

A Formal Total Synthesis of Salvadione

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The tricyclic 6-7-6 core structure of the triterpene salvadione (**1**) was obtained in an efficient manner from the aryl bromide **16** and the alkyl iodide **35** carrying a methylenecyclohexane group at the terminus. Alkylation of the anion derived from **16** with the iodide **35** gave the tethered system **36**. This compound was converted into the allylic bromide **40**. Finally, a

Lewis acid mediated intramolecular Friedel–Crafts alkylation furnished the target structure **13** in good overall yield. The synthesis of tricyclic compound **13** represents a formal total synthesis of salvadione (**1**).

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Introduction

The plant *salvia bucharica* is common in Central Asia and in many countries it is still in use as traditional medicine.^[1,2] The plant belongs to the family of Lamiaceae whose members have been the source of several antitumor compounds. Some years ago, the group of Ahmad isolated and characterized a range of interesting polycyclic triterpenes from *Salvia bucharica*, among them salvadione A^[3] (**1**), perovskone^[4] (**2**), and isoperadione^[5] (**3**) (Figure 1).

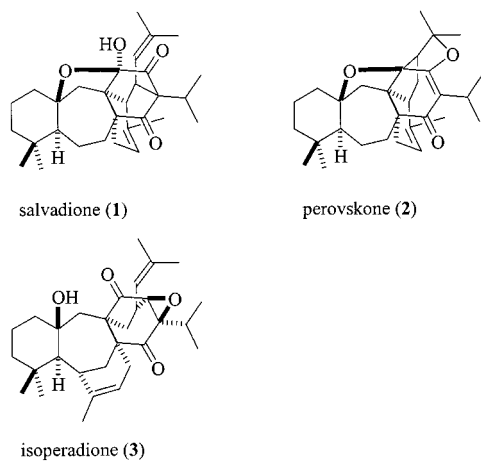


Figure 1. Structures of salvadione (**1**) and related compounds.

According to a biosynthetic proposal by Ahmad,^[2] these compounds originate from the tricyclic compound **6** and fragments derived from geranyl diphosphate (**4**). Thus, a

Diels–Alder reaction between quinone **6** and a diene of type **5** (*trans*- β -ocimene oxide) would form the cyclohexene ring resulting in compound **7**. Opening of the epoxide would yield compound **8** with an allylic system (X = phosphate or diphosphate). A subsequent intramolecular S_N2' reaction of the inherent 1,3-dicarbonyl system to the allylic system of **8** should then furnish salvadione A (**1**) (Figure 2). Of course, the order of the functionalization steps starting from **4** might be different.

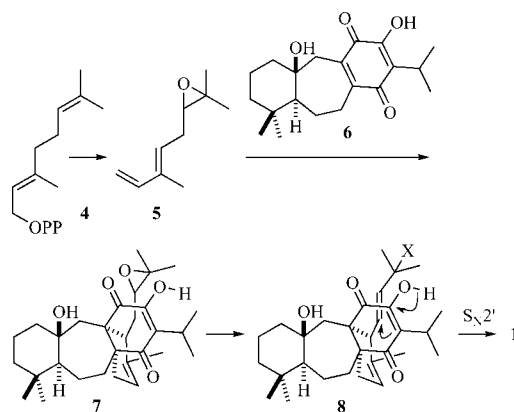


Figure 2. Proposed biosynthesis for salvadione (**1**) by an intermolecular Diels–Alder reaction.

In fact, based on this biosynthesis proposal, the group of Majetich recently completed the first total synthesis of salvadione A from quinone **9** and the triene **10** (Figure 3).^[6] The desired facial selectivity arises from the chair-like conformation of the cycloheptene annulated to the quinone. The quinone **9** also served as a key intermediate in the total synthesis of perovskone by the Majetich group.^[7] The tricyclic quinone **9** in turn was fashioned from the vinylcyclohexenone **12** by a Lewis acid induced cyclization reaction.^[7] A key intermediate was the tricyclic alkene **13**.

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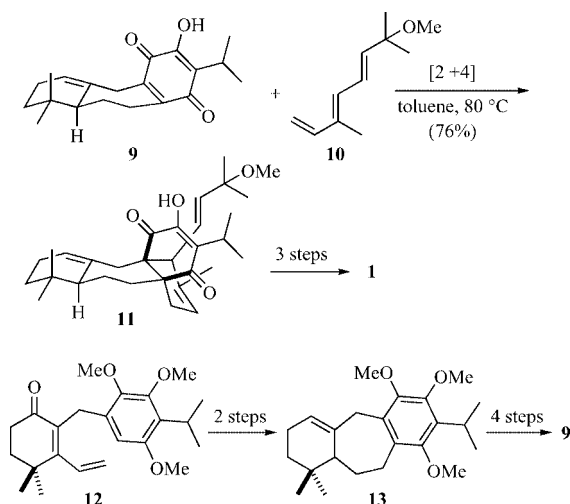


Figure 3. Key steps in the synthesis of salvadione (**1**) according to Majetich et al.

Results and Discussion

We reasoned that a short synthesis of the annulated hydroxyquinones such as **6** or **9** could be of interest, not only for the synthesis of salvadione-like structures, but also as starting point for generating structural diversity.^[8] At the outset we considered three possible strategies to build the seven-membered ring by two carbon–carbon bond-forming reactions (Figure 4). For example, strategy **A** could involve epoxide opening and an alkylation reaction. A possible scenario for strategy **B** would be an intramolecular attack of a benzylic anion to a ketone function. The connection to the aryl ring could be made by alkylation of an aryllithium intermediate with a primary iodide or tosylate. Strategy **C** would utilize key bond-forming reactions to the aromatic ring. This could be achieved by arylmetal intermediates or electrophilic aromatic substitution. In a way, **C** has elements of strategy **A** and **B**.

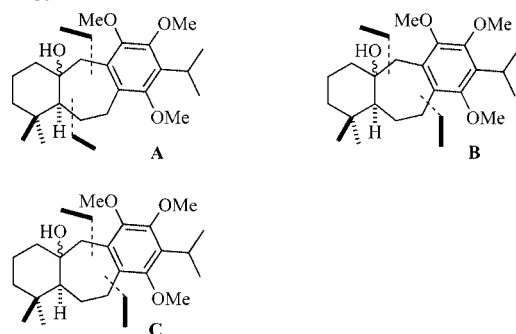
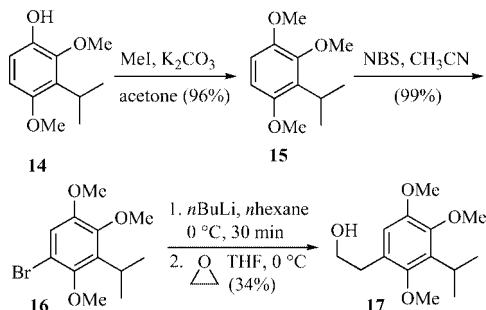


Figure 4. Possible disconnections in the central seven-membered ring.

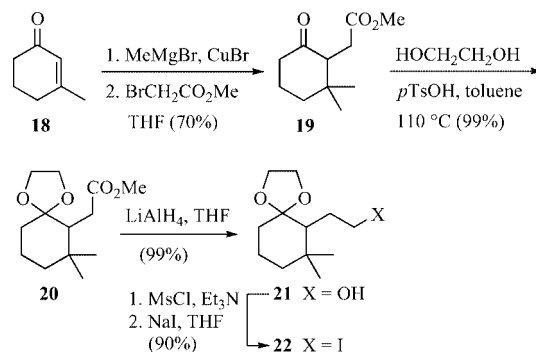
Our investigations started with the phenol **14**,^[9] obtained by oxidation of the corresponding isopropyl resorcin derivative^[10] with *meta*-chloroperbenzoic acid (*m*CPBA). Etherification (CH_3I , K_2CO_3) led to the fully protected trimethoxy compound **15**. The subsequent bromination was best achieved with NBS in acetonitrile resulting in almost quantitative yield of the bromide **16**.^[11] Considering strategy **A**,

extension of bromide **16** was performed by metalation with *n*-butyllithium in hexane followed by treatment of the aryllithium intermediate with oxirane to give the alcohol **17** in moderate yield (Scheme 1). Other products in this reaction were the corresponding styrene (26%), and the debrominated compound **15** (24%).



Scheme 1. Synthesis of the bromobenzene derivative **16** from phenol **14**.

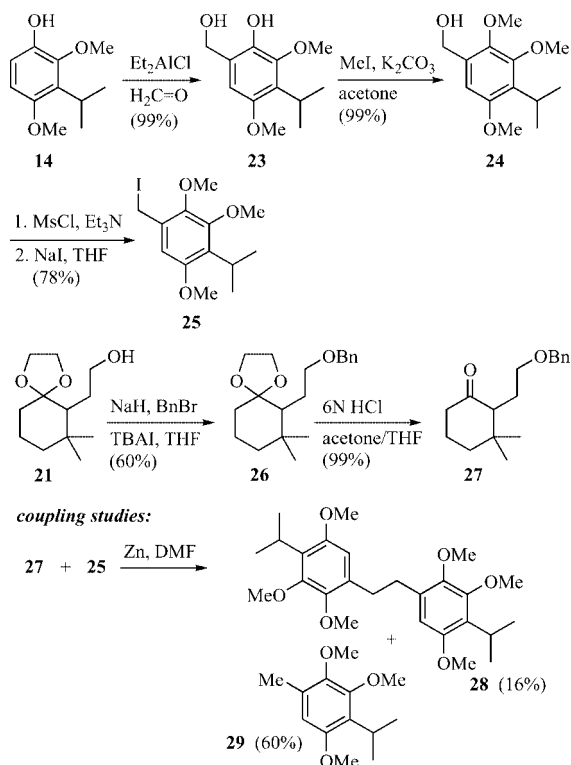
Suitable building blocks for the left part of the molecule were prepared from 3-methylcyclohexenone (**18**), which is available by a multicomponent reaction between acetoacetate and formaldehyde via the intermediacy of Hagemann's ester.^[12] Reaction of the cyclohexenone **18** with dimethylcuprate, followed by trapping of the enolate with the electrophile methyl 2-bromoacetate provided the keto ester **19** in good yield (Scheme 2).^[13–15] This was followed by acetalization of the keto function with glycol and reduction of the ester group with lithium aluminium hydride to provide the primary alcohol **21**. This compound is somewhat sensitive to acid in that it can undergo intramolecular transacetalization in the presence of traces of acid. Alcohol **21** was converted into the iodide **22** by mesylation and treatment of the intermediate mesylate with NaI (Scheme 2).



Scheme 2. Synthesis of the iodoalkane **22** from enone **18**.

