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Supporting Information

Regio-complementary synthesis of fluorinated bridged biphenyls

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A plausible reaction mechanism for the fluorination of 3-hydroxydienones 2.

To obtain some information on the reaction mechanism for the fluorination of 2 generating 4 and 9, we investigated the possibility of the migration of the phenyl group of 3. For instance, 3e was treated under the reaction conditions [Deoxofluor (6 equiv), iPr₂O, 50 °C, 1.5 h]; however, no reaction took place. We also examined a similar fluorination of the acetyl derivative of 2a, which also resulted in no reaction (see, footnote 24 of the main text). These facts propose the following reaction mechanism. Thus, the fluorination reagents, such as Deoxofluor and Xtalfluor-E, reacted with the enol moiety of 2 to give A, which generated the 5-membered intermediate B. The subsequent migration of the phenyl group onto the C6 position produced 4 as a major product (path a). As a side path, the phenyl migration took place onto the C2 position to give 9 (path b) and the second fluorination at the C4 position gave 3 (path c).
Experimental Section

General considerations

Reagents: Bu₄NF (1.0 M solution in THF) was purchased from Aldrich Chemical Co. and nBuLi (1.6 M solution in n-hexane) was purchased from Kanto Chemical Co. Anhydrous THF and anhydrous chloroform were purchased from Wako Pure Chemical Industries. All other reagents were purchased from Tokyo Chemical Industry Co., Aldrich Chemical Co., Kanto Chemical Co., Kishida Chemical Co., Nacalai Tesque or Wako Pure Chemical Industries and used without further purification. Flash chromatography was performed with silica gel 60 N, spherical neutral (40–50 μm) purchased from Kanto Chemical Co.

Analytical methods. IR spectra were obtained on a JASCO WS/IR-8000. ¹H NMR, ¹³C, and ¹⁹F NMR spectra were recorded on a JEOL JMN-A500 or ECA-500 (¹H: 500 MHz, ¹³C: 125 MHz, ¹⁹F: 470 MHz) instrument with chemical shifts reported in ppm relative to the residual deuterated solvent or the internal standard tetramethylsilane. Chemical shift of ¹⁹F NMR spectra reported in ppm relative to hexafluorobenzene (−164.9 ppm) as an internal standard. Mass spectra were measured on a Bruker micrOTOF, JEOL JMS-700 MStation, and JMS-T100TD spectrometer. Yield refers to isolated yields of compounds greater than 95% purity as determined by ¹H NMR analysis. ¹H NMR and melting points (where applicable) of all known compounds were taken. All new products were further characterized by elemental analysis or HRMS.

Oxidative Cyclization of 1 (Table 2), General Procedure: Under a nitrogen atmosphere, PhI(OAc)₂ (1.05 equiv) was added to a solution of 1 and MsOH (1 equiv) in DME (0.1 M) at 0 °C. The reaction mixture was stirred for 24 h at 5 °C before being quenched with a saturated aq. Na₂S₂O₃ solution and water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The purification of the residue by flash column chromatography afforded the spirodienone 2.

Dienone-phenol Rearrangement of 2 (Table 2), General Procedure: Under a nitrogen atmosphere, MsOH (1.0 equiv) was added to a solution of 2 in DME (0.1 M). The reaction mixture was stirred at 80 °C until the starting material was completely consumed monitored by TLC analysis. After cooling, the reaction was quenched with water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The purification of the residue by flash column chromatography afforded the bridged biphenyl 5.
Table 2, entry 1

3,3-Bis(methoxycarbonyl)-6,7,8-trimethoxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1'-(3'-hydroxycyclohexa-2',5'-dien-4'-one) (2a)

Following the general procedure, 2a (95 mg, 95%) was obtained from 1a (100 mg, 0.23 mmol).

A colorless solid: mp 159.0–162.0 °C. 1H NMR (500 MHz, CDCl 3) δ: 2.36 (1H, d, J = 15.0 Hz), 2.49 (1H, d, J = 15.0 Hz), 3.13 (1H, d, J = 16.5 Hz), 3.37 (1H, d, J = 16.5 Hz), 3.60 (3H, s), 3.75 (6H, s), 3.77 (3H, s), 3.85 (3H, s), 5.94 (1H, d, J = 3.0 Hz), 6.26 (1H, s), 6.38 (1H, d, J = 10.0 Hz), 6.51 (1H, s), 6.89 (1H, dd, J = 3.0, 10.0 Hz). 13C NMR (125 MHz, CDCl 3) δ: 35.0, 40.5, 42.7, 51.6, 52.9, 55.7, 60.5, 61.0, 107.3, 118.8, 122.9, 123.5, 129.0, 140.7, 146.0, 152.7, 153.2, 158.8, 171.1, 171.3, 181.5. IR (CHCl 3): 3447, 1734, 1647, 1238 cm −1. HRMS Calcd for C 22H 25O 9 [(M+H) ] m/z: 433.1493, found: 433.1503.

Dimethyl 5,7-dihydro-9,10-dihydroxy-1,2,3-trimethoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (5a)

Following the general procedure, 5a (100 mg, 99%) was obtained from 2a (100 mg, 0.23 mmol).

A colorless solid: mp 162.5–164.0 °C. 1H NMR (500 MHz, CDCl 3) δ: 2.727 (1H, d, J = 14.0 Hz), 2.731 (1H, d, J = 14.0 Hz), 3.09 (1H, d, J = 14.0 Hz), 3.10 (1H, d, J = 14.0 Hz), 3.54 (3H, s), 3.74 (3H, s), 3.75 (3H, s), 3.85 (3H, s), 3.90 (3H, s), 5.94 (1H, brs), 6.21 (1H, brs), 6.62 (1H, s), 6.83 (1H, s), 7.08 (1H, s). 13C NMR (125 MHz, CDCl 3) δ: 36.2, 37.1, 52.8, 52.9, 56.0, 60.8, 61.2, 64.5, 109.5, 116.5, 116.8, 125.7, 128.0, 128.2, 131.6, 141.3, 142.4, 143.0, 150.3, 151.9, 171.2, 171.3. IR (CHCl 3): 3595, 3554, 1732 cm −1. HRMS Calcd for C 22H 24NaO 9 [(M+Na) ] m/z: 455.1313, found: 455.1339.

Table 2, entry 2

Table 2

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3,3-Bis(methoxycarbonyl)-6,7-dimethoxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1’-(3’-hydroxycyclohexa-2’,5’-dien-4’-one) (2b)

Following the general procedure, 2b (385 mg, 77%) was obtained from 1b (500 mg, 1.23 mmol). A colorless solid: mp 108.0–109.0 ºC. ¹H NMR (500 MHz, CDCl₃) δ: 2.55 (1H, d, J = 15.0 Hz), 2.58 (1H, d, J = 15.0 Hz), 3.24 (1H, d, J = 16.5 Hz), 3.31 (1H, d, J = 16.5 Hz), 3.71 (3H, s), 3.74 (3H, s), 3.76 (3H, s), 3.86 (3H, s), 6.05 (1H, d, J = 3.0 Hz), 6.26 (1H, s), 6.328 (1H, s), 6.329 (1H, d, J = 10.0 Hz), 6.66 (1H, s), 6.88 (1H, dd, J = 3.0, 10.0 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 34.2, 38.3, 44.4, 52.1, 53.00, 53.02, 55.8, 55.9, 109.9, 111.8, 123.6, 123.8, 123.9, 125.3, 145.6, 148.2, 148.9, 157.8, 171.2, 171.5, 181.5. IR (CHCl₃): 3447, 1734, 1653, 1234 cm –¹. HRMS Calcd for C₂₁H₂₂NaO₈ [(M+Na)⁺] m/z: 425.1207, found: 425.1222.

Dimethyl 5,7-dihydro-9,10-dihydroxy-2,3-dimethoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (5b)

Following general procedure, 5b (386 mg, 96%) was obtained from 2a (402 mg, 1.00 mmol). A colorless solid: mp 176.0–177.0 ºC. ¹H NMR (500 MHz, CDCl₃) δ: 2.51–3.35 (4H, m), 3.75 (6H, s), 3.88 (3H, s), 3.90 (3H, s), 5.74 (1H, brs), 5.84 (1H, brs), 6.84 (1H, s), 6.86 (1H, s), 6.88 (1H, s), 6.91 (1H, s). ¹³C NMR (125 MHz, CDCl₃) δ: 36.4, 36.5, 52.8, 56.00, 56.02, 65.2, 111.2, 113.6, 114.9, 117.4, 127.6, 127.7, 132.7, 133.3, 142.5, 143.2, 147.7, 148.1, 171.6. IR (CHCl₃): 3597, 3557, 1732, 1236 cm –¹. HRMS Calcd for C₂₁H₂₂NaO₈ [(M+Na)⁺] m/z: 425.1207, found: 425.1191.

Table 2, entry 3

3,3-Bis(methoxycarbonyl)-6-methoxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1’-(3’-hydroxycyclohexa-2’,5’-dien-4’-one) (2c)

Under a nitrogen atmosphere, a solution of PhI(OAc)₂ (856 mg, 2.6 mmol) in DME (67 mL) was added to an ice-cold solution of 1c (948 mg, 2.5 mmol) in DME (60 mL) over 35 min. MsOH (3.3 mL, 51 mmol) was added at the same temperature. The reaction mixture was stirred for 18 h at 5 ºC before being quenched with water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The purification of the residue by flash column
chromatography (hexanes–EtOAc 2:1) gave 2c (containing ca. 3% of an unidentified compound, 434 mg, 46%). This compound was used for the subsequent fluorination reaction without further purification. Analytically pure 2c was obtained by recrystallization from Et₂O–hexanes. A colorless solid: mp 132.0–134.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 2.58 (1H, d, J = 13.0 Hz), 2.60 (1H, d, J = 13.0 Hz), 3.29 (1H, d, J = 17.0 Hz), 3.35 (1H, d, J = 17.0 Hz), 3.74 (3H, s), 3.75 (3H, s), 3.78 (3H, s), 6.03 (1H, d, J = 3.0 Hz), 6.24 (1H, s), 6.30 (1H, d, J = 10.0 Hz), 6.68 (1H, dd, J = 3.0, 8.5 Hz), 6.72 (1H, d, J = 3.0 Hz), 6.84 (1H, d, J = 8.5 Hz), 6.86 (1H, dd, J = 3.0, 10.0 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 34.9, 38.2, 44.0, 52.0, 53.0, 53.1, 55.2, 113.6, 114.1, 123.6, 123.7, 123.9, 129.2, 134.4, 145.4, 157.6, 159.1, 171.2, 171.4, 181.5. IR (CHCl₃): 3449, 1734, 1653, 1261 cm⁻¹. HRMS Calcd for C₂₀H₂₀NaO₇ [(M+Na)⁺] m/z: 395.1101, found: 395.1087.

**Dimethyl 5,7-dihydro-9,10-dihydroxy-3-methoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (5c)**

Following the general procedure, 5c (130 mg, 99%) was obtained from 2c (131 mg, 0.35 mmol). White amorphous. ¹H NMR (500 MHz, CDCl₃) δ: 2.60–3.35 (4H, m), 3.76 (6H, s), 3.83 (3H, s), 5.24 (2H, brs), 6.84 (1H, s), 6.86–6.90 (3H, m), 7.24 (1H, d, J = 9.0 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 36.3, 37.1, 52.8, 55.3, 64.6, 112.5, 115.1, 116.0, 117.2, 127.9, 128.9, 132.8, 133.4, 136.6, 142.2, 142.9, 158.6, 171.3. IR (CHCl₃): 3597, 3557, 1732, 1258 cm⁻¹. HRMS Calcd for C₂₀H₂₀NaO₇ [(M+Na)⁺] m/z: 395.1101, found: 395.1125.

