a crude product which was purified by column chromatography (SiO_2, 40% EtOAc in hexanes) to give a diastereomeric mixture of **7a** (0.16 g, 51%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.2 Hz, 2H), 7.47 (d, J = 7.2 Hz, 2H), 7.45−7.29 (m, 6H), 5.97 (d, J = 5.1 Hz, 1H), 5.84 (d, J = 8.2 Hz, 1H), 5.75 (d, J = 5.5 Hz, 1H), 5.61 (d, J = 4.2 Hz, 1H), 4.95 (d, J = 21.0 Hz, 1H), 4.86−4.81 (m, 1H), 3.24 (ddd, J = 20.5, 8.2, 3.3 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.6 to −173.9 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.7 (C), 136.2 (d, J = 4.9 Hz, C), 128.1 (2 × CH), 127.8 (2 × CH), 127.7 (2 × CH), 127.5 (2 × CH), 126.4 (2 × CH), 107.9 (d, J = 214.6 Hz, CF), 99.4 (CH), 96.0 (d, J = 21.6 Hz, CH), 85.1 (d, J = 23.5 Hz, CH), 77.3 (d, J = 6.7 Hz, CH), 58.5 (d, J = 20.6 Hz, CH); IR (neat) ν_{max} 3377br, 1495m, 1453m, 1271m, 1115s, 1059s, 1026s, 697s cm^{-1}; MS m/z (rel intens, %) 317 [$(M + 1)^+$,5], 316 (M^+, 5), 231 (18), 202 (24), 149 (87), 115 (66), 91 (65), 79 (71), 77 (100), 67 (75), 55 (83); HRMS (ESI-TOF) calcd for $C_{18}H_{17}FO_4Na$ [M + Na]$^+$ 339.1009, found 339.1006.

(3R,3aR*,6R*,6aS*)-3a-Fluoro-6-(4-methoxyphenyl)-3-phenylhexahydrofuro[3,4-c]furan-1,4-diol (**7b**).* According to general procedure D, the reaction of **2b** (0.39 g, 1.0 mmol) in THF and DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) gave a diastereomeric mixture of **7b** (0.16 g, 47%) as a colorless oil after column chromatography (SiO_2, 40% EtOAc in hexanes): ^{1}H NMR (400 MHz, acetone-d_6) δ 7.37−7.29 (m, 4H), 7.28−7.23 (m, 2H), 7.20−7.15 (m, 1H), 6.80−6.75 (m, 2H), 5.79 (d, J = 5.3 Hz, 1H), 5.67 (d, J = 8.2 Hz, 1H), 5.55 (d, J = 5.6 Hz, 1H), 5.38 (d, J = 4.2 Hz, 1H), 4.71 (d, J = 20.9 Hz, 1H), 4.67−4.63 (m, 1H), 3.65 (s, 3H), 3.07 (ddd, J = 20.9, 8.2, 3.4 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −173.8 to −173.9 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5 (C), 138.7 (C), 130.1 (2 × CH), 129.0 (2 × CH), 128.8 (C), 128.3 (CH), 127.3 (2 × CH), 114.0 (2 × CH), 108.6 (d, J = 214.1 Hz, CF), 100.1 (CH), 96.8 (d, J = 21.6 Hz, CH), 85.7 (d, J = 23.2 Hz, CH), 78.2 (d, J = 6.6 Hz, CH), 59.3 (d, J = 20.6 Hz, CH), 55.5 (CH_3); IR (neat) ν_{max} 3394br, 1514m, 1255s, 1023s, 841s cm^{-1}; MS m/z (rel intens, %) 346 (M^+, 8), 196 (32), 185 (29), 161 (38), 149 (100), 121 (59), 91 (63), 79 (79), 77 (86); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_5Na$ [M + Na]$^+$ 369.1109, found 369.1111.