Strategy **A** was early dismissed for two reasons. First, the yield of alcohol **17** was low, and the corresponding bromide (not shown) was obtained in moderate yield and prone to elimination; second, a model study concerning the tandem dimethylcuprate addition to the cyclohexenone **18**, followed by trapping of the enolate with ethyl iodide was not successful. With regard to strategy **B**, the phenol **14** was converted into the benzyl iodide **25** (Scheme 3). This was achieved by hydroxyalkylation of the phenol **14** with formaldehyde in

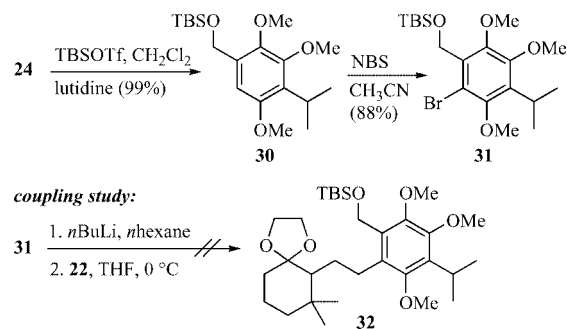
the presence of diethylaluminium chloride.^[16,17] Subsequently, the phenolic hydroxy function of **23** was selectively methylated to give rise to the trimethoxybenzene derivative **24**. Mesylation of the alcohol **24** and displacement of the mesylate with iodide furnished the benzyl iodide **25**. However, halogen/metal exchange followed by trapping with a suitable cyclohexanone did not lead to the desired tertiary alcohol. The lithium compound mainly led to the Wurtz coupling product **28** (56%). Metalation with zinc^[18] gave the reduced compound **29**, the natural product methyl-espintanol,^[19] as the major product. With added LiCl, CuCN, and BF₃ Et₂O, conditions that were developed for the efficient alkylation of benzylic halides,^[20] there was also no product formation.



Scheme 3. Synthesis of the benzyl iodide **25** and its attempted coupling with cyclohexanone **27**.

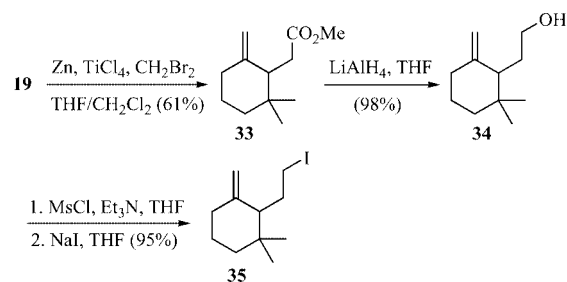
Next, a reversed bond-forming order was examined (Scheme 4). Accordingly, the alcohol **21** was converted into the iodide **22** via the corresponding mesylate (Scheme 2). On the aryl side, the bromide **31** was envisioned. This compound was available in two steps from the benzyl alcohol **24** by silylation to **30** and bromination.^[11] Unfortunately, transmetalation of the aryl bromide **31** with *n*-butyllithium with removal of the formed bromobutane, followed by addition of the iodide **22** did not give the desired coupling product **32**.

Therefore, we finally opted for strategy C. This strategy is characterized by the late stage formation of the two carbon–carbon bonds to the aryl ring. A corresponding building block for the cyclohexyl part, the iodide **35** with an *exo*-methylene group was prepared from the keto ester **19** by a



Scheme 4. Synthesis of the aryl bromide **31** and attempts to alkylate it with the iodide **22**.

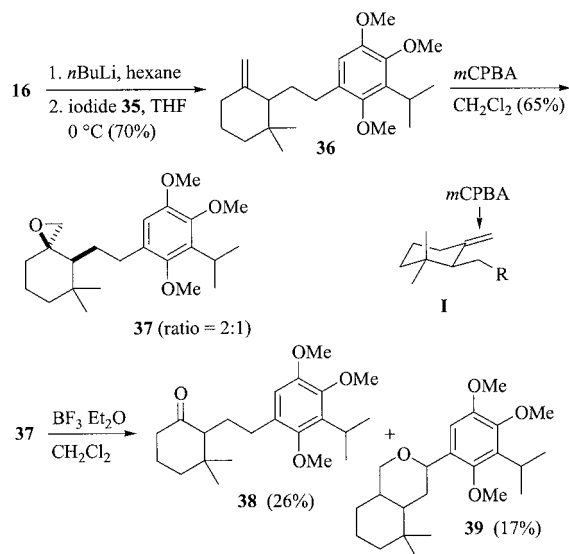
Lombardo reaction^[21] resulting in the unsaturated ester^[13] **33** (Scheme 5). Ester reduction to alcohol **34**, mesylation and conversion of the mesylate to the iodide **35** went well without any difficulties.



Scheme 5. Synthesis of the alkenyliodide **35**.

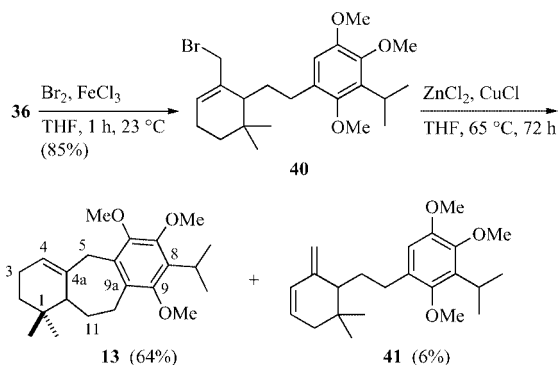
While metalation of the aryl bromide **16** with *n*BuLi and treatment with the iodide **22** was not successful, the coupling of the aryllithium species derived from **16** with the iodide **35** went smoothly in 70% yield (Scheme 6). Besides the alkylation product **36**, some unreacted iodide **35** (25%) as well as the debrominated aryl compound **15** were isolated. The next step called for epoxidation of the double bond and a subsequent 7-*endo-tet* cyclization. The epoxidation using *m*CPBA was slightly stereoselective to give a mixture of two diastereomers at a ratio of 61:39 (determined by ¹H NMR). Assuming a preferential axial attack of the peracid (cf. structure **1**, Scheme 6), the major diastereomer was tentatively assigned structure **37**.^[22,23] Activation of the epoxide function of **37** with BF₃ Et₂O produced the ketone **38** and the pyran **39**. Probably, an intramolecular hydride migration from the benzylic to the tertiary carbon atom is operative in the formation of **39**.

Eventually, we turned to an allylic electrophile on the side of the cyclohexane ring. Accordingly, allylic bromination of the *exo*-methylene compound **36** was initially investigated. While NBS gave a yield of 58%, bromination of **36** with bromine in the presence of iron(III) chloride turned out to be much more efficient, providing the allyl bromide **40** in 85% yield (Scheme 7). The crucial cyclization was studied under Friedel–Crafts conditions. For example, the desired product **13** was formed with FeCl₃ (21%) but the



Scheme 6. Alkylation of the metalated benzene **16** with iodide **35**, and attempts to cyclize the derived epoxide **37**.

major product was the diene **41**, resulting from HBr elimination. Similar results were obtained with ZnCl₂ (28% of **13**, 65% of **41**). Gratifyingly, the yield of **13** could be substantially improved by performing the cyclization with ZnCl₂ (10 equiv.) and CuCl (10 equiv.) in THF (reflux, 72 h).



Scheme 7. Intramolecular Friedel–Crafts alkylation of allyl bromide **40**.

The constitution of **13** could be inferred from spectroscopic data, with the ¹H NMR spectrum being the most supportive. Thus, there are no aromatic signals because of the fully substituted aromatic ring. In addition, only one olefinic proton is present. The methylene proton signals of the one carbon bridge appear at rather different chemical shifts, namely at δ = 3.03 and 3.78 ppm, respectively. Even though we could not get our hands on the spectroscopic data from the literature,^[6,7] the structure of **13** could be clearly assigned based on the NMR spectroscopic data. Since **13** has been used in the total syntheses of salvadione A by Majetich et al.,^[6] our route represents a formal total synthesis of this natural product. Starting from the enone **18** the longest linear sequence is 7 steps providing the tricycle **13** with a good overall yield.

Experimental Section

General: ¹H and ¹³C NMR: Bruker Avance 400 spectrometer; spectra were recorded at 295 K in CDCl₃; chemical shifts are calibrated to the residual proton and carbon resonance of the solvent: CDCl₃ (δ_H = 7.25 ppm; δ_C = 77.0 ppm), C₆D₆ (δ_H = 7.16 ppm; δ_C = 128.0 ppm). Melting points: Büchi Melting Point B-540; values are uncorrected. IR: Jasco FT/IR-430 apparatus. MS: Finnigan Triple-Stage-Quadrupole TSQ-70 (ionizing voltage of 70 eV). HRMS: Intectra AMD MAT-711A (EI) mass spectrometers. Flash chromatography: J. T. Baker silica gel, 43–60 μ m. Thin-layer chromatography: Macherey–Nagel Polygram Sil G/UV254 plates. All solvents used in the reactions were distilled before use. Dry tetrahydrofuran and toluene were distilled from sodium/benzophenone, whereas dry dichloromethane and triethylamine were distilled from CaH₂. Acetone and acetonitrile were dried by distillation from phosphorus pentoxide. Petroleum ether with a boiling range of 40–60 °C was used. Reactions were generally run under argon. All commercially available compounds were used as received, unless stated otherwise. The aromatic compounds 2-isopropyl-1,3-dimethoxybenzene, 3-isopropyl-2,4-dimethoxyphenol (**14**), and 2-isopropyl-1,3,4-trimethoxybenzene (**15**) were prepared according to Burnell^[10] from methyl 2,6-dimethoxybenzoate. 1-Bromo-3-isopropyl-2,4,5-trimethoxybenzene (**16**) was prepared according to Carreno et al.^[11] Cyclohexenone **18** was prepared according to Rieser.^[12a]

2-(3-Isopropyl-2,4,5-trimethoxyphenyl)ethanol (17): A solution of the aryl bromide^[11] **16** (0.13 g, 0.45 mmol) in dry *n*-hexane (3 mL) was treated with *n*BuLi (2.7 M in *n*-heptane, 0.18 mL, 0.47 mmol, 1.05 equiv.) at 0 °C, which results in a colorless precipitate. After stirring the mixture at 23 °C for 30 min, the solvent and bromobutane were removed in vacuo. The colorless residue was dissolved in THF (5 mL) and then treated dropwise with a solution of oxirane (0.22 mL, 4.5 mmol, 10 equiv.) in dry THF (3 mL) at 0 °C. The mixture was stirred at 0 °C for 1 h, and then at room temperature overnight. It was diluted with diethyl ether (10 mL) and saturated NH₄Cl solution (10 mL). After separation of the layers, the aqueous phase was washed with diethyl ether (3 $\times$ 7 mL). The combined organic layers were washed with water (10 mL), brine (5 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/ethyl acetate, 20:1) provided the alcohol **17** (0.039 g, 0.15 mmol, 34%), the corresponding styrene (**16**) (0.028 g, 0.12 mmol, 26%) and **15** (0.023 g, 0.11 mmol, 24%) as the major products, each of them as colorless oil.

