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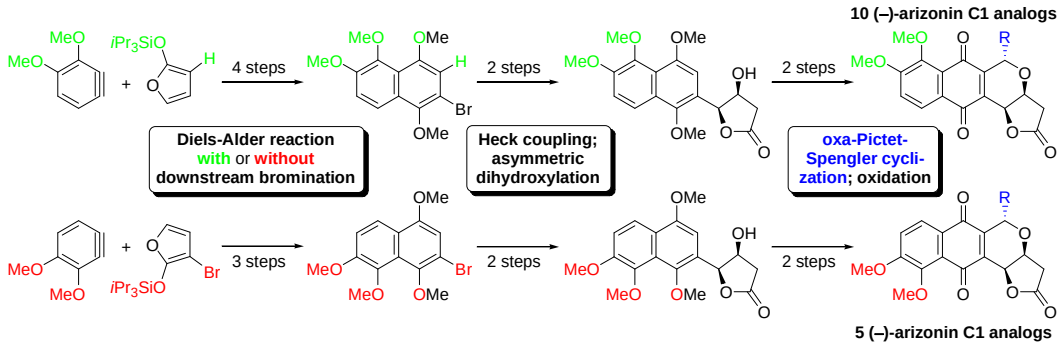
Markus Neumeyer,[a] Julia Kopp,[a] and Reinhard Brückner*[a]

Naphthoquinonopyrano-γ-lactones



Furans with directing power: 3,4-Dimethoxybenz-1-yne and 2-siloxylated furans with or without 3-bromine underwent Diels-Alder reactions with orientational selectivity. Hydrolysis gave a bromine-containing and a bromine-free naphthalene, respectively. Bromination of the latter provided a regioisomer of the former. In 4 steps, these compounds delivered unnatural naphthoquinonopyrano-γ-lactones. They resemble the natural product (–)-arizonin C1 and contain hexasubstituted naphthalene cores, too.

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Controlling the Substitution Pattern of Hexasubstituted Naphthalenes by Aryne/Siloxyfuran Diels-Alder Additions: Regio- and Stereocontrolled Synthesis of Arizonin C1 Analogs

Markus Neumeyer,[a] Julia Kopp,[a] and Reinhard Brückner*[a]

Dedicated to Waldemar Adam at the occasion of his 80th anniversary

Abstract: *3,4-Dimethoxybenz-1-yne and 2-siloxylated furans without or with a bromine atom at C-3 undergo Diels-Alder reactions with orientational selectivity. Hydrolysis furnished a bromine-free and a bromine-containing naphthalene, respectively. Bromination of the former provided a regioisomer of the latter. Either of the two compounds was processed to give a variety of unnatural naphthoquinonopyrano-γ-lactones. This occurred by a succession of (1) Heck coupling, (2) asymmetric dihydroxylation, (3) oxa-Pictet-Spengler cyclization, and (4) oxidation. The fifteen monomeric naphthoquinonopyrano-γ-lactone structures, which we reached resemble the natural product (–)-arizonin C1 or its C-5 epimer. Accordingly, they represent hexasubstituted naphthalenes likewise. The sixteenth naphthoquinonopyrano-γ-lactone is a dimer of sorts. Its moieties are bridged differently than in naturally occurring naphthoquinonopyrano-γ-lactone dimers.*

Natural Naphthoquinonopyrano-γ-lactones and Synthetic Analogs

The naphthoquinonopyrano-γ-lactone natural products exhibit a wide array of biological activity such as inhibition of Gram positive and negative bacteria, fungi, yeasts, and malignant tumors.[1] Not in the least therefore, these compounds have attracted the interest of natural product, synthetic, and medicinal chemists.[2] Figure 1 shows a selection of monomeric naphthoquinonopyrano-γ-lactone natural products: (+)-kalafungin (**1a**[3]), its naturally occurring enantiomer (–)-nanaomycin D (*ent*-**1a**[4]), (+)-frenolicin B (**1b**[5]), (–)-arizonin B1 (**2**[6]), and (–)-arizonin C1 (**3**[6]). Considerable efforts were directed towards the total synthesis of these compounds[7] and their congeners.[2] In that context a number of C5-epimers,[8,9] naphthoquinonopyrano-γ-lactones,[10] benzoquinonopyrano-γ-lactones,[11] and carbazole-

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Supporting Information for this article is provided via a link at the end of this document.

[1] M. A. Brimble, L. J. Duncalf, M. R. Nairn, *Nat. Prod. Rep.* **1999**, *16*, 267-281.
[2] Reviews: a) M. A. Brimble, M. R. Nairn, H. Prabarahan, *Tetrahedron* **2000**, *56*, 1937-1992; b) K. Tatsuta, S. Hosokawa, *Chem. Rev.* **2005**, *105*, 4707-4729; c) Review: K. Tatsuta, S. Hosokawa, *Science and Technology of Advanced Materials*, **2006**, *7*, 397-410; d) J. Sperry, P. Bachu, M. A. Brimble, *Nat. Prod. Rep.* **2008**, *25*, 376-400; e) K. Tatsuta, *J. Antibiot.* **2013**, *66*, 107-129; f) R. A. Fernandes, P. H. Patil, D. A. Chaudhari, *Eur. J. Org. Chem.* **2016**, 5778–5798; g) B. J. Naysmith, P. A. Hume, J. Sperry, M. A. Brimble, *Nat. Prod. Rep.* **2017**, 34, 25-61.
[3] a) M. E. Bergy, *J. Antibiot*. **1968**, *21*, 454-457; b) H. Hoeksema, W. C. Krueger, *J. Antibiot*. **1976**, *29*, 704-709 [ORD spectrum of *O*-methyl-(+)-kalafungin but not of (+)-kalafungin (**1a**)].
[4] S. Omura, H. Tanaka, Y. Okada, H. Marumo, *J. Chem. Soc., Chem. Commun*. **1976**, 320-321.
[5] a) Y. Iwai, A. Kora, Y. Takahashi, T. Hayashi, J. Awaya, R. Masuma, R. Oiwa, S. Omura, *J. Antibiot*. **1978**, *31*, 959-965 (without the sign of the specific rotation of the natural product); b) synthetic (+)-deoxyfrenolicin B and "deoxyfrenolicin B methyl ester of natural origin" were converted into synthetic (+)-frenolicin B by T. Masquelin, U. Hengartner, J. Streith, *Helv. Chim. Acta*, **1997**, *80*, 43-58; natural deoxyfrenolicin B being dextrorotatory (ref.[5a]) the correlations of ref.[5b establish the dextrorotation of natural (+)-frenolicin B (**1b**).
[6] a) J. E. Hochlowski, G. M. Brill, W. W. Andres, S. G. Spanton, J. B. McAlpine, *J. Antibiot.* **1987**, *40*, 401-407.
[7] With respect to the naphthoquinonopyrano-γ-lactone natural products **1**- **3** we are aware of the following total syntheses: (+)-kalafungin (**1a**): a) K. Tatsuta, K. Akimoto, M. Annaka, Y. Ohno, M. Kinoshita, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1699-1706; b) *J. Antibiot.* **1985**, 680-682; c) R. A. Fernandes, R. Brückner, *Synlett* **2005**, 1281-1285; d) C. D. Donner, *Tetrahedron Lett.* **2007**, *48*, 8888-8890; e) R. A. Fernandes, V. P. Chavan, S. V. Mulay A. Manchoju, *J. Org. Chem.* **2012**, *77*, 10455−10460; f) C. D. Donner, *Tetrahedron*, **2013**, *69*, 377-386; total syntheses of (–)-nanaomycin D (*ent*-**1a**): g) ref.[7a]; h) ref.[7b]; i) M. P. Winters, M. Stranberg, H. W. Moore, *J. Org. Chem.* **1994**, *59*, 7572-7574; j) ref.[7c]; k) N. P.S. Hassan, B. J. Naysmith, J. Sperry, M. A. Brimble, *Tetrahedron* **2015**, *71*, 7137-7143; total syntheses of (+)-frenolicin B (**1b**): l) G. A. Kraus, J. Li, *J. Am. Chem. Soc.* **1993**, *115*, 5859-5860; m) G. A. Kraus, J. Li, M. S. Gordon, J. H. Jensen, *J. Org. Chem.* **1995**, *60*, 1154-1159; n) ref.[5b]; o) R. Brückner, R. A. Fernandes, unpublished results; p) ref.[7e] q) Y. Zhang, X. Wang, M. Sunkara, Q. Ye, L. V. Ponomereva, Q.-B. She, A. J. Morris, J. S. Thorson, *Org. Lett.* **2013**, *15*, 5566-5569; total synthesis of (–)-arizonin B1 (**2**): r) M. Neumeyer, R. Brückner, *Eur. J. Org. Chem.* **2017**, in the press (DOI: 10.1002/ejoc.201700013); total syntheses of (–)-arizonin C1 (**3**): s) M. Mahlau, R. A. Fernandes, R. Brückner, *Eur. J. Org. Chem.* **2011**, 4765-4772; t) R. A. Fernandes, S. V. Mulay, V. P. Chavan, *Tetrahedron: Asymmetry* **2013**, *24*, 1548-1555; u) ref.[7r].
[8] a) Syntheses of racemic 5-*epi*-kalafungin = racemic 5-*epi*-nanaomycin D (5-*epi*-*rac*-**1a**) are unknown; syntheses of racemic 5-*epi*-frenolicin B (5-*epi*-*rac*-**1b**): b) P. Contant, M. Haess, J. Riegl, M. Scalone, M. Visnick, *Synthesis*, **1999**, 821-828; c) C. D. Donner, *Synthesis* **2010**, 415-420; synthesis of racemic 5-*epi*-arizonin B1 (5-*epi*-*rac*-**2**): d) M. A. Brimble, S. J. Phythian, *Tetrahedron Lett.* **1993**, *34*, 5813-5814; synthesis of racemic 5-*epi*-arizonin C1 (5-*epi*-*rac*-**3**): e) Ref.[8d].
[9] Syntheses of enantiomerically pure (–)-5-*epi*-kalafungin (5-*epi*-**1a**) or (+)-5-*epi*-nanaomycin D (5-*epi*-*ent*-**1a**): a) Ref.[7c]; b) ref.[7d]; c) ref.[7e]; d) ref.[7f]; syntheses of enantiomerically pure (–)-5-*epi*-frenolicin B (5-*epi*-**1b**): e) ref.[5b]; f) ref.[7o]; g) ref.[7e]; h) ref.[7f]; i) ref.[7q]; synthesis of enantiomerically pure (+)-5-*epi*-arizonin B1 (5-*epi*-**2**) j) ref.[7r]; synthesis of enantiomerically pure (+)-5-*epi*-arizonin C1 (5-*epi*-**3**): ref.[7r].
[10] For example: a) T. Masquelin, U. Hengartner, J. Streith, *Synthesis* **1995**, 780-786; b) C. Tödter, H. Lackner, *Liebigs Ann.* **1996**, 1385-1394; c) E. J. Salaski, G. Krishnamurthy, W.-D. Ding, K. Yu, S. S. Insaf, C. Eid, J. Shim, J. I. Levin, K. Tabei, L. Toral-Barza, W.-G. Zhang, L. A. McDonald, E. Honores, C.

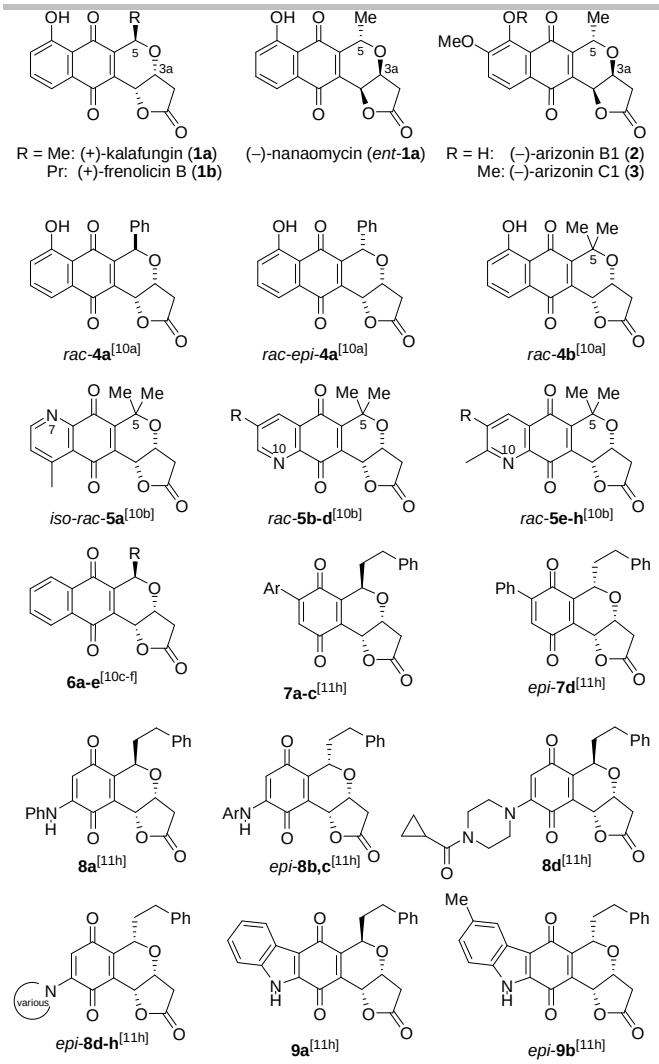
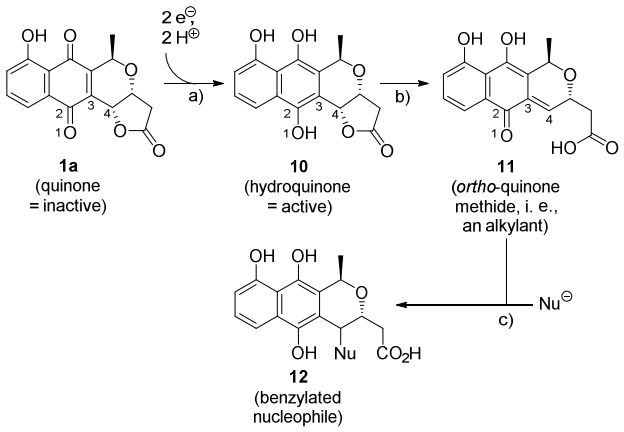


Figure 1. Selected monomeric naphthoquinonopyrano-γ-lactone natural products: (+)-kalafungin (**1a**), (+)-frenolicin B (**1b**), (–)-nanaomycin (*ent*-**1a**), (–)-arizonin B1 (**2**), and (–)-arizonin C1 (**3**). Synthetic pyrano-γ-lactone analogs with *trans*,*cis*-substituted dihydropyran moieties: naphthoquinonopyrano-γ-lactones (*rac*-**4a**, **6a-e**), benzoquinonopyrano-γ-lactones (**7a-c**-**8a**,**d**), and carbazolequinonopyrano-γ-lactones (**9a**); with *cis*,*cis*-substituted dihydropyran moieties: naphthoquinonopyrano-γ-lactones (*rac*-*epi*-**4a**) benzoquinonopyrano-γ-lactones (*epi*-**7d**, *epi*-**8a**,**b**,**d**-**h**) and the carbazolequinonopyrano-γ-lactone *epi*-**9b**; with C-5 dimethylated diyhdropyran moieties: naphthoquinonopyrano-γ-lactones (*rac*-**4b**, *iso*-*rac*-**5a**, and *rac*-**5b-h**).

zolequinonopyrano-γ-lactones [11h] were synthesized. They all are "analogs" of the naphthoquinonopyrano-γ-lactone natural products **1**-**3**.[12] Figure 1 shows most of them (**4** - **9**). *Rac*-**4a** differs from *rac*-kalafungin (*rac*-**1a**) by its phenyl instead of a methyl substituent.[10a] The kalafungin epimer *rac*-*epi*-**4a** contains a *cis*,*cis*- rather than *trans*,*cis*-dihydropyran. Compound *rac*-**4b** is monomethyl kalafungin (5-Me-*rac*-**1a**).[10a] Other 5,5-dimethylated naphthoquinonopyrano-γ-lactone analogs are quinolinequinones: *iso*-*rac*-**5a**, *rac*-**5b**-**d** (R = H, Me, OH), and *rac*-**5e**-**h** (R = OH, OMe, OBn, and NMe_2, respectively).[10b] 7-Deoxykalafungin (**6a**, R = Me) was targeted four times[10c-f] and analogs **6b**-**e** (R = H, alkyl ≠ methyl, aryl) thereof twice.[10c-d] Benzoquinonopyrano-γ-lactones with an aryl group (**7a**-**c**, Ar = 4-$MeOC_6H_4$, 4-ClC_6H_4, 2,4,6-$(MeO)_3C_6H_4$; *epi*-**7d**), an acyclic nitrogen substituent (**8a**; *epi*-**8b**-**c**, R = 4-MeC_6H_4, 4-FC_6H_4), a heterocyclic nitrogen substituent (**8d**; *epi*-**8d**-**h**, substituents too complex for showing) were studied, too,[11h] as were the carbazolequinonopyrano-γ-lactones **9a** and *epi*-**9b**.[11h]

The frenolicin B analogs *rac*-**4a** and *rac*-**4b** (Figure 1) increased the drug resistance of *Eimeria tenella* in vitro as much and by the same mode of action as the natural product frenolicin B (**1b**) [10a]. Some quinolinequinones *rac*-**5** are active against bacteria, fungi, and tumor cell lines.[10b] Brimble et al. proved 7-deoxykalafungin **6a** (R = Me; synthesis: ref.[10e]) is cytotoxic against three breast cancer cell lines.[13] (+)-Frenolicin B (**1b**) inhibits a serine/threonine kinase implicated in certain malignant tumors.[14] The deoxykalafungin analogs **6a-e**[10d] inhibit the same kinase by the surmised alkylation of a cysteine thiol group.[10c] Remarkably, antipode *ent*-**6e** is as active as **6e** itself.[10c] The naphthoquinonopyrano-γ-lactone analogs **7**-**9** proved cytotoxic against various tumor cell lines.[11h] Altogether, bioactivity in this class of compounds stretches beyond the natural products considerably.