(3R,3aR*,6R*,6aS*)-3a-Fluoro-3-(4-methoxyphenyl)-6-phenylhexahydrofuro[3,4-c]furan-1,4-diol (**7c**).* According to general procedure D, the reaction of **2c** (0.39 g, 1.0 mmol) in THF and DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) gave a diastereomeric mixture of **7c** (0.15 g, 43%) as a colorless oil after column chromatography (SiO_2, 40% EtOAc in hexanes): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.55−7.46 (m, 4H and 4H*), 7.46−7.35 (m, 2H and 2H*), 7.35−7.26 (m, 1H and 1H*), 6.97−6.86 (m, 2H and 2H*), 6.75 (d, J = 5.2 Hz, 1H*), 5.91 (d, J = 5.3 Hz, 1H), 5.83 (d, J = 8.2 Hz, 1H), 5.65 (d, J = 6.2 Hz, 1H), 5.64 (d, J = 6.2 Hz, 1H*), 5.55−5.46 (m, 1H and 2H*), 5.44 (d, J = 7.6 Hz, 1H*), 5.31 (d, J = 18.0 Hz, 1H*), 4.94−4.88 (m, 1H*), 4.86 (d, J = 21.1 Hz, 1H), 4.83−4.77 (m, 1H), 3.81 (s, 3H), 3.80 (s, 3H*), 3.27−3.11 (m, 1H and 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −167.7 to −168.0 (m, 1F*), −173.7 to −174.1 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.7 (C), 159.2 (C*), 137.9 (C), 137.6 (C*), 129.3 (2 × CH*), 129.2 (2 × CH), 128.1 (2 × CH), 128.0 (2 × CH*), 127.9 (C and C*), 127.4 (CH), 127.2 (CH*), 126.4 (2 × CH), 126.2 (2 × CH*), 113.1 (2 × CH), 112.8 (2 × CH*), 107.9 (d, J = 212.4 Hz, CF*), 107.7 (d, J = 214.1 Hz, CF), 99.2 (CH), 99.0 (CH*), 95.9 (d, J = 21.7 Hz, CH and CH*), 84.8 (d, J = 23.2 Hz, CH), 79.2 (d, J = 23.8 Hz, CH*), 77.5 (d, J = 5.7 Hz, CH*), 77.3 (d, J = 6.8 Hz, CH), 60.1 (d, J = 18.9 Hz, CH*), 58.5 (d, J = 20.7 Hz, CH), 54.6 (CH_3), 54.1 (CH_3*); IR (neat) ν_{max} 3365br, 1512s, 1249s, 1173s, 1007s, 837s cm^{-1}; MS m/z (rel intens, %) 346 (M^+, 1), 289 (16), 246 (16), 217 (19), 202 (23), 201 (57), 196 (100), 189 (26), 135 (47), 109 (44), 94 (40), 77 (49); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_5Na$ [M + Na]$^+$ 369.1109, found 369.1107.

(3R,3aR*,6R*,6aS*)-3a-Fluoro-3,6-bis(4-methoxyphenyl)hexahydrofuro[3,4-c]furan-1,4-diol (**7d**).* According to general procedure D, the reaction of **2d** (0.42 g, 1.0 mmol) in THF and DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) gave a diastereomeric mixture of **7d** (0.20 g, 48%) as a colorless oil after column chromatography (SiO_2, 50% EtOAc in hexanes): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.57−7.43 (m, 2H and 2H*), 7.36−7.24 (m, 1H and 1H*), 7.08−6.98 (m, 2H and 2H*), 6.96−6.81 (m, 3H and 3H*), 6.77−6.69 (m, 1H*), 5.96−5.87 (m, 1H), 5.80 (d, J = 8.2 Hz, 1H), 5.76−5.65 (m, 1H and 1H*), 5.56−5.47 (m, 1H and 1H*), 5.42 (d, J = 7.2 Hz, 1H*), 5.30 (d, J = 17.9 Hz, 1H*), 4.95 (dd, J = 5.3, 5.3 Hz, 1H*), 4.89−4.78 (m, 2H), 3.87−3.74 (m, 6H and 6H*), 3.27−3.10 (m, 1H and 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −167.7 to −168.0 (m, 1F*), −173.8 to −174.1 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 159.8 (C), 159.7 (C), 139.4 (C), 129.2 (2 × CH), 127.9 (C), 118.6 (CH), 113.1 (3 × CH), 112.8 (CH), 112.0 (CH), 107.7 (d, J = 215.0 Hz, CF), 92.0 (CH), 95.9 (d, J = 21.0 Hz, CH), 84.7 (d, J = 23.0 Hz, CH), 77.2 (d, J = 7.0 Hz, CH), 58.5 (d, J = 21.0 Hz, CH), 54.6 (2 × CH_3); IR (neat) ν_{max} 3365br, 1598m, 1515m, 1247s, 996s, 776s cm^{-1}; MS m/z (rel intens, %) 376 (M^+, 0.1), 319 (100), 318 (24), 305 (51), 291 (34), 276 (82), 261 (42), 253 (20), 222 (24), 202 (80), 178 (58), 176 (92), 135 (72); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_6Na$ [M + Na]$^+$ 399.1219, found 399.1215.

(3R,3aR*,6R*,6aS*)-3a-Fluoro-3,6-di-p-tolylhexahydrofuro[3,4-c]furan-1,4-diol (**7g**).* According to general procedure D, the reaction of compound **2g** (0.38 g, 1.0 mmol) in THF and DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) gave a diastereomeric mixture of **7g** (0.20 g, 58%) as a colorless oil after column chromatography (SiO_2, 40% EtOAc in hexanes): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 7.44 (d, J

