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Intramolecular Conjugate Ene Reaction of γ-Difluoromethyl- and γ-Trifluoromethyl-α,β-Unsaturated γ-Butyrolactones

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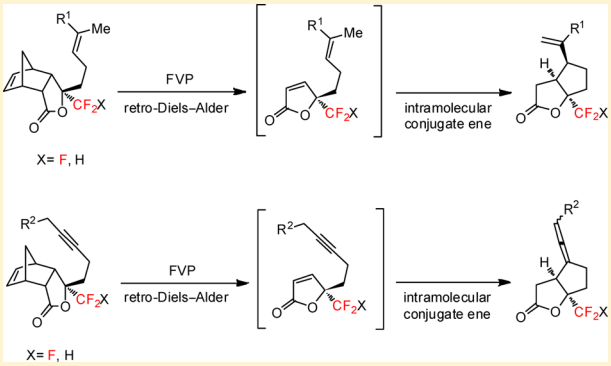
Supporting Information

ABSTRACT: A general synthetic strategy to cis-fused bicyclic γ-butyrolactones via the retro-Diels−Alder reaction/intramolecular conjugate ene cascade (RDA/ICE) reaction under the flash-vacuum pyrolysis of maleic anhydride adducts is developed. The reaction gave high yields of products with high stereoselectivity. The existence of the difluoromethyl or trifluoromethyl group at the γ-position of the in situ-generated homoalkenyl- or homoalkynyl-α,β-unsaturated γ-butyrolactones was found to accelerate the rate of the intramolecular conjugate ene reaction leading to γ-difluoromethylated and γ-trifluoromethylated cis-fused bicyclic γ-butyrolactones.



INTRODUCTION

Organofluorine compounds received dramatic attention due to their prevalent use in biological, pharmaceutical, agrochemical, and materials sciences.[1,2] The unique properties of the fluorine atom including, the high electronegativity, small size, and the high stability of the C−F bond cause the fluorine-containing molecules to possess unique and superior physical, biological, and chemical properties compared to the parent nonfluorinated ones. As a consequence, the development of a general approach of introducing fluorine atoms or fluorinated motifs into small organic compounds, particularly for the preparation of fluorinated analogs of biologically active natural compounds, has received increasing attention in recent years.[3] Our group has long been interested in the development of synthetic methods to incorporate trifluoromethyl and difluoromethyl moieties into small organic molecules. Recently, we have reported convenient strategies toward the synthesis of γ-trifluoromethyl- and γ-difluoromethyl-α,β-unsaturated γ-butyrolactones through Grignard reaction of the respective compounds **1** and **2** followed by flash-vacuum pyrolysis (FVP) to mediate the retro-Diels−Alder (RDA) reaction.[4,5]

An intramolecular ene reaction of the suitable dienes, enynes, enones, and related systems is a powerful method to readily access the carbocycles and heterocycles containing multiple substituents.[6] Both Lewis acid-catalyzed[7] and thermal[8] conditions were employed to promote the intramolecular ene reactions leading to cyclopentane and cyclopentanone derivatives with high regio- and stereoselectivity.

In a view of α,β-unsaturated γ-butyrolactones as synthetically useful intermediates for the elaboration of structurally complex molecules, we described herein an intramolecular conjugate ene (ICE) reaction under the FVP conditions of γ-trifluoromethyl- and γ-difluoromethyl-γ-(*E*)-homoalkenyl-α,β-unsaturated γ-butyrolactones (*E*)-**7** (X = F) and (*E*)-**8** (X = H), generated in situ from the corresponding adducts (*E*)-**3** and (*E*)-**4** and the intramolecular conjugate ene reaction of γ-trifluoromethyl-γ-homoalkynyl-α,β-unsaturated γ-butyrolactones **11** and **12**, obtained in situ from adducts **5** and **6** (Scheme 1). It is anticipated that the high level of electron-withdrawing ability of the γ-trifluoromethyl and γ-difluoromethyl motifs would have an activating effect to the adjacent α,β-unsaturated carbonyl moiety and would facilitate the intramolecular conjugate ene reaction. The results of the intramolecular conjugate ene reactions of (*E*)-**7**, (*E*)-**8**, **11**, and **12** will establish convenient routes to cis-fused bicyclic γ-butyrolactones **9** (X = F), **10** (X = H) and allenylated cis-fused bicyclic γ-butyrolactones **13** and **14** (Scheme 1). The fused bicyclic γ-butyrolactones are commonly found in the core structures of naturally derived compounds, thus synthetic approach that allows the access to fluorinated analogs of these types of compounds would remarkably extend the scope of fluorine research. It is worth noting that Inomata[9] previously reported an impressive stereoselective synthesis of 5,5-fused bicyclic γ-butyrolactones via a tandem retro-Diels−Alder-ene reaction that the alkenyl

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Scheme 1. Preparation of cis-Fused Bicyclic γ-Butyrolactones 9, 10, 13, and 14 via RDA/ICE Reaction

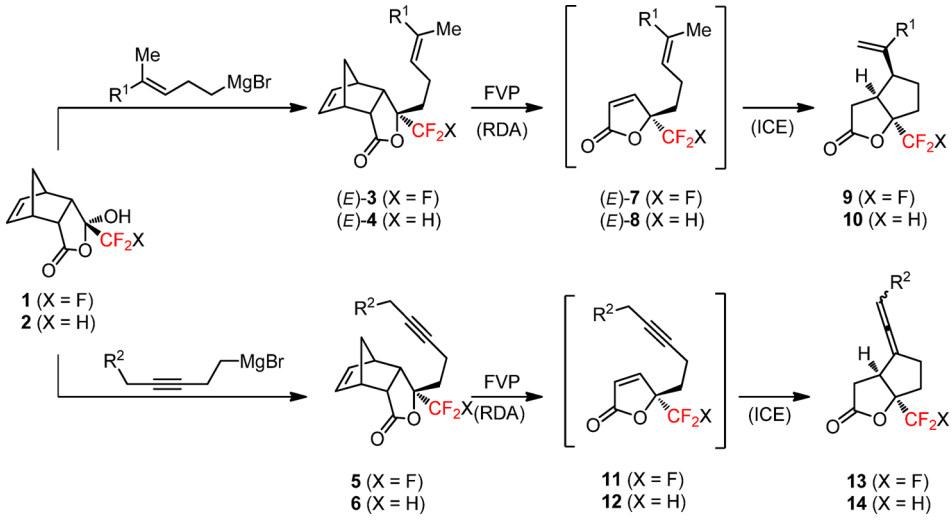
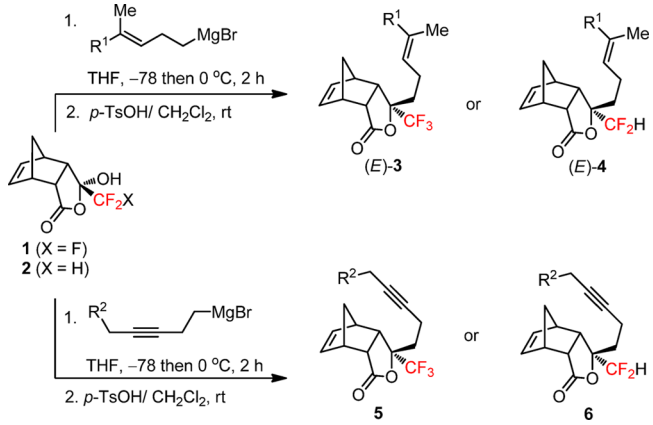


Table 1. Preparation of Compounds (*E*)-3 and (*E*)-4, 5, and 6



entry	substrate	Me / R^1 / MgBr (R^1)	R^2–MgBr (R^2)	(*E*)-**3** or (*E*)-**4** or **5** or **6** (% yield)[a]
1	**1**	Ph	–	**3a** (76)
2	**1**	Me	–	**3b** (82)
3	**1**	4-MeC_6H_4	–	**3c** (88)
4	**1**	2-$MeOC_6H_4$	–	**3d** (91)
5	**2**	Ph	–	**4a** (86)
6	**2**	Me	–	**4b** (95)
7	**2**	4-MeC_6H_4	–	**4c** (98)
8	**2**	2-$MeOC_6H_4$	–	**4d** (96)
9	**1**	–	H	**5a** (46)
10	**1**	–	Me	**5b** (66)
11	**1**	–	Pr	**5c** (67)
12	**2**	–	Pr	**6** (65)

[a]Isolated yield by column chromatography (SiO_2).

side chains were strongly activated by a trimethylsilyl substituent[10] and the resulting products were employed as precursors for synthesis of methyl jasmonate and methyl 6-*epi*-curcurbate.