Data for 17: R_f = 0.18 (petroleum ether/ethyl acetate, 3:1). ¹H NMR (250 MHz, CDCl₃): δ = 1.33 [d, J = 7.0 Hz, 6 H, CH(CH₃)₂], 2.13 (br. s, 1 H, OH), 2.84 (t, J = 6.4 Hz, 2 H, 1'-H), 3.37 [sept, J = 7.0 Hz, 1 H, CH(CH₃)₂], 3.67, 3.80, 3.83 (3 s, 3 H each, OCH₃), 3.83 (t, J = 6.4 Hz, 2 H, 2'-H), 6.59 (s, 1 H, H_{ar}) ppm. ¹³C NMR (62.9 MHz, CDCl₃): δ = 21.9 [CH(CH₃)₂], 26.1 [CH(CH₃)₂], 34.0 (C-1'), 55.9, 60.6, 61.9 (3 OCH₃), 63.4 (C-2'), 111.8 (C-6), 126.4 (C-1), 135.1 (C-3), 147.6 (C-5), 149.6 (C-2), 150.0 (C-4) ppm. IR (film): $\tilde{\nu}$ = 3418 (br. w), 2956 (m), 2935 (m), 1482 (s), 1428 (m), 1227 (s), 1113 (s), 1041 (s), 1013 (m) cm⁻¹. MS (EI): m/z (%) = 254 (96) [M]⁺, 239 (5) [M-CH₃]⁺, 223 (100), 208 (69), 192 (19), 177 (23), 161 (13), 84 (22). HRMS (EI): [M]⁺ calcd. for C₁₄H₂₂O₄ 254.151791, found 254.148503.

Data for the Vinyl Derivative 3-Isopropyl-1,2,4-trimethoxy-5-vinylbenzene: R_f = 0.40 (petroleum ether/ethyl acetate, 20:1). ¹H NMR (400 MHz, CDCl₃): δ = 1.33 [d, J = 7.2 Hz, 6 H, CH(CH₃)₂], 3.44 [sept, J = 7.2 Hz, 1 H, CH(CH₃)₂], 3.66, 3.84, 3.86 (3 s, 3 H each, OCH₃), 5.24 (dd, J = 10.8, 1.3 Hz, 1 H, CH₂), 5.63 (dd, J = 17.5,

1.3 Hz, 1 H, CH₂), 6.88 (s, 1 H, CH_{ar}), 6.96 (dd, *J* = 17.5, 10.8 Hz, 1 H, CH) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 21.9 [CH-(CH₃)₂], 25.8 [CH(CH₃)₂], 55.8, 60.8, 62.3 (3 OCH₃), 106.9 (C-6), 113.5 (CH₂), 126.1 (C-1), 132.0 (CH), 135.1 (C-3), 148.8 (C-5), 149.7 (C-2), 149.9 (C-4) ppm. IR (film): ν̄ = 2987 (m), 2957 (s), 1479 (s), 1404 (m), 1343 (m), 1223 (s), 1116 (s), 1042 (s), 1012 (m) cm⁻¹. MS (EI): *m/z* (%) = 236 (100) [M]⁺, 221 (53), 205 (12), 190 (18), 178 (29), 163 (64). HRMS (EI): [M]⁺ calcd. for C₁₄H₂₀O₃ 236.141231, found 236.142374.

Methyl (2,2-Dimethyl-6-oxocyclohexyl)acetate (19): To a solution of copper(I) bromide (0.717 g, 5.00 mmol, 0.050 equiv.) in dry THF (100 mL) was added methylmagnesium bromide (3.0 M in diethyl ether, 33.3 mL, 100 mmol, 1.0 equiv.) at 0 °C. After stirring at 0 °C for 30 min, enone^[12a] **18** (11.0 g, 100 mmol, 1.0 equiv.) was added slowly. The solution was stirred at 0 °C for further 2 h, before a solution of DMPU (125 mL, 1.04 mol, 10 equiv.) and methyl bromoacetate (18.4 mL, 200 mmol, 2.0 equiv.) was added dropwise at 0 °C. Stirring was continued at 0 °C for 1 h, then the mixture was allowed to reach room temperature and stirred overnight. After quenching the reaction by addition of saturated NH₄Cl solution (250 mL), the aqueous layer was extracted with diethyl ether (3 × 200 mL). The combined organic layers were washed with saturated NH₄Cl solution (2 × 100 mL) and brine (25 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Purification of the crude product by flash chromatography (petroleum ether/ethyl acetate, 5:1) provided the ester **19** (13.9 g, 70 mmol, 70%) as a colorless oil; *R*_f = 0.39 (petroleum ether/ethyl acetate, 5:1). ¹H NMR (400 MHz, CDCl₃): δ = 0.69 (s, 3 H, CH₃), 1.03 (s, 3 H, CH₃), 1.53–1.56 (m, 1 H, 3a-H), 1.70–1.82 (m, 2 H, 3b-H, 4a-H), 1.87–1.96 (m, 1 H, 4b-H), 2.19 (dd, *J* = 16.6, 3.1 Hz, 1 H, CH₂), 2.28–2.38 (m, 2 H, 5-H), 2.66 (dd, *J* = 16.6, 10.2 Hz, 1 H, CH₂), 2.81 (dd, *J* = 10.2, 3.0 Hz, 1 H, 1-H), 3.62 (s, 3 H, OCH₃) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 20.8 (CH₃), 22.6 (C-4), 28.5 (CH₂), 29.6 (CH₃), 38.9 (C-2), 40.2 (C-3), 41.0 (C-5), 51.6 (OCH₃), 56.2 (C-1), 173.6 (CO), 211.1 (CO) ppm. IR (film): ν̄ = 2959 (m), 1739 (s), 1712 (s), 1436 (m), 1371 (m), 1326 (m), 1267 (m), 1213 (m), 1171 (s), 1082 (m) cm⁻¹. MS (EI): *m/z* (%) = 198 (34) [M]⁺, 183 (54) [M-CH₃]⁺, 167 (68), 151 (100), 139 (27), 123 (32), 95 (33), 69 (44), 55 (35). HRMS (EI): [M]⁺ calcd. for C₁₁H₁₈O₃ 198.125581, found 198.126866.

Methyl (7,7-Dimethyl-1,4-dioxaspiro[4.5]dec-6-yl)acetate (20): A mixture of keto ester **19** (2.4 g, 12 mmol, 1.0 equiv.), ethylene glycol (2.7 mL, 48 mmol, 4.0 equiv.) and *para*-toluenesulfonic acid (0.046 g, 0.24 mmol, 0.020 equiv.) in dry toluene (20 mL) was refluxed in a Dean-Stark apparatus for 5 h. The cooled solution was diluted with ethyl acetate (100 mL) and then the mixture was washed with brine (2 × 30 mL). The organic layer was dried with MgSO₄, filtered and concentrated in vacuo. The acetal **20** (2.9 g, 12 mmol, 99%) was obtained pure as a colorless oil; *R*_f = 0.47 (petroleum ether/ethyl acetate, 5:1). ¹H NMR (400 MHz, CDCl₃): δ = 0.85 (s, 3 H, CH₃), 0.94 (s, 3 H, CH₃), 1.21–1.27 (m, 1 H, 8a-H), 1.24–1.31 (m, 1 H, 10a-H), 1.35–1.41 (m, 1 H, 8b-H), 1.44–1.51 (m, 1 H, 9a-H), 1.53–1.61 (m, 1 H, 9b-H), 1.73–1.79 (m, 1 H, 10b-H), 2.13–2.18 (m, 1 H, CH₂), 2.15–2.18 (m, 1 H, 6-H), 2.33 (dd, *J* = 15.9, 9.9 Hz, 1 H, CH₂), 3.62 (s, 3 H, OCH₃), 3.71–3.81 (m, 2 H, CH₂ acetal), 3.89–4.02 (m, 2 H, CH₂ acetal) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 19.4 (C-9), 21.3 (CH₃), 29.6 (CH₂), 31.3 (CH₃), 34.4 (C-10), 35.0 (C-7), 40.7 (C-8), 50.0 (C-6), 51.4 (OCH₃), 63.2 (C-2), 65.1 (C-3), 110.5 (C-5), 175.0 (CO) ppm. IR (film): ν̄ = 2949 (s), 2907 (m), 1739 (s), 1436 (m), 1273 (m), 1172 (m), 1141 (s), 1092 (m), 1056 (m), 1039 (m) cm⁻¹. MS (EI): *m/z* (%) = 242 (7) [M]⁺, 227 (17) [M-CH₃]⁺, 211 (27), 199 (82), 167 (22),

155 (46), 139 (22), 113 (50), 99 (100), 86 (27), 55 (30). HRMS (EI): [M]⁺ calcd. for C₁₃H₂₂O₄ 242.151719, found 242.152851.

2-(7,7-Dimethyl-1,4-dioxaspiro[4.5]dec-6-yl)ethanol (21): A cooled solution of ester **20** (2.90 g, 12.0 mmol) in dry THF (70 mL) was treated with LiAlH₄ (0.478 g, 12.6 mmol, 1.05 equiv.). The reaction mixture was then stirred at room temperature for 2 h, before it was treated with a mixture of THF/water/diethyl ether (96 mL/96 mL/120 mL) under ice-cooling. After separation of the layers, the aqueous phase was extracted with diethyl ether (3 × 100 mL). The combined organic layers were washed with brine (40 mL), dried with MgSO₄, filtered and concentrated in vacuo. The alcohol **21** (2.5 g, 12 mmol, 99%) was obtained as a colorless solid; m.p. 33 °C; *R*_f = 0.54 (petroleum ether/ethyl acetate, 2:1). ¹H NMR (400 MHz, C₆D₆): δ = 0.84 (s, 3 H, CH₃), 0.98 (s, 3 H, CH₃), 1.05 (ddd, *J* = 13.4, 13.1, 3.5 Hz, 1 H, 8'a-H), 1.12–1.20 (m, 1 H, 10'a-H), 1.24–1.36 (m, 2 H, 8'b-H, 9'a-H), 1.43–1.51 (m, 1 H, 2a-H), 1.49–1.52 (m, 1 H, 6'-H), 1.55–1.64 (m, 2 H, 9'b-H, 10'b-H), 1.66–1.76 (m, 1 H, 2b-H), 2.59 (br. s, 1 H, OH), 3.34–3.39 (m, 2 H, 1-H), 3.36–3.52 (m, 2 H, 2'-H), 3.60–3.80 (m, 2 H, 3'-H) ppm. ¹³C NMR (100 MHz, C₆D₆): δ = 20.0 (C-9'), 21.2 (CH₃), 28.0 (C-2), 31.2 (CH₃), 34.7 (C-10'), 35.9 (C-7'), 41.2 (C-8'), 51.0 (C-6'), 63.2 (C-1), 64.1 (C-3'), 65.0 (C-2'), 111.2 (C-5') ppm. IR (KBr): ν̄ = 3425 (br. s), 2945 (s), 1471 (m), 1389 (m), 1366 (m), 1348 (m), 1280 (m), 1211 (m), 1143 (m), 1079 (m) cm⁻¹. MS (EI): *m/z* (%) = 214 (1) [M]⁺, 199 (3) [M-CH₃]⁺, 171 (52), 155 (28), 113 (19), 99 (100), 86 (18). HRMS (EI): [M]⁺ calcd. for C₁₂H₂₂O₃ 214.156881, found 214.156184.