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= 7.9 Hz, 2H), 7.34 (d, J = 7.9 Hz, 2H), 7.22 (d, J = 7.9 Hz, 2H), 7.18 (d, J = 7.9 Hz, 2H), 5.87 (d, J = 5.3 Hz, 1H), 5.79 (d, J = 8.2 Hz, 1H), 5.66 (d, J = 5.6 Hz, 1H), 5.55 (d, J = 4.8 Hz, 1H), 4.88 (d, J = 21.4 Hz, 1H), 4.86−4.80 (m, 1H), 3.19 (ddd, J = 20.6, 8.2, 3.3 Hz, 1H), 2.35 (s, 3H), 2.34 (s, 1H); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −167.6 to −168.0 (m, 1F*), −173.7 to −174.0 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 138.7 (C), 138.3 (C), 136.2 (C), 134.6 (d, J = 4.8 Hz, C), 130.1 (2 × CH), 129.8 (2 × CH), 129.2 (2 × CH), 127.8 (2 × CH), 109.2 (d, J = 214.3 Hz, CF), 100.8 (CH), 97.3 (d, J = 21.6 Hz, CH), 86.4 (d, J = 23.5 Hz, CH), 78.7 (d, J = 6.7 Hz, CH), 59.9 (d, J = 20.4 Hz, CH), 21.7 (2 × CH_3); IR (neat) ν_{max} 3401br, 1515m, 1055s, 977s, 930m, 761m cm^{-1}; MS m/z (rel intens, %) 344 (M^+, 0.1), 202 (55), 163 (50), 147 (52), 128 (61), 115 (52), 91 (100), 77 (32); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_4Na$ [M + Na]$^+$ 367.1321, found 367.1324.

(3R,3aR*,6R*,6aS*)-6-(4-Bromo-3-methoxyphenyl)-3a-fluoro-3-(p-tolyl)hexahydrofuro[3,4-c]furan-1,4-diol (**7h**).* According to general procedure D, the reaction of compound **2h** (0.48 g, 1.0 mmol) in THF and DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) gave a diastereomeric mixture of **7h** (0.19 g, 43%) as a colorless oil after column chromatography (SiO_2, 40% EtOAc in hexanes): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 7.54 (d, J = 8.8 Hz, 1H), 7.45 (d, J = 7.9 Hz, 2H), 7.25 (d, J = 3.1 Hz, 1H), 7.18 (d, J = 7.9 Hz, 2H), 6.90 (dd, J = 8.8, 3.1 Hz, 1H), 6.09 (d, J = 5.7 Hz, 1H), 5.83 (d, J = 8.1 Hz, 1H), 5.76 (d, J = 5.7 Hz, 1H), 5.65 (d, J = 4.6 Hz, 1H), 4.94 (d, J = 21.0 Hz, 1H), 4.85−4.77 (m, 1H), 3.84 (s, 3H), 3.50−3.40 (m, 1H), 2.33 (s, 3H); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −167.8 to −168.0 (m, 1F*), −173.5 to −173.8 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 159.3 (C), 138.5 (C), 137.3 (C), 133.2 (d, J = 5.0 Hz, C), 133.0 (CH), 128.4 (2 × CH), 127.8 (2 × CH), 114.6 (CH), 114.2 (CH), 111.6 (C), 109.2 (d, J = 214.6 Hz, CF), 99.2 (CH), 96.0 (d, J = 21.8 Hz, CH), 85.2 (d, J = 23.4 Hz, CH), 76.9 (d, J = 7.2 Hz, CH), 56.9 (d, J = 21.0 Hz, CH), 55.0 (CH_3), 20.3 (CH_3); IR (neat) ν_{max} 3325br, 1468m, 1373m, 1237s, 1043s cm^{-1}; MS m/z (rel intens, %) 438 (M^+, 1), 321 (20), 275 (25), 213 (100), 91 (45); HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrFO_5Na$ [M + Na]$^+$ 461.0375, found 461.0370 and 463.0352.