Scheme 1. The in-vivo alkylation of nucleophiles, which causes the biological activity of naphthoquinonopyrano-γ-lactones according to ref.[15], exemplified for (+)-kalafungin (**1a**): a) reduction; b) 1,4-elimination; c) 1,4-addition [steps (b) and (c) combined represent an S_N1-substitution].

Hanna, A. Yamashita, B. Johnson, Z. Li, L. Laakso, D. Powell, T. S. Mansour, *J. Med. Chem.* **2009**, *52*, 2181-2184; d) C. N. Eid, J. Shim, J. Bikker, M. Lin, *J. Org. Chem.* **2009**, *74*, 423-426; e) P. A. Hume, J. Sperry, M. A. Brimble, *Org. Biomol. Chem.*, **2011**, *9*, 5423-5430; f) S. Korwar, T. Nguyen, K. C. Ellis, *Bioorg. Med. Chem. Lett.* **2014**, *24*, 271-274.

[11] Examples of racemic benzoquinonopyrano-γ-lactones: a) ref.[10b]; b) Z. Li, Y. Gao, Y. Tang, M. Dai, G. Wang, Z. Wang, Z. Yang, *Org. Lett.* **2008,** *10*, 3017-3020; c) Y. Cui, H. Jiang, Z. Li, N. Wu, Z. Yang, J. Quan, *Org. Lett.* **2009**, *11*, 4628-4631; d) ref.[8c]; examples of enantiomerically pure benzoquinonopyrano-γ-lactones: e) ref.[7i]; f) ref.[7l]; g) ref.[7m]; h) X. Jiang, M. Wang, S. Song, Y. Xu, Z. Miao, A. Zhang, *RSC Advances* **2015**, *5*, 27502-27508.

[12] More extensive treatises of the structural space of naphthoquinonopyrano-γ-lactones: ref.[2].

[13] A. M. Heapy, A. V. Patterson, J. B. Smaill, S. M. F. Jamieson, C. P. Guise, J. Sperry, P. A. Humea, K. Rathwell, M. A. Brimble, *Bioorg. Med. Chem.* **2013**, *21*, 7971-7980.

[14] L. Toral-Barza, W.-G. Zhang, X. Huang, L. A. McDonald, E. J. Salaski, L. R. Barbieri, W.-D. Ding, G. Krishnamurthy, Y. B. Hu, J. Lucas, V. S. Bernan, P. Cai, J. I. Levin, T. S. Mansour, J. J. Gibbons, R. T. Abraham, K. Yu, *Mol. Cancer Ther.* **2007**, *6*, 3028-3038.

The chemical basis of these bioactivities should be the bioreductive alkylation mechanism of Moore and Czerniak.[15] Scheme 1 exemplifies it for (+)-kalafungin (**1a**). Step 1 is believed to be an in-vivo reduction providing the naphthohydroquinone **10**. The lactone moiety ring-opens thereupon, forming quinone methide **11**. The latter is a Michael acceptor and therefore acts as an alkylating agent of nucleophilic sites in proteins.[15] Supporting evidence for this mode of action stems from reductive thioalkylations of a naphthoquinonopyrano-γ-lactone described by Brimble et al.[16] and a pertinent theoretical treatment.[17]

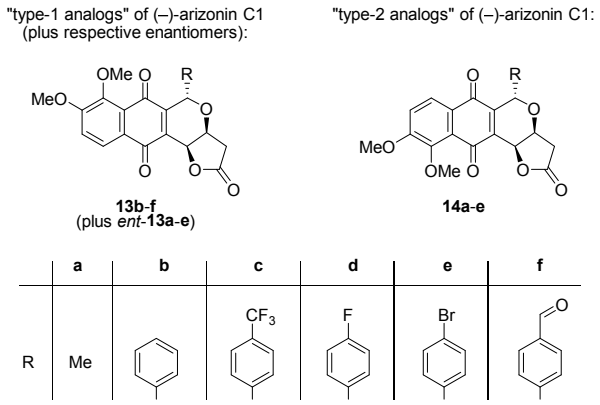


Figure 2. Synthetic naphthoquinonopyrano-γ-lactones reached in the present study. Compounds **13b**-**f**, their mirror images *ent*-**13b**-**f**, and the unnatural enantiomer *ent*-**13a** (≡ *ent*-**3**) of (–)-arizonin C1 (**3**) – summarizable as "type-1 analogs" of (–)-arizonin C1 (**3**) – are dimethoxylated at the same positions as their antecessor. Compounds **12a**-**e** – collectively called "type-2 analogs" of (–)-arizonin C1 (**3**) – are dimethoxylated at different positions. In addition to these analogs we synthesized the dimeric naphthoquinonopyrano-γ-lactone **46** (structure: Scheme 6).

This publication describes the synthesis of a 16-membered library of arizonin C1-like naphthoquinonopyrano-γ-lactones (structures: Figure 2). It includes the synthesis of the dimeric naphthoquinonopyrano-γ-lactone **45** (detailed in Scheme 6).

Orientationally Complementary Aryne/Siloxyfuran Diels-Alder Reactions for Synthesizing Naphthoquinonopyrano-γ-lactone Analogs of (–)-Arizonin C1

Each arizonin C1 analog of Figure 2 or Scheme 6 was prepared by an identical series of 4 late steps: 1) Heck-coupling;[18] 2) asymmetric dihydroxylation;[19] 3) oxa-Pictet-Spengler reaction;[20] oxidation of the naphthohydroquinone (details: below). This strategy equals one, which we followed in total syntheses of the naphthoquinonopyrano-γ-lactone natural products (+)-kalafungin (**1**),[7c] (–)-arizonin B1 (**2**),[7r] (–)-arizonin C1 (**3**),[7s] and (+)-γ-actinorhodin.[21,22] The difference between the present syntheses and our former ones is how we deemed to prepare the bromonaphthalene substrate of the Heck coupling. This is shown at the bottom of Scheme 2 and discussed in the next paragraph.

Scheme 2 depicts retrosynthetic analyses of the desired „type 1-analogs" (at left) and „type-2 analogs" (at right) of the naphthoquinonopyrano-γ-lactone pharmacophore. The former analogs possess scaffold **13**, the latter scaffold **14**. The upper half of Scheme 2 retraces the already-mentioned steps: (1) Heck couplings **19**→**17** and **20**→**18**; (2) asymmetric dihydroxylations **17**→**15** and **18**→**16**; (3) oxa-Pictet-Spengler cyclizations / (4) Ce(IV) oxidations (**15** → → **13** and **16** → → **14**). The lower half of Scheme 2 shows how we planned to reach the Heck substrates: after annulating 3,4-dimethoxybenz-1-yne (**26**) to the 2-siloxyfurans **27** or **28**, respectively. This should occur by tandems of regioselective[23] Diels-Alder reactions (→ tricycles **24**[24] and **25**, respectively) and in-situ ring-openings (→ naphthalene **22** and bromonaphthalene **23**, respectively). The naphthalene **22** should be (re)protected and brominated regioselectively[25] in order to reach the Heck substrate **19**. The bromonaphthalene **23** should be (re)protected to render the Heck substrate **20** directly.

The route delivering the aryne **26** and our desire to add it to the bromine-containing siloxyfuran **28** (Scheme 2, at bottom) deserve two comments. (1) To date this aryne seems to have been prepared solely by treating the bromotosylate *iso*-**29** with *n*BuLi.[26] This induces a Br/Li exchange and subsequent β-elimination of lithium *p*-toluenesulfinate. We wanted to proceed

[15] a) H. W. Moore, *Science* **1977**, *198*, 527-532.– b) H. W. Moore, R. Czerniak, *Med. Res. Rev.* **1981**, *1*, 249-280.

[16] Communication: M. A. Brimble, M. R. Nairn, *Tetrahedron Lett.* **1998**, *39*, 4879-4882; full paper: M. A. Brimble, M. R. Nairn, *J. Chem. Soc. Perkin Trans. 1*, **2000**, 317-322.

[17] P. A. Hume, M. A. Brimble, J. Reynisson, *Aust. J. Chem.* **2012**, *65*, 402-408.

[18] a) ref.[10d]; b) Y. Zhang, X. Wang, M. Sunkara, Q. Ye, L. V. Ponomereva, Q.-B. She, A. J. Morris, J. S. Thorson, *Org. Lett.* **2013**, *15*, 5566-5569; c) .[10f]; d) Y. Zhang, Q. Ye, X. Wang, Q.-B. She, J. S. Thorson, *Angew. Chem.* **2015**, *127*, 11371-11374; *Angew. Chem. Int. Ed.* **2015**, *54*, 11219-11222; e) ref.[7r].

[19] Such routes to "Nonracemic γ-Lactones From the Sharpless Asymmetric Dihydroxylation of β,γ-Unsaturated Carboxylic Esters" were the topic of a pertinent review: M. Neumeyer, R. Brückner, *Eur. J. Org. Chem.* **2016**, 5060-5087.

[20] a) Review: E. L. Larghi, T. S. Kaufman, *Eur. J. Org. Chem.* **2011**, 5195-5231; recent uses in the synthesis of naphthoquinonopyrano-γ-lactones: b) ref.[7e]; c) R. Bartholomäus, J. Bachmann, C. Mang, L. O. Haustedt, K. Harms, U. Koert, *Eur. J. Org. Chem.* **2013**, 180-190; d) ref.[7t]; e) S. V. Mulay, A. Bhowmik, R. A. Fernandes, *Eur. J. Org. Chem.* **2015**, 4931-4938; f) ref.[7r]; g) ref.[22].

[21] a) Correct structure: A. Zeeck, H. Zähner, M. Mardin, *Liebigs Ann. Chem.* **1974**, 1100-1125; b) tautomeric structure: B. Krone, A. Zeeck, *Liebigs Ann. Chem.* **1987**, 751-758; c) the specific rotation was not determined at a single wavelength; its value at 589 nm can be interpolated from the ORD spectrum (P. Christiansen, *Ph. D. Thesis*, Universität Göttingen, Germany, **1970**; ref.[21b]).

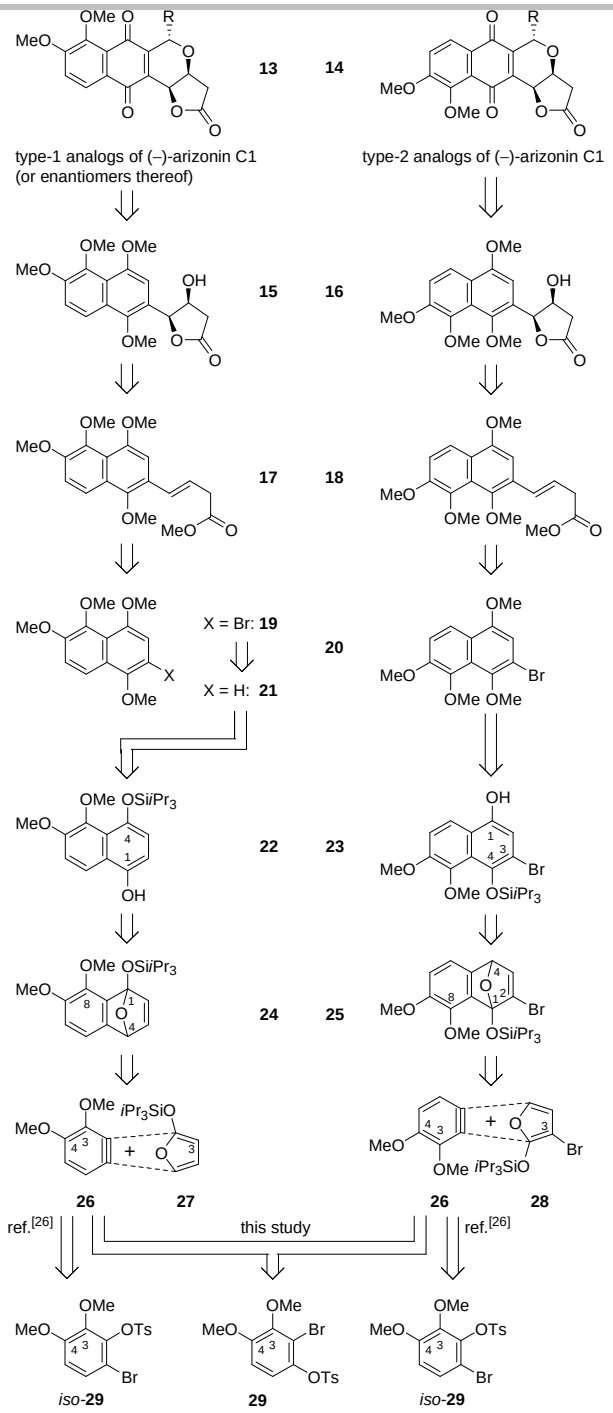
[22] Total synthesis: M. Neumeyer, R. Brückner, *Angew. Chem.* **2017**, in the press (DOI: 10.1002/anie.201611183, DOI: 10.1002/ange.201611183).

[23] Diels-Alder reactions of unsymmetric 3-alkoxybenz-1-ynes with 2-oxygenated furans are likely to deliver two regioisomers but usually one adduct predominates. Therein, the mentioned oxygen substituents are located close to each other, namely at C-1 and C-8 (naphthalene numbering; references: cf. footnote 30 in ref.[7r].). We call this the "proximal" Diels-Alder adduct. In contrast, the mentioned oxygen substituents wind up in a greater distance from one another in what we call the "distal" Diels-Alder adduct, namely at C-1 and C-5 (naphthalene numbering).

[24] We are aware of a single Diels-Alder reaction between an aryne and the siloxyfuran **27**: S. Narayan, W. R. Roush, *Org. Lett.* **2004**, *6*, 3789-3792. The aryne employed there was near-symmetric and reacted without regiocontrol.