**Table 2, entry 4**

3,3-Bis(methoxycarbonyl)-6,7-methylenedioxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1’-(3’-hydroxycyclohexa-2’,5’-dien-4’-one) (2d)

Under a nitrogen atmosphere, PhI(OAc)₂ (711 mg, 2.2 mmol) was added to a solution of 1d (816 mg, 2.1 mmol) and MsOH (0.41 mL, 6.3 mmol) in DME (21 mL) at 0 °C. The reaction mixture was stirred for 24 h at 5 °C before being quenched with water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered and concentrated *in vacuo*. The purification of the residue by flash column chromatography (hexanes–EtOAc 2:1) gave 2d (582 mg, 64%). A colorless solid: mp 178.0–180.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 2.53 (1H, d, J = 14.5 Hz),
2.56 (1H, d, \( J = 14.5 \) Hz), 3.19 (1H, d, \( J = 16.0 \) Hz), 3.26 (1H, d, \( J = 16.0 \) Hz), 3.72 (3H, s), 3.73 (3H, s), 5.87 (2H, s), 6.00 (1H, d, \( J = 3.0 \) Hz), 6.28 (1H, d, \( J = 10.0 \) Hz), 6.345 (1H, s), 6.354 (1H, s), 6.63 (1H, s), 6.84 (1H, dd, \( J = 3.0, 10.0 \) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 34.6, 37.9, 44.4, 52.0, 52.96, 52.98, 101.2, 107.3, 109.0, 123.7, 123.8, 124.9, 126.5, 145.5, 146.9, 147.5, 157.4, 171.0, 171.3, 181.3. IR (CHCl\(_3\)): 3451, 1734, 1653, 1265 cm\(^{-1}\). HRMS Calcd for C\(_{20}\)H\(_{18}\)NaO\(_8\) [(\( M+Na \))\(^+\)] \( m/z \): 409.0894, found: 409.0883.

Dimethyl 5,7-dihydro-9,10-dihydroxy-2,3-methylenedioxy-6\(H\)-dibenzo[\(a,c\)]cycloheptene-6,6-dicarboxylate (5d)

Following the general procedure, 5d (205 mg, 95\%) was obtained from 2d (215 mg, 0.56 mmol).
A colorless solid: mp 224.0–226.0 \(^\circ\)C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 2.60–3.30 (4H, m), 3.76 (6H, s), 5.00 (1H, br), 5.03 (1H, br), 5.96 (2H, s), 6.79 (1H, s), 6.81 (1H, s), 6.83 (1H, s), 6.86 (1H, s). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 36.2, 36.8, 52.8, 65.1, 101.0, 108.3, 110.6, 115.1, 117.3, 128.2, 128.8, 133.6, 133.7, 142.3, 142.9, 146.4, 147.0, 171.2. IR (KBr): 3437, 1728, 1701, 1258 cm\(^{-1}\). HRMS Calcd for C\(_{20}\)H\(_{18}\)NaO\(_8\) [(\( M+Na \))\(^+\)] \( m/z \): 409.0894, found: 409.0917.

Table 2, entry 5

6,7,8-trimethoxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1’-(3’-hydroxycyclohexa-2’,5’-dien-4’-one) (2e)

Following the general procedure, 2e (90 mg, 90\%) was obtained from 1e (100 mg, 0.31 mmol).
A colorless solid: mp 157.0–164.0 \(^\circ\)C. \(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \): 1.70–1.94 (4H, m), 2.76–2.84 (2H, m), 3.62 (3H, s), 3.75 (3H, s), 3.84 (3H, s), 6.28 (1H, d, \( J = 3.0 \) Hz), 6.35 (1H, s), 6.39 (1H, d, \( J = 10.0 \) Hz), 6.46 (1H, s), 7.08 (1H, dd, \( J = 3.0, 10.0 \) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \( \delta \): 20.1, 30.4, 37.4, 43.6, 55.8, 60.5, 61.0, 107.9, 120.9, 123.2, 124.2, 132.5, 140.3, 145.8, 152.7, 153.1, 160.4, 181.8. IR (CHCl\(_3\)): 3441, 1643, 1236 cm\(^{-1}\). HRMS Calcd for C\(_{19}\)H\(_{20}\)NaO\(_5\) [(\( M+Na \))\(^+\)] \( m/z \): 339.1203, found: 339.1193.
6,7-Dihydro-9,10-dihydroxy-1,2,3-trimethoxy-5\textit{H}-dibenzo[\textit{a,c}]cycloheptene (5e)

Under a nitrogen atmosphere, PhI(OAc)_2 (338 mg, 1.05 mmol) was added to a solution of 1e (316 mg, 1.00 mmol) and MsOH (57 \mu L, 1.00 mmol) in DME (10 mL) at 0 °C. The reaction mixture was stirred for 24 h at 5 °C. Na_2S_2O_3 (15.8 mg, 0.100 mmol) was added and the reaction mixture was stirred for another 24 h at 80 °C before being quenched with water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na_2SO_4), filtered and concentrated \textit{in vacuo}. The purification of the residue by flash column chromatography (hexanes–EtOAc 1:1) gave 5e (280 mg, 88%).

A colorless solid: mp 188.0–189.0 °C. \textit{\textup{1}}H NMR (500 MHz, CDCl_3) \text{\delta}: 1.99–2.07 (2H, m), 2.25–2.44 (4H, m), 3.55 (3H, s), 3.89 (3H, s), 3.91 (3H, s), 5.43 (1H, br), 5.59 (1H, br), 6.57 (1H, s), 6.77 (1H, s), 7.03 (1H, s). \textit{\textup{13}}C NMR (125 MHz, CDCl_3) \text{\delta}: 30.6, 31.7, 33.1, 56.1, 60.7, 61.2, 108.1, 115.1, 117.2, 125.9, 128.4, 133.1, 136.1, 140.7, 141.2, 143.0, 150.5, 152.0. IR (CHCl_3): 3599, 3557, 1236 cm\textsuperscript{-1}. HRMS Calcd for C_{18}H_{20}NaO_5 [(M+Na)^+ m/z]: 339.1203, found: 339.1175.

Table 2, entry 6

6,7-trimethoxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1'-(3'-hydroxycyclohexa-2',5'-dien-4'-one) (2f)

Following the general procedure, 2f (90 mg, 90%) was obtained from 1f (100 mg, 0.31 mmol).

A colorless solid: mp 161.0–165.0 °C. \textit{\textup{1}}H NMR (500 MHz, CDCl_3) \text{\delta}: 1.93–2.00 (4H, m), 2.80–2.86 (2H, m), 3.72 (3H, s), 3.85 (3H, s), 6.29–6.31 (2H, m), 6.35 (1H, s), 6.37 (1H, d, \textit{J} = 10.0 Hz), 6.81 (1H, s), 7.13 (1H, dd, \textit{J} = 3.0, 10.0 Hz). \textit{\textup{13}}C NMR (125 MHz, CDCl_3) \text{\delta}: 19.7, 29.2, 34.9, 45.2, 55.8, 56.0, 110.5, 112.3, 123.8, 125.0, 128.6, 145.5, 147.5, 148.4, 159.3, 181.8. IR (CHCl_3): 3447, 1651, 1256 cm\textsuperscript{-1}. HRMS Calcd for C_{17}H_{19}O_4 [(M+H)^+ m/z]: 287.1283, found: 287.1282.

6,7-Dihydro-9,10-dihydroxy-2,3-dimethoxy-5\textit{H}-dibenzo[\textit{a,c}]cycloheptene (5f)
Similarly to the preparation of 5e, 5f (257 mg, 86%) was obtained from 1f (300 mg, 1.03 mmol).

A colorless solid: mp 225.0–226.0 °C. 1H NMR (500 MHz, CDCl3) δ: 2.12 (2H, quint. J = 7.0 Hz), 2.39 (2H, t, J = 7.0 Hz), 2.44 (2H, t, J = 7.0 Hz), 3.90 (3H, s), 3.92 (3H, s), 4.97 (1H, br), 5.00 (1H, br), 6.76 (2H, s), 6.86 (1H, s), 6.90 (1H, s). 13C NMR (125 MHz, CDCl3) δ: 30.9, 31.2, 33.7, 56.3, 56.4, 112.5, 112.7, 115.5, 115.9, 132.4, 133.0, 133.1, 134.2, 142.0, 142.5, 147.9, 148.3. IR (KBr): 3476, 3449, 1273 cm–1. HRMS Calcd for C17H18NaO4 [(M+Na)+] m/z: 309.1097, found: 309.1077.

Table 2, entry 7

**9,10,11-Trimethoxy-6-toluenesulfonyl-6,7-dihydro-5H-dibenzo[c,e]azepine-2,3-diol (5g)**

Under a nitrogen atmosphere, PhI(OAc)2 (86 mg, 0.27 mmol) was added to a solution of 1g (120 mg, 0.25 mmol) in DME (25 mL) at 0 °C. The reaction mixture was stirred for 30 min at the same temperature. MsOH (0.82 mL, 12.7 mmol) was added to the reaction mixture and the reaction mixture was stirred for 1 h at 0 °C before being quenched with water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na2SO4), filtered and concentrated in vacuo. The purification of the residue by flash column chromatography (hexanes–EtOAc 2:3) gave 5g (115 mg, 86%, contaminated with ca. 10 % of 1g). Recrystallization from CHCl3 gave pure 5g (70 mg, 58%)

A colorless solid: mp 212.0–214.0 °C. 1H NMR (500 MHz, DMSO-d6) δ: 2.36 (3H, s), 3.26–3.40 (2H, m), 3.47 (3H, s), 3.72 (3H, s), 3.73 (3H, s), 4.33 (1H, d, J = 12.5 Hz), 4.45 (1H, d, J = 12.5 Hz), 6.61 (1H, s), 6.62 (1H, s), 6.87 (1H, s), 7.37 (2H, d, J = 8.0 Hz), 7.75 (2H, d, J = 8.0 Hz), 8.99 (1H, br), 9.04 (1H, br). 13C NMR (125 MHz, DMSO-d6) δ: 21.3, 48.6, 49.0, 56.2, 60.8, 109.9, 116.9, 117.1, 123.4, 126.1, 127.1, 127.7, 127.8, 130.0, 136.5, 142.3, 143.4, 145.0, 145.2, 150.3, 152.2. IR (KBr): 3418, 1599, 1333 cm–1. HRMS Calcd for C24H25NNaO7S [(M+Na)+] m/z: 494.1244, found: 494.1218.

**Fluorination of 2a–f (Table 4), General Procedure:** Under a nitrogen atmosphere, Xtalfluor-E (6 equiv) was added to a solution of 2 (1.0 equiv) and Et3N-HF (6 equiv) in iPr2O-CHCl3 (1:1, 0.2 M) at 0 °C. The reaction mixture was stirred for 1.5 h at 50 °C before being quenched with ice water. CH2Cl2 was added, the layers were separated, and the aqueous layer was extracted three times with CH2Cl2. The combined organic layer was washed with brine, dried (Na2SO4), filtered and concentrated in vacuo. The purification of the residue by flash column chromatography afforded 4 and 9.