(3R,3aR*,6R*,6aS*)-6-(4-Bromo-3-methoxyphenyl)-3a-fluoro-3-(4-methoxyphenyl)hexahydrofuro[3,4-c]furan-1,4-diol (**7i**).* According to general procedure D, the reaction of compound **2i** (0.50 g, 1.0 mmol) in THF and DIBALH (1 M solution in hexane, 6.0 mL, 6.0 mmol) gave a diastereomeric mixture of **7i** (0.19 g, 42%) as a colorless oil after column chromatography (SiO_2, 40% EtOAc in hexanes): ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.57−7.40 (m, 3H and 3H*), 7.32 (d, J = 3.1 Hz, 1H*), 7.26 (d, J = 3.0 Hz, 1H), 6.97−6.85 (m, 3H and 3H*), 6.13 (d, J = 5.6 Hz, 1H), 5.83 (d, J = 8.1 Hz, 1H), 5.79 (d, J = 5.7 Hz, 1H), 5.73 (d, J = 6.1 Hz, 1H*), 5.65−5.55 (m, 1H and 2H*), 5.46 (d, J = 7.2 Hz, 1H*), 5.34 (d, J = 17.9 Hz, 1H), 4.92 (d, J = 4.92 Hz, 1H), 4.83−4.47 (m, 1H), 4.47−4.42 (m, 1H*), 3.83 (s, 3H), 3.82 (s, 3H*), 3.81 (s, 3H), 3.80 (s, 3H*), 3.51−3.33 (m, 1H and 1H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −167.7 to −168.1 (m, 1F*), −173.6 (t, J = 20.3 Hz, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 164.9 (C), 164.5 (C), 143.7 (C), 138.2 (CH), 134.4 (2 × CH), 133.2 (d, J = 4.8 Hz, C), 119.8 (CH), 119.5 (CH), 118.4 (2 × CH), 116.8 (C), 112.6 (d, J = 214.1 Hz, CF), 104.3 (CH), 101.2 (d, J = 21.8 Hz, CH), 90.4 (d, J = 23.3 Hz, CH), 82.1 (d, J = 7.2 Hz, CH), 62.1 (d, J = 21.0 Hz, CH), 60.2 (CH_3), 59.8 (CH_3); IR (neat) ν_{max} 3409br, 1514m, 1248m, 1027s cm^{-1}; MS m/z (rel intens, %) 454 (M^+, 2), 337 (46), 229 (62), 202 (60), 196 (52), 145 (55), 135 (100), 109 (49), 77 (63); HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrFO_6Na$ [M + Na]$^+$ 477.0324, found 477.0326 and 479.0310.

Synthesis of 1-Fluoro-*exo,exo*-furofurans 3A and *exo,endo*-1-Fluoro-8-hydroxyfurofurans 8: General Procedure E. To the reaction mixture of **7** (0.2 mmol) and Et_3SiH (2.0 mmol) in CH_2Cl_2 (4 mL) was added dropwise $BF_3{\cdot}OEt_2$ (2.0 mmol) at −20 °C for 10 min. The reaction was stirred at −20 °C for 10 min and then at 0 °C for 1.5 to 2 h. It was quenched with sat. $NaHCO_3$ and extracted with EtOAc (10 mL × 3). The combined organic phase was washed with water (10 mL), brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave a crude product, which was purified by column chromatography (SiO_2) to give **3A** as a major product and a diastereomeric mixture of **8** as a minor product.

*Preparation of **3aA** and **8a**.* According to general procedure E, the reaction of **7a** (63 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3aA** (29 mg, 51%) as a pale yellow oil and a diastereomeric mixture of **8a** (20 mg, 33%) as a colorless oil after column chromatography (SiO_2, 5−25% EtOAc in hexanes).

Data for (1R,3aS*,4R*,6aR*)-3a-fluoro-1,4-diphenylhexahydrofuro[3,4-c]furan (**8a**):* ^{1}H NMR (400 MHz, acetone-d_6) δ 7.57−7.23 (m, 10H), 5.92 (d, J = 5.5 Hz, 1H), 5.82 (d, J = 6.9 Hz, 1H), 5.66 (d, J = 5.2 Hz, 1H), 4.60 (d, J = 22.4 Hz, 1H), 4.01 (dd, J = 9.0, 9.0 Hz, 1H), 3.52 (dddd, J = 22.4, 15.0, 9.0, 6.9 Hz, 1H), 3.17 (dd, J = 9.0, 9.0 Hz, 1H); ^{19}F NMR (376 MHz, acetone-d_6) δ −172.4 to −172.7 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6) δ 138.1 (C), 135.4 (C), 128.2 (2 × CH), 128.0 (CH), 127.9 (2 × CH), 127.5 (2 × CH), 127.2 (CH), 125.7 (2 × CH), 109.7 (d, J = 213.0 Hz, CF), 95.9 (d, J = 21.0 Hz, CH), 87.0 (d, J = 23.0 Hz, CH), 76.9 (d, J = 6.0 Hz, CH), 68.3 (CH_2), 52.7 (d, J = 22.0 Hz, CH); IR (neat) ν_{max} 3427br, 1451m, 1026s, 727s cm^{-1}; MS m/z (rel intens, %) 300 (M^+, 0.5), 253 (21), 202 (35), 189 (64), 163 (25), 147 (68), 145 (59), 128 (40), 117 (100), 115 (95), 105 (52), 91 (55), 77 (85); HRMS (ESI-TOF) calcd for $C_{18}H_{17}FO_3Na$ [M + Na]$^+$ 323.1059, found 323.1056.

*Preparation of **3bA** and **8b**.* According to general procedure E, the reaction of **7b** (69 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3bA** (30 mg, 47%) as a yellow oil and a diastereomeric mixture of **8b** (17 mg, 25%) as a colorless oil after column chromatography (SiO_2, 5−30% EtOAc in hexanes).