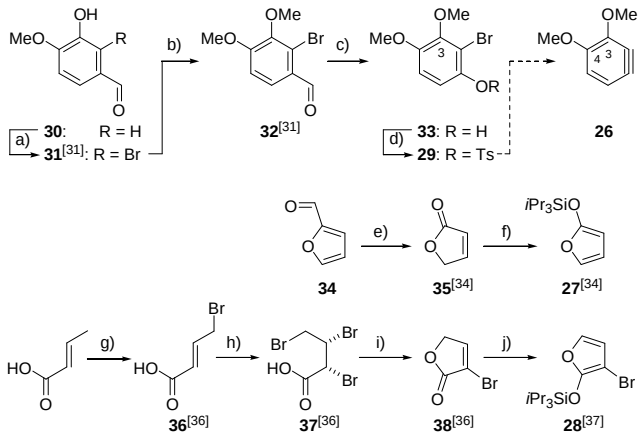
[25] References of C-6 brominations of 1-substituted 2-oxynaphthalenes: cf. footnote 27 in ref.[7r].

[26] Preparation of 3,4-dimethoxybenz-1-yne (**26**) from bromotosylate *iso*-**29**: a) R. G. F. Giles, A. B. Hughes, M. V. Sargent, *J. Chem. Soc. Perkin Trans. 1* **1991**, 1581-1587; b) M. A. Brimble, S. J. Phythian, *Tetrahedron Lett.* **1993**, *34*,



Scheme 2. Retrosynthetic analysis of arizonin C1 analogs. Type 1-analogs contain the natural naphthoquinone motif (**13**, left column), type 2-analogs are "methoxy-reversed" variations thereof (**14**, right column).

analogously employing the isomeric bromotosylate **29**. It is easier to make than *iso*-**29**.[27] (2) Employing *n*BuLi for generating 3,4-dimethoxybenz-1-yne (**26**) requires that Br/Li exchange in **29** (or *iso*-**29**) is faster than in the 3-bromo-2-siloxyfuran **28** (which is susceptible to a Br/Li exchange with *n*BuLi in THF at –78°C[28]). However, *n*BuLi and an iodotosylate gave an aryne when 2-bromofuran was present.[29] Likewise, *n*BuLi effected a dehydrofluorination providing an aryne in the presence of 3-bromofuran[30]. This meant that our preparation of the aryne **26** should not jeopardize the Br-containing siloxyfuran **28**.



Scheme 3. Syntheses of the Diels-Alder partners: bromotosylate **29** (preceding the aryne **26**), siloxyfurans **27** and **28**. Reagents and conditions: ***a)*** *Br_2 (1.0 equiv.), NaOAc (2 equiv.) Fe powder (8 mol-%), AcOH, room temp., 5 h; 73% (ref.[31]: 70%);* ***b)*** *KOH (1.6 equiv.) Me_2SO_4 (1.6 equiv.), H_2O, 60°C, 1 h; 74% (ref. [31]: 96%);* ***c)*** *mCPBA (1.5 equiv.), CH_2Cl_2, reflux, 14 h; aqueous KOH (10%, 4 equiv.), room temp., 3 h; 92%;* ***d)*** *TsCl (1.5 equiv.), NEt_3 (1.5 equiv.), CH_2Cl_2, 0°C → room temp., 4 d; 85%;* ***e)*** *N,N-dimethylethanolamine (34 mol-%), formic acid (2 equiv.), H_2O_2 (30% in H_2O, 2 equiv.), Na_2SO_4,, room temp., 16 h; 59% (ref.[34]: 58%);* ***f)*** *iPr_3SiOTf (1.2 equiv.),[35] NEt_3 (1.3 equiv.), CH_2Cl_2, 0°C → room temp., 1 h; 98% (ref.[34]: 94%);* ***g)*** *NBS (1.0 equiv.), AIBN (0.6 mol-%), CCl_4, reflux, 5 h;* ***h)*** *Br_2 (1.2 equiv.), 40°C, 5 h; 42% over the 2 steps (ref.[36]: 35%);* ***i)*** *H_2O, reflux, 4 h; 43% (ref.[36]: 31%);* ***j)*** *iPr_3SiOTf (1.2 equiv.),[35] NEt_3 (1.4 equiv.), CH_2Cl_2, 0°C → room temp., 2.5 h; 79% (ref.[37]: 90%).*

Our syntheses began with preparing the bromotosylate **29** and the siloxyfurans **27** and **28**, i. e., the precursor and substrates, respectively, of the mentioned Diels-Alder reactions (Scheme 3). For reaching the bromotosylate **29**, isovanillin (**30**) was *ortho*-brominated following the literature.[31] An *O*-methylation ensued first[31] (→ **31**), a Dakin oxidation[32] then, and formate hydrolysis thereafter(→ **33**).[33] A tosylation accomplished the bromotosylate **29** in 42% overall yield.

5813-5814; c) M. A. Brimble, S. J. Phythian, H. Prabaharan, *J. Chem. Soc. Perkin Trans 1*, **1995**, 2855-2860.

[27] This variation entailed no risk: We prepared the analogous aryne – containing 3-OBn instead of 3-OMe – from the OBn analog of bromotosylate **29** rather than from the OBn analog of bromotosylate *iso*-**29** earlier (ref. [7r]).

[28] a) Br/Li exchange: J. Boukouvalas, J.-X. Wang, O. Marion, B. Ndzi, *J. Org. Chem.* **2006**, *71*, 6670-6673; b) 3-lithiated 2-triisopropylsiloxyfurans (from an I/Li exchange) undergo no retro-[1.2]-Brook rearrangement at –78°C (as shown by quenching 3-lithio-4-methoxy-2-(triisopropylsiloxy)furan with CD_3OD at –78°C and working up at pH 5.5 to a 3-deuterated butenolide) according to F. F. Paintner, L. Allmendinger, G. Bauschke, *Synlett* **2005**, *18*, 2735-2738.

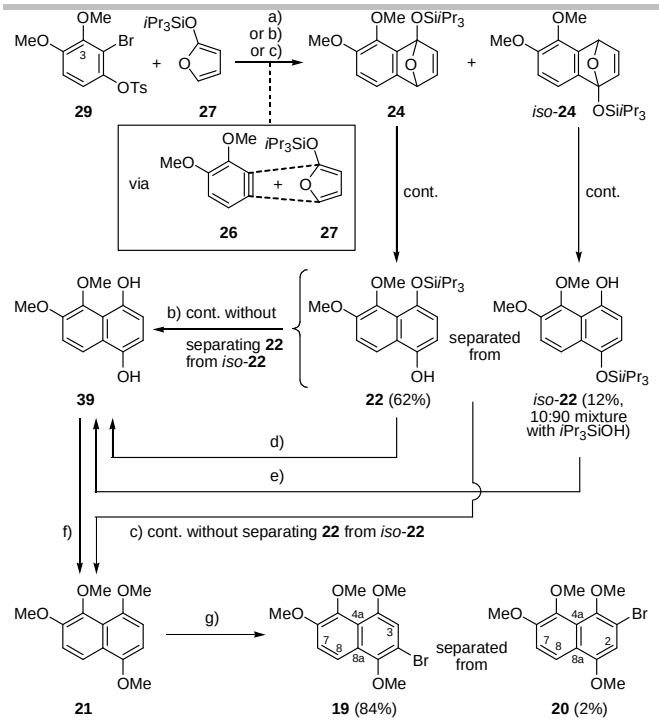
[29] G. E. Morton, A. G. M. Barrett, *J. Org. Chem.* **2005**, *70*, 3525-3529.

[30] R. G. F. Giles, M. V. Sargent, H. Sianipar, *J. Chem. Soc., Perkin Trans. 1* **1991**, 1571-1579.

[31] A. K. Sinhababu, R. T. Borchardt, *J. Org. Chem.* **1983**, *48*, 2356-2360.

[32] First reports: a) H. D. Dakin, *Proc. Chem. Soc., London,* **1909**, *25*, 194–195; b) H. D. Dakin, *Am. Chem. J.* **1909**, *42*, 477-498.

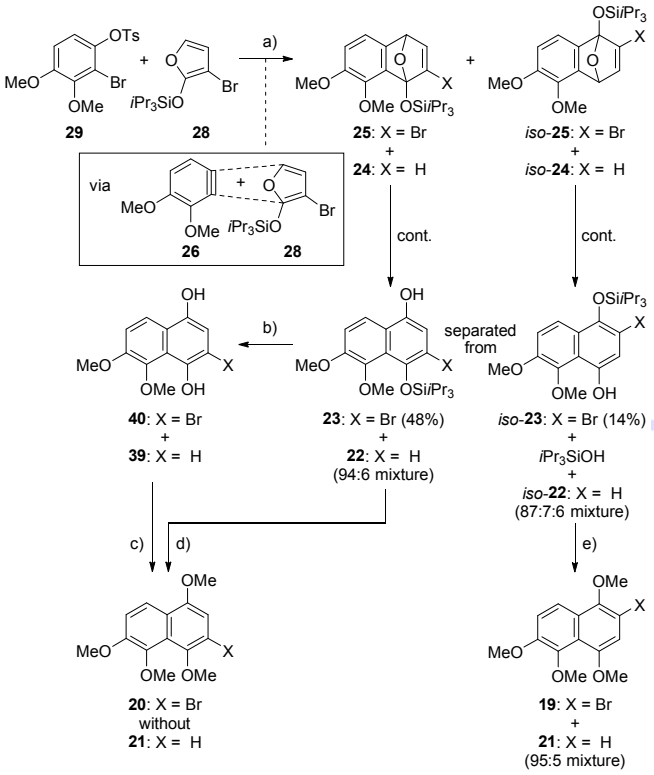
[33] A Dakin oxidation delivering **33** had not been known prior to our study. We based it on a procedure described by M. Altemöller, T. Gehring, J. Cudaj, J. Podlech, H. Goesmann, C. Feldmann, A. Rothenberger, *Eur. J. Org. Chem.* **2009**, 2130-2140.



Scheme 4. Synthesizing the bromotetramethoxynaphthalene **19** – preceding our "type 1" arizonin C1 analogs – by an aryne/siloxyfuran Diels-Alder addition and an ensuing bromination. Reagents and conditions: ***a)*** ***27*** *(1.5 equiv.), THF, –78°C; dropwise addition of nBuLi (2.60 M in hexane, 1.0 equiv.), THF, –78°C; 5 min; –78°C → room temp., 45 min;* ***22****: 62%, iso-****22****: 12% (as a 10:90 mixture with iPr₃SiOH);* ***b)*** *same as* ***(a)****; cooling to 0°C; addition of Bu₄NF (in THF, 1.5 equiv.), 0°C → room temp., 8 min; 82% over the 2 steps;* ***c)*** *same as* ***(b)*** *but 15 min instead of 8 min; addition of Me₂SO₄ (10 equiv.) KOH (8 equiv.), Bu₄NBr (5 mol-%), THF/H₂O (2:1), 0°C → room temp., 17 h; 79% over the 3 steps;* ***d)*** *Bu₄NF (in THF, 1.5 equiv.), THF, 0°C → room temp., 15 min; 90%;* ***e)*** *same as* ***(d)****; 86%;* ***f)*** *Me₂SO₄ (10 equiv.), KOH (8 equiv.), Bu₄NBr (5 mol-%), THF/H₂O (2:1), 0°C → room temp., 17 h; 96%;* ***g)*** *NBS (1.0 equiv.), DMF, room temp., 16 h;* ***19****: 84%;* ***20****: 2%.*

The bromine-free siloxyfuran **27** was obtained from furfural.[34] A Dakin oxidation[32] and hydrolysis provided 59% of the butenolide **39** as reported.[34] *O*-protection with freshly prepared *i*Pr$_3$SiOTf[35] delivered 98% of the siloxyfuran **27**.[34] The bromine-containing (triisopropylsiloxy)furan **28** was prepared like the analogous (trimethylsiloxy)furan, which we used for synthesizing the carotenoid butenolide pyrrhoxanthin.[36] I. e., we undertook a Wohl-Ziegler bromination of crotonic acid as before (→**36**),[36] added bromine as before (→**37**),[36] and lactonized / eliminated in refluxing H_2O as before (→**39**).[36] We then introduced the triisopropylsilyl group following another procedure[37] (→**28**).

We synthesized the bromotetramethoxy naphthalene **19** almost without producing the isomer **20** as a waste (Scheme 4). At –78°C, we treated a solution of the bromotosylate **29** and 1.5 equiv. of the bromine-free siloxyfuran **27** in THF with *n*BuLi, like suggested by related literature reports.[26] This generated the aryne **26**. It engaged in a Diels-Alder addition with **27** immediately. Two orientational isomers resulted, namely mainly the "proximal"[23] adduct **24** and some "distal"[23] adduct *iso*-**24**. An aqueous acidic work-up and flash chromatography on silica gel[38] delivered the respective ring-opening products. These were 62% of the naphthohydroquinonetriether **22** and, within a 10:90 mixture with *i*Pr$_3$SiOH, 12% of the isomeric triether *iso*-**22**. Both compounds gave the same naphthohydroquinonediether **39** by desilylation. However, it was better to desilylate the crude mixture of Diels-Alder adducts **24**/*iso*-**24** directly. This gave **39** in 82% yield over the 2 steps. Double *O*-methylation provided the naphthohydroquinonetetraether **21** in 79% yield over all 3 steps. It was brominated with NBS in DMF at room temperature as regioselectively as found for an analogous compound recently.[7r] This allowed to isolate the (desired) bromonaphthalene **19** in 84% yield and to separate the (presently undesired) bromonaph-



Scheme 5. Synthesizing the bromotetramethoxynaphthalene **20** – preceding our "type 2" arizonin C1 analogs – by an aryne/siloxyfuran Diels-Alder addition. *Reagents and conditions:* ***a)*** ***28*** *(1.5 equiv.), THF, –78°C; dropwise addition of nBuLi (in hexane, 1.0 equiv.), THF, –78°C; 5 min; –78°C → room temp., 45 min;* ***23****: 48%, iso-****23****: 14%;* ***b)*** *Bu₄NF (in THF, 1.1 equiv.), THF, 0°C, 45 min; 29%;* ***c)*** *Na₂S₂O₄ (9 mol-%), Bu₄NBr (8 mol-%), KOH (9 equiv.), Me₂SO₄ (10 equiv.) THF/H₂O (2:1), room temp., 16 h; 85% (25% over the 2 steps);* ***d)*** *Bu₄NF (in THF, 1.1 equiv.), THF, room temp., 15 min; addition of KOH (1.4 M in H₂O, 7.2 equiv.), Me₂SO₄ (10 equiv.), THF/H₂O (2:1), 0°C → room temp., 14 h; 25% over the 2 steps;* **e)** same as **(d)**; *72% over the 2 steps.*

[34] E. K. Kemppainen, G. Sahoo, A. Valkonen, P. M. Pihko, *Org. Lett.* **2012**, *14*, 1086-1089.

[35] We prepared *i*Pr$_3$SiOTf from *i*Pr$_3$SiH and TfOH (1.2 equiv.) immediately prior to use, adopting conditions from: a) A. G. Sancho, X. Wang, B. Sui, D. P. Curran, *Adv. Synth. Cat.* **2009**, *351,* 1035-1040. b) E. J. Corey, H. Cho, C. Rücker, D. H. Hua, *Tetrahedron Lett.* **1981**, *22*, 3455-3458.

[36] J. Burghart, R. Brückner, *Angew. Chem.* **2008**, *120,* 7777-7782; *Angew. Chem. Int. Ed.* **2008**, *47*, 7664-7668.

[37] J. Boukouvalas, J. X. Wang, O. Marion, B. Ndzi, *J. Org. Chem.* **2006**, *71*, 6670-6673.

[38] W. C. Still, M. Kahn, A. Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

thalene **20** in just 2% yield.[39] The major product (**19**) was incorporated in the type-1 arizonin C models as described after the next paragraph.