Table 4, entry 1

Following the general procedure, 4a (22 mg, 74%) and 9a (6.0 mg, 18%) were obtained from 2a
Dimethyl 10-fluoro-5,7-dihydro-9-hydroxy-1,2,3-trimethoxy-6H-dibenzo[\(a,c]\]cycloheptene-6,6-dicarboxylate (4a)

A colorless solid: mp 146.0–147.0 ºC. \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 2.72 (1H, d, \(J = 14.5\) Hz), 2.76 (1H, d, \(J = 14.5\) Hz), 3.13 (1H x 2, d, \(J = 14.5\) Hz), 3.60 (3H, s), 3.76 (6H, s), 3.87 (3H, s), 3.90 (3H, s), 5.39 (1H, br), 6.63 (1H, s), 6.93 (1H, d, \(J = 9.0\) Hz), 7.26 (1H, d, \(J = 11.5\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ: 36.2, 37.0, 52.8, 52.9, 56.0, 60.8, 61.1, 64.4, 109.4, 117.1 (d, \(J = 18.0\) Hz), 118.3, 124.8, 128.5 (d, \(J = 7.0\) Hz), 131.4, 132.3 (d, \(J = 3.5\) Hz), 141.6, 142.2 (d, \(J = 14.5\) Hz), 150.0 (d, \(J = 238\) Hz), 150.6, 152.4, 170.8, 171.0. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) δ: –146.5 (1F, dd, \(J = 9.0, 11.5\) Hz). IR (CHCl\(_3\)): 3578, 1734, 1254 cm\(^{-1}\). HRMS Calcd for C\(_{22}\)H\(_{23}\)FNaO\(_8\) [(\(M+Na\)] \(m/z\): 457.1269, found: 457.1289.

Dimethyl 10-fluoro-5,7-dihydro-11-hydroxy-1,2,3-trimethoxy-6H-dibenzo[\(a,c]\]cycloheptene-6,6-dicarboxylate (9a)

A colorless solid: mp 104.0–109.0 ºC. \(^1\)H NMR (500 MHz, CDCl\(_3\)) δ: 2.71 (1H, d, \(J = 14.0\) Hz), 2.73 (1H, d, \(J = 14.0\) Hz), 3.13 (1H, d, \(J = 14.0\) Hz), 3.20 (1H, d, \(J = 14.0\) Hz), 3.70 (3H, s), 3.76 (3H, s), 3.77 (3H, s), 3.90 (3H, s), 3.93 (3H, s), 6.70 (1H, s), 6.81 (1H, dd, \(J = 5.0, 8.0\) Hz), 6.99 (1H, s), 7.01 (1H, d, \(J = 8.0, 10.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) δ: 36.8, 36.9, 52.88, 52.92, 56.1, 61.3, 62.2, 64.2, 110.9, 115.1 (d, \(J = 18.0\) Hz), 121.3 (d, \(J = 2.0\) Hz), 122.1 (d, \(J = 7.0\) Hz), 126.4, 131.9 (d, \(J = 3.5\) Hz), 132.4, 141.4, 141.5 (d, \(J = 12.0\) Hz), 149.4, 152.9 (d, \(J = 241\) Hz), 153.1, 170.6, 170.8. \(^{19}\)F NMR (470 MHz, CDCl\(_3\)) δ: –138.9 (1F, dd, \(J = 5.0, 10.0\) Hz). IR (CHCl\(_3\)): 3327, 1732, 1240 cm\(^{-1}\). HRMS Calcd for C\(_{22}\)H\(_{23}\)FNaO\(_8\) [(\(M+Na\)] \(m/z\): 457.1269, found: 457.1271.

Table 4, entry 2

Following the general procedure, 4b (26 mg, 54%) and 9b (14 mg, 28%) were obtained from 2b (47.0 mg, 0.124 mmol).
Dimethyl 10-fluoro-5,7-dihydro-9-hydroxy-2,3-dimethoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (4b)
A colorless solid: mp 172.0–173.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 2.60–3.38 (4H, m), 3.75 (6H, s), 3.906 (3H, s), 3.912 (3H, s), 5.40 (1H, br), 6.82 (1H, s), 6.86 (1H, s), 7.00 (1H, d, J = 9.0 Hz), 7.09 (1H, d, J = 11.5 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 36.4, 36.5, 52.8, 56.0, 65.0, 65.0, 111.1, 113.5, 114.8 (d, J = 18.0 Hz), 119.2, 127.7, 131.6, 132.1 (d, J = 3.5 Hz), 133.4 (d, J = 6.0 Hz), 142.1 (d, J = 14.5 Hz), 148.1, 148.3, 150.4 (d, J = 236 Hz), 171.1. ¹⁹F NMR (470 MHz, CDCl₃) δ: -146.0–-145.9 (1F, m). IR (CHCl₃): 3577, 1732, 1275 cm⁻¹. HRMS Calcd for C₂₁H₂₁FNaO₇ [(M+Na)⁺] m/z: 427.1164, found: 427.1164.

Dimethyl 10-fluoro-5,7-dihydro-11-hydroxy-2,3-dimethoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (9b)
White amorphous. ¹H NMR (500 MHz, CDCl₃) δ: 2.67 (1H, d, J = 14.5 Hz), 2.79 (1H, d, J = 14.5 Hz), 3.18 (1H, d, J = 14.0 Hz), 3.19 (1H, d, J = 14.0 Hz), 3.74 (3H, s), 3.75 (3H, s), 3.88 (3H, s), 3.91 (3H, s), 5.33 (1H, d, J = 5.0 Hz), 6.83 (1H, dd, J = 5.0, 8.0 Hz), 6.89 (1H, s), 6.99 (1H, dd, J = 8.0, 10.0 Hz), 7.11 (1H, s). ¹³C NMR (125 MHz, CDCl₃) δ: 36.2, 36.7, 52.8, 55.96, 56.02, 64.7, 112.4, 112.4, 113.9 (d, J = 18.0 Hz), 121.8 (d, J = 7.0 Hz), 126.4 (d, J = 2.5 Hz), 127.8, 128.9, 132.2, 140.1, 147.7, 148.4, 150.8 (d, J = 232 Hz), 170.9, 171.0. ¹⁹F NMR (470 MHz, CDCl₃) δ: -143.6 (1F, td, J = 5.0, 10.0 Hz). IR (CHCl₃): 3566, 1732, 1215 cm⁻¹. HRMS Calcd for C₂₁H₂₁FNaO₇ [(M+Na)⁺] m/z: 427.1164, found: 427.1162.

Table 4, entry 3
Following the general procedure, 4c (27 mg, 54%) and 9c (16 mg, 32%) were obtained from 2c (50 mg, 0.134 mmol).
Dimethyl 2-fluoro-5,7-dihydro-3-hydroxy-9-methoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (4c)

White amorphous. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 2.60–3.30 (4H, m), 3.77 (6H, s), 3.83 (3H, s), 5.42 (1H, d, $J = 3.5$ Hz), 6.86–6.91 (2H, m), 6.95 (1H, d, $J = 9.0$ Hz), 7.06 (1H, d, $J = 11.0$ Hz), 7.23 (1H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 36.3, 37.1, 52.9, 55.3, 64.4, 112.7, 114.9 (d, $J = 18.0$ Hz), 116.0, 118.9, 128.9, 131.7, 132.1, 133.2 (d, $J = 6.0$ Hz), 136.5, 142.1 (d, $J = 14.5$ Hz), 150.4 (d, $J = 235$ Hz), 158.8, 171.1. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$: –145.9– –145.7 (1F, m). IR (CHCl$_3$): 3578, 3566, 1732 cm$^{-1}$. HRMS Calcd for C$_{20}$H$_{20}$FNaO$_6$ [(M+Na)$^+$] $m/z$: 397.1058, found: 397.1053.

Dimethyl 2-fluoro-5,7-dihydro-1-hydroxy-9-methoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (9c)

White amorphous. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 2.72 (1H, d, $J = 14.5$ Hz), 2.86 (1H, d, $J = 14.5$ Hz), 3.16 (1H, d, $J = 10.5$ Hz), 3.19 (1H, d, $J = 10.5$ Hz), 3.75 (3H, s), 3.76 (3H, s), 3.84 (3H, s), 5.25 (1H, d, $J = 4.5$ Hz), 6.79 (1H, dd, $J = 6.0$, 8.5 Hz), 6.89–6.94 (2H, m), 6.98 (1H, dd, $J = 8.5$, 10.5 Hz), 7.50 (1H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 36.6, 36.8, 52.8, 55.3, 64.1, 112.1, 113.8 (d, $J = 18.0$ Hz), 116.5, 121.5 (d, $J = 7.0$ Hz), 126.7, 127.6, 130.4, 132.0, 137.7, 140.1, 150.9 (d, $J = 236$ Hz), 159.2, 170.9. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$: –143.5– –143.4 (1F, m). IR (CHCl$_3$): 3572, 1732 cm$^{-1}$. HRMS Calcd for C$_{20}$H$_{19}$FNaO$_6$ [(M+Na)$^+$] $m/z$: 397.1058, found: 397.1051.

Table 4, entry 4

Under a nitrogen atmosphere, Deoxofluor (0.29 mL, 1.55 mmol) was added to a solution of 2d (100 mg, 0.26 mmol) in CHCl$_3$ (1.30 mL) at 0 °C. The reaction mixture was stirred for 1.5 h at 50 °C before being quenched with ice water. CH$_2$Cl$_2$ was added, the layers were separated, and the aqueous layer was extracted three times with CH$_2$Cl$_2$. The combined organic layer was washed with brine, dried (Na$_2$SO$_4$), filtered and concentrated in vacuo. The purification of the residue by flash column chromatography (hexanes–EtOAc 2:1) afforded 4d (26 mg, 26%) and 9d (15.0 mg, 15%).
Dimethyl 5,7-dihydro-10-fluoro-9-hydroxy-2,3-methylenedioxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (4d)

A colorless solid: mp 181.0–183.0 ºC. ¹H NMR (500 MHz, CDCl₃) δ: 2.68–2.83 (2H, m), 3.09–3.20 (2H, m), 3.76 (6H, s), 5.10–5.80 (1H, m), 5.97 (2H, s), 6.79 (1H, s), 6.80 (1H, s), 6.95 (1H, d, J = 9.0 Hz), 7.03 (1H, d, J = 11.5 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 36.3, 36.7, 52.9, 64.9, 101.1, 108.2, 110.6, 115.0 (J = 19.0 Hz), 119.0, 128.8, 132.0 (J = 3.5 Hz), 132.9, 133.3 (J = 7.0 Hz), 142.3 (J = 14.0 Hz), 146.7, 147.1, 150.4 (J = 236 Hz), 171.1. ¹⁹F NMR (470 MHz, CDCl₃) δ: −146.0–−145.5 (1F, m). IR (CHCl₃): 3599, 3557, 1730 cm⁻¹. HRMS Calcd for C₂₀H₁₇FNaO₇ [(M+Na)⁺] m/z: 411.0851, found: 411.0868.