Data for (1R,3aS*,4R*,6aR*)-3a-fluoro-1-(4-methoxyphenyl)-4-phenylhexahydrofuro[3,4-c]furan (**8b**):* ^{1}H NMR (400 MHz, acetone-d_6) δ 7.52−7.43 (m, 2H), 7.42−7.30 (m, 5H), 7.00−6.93 (m, 2H), 5.86 (d, J = 5.4 Hz, 1H), 5.76 (d, J = 6.8 Hz, 1H), 5.64 (d, J = 5.2 Hz, 1H), 4.60 (d, J = 22.4 Hz, 1H), 4.00 (dd, J = 8.9, 8.9 Hz, 1H), 3.82 (s, 3H), 3.54−3.37 (m, 1H), 3.23 (dd, J = 8.9, 8.9 Hz, 1H); ^{19}F NMR (376 MHz, acetone-d_6) δ −172.4 to −172.8 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6) δ 159.1 (C), 135.5 (C), 129.9 (C), 127.8 (2 × CH), 127.5 (2 × CH), 127.0 (2 × CH), 113.6 (2 × CH), 109.7 (d, J = 214.0 Hz, CF), 95.8 (d, J = 21.0 Hz, CH), 86.9 (d, J = 23.0 Hz, CH), 76.7 (d, J = 6.0 Hz, CH), 68.2 (CH_2), 54.6 (CH_3), 52.8 (d, J = 22.0 Hz, CH); IR (neat) ν_{max} 3377br, 1513m, 1027s, 816s, 737s cm^{-1}; MS m/z (rel intens, %) 330 (M^+, 21), 223 (60), 196 (67), 194 (43), 136 (88), 118 (100), 110 (37), 91 (36), 77 (48); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_4Na$ [M + Na]$^+$ 353.1164, found 353.1182.

*Preparation of **3cA** and **8c**.* According to general procedure E, the reaction of **7c** (69 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3cA** (26 mg, 42%) as a white solid and a diastereomeric mixture of **8c** (24 mg, 36%) as a colorless oil after column chromatography (SiO_2, 5−30% EtOAc in hexanes).

Data for (1R,3aS*,4R*,6aR*)-3a-fluoro-4-(4-methoxyphenyl)-1-phenylhexahydrofuro[3,4-c]furan (**8c**):* ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.35−7.20 (m, 5H and 5H*), 7.20−7.11 (m, 2H and 2H*), 6.79 (d, J = 8.7 Hz, 2H), 6.75 (d, J = 8.8 Hz, 2H*), 6.68 (d, J = 5.2 Hz, 1H*), 5.75 (d, J = 5.5 Hz, 1H), 5.67 (d, J = 6.8 Hz, 1H), 5.44 (d, J = 5.4 Hz, 1H), 5.40 (dd, J = 14.6, 5.2 Hz, 1H*), 5.23 (d, J = 6.2 Hz, 1H*), 4.91 (d, J = 21.2 Hz, 1H*), 4.37 (d, J = 22.6 Hz, 1H), 3.82 (dd, J = 9.0, 9.0 Hz, 1H), 3.71 (dd, J = 9.3, 9.3 Hz, 1H*), 3.67 (s, 3H), 3.65 (s, 3H*), 3.43−3.25 (m, 1H and 1H*), 3.05 (dd, J = 9.3, 9.3 Hz, 1H*), 2.99 (dd, J = 9.0, 9.0 Hz, 1H); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −165.9 to −166.3 (m, 1F*), −172.5 to −172.8 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.8 (C and C*), 138.1 (2 × C and 2 × C*), 129.1 (2 × CH*), 129.0 (2 × CH), 128.2 (2 × CH), 128.1 (2 × CH*), 127.2

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(CH and CH*), 125.7 (2 × CH), 125.3 (2 × CH*), 113.3 (2 × CH), 112.9 (2 × CH*), 111.3 (d, J = 213.5 Hz, CF*), 109.4 (d, J = 214.1 Hz, CF), 100.7 (d, J = 39.8 Hz, CH*), 95.8 (d, J = 21.1 Hz, CH), 86.8 (d, J = 23.2 Hz, CH), 82.5 (d, J = 23.5 Hz, CH*), 76.9 (d, J = 5.4 Hz, CH), 74.2 (CH*), 68.1 (CH_2), 67.3 (CH_2*), 54.9 (d, J = 20.1 Hz, CH*), 54.6 (CH_3), 54.5 (CH_3*), 52.7 (d, J = 22.2 Hz, CH); IR (neat) ν_{max} 3442br, 1514m, 1242s, 1175m, 1042s, 984s, 779s, 704s cm^{-1}; MS m/z (rel intens, %) 330 (M^+, 14), 223 (55), 219 (34), 196 (72), 192 (16), 147 (38), 135 (71), 117 (100), 115 (70), 91 (59), 77 (55); HRMS (ESI-TOF) calcd for $C_{19}H_{19}FO_4Na$ [M + Na]$^+$ 353.1164, found 353.1175.

*Preparation of **3dA** and **8d**.* According to general procedure E, the reaction of **7d** (75 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3dA** (36 mg, 52%) as a pale yellow solid and a diastereomeric mixture of **8d** (21 mg, 29%) as a colorless oil after column chromatography (SiO_2, 10−30% EtOAc in hexanes).