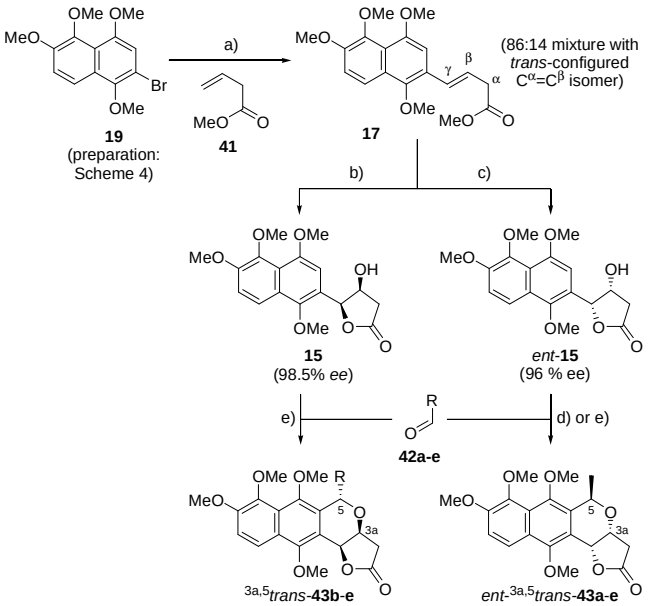
Scheme 5 shows how the bromonaphthalene **20**, a 2% side-product of the bromination of Scheme 4 (bottom line), was accessed better. This was in the sequel of a Diels-Alder reaction between the aryne **26** (generated as in Scheme 4) and the brominated silyoxyfuran **28** (synthesis: Scheme 3). Acidic workup and separation by flash chromatography on silica gel[38] afforded 48% of the ring-opening product **23** of the "proximal"[23] Diels-Alder adduct **25** as opposed to 14% of the ring-opening product *iso*-**23** resulting from the "distal"[23] adduct *iso*-**25**. Both compounds were admixed with up to 7 rel-% of the debrominated analogs **24** and *iso*-**24**, respectively. Their presence means that the Diels-Alder adducts **25** and *iso*-**25** preceding them, already contained the respective debrominated materials **24** and *iso*-**24**. This indicates that generating the aryne **26** without subjecting the siloxyfuran **28** to a parallel Br/Li exchange[28a] or the Diels-Alder adducts **25** and *iso*-**25** to a later Br/Li exchange is a narrow balance. Desilylating the ring-opening product **23** and performing a double *O*-methylation afforded the bromonaphthalene **20**. It was a key intermediate for synthesizing our type-2 arizonin C models. They are presented in the penultimate Section.

Elaboration of Bromotetramethoxynaphthalene 19 Into Naphthoquinonopyrano-γ-lactones Dimethoxylated Like (–)-Arizonin C1

This Section and the following one detail how we converted the bromonaphthalene **19** (preparation: Scheme 4) into the naphthohydroquinonopyranolactones **43** (Table 1). Oxidation advanced them to the corresponding quinones – or type-1 arizonin C1 models – **13** of Table 2.

The chemistry of Table 1 begins with a Heck-coupling between the bromonaphthalene **19** and the butenoate **41** (method: ref.[18]). It furnished an 86:14 mixture of the deconjugated ester **17** (desired) and the isomeric *trans*-configured conjugated ester (undesired). Without separating these compounds we subjected them to an $NaHCO_3$-buffered[40] asymmetric Sharpless dihydroxylation. Using $(DHQ)_2PHAL$ or $(DHQD)_2PHAL$ as a chiral auxiliary we obtained the β-hydroxy-γ-lactone **15** with 98.5% *ee* and its antipode *ent*-**15** with 96% *ee*, respectively. I. e., the β,γ-dihydroxyesters, formed initially, transesterified under the dihydroxylation conditions giving lactones although they implied less base-catalysis than usually.[19] Next, the lactones **15** and *ent*-**15** were diversified in a total of nine oxa-Pictet-Spengler cyclizations.[20] As a reaction partner we employed acetaldehyde (7.5 equiv.) and four aromatic benzaldehydes (Ar = Ph, 4-F_3C-C_6H_4, 4-F-C_6H_4, 4-Br-C_6H_4; 3.0 equiv.). $BF_3{\cdot}OEt_2$ (10 or 4.0 equiv., respectively) was used as a promotor. Acetaldehyde rendered the naphthohydroquinonopyranolactone **43a** with a modest ^{3a,5}*trans*-selectivity. It was isolated as a 78:22 ^{3a,5}*trans*:^{3a,5}*cis*-mixture, which was inseparable by flash chromatography on silica gel.[38] In contrast, the aromatic aldehydes gave the naphthohydroquinonopyranolactones **43b**-**e** – and their enantiomers *ent*-**43b**-**e** – with 100:0 ^{3a,5}*trans*-selectivity[41] (except *ent*-**43d**).

Table 1. Preparing the tetracyclic naphthohydroquinones **43** en route to "type-1 analogs" of (–)-arizonin C1: (a) Heck coupling; (b) Sharpless dihydroxylation / lactonization tandems; (c) oxa-Pictet Spengler cyclizations



42, 43	R	Step	Yield	43b-e (^{3a,5}*trans* : ^{3a,5}*cis*)	Yield	*ent*-43b-e (^{3a,5}*trans* : ^{3a,5}*cis*)
a	Me	d)	—	—	93%	78:22
b	C_6H_5	e)	89%	100:0	67%	100:0
c	4-F_3C–C_6H_4	e)	91%	100:0	64%	100:0
d	4-F–C_6H_4	e)	91%	100:0	62%	95:5
e	4-Br–C_6H_4	e)	96%	100:0	68%	100:0

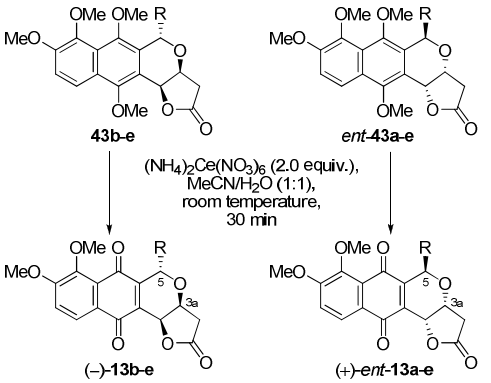
Reagents and conditions: ***a) 41*** *(3 equiv), $Pd_2dba_3{\cdot}CHCl_3$ (2.0 mol-%), $P(tBu)_3$ (8 mol-%), Cy_2NMe (3 equiv.), toluene, reflux, 2 d; 83% (of a 86:14 mixture of* ***17*** *with the trans-configured $C^{\alpha}=C^{\beta}$ isomer);* ***b)*** *$K_2OsO_2(OH)_4$ (0.4 mol-%), $(DHQ)_2PHAL$ (1.0 mol-%), $K_3Fe(CN)_6$ (3 equiv.), K_2CO_3 (3 equiv.), $NaHCO_3$ (3 equiv.), $MeSO_2NH_2$ (1.0 equiv.), $tBuOH/H_2O$ (1:1), room temp., 2 d; 66%, 98.5% ee (ref.[7s]: 71%, 99.2% ee);* ***c)*** *same as* ***(b)****, but $(DHQD)_2PHAL$ instead of $(DHQ)_2PHAL$; 58%, 96% ee;* ***d) 42a*** *(7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min;* ***e) 42b-e*** *(3 equiv.), $BF_3{\cdot}OEt_2$ (4 equiv.), CH_2Cl_2, 0°C → room temp., 30 min.*

[39] The structures **19** and **20** were differentiated as follows. (1) The most deshielded aromatic proton in either compound resonates as a dublet. It must be 8-H (numbering: cf. Scheme 4; in **19**: δ = 7.74 ppm; in **20**: δ = 8.00 ppm) rather than 7-H for complying with the chemical shift ordering in any naphthalene, which contains no strongly (de)shielding substituents. (2) In either compound, the *aromatic singlet* must be due to the isolated proton between Br and MeO. This proton would be 3-H in **19** (δ = 6.86 ppm) but 2-H in **20** (δ = 6.78 ppm). (3) The latter shifts were too similar for inferring whether they originate from **19** or **20**. We therefore probed the HMBC spectra (500 MHz / 126 MHz) of these compounds for $^3J_{C,H}$-based cross-peaks relating the bridgehead ^{13}C nuclei to the pair of protons at C-8 and between Br and MeO. The bromonaphthalene **19** displayed two such (!) crosspeaks for ^{13}C-4a (regarding 8-^1H and 3-^1H) but zero such (!) crosspeaks for ^{13}C-8a. In contrast, the bromonaphthalene **20** showed one such (!) crosspeak both for ^{13}C-4a (regarding 8-^1H) and ^{13}C-8a (regarding 2-^1H). This makes the distinction of **19** and **20** unequivocal.

[40] Method: K. P. M. Vanhessche, Z.-M. Wang, K. B. Sharpless, *Tetrahedron Lett.* **1994**, *35*, 3469-3472.

[41] The oxa-Pictet-Spengler products **43b**-**e** and *ent*-**43b**-**e** are ^{3a,5}*trans*- rather than ^{3a,5}*cis*-configured for the following reason: The (at first: alleged) *trans*-orientation of 5-Ar and 3a-C implies that the 5-Ar bond and the 3a-H bond are *cis*-oriented. Therefore, 5-Ar-H^{ortho} and 3a-H reside close to each other. In the

Table 2. Accomplishing nine "type-1 analogs" **13** of (–)-arizonin C1



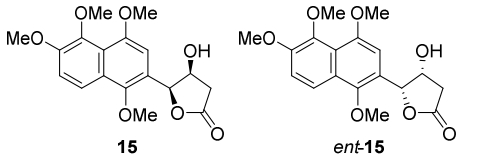
43, 13	R	(–)-13b-e Yield	(–)-13b-e (^{3a,5}*trans* : ^{3a,5}*cis*)	(+)-*ent*-13a-e Yield	(+)-*ent*-13a-e (^{3a,5}*trans* : ^{3a,5}*cis*)
a	Me	—	—	84%	75:25
				25%	flash chromatogr. 90:10
					HPLC 100:0
b	C_6H_5	99%	100:0	61%	100:0
c	4-F_3C-C_6H_4	94%	100:0	64%	100:0
d	4-F-C_6H_4	75%	100:0	62%	95:5
e	4-Br-C_6H_4	88%	100:0	89%	100:0

The naphthohydroquinonopyranolactones **43b**-**e** and their oppositely configured congeners *ent*-**43a**-**e** were oxidized with $(NH_4)_2Ce(NO_3)_6$ (Table 2). This provided the naphthoquinonopyranolactones (–)-**13b**-**e** and (+)-*ent*-**13a**-**e**, respectively, in yields of 61-99%. They all constitute "type 1" arizonin C1 models. Specifically, oxidation of the 78:22 mixture of ^{3a,5}*trans*- and ^{3a,5}*cis*-*ent*-**43a** provided a 75:25 mixture of ^{3a,5}*trans*- and ^{3a,5}*cis*-*ent*-**13a**. Re-purification by flash chromatography[38] increased the *trans*:*cis* ratio to 90:10. HPLC afforded the naphthoquinonopyrano-γ-lactone ^{3a,5}*trans*-**13a** analytically pure. It equals the unnatural enantiomer (+)-*ent*-**13a** ≡ (+)-*ent*-**3** of (–)-arizonin C1. The other "type 1" arizonin C1 models included in Table 2 had the identical isomeric composition as the respective precursor.

Getting hold of the hydroxylactones **15** and *ent*-**15** by the Sharpless dihydroxylations of Table 1, we determined that **15** is (slightly) levorotatory and *ent*-**15** (slightly) dextrorotatory (Table 3, entry 1). This contrasts with Fernandes's report of the opposite senses of rotation (Table 3, entry 2).[7t] Yet the specimen to which they assigned the stereostructure *ent*-**15** ["levorotatory"] and we, too ["dextrorotatory"], delivered (+)-*ent*-arizonin C1 in their laboratory (ref.[7t]) as well as in ours (Table 1/Table 2). This means that they or us published the specific rotation of the hydroxylactones **15** and *ent*-**15** with the incorrect sign. Accordingly, **15** and *ent*-**15** offer no stereochemical reference point.

NOESY spectrum (400 and 500 MHz, respectively, $CDCl_3$) this causes 5-Ar-H^{ortho} to correlate with 3a-H.

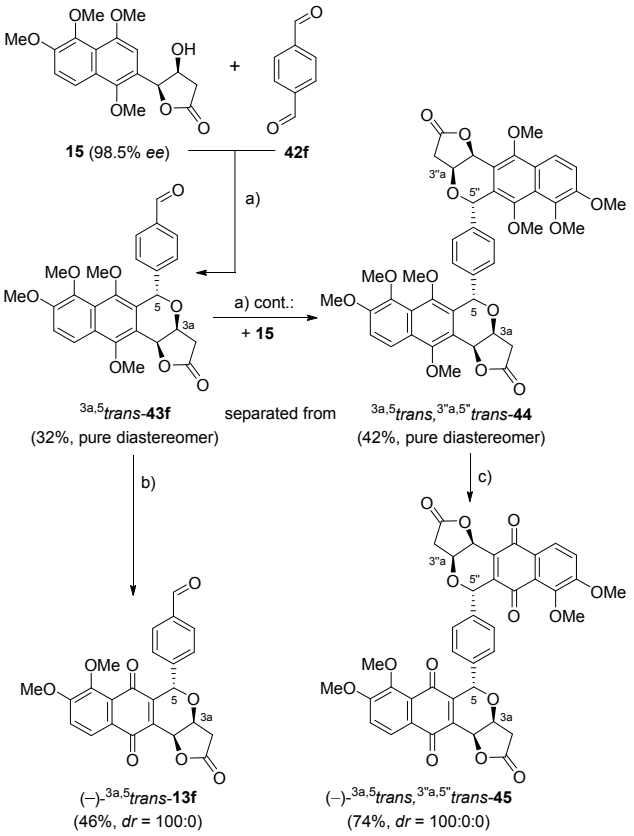
Table 3. Impurity effects on the specific rotations ($[\alpha]_D^{20}$ in $CHCl_3$) of enantiomerically pure hydroxylactones **15** and *ent*-**15**: a caveat regarding configurational assignments in this field



Entry		**15**	*ent*-**15**
1	this work	–5.5 (*c* 0.45, $CHCl_3$)	+3.1 (*c* 0.45, $CHCl_3$)
2	Fernandes et al.[7t]	+5.2 (*c* 0.46, $CHCl_3$)	–4.6 (*c* 0.5, $CHCl_3$)

A Bis(pyrano-γ-lactone) Analog of (–)-Arizonin C1

The perfect ^{3a,5}*trans*-selectivites, with which hydroxylactone **15** and the aromatic aldehydes **42b**-**e** oxa-Pictet-Spengler cyclized (Table 1), manifested itself also when the same lactone and terephthalaldehyde (**42f**) oxa-Pictet-Spengler cyclized in the presence of $BF_3{\cdot}OEt_2$ (Scheme 6). The product structure depended on how many aldehyde groups reacted. The only reaction conditions, which we tested, allowed either course. One aldehyde group reacted to give rise to the "simple" oxa-Pictet-



Scheme 6. Modifying the follow-up chemistry of the hydroxylactone **15** of Table 1: (a) oxa-Pictet-Spengler cyclizations providing the naphthohydroquinones **43** and **44**; (b) and (c) oxidation to "type-1 analogs" of (–)-arizonin C1. *Reagents and conditions:* ***a)*** *Terephthalaldehyde (0.52-fold molar amount), $BF_3{\cdot}OEt_2$ (2.06 equiv.), CH_2Cl_2, 0°C → room temp., 30 min; ^{3a,5}trans-**43f**: 32%; ^{3a,5}trans,$^{3"a,5"}$trans-**44**: 42%;* ***b)*** *$(NH_4)_2Ce(NO_3)_6$ (2.0 equiv.), MeCN/H_2O (1:1), room temp., 30 min; 46%;* ***c)*** *$(NH_4)_2Ce(NO_3)_6$ (4.0 equiv.), MeCN/H_2O (1:1), room temp., 30 min; 74%.*

Spengler product ^{3a,5}*trans*-**43f** (32% yield), both aldehyde functions reacted to form the "double" oxa-Pictet-Spengler product ^{3a,5}*trans*,$^{3''a,5''}$*trans*-**44** (42% yield; eluted second to ^{3a,5}*trans*-**43f** from the flash chromatography column[38]). These structures were distinguished ^{1}H-NMR spectroscopically:

- The "simple" oxa-Pictet-Spengler product ^{3a,5}*trans*-**43f** displayed an aldehyde as a 1-proton singlet at δ = 9.99 ppm. In contrast, ^{3a,5}*trans*,$^{3''a,5''}$*trans*-**44** did not.
- The "double" oxa-Pictet-Spengler product ^{3a,5}*trans*,$^{3''a,5''}$*trans*-**44** displayed the *para*-phenylene moiety as a 4-proton singlet at δ = 7.05 ppm. Oppositely, ^{3a,5}*trans*-**43f** did not.
- The "double" oxa-Pictet-Spengler product ^{3a,5}*trans*,$^{3''a,5''}$*trans*-**44** showed a *common* set of resonances for the two pyranolactone moieties. This excludes a ^{3a,5}*trans*,$^{3''a,5''}$*cis*-configuration but allows for a ^{3a,5}*cis*,$^{3''a,5''}$*cis*-configuration.
- A NOESY experiment analogous to that in footnote[41] was supportive of **44** being ^{3a,5}*trans*,$^{3''a,5''}$*trans*-configured and incompatible with its being ^{3a,5}*cis*,$^{3''a,5''}$*cis*-configured.