RESULTS AND DISCUSSION

Our investigation began with the synthesis of the requisite precursors (*E*)-**3** and (*E*)-**4**, **5**, and **6** which are considered as masked γ-fluoromethylated α,β-unsaturated γ-butyrolactones (*E*)-**7**, (*E*)-**8**, **11**, and **12**, respectively. Indeed, compounds **1** and **2** were prepared according to our previously reported method.[4,5] Next, treatment of **1** or **2** with appropriate (*E*)-homoalkenyl- or homoalkynylmagnesium bromides at −78 °C then stirring at 0 °C for 2 h followed by acid-catalyzed lactonization yielded compounds (*E*)-**3** and (*E*)-**4**, **5**, and **6** in moderate to high yields, each as a single isomer. The results are summarized in Table 1. The relative stereochemistries of compounds (*E*)-**3**, (*E*)-**4**, **5**, and **6** were assigned on the same basis of our previously reported works.[4,5]

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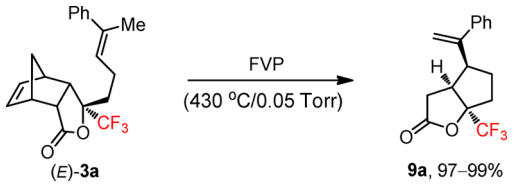
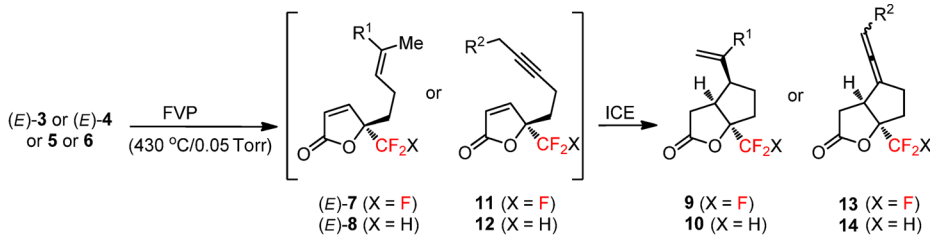
Having the key precursors (*E*)-**3** and (*E*)-**4**, **5**, and **6** in hands, the retro-Diels–Alder reaction/intramolecular conjugate ene cascade (RDA/ICE) reaction was investigated. Compound (*E*)-**3a** bearing a homoalkenyl group was chosen as a benchmark substrate for the optimization of reaction conditions. On the basis of reaction optimization, it was found that the flash-vacuum pyrolysis (FVP) of (*E*)-**3a** at 430 °C/0.05 Torr afforded a single isomer of a cis-fused bicyclic γ-butyrolactone **9a** as a sole product in excellent yields (97–99%) (Scheme 2). The FVP carried out at lower temperature (250 °C/0.05 Torr) led to inferior results. It should also be mentioned that the RDA/ICE reaction of (*E*)-**3a** under thermal conditions (refluxing diphenyl ether, 3 h) gave **9a** in 65% yield after column chromatography.

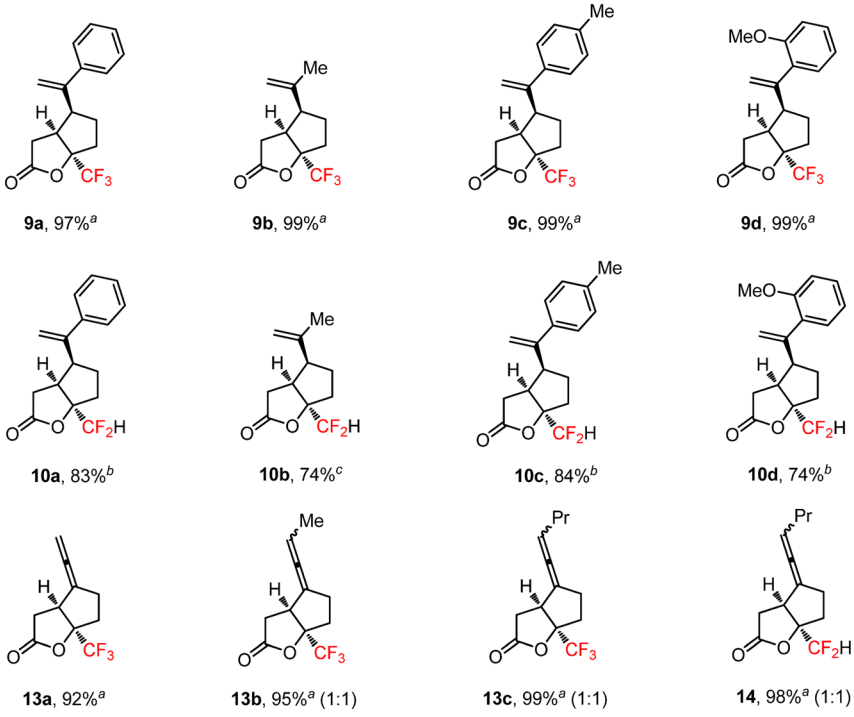
Scheme 2. FVP Conditions for the RDA/ICE Reaction



Under the optimized FVP reaction conditions as for (*E*)-**3a**, the RDA/ICE of (*E*)-**3b–d**, (*E*)-**4a–d**, **5a–c**, and **6** were investigated, and the results are summarized in Table 2. The FVP of (*E*)-**3b–d** gave high yields (99%) of the corresponding trifluoromethylated cis-fused bicyclic γ-butyrolactones **9b–d**, each as a single isomer. To our delight, under similar FVP conditions, when alkynylated adducts **5a–c** and **6** were employed as substrates, the corresponding trifluoromethylated cis-fused allenylated bicyclic γ-butyrolactones **13a–c** and **14** were obtained in high yields (92–99%). It is worth to emphasize here that, after FVP and without chromatographic purification, compounds **9**, **13**, and **14** were obtained as analytically pure compounds. The importance of the γ-trifluoromethyl group in facilitating the rate of the RDA/ICE reaction was realized when the adduct (*E*)-**4a**, containing γ-difluoromethyl moiety, was subjected to the optimized FVP reaction conditions. The reaction afforded the expected γ-difluoromethylated cis-fused bicyclic γ-butyrolactone **10a** along with the unreacted γ-difluoromethyl-α,β-unsaturated γ-butyrolactone (*E*)-**8a** (**10a**:**8a** = 10:1) as determined by the ^{19}F-NMR analysis of the crude pyrolysate. After careful chromato-

Table 2. Preparation of 9, 10, 13, and 14 by the RDA/ICE Reaction of (*E*)-3 and (*E*)-4, 5, and 6





[a]Yield of analytical pure product after FVP. [b]Isolated yield by preparative thin-layer chromatography (SiO_2). [c]Isolated yield by column chromatography (SiO_2).

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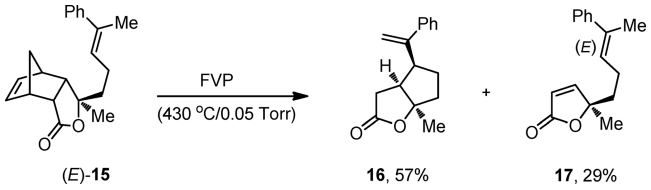
graphic separation (preparative thin-layer chromatography on silica gel), a bicyclic γ-butyrolactone **10a** was obtained in 83% yield as a single isomer. Similar results were observed when (*E*)-**4b−d** were subjected to the FVP conditions. In all cases, mixtures of the corresponding products **10b−d** together with trace amount of the corresponding unreacted γ-difluoromethylated intermediates (*E*)-**8** were obtained after FVP. Each pair of (*E*)-**8** and **10** can be readily separated by chromatographic purification on silica gel to provide **10b−d** in 74−84% yields. The observed experimental results of the ICE reaction of the γ-difluoromethylated compounds (*E*)-**8** implied that the ICE reaction of (*E*)-**8** was not so efficient as that of the γ-trifluoromethylated compounds (*E*)-**7**. The activating effect of the γ-trifluoromethyl moiety in the ICE step was notable and was further emphasized by exposure of compound (*E*)-**15**, bearing a methyl group at the γ-position of the γ-lactone ring, to the standard FVP conditions for the RDA/ICE reaction (430 °C/0.05 Torr) (Scheme 3). The FVP of (*E*)-**15** yielded a

Scheme 3. FVP of γ-Methylated Compound (*E*)-15



RDA/ICE product, bicyclic γ-butyrolactone **16** (57% yield), as a single isomer and a RDA product, α,β-unsaturated γ-butyrolactone (*E*)-**17** (29% yield), after chromatographic purification (SiO_2). At this point, it can be concluded that the γ-trifluoromethyl and the γ-difluoromethyl moieties in α,β-unsaturated γ-butyrolactones (*E*)-**7**, (*E*)-**8**, **11**, and **12** enhanced the efficiency of the ICE process.

The exclusive formation of cis-fused bicyclic γ-butyrolactones **9**, **10**, and **16** through the intramolecular conjugate ene reaction of the in situ-generated α,β-unsaturated γ-butyrolactones (*E*)-**7**, (*E*)-**8**, and **17**, respectively, was proposed to proceed through the transition state **TS-A** (Figure 1). Similarly, the intra-

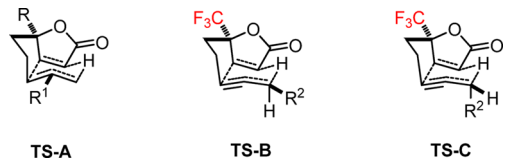


Figure 1. Proposed transition states for the formation of cis-fused bicyclic γ-butyrolactones **9**, **10**, **13**, and **14**.

molecular conjugate ene reaction of the in situ-generated α,β-unsaturated γ-butyrolactones **11** and **12** was proposed to proceed through the transition states **TS-B** and **TS-C**, providing the desired cis-fused allenylated bicyclic γ-butyrolactones **13b−c** and **14** as a 1:1 mixture of isomers.

CONCLUSION

We have successfully established a convenient route to access γ-difluoromethylated and γ-trifluoromethylated cis-fused bicyclic γ-butyrolactones **9**, **10**, **13**, and **14** via the RDA/ICE reaction. The reaction proceeded with high stereoselectivity leading only to the cis-fused bicyclic γ-butyrolactones. The presence of a difluoromethyl or a trifluoromethyl group at the γ-position of the in situ-generated homoalkenyl- or homoalkynyl-α,β-unsaturated γ-butyrolactones (*E*)-**7**, (*E*)-**8**, **11**, and **12** was found to have an enhanced effect on the rate of the RDA/ICE reaction of (*E*)-**3** and (*E*)-**4**, **5**, and **6**. The obtained γ-difluoromethylated and γ-trifluoromethylated cis-fused bicyclic γ-butyrolactones may be found useful as synthetic intermediates for the synthesis of higher functionalized molecules.