Data for (1R,3aS*,4R*,6aR*)-3a-fluoro-1,4-bis(4-methoxyphenyl)hexahydrofuro[3,4-c]furan (**8d**):* ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.31−7.22 (m, 2H and 2H*), 7.19−7.13 (m, 1H and 1H*), 6.90−6.70 (m, 5H and 5H*), 6.68 (d, J = 5.2 Hz, 1H*), 5.76 (d, J = 5.5 Hz, 1H), 5.63 (d, J = 6.8 Hz, 1H), 5.42 (d, J = 5.4 Hz, 1H), 5.38 (dd, J = 14.7, 5.3 Hz, 1H*), 5.20 (d, J = 6.2 Hz, 1H*), 4.91 (d, J = 21.1 Hz, 1H*), 4.36 (d, J = 22.6 Hz, 1H), 3.85 (dd, J = 9.1, 9.1 Hz, 1H), 3.75 (dd, J = 9.0, 9.0 Hz, 1H*), 3.68 (s, 3H and 3H*), 3.67 (s, 3H), 3.65 (s, 3H*), 3.43−3.24 (m, 1H and 1H*), 3.08 (dd, J = 9.5, 9.5 Hz, 1H*), 3.02 (dd, J = 8.9, 8. Hz, 1H); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −166.0 to −166.3 (m, 1F*), −172.6 to −172.8 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.9 (2 × C), 159.8 (2 × C*), 139.8 (2 × C), 139.7 (2 × C*), 129.3 (CH), 129.2 (CH*), 129.1 (2 × CH*), 128.9 (2 × CH), 117.8 (CH), 117.4 (CH*), 113.3 (2 × CH), 112.9 (2 × CH*), 112.6 (CH*), 112.5 (CH), 111.4 (CH), 111.0 (CH*), 110.5 (d, J = 211.3 Hz, CF*), 109.4 (d, J = 213.7 Hz, CF), 100.7 (d, J = 40.1 Hz, CH*), 95.8 (d, J = 21.0 Hz, CH), 86.8 (d, J = 23.1 Hz, CH), 82.5 (d, J = 23.4 Hz, CH*), 76.8 (d, J = 5.3 Hz, CH), 74.2 (d, J = 2.9 Hz, CH*), 68.1 (CH_2), 67.3 (d, J = 4.2 Hz, CH_2*), 54.9 (d, J = 20.9 Hz, CH*), 54.6 (CH_3 and CH_3*), 52.7 (d, J = 22.2 Hz, CH); IR (neat) ν_{max} 3450br, 1514m, 1242s, 1175m, 1028s, 780s, 704s cm^{-1}; MS m/z (rel intens, %) 360 (M^+, 2), 180 (35), 147 (62), 135 (100), 91 (51), 77 (32); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_5Na$ [M + Na]$^+$ 383.1270, found 383.1266.

*Preparation of **3gA** and **8g**.* According to general procedure E, the reaction of **7g** (69 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3gA** (40 mg, 64%) as a white solid and a diastereomeric mixture of **8g** (12 mg, 18%) as a colorless oil after column chromatography (SiO_2, 5−25% EtOAc in hexanes).

data for (1R,3aS*,4R*,6aR*)-3a-fluoro-1,4-di-p-tolylhexahydrofuro[3,4-c]furan (**8g**):* ^{1}H NMR (400 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 7.20 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 7.9 Hz, 2H), 7.06 (d, J = 7.7 Hz, 2H), 7.04 (d, J = 7.7 Hz, 2H), 5.71 (d, J = 5.5 Hz, 1H), 5.62 (d, J = 6.8 Hz, 1H), 5.45 (d, J = 5.3 Hz, 1H), 4.38 (d, J = 22.5 Hz, 1H), 3.83 (dd, J = 9.0, 9.0 Hz, 1H), 3.50−3.15 (m, 1H), 3.02 (d, J = 9.0, 9.0 Hz, 1H), 2.18 (s, 6H); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −165.8 to −166.2 (m, 1F*), −172.5 to −172.7 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer could not be detected due to low intensity) δ 137.5 (C), 136.7 (C), 135.0 (C), 132.3 (d, J = 4.2 Hz, C), 128.8 (2 × CH), 128.5 (2 × CH), 127.5 (2 × CH), 125.7 (2 × CH), 109.6 (d, J = 214.3 Hz, CF), 95.8 (d, J = 21.0 Hz, CH), 86.9 (d, J = 23.5 Hz, CH), 76.8 (d, J = 5.4 Hz, CH), 68.2 (CH_2), 52.7 (d, J = 22.1 Hz, CH), 20.3 (CH_3), 20.2 (CH_3); IR (neat) ν_{max} 3449br, 1517m, 1219s, 1043s, 760s cm^{-1}; MS m/z (rel intens, %) 329 [(M + 1)$^+$, 0.5], 328 (M^+, 0.5), 202 (39), 159 (34), 146 (56), 131 (63), 91 (100); HRMS (ESI-TOF) calcd for $C_{20}H_{21}FO_3Na$ [M + Na]$^+$ 351.1372, found 351.1374.