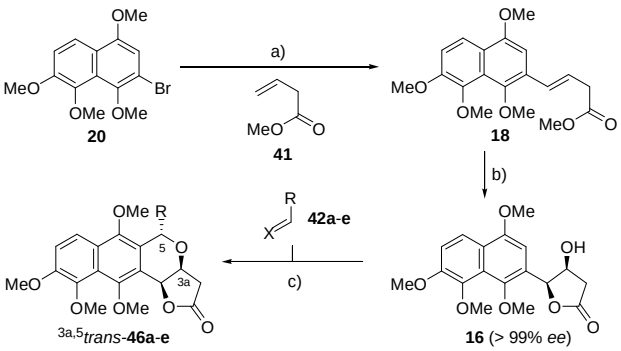
Finishing up, we oxidized the "simple" oxa-Pictet-Spengler product ^{3a,5}*trans*-**43f** with $(NH_4)_2Ce(NO_3)_6$ (Scheme 6). This gave the naphthoquinonopyranolactone **13f** in 46% yield. It is the tenth type-1 arizonin C1 analog of our study. The "double" oxa-Pictet-Spengler product ^{3a,5}*trans*,$^{3''a,5''}$*trans*-**44** was oxidized with $(NH_4)_2Ce(NO_3)_6$, too. This provided the naphthoquinonopyranolactone ^{3a,5}*trans*,$^{3''a,5''}$*trans*-**45** in 74% yield. It constitutes a dimeric arizonin C1 analog of sorts.

Elaboration of Bromotetramethoxynaphthalene 20 Into Naphthoquinonopyrano-γ-lactones Dimethoxylated Unlike (–)-Arizonin C1

This Section describes how we processed the bromonaphthalene **20** from Scheme 5 via the naphthohydroquinonopyranolactones **46** (Table 4) to the naphthoquinonopyranolactones **14a**-**e**, i. e., type-2 arizonin C1 models (Table 5).

We proceeded as delineated in the previous Section for the preparation of the type-1 arizonin C1 models **13** and *ent*-**13**. I. e., we started by a Heck-coupling of the bromonaphthalene **20** and methyl but-3-enoate (**41**; Table 4). The resulting unsaturated ester **18** (61%, 92:8 mixture with a C=C-shifted isomer) was Sharpless-dihydroxylated.[40] This led to the lactone **16** in 60% yield and with >99% *ee*. Oxa-Pictet-Spengler cyclizations furnished the naphthohydroquinonopyranolactones **46**. This occurred with a 81:19 preference for the ^{3a,5}*trans*-isomer using acetaldehyde (→ **46a**) and with 100:0 selectivities using aromatic aldehydes (→ **46b**-**e**). Oxidation with $(NH_4)_2Ce(NO_3)_6$ afforded the corresponding naphthoquinonopyranolactones **14a**-**e** (Table 5). This went along with a complete or an almost complete retention of the ^{3a,5}*trans*-configuration.

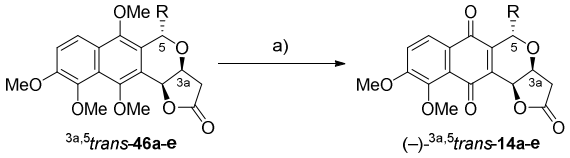
Table 4. Preparing naphthohydroquinone precursors **46** of "type-2 analogs" of (–)-arizonin C1: (a) Heck coupling; (b) Sharpless dihydroxylation / lactonization tandem; (c) oxa-Pictet Spengler cyclizations



42, 46	R	X	Yield	^{3a,5}*trans* : ^{3a,5}*cis*
a	Me[a]	O	63%	81:19 (flash chromatogr.)
			27%	94:6
a	Me[a]	$(OMe)_2$	75%	52:48
b	C_6H_5	O	86%	100:0
c	4-F_3C-C_6H_4	O	68%	100:0
d	4-F-C_6H_4	O	60%	100:0
e	4-Br-C_6H_4	O	86%	100:0

Reagents and conditions: ***a) 41*** *(3 equiv), $Pd_2dba_3{\cdot}CHCl_3$ (2.0 mol-%), $P(tBu)_3$ (8.0 mol-%), Cy_2NMe (3 equiv.), toluene, reflux, 2 d; 61% (of a 92:8 mixture of* ***18*** *with the trans-configured C^{α}=C^{β} isomer);* ***b)*** *$K_2OsO_2(OH)_4$ (0.4 mol-%), $(DHQ)_2PHAL$ (1.0 mol-%), $K_3Fe(CN)_6$ (3.1 equiv.), K_2CO_3 (3.2 equiv.), $NaHCO_3$ (3.2 equiv.), $MeSO_2NH_2$ (1.0 equiv.), tBuOH/H_2O (1:1), room temp., 15 h; 60%, >99% ee;* ***c)*** *RCH=X (3 equiv.), $BF_3{\cdot}OEt_2$ (4 equiv.), CH_2Cl_2, 0°C → room temp., 30 min.* [a] RCH=X: 7.5 equiv., $BF_3{\cdot}OEt_2$: 10 equiv.

Table 5. Accomplishing five "type-1 analogs" **13** of (–)-arizonin C1



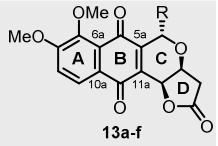
Reagents and conditions: a) $(NH_4)_2Ce(NO_3)_6$ (2.0 equiv.), MeCN/H_2O (3:2 or 1:1), room temperature, 30 min; yields and ^{3a,5}trans : ^{3a,5}cis selectivity see table.

46, 14	R	46 *d.r.*	14 Yield	14 ^{3a,5}*trans* : ^{3a,5}*cis*
a	Me	94:6	68%	97:3
b	C_6H_5	100:0	86%	94:6 (recrystallization)
			55%	100:0
c	4-F_3C-C_6H_4	100:0	90%	100:0
d	4-F-C_6H_4	100:0	93%	100:0
e	4-Br-C_6H_4	100:0	70%	95:5

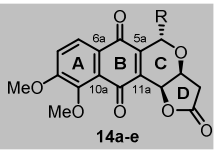
Distinguishing Naphthoquinonopyrano-γ-lactones Dimethoxylated Like or Unlike (–)-Arizonin C1 NMR-Spectroscopically

(–)-Arizonin C1 (**3**) equals the naphthoquinonopyranolactone numbered **13a** in (Table 6). The type-1 arizonin C1 analogs synthesized in the present study comprise the naphthoquinonopyranolactones **13b**-**f** (Table 6). In addition we synthesized the naphthoquinonopyranolactones **14a**-**f** (*ibid.*). Dubbed type-2 arizonin

Table 6. Pertinent ^{13}C NMR resonances (recorded at 101 or 126 MHz in $CDCl_3$) for distinguishing the naphthoquinonopyrano-γ-lactones **13a-f** and **14a-e** from this work. Where we could not attribute $\delta_{C\text{-}5a}$ and $\delta_{C\text{-}11a}$ individually, they are collected group-wise and separated by a comma.[42]

type-1 analogs: 

13a-f

type-2 analogs: 

14a-e

	R	A-ring/B-ring junction: type-1 analogs $\delta_{C\text{-}6a}$ / ppm	$\delta_{C\text{-}10a}$ / ppm	$\Delta\delta$ / ppm	A-ring/B-ring junction: type-2 analogs $\delta_{C\text{-}6a}$ / ppm	$\delta_{C\text{-}10a}$ / ppm	$\Delta\delta$ / ppm	B-ring/C-ring junction: type-1 analogs $\delta_{C\text{-}5a}$ / ppm	$\delta_{C\text{-}11a}$ / ppm	$\lvert\Delta\delta$ / ppm$\rvert$	B-ring/C-ring junction: type-2 analogs $\delta_{C\text{-}5a}$ / ppm	$\delta_{C\text{-}11a}$ / ppm	$\lvert\Delta\delta$ / ppm$\rvert$
a	Me	124.97	125.26	–0.29	125.56	124.92	0.64	150.61	133.20	17.41	148.29	135.26	13.03
b	C_6H_5	124.86	125.52	–0.66	125.41	125.09	0.32	147.57, 135.48		12.09	145.31, 137.54		7.77
c	4-F_3C–C_6H_4	124.70	125.41	–0.71	125.17	125.03	0.14	146.62, 135.89		10.73	144.43, 137.89		6.54
d	4-F–C_6H_4	124.80	125.47	–0.67	125.27	125.04	0.23	147.26, 135.57		11.69	145.02, 137.58		7.44
e	4-Br–C_6H_4	124.80	125.51	–0.71	125.28	125.07	0.21	146.96, 135.71		11.25	144.74, 137.71		7.03
f	4-OHC–C_6H_4	124.71	125.42	–0.71	—	—	—	146.60, 135.85		10.75	—	—	—
		hardly negative			hardly positive			~11-12 ppm			~ 7-8 ppm		

C1 analogs, the latter are constitutional isomers of the former compounds. Each pair **13**/**14** of isomers differs by the orientation of the A-ring substituents relative to the C-ring substituents (one of which is the D-ring). We were able to assign each ^{13}C-NMR shift of the respective A/B/C/D scaffolds **a-f** nucleus-specifically – except that we could not differentiate C5a and C-11a unless the substitution pattern was **a**. These assignments stem from analyzing the cross-peaks in HBMC spectra [400 MHz (^1H) / 101 MHz (^{13}C) or 500 MHz (^1H) / 126 MHz (^{13}C)] in terms of the underlying $^2J_{C,H}$ and $^3J_{C,H}$ couplings.[42] The essence of these analyses is embedded in the chemical shifts of four quaternary ^{13}C nuclei per compound: the atoms C-6a/C-10a at the A-ring/B-ring junction ("benzene/quinone junction") and the atoms C-5a/C-11a at the B-ring/C-ring junction ("quinone/pyran junction").

Table 6 shows that the chemical shifts of the four mentioned ^{13}C nuclei can be combined pairwise in each compound such that they seem to become structure-revealing:

1) $\Delta\delta \equiv \delta_{C\text{-}6a} - \delta_{C\text{-}10a}$ is a small negative number in type-**13** naphthoquinonopyranolactones but a small positive number in type-**14** naphthoquinonopyranolactones.
2) The absolute value of $\Delta'\delta \equiv \delta_{C\text{-}5a} - \delta_{C\text{-}11a}$ is 11-12 ppm in type-**13** naphthoquinonopyranolactones but 7-8 ppm in type-**14** naphthoquinonopyranolactones.

Elucidating the structure of naphthoquinonopyranolactone natural products often entails localizing substituents in their A-ring relative to their C-ring/D-ring moiety. This used to be not easy. Good illustrations are how long it took to prove the location of the biaryl bond in the dimeric naphthoquinonopyrano-γ-lactone natural products actinorhodin[43] and γ-actinorhodin.[44] Another pertinent example is the controversy about where the naphthoquinonopyranolactone-*C*-glycoside medermycin is glycosylated.[45] In this regard, systematic NMR analyses like that of Table 6 may hold a potential, which has not yet been exploited.

Conclusion

To sum up we have made 15 naphthoquinonopyrano-γ-lactone analogs dimethoxylated like (**13**, "type 1" analogs) or unlike (**14**, "type 2" analogs) (–)-arizonin C1 (**3**). Both substitution patterns were reached from naphthalenes, which emerged from an orientationally selective Diels-Alder reaction between 3,4-dimethoxybenz-1-yne and a 2-siloxylated furan. The latter was bromine-free (**27**; → → **13**) or 3-brominated (**28**; → → **14**). This allowed to process the respective Diels-Alder product such that a Heck coupling, an SAD, and an oxa-Pictet-Spengler reaction established the remaining rings in a regiocomplementary fashion.

As numerous naphthoquinonopyrano-γ-lactones have proved bioactive, we had our models **13** and **14** tested in vitro against B16-melanoma tumor cells.[46] The best potency was observed for *ent*-**13b** (LD_{50} = 2.9 μM). However, adding the other models to phosphate-buffered saline (containing 1% DMSO) in amounts corresponding to concentrations of 3 μM *if dissolved completely* did not render solutions but suspensions. This left their cell toxicity unknown.

Experimental Section

General Working Technique and Analytic Techniques

Working technique: If not indicated differently, all reactions were carried out under a nitrogen atmosphere. Reaction flasks were dried in vacuo

[42] Details: Experimental Section

[43] Structure known except the location of the biaryl bond: a) A. Zeeck, P. Christiansen, *Liebigs Ann. Chem.* **1969**, *724*, 172-182; b) P. Christiansen, *Ph. D. Thesis*, Universität Göttingen, Germany, **1970**; c) biaryl bond localized by C. P. Gorst-Allman, B. A. M. Rudd, C. Chang, H. G. Floss, *J. Org. Chem.* **1981**, *46*, 455-456 in isotopologs gained by biosynthesis.

[44] a) 1974: Biaryl bond position inferred from analogy: ref.[21a]; b) 2017: biaryl bond position proved by NOESY and HMBC experiments with totally synthetic material: ref.[22].

[45] a) Structure assignment by total synthesis: K. Tatsuta, H. Ozeki, M. Yamaguchi, M. Tanaka, T. Okui, *Tetrahedron Lett.* **1990**, *31*, 5495-5498; b) structure revision: P.-M. Léo, C. Morin, C. Philouze, *Org. Lett.* **2002**, *4*, 2711-2714; c) revision of the structure revision: G. T. Williamson, L. A. McDonald, L. R. Barbieri, G. T. Carter, *Org. Lett.* **2002**, *4*, 4695-4662.