Dimethyl 5,7-dihydro-10-fluoro-11-hydroxy-2,3-methylenedioxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (9d)

A colorless solid: mp 207.0–211.0 ºC. ¹H NMR (500 MHz, CDCl₃) δ: 2.72 (1H, d, J = 14.0 Hz), 2.77 (1H, d, J = 14.0 Hz), 3.11 (1H, d, J = 14.5 Hz), 3.15 (1H, d, J = 14.5 Hz), 3.74 (3H, s), 3.76 (3H, s), 5.29 (1H, d, J = 5.0 Hz), 5.995 (1H, J = 2.0 Hz), 6.002 (1H, d, J = 2.0 Hz), 6.89 (1H, dd, J = 5.0, 8.0 Hz), 6.82 (1H, s), 6.98 (1H, dd, J = 8.0, 10.0 Hz), 7.06 (1H, s). ¹³C NMR (125 MHz, CDCl₃) δ: 36.4, 36.5, 52.8, 52.9, 64.6, 101.2, 109.7, 110.7, 113.9 (J = 18.0 Hz), 121.6 (J = 7.0 Hz), 127.6 (J = 18.0 Hz), 129.9, 132.2, 140.1 (J = 14.5 Hz), 146.6, 147.1, 150.8 (J = 236 Hz), 170.86, 170.94. ¹⁹F NMR (470 MHz, CDCl₃) δ: −143.8–−143.7 (1F, m). IR (CHCl₃): 3692, 3568, 1732 cm⁻¹. HRMS Calcd for C₂₀H₁₇FO₇ [(M+Na)⁺] m/z: 411.0851, found: 411.0826.

Table 4, entry 5

Similarly to the preparation of 4d and 9d, 4e (53 mg, 52%) and 9e (4.0 mg, 4%) were obtained from 2e (100 mg, 0.32 mmol). The flash column chromatography of the crude product was conducted using hexanes–EtOAc–Et₃N 100:20:1 as an eluent.
6,7-Dihydro-10-fluoro-9-hydroxy-1,2,3-trimethoxy-5H-dibenzo[a,c]cycloheptene (4e)
A colorless solid: mp 145.0–146.0 ºC. 1H NMR (500 MHz, CDCl₃) δ: 2.02–2.07 (2H, m), 2.23–2.48 (4H, m), 3.60 (3H, s), 3.90 (3H, s), 3.91 (3H, s), 6.57 (1H, s), 6.87 (1H, d, J = 9.0 Hz), 7.23 (1H, d, J = 12.5 Hz). 13C NMR (125 MHz, CDCl₃) δ: 30.6, 31.5, 32.9, 55.9, 60.7, 61.1, 107.7, 116.6, 116.9 (d, J = 18.0 Hz), 125.0, 128.4, (d, J = 6.0 Hz), 135.9, 136.5 (d, J = 2.5 Hz), 140.6, 142.0 (d, J = 14.5 Hz), 149.2 (d, J = 234 Hz), 150.6, 152.3. 19F NMR (470 MHz, CDCl₃) δ: –148.1 (1F, dd, J = 9.0, 12.5 Hz). IR (CHCl₃): 3580, 1236 cm –1. HRMS Calcd for C₁₈H₁₉FNaO₄ [(M+Na)+] m/z: 341.1160, found: 341.1163.

Table 4, entry 6
Similarly to the preparation of 4d and 9d, 4f (23 mg, 23%) and 9f (7.0 mg, 7%) were obtained from 2f (100 mg, 0.35 mmol).

6,7-Dihydro-10-fluoro-11-hydroxy-1,2,3-trimethoxy-5H-dibenzo[a,c]cycloheptene (9e)
White amorphous. 1H NMR (500 MHz, CDCl₃) δ: 2.00–2.55 (6H, m), 3.68 (3H, s), 3.92 (3H, s), 3.93 (3H, s), 6.67 (1H, s), 6.77 (1H, dd, J = 5.0, 8.5 Hz), 6.89 (1H, s), 7.03 (1H, d, J = 8.5, 10.5 Hz). 13C NMR (125 MHz, CDCl₃) δ: 31.1, 31.5, 33.1, 56.0, 61.4, 62.1, 109.2, 114.8 (d, J = 19.0 Hz), 120.3 (d, J = 7.0 Hz), 121.2 (d, J = 2.5 Hz), 126.4, 136.4 (d, J = 2.5 Hz), 137.0, 140.4, 141.2 (d, J = 13.0 Hz), 149.4, 152.2 (d, J = 240 Hz), 153.1. 19F NMR (470 MHz, CDCl₃) δ: –140.9 (1F, dd, J = 5.0, 10.5 Hz). IR (CHCl₃): 3334, 1236 cm –1. HRMS Calcd for C₁₈H₂₀FO₄ [(M+H)+] m/z: 319.1340, found: 319.1361.

6,7-Dihydro-10-fluoro-9-hydroxy-2,3-dimethoxy-5H-dibenzo[a,c]cycloheptene (4f)
A colorless solid: mp 168.0–172.0 ºC. 1H NMR (500 MHz, CDCl₃) δ: 2.14 (2H, quint., J = 7.0 Hz), 2.40 (2H, t, J = 7.0 Hz), 2.43 (2H, t, J = 7.0 Hz), 3.91 (3H, s), 3.82 (3H, s), 6.76 (1H, s), 6.83 (1H, s), 6.88 (1H, d, J = 9.0 Hz), 7.08 (1H, d, J = 11.5 Hz). 13C NMR (125 MHz, CDCl₃) δ: 30.9, 33.4,
56.0, 56.1, 111.5, 111.9, 114.8 (d, \( J = 18.0 \) Hz), 117.3, 131.9 (d, \( J = 2.5 \) Hz), 133.6 (d, \( J = 13.0 \) Hz), 136.3 (d, \( J = 2.5 \) Hz), 142.1 (d, \( J = 14.5 \) Hz), 147.5, 148.0, 150.0 (d, \( J = 237 \) Hz). \(^{19}\text{F} \) NMR (470 MHz, CDCl\(_3\)) \( \delta = -147.8 \) (1F, dd, \( J = 9.0, 11.5 \) Hz). IR (CHCl\(_3\)): 3579, 1275 cm\(^{-1}\). HRMS Calcd for \( \text{C}_{17}\text{H}_{17}\text{FNaO}_3 \) [(\( M+\text{Na}\))\(^{+}\)]\( m/z \): 311.1054, found: 311.1043.

6,7-Dihydro-10-fluoro-11-hydroxy-2,3-dimethoxy-5H-dibenzo[\( a,c \)]cycloheptene (9f)
A colorless solid: mp 69.0–74.0 °C. \(^1\text{H} \) NMR (500 MHz, CDCl\(_3\)) \( \delta = 2.04–2.52 \) (6H, m), 3.89 (3H, s), 3.94 (3H, s), 6.74 (1H, dd, \( J = 5.0, 8.5 \) Hz), 6.82 (1H, s), 6.98 (1H, dd, \( J = 8.5, 10.5 \) Hz), 7.07 (1H, s). \(^{13}\text{C} \) NMR (125 MHz, CDCl\(_3\)) \( \delta = 30.6, 31.0, 33.2, 55.9, 56.1, 112.3 \) (d, \( J = 19.0 \) Hz), 113.8 (d, \( J = 18.0 \) Hz), 119.7 (d, \( J = 7.0 \) Hz), 126.2, 127.9, 133.3, 136.5 (d, \( J = 3.5 \) Hz), 139.9 (d, \( J = 13.0 \) Hz), 147.0, 148.4, 150.2 (d, \( J = 237 \) Hz). \(^{19}\text{F} \) NMR (470 MHz, CDCl\(_3\)) \( \delta = -144.9 \) (1F, dd, \( J = 5.0, 10.5 \) Hz). IR (CHCl\(_3\)): 3574, 3545, 1238 cm\(^{-1}\). HRMS Calcd for \( \text{C}_{17}\text{H}_{17}\text{FNaO}_3 \) [(\( M+\text{Na}\))\(^{+}\)]\( m/z \): 311.1054, found: 311.1073.

Fluorination of 5a–g (Table 4), General Procedure: Under a nitrogen atmosphere, PhI(OAc)\(_2\) (1.05 equiv) was added to a mixture of 5 (1.0 equiv) and MgO (2.3 equiv) in CHCl\(_3\) (0.2 M) at 0 °C, and the reaction mixture was stirred at the same temperature for 5 min. Deoxofluor (6 equiv) was added, and the reaction mixture was stirred for 1 h at 40 °C before being quenched with ice water. CH\(_2\)Cl\(_2\) was added, the layers were separated, and the aqueous layer was extracted three times with CH\(_2\)Cl\(_2\). The combined organic layer was dried (Na\(_2\)SO\(_4\)), filtered and concentrated in vacuo. The residue was dissolved in EtOH (0.2 M), and NaBH\(_4\) (5.0 equiv) was added to the solution at 0 °C. The reaction mixture was stirred overnight at room temperature before being quenched with 1N HCl. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na\(_2\)SO\(_4\)), filtered and concentrated in vacuo. Purification of the residue by flash column chromatography afforded 4 and 7.

Table 4, entry 7
Following the general procedure, 4a (24.0 mg, 23%) and 7a (43 mg, 43%) were obtained from 5a (100 mg, 0.23 mmol). Spectral data of 4a was identical to those of the authentic sample obtained from 2a.
Dimethyl 5,7-dihydro-9-fluoro-10-hydroxy-1,2,3-trimethoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (7a)

A colorless solid: mp 188.5–189.5 ºC. 1H NMR (500 MHz, CDCl₃): 2.68 (1H, d, J = 14.0 Hz), 2.73 (1H, d, J = 14.0 Hz), 3.13 (1H, d, J = 13.0 Hz), 3.15 (1H, d, J = 13.0 Hz), 3.61 (3H, s), 3.76 (6H, s), 3.88 (3H, s), 3.90 (3H, s), 5.26 (1H, br), 6.64 (1H, s), 7.03 (1H, d, J = 11.0 Hz), 7.17 (1H, d, J = 9.0 Hz). 13C NMR (125 MHz, CDCl₃) δ: 36.0, 37.0, 52.8, 52.9, 56.0, 60.9, 61.1, 64.3, 109.4, 116.7 (d, J = 18.0 Hz), 119.0, 124.9, 128.3 (d, J = 6.0 Hz), 131.3, 132.5 (d, J = 3.5 Hz), 141.6, 142.1 (d, J = 13.0 Hz), 149.6 (d, J = 237 Hz), 150.7, 152.5, 170.9, 171.0. 19F NMR (470 MHz, CDCl₃): –145.4– –145.2 (1F, m). IR (CHCl₃): 3580, 1732, 1238 cm⁻¹. HRMS Calcd for C₂₂H₂₃FNaO₈ [(M+Na)+] m/z: 457.1269, found: 457.1292.

Table 4, entry 8

Following the general procedure, a mixture of 4b and 7b (55 mg, 55%, 4b: 7b = 1:2) were obtained from 5b (100 mg, 0.25 mmol). A colorless oil. IR (CHCl₃): 3580, 3437, 1732, 1265 cm⁻¹. HRMS Calcd for C₂₁H₂₁FO₇ [(M+H)+] m/z: 404.1266, found: 404.1273. 1H NMR data of 4b was identical to those of the authentic sample obtained from 2b.

Dimethyl 5,7-dihydro-9-fluoro-10-hydroxy-2,3-dimethoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (7b)

1H NMR (500 MHz, CDCl₃): 2.60–3.40 (4H, m), 3.75 (6H, s), 3.89 (3H, s), 3.91 (3H, s), 5.53 (1H, d, J = 3.5 Hz), 6.85 (1H, s), 6.87 (1H, s), 7.02 (1H, d, J = 8.5 Hz), 7.08 (1H, d, J = 11.0 Hz). 13C NMR (125 MHz, CDCl₃) δ: 36.2, 36.5, 52.8, 56.0, 65.0, 111.2, 113.6, 116.6, 117.4 (d, J = 19.0 Hz), 127.7, 128.0 (d, J = 6.0 Hz), 131.8, 137.3, 142.7 (d, J = 14.5 Hz), 148.2, 148.3, 149.7 (d, J = 239 Hz), 171.2. 19F NMR (470 MHz, CDCl₃): –146.0– –145.8 (1F, m).