6-(2-Iodoethyl)-7,7-dimethyl-1,4-dioxaspiro[4.5]decane (22): A solution of alcohol **21** (0.21 g, 1.0 mmol) in dry THF (7 mL) was treated at 0 °C with Et₃N (121 mg, 168 μL, 1.2 equiv.) and mesyl chloride (108 mg, 76 μL, 1.1 equiv.). The cooling bath was removed and the mixture stirred at room temperature for 1 h. Subsequently, NaI (4 equiv.) and THF (4 mL) were added and stirring was continued for 14 h. After the addition of diethyl ether (10 mL) and water (10 mL), the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with a 10% aqueous Na₂S₂O₅ solution (2 × 4 mL), brine (3 mL), dried with MgSO₄, filtered, and concentrated in vacuo. This way, the iodide **22** (0.29 g, 0.90 mmol, 90%) was obtained as a slightly yellow oil; *R*_f = 0.65 (petroleum ether/ethyl acetate, 10:1). ¹H NMR (400 MHz, C₆D₆): δ = 0.83 (s, 3 H, CH₃), 0.90 (s, 3 H, CH₃), 1.02 (ddd, *J* = 13.4, 13.1, 3.5 Hz, 1 H, 8a-H), 1.10–1.18 (m, 1 H, 10a-H), 1.18–1.24 (m, 1 H, 8b-H), 1.25–1.30 (m, 1 H, 9a-H), 1.29–1.33 (m, 1 H, 6-H), 1.50–1.62 (m, 2 H, 9b-H, 10b-H), 1.78–1.87 (m, 1 H, 1'a-H), 2.03–2.13 (m, 1 H, 1'b-H), 3.15 (ddd, *J* = 9.2, 8.1, 8.0 Hz, 1 H, 2'a-H), 3.23–3.34 (m, 2 H, 2-H), 3.34–3.45 (m, 3 H, 3-H, 2'b-H) ppm. ¹³C NMR (100 MHz, C₆D₆): δ = 9.2 (C-2'), 19.9 (C-9), 21.3 (CH₃), 30.7 (C-1'), 31.3 (CH₃), 35.0 (C-10), 35.5 (C-7), 41.4 (C-8), 54.5 (C-6), 63.1 (C-2), 65.0 (C-3), 111.4 (C-5) ppm. IR (film): ν̄ = 2948 (s), 2878 (s), 1457 (m), 1367 (m), 1268 (m), 1164 (m), 1110 (m), 1090 (s), 1030 (m) cm⁻¹. MS (EI): *m/z* (%) = 309 (3) [M]⁺, 281 (14), 197 (100), 127 (9), 113 (11), 99 (46), 86 (9). HRMS (EI): [M]⁺ calcd. for C₁₁H₁₈IO₂ 309.035174, found 309.034101.

6-(Hydroxymethyl)-3-isopropyl-2,4-dimethoxyphenol (23): To a stirred mixture of phenol^[10] **14** (1.74 g, 8.87 mmol, 1.00 equiv.) and dried paraformaldehyde (0.533 g, 17.7 mmol, 2.0 equiv.) (heated in vacuo for some time) in dichloromethane (17 mL) was added diethylaluminum chloride (1.0 M in *n*-hexane, 10.2 mL, 10.2 mmol, 1.15 equiv.) dropwise at 0 °C. The mixture was stirred at 0 °C for 30 min, and then at room temperature overnight. The mixture was diluted with water (75 mL) and ethyl acetate (75 mL). The phases

were separated and the aqueous phase was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with water (50 mL), brine (25 mL), dried with MgSO₄, filtered and concentrated in vacuo. The diol **23** (1.99 g, 8.79 mmol, 99%) was obtained as a colorless solid with sufficient purity to be used in the next step; m.p. 77 °C; *R*_f = 0.55 (petroleum ether/ethyl acetate, 1:1). ¹H NMR (400 MHz, CDCl₃): δ = 1.31 [d, *J* = 7.1 Hz, 6 H, CH(CH₃)₂], 2.32 (br. s, 1 H, OH), 3.36 [sept, *J* = 7.1 Hz, 1 H, CH(CH₃)₂], 3.75 (s, 3 H, OCH₃), 3.77 (s, 3 H, OCH₃), 4.70 (s, 2 H, CH₂), 5.90 (br. s, 1 H, OH), 6.53 (s, 1 H, CH_{ar}) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 21.0 [CH(CH₃)₂], 25.8 [CH(CH₃)₂], 55.9 (OCH₃), 61.7 (OCH₃), 62.2 (CH₂), 107.4 (C-5), 123.7 (C-3), 129.4 (C-6), 141.4 (C-1), 145.4 (C-2), 152.3 (C-4) ppm. IR (KBr): ν̄ = 3506 (s), 3413 (s), 2984 (s), 2960 (s), 2875 (s), 2837 (s), 1740 (m), 1591 (m), 1488 (m), 1469 (m), 1421 (m), 1360 (m), 1338 (m), 1187 (m), 1132 (m), 1060 (m) cm⁻¹. MS (EI): *m/z* (%) = 226 (37) [M]⁺, 208 (96) [M–H₂O]⁺, 193 (100), 175 (15), 165 (46), 161 (53), 135 (16). HRMS (EI): [M]⁺ calcd. for C₁₂H₁₈O₄ 226.120491, found 226.121266.

(4-Isopropyl-2,3,5-trimethoxyphenyl)methanol (24): To a stirred mixture of diol **23** (2.01 g, 8.87 mmol, 1.0 equiv.) and potassium carbonate (5.45 g, 39.4 mmol, 4.4 equiv.) in acetone (50 mL) was added methyl iodide (3.86 mL, 62.1 mmol, 7.0 equiv.) followed by refluxing of the mixture for 6 h. After cooling, half-concentrated aqueous NH₄Cl solution (75 mL) was added and the mixture extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with brine (20 mL), dried with MgSO₄, filtered, and concentrated in vacuo. This way, the hydroxymethyl derivative **24** (2.11 g, 8.78 mmol, 99%) was obtained as a colorless solid; m.p. 39 °C; *R*_f = 0.46 (petroleum ether/ethyl acetate, 2:1). ¹H NMR (400 MHz, CDCl₃): δ = 1.29 [d, *J* = 7.1 Hz, 6 H, CH(CH₃)₂], 2.13–2.17 (br. m, 1 H, OH), 3.48 [sept, *J* = 7.1 Hz, 1 H, CH(CH₃)₂], 3.77, 3.81, 3.83 (3 s, 3 H each, OCH₃), 4.65 (d, *J* = 4.5 Hz, 2 H, CH₂), 6.58 (s, 1 H, CH_{ar}) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 21.1 [CH(CH₃)₂], 25.1 [CH(CH₃)₂], 55.7 (OCH₃), 60.8 (2 OCH₃), 61.6 (CH₂), 106.4 (C-6), 130.2 (C-4), 131.6 (C-1), 145.1 (C-2), 151.6 (C-3), 154.7 (C-5) ppm. IR (KBr): ν̄ = 3309 (br. s), 2953 (s), 2871 (m), 2834 (m), 1604 (m), 1580 (m), 1455 (s), 1409 (s), 1357 (m), 1339 (m), 1241 (m), 1192 (m), 1130 (s), 1071 (m), 1029 (m) cm⁻¹. MS (EI): *m/z* (%) = 240 (100) [M]⁺, 225 (56) [M–CH₃]⁺, 207 (46) [M–CH₃–H₂O]⁺, 177 (12), 155 (15), 140 (27), 123 (19). HRMS (EI): [M]⁺ calcd. for C₁₃H₂₀O₄ 240.136141, found 240.137270.

1-(Iodomethyl)-4-isopropyl-2,3,5-trimethoxybenzene (25): A solution of alcohol **24** (1.09 g, 4.54 mmol) in dry THF (30 mL) was treated at 0 °C with Et₃N (551 mg, 5.44 mmol, 0.76 mL, 1.2 equiv.) and mesyl chloride (572 mg, 5.0 mmol, 0.39 mL, 1.1 equiv.). The cooling bath was removed and the mixture stirred at room temperature for 1 h. Subsequently, NaI (2.72 g, 18.2 mmol, 4 equiv.) and THF (18 mL) were added and stirring continued for 14 h. After the addition of diethyl ether (40 mL) and water (40 mL), the layers were separated and the aqueous layer extracted with diethyl ether (3 × 40 mL). The combined organic layers were washed with a 10% aqueous Na₂S₂O₅ solution (2 × 20 mL), brine (15 mL), dried with MgSO₄, filtered, and concentrated in vacuo. This way, the iodide **25** (1.24 g, 3.54 mmol, 78%) was obtained as a slightly yellow solid; m.p. 41 °C; *R*_f = 0.76 (petroleum ether/ethyl acetate, 10:1). ¹H NMR (400 MHz, CDCl₃): δ = 1.28 [d, *J* = 7.1 Hz, 6 H, CH(CH₃)₂], 3.46 [sept, *J* = 7.1 Hz, 1 H, CH(CH₃)₂], 3.76, 3.79, 3.92 (3 s, 3 H each, OCH₃), 4.47 (s, 2 H, CH₂), 6.55 (s, 1 H, CH_{ar}) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 0.7 (CH₂), 21.1 [CH(CH₃)₂], 25.3 [CH(CH₃)₂], 55.7, 59.7, 60.7 (3 OCH₃), 107.5 (C-6), 129.9 (C-4), 131.3 (C-1), 145.2 (C-2), 151.9 (C-3), 154.5 (C-5) ppm. IR (KBr): ν̄ = 2956 (s), 2933 (s), 2867 (m), 2836 (m), 1599 (m), 1575

(m), 1479 (s), 1455 (s), 1406 (s), 1236 (m), 1142 (m), 1061 (m), 1026 (m) cm⁻¹. HRMS (ESI): [M+Na]⁺ calcd. for C₁₃H₁₉INaO₃ 373.02711, found 373.02725.