*Preparation of **3hA** and **8h**.* According to general procedure E, the reaction of **7h** (88 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3hA** (44 mg, 54%) as a white solid and a diastereomeric mixture of **8h** (18 mg, 21%) as a colorless oil after column chromatography (SiO_2, 5−25% EtOAc in hexanes).

Data for (1R,3aS*,4R*,6aR*)-1-(4-bromo-3-methoxyphenyl)-3a-fluoro-4-(p-tolyl)hexahydrofuro[3,4-c]furan (**8h**):* ^{1}H NMR (400 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 7.43−7.35 (m, 1H and 1H*), 7.26 (d, J = 8.0 Hz, 2H*), 7.22 (d, J = 7.9 Hz, 2H), 7.16 (d, J = 3.0 Hz, 1H*), 7.12 (d, J = 2.9 Hz, 1H), 7.05 (d, J = 7.9 Hz, 2H), 7.01 (d, J = 8.0 Hz, 2H*), 6.80−6.71 (m, 1H and 2H*), 5.93 (d, J = 5.9 Hz, 1H), 5.61 (d, J = 7.0 Hz, 1H), 5.53 (d, J = 5.6 Hz, 1H), 5.49 (dd, J = 14.2, 5.3 Hz, 1H*), 5.24 (d, J = 6.4 Hz, 1H*), 4.97 (d, J = 21.2 Hz, 1H*), 4.44 (d, J = 23.0 Hz, 1H), 3.87 (dd, J = 8.8, 8.8 Hz, 1H), 3.75−3.65 (m, 3H and 4H*), 3.64−3.47 (m, 1H and 1H*), 3.08 (dd, J = 9.3, 9.3 Hz, 1H*), 3.00 (dd, J = 8.8, 8.8 Hz, 1H), 2.19 (s, 3H), 2.18 (s, 3H*); ^{19}F NMR (376 MHz, acetone-d_6, minor isomer marked with an asterisk) δ −165.3 to −165.7 (m, 1F*), −172.5 to −172.8 (m, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer marked with an asterisk) δ 159.3 (C and C*), 138.6 (C), 138.4 (C*), 137.6 (C), 136.8 (C*), 133.3 (CH and CH*), 133.2 (C*), 132.2 (C), 128.5 (2 × CH), 128.1 (2 × CH*), 127.8 (2 × CH*), 127.5 (2 × CH), 114.8 (CH*), 114.6 (CH), 114.4 (CH), 114.2 (CH*), 110.5 (C), 110.0 (C*), 109.2 (d, J = 213.7 Hz, CF and CF*), 100.3 (d, J = 40.3 Hz, CH*), 95.2 (d, J = 21.1 Hz, CH), 86.7 (d, J = 23.1 Hz, CH), 82.6 (d, J = 23.7 Hz, CH*), 77.0 (d, J = 6.1 Hz, CH), 74.5 (CH*), 67.6 (CH_2), 66.7 (CH_2*), 55.0 (CH_3 and CH_3*), 53.3 (d, J = 21.7 Hz, CH*), 51.1 (d, J = 22.7 Hz, CH), 20.3 (CH_3 and CH_3*); IR (neat) ν_{max} 3387br, 1471m, 1296m, 1043s cm^{-1}; MS m/z (rel intens, %) 424 [(M + 2)$^+$, 9], 422 (M^+, 13), 297 (32), 187 (100), 147 (80), 146 (67), 91 (75); HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrFO_4Na$ [M + Na]$^+$ 445.0426, found 445.0430 and 447.0417.

*Preparation of **3iA** and **8i**.* According to general procedure E, the reaction of **7i** (91 mg, 0.2 mmol), Et_3SiH (0.32 mL, 2.0 mmol), and $BF_3{\cdot}OEt_2$ (0.25 mL, 2.0 mmol) in CH_2Cl_2 gave **3iA** (52 mg, 61%) as a white solid and a diastereomeric mixture of **8i** (16 mg, 18%) as a colorless oil after column chromatography (SiO_2, 5−25% EtOAc in hexanes).