Table 4, entry 9

Following the general procedure, 7c (30 mg, 37%) and 4c (13.4 mg, 17%) were obtained from 5c (70 mg, 0.21 mmol). Spectral data of 4c was identical to those of the authentic sample obtained from 2c.
3-Fluoro-5,7-dihydro-2-hydroxy-9-methoxy-6H-dibenzo[a,c]cycloheptene-6,6-dicarboxylate (7c)
White amorphous. $^1$H NMR (500 MHz, CDCl$_3$) δ: 2.52–3.42 (4H, br), 3.76 (6H, s), 3.83 (3H, s), 5.30 (1H, d, $J = 3.5$ Hz), 6.86–6.92 (2H, m), 7.00 (1H, d, $J = 9.0$ Hz), 7.04 (1H, d, $J = 11.0$ Hz), 7.23–7.26 (1H, m). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 36.2, 37.0, 52.9, 55.3, 64.3, 112.7, 116.0, 116.7, 117.0, 117.2, 127.7 (d, $J = 6.0$ Hz), 129.1, 132.1, 136.5, 137.1 (d, $J = 5.0$ Hz), 142.7 (d, $J = 14.5$ Hz), 149.7 (d, $J = 236$ Hz), 159.0, 171.1. $^{19}$F NMR (470 MHz, CDCl$_3$) δ: –146.5– –146.3 (1F, m). IR (CHCl$_3$): 3580, 1732 cm$^{-1}$. HRMS Calcd for C$_{20}$H$_{19}$FNaO$_6$ [(M+Na)$^+$] m/z: 397.1058, found: 397.1082.

Table 4, entry 10
Following the general procedure, 4d (28 mg, 25%) and 7d (52 mg, 41%) were obtained from 5d (130 mg, 0.34 mmol). Spectral data of 4d was identical to those of the authentic sample obtained from 2d.

5,7-Dihydro-9-fluoro-10-hydroxy-2,3-methylenedioxy-6H-dibenzo[a,c]cycloheptene (7d)
A colorless solid: mp 181.0–183.0 ºC. $^1$H NMR (500 MHz, CDCl$_3$) δ: 2.64–2.82 (2H, m), 3.07–3.22 (2H, m), 3.76 (6H, s), 5.46 (1H, br), 5.97 (2H, s), 6.80 (1H, s), 6.81 (1H, s), 6.96 (1H, d, $J = 8.5$ Hz), 7.03 (1H, d, $J = 11.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 36.1, 36.6, 52.9, 64.9, 101.1, 108.4, 110.6, 116.8, 117.2 (d, $J = 18.0$ Hz), 127.8 (d, $J = 6.0$ Hz), 128.8, 133.0, 137.1 (d, $J = 9.0$ Hz), 142.8 (d, $J = 14.5$ Hz), 146.8, 147.1, 150.0 (d, $J = 237$ Hz), 171.1. $^{19}$F NMR (470 MHz, CDCl$_3$) δ: –145.7– –145.5 (1F, m). IR (CHCl$_3$): 3578, 1732 cm$^{-1}$. HRMS Calcd for C$_{20}$H$_{17}$FNaO$_7$ [(M+Na)$^+$] m/z: 411.0851, found: 411.0868.

Table 4, entry 11
Following the general procedure, 4e (25 mg, 25%) and 7e (41 mg, 41%) were obtained from 5e (100 mg, 0.32 mmol). Spectral data of 4e was identical to those of the authentic sample obtained from 2e.
5,7-Dihydro-9-fluoro-10-hydroxy-1,2,3-trimethoxy-6H-dibenzo[a,c]cycloheptene (7e)
A colorless solid: mp 174.0–175.0 ºC. 1H NMR (500 MHz, CDCl3) δ: 2.00–2.07 (2H, m), 2.23–2.45 (4H, m), 3.60 (3H, s), 3.89 (3H, s), 3.90 (3H, s), 5.00 (1H, br), 6.57 (1H, s), 6.93 (1H, d, J = 11.0 Hz), 7.14 (1H, d, J = 9.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 30.4, 31.4, 32.9, 55.9, 60.7, 61.1, 107.6, 114.9 (d, J = 18.0 Hz), 119.0, 125.0, 132.4 (d, J = 2.5 Hz), 132.5 (d, J = 5.0 Hz), 135.8, 140.6, 141.2 (d, J = 13.0 Hz), 149.8 (d, J = 237 Hz), 150.6, 152.3. 19F NMR (470 MHz, CDCl3) δ: –145.5 (1F, dd, J = 9.0, 11.0 Hz). IR (CHCl3): 3599, 3557 cm –1. HRMS Calcd for C18H20FNaO5 [(M+Na)+] m/z: 339.1203, found: 339.1175.

Table 4, entry 12
Following the general procedure, 4f (32 mg, 32%) and 7f (44 mg, 44%) were obtained from 5f (100 mg, 0.349 mmol). Spectral data of 4f was identical to those of the authentic sample obtained from 2f.

5,7-Dihydro-9-fluoro-10-hydroxy-2,3-dimethoxy-6H-dibenzo[a,c]cycloheptene (7f)
A colorless solid: mp 189.0–190.0 ºC. 1H NMR (500 MHz, CDCl3) δ: 2.13 (2H, quint., J = 7.0 Hz), 2.39 (2H, t, J = 7.0 Hz), 2.43 (2H, t, J = 7.0 Hz), 3.91 (3H, s), 3.93 (3H, s), 5.03 (1H, d, J = 4.0 Hz), 6.76 (1H, s), 6.86 (1H, s), 6.95 (1H, d, J = 11.0 Hz), 7.02 (1H, d, J = 8.5 Hz). 13C NMR (125 MHz, CDCl3) δ: 30.7, 30.9, 33.5, 55.9, 56.0, 111.6, 111.8, 115.4 (d, J = 18.0 Hz), 116.8, 131.9, 132.5 (d, J = 6.0 Hz), 137.6 (d, J = 3.5 Hz), 141.6 (d, J = 14.5 Hz), 147.5, 148.1, 149.7 (d, J = 253 Hz). 19F NMR (470 MHz, CDCl3) δ: –147.0– –146.9 (1F, m). IR (KBr): 3429, 1504, 1273 cm –1. HRMS Calcd for C17H17FNaO3 [(M+Na)+] m/z: 311.1054, found: 311.1047.

Table 4, entry 13
Following the general procedure, a mixture of 7g and 4g (30 mg, 7g: 4g = 6: 1) were obtained from 5g (40 mg, 0.081 mmol). Further purification by preparative HPLC (Kanto, Mightysil, RP-18, GP250-10, water–CH3CN 1:1, flow 3.0 mL/min) gave 7g (25 mg, 62%, RT = 30.9 min) and 4g (4.0 mg, 10%, RT = 38.2 min).
3-Fluoro-9,10,11-trimethoxy-6-toluenesulfonyl-6,7-dihydro-5H-dibenzo[c,e]azepin-2-ol (7g)

A colorless solid: mp 248.0–250.0 °C. $^1$H NMR (500 MHz, acetone-d$_6$) δ: 2.41 (3H, s), 3.43 (1H, d, $J = 12.5$ Hz), 3.50 (1H, d, $J = 12.5$ Hz), 3.58 (3H, s), 3.80 (3H, s), 3.86 (3H, s), 4.52 (1H, d, $J = 8.0$ Hz), 4.54 (1H, d, $J = 8.0$ Hz), 6.72 (1H, s), 6.99 (1H, d, $J = 11.5$ Hz), 7.15 (1H, d, $J = 9.0$ Hz), 7.40 (2H, d, $J = 8.0$ Hz), 7.81 (2H, d, $J = 8.0$ Hz), 8.77 (1H, br). $^{13}$C NMR (125 MHz, acetone-d$_6$) δ: 21.1, 48.5, 49.4, 56.1, 60.7, 60.9, 109.9, 117.4 (d, $J = 18.0$ Hz), 119.7, 124.8 (d, $J = 6.0$ Hz), 125.6, 128.3, 128.7, 130.3, 133.5 (d, $J = 3.5$ Hz), 137.5, 143.2, 144.0, 144.8 (d, $J = 13.0$ Hz), 150.9 (d, $J = 241$ Hz), 151.1, 153.9. $^{19}$F NMR (470 MHz, acetone-d$_6$) δ: −145.5 (1F, dd, $J = 9.0, 11.0$ Hz). IR (KBr): 3352, 1493, 1319 cm$^{-1}$. HRMS Caled for C$_{24}$H$_{24}$FNNaO$_6$S [$(M+Na)^+$] $m/z$: 496.1201, found: 496.1201.

2-Fluoro-9,10,11-trimethoxy-6-toluenesulfonyl-6,7-dihydro-5H-dibenzo[c,e]azepin-3-ol (4g)

A colorless solid: mp >360 °C. $^1$H NMR (500 MHz, acetone-d$_6$) δ: 2.40 (3H, s), 3.45 (1H, d, $J = 13.0$ Hz), 3.48 (1H, d, $J = 13.0$ Hz), 3.57 (3H, s), 3.80 (3H, s), 3.84 (3H, s), 4.52 (1H, d, $J = 13.0$ Hz), 4.56 (1H, d, $J = 13.0$ Hz), 6.70 (1H, s), 6.93 (1H, d, $J = 9.0$ Hz), 7.22 (1H, d, $J = 12.5$ Hz), 7.40 (2H, d, $J = 8.0$ Hz), 7.80 (2H, d, $J = 8.0$ Hz), 8.93 (1H, br). $^{13}$C NMR (125 MHz, acetone-d$_6$) δ: 20.2, 47.9, 48.6, 55.1, 59.78, 59.80, 109.0, 116.8 (d, $J = 19.0$ Hz), 118.3 (d, $J = 2.5$ Hz), 124.5, 127.3, 127.7, 128.6 (d, $J = 3.5$ Hz), 129.4, 136.4, 142.2, 143.1, 143.8 (d, $J = 12.0$ Hz), 150.1, 150.3 (d, $J = 242$ Hz), 152.8. $^{19}$F NMR (470 MHz, CDCl$_3$) δ: −139.6−139.4 (1F, m). IR (KBr): 3399, 1524, 1250 cm$^{-1}$. HRMS Caled for C$_{24}$H$_{24}$FNNaO$_6$S [$(M+Na)^+$] $m/z$: 496.1201, found: 496.1230.
Synthesis of substrates (1a–g)

Synthesis of 1a–d

Dimethyl 2-[3,4-bis(benzyloxy)benzylidene]malonate (S1)

Under a nitrogen atmosphere, dimethyl malonate (5.6 g, 43 mmol) was added to a solution of a mixture of 3,4-dibenzyloxybezaldehyde (12.3 g, 39 mmol), piperidine (0.50 mL, 5.0 mmol) and AcOH (1.0 mL, 17.3 mmol) in toluene (80 mL). The resulting solution was refluxed using a Dean-Stark condenser for 3 h. After cooling, the reaction mixture was concentrated in vacuo. The solvents were evaporated, and the residue was triturated with hexanes. The resultant solid was filtered and washed with hexanes and water to afford S1 (16.7 g, quant.).