6-[2-(Benzyloxy)ethyl]-7,7-dimethyl-1,4-dioxaspiro[4.5]decane (26): To a cooled (0 °C) solution of alcohol **21** (0.43 g, 2.0 mmol, 1.0 equiv.) in dry THF (5 mL) was added NaH (58 mg, 2.4 mmol, 1.2 equiv.). The mixture was stirred at 0 °C for 15 min before benzyl bromide (0.29 mL, 2.4 mmol, 1.2 equiv.) and tetrabutylammonium iodide (7 mg, 20 μmol, 0.01 equiv.) were added. After being stirred at room temperature overnight, water (15 mL) was carefully added and the mixture extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/ethyl acetate, 10:1) provided the benzyl ether **26** (0.35 g, 1.2 mmol, 60%) as a colorless oil; *R*_f = 0.50 (petroleum ether/ethyl acetate, 10:1). ¹H NMR (400 MHz, C₆D₆): δ = 0.97 (s, 3 H, CH₃), 1.07 (s, 3 H, CH₃), 1.07–1.14 (m, 1 H, 8a-H), 1.21–1.25 (m, 1 H, 10a-H), 1.27–1.31 (m, 1 H, 8b-H), 1.32–1.40 (m, 1 H, 9a-H), 1.54 (dd, *J* = 6.8, 2.0 Hz, 1 H, 6-H), 1.61–1.63 (m, 2 H, 9b-H, 10b-H), 1.75–1.83 (m, 1 H, 1'a-H), 1.91–2.00 (m, 1 H, 1'b-H), 3.36–3.55 (m, 2 H, 2-H, 3-H), 3.55–3.62 (m, 1 H, 2'a-H), 3.72–3.78 (m, 1 H, 2'b-H), 4.47 (s, 2 H, CH₂Ph), 7.08–7.21 (m, 3 H, CH_{ar}), 7.36–7.38 (m, 2 H, CH_{ar}) ppm. ¹³C NMR (100 MHz, C₆D₆): δ = 20.1 (C-9), 21.5 (CH₃), 25.6 (C-1'), 31.6 (CH₃), 35.2 (C-10), 35.7 (C-7), 41.3 (C-8), 49.7 (C-6), 63.3 (C-2), 65.2 (C-3), 72.6 (C-2'), 72.8 (CH₂Ph), 111.7 (C-5), 127.4 (CH_{ar}), 127.6 (CH_{ar}), 128.4 (CH_{ar}), 139.9 (C_{ar}) ppm. IR (film): ν̄ = 2947 (s), 2870 (s), 1455 (m), 1366 (m), 1147 (m), 1083 (s), 1036 (m) cm⁻¹. MS (EI): *m/z* (%) = 304 (5) [M]⁺, 261 (6) [M–C₂H₄O]⁺, 213 (100), 183 (12), 170 (22), 155 (54), 127 (20), 113 (22), 99 (97), 91 (54). HRMS (EI): [M–C₂H₄O]⁺ calcd. for C₁₇H₂₄O₂ 260.177621, found 260.176811.

2-[2-(Benzyloxy)ethyl]-3,3-dimethylcyclohexanone (27): A solution of acetal **26** (0.15 g, 0.48 mmol) in THF (2.5 mL), acetone (1 mL) and 6 N HCl (0.25 mL) was refluxed for 3 h. After cooling, the mixture was diluted with diethyl ether (15 mL), washed with saturated NaHCO₃ solution (2 × 10 mL) and brine (5 mL). The organic layer was dried with MgSO₄, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/ethyl acetate, 10:1) to provide ketone **27** (0.13 g, 0.48 mmol, 99%) as a colorless oil; *R*_f = 0.36 (petroleum ether/ethyl acetate, 10:1). ¹H NMR (400 MHz, CDCl₃): δ = 0.70 (s, 3 H, CH₃), 1.00 (s, 3 H, CH₃), 1.49–1.64 (m, 3 H, 4-H, 1'a-H), 1.68–1.88 (m, 2 H, 5-H), 1.90–1.99 (m, 1 H, 1'b-H), 2.15–2.30 (m, 3 H, 6-H, 2-H), 3.24–3.30 (m, 1 H, 2'a-H), 3.42–3.47 (m, 1 H, 2'b-H), 4.35 (d, *J* = 11.9 Hz, 1 H, CH₂Ph), 4.43 (d, *J* = 11.9 Hz, 1 H, CH₂Ph), 7.18–7.29 (m, 5 H, CH_{ar}) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 21.7 (CH₃), 23.1 (C-5), 24.1 (C-1'), 29.5 (CH₃), 39.5 (C-4), 39.6 (C-3), 41.4 (C-6), 57.0 (C-2), 69.4 (C-2'), 72.7 (CH₂Ph), 127.4 (CH_{ar}), 127.6 (CH_{ar}), 128.3 (CH_{ar}), 138.6 (C_{ar}), 213.0 (CO) ppm. IR (film): ν̄ = 2961 (s), 2933 (s), 2870 (m), 1709 (s), 1455 (m), 1369 (m), 1264 (w), 1101 (m), 1076 (m) cm⁻¹. MS (EI): *m/z* (%) = 261 (8) [M]⁺, 216 (14), 169 (28), 153 (73), 137 (24), 111 (100), 91 (98). HRMS (EI): [M]⁺ calcd. for C₁₇H₂₄O₂ 260.177621, found 260.176298.

1-({tert-Butyl(dimethyl)silyloxy}methyl)-4-isopropyl-2,3,5-trimethoxybenzene (30): To a solution of alcohol **24** (2.31 g, 9.62 mmol) and 2,6-lutidine (2.79 mL, 24.05 mmol, 2.5 equiv.) in dry dichloromethane (40 mL) was added dropwise *tert*-butyldimethylsilyl triflate (2.43 mL, 10.58 mmol, 1.1 equiv.) at 0 °C. The stirred mixture was allowed to reach room temperature and then treated with water (40 mL). After separation of the layers, the aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic

layers were washed with 1 N HCl (20 mL), brine (10 mL), dried with MgSO_4 , filtered and concentrated in vacuo. The silyl ether **30** (3.38 g, 9.53 mmol, 99%) was obtained as a colorless oil, pure enough for further usage; $R_f = 0.40$ (petroleum ether/diethyl ether, 25:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.12$ (s, 6 H, SiCH_3), 0.96 [s, 9 H, $\text{C}(\text{CH}_3)_3$], 1.29 [d, $J = 7.1$ Hz, 6 H, $\text{CH}(\text{CH}_3)_2$], 3.47 [sept, $J = 7.1$ Hz, 1 H, $\text{CH}(\text{CH}_3)_2$], 3.77 (s, 6 H, OCH_3), 3.80 (s, 3 H, OCH_3), 4.74 (s, 2 H, CH_2), 6.77 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = -5.3$ (SiCH_3), 18.4 [$\text{C}(\text{CH}_3)_3$], 21.2 [$\text{CH}(\text{CH}_3)_2$], 25.1 [$\text{CH}(\text{CH}_3)_2$], 25.9 [$\text{C}(\text{CH}_3)_3$], 55.6 (OCH_3), 60.0 (CH_2), 60.4 (OCH_3), 60.8 (OCH_3), 105.1 (C-6), 128.8 (C-4), 132.3 (C-2), 143.7 (C-1), 151.2 (C-3), 154.6 (C-5) ppm. IR (film): $\tilde{\nu} = 2955$ (s), 2932 (s), 2857 (m), 1463 (m), 1411 (s), 1370 (m), 1255 (m), 1134 (s), 1110 (m), 1061 (m), 1031 (m) cm^{-1} . MS (EI): m/z (%) = 354 (6) [$\text{M}]^+$, 297 (38), 282 (100), 267 (37), 147 (13), 84 (19). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{19}\text{H}_{34}\text{O}_4\text{Si}$ 354.222622, found 354.221243.

2-Bromo-1-((tert-butyl(dimethyl)silyl)oxy)methyl-4-isopropyl-2,3,5-trimethoxybenzene (31): A solution of the benzene derivative **30** (3.61 g, 9.62 mmol) and *N*-bromosuccinimide (NBS) (1.8 g, 10.1 mmol, 1.05 equiv.) in acetonitrile (140 mL) was stirred at room temperature for 1 h. The solvent was removed in vacuo and the residue taken up in CCl_4 (50 mL) at 0 °C. The slurry was stirred at 0 °C for 15 min, filtered, and the filtrate concentrated in vacuo. This way, the aryl bromide **31** (3.67 g, 8.47 mmol, 88%) was obtained as colorless oil, suitable for further transformations; $R_f = 0.48$ (petroleum ether/diethyl ether, 25:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.15$ (s, 6 H, SiCH_3), 0.93 [s, 9 H, $\text{C}(\text{CH}_3)_3$], 1.31 [d, $J = 7.1$ Hz, 6 H, $\text{CH}(\text{CH}_3)_2$], 3.44 [sept, $J = 7.1$ Hz, 1 H, $\text{CH}(\text{CH}_3)_2$], 3.77, 3.83, 3.86 (3 s, 3 H each, OCH_3), 4.79 (s, 2 H, CH_2) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = -5.2$ (SiCH_3), 18.6 [$\text{C}(\text{CH}_3)_3$], 21.9 [$\text{CH}(\text{CH}_3)_2$], 26.0 [$\text{C}(\text{CH}_3)_3$], 26.8 [$\text{CH}(\text{CH}_3)_2$], 60.3 (CH_2), 60.4, 61.4, 61.5 (3 OCH_3), 115.1 (C-2), 132.4 (C-4), 136.3 (C-6), 149.6 (C-1), 151.3 (C-3), 152.3 (C-5) ppm. IR (film): $\tilde{\nu} = 2956$ (s), 2934 (s), 2857 (m), 1454 (s), 1404 (s), 1341 (m), 1252 (m), 1123 (m), 1086 (s), 1045 (m), 1029 (s) cm^{-1} . MS (EI): m/z (%) = 419 (2) [$\text{M}-\text{CH}_3$, $^{81}\text{Br}^+$], 417 (2) [$\text{M}-\text{CH}_3$, $^{79}\text{Br}^+$], 377 (80), 375 (87), 362 (100), 360 (98), 347 (23), 345 (22), 282 (27), 147 (50), 84 (36). HRMS (EI): [$\text{M}-\text{CH}_3$] $^+$ calcd. for $\text{C}_{18}\text{H}_{30}\text{BrO}_4\text{Si}$ 417.109619, found 417.111320.