EXPERIMENTAL SECTION

General Procedures. ^{1}H NMR spectra were recorded on a 400 MHz spectrometer and reported in ppm. Proton-decoupled ^{13}C NMR spectra were recorded on a 100 MHz spectrometer and reported in ppm. ^{19}F NMR spectra were recorded on a 376 MHz spectrometer and reported in ppm. Reactions were monitored by thin-layer chromatography visualized by UV and a solution of $KMnO_4$. Tetrahydrofuran (THF) was distilled from sodium-benzophenone ketyl. Dichloromethane (CH_2Cl_2) was dried over calcium hydride before distillation and stored over molecular sieves (4 Å). All glassware including needles and syringes were oven-dried and kept in a desiccator before use. The products were purified by column chromatography on silica gel or preparative thin-layer chromatography. Compounds **1** and **2** were prepared according to our previous reports.[4,5]

(3R,3aS*,4R*,7S*,7aR*)-3-((E)-4-Phenylpent-3-en-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**3a**). General Procedure A.* To a stirred suspension of magnesium (turning) (304 mg, 12.5 mmol) in dry THF (2 mL), a solution of (*E*)-(5-bromopent-2-en-2-yl)benzene[11] (563 mg, 2.5 mmol) in dry THF (3 mL) was added dropwise under an argon atmosphere at room temperature. The reaction was allowed to stir at room temperature for 2 h, then the resulting alkenyl Grignard reagent was transferred via a syringe to react with **1** (117 mg, 0.5 mmol) dissolved in dry THF (5 mL) at −78 °C.[4] After the addition, the reaction mixture was brought to 0 °C and stirred for 2 h then quenched with 10% HCl (5 mL) and extracted with EtOAC (4 × 15 mL). The combined organic phases were washed with brine, dried over anhydrous Na_2SO_4, filtered, and concentrated to provide the crude product which was subsequently treated with a catalytic amount of *p*-TsOH in dry CH_2Cl_2 (10 mL) at room temperature for overnight. The reaction was quenched with water and extracted with CH_2Cl_2 (4 × 10 mL). The combined organic phases were washed with brine and dried over anhydrous Na_2SO_4. After filtration and removal of solvent under vacuo, the crude product was purified by column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes) to afford **3a** (138 mg, 76% yield) as a colorless viscous oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.14 (m, 5H), 6.21 (dd, *J* = 5.7, 3.0 Hz, 1H), 6.18−6.10 (m, 1H), 5.59 (dt, *J* = 7.0, 1.2 Hz, 1H), 3.43 (dd, *J* = 8.7, 5.1 Hz, 1H), 3.21 (br s, 1H), 3.17 (br s, 1H), 2.93 (dd, *J* = 8.7, 3.3 Hz, 1H), 2.37−2.17 (m, 2H), 1.97 (s, 3H), 1.91 (dd, *J* = 8.8, 8.2 Hz, 2H), 1.68 (d, *J* = 8.7 Hz, 1H), 1.44 (d, *J* = 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −71.89 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8 (CO), 143.2 (C), 136.8 (C), 135.8 (CH), 135.1 (q, *J* = 4.7 Hz, CH), 128.2 (2 × CH), 126.9 (CH), 125.6 (2 × CH), 125.2 (CH), 124.0 (q, *J* = 282.3 Hz, CF_3), 83.9 (q, *J* = 30.9 Hz, C), 54.2 (CH_2), 48.2 (CH), 47.9 (CH), 45.6 (CH), 44.2 (CH), 38.1 (CH_2), 22.2 (CH_2), 15.9 (CH_3); IR (neat) ν_{max} 2987s, 1790s, 1598w, 1495m, 1446s, 1329s, 1162s, 760s, 732s, 698s cm^{-1}; MS *m*/*z* (%) relative intensity 362 (M^+, 59), 347 (18), 294 (10), 260 (10), 128 (100), 65 (41); HRMS (ESI-TOF) calcd for $C_{21}H_{21}F_3O_2Na$ $[M + Na]^+$ 385.1391, found 385.1406.

(3R,3aS*,4R*,7S*,7aR*)-3-(4-Methylpent-3-en-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**3b**).* According to the general procedure A, the addition (4-methylpent-3-en-1-yl)magnesium bromide to **1** (117 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **3b** (123 mg, 82% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, *J* = 5.7, 3.0 Hz, 1H), 6.16−6.08 (m, 1H), 4.97 (tt, *J* = 7.0, 1.4 Hz, 1H), 3.39 (dd, *J* = 8.8, 5.2 Hz, 1H), 3.22−3.16 (m, 1H), 3.15 (br s, 1H), 2.88 (dd, *J* = 8.8, 3.3 Hz, 1H), 2.14−1.93 (m, 2H), 1.78 (dd, *J* =

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9.0, 8.1 Hz, 2H), 1.67 (td, J = 8.6, 1.6 Hz, 1H), 1.62 (s, 3H), 1.54 (s, 3H), 1.42 (d, J = 8.6 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −72.00 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9 (CO), 135.7 (CH), 135.1 (q, J = 4.6 Hz, CH), 133.6 (C), 124.1 (q, J = 282.1 Hz, CF_3), 121.9 (CH), 84.0 (q, J = 30.7 Hz, C), 54.1 (CH_2), 48.3 (CH), 47.7 (CH), 45.6 (CH), 44.2 (CH), 38.4 (CH_2), 25.6 (CH_3), 21.5 (CH_2), 17.7 (CH_3); IR (neat) ν_{max} 2979s, 1789s, 1579w, 1455m, 1378m, 1329s, 1164s, 813m, 733s cm^{-1}; MS m/z (%) relative intensity 301 (M^+ + 1, 100), 300 (M^+, 95), 272 (22), 233 (27), 164 (20), 151 (24), 122 (15), 65 (45); HRMS (ESI-TOF) calcd for $C_{16}H_{19}F_3O_2Na$ [M + Na]$^+$ 323.1235, found 323.1239.

(3R,3aS*,4R*,7S*,7aR*)-3-((E)-4-(p-Tolyl)pent-3-en-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**3c**).* According to the general procedure A, the addition of (*E*)-(4-(*p*-tolyl)pent-3-en-1-yl)magnesium bromide to **1** (117 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **3c** (166 mg, 88% yield) as a white solid after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). mp 72−74 °C (EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.1 Hz, 2H), 7.12 (d, J = 8.1 Hz, 2H), 6.28 (dd, J = 5.7, 3.1 Hz, 1H), 6.25−6.17 (m, 1H), 5.63 (dt, J = 7.0, 1.1 Hz, 1H), 3.49 (dd, J = 8.8, 5.1 Hz, 1H), 3.28 (br s, 1H), 3.24 (br s, 1H), 3.00 (dd, J = 8.8, 3.3 Hz, 1H), 2.43−2.23 (m, 2H), 2.34 (s, 3H), 2.02 (s, 3H), 1.97 (dd, J = 8.7, 8.3 Hz, 2H), 1.75 (d, J = 8.7 Hz, 1H), 1.50 (d, J = 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −71.89 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9 (CO), 140.3 (C), 136.6 (C), 136.5 (C), 135.7 (CH), 135.1 (q, J = 4.8 Hz, CH), 128.9 (2 × CH), 125.5 (2 × CH), 124.4 (CH), 124.1 (q, J = 281.2 Hz, CF_3), 83.9 (q, J = 30.8 Hz, C), 54.1 (CH_2), 48.2 (CH), 47.9 (CH), 45.6 (CH), 44.2 (CH), 38.2 (CH_2), 22.2 (CH_2), 21.0 (CH_3), 15.9 (CH_3); IR ($CHCl_3$) ν_{max} 3029w, 1782s, 1513w, 1453w, 1169s, 814m cm^{-1}; MS m/z (%) relative intensity 376 (M^+, 14), 375 (64), 374 (24), 272 (8), 159 (13), 128 (94), 65 (9); HRMS (ESI-TOF) calcd for $C_{22}H_{23}F_3O_2Na$ [M + Na]$^+$ 399.1548, found 399.1549.

(3R,3aS*,4R*,7S*,7aR*)-3-((E)-4-(2-Methoxyphenyl)pent-3-en-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**3d**).* According to the general procedure A, the addition of (*E*)-(4-(2-methoxyphenyl)pent-3-en-1-yl)magnesium bromide to **1** (117 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **3d** (179 mg, 91% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (ddd, J = 8.0, 7.6, 1.7 Hz, 1H), 7.00 (dd, J = 7.4, 1.7 Hz, 1H), 6.83 (ddd, J = 7.6, 7.4, 0.9 Hz, 1H), 6.79 (d, J = 8.0 Hz, 1H), 6.20 (dd, J = 5.6, 3.0 Hz, 1H), 6.17−6.09 (m, 1H), 5.28 (dt, J = 6.9, 1.2 Hz, 1H), 3.74 (s, 3H), 3.43 (dd, J = 8.8, 5.2 Hz, 1H), 3.20 (br s, 1H), 3.16 (br s, 1H), 2.94 (dd, J = 8.8, 3.3 Hz, 1H), 2.34−2.15, (m, 2H), 1.95−1.87 (m, 2H), 1.90 (s, 3H), 1.67 (d, J = 8.6 Hz, 1H), 1.43 (d, J = 8.6 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −71.87 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9 (CO), 156.5 (C), 137.0 (C), 135.7 (CH), 135.1 (q, J = 4.6 Hz, CH), 134.2 (C), 129.4 (CH), 128.1 (CH), 126.8 (CH), 124.1 (q, J = 282.2 Hz, CF_3), 120.5 (CH), 110.7 (CH), 84.0 (q, J = 30.8 Hz, C), 55.3 (CH_3), 54.1 (CH_2), 48.3 (CH), 47.7 (CH), 45.6 (CH), 44.2 (CH), 38.0 (CH_2), 21.8 (CH_2), 17.2 (CH_3); IR (neat) ν_{max} 3072w, 2955m, 1789s, 1597m, 1489s, 1435m, 1164s, 756s cm^{-1}; MS m/z (%) relative intensity 293 (M^+ + 1, 16), 292 (M^+, 44), 147 (26), 132 (33), 118 (16), 77 (15); HRMS (ESI-TOF) calcd for $C_{22}H_{23}F_3O_3Na$ [M + Na]$^+$ 415.1497, found 415.1496.