A colorless solid: mp 91.0–93.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 3.79 (3H, s), 3.83 (3H, s), 5.14 (2H, s), 5.20 (2H, s), 6.91 (1H, d, J = 8.0 Hz), 7.02 (1H, dd, J = 2.0, 8.0 Hz), 7.07 (1H, d, J = 2.0 Hz), 7.30–7.47 (10H, m), 7.65 (1H, s). ¹³C NMR (125 MHz, CDCl₃) δ: 52.5, 52.6, 70.7, 71.1, 113.9, 115.2, 123.0, 124.5, 125.7, 127.0, 127.2, 127.91, 127.93, 128.50, 128.53, 136.4, 136.6, 142.6, 148.6, 151.2, 164.7, 167.5. IR (CHCl₃): 1726, 1238 cm⁻¹. HRMS Calcd for C₂₆H₂₄NaO₆ [(M+Na)⁺] m/z: 455.1465, found: 455.1453.
Dimethyl 2-[3,4-bis(benzyloxy)benzyl]malonate (S2)

Under a nitrogen atmosphere, NaBH₄ (1.75 g, 46 mmol) was added to a solution of S1 (10.0 g, 23 mmol) in MeOH–MeCN (1:1, 230 mL) at 0 °C. The reaction mixture was stirred for 1 h before being quenched with NH₄Cl. The solvents were evaporated, and water (100 mL) was added. The layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes–EtOAc 3:1) to give S2 (7.9 g, 75%). A colorless solid: mp 69.0–69.5 °C. ¹H NMR (500 MHz, CDCl₃): 3.11 (2H, d, J = 7.5 Hz), 3.59 (1H, t, J = 7.5 Hz), 3.66 (6H, s), 5.12 (4H, s), 6.70 (1H, dd, J = 2.0, 8.0 Hz), 6.79 (1H, d, J = 2.0 Hz), 6.84 (1H, d, J = 8.0 Hz), 7.27–7.46 (10H, m). ¹³C NMR (125 MHz, CDCl₃): 34.3, 52.6, 53.7, 71.2, 71.3, 115.1, 115.7, 121.7, 127.25, 127.31, 127.7, 127.8, 128.4, 131.0, 137.2, 137.3, 147.8, 148.8, 169.2. IR (CHCl₃): 1732, 1512 cm⁻¹. HRMS Calcd for C₂₆H₂₆NaO₆ [(M+Na)⁺] m/z: 457.1622, found: 457.1607.

Dimethyl 2-[3,4-bis(benzyloxy)benzyl]-2-(3,4,5-trimethoxybenzyl)malonate (S3)

Under a nitrogen atmosphere, a solution of S2 (10.0 g, 23.0 mmol, dried by azeotropic distillation with toluene before use) in anhydrous THF (20 mL) was added to a suspension of NaH (1.00 g, 55% w/w, washed with hexanes before use) in anhydrous THF (8 mL) at 0 °C, and the reaction mixture was stirred for 10 min at room temperature. A solution of 3,4,5-trimethoxybenzyl chloride (3.1 g, 14.4 mmol, dried by azeotropic distillation with toluene before use) in THF (30 mL) and nBu₄NI (212 mg, 0.58 mmol) were added to the reaction mixture at 0 °C, and the resulting mixture was stirred at 50 °C for 24 h before being quenched with a saturated aq. NH₄Cl solution. The layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes–EtOAc 12:5) to give S3 (5.4 g, 76%). A pale yellow oil: ¹H NMR (500 MHz, CDCl₃): 3.12 (2H, s), 3.15 (2H, s), 3.61 (6H, s), 3.80 (6H, s), 3.83 (3H, s), 5.12 (2H, s), 5.14 (2H, s), 6.33 (2H, s), 6.65 (1H, dd, J = 2.0, 8.5 Hz), 6.76 (1H, d, J = 2.0 Hz), 6.84 (1H, d, J = 8.5 Hz), 7.25–7.45 (10H, m). ¹³C NMR (125 MHz, CDCl₃): 39.0, 39.6,
52.2, 55.9, 60.3, 60.8, 71.1, 71.3, 106.9, 114.6, 117.2, 123.0, 127.19, 127.24, 127.71, 127.73, 128.4, 129.2, 131.7, 136.8, 137.1, 137.2, 148.0, 148.4, 152.7, 171.3. IR (CHCl₃): 1728, 1290 cm⁻¹. HRMS Calcd for C₃₆H₃₈NaO₉ [(M+Na)⁺] m/z: 637.2408, found: 637.2396.

**Dimethyl 2-[3,4-bis(benzyloxy)benzyl]-2-(3,4-dimethoxybenzyl)malonate (S4)**

Similarly to the preparation of S₃, S₄ (4.3 g, 79%) was obtained from S₂ (4.0 g, 9.2 mmol) and 3,4-dimethoxybenzyl chloride (2.2 g, 11.5 mmol).

A pale yellow oil: ¹H NMR (500 MHz, CDCl₃) δ: 3.11 (2H, s), 3.12 (2H, s), 3.60 (6H, s), 3.81 (3H, s), 3.86 (3H, s), 5.12 (2H, s), 6.62–6.67 (3H, m), 6.74–6.78 (2H, m), 6.84 (1H, d, J = 8.0 Hz), 7.25–7.45 (10H, m). ¹³C NMR (125 MHz, CDCl₃) δ: 38.94, 38.96, 52.2, 55.7, 55.8, 60.5, 71.2, 71.3, 110.8, 113.2, 114.7, 117.3, 122.1, 123.0, 127.2, 127.7, 128.4, 128.5, 129.4, 137.2, 137.3, 147.9, 148.0, 148.4, 148.5, 171.4. IR (CHCl₃): 3038, 3009, 1728, 1518 cm⁻¹. HRMS Calcd for C₃₅H₃₆NaO₈ [(M+Na)⁺] m/z: 607.2302, found: 607.2277.

**Dimethyl 2-[3,4-bis(benzyloxy)benzyl]-2-(3-methoxybenzyl)malonate (S5)**

Similarly to the preparation of S₃, S₅ (4.7 g, 84%) was obtained from S₂ (4.0 g, 9.2 mmol) and 3-methoxybenzyl chloride (1.7 g, 11.5 mmol).

A pale yellow oil: ¹H NMR (500 MHz, CDCl₃) δ: 3.11 (2H, s), 3.14 (2H, s), 3.60 (6H, s), 3.76 (3H, s), 5.12 (2H, s), 5.14 (2H, s), 6.63–6.69 (3H, m), 6.74–6.78 (2H, m), 6.84 (1H, d, J = 8.0 Hz), 7.18 (1H, t, J = 8.0 Hz), 7.26–7.45 (10H, m). ¹³C NMR (125 MHz, CDCl₃) δ: 38.7, 39.2, 52.2, 55.1, 60.3, 71.2, 112.1, 114.7, 116.0, 117.2, 122.3, 123.0, 127.3, 127.7, 128.4, 129.2, 129.3, 137.2, 137.3, 137.6, 147.9, 148.4, 159.4, 171.3. IR (CHCl₃): 1730, 1263 cm⁻¹. HRMS Calcd for C₃₄H₃₅O₇ [(M+H)⁺] m/z: 555.2377, found: 555.2381.
Dimethyl 2-[3,4-bis(benzyloxy)benzyl]-2-(3,4-methylenedioxybenzyl)malonate (S6)

Similarly to the preparation of S3, S6 (1.34 g, 95%) was obtained from S2 (1.00 g, 2.3 mmol) and piperonyl chloride (496 mg, 2.9 mmol).

A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 3.14 (2H, s), 3.17 (2H, s), 3.62 (6H, s), 5.17 (2H, s), 5.18 (2H, s), 5.92 (2H, s), 6.60 (1H, dd, $J = 2.0, 8.0$ Hz), 6.67 (1H, d, $J = 2.0$ Hz), 6.71 (1H, dd, $J = 2.0, 8.0$ Hz), 6.73 (1H, d, $J = 8.0$ Hz), 6.83 (1H, d, $J = 2.0$ Hz), 6.89 (1H, d, $J = 8.0$ Hz), 7.29–7.52 (10H, m). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 38.7, 38.9, 52.0, 60.4, 70.99, 71.04, 100.8, 107.8, 110.1, 114.5, 117.1, 122.8, 123.0, 127.08, 127.13, 127.6, 128.28, 128.30, 129.1, 129.5, 137.1, 137.2, 146.3, 147.3, 147.8, 148.3, 171.1. IR (CHCl$_3$): 1730, 1246 cm$^{-1}$. HRMS Calcd for C$_{34}$H$_{32}$NaO$_8$ [(M+Na)$^+$] $m/z$: 591.1989, found: 591.2000.

Dimethyl 2-(3,4-dihydroxybenzyl)-2-(3,4,5-trimethoxybenzyl)malonate (1a)

THF (44 mL) was added to a mixture of S3 (5.4 g, 8.8 mmol) and Pd/C (10% Pd on carbon, 530 mg) at room temperature under a nitrogen atmosphere. The flask was evacuated and back-filled with hydrogen. The reaction mixture was stirred overnight at room temperature under a hydrogen atmosphere (1 atm) using a balloon and filtered through a Celite pad. The Celite pad was washed with EtOAc, and the combined organic layer was concentrated in vacuo. The resulting oil was purified by flash column chromatography (hexanes–EtOAc 1:1) to afford 1a (3.6 g, 94%).

A colorless solid: mp 155.5–156.0 °C. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$: 3.13 (2H, s), 3.15 (2H, s), 3.68 (6H, s), 3.82 (6H, s), 3.83 (3H, s), 5.22 (1H, brs), 5.42 (1H, brs), 6.35 (2H, s), 6.55 (1H, dd, $J = 2.0, 8.0$ Hz), 6.66 (1H, d, $J = 2.0$ Hz), 6.76 (1H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$: 38.9, 39.5, 52.4, 56.0, 60.4, 60.9, 107.1, 115.1, 117.1, 122.3, 128.7, 131.8, 136.8, 142.7, 143.4, 152.8, 171.5. IR (CHCl$_3$): 3595, 3555, 1728, 1238 cm$^{-1}$. HRMS Calcd for C$_{24}$H$_{26}$NaO$_9$ [(M+Na)$^+$] $m/z$: 457.1469, found: 457.1480.
Dimethyl 2-(3,4-dihydroxybenzyl)-2-(3,4-dimethoxybenzyl)malonate (1b)

Similarly to the preparation of 1a, 1b (3.1 g, quant.) was obtained from S4 (4.2 g, 7.3 mmol).

White amorphous. $^1$H NMR (500 MHz, CDCl$_3$) δ: 3.11 (2H, s), 3.15 (2H, s), 3.69 (6H, s), 3.81 (3H, s), 3.83 (3H, s), 5.80 (1H, brs), 5.87 (1H, s), 6.54 (1H, dd, $J = 2.0$, 8.0 Hz), 6.64–6.70 (3H, m), 6.72 (1H, d, $J = 8.0$ Hz), 6.76 (1H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 38.8, 38.9, 52.4, 55.7, 60.6, 110.9, 113.3, 115.1, 117.0, 122.1, 122.3, 128.4, 128.5, 142.7, 143.5, 147.9, 148.3, 171.7. IR (CHCl$_3$): 3597, 3557, 1728, 1281, 1261 cm$^{-1}$. HRMS Calcd for C$_{21}$H$_{24}$NaO$_8$ [(M+Na)$^+$] m/z: 427.1363, found: 427.1340.