Methyl (2,2-Dimethyl-6-methylenecyclohexyl)acetate (33): To a suspension of zinc (1.44 g, 22 mmol, 11 equiv.) and dibromomethane (0.51 mL, 7.2 mmol, 3.6 equiv.) in dry THF (13 mL) was added dropwise TiCl_4 (0.57 mL, 5.2 mmol, 2.6 equiv.) at -40 °C. The mixture was stirred at 5 °C for 3 d before it was added to a solution of ester **19** (0.40 g, 2.0 mmol, 1.0 equiv.) in dry dichloromethane (15 mL) at 5 °C. The resulting mixture was stirred at 5 °C overnight, then diluted with diethyl ether (30 mL) and treated with a cold saturated NaHCO_3 solution (30 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (3 $\times$ 25 mL). The combined organic layers were washed with brine (15 mL), dried with MgSO_4 , filtered, and concentrated in vacuo. Purification of the crude product by flash chromatography (petroleum ether/ethyl acetate, 15:1) provided the unsaturated ester **33** (0.24 g, 1.2 mmol, 61%) as a colorless oil; $R_f = 0.51$ (petroleum ether/ethyl acetate, 15:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.77$ (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3), 1.30–1.37 (m, 1 H, 3a-H), 1.39–1.45 (m, 1 H, 3b-H), 1.48–1.58 (m, 2 H, 4-H), 2.00–2.07 (m, 1 H, CH_2), 2.17–2.23 (m, 1 H, CH_2), 2.37–2.53 (m, 3 H, 1-H, 5-H), 3.62 (s, 3 H, OCH_3), 4.54 (s, 1 H, $\text{C}=\text{CH}_2$), 4.73 (s, 1 H, $\text{C}=\text{CH}_2$) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 23.6$ (C-4), 23.7 (CH_3), 28.7 (CH_3), 33.3 (C-5), 34.1 (CH_2), 34.9 (C-2), 38.2 (C-3), 49.8 (C-1), 51.5 (OCH_3), 108.4 ($\text{C}=\text{CH}_2$), 148.9 (C-6), 174.0 (CO) ppm. IR (film): $\tilde{\nu} = 2955$ (s), 2931 (s), 2868 (m), 1742 (s), 1436 (m), 1158 (m) cm^{-1} .

MS (EI): m/z (%) = 196 (8) [$\text{M}]^+$, 181 (49) [$\text{M}-\text{CH}_3$] $^+$, 149 (22), 122 (76), 107 (69), 93 (25), 81 (43), 69 (100). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{12}\text{H}_{20}\text{O}_2$ 196.146321, found 196.147720.

2-(2,2-Dimethyl-6-methylenecyclohexyl)ethanol (34): To a solution of ester **33** (0.25 g, 1.3 mmol, 1 equiv.) in dry THF (8 mL) was slowly added lithium aluminium hydride (0.052 g, 1.4 mmol, 1.05 equiv.). After stirring at room temperature for 2 h, a 1:1 mixture (10 mL) of THF and water was carefully added at 0 °C followed by addition of diethyl ether (13 mL). The layers were separated, and the aqueous layer was extracted with diethyl ether (2 $\times$ 13 mL). The combined organic layers were washed with brine (4 mL), dried with MgSO_4 , filtered, and concentrated in vacuo, yielding pure alcohol **34** (0.21 g, 1.3 mmol, 98%) as a colorless oil; $R_f = 0.38$ (petroleum ether/ethyl acetate, 5:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.84$ (s, 3 H, CH_3), 0.91 (s, 3 H, CH_3), 1.19–1.25 (m, 1 H, 3'a-H), 1.42–1.48 (m, 1 H, 3'b-H), 1.47–1.58 (m, 2 H, 4'-H), 1.62–1.77 (m, 2 H, 2-H), 1.88 (dd, $J = 15.0$, 7.4 Hz, 1 H, 1'-H), 2.00–2.13 (m, 2 H, 5'-H), 3.50–3.65 (m, 2 H, CH_2OH), 4.61 (d, $J = 2.0$ Hz, 1 H, CH_2), 4.76 (d, $J = 2.0$ Hz, 1 H, CH_2) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 23.5$ (C-4'), 26.6 (CH_3), 28.0 (CH_3), 29.6 (C-2), 32.1 (C-5'), 34.6 (C-2'), 35.7 (C-3'), 50.9 (C-1'), 62.2 (C-1), 109.1 (CH_2), 150.0 (C-6') ppm. IR (film): $\tilde{\nu} = 3361$ (br. m), 2932 (s), 2867 (m), 1052 (m) cm^{-1} . MS (EI): m/z (%) = 168 (3) [$\text{M}]^+$, 153 (31) [$\text{M}-\text{CH}_3$] $^+$, 124 (45), 109 (83), 95 (28), 81 (67), 69 (100), 41 (56). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{11}\text{H}_{20}\text{O}$ 168.151411, found 168.151928.

2-(2-Iodoethyl)-1,1-dimethyl-3-methylenecyclohexane (35): To a solution of alcohol **34** (0.27 g, 1.6 mmol, 1 equiv.) in dry THF (11 mL) were added triethylamine (0.26 mL, 1.9 mmol, 1.2 equiv.) and mesyl chloride (0.14 mL, 1.8 mmol, 1.1 equiv.) at 0 °C. The solution was allowed to reach room temperature and stirred for 1 h, before sodium iodide (0.96 g, 6.4 mmol, 4.0 equiv.) and dry THF (6 mL) were added. After stirring the mixture at room temperature overnight, diethyl ether (16 mL) and water (16 mL) were added. The layers were separated, and the aqueous layer was extracted with diethyl ether (2 $\times$ 16 mL). The combined organic layers were washed with diluted $\text{Na}_2\text{S}_2\text{O}_5$ solution (2 $\times$ 6 mL), brine (5 mL), dried with MgSO_4 , filtered, and concentrated in vacuo to yield pure iodide **35** (0.42 g, 1.5 mmol, 95%) as a colorless oil; $R_f = 0.40$ (petroleum ether/ethyl acetate, 5:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.83$ (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 1.18–1.27 (m, 1 H, 6a-H), 1.38–1.45 (m, 1 H, 6b-H), 1.46–1.57 (m, 2 H, 5-H), 1.83–2.03 (m, 5 H, 1'a-H, 2-H, 1'b-H, 4-H), 2.89–2.96 (m, 1 H, 2'a-H), 3.19–3.25 (m, 1 H, 2'b-H), 4.64 (d, $J = 2.0$ Hz, 1 H, CH_2), 4.81 (d, $J = 2.0$ Hz, 1 H, CH_2) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 6.5$ (C-2'), 23.4 (C-5), 26.5 (CH_3), 28.1 (CH_3), 30.8 (C-1'), 32.0 (C-4), 34.6 (C-1), 36.1 (C-6), 54.4 (C-2), 110.1 (CH_2), 147.5 (C-3) ppm. IR (film): $\tilde{\nu} = 2931$ (s), 2866 (m), 1645 (m), 1449 (m), 1365 (m) cm^{-1} . MS (EI): m/z (%) = 278 (29) [$\text{M}]^+$, 235 (22), 151 (20), 123 (18), 109 (52), 95 (100), 81 (44), 69 (62), 41 (26). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{11}\text{H}_{19}\text{I}$ 278.05315, found 278.05365.

1-[2-(2,2-Dimethyl-6-methylenecyclohexyl)ethyl]-3-isopropyl-2,4,5-trimethoxybenzene (36): To a solution of aryl bromide **16** (2.3 g, 8.0 mmol, 1.0 equiv.) in dry *n*-hexane (25 mL) was added *n*BuLi (2.7 M in *n*-heptane, 3.4 mL, 8.4 mmol, 1.05 equiv.) dropwise at 0 °C resulting in a colorless precipitate. The mixture was stirred at room temperature for 30 min before the solvent and all volatile compounds were removed in vacuo. The slightly yellow residue was dissolved in dry THF (25 mL) at -78 °C, then the iodide **35** (2.2 g, 8.0 mmol, 1.0 equiv.) was slowly added at -78 °C. The solution was allowed to reach 0 °C and stirred at this temperature overnight. After diluting the mixture with diethyl ether (100 mL), the reaction

was quenched by addition of half-saturated aqueous NH_4Cl solution (100 mL), the layers were separated, and the aqueous layer was extracted with diethyl ether (3×70 mL). The combined organic layers were washed with diluted $\text{Na}_2\text{S}_2\text{O}_5$ solution (50 mL) and brine (25 mL), dried with MgSO_4 , filtered, and concentrated in vacuo. Purification of the crude product by flash chromatography (petroleum ether/ethyl acetate, 20:1) provided the desired coupling product **36** (2.0 g, 5.6 mmol, 70%) as a colorless oil together with some unreacted iodide **35** (0.56 g, 2.0 mmol, 25%).

Data for Coupling Product 36: $R_f = 0.46$ (petroleum ether/ethyl acetate, 20:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.83$ (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 1.18–1.28 (m, 1 H, 3''a-H), 1.33 [d, $J = 7.1$ Hz, 3 H, $\text{CH}(\text{CH}_3)_2$], 1.34 [d, $J = 7.1$ Hz, 3 H, $\text{CH}(\text{CH}_3)_2$], 1.42–1.49 (m, 1 H, 3''b-H), 1.50–1.57 (m, 2 H, 4''-H), 1.63–1.76 (m, 2 H, 2''-H), 1.80 (dd, $J = 11.1$, 3.1 Hz, 1 H, 1''-H), 2.02–2.08 (m, 1 H, 5''a-H), 2.13–2.20 (m, 1 H, 5''b-H), 2.27 (ddd, $J = 11.3$, 8.1, 5.6 Hz, 1 H, 1'a-H), 2.57 (ddd, $J = 11.3$, 8.7, 5.1 Hz, 1 H, 1'b-H), 3.40 [sept, $J = 7.1$ Hz, 1 H, $\text{CH}(\text{CH}_3)_2$], 3.64, 3.82, 3.83 (3 s, 3 H each, OCH_3), 4.67 (d, $J = 2.1$ Hz, 1 H, $\text{C}=\text{CH}_2$), 4.83 (d, $J = 2.1$ Hz, 1 H, $\text{C}=\text{CH}_2$), 6.55 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 22.0$ [$\text{CH}(\text{CH}_3)_2$], 23.7 (C-4''), 26.1 (CH_3), 26.3 [$\text{CH}(\text{CH}_3)_2$], 27.9 (C-2''), 28.4 (CH_3), 29.4 (C-1'), 32.5 (C-5'), 35.0 (C-2''), 36.3 (C-3''), 54.5 (C-1''), 55.9, 60.6, 61.9 (3 OCH_3), 109.0 ($\text{C}=\text{CH}_2$), 111.2 (CH_{ar}), 130.9 (C-1), 134.9 (C-3), 146.8 (C-5), 149.3 ($\text{C}=\text{CH}_2$), 149.4 (C-4), 149.7 (C-2) ppm. IR (film): $\tilde{\nu} = 2935$ (s), 2867 (m), 1482 (s), 1456 (m), 1427 (m), 1344 (m), 1225 (s), 1116 (s), 1044 (s), 1016 (m) cm^{-1} . MS (EI): m/z (%) = 360 (46) [$\text{M}]^+$, 236 (100), 221 (85), 208 (66), 193 (25), 179 (24), 161 (18). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{23}\text{H}_{36}\text{O}_3$ 360.26645, found 360.26900.