(3R,3aS*,4R*,7S*,7aR*)-3-(Difluoromethyl)-3-((E)-4-phenylpent-3-en-1-yl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**4a**).* According to the general procedure A, the addition of (*E*)-(4-phenylpent-3-en-1-yl)magnesium bromide to **2** (108 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **4a** (148 mg, 86% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes).[4,5] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31−7.12 (m, 5H), 6.26 (dd, J = 5.6, 3.0 Hz, 1H), 6.13−6.07 (m, 1H), 5.71 (dd, J = 56.9, 53.6 Hz, 1H), 5.62 (dd, J = 7.0, 6.5 Hz, 1H), 3.40 (dd, J = 8.9, 5.1 Hz, 1H), 3.25 (br s, 1H), 3.19 (br s, 1H), 2.88 (dd, J = 9.0, 3.5 Hz, 1H), 2.33−2.13 (m, 2H), 2.01−1.90 (m, 1H), 1.97 (s, 3H), 1.86−1.76 (m, 1H), 1.66 (d, J = 8.7 Hz, 1H), 1.42 (d, J = 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.11 (dd, J = 295.3, 53.6 Hz, 1F), −129.76 (dd, J = 295.3, 57.0 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0 (CO), 143.3 (C), 137.2 (CH), 136.3 (C), 134.2 (CH), 128.2 (2 × CH), 126.8 (CH), 125.9 (CH), 125.6 (2 × CH), 114.8 (dd, J = 249.8, 240.8 Hz, CF_2H), 84.7 (dd, J = 29.8, 20.8 Hz, C), 53.6 (CH_2), 48.2 (CH), 47.3 (d, J = 3.5 Hz, CH), 45.5 (d, J = 1.6 Hz, CH), 44.5 (CH), 34.0 (d, J = 5.1 Hz, CH_2), 21.7 (CH_2), 15.9 (CH_3); IR (neat) ν_{max} 2987s, 1778s, 1598w, 1495m, 1445m, 1324m, 1166s, 759s, 730s, 699s cm^{-1}; MS m/z (%) relative intensity 345 (M^+ + 1, 14), 344 (M^+, 45), 343 (15), 294 (8), 192 (15), 178 (26), 129 (100), 65 (28); HRMS (ESI-TOF) calcd for $C_{21}H_{22}F_2O_2Na$ [M + Na]$^+$ 367.1486, found 367.1484.

(3R,3aS*,4R*,7S*,7aR*)-3-(Difluoromethyl)-3-(4-methylpent-3-en-1-yl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**4b**).* According to the general procedure A, the addition of (4-methylpent-3-en-1-yl)magnesium bromide to **2** (108 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **4b** (134 mg, 95% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (dd, J = 5.6, 3.0 Hz, 1H), 6.10 (dd, J = 5.6, 2.5 Hz, 1H), 5.68 (dd, J = 57.0, 53.7 Hz, 1H), 5.00 (t, J = 6.3 Hz, 1H), 3.37 (dd, J = 8.9, 5.1 Hz, 1H), 3.24 (br s, 1H), 3.17 (br s, 1H), 2.85 (dd, J = 8.9, 3.5 Hz, 1H), 2.10−1.89 (m, 2H), 1.87−1.76 (m, 1H), 1.73−1.66 (m, 1H), 1.65 (d, J = 8.6 Hz, 1H), 1.62 (s, 3H), 1.54 (s, 3H), 1.42 (d, J = 8.6 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.27 (dd, J = 295.3, 53.6 Hz, 1F), −130.01 (dd, J = 295.3, 57.2 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0 (CO), 137.1 (CH), 134.2 (CH), 133.1 (C), 122.4 (CH), 114.7 (dd, J = 249.6, 240.9 Hz, CF_2H), 84.8 (dd, J = 29.7, 20.9 Hz, C), 53.5 (CH_2), 48.2 (CH), 47.1 (d, J = 3.6 Hz, CH), 45.4 (d, J = 1.9 Hz, CH), 44.5 (CH), 34.1 (d, J = 5.2 Hz, CH_2), 25.6 (CH_3), 20.8 (CH_2), 17.7 (CH_3); IR (neat) ν_{max} 2973s, 1778s, 1650w, 1454m, 1350m, 1165s, 1069s, 735m, 724m cm^{-1}; MS m/z (%) relative intensity 282 (M^+, 5), 214 (11), 200 (6), 150 (10), 128 (15), 108 (6), 65 (14); HRMS (ESI-TOF) calcd for $C_{16}H_{20}F_2O_2Na$ [M + Na]$^+$ 305.1329, found 305.1330.

(3R,3aS*,4R*,7S*,7aR*)-3-(Difluoromethyl)-3-((E)-4-(p-tolyl)-pent-3-en-1-yl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**4c**).* According to the general procedure A, the addition of (*E*)-(4-(*p*-tolyl)pent-3-en-1-yl)magnesium bromide to **2** (108 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **4c** (176 mg, 98% yield) as a white solid after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). mp 102−104 °C (EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 (d, J = 8.0 Hz, 2H), 7.12 (d, J = 8.0 Hz, 2H), 6.34 (dd, J = 5.7, 3.1 Hz, 1H), 6.21−6.15 (m, 1H), 5.78 (dd, J = 56.8, 53.6 Hz, 1H), 5.67 (dd, J = 8.1, 6.2 Hz, 1H), 3.48 (dd, J = 8.9, 5.1 Hz, 1H), 3.33 (br s, 1H), 3.27 (br s, 1H), 2.96 (dd, J = 8.9, 3.5 Hz, 1H), 2.39−2.20 (m, 2H), 2.33 (s, 3H), 2.07−1.97 (m, 1H), 2.02 (s, 3H), 1.93−1.83 (m, 1H), 1.74 (d, J = 8.7 Hz, 1H), 1.50 (d, J = 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.13 (dd, J = 295.2, 53.4 Hz, 1F), −129.79 (dd, J = 295.2, 56.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0 (CO), 140.5 (C), 137.2 (CH), 136.5 (C), 136.1 (C), 134.2 (CH), 128.9 (2 × CH), 125.4 (2 × CH), 125.1 (CH), 114.8 (dd, J = 249.8, 240.9 Hz, CF_2H), 84.7 (dd, J = 29.7, 20.8 Hz, C), 53.6 (CH_2), 48.2 (CH), 47.3 (d, J = 3.5 Hz, CH), 45.5 (d, J = 1.3 Hz, CH), 44.5 (CH), 34.0 (d, J = 5.1 Hz, CH_2), 21.6 (CH_2), 21.0 (CH_3), 15.9 (CH_3); IR (KBr) ν_{max} 2950m, 1769s, 1638w, 1167s, 1048s, 813s, 721m cm^{-1}; MS m/z (%) relative intensity 359 (M^+ + 1, 12), 358 (M^+, 51), 357 (100), 192 (14), 178 (9), 138 (10), 77 (10); HRMS (ESI-TOF) calcd for $C_{22}H_{24}F_2O_2Na$ [M + Na]$^+$ 381.1642, found 381.1643.

(3R,3aS*,4R*,7S*,7aR*)-3-(Difluoromethyl)-3-((E)-4-(2-methoxyphenyl)pent-3-en-1-yl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**4d**).* According to the general procedure A, the addition of (*E*)-(4-(2-methoxyphenyl)pent-3-en-1-yl)magnesium bromide to **2** (108 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at −78 °C for 2 h and at 0 °C for 2 h gave **4d** (180 mg, 96% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (ddd, J = 8.3, 7.3, 1.6 Hz, 1H), 7.01 (dd, J = 7.4, 1.4 Hz, 1H), 6.83 (dd, J = 7.4, 7.3, 1H), 6.78 (d, J = 8.3, Hz, 1H), 6.26 (dd, J = 5.6, 3.0 Hz, 1H), 6.14−6.08 (m, 1H), 5.71 (dd, J = 56.8, 53.7 Hz, 1H), 5.32 (t, J = 6.8 Hz, 1H), 3.74 (s, 3H), 3.42 (dd, J = 9.0, 5.0 Hz, 1H), 3.25 (br s, 1H), 3.19 (br s, 1H), 2.91 (dd, J = 9.0, 3.5 Hz, 1H), 2.31−2.11 (m,

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2H), 2.00−1.87 (m, 1H), 1.90 (s, 3H), 1.86−1.76 (m, 1H), 1.66 (d, J = 8.7 Hz, 1H), 1.42 (d, J = 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.17 (dd, J = 295.5, 53.8 Hz, 1F), −129.87 (dd, J = 295.5, 57.0 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.0 (CO), 156.6 (C), 137.2 (CH), 136.6 (C), 134.4 (C), 134.3 (CH), 129.5 (CH), 128.0 (CH), 127.5 (CH), 120.5 (CH), 114.8 (dd, J = 249.7, 241.0 Hz, CF_2H), 110.7 (CH), 84.8 (dd, J = 29.7, 20.9 Hz, C), 55.4 (CH_3), 53.6 (CH_2), 48.3 (CH), 47.3 (d, J = 3.5 Hz, CH), 45.5 (d, J = 1.7 Hz, CH), 44.5 (CH), 33.9 (d, J = 5.2 Hz, CH_2), 21.3 (CH_2), 17.2 (CH_3); IR (neat) ν_{max} 3068w, 2953s, 1778s, 1650w, 1597m, 1578m, 1489s, 1248s, 1166s, 756s cm^{-1}; MS m/z (%) relative intensity 374 (M^+, 21), 174 (39), 160 (76), 147 (31), 136 (47), 118 (31), 106 (22), 92 (33), 77 (35); HRMS (ESI-TOF) calcd for $C_{22}H_{24}F_2O_3Na$ [M + Na]$^+$ 397.1591, found 397.1593.