Dimethyl 2-(3,4-dihydroxybenzyl)-2-(3-methoxybenzyl)malonate (1c)

Similarly to the preparation of 1a, 1c (3.0 g, quant.) was obtained from S5 (4.4 g, 7.1 mmol).

A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) δ: 3.11 (2H, s), 3.19 (2H, s), 3.66 (6H, s), 3.77 (3H, s), 5.88 (2H, brs), 6.55 (1H, dd, $J = 2.0$, 8.0 Hz), 6.68 (1H, d, $J = 2.0$ Hz), 6.69–6.74 (3H, m), 6.78 (1H, dd, $J = 8.0$ Hz), 7.18 (1H, t, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: 38.6, 39.1, 52.4, 55.1, 60.6, 112.2, 115.1, 116.1, 117.1, 122.4, 128.5, 129.2, 137.5, 142.7, 143.5, 159.3, 171.6. IR (CHCl$_3$): 3597, 3555, 3412, 1728, 1603 cm$^{-1}$. HRMS Calcd for C$_{20}$H$_{22}$NaO$_7$ [(M+Na)$^+$] m/z: 397.1258, found: 397.1239.

Dimethyl 2-(3,4-dihydroxybenzyl)-2-(3,4-methylenedioxybenzyl)malonate (1d)

Similarly to the preparation of 1a, 1d (905 mg, quant.) was obtained from S6 (1.30 g, 2.1 mmol).

A colorless oil: $^1$H NMR (500 MHz, CDCl$_3$) δ: 3.10 (2H, s), 3.13 (2H, s), 3.66 (6H, s), 5.63 (1H, brs), 5.68 (1H, brs), 5.92 (2H, s), 6.56 (1H, dd, $J = 2.0$, 8.0 Hz), 6.59 (1H, dd, $J = 2.0$, 8.0 Hz), 6.64
(1H, d, J = 2.0 Hz), 6.68 (1H, d, J = 2.0 Hz), 6.706 (1H, d, J = 8.0 Hz), 6.712 (1H, d, J = 8.0 Hz).

$^{13}$C NMR (125 MHz, CDCl$_3$) δ: 38.8, 39.1, 52.4, 60.8, 100.9, 108.1, 110.3, 115.1, 117.0, 122.4, 123.2, 128.6, 129.5, 142.6, 143.4, 146.5, 147.4, 171.6. IR (CHCl$_3$): 3674, 1730, 1240 cm$^{-1}$. HRMS Calcd for C$_{20}$H$_{20}$NaO$_8$ [(M+Na)$^+$] m/z: 411.1050, found: 411.1044.

**Synthesis of 1e and 1f**

3,4-Bis(tert-butyldimethylsilyloxy)benzaldehyde (S7)$^2$

Under a nitrogen atmosphere, imidazole (7.4 g, 109 mmol) and TBSCl (13.7 g, 91 mmol) were added to an ice-cold solution of 3,4-dihydroxybenzaldehyde (5.0 g, 36 mmol) in anhydrous DMF (72 mL), and the reaction mixture was stirred overnight at room temperature before being quenched with a saturated aq. NH$_4$Cl solution. Hexanes (50 mL) were added and the layers were separated. The aqueous layer was extracted three times with hexanes. The combined organic layer was washed three times with water and then with brine, dried (Na$_2$SO$_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes–EtOAc 20:1) to give S7 (8.7 g, 65%). The $^1$H NMR and $^{13}$C NMR data of S7 were in good agreement with those reported in ref. 2.
1-[3,4-Bis(tert-butyldimethylsilyloxy)phenyl]-3-(3,4,5-trimethoxyphenyl)prop-2-yn-1-ol (S8)
Under a nitrogen atmosphere, nBuLi (1.6 M in hexanes, 32.0 mL, 51.0 mmol) was added to a solution of 5-(2,2-dibromovinyl)-1,2,3-trimethoxybenzene\(^3\) (6.0 g, 17.0 mmol) in anhydrous THF (85 mL) at –78 °C. The reaction mixture was stirred at 0 °C for 30 min, and a solution of S7 (6.2 g, 17.0 mmol) in THF (20 mL) was added at the same temperature. The reaction mixture was warmed up to room temperature and stirred for another 15 min at room temperature before being quenched with a saturated aq. NH\(_4\)Cl solution. The layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na\(_2\)SO\(_4\)), filtered and concentrated \textit{in vacuo}. The residue was purified by flash column chromatography (hexanes–EtOAc 3:1) to afford S8 (9.3 g, 98%).

A colorless oil: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.20 (6H, s), 0.22 (6H, s), 0.99 (18H, s), 2.47 (1H, brs), 3.84 (6H, s), 3.86 (3H, s), 5.56 (1H, s), 6.71 (2H, s), 6.84 (1H, d, \(J = 8.0\) Hz), 7.04 (1H, dd, \(J = 2.0, 8.0\) Hz), 7.13 (1H, d, \(J = 2.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): –4.2, –4.13, –4.10, 18.4, 25.8, 25.9, 56.0, 60.9, 64.6, 86.2, 87.9, 108.8, 117.5, 119.7, 119.8, 120.9, 133.8, 138.8, 146.8, 147.0, 152.9. IR (CHCl\(_3\)): 3588, 2359, 2338, 1504, 1238 cm \(^{-1}\). HRMS Calcd for C\(_{30}\)H\(_{46}\)NaO\(_6\)Si\(_2\) [\((\text{M}+\text{Na})^+\)] m/z: 581.2725, found: 581.2742.

1-[3,4-Bis(tert-butyldimethylsilyloxy)phenyl]-3-(3,4-dimethoxyphenyl)prop-2-yn-1-ol (S9)
Similarly to the preparation of S8, S9 (4.8 g, 97%) was obtained from S7 (3.4 g, 9.3 mmol) and 4-(2,2-dibromovinyl)-1,2-dimethoxybenzene\(^4\) (3.0 g, 9.3 mmol).

A colorless oil: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.20 (6H, s), 0.22 (6H, s), 0.99 (18H, s), 2.17 (1H, brs), 3.87 (3H, s), 3.89 (3H, s), 5.56 (1H, s), 6.80 (1H, d, \(J = 8.0\) Hz), 6.84 (1H, d, \(J = 8.0\) Hz), 6.97 (1H, d, \(J = 2.0\) Hz), 7.04 (1H, dd, \(J = 2.0, 8.0\) Hz), 7.08 (1H, dd, \(J = 2.0, 8.0\) Hz), 7.14 (1H, d, \(J = 2.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): –4.15, –4.13, –4.10, 18.4, 25.8, 25.9, 56.0, 60.9, 64.6, 86.4, 87.3, 110.8, 114.3, 114.6, 119.75, 119.85, 120.9, 125.0, 133.9, 146.9, 147.1, 148.5, 149.6. IR (CHCl\(_3\)): 3588, 2359, 2340, 1601, 1514, 1296, 1256 cm \(^{-1}\). HRMS Calcd for C\(_{29}\)H\(_{44}\)NaO\(_6\)Si\(_2\)
[(M+Na)\(^+\)] m/z: 551.2619, found: 551.2593.

1-[3,4-Bis(tert-butyldimethylsilyloxy)phenyl]-3-(3,4,5-trimethoxyphenyl)propane (S10)
MeOH (152 mL) and AcOH (15 mL) were added to a mixture of S8 (8.5 g, 15.2 mmol) and Pd/C (10% Pd on carbon, 1.70 g) at room temperature under a nitrogen atmosphere. The flask was evacuated and back-filled with hydrogen. The reaction mixture was stirred at room temperature for 107 h under a hydrogen atmosphere (1 atm) using a balloon, and Et\(_3\)N (37 mL) was added. The resulting mixture was filtered through a Celite pad, and the Celite pad was washed with EtOAc. Water was added, and the organic layer was separated, washed with water and brine, dried (Na\(_2\)SO\(_4\)), filtered and concentrated \textit{in vacuo}. The residue was purified by flash column chromatography (hexanes–EtOAc 10:1) to afford S10 (6.8 g, 87%).

A colorless oil: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.19 (6H, s), 0.20 (6H, s), 0.98 (9H, s), 0.99 (9H, s), 1.89 (2H, quint, \(J = 7.0\) Hz), 2.54 (2H, \(t, J = 7.0\) Hz), 2.56 (2H, \(t, J = 7.0\) Hz), 3.83 (3H, s), 3.85 (6H, s), 6.38 (2H, s), 6.62 (1H, dd, \(J = 2.0, 8.0\) Hz), 6.67 (1H, d, \(J = 2.0\) Hz), 6.74 (1H, d, \(J = 8.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): –4.11, –4.08, 18.4, 25.9, 33.1, 34.7, 35.7, 56.0, 60.9, 105.1, 120.7, 121.3, 235.2, 135.9, 138.3, 144.8, 146.4, 153.0. IR (CHCl\(_3\)): 1589, 1294, 1254 cm\(^{-1}\). HRMS Calcd for C\(_{30}\)H\(_{50}\)NaO\(_5\)Si\(_2\) [(M+Na)\(^+\)] m/z: 569.3089, found: 569.3073.

1-[3,4-Bis(tert-butyldimethylsilyloxy)phenyl]-3-(3,4-dimethoxyphenyl)propane (S11)
Similarly to the preparation of S10, S11 (2.4 g, 48%) was obtained from S9 (4.8 g, 9.0 mmol).

A colorless oil: \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\): 0.19 (6H, s), 0.20 (6H, s), 0.98 (9H, s), 1.00 (9H, s), 1.88 (2H, quint, \(J = 7.5\) Hz), 2.53 (1H, \(t, J = 7.5\) Hz), 2.57 (1H, \(t, J = 7.5\) Hz), 3.86 (3H, s), 3.87 (3H, s), 6.62 (1H, dd, \(J = 2.0, 8.0\) Hz), 6.67 (1H, d, \(J = 2.0\) Hz), 6.70 (1H, d, \(J = 2.0\) Hz), 6.72 (1H, dd, \(J = 2.0, 8.0\) Hz), 6.74 (1H, d, \(J = 8.0\) Hz), 6.80 (1H, d, \(J = 8.0\) Hz). \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\): –4.14, –4.08, 18.4, 25.9, 33.2, 34.6, 34.9, 55.7, 55.9, 111.1, 111.6, 120.1, 120.7, 121.2, 121.3, 135.1, 135.4, 144.7, 146.4, 147.0, 148.7. IR (CHCl\(_3\)): 2957, 2932, 1514 cm\(^{-1}\). HRMS Calcd for C\(_{29}\)H\(_{49}\)O\(_4\)Si\(_2\) [(M+H)\(^+\)] m/z: 517.3169, found: 517.3165.
4-[3-(3,4,5-Trimethoxyphenyl)propyl]benzene-1,2-diol (1e)
Under a nitrogen atmosphere, AcOH (2.1 mL, 37 mmol) and TEA·3HF (5.1 mL, 31 mmol) were added to an ice-cold solution of S10 (6.8 g, 12.4 mmol) in THF (25 mL). The reaction mixture was stirred overnight at room temperature before being quenched with water. EtOAc was added, the layers were separated, and the aqueous layer was extracted three times with EtOAc. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes–EtOAc 1:1) to afford 1e (3.8 g, 96%).
A colorless solid: mp 109.0–111.0 ºC. ¹H NMR (500 MHz, CDCl₃) δ: 1.85–1.93 (2H, m), 2.55 (2H, t, J = 8.0 Hz), 2.57 (2H, t, J = 7.5 Hz), 3.83 (3H, s), 3.84 (6H, s), 5.05 (1H, s), 5.21 (1H, s), 6.38 (2H, s), 6.62 (1H, dd, J = 2.0, 8.0 Hz), 6.72 (1H, d, J = 2.0 Hz), 6.78 (1H, d, J = 8.0 Hz). ¹³C NMR (125 MHz, CDCl₃) δ: 33.0, 34.7, 35.7, 56.0, 60.9, 105.2, 115.2, 115.5, 120.8, 135.4, 135.9, 138.2, 141.4, 143.5, 153.0. IR (CHCl₃): 3599, 3557, 1238 cm⁻¹. HRMS Calcd for C₁₈H₂₃O₅ [(M+H)⁺] m/z: 319.1540, found: 319.1533.