4-[2-(3-Isopropyl-2,4,5-trimethoxyphenyl)ethyl]-5,5-dimethyl-1-oxaspiro[2.5]octane (37) (2:1 Diastereomeric Mixture): A solution of alkene **36** (0.18 g, 0.50 mmol, 1.0 equiv.) in dry dichloromethane (1 mL) was treated with *m*CPBA (0.17 g, 1.0 mmol, 2.0 equiv.) followed by stirring of the mixture at room temperature for 5 min. Then the mixture was diluted with dichloromethane (2 mL) and stirred at room temperature overnight. For the workup, a saturated NaHCO_3 solution (5 mL) was added, and stirring continued for 30 min, before diethyl ether was added (15 mL). After separation of the layers, the organic layer was washed with brine (5 mL), dried with MgSO_4 , filtered, and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/ethyl acetate, 10:1) provided the epoxide **37** (0.12 g, 0.32 mmol, 65%) as a colorless oil; $R_f = 0.39$ (petroleum ether/ethyl acetate, 10:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.86$ (s, 2 H, CH_3), 0.94 (s, 1 H, CH_3), 0.99 (s, 1 H, CH_3), 1.97 (s, 2 H, CH_3), 1.10–1.30 (m, 3 H, 4-H, 6a-H, 1'a-H), 1.33 [d, $J = 7.1$ Hz, 6 H, $\text{CH}(\text{CH}_3)_2$], 1.38–1.53 (m, 2 H, 1'a-H, 2'a-H, 6b-H), 1.54–1.81 (m, 4 H, 7a-H, 1'b-H, 2'b-H, 7b-H), 2.44–2.55 (m, 1 H, 8a-H), 2.52 (d, $J = 4.7$ Hz, 0.67 H, 2a-H), 2.57 (d, $J = 4.7$ Hz, 0.33 H, 2a-H), 2.61–2.72 (m, 1 H, 8b-H), 2.66 (d, $J = 4.7$ Hz, 0.67 H, 2b-H), 2.68 (d, $J = 4.7$ Hz, 0.33 H, 2b-H), 3.39 [sept, $J = 7.1$ Hz, 1 H, $\text{CH}(\text{CH}_3)_2$], 3.65 (s, 2 H, OCH_3), 3.66 (s, 1 H, OCH_3), 3.81 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 6.55 (s, 0.67 H, CH_{ar}), 6.59 (s, 0.33 H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 20.7$ (C-7), 21.0 (C-7), 22.0 [$\text{CH}(\text{CH}_3)_2$], 25.4 (CH_3), 26.1 [$\text{CH}(\text{CH}_3)_2$], 26.6 (CH_3), 27.8 (2 peaks, C-2'), 28.2 (CH_3), 28.9 (CH_3), 31.0 (C-1'), 31.1 (C-8), 31.3 (C-8), 32.1 (C-1'), 35.7 (C-6), 36.1 (C-5), 37.1 (C-6), 50.2 (C-4), 50.4 (C-4), 51.3 (C-2), 54.1 (C-2), 55.9 (OCH_3), 59.9 (C-3), 60.0 (C-3), 60.6 (OCH_3), 61.9 (2 peaks, OCH_3), 111.2 (CH_{ar}), 130.4 (C-1''), 130.6 (C-1''), 134.9 (C-3''), 135.0 (C-3''), 146.9 (C-5''), 147.0 (C-5''), 149.4 (2 peaks, C-4''), 149.7 (C-2'') ppm. IR (film): $\tilde{\nu} = 2938$ (s), 2869 (m), 1482 (s), 1456 (m), 1428 (m), 1226 (s), 1115 (s), 1043 (s), 1015 (m) cm^{-1} . MS (EI): m/z (%) = 376 (11) [$\text{M}]^+$, 236 (100), 221 (61), 208 (13), 164 (12).

HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{23}\text{H}_{36}\text{O}_4$ 376.261342, found 376.259678.

2-[2-(3-Isopropyl-2,4,5-trimethoxyphenyl)ethyl]-3,3-dimethylcyclohexanone (38): A solution of epoxide **37** (25 mg, 66 μmol , 1.0 equiv.) in dry dichloromethane was treated with $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (9 μL , 69 μmol , 1.05 equiv.) at room temperature followed by stirring of the mixture at room temperature overnight. Thereafter, the mixture was diluted with diethyl ether (5 mL) and water (5 mL). After separation of the layers, the aqueous phase was extracted with diethyl ether (3×5 mL). The combined organic layers were washed with brine (2 mL), dried with MgSO_4 , filtered and concentrated in vacuo. Purification of the residue by flash chromatography (petroleum ether/ethyl acetate, 10:1) provided ketone **38** (6 mg, 17 μmol , 26%) and the pyran **39** (4 mg, 11 μmol , 17%) as colorless oils.

Data for Ketone 38: $R_f = 0.40$ (petroleum ether/ethyl acetate, 10:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.76$ (s, 3 H, CH_3), 0.99 (s, 3 H, CH_3), 1.32 [d, $J = 7.1$ Hz, 6 H, $\text{CH}(\text{CH}_3)_2$], 1.52–1.64 (m, 2 H, 1'a-H, 4-H), 1.75–1.95 (m, 2 H, 5-H), 1.96–2.03 (m, 1 H, 1'b-H), 2.14 (dm, $J = 10.5$ Hz, 1 H, 2-H), 2.25–2.33 (m, 1 H, 6a-H), 2.35–2.42 (m, 2 H, 6b-H, 2'a-H), 2.55 (ddd, $J = 13.5$, 10.5, 4.6 Hz, 1 H, 2'b-H), 3.39 [sept, $J = 7.1$ Hz, 1 H, $\text{CH}(\text{CH}_3)_2$], 3.63, 3.81, 3.82 (3 s, 3 H each, OCH_3), 6.58 (s, 1 H, CH_{ar}) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 22.0$ [$\text{CH}(\text{CH}_3)_2$], 22.1 (CH_3), 23.2 (C-5), 25.4 (C-1'), 26.0 [$\text{CH}(\text{CH}_3)_2$], 29.4 (CH_3), 29.4 (C-2'), 39.2 (C-4), 39.9 (C-3), 41.3 (C-6), 55.8 (OCH_3), 60.5 (C-2), 60.6 (OCH_3), 61.9 (OCH_3), 111.2 (C-6''), 130.1 (C-1''), 134.9 (C-3''), 146.8 (C-5''), 149.4 (C-4''), 149.7 (C-2''), 213.5 (C-1) ppm. IR (film): $\tilde{\nu} = 2956$ (s), 2871 (m), 1709 (s), 1482 (s), 1458 (m), 1428 (m), 1227 (s), 1114 (m), 1043 (s), 1014 cm^{-1} . MS (EI): m/z (%) = 362 (32) [$\text{M}]^+$, 331 (2), 236 (100), 221 (40), 208 (26), 193 (9), 179 (10), 161 (8). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{22}\text{H}_{34}\text{O}_4$ 362.245692, found 362.247185.

Data for Pyran 39 [3-(3-Isopropyl-2,4,5-trimethoxyphenyl)-5,5-dimethylcyclohex-1H-isochromene]: $R_f = 0.69$ (petroleum ether/ethyl acetate, 10:1). ^1H NMR (400 MHz, CDCl_3): $\delta = 0.85$ (s, 3 H, CH_3), 0.87 (s, 3 H, CH_3), 0.82–0.86 (m, 1 H, 8-H), 1.14–1.20 (m, 1 H, 4a-H), 1.19–1.27 (m, 1 H, 6-H), 1.26–1.32 (m, 1 H, 4-H), 1.32 [d, $J = 7.1$ Hz, 3 H, $\text{CH}(\text{CH}_3)_2$], 1.33 [d, $J = 7.1$ Hz, 3 H, $\text{CH}(\text{CH}_3)_2$], 1.41–1.46 (m, 1 H, 6-H), 1.49–1.56 (m, 2 H, 8-H, 7-H), 1.56–1.65 (m, 1 H, 8a-H), 1.79 (d, $J = 12.9$ Hz, 1 H, 4-H), 3.20 (dd, $J = 11.0$, 10.9 Hz, 1 H, 1-H), 3.39 [sept, $J = 7.1$ Hz, 1 H, $\text{CH}(\text{CH}_3)_2$], 3.68 (s, 3 H, OCH_3), 3.82 (s, 3 H, OCH_3), 3.85 (s, 3 H, OCH_3), 3.20 (dd, $J = 11.0$, 4.3 Hz, 1 H, 1-H), 4.64 (dd, $J = 10.8$, 1.6 Hz, 1 H, 3-H), 6.84 (s, 1 H, H aromatic) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 20.0$ (CH_3), 21.4 (C-7), 21.9 [$\text{CH}(\text{CH}_3)_2$], 26.0 [$\text{CH}(\text{CH}_3)_2$], 28.4 (C-8), 29.8 (CH_3), 32.5 (C-5), 33.6 (C-4), 36.2 (C-8a), 41.9 (C-6), 50.2 (C-4a), 55.9 (OCH_3), 60.6 (OCH_3), 62.7 (OCH_3), 74.3 (C-1), 75.5 (C-3), 108.1 (CH aromatic), 130.9 (C-1'), 134.6 (C-3), 148.2 (C-5'), 148.4 (C-2'), 149.9 (C-4) ppm. IR (film): $\tilde{\nu} = 2939$ (s), 2870 (m), 2844 (m), 1482 (s), 1456 (s), 1428 (m), 1367 (m), 1344 (m), 1222 (m), 1115 (s), 1042 (s), 1013 (m) cm^{-1} . MS (EI): m/z (%) = 376 (100) [$\text{M}]^+$, 345 (58), 237 (16), 223 (40), 208 (36), 195 (26), 149 (23), 84 (47). HRMS (EI): [$\text{M}]^+$ calcd. for $\text{C}_{23}\text{H}_{36}\text{O}_4$ 376.261342, found 376.264189.