(3R,3aS*,4R*,7S*,7aR*)-3-(Pent-3-yn-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**5a**).* According to the general procedure A, the addition of pent-3-yn-1-ylmagnesium bromide[12] to **1** (117 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **5a** (65 mg, 46% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (dd, J = 5.5, 2.8 Hz, 1H), 6.15−6.05 (m, 1H), 3.44 (dd, J = 8.7, 5.2 Hz, 1H), 3.20 (br s, 1H), 3.14 (br s, 1H), 2.98 (dd, J = 8.7, 3.3 Hz, 1H), 2.29−2.21, (m, 2H), 2.09−1.92 (m, 2H), 1.72−1.64 (m, 1H), 1.69 (t, J = 2.4 Hz, 3H), 1.40 (d, J = 8.7 Hz, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −72.19 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7 (CO), 135.9 (CH), 135.0 (q, J = 4.6 Hz, CH), 123.9 (q, J = 282.2 Hz, CF_3), 83.4 (q, J = 30.9 Hz, C), 78.0 (C), 76.8 (C), 54.2 (CH_2), 48.1 (CH), 47.7 (CH), 45.6 (CH), 44.1 (CH), 37.6 (CH_2), 13.1 (CH_2), 3.4 (CH_3); IR (neat) ν_{max} 2963m, 2225w, 1790s, 1455m, 1378m, 1330m, 1263m, 1165s, 1094s, 734m cm^{-1}; MS m/z (%) relative intensity 284 (M^+, 3), 239 (23), 211 (19), 200 (16), 191 (23), 177 (25), 161 (17), 129 (32), 57 (17); HRMS (ESI-TOF) calcd for $C_{15}H_{15}F_3O_2Na$ [M + Na]$^+$ 307.0922, found 307.0928.

(3R,3aS*,4R*,7S*,7aR*)-3-(Hex-3-yn-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**5b**).* According to the general procedure A, the addition of hex-3-yn-1-ylmagnesium bromide[12] to **1** (117 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **5b** (98 mg, 66% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, J = 5.7, 3.0 Hz, 1H), 6.14−6.06 (m, 1H), 3.46 (dd, J = 8.8, 5.2 Hz, 1H), 3.22−3.17 (m, 1H), 3.14 (br s, 1H), 3.03 (dd, J = 8.8, 3.3 Hz, 1H), 2.31−2.23 (m, 2H), 2.11−1.94 (m, 4H), 1.67 (dt, J = 8.6, 1.5 Hz, 1H), 1.41 (d, J = 8.6 Hz, 1H), 1.03 (t, J = 7.5 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −72.17 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7 (CO), 135.8 (CH), 135.0 (q, J = 4.6 Hz, CH), 123.9 (q, J = 282.2 Hz, CF_3), 83.5 (q, J = 31.0 Hz, C), 83.0 (2 × C), 54.1 (CH_2), 48.1 (CH), 47.6 (CH), 45.5 (CH), 44.1 (CH), 37.5 (CH_2), 14.0 (CH_3), 13.1 (d, J = 1.1 Hz, CH_2), 12.2 (CH_2); IR (neat) ν_{max} 2979m, 2215w, 1790s, 1678w, 1455m, 1330m, 1178s, 1094s, 733m cm^{-1}; MS m/z (%) relative intensity 299 (M^+ + 1, 9), 298 (M^+, 4), 251 (13), 239 (10), 211 (34), 200 (16), 191 (25), 178 (40), 161 (20), 129 (25), 57 (9); HRMS (ESI-TOF) calcd for $C_{16}H_{17}F_3O_2Na$ [M + Na]$^+$ 321.1078, found 321.1085.

(3R,3aS*,4R*,7S*,7aR*)-3-(Oct-3-yn-1-yl)-3-(trifluoromethyl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**5c**).* According to the general procedure A, the addition of oct-3-yn-1-ylmagnesium bromide[12,13] to **1** (117 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **5c** (109 mg, 67% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, J = 5.5, 3.0 Hz, 1H), 6.14−6.07 (m, 1H), 3.45 (dd, J = 8.7, 5.2 Hz, 1H), 3.19 (br s, 1H), 3.14 (br s, 1H), 3.03 (dd, J = 8.7, 3.3 Hz, 1H), 2.27 (dd, J = 7.7, 6.8 Hz, 2H), 2.10−1.93 (m, 4H), 1.67 (d, J = 8.6 Hz, 1H), 1.43−1.26 (m, 5H), 0.83 (t, J = 7.1 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −72.14 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7 (CO), 135.8 (CH), 135.0 (q, J = 4.6 Hz, CH), 123.9 (q, J = 282.2 Hz, CF_3), 83.5 (q, J = 30.9 Hz, C), 81.6 (C), 77.6 (C), 54.1 (CH_2), 48.0 (CH), 47.6 (CH), 45.5 (CH), 44.1 (CH), 37.6 (CH_2), 30.9 (CH_2), 21.9 (CH_2), 18.3 (CH_2), 13.5 (CH_3), 13.1 (d, J = 1.1 Hz, CH_2); IR (neat) ν_{max} 2959m, 2232w, 1790s, 1456w, 1330m, 1177s, 1094s, 733m cm^{-1}; MS m/z (%) relative intensity 326 (M^+, 20), 239 (28), 211 (22), 199 (32), 178 (24), 161 (15), 129 (22), 66 (100); HRMS (ESI-TOF) calcd for $C_{18}H_{21}F_3O_2Na$ [M + Na]$^+$ 349.1391, found 349.1392.

(3R,3aS*,4R*,7S*,7aR*)-3-(Difluoromethyl)-3-(oct-3-yn-1-yl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**6**).* According to the general procedure A, the addition of oct-3-yn-1-ylmagnesium bromide[12,13] to **2** (108 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C then stirring at 0 °C for 2 h gave **6** (100 mg, 65% yield) as a colorless viscous oil after column chromatography (SiO_2, 30% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (dd, J = 5.6, 3.0 Hz, 1H), 6.08 (dd, J = 5.6, 3.0 Hz, 1H), 5.67 (dd, J = 56.8, 53.6 Hz, 1H), 3.44 (dd, J = 9.0, 5.1 Hz, 1H), 3.24 (br s, 1H), 3.17 (br s, 1H), 3.00 (dd, J = 9.0, 3.5 Hz, 1H), 2.30−2.20 (m, 2H), 2.10−2.00 (m, 3H), 1.95−1.85 (m, 1H), 1.65 (d, J = 8.7 Hz, 1H), 1.44−1.28 (m, 5H), 0.83 (t, J = 7.2 Hz, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −126.17 (dd, J = 295.3, 53.2 Hz, 1F), −129.87 (dd, J = 296.3, 55.6 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9 (CO), 137.3 (CH), 134.1 (CH), 114.7 (dd, J = 250.0, 241.1 Hz, CF_2H), 84.3 (dd, J = 29.8, 20.6 Hz, C), 81.3 (C), 78.2 (C), 53.6 (CH_2), 48.0 (CH), 47.0 (d, J = 3.7 Hz, CH), 45.4 (d, J = 1.8 Hz, CH), 44.5 (CH), 33.7 (d, J = 5.2 Hz, CH_2), 30.9 (CH_2), 21.9 (CH_2), 18.3 (CH_2), 13.6 (CH_3), 12.6 (CH_2); IR (neat) ν_{max} 2957m, 1778s, 1453w, 1325w, 1163s, 1059s, 726m cm^{-1}; MS m/z (%) relative intensity 309 (M^+ + 1, 1), 326 (M^+, 2), 239 (8), 211 (13), 199 (15), 178 (42), 161 (17), 129 (33), 66 (100); HRMS (ESI-TOF) calcd for $C_{18}H_{22}F_2O_2Na$ [M + Na]$^+$ 331.1486, found 331.1484.