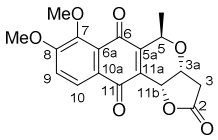
[46] We express our gratitude to Dr. L. O. Haustedt (AnalytiCon Discovery, Potsdam) for these experiments.

with a heat gun prior to use. Small amounts of liquids were added with a syringe through a rubber septum. If solids were suspended, the flask was evacuated again and flushed with nitrogen prior to addition of the solvent. If solids were added to a reaction this was carried out in a nitrogen counter flow. **Solvents for reactions:** Tetrahydrofuran (THF) and toluene were distilled over potassium under a nitrogen atmosphere prior to use. Diethyl ether (Et_2O) was distilled over a sodium/potassium alloy under a nitrogen atmosphere. Dichloromethane (CH_2Cl_2), acetonitrile (MeCN), N,N,N',N'-tetramethylethylenediamine (TMEDA), and triethylamine (NEt_3) were distilled over CaH_2 and also under a nitrogen atmosphere. Other solvents and reagents were purchased and – if not indicated – used without further purification. **Organolithium reagents** were stored in a fridge in Schlenk flasks with PTFE screw caps and PTFE valves. Prior to use, they were titrated using N-pivaloyl-*o*-toluidine.[47] **Solvents for extraction and flash chromatography** [i.e. methyl *tert*-butyl ether (*t*BuOMe), dichloromethane (CH_2Cl_2), petroleum ether (PE 30/50), toluene (PhMe), ethyl acetate (EtOAc or EE), cyclohexane (C_6H_{12} or CH), and diethyl ether (Et_2O) were purchased in technical quality] and distilled using a rotary evaporator to free them from high boiling fractions. **Flash chromatography:**[38] Macherey-Nagel silica gel 60® (230-400 mesh) was used for flash chromatography. All eluents were distilled prior to use. Chromatography conditions are documented as following: "[diameter d = y cm height h = x cm, eluent a/eluent b = v_a:v_b, fraction volume = e mL] furnished the product (Fx-y, yield in g and %)" example: "flash chromatography [d = 1.5 cm, h = 12 cm, CH/EE 5:1, F = 6 mL] furnished the product (F9-13, 26.9 mg, 78%) as a colorless oil.". **Thin layer chromatography** was carried out on Merck silica TLC plates (silica gel 60 F254). The chromatograms were marked under UV light and were subsequently stained in one of the three following solutions: 1. Cer-(IV)-phosphomolybdic acid: $Ce(SO_4)_2$ (10 g), phosphomolybdic acid (20 g), conc. H_2SO_4 (80 mL), and H_2O (1 L). 2. $KMnO_4$: $KMnO_4$ (2.5 g), K_2CO_3 (12.5 g), H_2O (500 mL). 3. vanillin: vanillin (2.5 g), acetic acid (50 mL), conc. H_2SO_4 (16 mL), MeOH (480 mL). **Nuclear magnetic resonance (NMR) spectra** were recorded by Dr. M. Keller, Ms. M. Schonhard, and Mr. F. Reinbold (all Inst. f. Org. Chemie, Albert-Ludwigs-Universität Freiburg) on a Bruker Avance III 500 spectrometer (500 MHz for ^{1}H, 125 MHz for ^{13}C, and 478 MHz for ^{19}F), a Bruker Avance II 400 spectrometer (400 MHz and 100 MHz for ^{1}H and ^{13}C respectively), a Bruker Avance III 300 spectrometer, and a Bruker DRX 250 spectrometer (250 MHz for ^{1}H, 63 MHz for ^{13}C). Spectra were referenced internally by the ^{1}H- and ^{13}C-NMR signals of the solvent [$CDCl_3$: δ_{CHCl_3} = 7.26 ppm (^{1}H) and δ_{CDCl_3} = 77.10 ppm (^{13}C)]. ^{1}H-NMR data are reported as follows: chemical shift (δ in ppm), multiplicity (s for singlet; d for dublet; t for triplet; m for multiplet; m_c for symmetrical multiplet; br for broad signal), coupling constant(s) (in Hz; *J* means ^3J couplings unless otherwise noted), integral, and specific assignment. ^{13}C-NMR data are reported in terms of chemical shift and assignment. For AB signals the high-field part was named A and the low-field part B. **Elemental analyses (EA)** were performed by Ms A. Siegel on a Vario EL analyzer from Elementar. **High resolution mass spectra (HRMS)** were recorded by Dr. J Wörth and C. Warth on a Thermo Exactive mass spectrometer equipped with an orbitrap analyzer. Ionization methods: Electron spray ionization (ESI; spray voltage: 2.5-4 kV) or atmospheric pressure chemical ionization (APCI; spray current: 5 µA). **HPLC:** Determinations of the enantiomeric excess (*ee*) were conducted by Dr. R. Krieger and A. Schuschkowski, and X. Iwanowa (all Inst. f. Org. Chemie, Albert-Ludwigs-Universität Freiburg) using a Merck Hitachi LaChrom (pump: L-7100. UV detector: D-7400, oven: L-7360; columns: Chiralpak AD-3, AD-H, IA, Chiralcel OD-3, 25 cm, 4.6 mm). Further details for chiral HPLC are given in the following experimental section. **Optical rotation** was measured on a Perkin-Elmer polarimeter 241 or 341 at 589 nm (λ = D, Na-D-lamp) or 546 nm, 436 nm, 365 nm (Hg-lamp). $[\alpha]_\lambda^{20}$ values were calculated by the following equation: $[\alpha]_\lambda^{20} = (\alpha_{exp} \cdot 100)/(c \cdot d)$, where λ is the wavelength, α_{exp} is the experimental result (given as arithmetic mean of 10 measurements), *c* is the concentration [g/100 mL], and d is the length of the cell [dm]. Solvent and concentration were given in brackets. **Melting points** were determined in a Büchi melting point apparatus using open glass capillaries.[48] **Boiling points** were measured in the head of the distillation column and are uncorrected. If no pressure is indicated the distillation was performed under ambient pressure. **IR spectra** were obtained on an FT-IR Perkin Elmer Paragon 1000 spectrometer for a film of the substance on a NaCl crystal plate.

General procedure A: Representative $(NH_4)_2Ce(NO_3)_6$ Oxidation to the Arizonin C1 analog 13b:

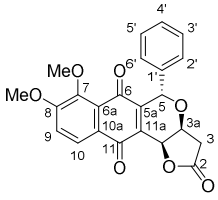
(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-5-phenyl-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (**43b**, 58.1 mg, 133 µmol) was suspended in acetonitrile (1.3 mL). At room temperature a freshly prepared solution of $(NH_4)_2Ce(NO_3)_6$ (145.8 mg, 266 µmol, 2.0 equiv.) in H_2O (1.3 mL) was added dropwise. The reaction mixture was stirred for 30 min and afterwards diluted with CH_2Cl_2 (10 mL). The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (4 × 8 mL). The combined organic extracts were washed with brine (8 mL) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 2:1 (F1-13), CH/EE 1:1 (F14-29),] afforded the title compound [F15-26, R_f (2:1) = 0.2, 53.3 mg, 99%, *dr* = 100:0] as an orange solid.

(3aR,5R,11bR)-7,8-dimethoxy-5-methyl-3,3a,5,11b-tetrahydro-2H-benzo[g]furo[3,2-c]isochromene-2,6,11-trione (+)-*ent*-^{3a,5}*trans*-13a ≡ (+)-*ent*-3



Following the **General Procedure B** (see below) β-hydroxy-γ-lactone **15** (75.0 mg, 0.22 mmol), acetaldehyde (0.09 mL, 0.07 g, 1.65 mmol, 7.5 equiv.) and $BF_3{\cdot}OEt_2$ (0.27 mL, 0.31 g, 2.2 mmol, 10 equiv.) were reacted in CH_2Cl_2 (2 mL). Purification by flash chromatography [d = 1.5 cm, h = 10 cm, F = 8 ml; CH/EE 2:1] afforded a 78:22 mixture of 3a,5trans:3a,5cis-mixture of **43a** (F6-14, R_f (2:1) = 0.3, 75.0 mg, 93%, *ds* = 78:22). Following the **General Procedure A** the title compound was prepared from the 78:22 mixture of **43a** (75.0 mg, 0.20 mmol) dissolved in MeCN (2 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (219.0 mg, 0.40 mmol, 2.0 equiv.) in H_2O (2 mL). Purification by flash chromatography [d = 1.5 cm, h = 18 cm, F = 8 mL; CH/EE 1:1] afforded the title compound [F14-24, R_f (1:1) = 0.25, 58.0 mg, 84%, *dr* = 75:25] as an orange solid. An analytical sample was obtained by preparative HPLC [Phenomenex Luna 5µ C18, 100 Å column, $\lambda_{detector}$ = 265 nm, MeCN/H_2O (50:50), flow rate = 10 mL/min, t_R (*ent*-^{3a,5}*trans*-**13a**) = 14.2 min, t_R (*ent*-^{3a,5}*cis*-**13a**) = 15.3 min. **Optical rotation of *ent*-^{3a,5}*trans*-13a ≡ (+)-*ent*-3:** $[\alpha]_D^{20}$ = +120.0 (*c* = 0.28, MeOH). For reference values and complete analytical data see ref.[7r].

(3a*S*,5*S*,11b*S*)-7,8-Dimethoxy-5-phenyl-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6,11-trione (13b)



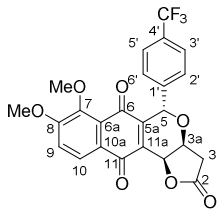
Following the **General Procedure A** the title compound was prepared from **43b** (58.1 mg, 133 µmol) dissolved in MeCN (1.3 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (145.8 mg, 266 µmol, 2.0 equiv.) in H_2O (1.3 mL). Purification by flash chromatography [d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 2:1 (F1-13), CH/EE 1:1 (F14-29)] afforded the title compound [F15-26, R_f (2:1) = 0.2, 53.3 mg, 99%, *dr* = 100:0] as an orange solid. Note: The optical antipode *ent*-**13b** was synthesized analogously in 61% yield (*dr* = 100:0).– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A =

[47] J. Suffert, *J. Org. Chem.* **1989**, *54*, 509-510.

[48] The melting points are neither corrected nor uncorrected, as these terms refer to total immersion thermometers. In our laboratory, like in most modern laboratories, only partial immersion thermometers are used, which per definition need no correction for immersion depth, as they are intended to be only partially immersed: G. V. D. Tiers, *J. Chem. Educ.* **1990**, *67*, 258-259.

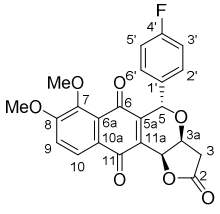
2.63, δ_B = 2.82, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.4 Hz, 3-H^A and 3-H^B), 3.85 (s, 3H, 7-OMe), 3.98 (s, 3H, 8-OMe), 4.29 (dd, 1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.29 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 6.04 (s, 1H, 5-H), 7.22-7.26 (m, 2H, 2'-H and 6'-H), 7.25 (d, 1H, $J_{9,10}$ = 8.4 Hz, 9-H), 7.34-7.38 (m, 3H, 3'-H, 4'-H and 5'-H), 8.05 (d, 1H, $J_{10,9}$ = 8.7 Hz, 10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.82 (3-H^B) ↔ δ = 5.29 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.98 (8-OMe) ↔ δ = 7.25 (9-H), δ = 7.22-7.26 (2'-H and 6'-H) ↔ δ = 4.29 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.22-7.26 (2'-H and 6'-H) ↔ δ = 6.04 (5-H). **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 36.70 (C-3), 56.47 (8-OCH_3), 61.31 (7-OCH_3), 66.98 (C-3a), 69.24 (C-11b), 72.18 (C-5), 116.33 (C-9), 124.86 (C-6a), 125.11 (C-10), 125.52 (C-10a), 128.62 (C-2' and C-6'), 128.96 (C-3' and C-5'), 129.15 (C-4'), 135.48 and 147.57 (C-5a and C-11a), 136.30 (C-1'), 149.81 (C-7), 159.41 (C-8), 174.16 (C-2), 181.32 (C-11), 181.99 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 36.70 (C-3) ↔ [δ_A = 2.63 (3-H^A) and δ_B = 2.82 (3-H^B)], δ = 56.47 (8-OCH_3) ↔ δ = 3.98 (8-OMe), δ = 61.31 (7-OCH_3) ↔ δ = 3.85 (7-OMe), δ = 66.98 (C-3a) ↔ δ = 4.29 (3a-H), δ = 69.24 (C-11b) ↔ δ = 5.29 (11b-H), δ = 72.18 (C-5) ↔ δ = 6.04 (5-H), δ = 116.33 (C-9) ↔ δ = 7.25 (9-H), δ = 125.11 (C-10) ↔ δ = 8.05 (10-H), δ = 128.62 (C-2' and C-6') ↔ δ = 7.22-7.26 (2'-H and 6'-H), δ = 128.96 (C-3' and C-5') ↔ δ = 7.34-7.38 (3'-H, 4'-H and 5'-H), δ = 129.15 (C-4') ↔ δ = 7.34-7.38 (3'-H, 4'-H and 5'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances[δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 124.86 (C-6a) ↔ δ = 8.05 (10-H), δ = 125.52 (C-10a) ↔ δ = 7.25 (9-H), [δ = 135.48 and 147.57 (C-5a and C-11a) ↔ δ = 5.29 (11b-H), δ = 135.48 and 147.57 (C-5a and C-11a) ↔ δ = 6.04 (5-H) could not be assigned unambiguously], δ = 136.30 (C-1') ↔ δ = 6.04 (5-H), δ = 136.30 (C-1') ↔ δ = 7.34-7.38 (3'-H and 5'-H), δ = 149.81 (C-7) ↔ δ = 3.85 (7-OMe), δ = 149.81 (C-7) ↔ δ = 7.25 (9-H), δ = 159.41 (C-8) ↔ δ = 3.98 (8-OMe), δ = 159.41 (C-8) ↔ δ = 7.25 (9-H), δ = 159.41 (C-8) ↔ δ = 8.05 (10-H), δ = 174.16 (C-2) ↔ [δ_A = 2.63 (3-H^A) and δ_B = 2.82 (3-H^B)], δ = 174.16 (C-2) ↔ 4.29(3a-H), δ = 181.32 (C-11) ↔ δ = 5.29 (11b-H), δ = 181.32 (C-11) ↔ δ = 8.05 (10-H), δ = 181.99 (C-6) ↔ δ = 6.04 (5-H). **Melting point:** 228-234°C (decomposition). **Optical rotation of 13b:** $[\alpha]_D^{20}$ = –260.3 (*c* = 0.49, $CHCl_3$). **Optical rotation of *ent*-13b:** $[\alpha]_D^{20}$ = +275.3 (*c* = 0.79, $CHCl_3$). **HRMS** (pos. ESI): calcd. for $C_{23}H_{18}O_7Na$ [M+Na]$^+$ = 429.09447; found 429.09445 (–0.05 ppm). **IR (film):** *v* = 3060, 2940, 2850, 1785, 1665, 1625, 1575, 1485, 1450, 1400, 1335, 1275, 1230, 1200, 1155, 1095, 1075, 1050, 1015, 995, 970, 945, 905, 885, 845, 820, 795, 765, 735, 700 cm^{-1}.