1-[2-[2-(Bromomethyl)-6,6-dimethylcyclohex-2-en-1-yl]ethyl]-3-isopropyl-2,4,5-trimethoxybenzene (40): A suspension of dry FeCl_3 (0.034 g, 0.21 mmol, 1.05 equiv.) in dry THF (5 mL) was treated with bromine (0.011 mL, 0.21 mmol, 1.05 equiv.). After stirring at room temperature for 45 min, compound **36** (0.071 g, 0.20 mmol, 1.0 equiv.) was added. The mixture was stirred at room temperature for another 60 min, before it was diluted with diethyl ether (10 mL) and water (15 mL). The layers were separated, and the aqueous

layer was extracted with diethyl ether (3×15 mL). The combined organic layers were washed with saturated NaHCO₃ solution (10 mL) and brine (5 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Purification of the crude product by flash chromatography (petroleum ether/diethyl ether, 25:1) provided the bromide **40** (0.074 g, 0.17 mmol, 85%) as a colorless oil; *R*_f = 0.34 (petroleum ether/diethyl ether, 25:1). ¹H NMR (400 MHz, CDCl₃): δ = 0.90 (s, 3 H, CH₃), 1.04 (s, 3 H, CH₃), 1.15–1.21 (m, 1 H, 5''-H), 1.34 [d, *J* = 7.1 Hz, 6 H, CH(CH₃)₂], 1.46–1.58 (m, 2 H, 5''-b-H, 2'-a-H), 1.74–1.83 (m, 1 H, 2'-b-H), 1.97–2.00 (m, 1 H, 1''-H), 2.03–2.07 (m, 2 H, 4''-H), 2.60–2.64 (m, 2 H, 1'-H), 3.38 [sept, *J* = 7.1 Hz, 1 H, CH(CH₃)₂], 3.66, 3.82, 3.83 (3 s, 3 H each, OCH₃), 3.98 (d, *J* = 9.6 Hz, 1 H, CH₂Br), 4.07 (d, *J* = 9.6 Hz, 1 H, CH₂Br), 5.79 (dd, *J* = 3.5, 3.4 Hz, 1 H, 3''-H), 6.55 (s, 1 H, 6-H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 22.0 [CH(CH₃)₂], 23.3 (C-4''), 26.1 [CH(CH₃)₂], 26.8 (CH₃), 27.6 (CH₃), 30.8 (C-5''), 31.5 (C-1'), 32.2 (C-6''), 33.0 (C-2'), 39.2 (CH₂Br), 44.4 (C-1''), 55.9, 60.6, 61.9 (3 OCH₃), 111.3 (CH_{ar}), 127.3 (C-3''), 130.3 (C-1), 135.0 (C-3), 138.0 (C-2'), 147.1 (C-5), 149.4 (C-4), 149.6 (C-2) ppm. IR (film): ν̄ = 2954 (s), 2870 (m), 1482 (s), 1456 (m), 1428 (m), 1226 (s), 1114 (s), 1043 (s) cm⁻¹. MS (EI): *m/z* (%) = 440 (30) [M, ⁸¹Br]⁺, 438 (32) [M, ⁷⁹Br]⁺, 358 (22), 317 (25), 302 (20), 266 (48), 236 (100), 223 (99), 208 (86), 193 (46), 123 (51), 84 (33). HRMS (EI): [M]⁺ calcd. for C₂₃H₃₅BrO₃ 438.176903, found 438.173246.

8-Isopropyl-6,7,9-trimethoxy-1,1-dimethyl-2,3,5,10,11,11a-hexahydro-1H-dibenzo[a,d][7]annulene (13): To a solution of allyl bromide **40** (0.044 g, 0.10 mmol, 1.0 equiv.) in dry THF (10 mL) was added dry zinc chloride (0.14 g, 1.0 mmol, 10 equiv.) and dry copper(I) chloride (0.099 g, 1.0 mmol, 10 equiv.). After refluxing the mixture for 72 h, it was cooled to room temperature, treated with water (7 mL) and 1 N HCl (1 mL). The aqueous layer was extracted with diethyl ether (3×7 mL). The combined organic layers were washed with brine (3 mL), dried with MgSO₄, filtered, and concentrated in vacuo. Flash chromatography (petroleum ether/diethyl ether, 25:1) of the residue provided the desired tricycle **13** (0.023 g, 0.064 mmol, 64%) as a colorless solid, together with some recovered starting material **40** (0.008 g, 0.022 mmol, 22%) and byproduct **41** (0.002 g, 0.006 mmol, 6%) as a colorless oil.

Data for Product 13: M.p. 109 °C. *R*_f = 0.49 (petroleum ether/diethyl ether, 25:1). ¹H NMR (400 MHz, CDCl₃): δ = 0.87 (s, 3 H, CH₃), 0.91 (s, 3 H, CH₃), 1.06–1.11 (m, 1 H, 2-H), 1.10–1.18 (m, 1 H, 11-H), 1.28–1.32 (m, 1 H, 2-H), 1.31 [d, *J* = 7.1 Hz, 3 H, CH(CH₃)₂], 1.33 [d, *J* = 7.1 Hz, 3 H, CH(CH₃)₂], 1.76–1.82 (m, 1 H, 11a-H), 1.87–2.02 (m, 2 H, 3-H), 2.04–2.11 (m, 1 H, 11-H), 2.55 (ddd, *J* = 12.2, 7.7, 2.3 Hz, 1 H, 10-H), 3.03 (d, *J* = 14.7 Hz, 1 H, 5-H), 3.14 (ddd, *J* = 10.7, 8.4, 2.3 Hz, 1 H, 10-H), 3.39 [sept, *J* = 7.1 Hz, 1 H, CH(CH₃)₂], 3.63 (s, 3 H, OCH₃), 3.76 (s, 3 H, OCH₃), 3.78 (d, *J* = 14.7 Hz, 1 H, 5-H), 3.85 (s, 3 H, OCH₃), 5.47–5.50 (m, 1 H, 4-H) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 22.2 [CH(CH₃)₂], 22.3 [CH(CH₃)₂], 23.2 (C-3), 26.0 [CH(CH₃)₂], 26.0 (C-10), 27.2 (CH₃), 27.4 (CH₃), 29.6 (C-11), 31.5 (C-2), 32.1 (C-1), 35.3 (C-5), 51.4 (C-11a), 60.3, 60.4, 62.3 (3 OCH₃), 121.4 (C-4), 130.2 (C-9a), 132.0 (C-7), 133.7 (C-8), 138.2 (C-4a), 146.6 (C-6), 150.7 (C-7), 151.3 (C-9) ppm. IR (KBr): ν̄ = 2912 (s), 2867 (m), 2832 (m), 1449 (s), 1411 (m), 1341 (m), 1125 (m), 1097 (m), 1039 (s) cm⁻¹. MS (EI): *m/z* (%) = 358 (100) [M]⁺, 343 (22) [M-CH₃]⁺, 302 (8), 278 (6), 223 (18), 165 (6), 128(7). HRMS (EI): [M]⁺ calcd. for C₂₃H₃₄O₃ 358.250781, found 358.253657.

Data for Byproduct 1-[2-(6,6-Dimethyl-2-methylenecyclohex-3-en-1-yl)ethyl]-3-isopropyl-2,4,5-trimethoxybenzene (41): *R*_f = 0.40 (petroleum ether/diethyl ether, 25:1). ¹H NMR (400 MHz, CDCl₃): δ = 0.87 (s, 3 H, CH₃), 0.97 (s, 3 H, CH₃), 1.30–1.36 (m, 1 H, 2'-H),

1.32 [two peaks, d, *J* = 7.1 Hz, 6 H, CH(CH₃)₂], 1.71 [dd, *J* = 18.4, 5.3 Hz, 1 H, CH₂C(Me)₂], 1.75–1.85 (m, 2 H, 2'-H, 1''-H), 2.05 [dm, *J* = 18.4 Hz, 1 H, 1 H, CH₂C(Me)₂], 2.38 (ddd, *J* = 13.7, 11.7, 5.5 Hz, 1 H, 1'-H), 2.66 (ddd, *J* = 13.6, 11.7, 4.5 Hz, 1 H, 1'-H), 3.40 [sept, *J* = 7.1 Hz, 1 H, CH(CH₃)₂], 3.62, 3.81, 3.82 (3 s, 3 H each, OCH₃), 4.82–4.83 (m, 1 H, CH₂=C), 4.94–4.95 (m, 1 H, CH₂=C), 5.61–5.67 (m, 1 H, CH₂CH=CH), 6.06 (dm, *J* = 9.9 Hz, 1 H, CH₂CH=CH), 6.53 (s, 1 H, H aromatic) ppm. ¹³C NMR (100 MHz, CDCl₃): δ = 22.0 [2 peaks, CH(CH₃)₂], 26.0 [CH(CH₃)₂], 27.6 (CH₃), 28.2 (CH₃), 28.7 (C-1'), 29.4 (C-2'), 32.8 (CMe₂), 36.4 (CH₂CMe₂), 52.1 (C-1''), 55.9, 60.6, 61.9 (3 OCH₃), 111.1 (C-CH aromatic), 112.8 (CH₂=C), 127.3 [CH₂CH=CH (C-4'')], 127.8 [CH₂CH=CH (C-3'')], 130.7 (C-1), 134.9 (C-3), 145.8 (C-5), 146.7 (CH₂=C), 149.3 (C-4), 149.7 (C-2) ppm. IR (film): ν̄ = 2954 (s), 2870 (m), 1482 (s), 1456 (m), 1427 (m), 1225 (s), 1114 (s), 1044 (s), 1015 (m) cm⁻¹. MS (EI): *m/z* (%) = 358 (5) [M]⁺, 266 (4), 236 (100), 221 (32), 208 (11), 164 (9), 86 (19), 84 (33). HRMS (EI): [M]⁺ calcd. for C₂₃H₃₄O₃ 358.250781, found 358.252952.

Supporting Information (see footnote on the first page of this article): Experimental details for the attempted coupling of benzyl iodide **25** with ketone **27**; ¹H and ¹³C NMR spectra of all new compounds.

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