(3aS,4S*,6aR*)-4-(1-Phenylvinyl)-6a-(trifluoromethyl)-hexahydro-2H-cyclopenta[b]furan-2-one (**9a**). General Procedure B.* Compound **3a** (36 mg, 0.1 mmol) was placed in a flash-vacuum pyrolysis apparatus (conditions: oven temperature 220 °C, column temperature 430 °C, pressure 0.05 Torr)[4,5] to provide **9a** (29 mg, 97%) as a white solid. mp 64−66 °C (EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40−7.28 (m, 5H), 5.47 (s, 1H), 5.13 (d, J = 1.6 Hz, 1H), 3.46−3.37 (m, 1H), 3.04−2.95 (m, 1H), 2.39 (dd, J = 19.2, 5.1 Hz, 1H), 2.29 (dd, J = 19.2, 10.8 Hz, 1H), 2.30−2.22 (m, 1H), 2.19−2.08 (m, 2H), 1.92−1.79 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.40 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1 (CO), 146.4 (C), 140.4 (C), 128.8 (2 × CH), 128.2 (CH), 126.1 (2 × CH), 124.3 (q, J = 278.8 Hz, CF_3), 115.6 (CH_2), 91.9 (q, J = 31.5 Hz, C), 47.3 (CH), 40.7 (CH), 32.0 (CH_2), 29.2 (CH_2), 26.3 (CH_2); IR (KBr) ν_{max} 2974m, 1798s, 1635w, 1446m, 1314m, 1175s, 698s cm^{-1}; MS m/z (%) relative intensity 296 (M^+, 18), 219 (17), 194 (27), 127 (88), 126 (100); HRMS (ESI-TOF) calcd for $C_{16}H_{15}F_3O_2Na$ [M + Na]$^+$ 319.0922, found 319.0923.

(3aS,4S*,6aR*)-4-(Prop-1-en-2-yl)-6a-(trifluoromethyl)-hexahydro-2H-cyclopenta[b]furan-2-one (**9b**).* According to the general procedure B, flash-vacuum pyrolysis of **3b** (30 mg, 0.1 mmol) provided **9b** (23 mg, 99%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.94 (d, J = 1.3 Hz, 1H), 4.72 (s, 1H), 3.12−3.04 (m, 1H), 2.65−2.57 (m, 1H), 2.56 (dd, J = 19.1, 11.1 Hz, 1H), 2.35 (dd, J = 19.1, 4.8 Hz, 1H), 2.12 (dd, J = 13.8, 6.2 Hz, 1H), 1.96 (dt, J = 13.8, 6.3 Hz, 1H), 1.89−1.81 (m, 1H), 1.71−1.57 (m, 1H), 1.63 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.41 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2 (CO), 142.2 (C), 124.4 (q, J = 278.9 Hz, CF_3), 113.4 (CH_2), 92.0 (q, J = 31.4 Hz, C), 49.8 (CH), 40.4 (CH), 32.1 (CH_2), 28.9 (CH_2), 25.8 (CH_2), 22.7 (CH_3); IR (neat) ν_{max} 2973m, 1802s, 1651m, 1445m, 1369s, 1312s, 1168s, 1083s, 901m, 731m cm^{-1}; MS m/z (%) relative intensity 235 (M^+ + 1, 31), 234 (M^+, 10), 194 (43), 127 (49), 126 (7), 105 (36), 79 (13); HRMS (ESI-TOF) calcd for $C_{11}H_{13}F_3O_2Na$ [M + Na]$^+$ 257.0765, found 257.0762.

(3aS,4S*,6aR*)-4-(1-(p-Tolyl)vinyl)-6a-(trifluoromethyl)-hexahydro-2H-cyclopenta[b]furan-2-one (**9c**).* According to the general procedure B, flash-vacuum pyrolysis of **3c** (38 mg, 0.1 mmol) provided **9c** (31 mg, 99%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (d, J = 8.2 Hz, 2H), 7.09 (d, J = 8.2 Hz, 2H), 5.36 (s, 1H), 5.01 (d, J = 1.5 Hz, 1H), 3.37−3.27 (m, 1H), 2.97−2.88 (m, 1H), 2.31 (dd, J = 19.3, 5.1 Hz, 1H), 2.28 (s, 3H), 2.22 (dd, J = 19.3, 10.9 Hz, 1H), 2.20−2.14 (m, 1H), 2.12−1.99 (m, 2H), 1.84−

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1.71 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.41 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1 (CO), 146.2 (C), 138.1 (C), 137.5 (C), 129.5 (2 × CH), 125.9 (2 × CH), 124.3 (q, J = 278.8 Hz, CF_3), 114.7 (CH_2), 91.8 (q, J = 31.4 Hz, C), 47.3 (CH), 40.8 (CH), 32.0 (CH_2), 29.2 (CH_2), 26.3 (CH_2), 21.1 (CH_3); IR (neat) ν_{max} 3091w, 3026w, 2969m, 1800s, 1628w, 1513m, 1367m, 1151s, 1078s, 826s, 731m cm^{-1}; MS m/z (%) relative intensity 311 (M^+ + 1, 5), 310 (M^+, 5), 228 (2), 175 (100), 152 (4), 128 (21); HRMS (ESI-TOF) calcd for $C_{17}H_{17}F_3O_2Na$ [M + Na]$^+$ 333.1078, found 333.1075.

(3aS,4S*,6aR*)-4-(1-(2-Methoxyphenyl)vinyl)-6a-(trifluoromethyl)hexahydro-2H-cyclopenta[b]furan-2-one* (**9d**). According to the general procedure B, flash-vacuum pyrolysis of **3d** (39 mg, 0.1 mmol) provided **9d** (32 mg, 99%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (ddd, J = 8.0, 7.3, 1.6 Hz, 1H), 7.01 (dd, J = 7.8, 1.6 Hz, 1H), 6.87 (ddd, J = 7.8, 7.3, 0.9 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 5.20 (s, 1H), 5.12 (s, 1H), 3.76 (s, 3H), 3.56−3.46 (m, 1H), 2.81−2.72 (m, 1H), 2.45 (dd, J = 19.3, 5.3 Hz, 1H), 2.28 (dd, J = 19.3, 11.2 Hz, 1H), 2.14 (dd, J = 13.1, 6.5 Hz, 1H), 2.08−1.97 (m, 2H), 1.78−1.63 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −80.52 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.4 (CO), 156.3 (C), 146.0 (C), 130.5 (C), 129.8 (CH), 129.2 (CH), 124.4 (q, J = 278.8 Hz, CF_3), 120.9 (CH), 117.1 (CH_2), 111.0 (CH), 92.0 (q, J = 31.9 Hz, C), 55.4 (CH_3), 47.9 (CH), 41.0 (CH), 32.2 (CH_2), 29.6 (CH_2), 26.2 (CH_2); IR (KBr) ν_{max} 3075w, 2965m, 1800s, 1629w, 1598m, 1490s, 1164s, 1023s, 756s cm^{-1}; MS m/z (%) relative intensity 326 (M^+, 19), 227 (17), 159 (100), 136 (16), 135 (16), 105 (13); HRMS (ESI-TOF) calcd for $C_{17}H_{17}F_3O_3Na$ [M + Na]$^+$ 349.1027, found 349.1031.

(3aS,4S*,6aR*)-6a-(Difluoromethyl)-4-(1-phenylvinyl)-hexahydro-2H-cyclopenta[b]furan-2-one* (**10a**). According to the general procedure B, flash-vacuum pyrolysis of **4a** (34 mg, 0.1 mmol) provided **10a** (23 mg, 83%) as a colorless oil after preparative thin-layer chromatography (SiO_2, 5% MeOH in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34−7.21 (m, 5H), 5.79 (dd, J = 55.9, 55.8 Hz, 1H), 5.38 (s, 1H), 5.05 (d, J = 1.3 Hz, 1H), 3.33−3.23 (m, 1H), 2.97−2.88 (m, 1H), 2.30 (dd, J = 19.2, 5.0 Hz, 1H), 2.19 (dd, J = 19.2, 10.9 Hz, 1H), 2.12−1.91 (m, 3H), 1.85−1.73 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −130.39 (dd, J = 289.2, 55.8 Hz, 1F), −131.38 (dd, J = 289.2, 55.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8 (CO), 146.9 (C), 140.7 (C), 128.7 (2 × CH), 128.0 (CH), 126.1 (2 × CH), 115.2 (CH_2), 113.9 (dd, J = 243.8, 243.8 Hz, CF_2H), 93.1 (dd, J = 25.8, 23.6 Hz, C), 47.3 (CH), 39.4 (CH), 31.8 (CH_2), 29.7 (CH_2), 26.3 (CH_2); IR (neat) ν_{max} 2925m, 1783s, 1633m, 1495m, 1314m, 1191s, 1066s, 701m cm^{-1}; MS m/z (%) relative intensity 279 (M^+ + 1, 5), 278 (M^+, 6), 277 (3), 194 (16), 154 (8), 140 (4), 126 (3), 77 (23); HRMS (ESI-TOF) calcd for $C_{16}H_{16}F_2O_2Na$ [M + Na]$^+$ 301.1016, found 301.1018.

(3aS,4S*,6aR*)-6a-(Difluoromethyl)-4-(prop-1-en-2-yl)-hexahydro-2H-cyclopenta[b]furan-2-one* (**10b**). According to the general procedure B, flash-vacuum pyrolysis of **4b** (28 mg, 0.1 mmol) provided **10b** (16 mg, 74%) as a colorless oil after column chromatography (SiO_2, 3% MeOH in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (dd, J = 56.0, 55.7 Hz, 1H), 4.92 (s, 1H), 4.71 (s, 1H), 3.11−3.02 (m, 1H), 2.58−2.50 (m, 1H), 2.51 (dd, J = 19.1, 11.1 Hz, 1H), 2.32 (dd, J = 19.1, 4.8 Hz, 1H), 2.00 (dd, J = 13.2, 6.0 Hz, 1H), 1.88 (ddd, J = 6.7, 6.2, 1.7 Hz, 1H), 1.86−1.76 (m, 1H), 1.71−1.62 (m, 1H), 1.63 (s, 3H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −130.38 (dd, J = 289.7, 55.8 Hz, 1F), −131.47 (dd, J = 289.7, 55.6 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9 (CO), 142.7 (C), 114.0 (dd, J = 243.9, 243.8 Hz, CF_2H), 113.0 (CH_2), 93.2 (dd, J = 26.4, 23.4 Hz, C), 49.8 (CH), 38.9 (CH), 31.9 (CH_2), 29.4 (CH_2), 25.8 (CH_2), 22.8 (CH_3); IR (neat) ν_{max} 2927s, 2856m, 1789s, 1650m, 1444m, 1380m, 1235m, 1193s, 1070s cm^{-1}; MS m/z (%) relative intensity 216 (M^+, 2), 211 (12), 208 (16), 178 (9), 151 (5), 97 (10); HRMS (ESI-TOF) calcd for $C_{11}H_{14}F_2O_2Na$ [M + Na]$^+$ 239.0860, found 239.0858.