(3a*S*,5*S*,11b*S*)-7,8-Dimethoxy-5-(4-(trifluoromethyl)phenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6,11-trione (13c)



Following the **General Procedure A** the title compound was prepared from **43c** (68.6 mg, 136 µmol) suspended in MeCN (1.4 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (149.1 mg, 272 µmol, 2.0 equiv.) in H_2O (1.4 mL). After workup the solvent was removed in vacuo to afford the title compound (60.6 mg, 94%, *dr* = 100:0) in pure form as an orange solid. Note: The optical antipode *ent*-**13c** was synthesized analogously in 64% yield (*dr* = 100:0).– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.64, δ_B = 2.85, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.86 (s, 3H, 7-OMe, exclusion principle), 3.99 (s, 3H, 8-OMe), 4.24 (dd, 1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.29 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 6.06 (s, 1H, 5-H), 7.27 (d, 1H, $J_{9,10}$ = 8.2 Hz, 9-H), 7.38 (br. d, 2H, $J_{2',3'}$ = $J_{6',5'}$ = 8.0 Hz, 2'-H and 6'-H), 7.63 (br. d, 2H, $J_{3',2'}$ = $J_{5',6'}$ = 8.0 Hz, 3'-H and 5'-H), 8.05 (d, 1H, $J_{10,9}$ = 8.7 Hz, 10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.85 (3-H^B) ↔ δ = 5.29 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.99 (8-OMe) ↔ δ = 7.27 (9-H), δ = 7.38 (2'-H and 6'-H) ↔ δ = 4.24 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.38 (2'-H and 6'-H) ↔ δ = 6.06 (5-H). **^{19}F NMR** (470.72 MHz, $CDCl_3$): δ = –62.85 (s, 3F, CF_3). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 36.66 (C-3), 56.50 (8-OCH_3), 61.31 (7-OCH_3), 67.31 (C-3a), 68.95 (C-11b), 71.56 (C-5), 116.51 (C-9), 123.83 (q, 1C, $^1J_{C,F}$ = 272.4 Hz, 4'-CF_3), 124.70 (C-6a), 125.26 (C-10), 125.41 (C-10a), 125.98 (q, 2C, $^3J_{C,F}$ = 4.0 Hz, C-3' and C-5'), 128.98 (C-2' and C-6'), 131.33 (q, 1C, $^2J_{C,F}$ = 32.7 Hz, C-4'), 135.89 and 146.62 (C-5a and C-11a), 140.38 (C-1'), 149.92 (C-7), 159.52 (C-8), 173.81 (C-2), 181.07 (C-11), 182.06 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 36.66 (C-3) ↔ [δ_A = 2.64 (3-H^A) and δ_B = 2.85 (3-H^B)], δ = 56.50 (8-OCH_3) ↔ δ = 3.99 (8-OMe), δ = 61.31 (7-OCH_3) ↔ δ = 3.86 (7-OMe), δ = 67.31 (C-3a) ↔ δ = 4.24 (3a-H), δ = 68.95 (C-11b) ↔ δ = 5.29 (11b-H), δ = 71.56 (C-5) ↔ δ = 6.06 (5-H), δ = 116.51 (C-9) ↔ δ = 7.27 (9-H), δ = 125.26 (C-10) ↔ δ = 8.05 (10-H), δ = 125.98 (C-3' and C-5') ↔ δ = 7.63 (3'-H and 5'-H), δ = 128.98 (C-2' and C-6') ↔ δ = 7.38 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 124.70 (C-6a) ↔ δ = 8.05 (10-H), δ = 125.41 (C-10a) ↔ δ = 7.27 (9-H), δ = 131.33 (C-4') ↔ δ = 7.38 (2'-H and 6'-H), [δ = 135.89 and 146.62 (C-5a and C-11a) ↔ δ = 5.29 (11b-H), δ = 135.89 and 146.62 (C-5a and C-11a) ↔ δ = 6.06 (5-H) could not be assigned unambiguously], δ = 140.38 (C-1') ↔ δ = 6.06 (5-H), δ = 140.38 (C-1') ↔ δ = 7.63 (3'-H and 5'-H), δ = 149.92 (C-7) ↔ δ = 3.86 (7-OMe), δ = 149.92 (C-7) ↔ δ = 7.27 (9-H), δ = 159.52 (C-8) ↔ δ = 3.99 (8-OMe), δ = 159.52 (C-8) ↔ δ = 7.27 (9-H), δ = 159.52 (C-8) ↔ δ = 8.05 (10-H), δ = 173.81 (C-2) ↔ [δ_A = 2.64 (3-H^A) and δ_B = 2.85 (3-H^B)], δ = 173.81 (C-2) ↔ 4.24(3a-H), δ = 181.07 (C-11) ↔ δ = 5.29 (11b-H), δ = 181.07 (C-11) ↔ δ = 8.05 (10-H), δ = 182.06 (C-6) ↔ δ = 6.06 (5-H). **Melting point:** 228-234°C (decomposition). **Optical rotation of 13c:** $[\alpha]_D^{20}$ = –202.7 (*c* = 0.588, $CHCl_3$). **Optical rotation of *ent*-13c:** $[\alpha]_D^{20}$ = +167.8 (*c* = 0.83, $CHCl_3$). **HRMS** (pos. ESI): calcd. for $C_{24}H_{17}F_3O_7Na$ [M+Na]$^+$ = 497.08186; found 497.08206 (+0.41 ppm). **IR (film):** *v* = 3345, 2940, 2855, 1785, 1665, 1620, 1575, 1485, 1455, 1415, 1330, 1275, 1230, 1200, 1165, 1125, 1095, 1065, 1020, 1000, 975, 910, 885, 860, 830, 795, 780, 765, 735, 700, 655 cm^{-1}.

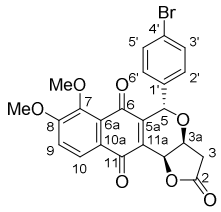
(3a*S*,5*S*,11b*S*)-7,8-Dimethoxy-5-(4-fluorophenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6,11-trione (13d)



Following the **General Procedure A** the title compound was prepared from **43d** (55.7 mg, 123 µmol) suspended in MeCN (1.2 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (134.4 mg, 245 µmol, 2.0 equiv.) in H_2O (1.2 mL). Purification by flash chromatography [d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 2:1 (F1-13), CH/EE 1:1 (F14-26),] afforded the title compound [F14-25, R_f (2:1) = 0.2, 38.8 mg, 75%, *dr* = 100:0] as an orange solid. Note: The optical antipode *ent*-**13d** was synthesized analogously in 62% yield (*dr* = 95:5).– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.63, δ_B = 2.84, J_{AB} = 17.9 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.86 (s, 3H, 7-OMe), 3.99 (s, 3H, 8-OMe), 4.24 (dd, 1H, $J_{3a,B}$ = 5.3 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.28 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 6.01 (s, 1H, 5-H), 7.05 (m, 2H, 3'-H and 5'-H), 7.23 (m, 2H, 2'-H and 6'-H), 7.26 (d, 1H, $J_{9,10}$ = 8.7 Hz, 9-H), 8.05 (d, 1H, $J_{10,9}$ = 8.7 Hz, 10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum

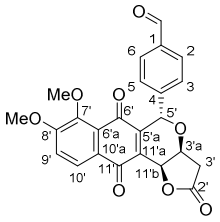
(500.32 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.84 (3-H^B) ↔ δ = 5.28 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.99 (8-OMe) ↔ δ = 7.26 (9-H), δ = 7.23 (2'-H and 6'-H) ↔ δ = 4.27 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.23 (2'-H and 6'-H) ↔ δ = 6.01 (5-H). **^{19}F NMR** (470.72 MHz, $CDCl_3$): δ = –112.17 ppm. **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 36.66 (C-3), 56.49 (8-OCH_3), 61.32 (7-OCH_3), 66.92 (C-3a), 69.09 (C-11b), 71.44 (C-5), 115.99 (d, 2C, $^2J_{C,F}$ = 21.7 Hz, C-3' and C-5'), 116.42 (C-9), 125.18 (C-10), 124.80 (C-6a), 125.47 (C-10a), 130.42 (d, 2C, $^3J_{C,F}$ = 8.7 Hz, C-2' and C-6'), 132.34 (d, 1C, $^4J_{C,F}$ = 3.4 Hz, C-1'), 135.57 and 147.26 (C-5a and C-11a), 149.86 (C-7), 159.47 (C-8), 163.08 (d, 1C, $^1J_{C,F}$ = 247.5 Hz, C-4'), 173.99 (C-2), 181.22 (C-11), 181.99 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 36.66 (C-3) ↔ [δ_A = 2.63 (3-H^A) and δ_B = 2.84 (3-H^B)], δ = 56.49 (8-OCH_3) ↔ δ = 3.99 (8-OMe), δ = 61.32 (7-OCH_3) ↔ δ = 3.86 (7-OMe), δ = 66.92 (C-3a) ↔ δ = 4.27 (3a-H), δ = 69.09 (C-11b) ↔ δ = 5.28 (11b-H), δ = 71.44 (C-5) ↔ δ = 6.01 (5-H), δ = 115.99 (C-3' and C-5') ↔ δ = 7.05 (3'-H and 5'-H), δ = 116.42 (C-9) ↔ δ = 7.26 (9-H), δ = 125.18 (C-10) ↔ δ = 8.05 (10-H), δ = 130.42 (C-2' and C-6') ↔ δ = 7.23 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 124.80 (C-6a) ↔ δ = 8.05 (10-H), δ = 125.47 (C-10a) ↔ δ = 7.26 (9-H), δ = 132.34 (C-1') ↔ δ = 6.01 (5-H), δ = 132.34 (C-1') ↔ δ = 7.05 (3'-H and 5'-H), [δ = 135.57 and 147.26 (C-5a and C-11a) ↔ δ = 5.28 (11b-H), δ = 135.57 and 147.26 (C-5a and C-11a) ↔ δ = 6.01 (5-H) could not be assigned unambiguously], δ = 149.86 (C-7) ↔ δ = 3.86 (7-OMe), δ = 149.86 (C-7) ↔ δ = 7.26 (9-H), δ = 159.47 (C-8) ↔ δ = 3.99 (8-OMe), δ = 159.47 (C-8) ↔ δ = 7.26 (9-H), δ = 159.47 (C-8) ↔ δ = 8.05 (10-H), δ = 173.99 (C-2) ↔ [δ_A = 2.63 (3-H^A) and δ_B = 2.84 (3-H^B)], δ = 173.99 (C-2) ↔ 4.27(3a-H), δ = 181.22 (C-11) ↔ δ = 5.28 (11b-H), δ = 181.22 (C-11) ↔ δ = 8.05 (10-H), δ = 181.99 (C-6) ↔ δ = 6.01 (5-H). **Melting point:** 231-232°C (decomposition). **Optical rotation of 11d:** $[\alpha]_D^{20}$ = –206.7 (*c* = 0.388, $CHCl_3$). **Optical rotation of *ent*-13d:** $[\alpha]_D^{20}$ = +171.0 (*c* = 0.41, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{23}H_{17}FO_7Na$ $[M+Na]^+$ = 447.08505; found 447.08508 (+0.07 ppm). **IR (film):** *v* = 2935, 2850, 1785, 1665, 1605, 1575, 1510, 1485, 1455, 1405, 1335, 1275, 1230, 1200, 1155, 1090, 1080, 1050, 1000, 975, 945, 910, 885, 855, 840, 795, 685 cm^{-1}.

(3a*S*,5*S*,11b*S*)-7,8-Dimethoxy-5-(4-bromoophenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6,11-trione (13e)



Following the **General Procedure A** the title compound was prepared from **43e** (71.0 mg, 138 µmol) suspended in MeCN (1.4 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (151.3 mg, 276 µmol, 2.0 equiv.) in H_2O (1.4 mL). Purification by flash chromatography (d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 2:1) afforded the title compound [F16-25, R_f (2:1) = 0.2, 59.0 mg, 88%, *dr* = 100:0] as an orange solid. Note: The optical antipode *ent*-**13e** was synthesized analogously in 89% yield (*dr* = 100:0).– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.63, δ_B = 2.83, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.86 (s, 3H, 7-OMe), 3.99 (s, 3H, 8-OMe), 4.26 (dd, 1H, $J_{3a,B}$ = 5.3 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.27 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 5.97 (s, 1H, 5-H), 7.12 (m, 2H, 2'-H and 6'-H), 7.26 (d, 1H, $J_{9,10}$ = 8.7 Hz, 9-H), 7.50 (m, 2H, 3'-H and 5'-H), 8.05 (d, 1H, $J_{10,9}$ = 8.6 Hz, 10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.83 (3-H^B) ↔ δ = 5.27 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.99 (8-OMe) ↔ δ = 7.26 (9-H), δ = 7.12 (2'-H and 6'-H) ↔ δ = 4.26 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.12 (2'-H and 6'-H) ↔ δ = 5.97 (5-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 36.66 (C-3), 56.50 (8-OCH_3), 61.32 (7-OCH_3), 67.10 (C-3a), 69.03 (C-11b), 71.57 (C-5), 116.47 (C-9), 125.17 (C-10), 130.23 (C-2' and C-6'), 132.17 (C-3' and C-5'), 123.44 (C-4'), 124.80 (C-6a), 125.51 (C-10a), 135.51 (C-1'), 135.71 and 146.96 (C-5a and C-11a), 149.93 (C-7), 159.50 (C-8), 173.85 (C-2), 181.14 (C-11), 181.98 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 36.66 (C-3) ↔ [δ_A = 2.63 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 56.50 (8-OCH_3) ↔ δ = 3.99 (8-OMe), δ = 61.32 (7-OCH_3) ↔ δ = 3.86 (7-OMe), δ = 67.10 (C-3a) ↔ δ = 4.26 (3a-H), δ = 69.03 (C-11b) ↔ δ = 5.27 (11b-H), δ = 71.57 (C-5) ↔ δ = 5.97 (5-H), δ = 116.47 (C-9) ↔ δ = 7.26 (9-H), δ = 125.17 (C-10) ↔ δ = 8.05 (10-H), δ = 130.23 (C-2' and C-6') ↔ δ = 7.12 (2'-H and 6'-H), δ = 132.17 (C-3' and C-5') ↔ δ = 7.50 (3'-H and 5'-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 123.44 (C-4') ↔ δ = 7.12 (2'-H and 6'-H), δ = 123.44 (C-4') ↔ 7.50 (3'-H and 5'-H), δ = 124.80 (C-6a) ↔ δ = 8.05 (10-H), δ = 125.51 (C-10a) ↔ δ = 7.26 (9-H), δ = 135.51 (C-1') ↔ δ = 5.97 (5-H), δ = 135.51 (C-1') ↔ δ = 7.50 (3'-H and 5'-H), [δ = 135.71 and 146.96 (C-5a and C-11a) ↔ δ = 5.27 (11b-H), δ = 135.71 and 146.96 (C-5a and C-11a) ↔ δ = 5.97 (5-H) could not be assigned unambiguously], δ = 149.93 (C-7) ↔ δ = 3.85 (7-OMe), δ = 149.93 (C-7) ↔ δ = 7.26 (9-H), δ = 159.50 (C-8) ↔ δ = 3.99 (8-OMe), δ = 159.50 (C-8) ↔ δ = 7.26 (9-H), δ = 159.50 (C-8) ↔ δ = 8.05 (10-H), δ = 173.85 (C-2) ↔ [δ_A = 2.63 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 173.85 (C-2) ↔ 4.26(3a-H), δ = 181.14 (C-11) ↔ δ = 5.27 (11b-H), δ = 181.14 (C-11) ↔ δ = 8.05 (10-H), δ = 181.98 (C-6) ↔ δ = 5.97 (5-H). **Melting point:** 238-243°C (decomposition). **Optical rotation of 13e:** $[\alpha]_D^{20}$ = –225.3 (*c* = 0.41, $CHCl_3$). **Optical rotation of *ent*-13e:** $[\alpha]_D^{20}$ = +229.7 (*c* = 0.48, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{23}H_{17}{}^{79}BrO_7Na$ $[M+Na]^+$ = 507.00499; found 507.00497 (–0.02 ppm) and calcd. for $C_{23}H_{17}{}^{81}BrO_7Na$ $[M+Na]^+$ = 509.00294; found 507.00296 (+0.04 ppm). **IR (film):** *v* = 2940, 2845, 1785, 1665, 1575, 1485, 1450, 1400, 1335, 1275, 1230, 1195, 1150, 1095, 1075, 1050, 1010, 1000, 975, 945, 910, 885, 855, 825, 790, 730, 695 cm^{-1}.