Data for (1R,3aS*,4R*,6aR*)-3-(4-bromo-3-methoxyphenyl)-6a-fluoro-6-(4-methoxyphenyl)hexahydrofuro[3,4-c]furan-1-ol (**8i**):* ^{1}H NMR (400 MHz, $CDCl_3$, minor isomer marked with an asterisk) δ 7.39−7.31 (m, 1H and 1H*), 7.30−7.23 (m, 2H and 2H*), 7.13−7.07 (m, 1H and 1H*), 6.88−6.80 (m, 2H and 2H*), 6.71 (m, 1H and 1H*), 5.71 (d, J = 6.9 Hz, 1H), 5.54 (dd, J = 13.6, 4.3 Hz, 1H*), 5.47 (s, 1H), 5.32 (d, J = 6.8 Hz, 1H*), 5.23 (s, 1H and 1H*), 4.99 (d, J = 21.3 Hz, 1H*), 4.37 (d, J = 23.3 Hz, 1H), 3.99 (dd, J = 9.3, 9.3 Hz, 1H), 3.90−3.65 (m, 7H and 8H*), 3.17 (dd, J = 9.8, 9.8 Hz, 1H*), 3.09 (dd, J = 9.3, 9.3 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$, minor isomer marked with an asterisk) δ −165.5 to −165.8 (m, 1F*), −171.7 (t, J = 23.1 Hz, 1F); ^{13}C NMR (100 MHz, acetone-d_6, minor isomer could not be detected) δ 161.2 (C), 160.7 (2 × C), 140.1 (C), 134.6 (CH), 130.4 (2 × CH), 116.0 (CH), 115.8 (CH), 114.7 (2 × CH), 112.0 (C), 110.6 (d, J = 200.7 Hz, CF), 96.8 (d, J = 21.0 Hz, CH), 87.9 (d, J = 22.9 Hz, CH), 78.4 (d, J = 6.2 Hz, CH), 68.9 (CH_2), 56.4 (CH_3), 56.0 (CH_3), 52.5 (d, J = 22.6 Hz, CH); IR (neat) ν_{max} 3389br, 1250s, 1028s cm^{-1}; MS m/z (rel intens, %) 439 [(M + 1)$^+$, 9], 438 (M^+, 10), 359 (19), 313 (21), 203 (30), 177 (31), 146 (100), 135 (95), 121 (34), 91 (30), 77 (39); HRMS (ESI-TOF) calcd for $C_{20}H_{20}BrFO_5Na$ [M + Na]$^+$ 461.0375, found 461.0372 and 463.0356.

Synthesis of 1-Fluoromembrine [(1S*,2R*,5R*,6S*)-6-(3,4-Dimethoxyphenyl)-1-fluoro-2-(4-methoxyphenyl)-3,7-dioxabicyclo[3.3.0]octane] (3jA). To a mixture of **3iA** (42 mg, 0.1 mmol) and CuI (2 mg, 0.01 mmol) in dry DMF (2 mL) was added a dissolved sodium metal (23 mg, 1.0 mmol) in dry MeOH (1 mL) at room temperature. The reaction mixture was heated at 120 °C for 16 h. It was quenched with satd NH_4Cl and extracted with EtOAc (10 mL × 3). The combined organic phase was washed with water (10 mL × 2) and brine (10 mL) and dried over anhydrous Na_2SO_4. Filtration followed by evaporation gave a crude product which was purified by column chromatography (SiO_2, 5% EtOAc in hexanes) to give **3jA** (25 mg, 67%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J

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= 8.5 Hz, 2H), 7.10 (d, J = 2.2 Hz, 1H), 6.19 (d, J = 8.5 Hz, 2H), 6.84−6.75 (m, 2H), 5.10 (d, J = 5.2 Hz, 1H), 4.74 (d, J = 20.7 Hz, 1H), 4.74 (dd, J = 9.0, 9.0 Hz, 1H), 4.25−4.08 (m, 2H), 3.94 (dd, J = 9.0, 7.2 Hz, 1H), 3.81 (s, 3H), 3.80 (3, 3H), 3.79 (s, 3H), 3.28−3.11 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −163.9 to −164.3 (m, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (C), 153.8 (C), 150.2 (C), 130.3 (C), 128.9 (2 × CH), 126.8 (C), 113.7 (2 × CH), 112.8 (CH), 111.5 (CH), 111.3 (d, J = 202.8 Hz, CF), 111.1 (CH), 85.0 (d, J = 23.4 Hz, CH), 81.8 (d, J = 5.4 Hz, CH), 72.5 (d, J = 31.1 Hz, CH_2), 72.2 (CH_2), 59.4(d, J = 20.1 Hz, CH), 55.8 (CH_3), 55.7 (CH_3), 55.3 (CH_3); IR (neat) ν_{max} 1514s, 1497s, 1249s, 1046s cm^{-1}; MS m/z (rel intens, %) 375 [$(M + 1)^+$, 12], 374 (M^+, 43), 177 (100), 165 (57), 136 (58), 91 (27), 77 (37); HRMS (ESI-TOF) calcd for $C_{21}H_{23}FO_5Na$ [$M + Na]^+$ 397.1427, found 397.1428.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic data of all compounds (^{1}H, ^{13}C, and ^{19}F NMR spectra), NOE spectra of **3aA**, **3aB**, and **5a**, and NOESY spectrum of **3aA**. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b00970.

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Notes

The authors declare no competing financial interest.

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