(3aS,4S*,6aR*)-6a-(Difluoromethyl)-4-(1-(p-tolyl)vinyl)-hexahydro-2H-cyclopenta[b]furan-2-one* (**10c**). According to the general procedure B, flash-vacuum pyrolysis of **4c** (36 mg, 0.1 mmol) provided **10c** (25 mg, 84%) as a colorless oil after preparative thin-layer chromatography (SiO_2, 5% MeOH in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, J = 8.1 Hz, 2H), 7.09 (d, J = 8.1 Hz, 2H), 5.78 (dd, J = 55.9, 55.8 Hz, 1H), 5.35 (s, 1H), 5.00 (d, J = 1.0 Hz, 1H), 3.30−3.21 (m, 1H), 2.98−2.88 (m, 1H), 2.29 (dd, J = 19.2, 5.1 Hz, 1H), 2.28 (s, 3H), 2.19 (dd, J = 19.2, 10.9 Hz, 1H), 2.12−1.90 (m, 3H), 1.84−1.72 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −130.39 (dd, J = 290.0, 56.4 Hz, 1F), −131.39 (dd, J = 290.0, 55.8 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9 (CO), 146.6 (C), 137.9 (C), 137.7 (C), 129.4 (2 × CH), 126.0 (2 × CH), 114.4 (CH_2), 114.0 (dd, J = 243.9, 243.9 Hz, CF_2H), 93.1 (dd, J = 25.4, 23.9 Hz, C), 47.3 (CH), 39.4 (CH), 31.8 (CH_2), 29.7 (CH_2), 26.3 (CH_2), 21.1 (CH_3); IR (neat) ν_{max} 3090w, 3026w, 1783s, 1626w, 1513m, 1190s, 1124s, 1069s, 826m, 732m cm^{-1}; MS m/z (%) relative intensity 293 (M^+ + 1, 9), 292 (M^+, 11), 291 (5), 227 (26), 175 (100), 140 (8), 91 (9); HRMS (ESI-TOF) calcd for $C_{17}H_{18}F_2O_2Na$ [M + Na]$^+$ 315.1173, found 315.1176.

(3aS,4S*,6aR*)-6a-(Difluoromethyl)-4-(1-(2-methoxyphenyl)-vinyl)hexahydro-2H-cyclopenta[b]furan-2-one* (**10d**). According to the general procedure B, flash-vacuum pyrolysis of **4d** (37 mg, 0.1 mmol) provided **10d** (23 mg, 74%) as a white solid after preparative thin-layer chromatography (SiO_2, 5% MeOH in hexanes). mp 106−107 °C (EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (ddd, J = 8.1, 7.3, 1.4 Hz, 1H), 7.00 (dd, J = 7.4, 1.5 Hz, 1H), 6.86 (dd, J = 7.4, 7.3 Hz, 1H), 6.82 (d, J = 8.1 Hz, 1H), 5.74 (dd, J = 56.0, 55.7 Hz, 1H), 5.18 (s, 1H), 5.12 (s, 1H), 3.75 (s, 3H), 3.48−3.37 (m, 1H), 2.80−2.70 (m, 1H), 2.43 (dd, J = 19.2, 5.3 Hz, 1H), 2.24 (dd, J = 19.2, 11.2 Hz, 1H), 2.07−1.87 (m, 3H), 1.78−1.64 (m, 1H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −130.41 (dd, J = 288.2, 55.1 Hz, 1F), −131.54 (dd, J = 288.2, 55.1 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2 (CO), 156.4 (C), 146.4 (C), 130.8 (C), 129.8 (CH), 129.0 (CH), 120.8 (CH), 116.8 (CH_2), 114.0 (dd, J = 243.9, 243.8 Hz, CF_2H), 110.9 (CH), 93.2 (dd, J = 25.9, 23.4 Hz, C), 55.4 (CH_3), 47.9 (CH), 39.6 (CH), 31.9 (CH_2), 30.0 (CH_2), 26.1 (CH_2); IR (KBr) ν_{max} 3089w, 3012w, 2958w, 1779s, 1619w, 1491w, 1252m, 1162m, 1117m, 1065s, 1018s, 759m cm^{-1}; MS m/z (%) relative intensity 309 (M^+ + 1, 8), 308 (M^+, 2), 277 (2), 201 (25), 187 (23), 175 (34), 123 (22), 107 (25); HRMS (ESI-TOF) calcd for $C_{17}H_{18}F_2O_3Na$ [M + Na]$^+$ 331.1122, found 331.1120.

(3aS,6aR*)-6a-(Trifluoromethyl)-4-vinylidenehexahydro-2H-cyclopenta[b]furan-2-one* (**13a**). According to the general procedure B, flash-vacuum pyrolysis of **5a** (28 mg, 0.1 mmol) provided **13a** (20 mg, 92%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.93−4.80 (m, 2H), 3.55−3.47 (m, 1H), 2.91 (dd, J = 18.2, 9.2 Hz, 1H), 2.70−2.47 (m, 3H), 2.17 (dd, J = 7.8, 7.4 Hz, 2H); ^{19}F NMR (376 MHz, $CDCl_3$) δ −79.83 (s, 3 × F); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.8 (C), 174.5 (CO), 124.3 (q, J = 279.8 Hz, CF_3), 103.8 (C), 91.8 (q, J = 31.1 Hz, C), 79.7 (CH_2), 43.0 (CH), 35.2 (CH_2), 31.4 (CH_2), 28.3 (CH_2); IR (neat) ν_{max} 2964s, 1966w, 1807s, 1682w, 1442m, 1366m, 1265s, 1164s, 1070s, 802m cm^{-1}; MS m/z (%) relative intensity 219 (M^+ + 1, 15), 218 (M^+, 42), 217 (27), 159 (49), 133 (39), 122 (23), 105 (61), 77 (100); HRMS (ESI-TOF) calcd for $C_{10}H_9F_3O_2Na$ [M + Na]$^+$ 241.0452, found 241.0451.

(3aS,6aR*)-4-(Prop-1-en-1-ylidene)-6a-(trifluoromethyl)-hexahydro-2H-cyclopenta[b]furan-2-one* (**13b**). According to the general procedure B, flash-vacuum pyrolysis of **5b** (30 mg, 0.1 mmol) provided a 1:1 mixture of **13b** (22 mg, 95%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, interpreted for two isomers) δ 5.32−5.20 (m, 2H), 3.50−3.40 (m, 2H), 2.91 and 2.87 (each dd, J = 14.8, 9.2 and 14.6, 9.3 Hz, respectively, 2H), 2.64−2.43 (m, 6H), 2.20−2.12 (m, 4H), 1.62 and 1.61 (each d, J = 7.1 and 7.0 Hz, respectively, 6H); ^{19}F NMR (376 MHz, $CDCl_3$, interpreted for two isomers) δ −79.85 (s, 6 × F); ^{13}C NMR (100 MHz, $CDCl_3$, interpreted for two isomers) δ 199.1 (C), δ 199.0 (C), 174.8 (CO), 174.7 (CO), 124.4 (q, J = 279.9 Hz, CF_3), 124.3 (q, J = 279.7 Hz, CF_3), 104.2 (C), 103.8 (C), 91.8 (q, J = 30.8 Hz, C), 91.7 (q, J = 30.8 Hz, C), 91.1 (CH), 91.0 (CH), 43.3 (CH), 42.9 (CH), 35.9 (CH_2), 35.3 (CH_2), 31.3 (2× CH_2), 28.5 (2 × CH_2), 14.5 (CH_3), 14.4 (CH_3); IR ($CHCl_3$) ν_{max} 3020m, 2928m, 1804s, 1462w, 1368w, 1262s, 1188s, 1098s, 1015s cm^{-1}; MS m/z (%) relative intensity 233 (M^+ + 1, 10), 232 (M^+, 7), 219 (26), 159 (34), 133 (43), 122 (18), 105 (18), 77 (70); HRMS (ESI-TOF) calcd for $C_{11}H_{11}F_3O_2Na$ [M + Na]$^+$ 255.0609, found 255.0612.