4-[3-(3,4-Dimethoxyphenyl)propyl]benzene-1,2-diol (1f)
Similarly to the preparation of 1e, 1f (1.20 g, quant.) was obtained from S11 (2.4 g, 4.3 mmol).
A colorless solid: mp 119.0–120.0 ºC. ¹H NMR (500 MHz, CDCl₃) δ: 1.88 (2H, quint. J = 7.5 Hz), 2.53 (1H, t, J = 7.5 Hz), 2.57 (1H, t, J = 7.5 Hz), 3.856 (3H, s), 3.863 (3H, s), 5.04 (1H, brs), 5.18 (1H, brs), 6.62 (1H, dd, J = 2.0, 8.0 Hz), 6.68–6.81 (5H, m). ¹³C NMR (125 MHz, CDCl₃) δ: 33.2, 34.6, 34.9, 55.8, 55.9, 111.1, 111.7, 115.2, 115.5, 120.2, 120.8, 134.9, 135.6, 141.3, 143.4, 147.0, 148.7. IR (CHCl₃): 3599, 3559, 1607, 1591 cm⁻¹. HRMS Calcd for C₁₇H₂₁O₄ [(M+H)⁺] m/z: 289.1440, found: 289.1410.
Synthesis of 1g

\[ \text{OH} \]
\[ \text{CN} \]

1) TBSCI  
imidazole  
2) LAH, THF  
3) TsCl, TEA  
CH\_2\_Cl\_2

\[ \text{OTBS} \]
\[ \text{TBSHN} \]
\[ \text{TsHN} \]

\[ \text{S12} \]

\[ \text{MeO} \]
\[ \text{OMe} \]
\[ \text{OMe} \]
\[ \text{OMe} \]

\[ \text{DIAD} \]
\[ \text{PPH}_3 \]

\[ \text{THF} \]

\[ \text{Ts} \]

\[ \text{S13} \]

\[ \text{OH} \]
\[ \text{OH} \]
\[ \text{MeO} \]
\[ \text{OMe} \]
\[ \text{OMe} \]
\[ \text{OMe} \]

\[ \text{1g} \]

N-(3,4-Bis(tert-butyldimethylsilyloxy)benzyl)-4-methylbenzenesulfonamide (S12)
Under a nitrogen atmosphere, imidazole (6.1 g, 90 mmol) and TBSCI (11.4 g, 75 mmol) were added to a solution of 3,4-dihydroxybenzonitrile (4.1 g, 30 mmol) in anhydrous DMF (60 mL). The reaction mixture was stirred overnight at room temperature before being quenched with water. Hexanes and EtOAc were added, the layers were separated, and the aqueous layer was extracted three times with hexanes–EtOAc (10:1). The combined organic layer was washed two times with water and brine, dried (Na\_2SO\_4), filtered and concentrated \textit{in vacuo}. The residue was dissolved in anhydrous Et\_2O (70 mL), which was added to an ice-cold suspension of LiAlH\_4 (2.3 g, 61 mmol) in anhydrous Et\_2O (80 mL). The reaction mixture was stirred for 2 h at room temperature. Water (2.3 mL), 15% NaOH (2.3 mL) and water (6.9 mL) were dropwise added to the ice-cold reaction mixture in this order. The resultant mixture was stirred vigorously for 30 min and filtered through a Celite pad. The Celite pad was washed with EtOAc, and the combined organic layer was concentrated \textit{in vacuo}. The residue was dissolved in CH\_2Cl\_2 (100 mL), and Et\_3N (8.3 mL, 60 mmol) and TsCl (6.9 g, 36 mmol) were added at 0 °C. The reaction mixture was stirred overnight at room temperature before being quenched with a saturated aq. NH\_4Cl solution. The layers were separated, and the aqueous layer was extracted three times with CH\_2Cl\_2. The combined organic layer was washed with water and brine, dried (Na\_2SO\_4), filtered and concentrated \textit{in vacuo}. The residue was
purified by flash column chromatography (hexanes–EtOAc 10:1) to afford S12 (15.4 g, 89%).

A colorless solid: mp 78.0–80.0 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.15 (6H, s), 0.17 (6H, s), 0.96 (18H, s), 2.44 (3H, s), 3.99 (2H, d, $J = 6.0$ Hz), 4.48 (1H, t, $J = 6.0$ Hz), 6.60 (1H, dd, $J = 2.0$, 8.0 Hz), 6.65 (1H, d, $J = 2.0$ Hz), 6.71 (1H, d, $J = 8.0$ Hz), 7.31 (2H, d, $J = 8.0$ Hz), 7.76 (2H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: –4.15, –4.13, 18.37, 18.41, 21.5, 25.9, 46.9, 120.8, 120.9, 121.0, 127.2, 129.2, 129.7, 136.9, 143.5, 146.7, 147.0. IR (CHCl$_3$): 3374, 1302 cm$^{-1}$. HRMS Calcd for C$_{26}$H$_{43}$NNaO$_4$SSi$_2$ [($M$+Na)$^+$] m/z: 544.2344, found: 544.2351.

$N$-[(3,4-Bis(tert-butyldimethylsilyloxy)benzyl]-4-methyl-$N$-(3,4,5-trimethoxybenzyl)benzenesulfonamide (S13)

Under a nitrogen atmosphere, diisopropyl azodicarboxylate (1.9 M in toluene, 3.1 mL, 5.9 mmol) was added to a solution of 3,4,5-trimethoxybenzyl alcohol (1.17 g, 5.9 mmol), PPh$_3$ (1.55 g, 5.9 mmol) and S12 (1.54 g, 2.96 mmol) in THF (10.0 mL). The reaction mixture was stirred overnight at room temperature. The solvent was evaporated and the residue was purified by flash column chromatography (hexanes–EtOAc 15:1) to afford S13 (1.82 g, 82%).

A colorless solid: mp 118.0–120.0 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 0.14 (6H, s), 0.18 (6H, s), 0.96 (9H, s), 0.97 (6H, s), 2.42 (3H, s), 3.67 (6H, s), 3.79 (3H, s), 4.20 (2H, s), 4.24 (2H, s), 6.18 (2H, s), 6.54 (1H, dd, $J = 2.0$, 8.0 Hz), 6.68 (1H, d, $J = 2.0$ Hz), 6.70 (1H, d, $J = 8.0$ Hz), 7.30 (2H, d, $J = 8.0$ Hz), 7.76 (2H, d, $J = 8.0$ Hz). $^{13}$C NMR (125 MHz, CDCl$_3$) δ: –4.20, –4.15, 18.35, 18.43, 21.5, 25.9, 49.8, 50.2, 55.8, 60.8, 105.2, 120.6, 121.3, 121.8, 127.1, 128.6, 129.7, 131.3, 137.1, 138.2, 143.1, 146.5, 146.9, 153.0. IR (CHCl$_3$): 2957, 1595, 1508, 1254, 1238 cm$^{-1}$. HRMS Calcd for C$_{36}$H$_{55}$NNaO$_7$SSi$_2$ [($M$+Na)$^+$] m/z: 724.3130, found: 724.3145.

$N$-(3,4-Dihydroxybenzyl)-4-methyl-$N$-(3,4,5-trimethoxybenzyl)benzenesulfonamide (1g)

Similarly to the preparation of 1e, 1g (1.10 g, 97%) was obtained from S13 (1.80 g, 2.4 mmol).

A pale yellow solid: mp 143.0–144.0 °C. $^1$H NMR (500 MHz, CDCl$_3$) δ: 2.44 (3H, s), 3.67 (6H, s),
3.79 (3H, s), 4.19 (2H, s), 4.22 (2H, s), 5.26 (1H, brs), 5.29 (1H, brs), 6.15 (2H, s), 6.51 (1H, dd, J = 2.0, 8.0 Hz), 6.70 (1H, d, J = 2.0 Hz), 6.71 (1H, d, J = 8.0 Hz), 7.33 (2H, d, J = 8.0 Hz), 7.76 (2H, d, J = 8.0 Hz). 13C NMR (125 MHz, CDCl3) δ: 21.5, 50.4, 50.9, 55.9, 60.9, 105.4, 114.9, 115.7, 121.5, 127.2, 128.5, 129.8, 131.4, 137.0, 137.6, 143.3, 143.4, 143.5, 152.9. IR (CHCl3): 3564, 1329, 1236 cm⁻¹. HRMS Calcd for C24H27NNaO7S [(M+Na)⁺] m/z: 496.1400, found: 496.1401.

Synthesis of 10

[Chemical structure image]

3,3-Bis(methoxycarbonyl)-6,7,8-trimethoxy-1,2,3,4-tetrahydroxynaphthalene-1-spiro-1’-(3’-acetoxycyclohexa-2’,5’-dien-4’-one) (10)

Under a nitrogen atmosphere, pyridine (28 μL, 0.35 mmol), Ac₂O (22 μL, 0.23 mmol) and DMAP (2 mg) were added to an ice-cold solution of 2a (50 mg, 0.116 mmol) in CH₂Cl₂ (1.1 mL). The reaction mixture was stirred for 1 h at room temperature before being quenched with water. The layers were separated, and the aqueous layer was extracted three times with CH₂Cl₂. The combined organic layer was washed with brine, dried (Na₂SO₄), filtered and concentrated in vacuo. The residue was purified by flash column chromatography (hexanes–EtOAc 1:1) to afford 10.

A colorless solid: mp 52.0–54.0 °C. ¹H NMR (500 MHz, CDCl₃) δ: 2.24 (3H, s), 2.47 (1H, d, J = 14.5 Hz), 2.51 (1H, d, J = 14.5 Hz), 3.19 (1H, d, J = 16.0 Hz), 3.30 (1H, d, J = 16.0 Hz), 3.67 (3H, s), 3.72 (3H, s), 3.74 (3H, s), 3.75 (3H, s), 3.84 (3H, s), 6.29 (1H, d, J = 10.0 Hz), 6.42 (1H, d, J = 3.0 Hz), 6.50 (1H, s), 6.75 (1H, d, J = 3.0, 10.0 Hz). 13C NMR (125 MHz, CDCl₃) δ: 20.4, 34.9, 40.3, 43.3, 51.6, 52.9, 53.0, 55.8, 60.5, 61.0, 107.2, 118.1, 125.8, 129.0, 140.2, 140.6, 144.2, 152.8, 153.5, 155.2, 168.3, 171.1, 178.9. IR (CHCl₃): 1765, 1734, 1672, 1238 cm⁻¹. HRMS Calcd for C2₄H₂₆NaO₁₀ [(M+Na)⁺] m/z: 497.1424, found: 497.1435.

References
Diagram of a compound labeled as 4b with chemical structures and spectral data.
X : parts per Million : 19F
X: parts per Million: 19F
9f

X: parts per Million: 19F