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(3aS,6aR*)-4-(Pent-1-en-1-ylidene)-6a-(trifluoromethyl)-hexahydro-2H-cyclopenta[b]furan-2-one (**13c**).* According to the general procedure B, flash-vacuum pyrolysis of **5c** (35 mg, 0.1 mmol) provided a 1:1 mixture of **13c** (26 mg, 99%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, interpreted for two isomers) δ 5.35−5.20 (m, 2H), 3.50−3.40 (m, 2H), 2.91 and 2.87 (each dd, J = 12.8, 9.2 and 12.9, 9.2 Hz, respectively, 2H), 2.62−2.43 (m, 6H), 2.16 (dd, J = 7.1, 6.7 Hz, 4H), 1.93 and 1.92 (each q, J = 7.1 and 7.1 Hz, respectively, 4H), 1.34 (sept, J = 7.2 Hz, 4H), 0.86 and 0.85 (each t, J = 7.3, 7.4 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$, interpreted for two isomers) δ −79.88 (s, 6 × F); ^{13}C NMR (100 MHz, $CDCl_3$, interpreted for two isomers) δ 198.3 (C), δ 198.2 (C), 174.8 (CO), 174.7 (CO), 124.4 (q, J = 279.9 Hz, CF_3), 124.3 (q, J = 279.8 Hz, CF_3), 104.6 (C), 104.2 (C), 96.4 (CH), 96.1 (CH), 91.8 (q, J = 30.9 Hz, C), 91.7 (q, J = 30.9 Hz, C), 43.3 (CH), 43.0 (CH), 35.8 (CH_2), 35.2 (CH_2), 31.3 (2× CH_2), 31.0 (CH_2), 30.8 (CH_2), 28.7 (CH_2), 28.6 (CH_2), 22.2 (CH_2), 22.1 (CH_2), 13.6 (CH_3), 13.5 (CH_3); IR ($CHCl_3$) ν_{max} 2962m, 1808s, 1456w, 1366m, 1312m, 1183s, 1070s cm^{-1}; MS m/z (%) relative intensity 261 (M^+ + 1, 22), 260 (M^+, 11), 232 (100), 150 (10), 135 (33), 122 (11), 105 (17), 77 (36); HRMS (ESI-TOF) calcd for $C_{13}H_{15}F_3O_2Na$ [M + Na]$^+$ 283.0922, found 283.0923.

(3aS,6aR*)-6a-(Difluoromethyl)-4-(pent-1-en-1-ylidene)-hexahydro-2H-cyclopenta[b]furan-2-one (**14**).* According to the general procedure B, flash-vacuum pyrolysis of **6** (33 mg, 0.1 mmol) provided a 1:1 mixture of **14** (24 mg, 98%) as a pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, interpreted for two isomers) δ 5.82 and 5.81 (each dd, J = 55.4, 55.3 and 55.4, 55.4 Hz, respectively, 2H), 5.31−5.20 (m, 2H), 3.46−3.38 (m, 2H), 2.88 and 2.84 (each dd, J = 13.0, 9.3 and 13.1, 9.3 Hz, respectively, 2H), 2.64−2.51 (m, 2H), 2.46 (dd, J = 10.0, 9.7 Hz, 4H), 2.10−1.97 (m, 4H), 1.93 and 1.92 (each q, J = 7.1 and 7.1 Hz, respectively, 4H), 1.34 (sept, J = 7.3 Hz, 4H), 0.86 and 0.85 (each t, J = 7.4, 7.4 Hz, 6H); ^{19}F NMR (376 MHz, $CDCl_3$, interpreted for two isomers) δ −130.91 (dd, J = 55.1, 12.2 Hz, 1F), −130.94 (dd, J = 55.1, 10.3 Hz, 1F); ^{13}C NMR (100 MHz, $CDCl_3$, interpreted for two isomers) δ 198.2 (C), δ 198.1 (C), 175.6 (CO), 175.5 (CO), 114.3 (dd, J = 244.6, 244.5 Hz, CF_2H), 114.2 (dd, J = 244.6, 244.4 Hz, CF_2H), 105.1 (C), 104.8 (C), 95.9 (CH), 95.6 (CH), 93.0 (dd, J = 23.8, 23.4 Hz, C), 92.9 (dd, J = 23.7, 23.5 Hz, C), 41.9 (CH), 41.6 (CH), 36.4 (CH_2), 35.9 (CH_2), 31.6 (2× CH_2), 31.0 (CH_2), 30.9 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 22.3 (CH_2), 22.1 (CH_2), 13.6 (CH_3), 13.5 (CH_3); IR (neat) ν_{max} 2961m, 1793s, 1438w, 1390w, 1175m, 1063s cm^{-1}; MS m/z (%) relative intensity 243 (M^+ + 1, 84), 242 (M^+, 9), 194 (17), 149 (15), 135 (57), 121 (19), 105 (42), 91 (100); HRMS (ESI-TOF) calcd for $C_{13}H_{16}F_2O_2Na$ [M + Na]$^+$ 265.1016, found 265.1019.

(3R,3aS*,4R*,7S*,7aR*)-3-Methyl-3-((E)-4-phenylpent-3-en-1-yl)-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3H)-one (**15**).* According to the general procedure A, the addition of (*E*)-(4-phenylpent-3-en-1-yl)magnesium bromide to (3*R**,3a*S**,4*R**,7-*S**,7a*R**)-3-hydroxy-3-methyl-3a,4,7,7a-tetrahydro-4,7-methanoisobenzofuran-1(3*H*)-one[4,14] (90 mg, 0.5 mmol) in dry THF (5 mL) at −78 °C, then stirring at 0 °C for 2 h afforded **15** (106 mg, 69% yield) as a colorless viscous oil after column chromatography (SiO_2, 60% CH_2Cl_2 in hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.12 (m, 5H), 6.19 (br s, 2H), 5.62 (t, J = 6.8 Hz, 1H), 3.37 (dd, J = 8.8, 5.1 Hz, 1H), 3.20 (br s, 1H), 2.98 (br s, 1H), 2.73 (dd, J = 8.9, 3.6 Hz, 1H), 2.29−2.13 (m, 2H), 1.95 (s, 3H), 1.65 (dd, J = 7.9, 7.6 Hz, 2H), 1.57 (d, J = 8.4 Hz, 1H), 1.36 (d, J = 8.4 Hz, 1H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5 (CO), 143.5 (C), 135.9 (CH), 135.6 (C), 134.7 (CH), 128.1 (2 × CH), 126.7 (CH), 126.6 (CH), 125.5 (2 × CH), 86.0 (C), 52.8 (CH_2), 50.6 (CH), 49.3 (CH), 45.5 (CH), 45.1 (CH), 44.6 (CH_2), 22.8 (CH_2), 21.7 (CH_3), 15.8 (CH_3); IR (neat) ν_{max} 3063w, 2974s, 1756s, 1684w, 1495m, 1446m, 1382m, 1260m, 981m, 760s, 700s cm^{-1}; MS m/z (%) relative intensity 308 (M^+, 5), 307 (9), 262 (11), 185 (11), 172 (10) 159 (18), 145 (100), 132 (24), 118 (26), 78 (39), 77 (48); HRMS (ESI-TOF) calcd for $C_{21}H_{24}O_2Na$ [M + Na]$^+$ 331.1674, found 331.1676.

(3aS,4S*,6aR*)-6a-Methyl-4-(1-phenylvinyl)hexahydro-2H-cyclopenta[b]furan-2-one (16) and (E)-5-Methyl-5-(4-phenylpent-3-en-1-yl)furan-2(5H)-one (**17**).* According to the general procedure B, flash-vacuum pyrolysis of **15** (31 mg, 0.1 mmol) provided **16** as a white solid (14 mg, 57%) together with **17** as a colorless oil (7 mg, 29%) after preparative thin-layer chromatography (SiO_2, 5% MeOH in hexanes). **16**; mp 81−83 °C (EtOAc/Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.15 (m, 5H), 5.34 (s, 1H), 5.04 (s, 1H), 3.30−3.20 (m, 1H), 2.45 (ddd, J = 9.8, 8.4, 5.0 Hz, 1H), 2.29 (dd, J = 19.4, 5.5 Hz, 1H), 2.22 (dd, J = 19.4, 10.3 Hz, 1H), 2.14 (dd, J = 12.9, 5.0 Hz, 1H), 1.91−1.84 (m, 1H), 1.80−1.62 (m, 2H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1 (CO), 147.6 (C), 141.3 (C), 128.6 (2 × CH), 127.8 (CH), 126.2 (2 × CH), 114.9 (CH_2), 94.5 (C), 47.6 (CH), 45.8 (CH), 38.8 (CH_2), 30.8 (CH_2), 27.3 (CH_2), 26.6 (CH_3); IR (neat) ν_{max} 3057w, 2967s, 1732s, 1626m, 1496m, 1382m, 1276m, 1176m, 956m, 781m cm^{-1}; MS m/z (%) relative intensity 243 (M^+ + 1, 57), 242 (M^+, 21), 196 (39), 165 (18), 128 (100), 77 (30); HRMS (ESI-TOF) calcd for $C_{16}H_{18}O_2Na$ [M + Na]$^+$ 265.1204, found 265.1206. **17**; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 5.6 Hz, 1H), 7.29−7.13 (m, 5H), 5.98 (d, J = 5.6 Hz, 1H), 5.59 (dt, J = 7.1, 1.3 Hz, 1H), 2.22−2.02 (m, 2H), 1.98−1.90 (m, 1H), 1.93 (s, 3H), 1.79 (ddd, J = 14.0, 10.5, 5.7 Hz, 1H), 1.45 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5 (CO), 160.1 (CH), 143.5 (C), 136.0 (C), 128.2 (2 × CH), 126.8 (CH), 126.4 (CH), 125.6 (2 × CH), 120.6 (CH), 88.7 (C), 38.0 (CH_2), 24.2 (CH_3), 23.2 (CH_2), 15.9 (CH_3); IR (neat) ν_{max} 3085w, 2925s, 1755s, 1603w, 1495w, 1448m, 1261s, 1026s, 780m cm^{-1}; MS m/z (%) relative intensity 243 (M^+ + 1, 29), 242 (M^+, 25), 196 (25), 117 (40), 106 (11), 93 (16), 77 (86); HRMS (ESI-TOF) calcd for $C_{16}H_{18}O_2Na$ [M + Na]$^+$ 265.1204, found 265.1208.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01562.

Copies of ^{1}H, ^{13}C, and ^{19}F NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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