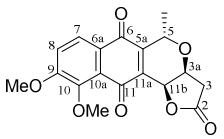
4-((3a*S*,5*S*,11b*S*)-7,8-Dimethoxy-2,6,11-trioxo-3,3a,5,6,11,11b-hexahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-5-yl)benzaldehyde (13f)



Following the **General Procedure A** the title compound was prepared from **43f** (14.5 mg, 31.2 µmol) suspended in MeCN (1 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (34.2 mg, 62.4 µmol, 2.0 equiv.) in H_2O (1 mL). Purification by flash chromatography (d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 3:2) afforded the title compound [F12-17, R_f (3:2) = 0.2, 6.3 mg, 46%, *dr* = 100:0] as an orange solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.65, δ_B = 2.85, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3'a}$ = 5.3 Hz, 3'-H^A and 3'-H^B), 3.86 (s, 3H, 7'-OMe), 3.99 (s, 3H, 8'-OMe), 4.24 (dd, 1H, $J_{3'a,B}$ = 5.3 Hz, $J_{3'a,11'b}$ = 3.1 Hz, 3'a-H), 5.30 (d, 1H, $J_{11'b,3'a}$ = 3.1 Hz, 11'b-H), 6.07 (s, 1H, 5'-H), 7.27 (d, 1H, $J_{9',10'}$ = 8.7 Hz, 9'-H), 7.43 (m_c, 2H, 3-H and 5-H), 7.89 (m_c, 2H, 2-H, and 6-H), 8.06 (d, 1H, $J_{10',9'}$ = 8.6 Hz, 10'-H), 10.02 (s, 1H, 1-CHO). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 2.85 (3'-H^B) ↔ δ = 5.30 (11'b-H, this cross-peak proves that 3'-H^B and 11'b-H are oriented *cis* relative to one another), δ = 3.99 (8'-OMe) ↔ δ = 7.27 (9'-H), δ = 7.43 (3-H and 5-H) ↔ δ = 4.24 (3'a-H, this cross-peak proves that the phenyl ring and 3'a-H are oriented *cis* relative to one another), δ = 7.43 (3-H and 5-H) ↔ δ = 6.07 (5'-H), δ = 7.89 (2-H and 6-H) ↔ δ = 10.02 (1-CHO). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 36.69 (C-3'), 56.51 (8'-OCH_3), 61.32 (7'-OCH_3), 67.41 (C-3'a), 68.95 (C-11'b), 71.73 (C-5'), 116.52 (C-9'), 124.71 (C-6'a), 125.28 (C-10'), 125.42 (C-10'a), 129.27 (C-3 and C-5), 130.23 (C-2 and C-6), 135.86 and

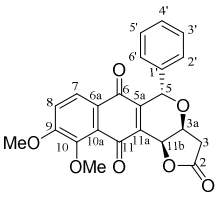
146.60 (C-5'a and C-11'a), 136.74 (C-1), 142.86 (C-4), 149.92 (C-7'), 159.52 (C-8'), 173.79 (C-2'), 181.06 (C-11'), 182.07 (C-6'), 191.52 (1-CHO). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 36.69 (C-3') ↔ [δ_A = 2.65 (3'-H^A) and δ_B = 2.85 (3'-H^B)], δ = 56.51 (8'-OCH_3) ↔ δ = 3.99 (8'-OMe), δ = 61.32 (7'-OCH_3) ↔ δ = 3.86 (7'-OMe), δ = 67.41 (C-3'a) ↔ δ = 4.24 (3'a-H), δ = 68.95 (C-11'b) ↔ δ = 5.30 (11'b-H), δ = 71.73 (C-5') ↔ δ = 6.07 (5'-H), δ = 116.52 (C-9') ↔ δ = 7.27 (9'-H), δ = 125.28 (C-10') ↔ δ = 8.06 (10'-H), δ = 129.27 (C-3 and C-5) ↔ δ = 7.43 (3-H and 5-H), δ = 130.23 (C-2 and C-6) ↔ δ = 7.89 (2-H and 6-H), δ = 191.52 (1-CHO) ↔ δ = 10.02 (1-CHO). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 124.71 (C-6'a) ↔ δ = 8.06 (10'-H), δ = 125.42 (C-10'a) ↔ δ = 7.27 (9'-H), [δ = 135.86 and 146.60 (C-5'a and C-11'a) ↔ δ = 5.30 (11'b-H), δ = 135.86 and 146.60 (C-5'a and C-11'a) ↔ δ = 6.07 (5'-H) could not be assigned unambiguously], δ = 136.74 (C-1) ↔ δ = 7.43 (3-H and 5-H), δ = 136.74 (C-1) ↔ δ = 10.02 (1-CHO), δ = 142.86 (C-4) ↔ δ = 6.07 (5'-H), δ = 142.86 (C-4) ↔ δ = 7.89 (2-H and 6-H), δ = 149.92 (C-7') ↔ δ = 3.86 (7'-OMe), δ = 149.92 (C-7') ↔ δ = 7.27 (9'-H), δ = 159.52 (C-8') ↔ δ = 3.99 (8'-OMe), δ = 159.52 (C-8') ↔ δ = 7.27 (9'-H), δ = 159.52 (C-8') ↔ δ = 8.06 (10'-H), δ = 173.79 (C-2') ↔ [δ_A = 2.65 (3'-H^A) and δ_B = 2.85 (3'-H^B)], δ = 173.79 (C-2') ↔ 4.24 (3'a-H), δ = 181.06 (C-11') ↔ δ = 8.06 (10'-H), δ = 182.07 (C-6') ↔ δ = 6.07 (5'-H). **Optical rotation:** $[\alpha]_D^{20}$ = –193.6 (*c* = 0.58, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{24}H_{18}O_8Na$ [M+Na]$^+$ = 457.08939; found 457.08929 (–0.21 ppm). **IR (film):** *v* = 2925, 2850, 1785, 1705, 1665, 1610, 1575, 1485, 1460, 1410, 1335, 1275, 1230, 1155, 1075, 1055, 1005, 975, 910, 825 cm^{-1}.

(3a*S*,5*S*,11b*S*)-9,10-Dimethoxy-5-methyl-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*] isochromen-2,6,11(5*H*,11b*H*)-trione (14a)



Following the **General Procedure A** the title compound was prepared from **46a** (8.2 mg, 22 µmol) dissolved in MeCN (1 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (24.1 mg, 44.0 µmol, 2.0 equiv.) in H_2O (1 mL). Purification by flash chromatography [d = 1 cm, h = 13 cm, F = 8 mL; CH/EE 1:1 (F1-13)] afforded the title compound [F4-8, R_f (1:1) = 0.30, 5.1 mg, 68%, *dr* = 97:3] as an orange solid].– **^{1}H-NMR** (500.32 MHz, $CDCl_3$, spectrum contains resonances of grease at δ = 0.85 and 1.25 ppm): δ = 1.53 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6:9 Hz, 5-CH_3), AB signal (δ_A = 2.68 and δ_B = 2.96, J_{AB} = 17.7 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.2 Hz, 3-H^A and 3-H^B), 3.94 (s, 3H, 10-OMe), 3.99 (s, 3H, 9-OMe), 4.66 (dd, 1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.0 Hz, 3a-H), 5.03 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.9 Hz, 5-H), 5.30 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 7.21 (d, 1H, $J_{7,8}$ = 8.6 Hz, 7-H), 7.94 (d, 1H, $J_{8,7}$ = 8.6 Hz, 8-H). 9-OMe was distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.96 (3-H^B) ↔ δ = 5.30 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 1.53 (5-C*H*$_3$) ↔ δ = 4.66 (3a-H, this cross-peak proves that 5-CH_3 and 3a-H are oriented *cis* relative to one another), δ = 3.99 (9-OMe) ↔ δ = 7.21 (8-H). **^{13}C-NMR** (125.81 MHz, $CDCl_3$, spectrum contains a resonance of grease at δ = 29.79 ppm): δ = 18.59 (5-CH_3), 37.10 (C-3), 56.47 (9-OCH_3), 61.49 (10-OCH_3), 66.58 (C-5), 66.65 (C-3a), 69.00 (C-11b), 115.95 (C-8), 124.86 (C-7), 124.92 (C-10a), 125.56 (C-6a), 135.26 (C-11a), 148.29 (C-5a), 149.79 (C-10), 159.63 (C-9), 174.26 (C-2), 181.57 (C-11), 182.08 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 18.59 (5-CH_3) ↔ δ = 1.53 (5-C*H*$_3$), δ = 37.10 (C-3) ↔ δ_A = 2.68 and δ_B = 2.96 (3-H^A and 3-H^B), δ = 56.47 (9-OCH_3) ↔ δ = 3.99 (9-OMe), δ = 61.49 (10-OCH_3) ↔ δ = 3.94 (10-OMe), δ = 66.58 (C-5) ↔ δ = 5.03 (5-H), δ = 66.65 (C-3a) ↔ δ = 4.66 (3a-H), δ = 69.00 (C-11b) ↔ δ = 5.30 (11b-H), δ = 115.95 (C-8) ↔ δ = 7.21 (8-H), δ = 124.86 (C-7) ↔ δ = 7.94 (7-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 124.92 (C-10a) ↔ δ = 7.94 (7-H), δ = 125.56 (C-6a) ↔ δ = 7.21 (8-H), δ = 135.26 (C-11a) ↔ δ = 5.03(5-H), δ = 135.26 (C-11a) ↔ δ = 5.30 (11b-H), δ = 148.29 (C-5a) ↔ δ = 1.53 (5-C*H*$_3$), δ = 148.29 (C-5a) ↔ δ = 5.03 (5-H), δ = 148.29 (C-5a) ↔ δ = 5.30 (11b-H), δ = 149.79 (C-10) ↔ δ = 3.94 (10-OMe), δ = 149.79 (C-10) ↔ δ = 7.21 (8-H), δ = 149.79 (C-10) ↔ δ = 7.94 (7-H), δ = 159.63 (C-9) ↔ δ = 3.99 (9-OMe), δ = 159.63 (C-9) ↔ δ = 7.21 (8-H), δ = 159.63 (C-9) ↔ δ = 7.94 (7-H), δ = 174.26 (C-2) ↔ δ_A = 2.68 (3-H^A), δ = 174.26 (C-2) ↔ δ_B = 2.96 (3-H^B), δ = 174.26 (C-2) ↔ δ = 4.66 (3a-H), δ = 181.57 (C-11) ↔ δ = 5.30 (11b-H), δ = 182.08 (C-6) ↔ δ = 7.94 (7-H). **Optical rotation:** $[\alpha]_D^{20}$ = −122.7 (c = 0.410, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{18}H_{16}O_7$ [M+Na]$^+$ = 367.07882; found 367.07907 (+0.67 ppm). **IR (film):** v = 2925, 2850, 1785, 1740, 1665, 1645, 1575, 1485, 1460, 1415, 1395, 1370, 1335, 1270, 1235, 1200, 1155, 1125, 1085, 1060, 1050, 1005, 995, 950, 900, 850 cm^{-1}.

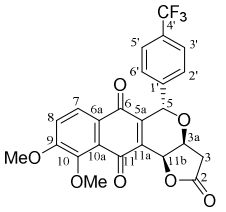
(3a*S*,5*S*,11b*S*)-5-Phenyl-9,10-dimethoxy-3,3a-dihydro-2*H*-benzo[g]furo[3,2-*c*] isochromen-2,6,11(5*H*,11b*H*)-trione (14b)



Following the **General Procedure A** the title compound was prepared from **46b** (23.4 mg, 53.6 µmol) dissolved in MeCN (4 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (59.1 mg, 108 µmol, 2.0 equiv.) in H_2O (2 mL). Purification by flash chromatography [d = 1 cm, h = 12 cm, F = 8 mL; CH/EE 2:1 (F1-16)] afforded the pure product [F5-10, R_f (2:1) = 0.20, 17.6 mg, 80%, *dr* = 94:6] as a yellow oil To separate the two diastereomers, the obtained product was completely dissolved in CH_2Cl_2 (2 mL) and heptane (1.5 mL) was added. CH_2Cl_2 was allowed to slowly vaporize over 3 d. The solvent was removed with a pipet to furnish **14b** as a yellow oil (12.0 mg, 55%).– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.63 and δ_B = 2.84, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.97 (s, 3H, 10-OMe), 3.99 (s, 3H, 9-OMe), 4.30 (dd, 1H, $J_{3a,B}$ = 5.3 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.32 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 6.00 (s, 1H, 5-H), 7.21 (d, 1H, $J_{8,7}$ = 8.8 Hz, 8-H), 7.21-7.26 (m, 2H, 2'-H and 6'-H), 7.34-7.38 (m, 3H, 3'-H, 4'-H and 5'-H), 7.89 (d, 1H, $J_{7,8}$ = 8.6 Hz, 7-H). 9-OMe was distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 2.84 (3-H^B) ↔ δ = 5.32 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.21-7.26 (2'-H and 6'-H) ↔ δ = 4.30 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.21-7.26 (2'-H and 6'-H) ↔ δ = 6.00 (5-H), δ = 3.99 (9-OMe) ↔ δ = 7.21 (8-H). **^{13}C-NMR** (100.61 MHz, $CDCl_3$): δ = 36.74 (C-3), 56.50 (9-OCH_3), 61.52 (10-OCH_3), 67.19 (C-3a), 69.20 (C-11b), 71.94 (C-5), 116.10 (C-8), 125.09 (C-7), 125.09 (C-10a), 125.41 (C-6a), 128.59 (C-2' and C-6'), 128.96 (C-3' and C-5'), 129.16 (C-4'), 136.37 (C-1'), 137.54 and 145.31 (C-5a and C-11a), 149.94 (C-10), 159.75 (C-9), 174.15 (C-2), 181.43 (C-11), 181.73 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 36.74 (C-3) ↔ δ_A = 2.63 and δ_B = 2.84 (3-H^A and 3-H^B), δ = 56.50 (9-OCH_3) ↔ δ = 3.99 (9-OMe), δ = 61.52 (10-OCH_3) ↔ δ = 3.97 (10-OMe), δ = 67.19 (C-3a) ↔ δ = 4.30 (3a-H), δ = 69.20 (C-11b) ↔ δ = 5.32 (11b-H), δ = 71.94 (C-5) ↔ δ = 6.00 (5-H), δ = 116.10 (C-8) ↔ δ = 7.21 (8-H), δ = 125.09 (C-7) ↔ δ = 7.89 (7-H), δ = 128.59 (C-2' and C-6') ↔ δ = 7.21-7.26 (2'-H and 6'-H), δ = 128.96 (C-3' and C-5') ↔ δ = 7.34-7.38 (3'-H, 4'-H and 5'-H), δ = 129.16 (C-4') ↔ δ = 7.34-7.38 (3'-H, 4'-H and 5'-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 125.09 (C-10a) ↔ δ = 7.89 (7-H), δ = 125.41 (C-6a) ↔ δ = 7.21 (8-H), δ = 136.37 (C-1') ↔ δ = 6.00 (5-H), δ = 136.37 (C-1') ↔ δ = 7.34-7.38 (3'-H, 4'-H and 5'-H), [δ = 137.54 and 145.31 (C-5a and C-11a) ↔ δ = 5.32 (11b-H), δ = 137.54 and 145.31 (C-5a and C-11a) ↔

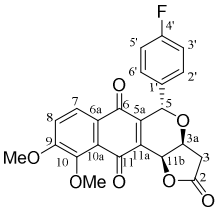
δ = 6.00 (5-H) could not be assigned unambiguously], δ = 149.94 (C-10) ↔ δ = 3.97 (10-OMe), δ = 149.94 (C-10) ↔ δ = 7.21 (8-H), δ = 159.75 (C-9) ↔ δ = 3.99 (9-OMe), δ = 159.75 (C-9) ↔ δ = 7.21 (8-H), δ = 159.75 (C-9) ↔ δ = 7.89 (7-H), δ = 174.15 (C-2) ↔ δ_A = 2.63 (3-H^A), δ = 174.15 (C-2) ↔ δ_B = 2.84 (3-H^B), δ = 174.15 (C-2) ↔ δ = 4.30 (3a-H), δ = 181.43 (C-11) ↔ δ = 5.32 (11b-H), δ = 181.73 (C-6) ↔ δ = 6.30 (5-H), δ = 181.73 (C-6) ↔ δ = 7.89 (7-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = −75.8 (c = 0.530, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{23}H_{18}O_7$ $[M+Na]^+$ = 429.09447; found 429.09464 (+0.38 ppm). **IR (film):** v = 2925, 2850, 1785, 1665, 1645, 1575, 1485, 1455, 1415, 1395, 1335, 1275, 1230, 1200, 1155, 1090, 1055, 1025, 1000, 970, 950, 925, 900 cm^{-1}.

(3a*S*,5*S*,11b*S*)-9,10-Dimethoxy-5-(4-(trifluoromethyl)phenyl)-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6-11(5*H*,11b*H*)-trione (14c)



Following the **General Procedure A** the title compound was prepared from **46c** (21.8 mg, 43.2 µmol) dissolved in MeCN (3 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (47.4 mg, 86.5 µmol, 2.0 equiv.) in H_2O (2 mL). Purification by flash chromatography [d = 1 cm, h = 13.5 cm, F = 8 mL; CH/EE 3:1 (F1-10), 2:1 (F11-20)] afforded the pure product (F10-16, R_f (2:1) = 0.25, 17.6 mg, 93%) as a yellow oil.– **^{1}H-NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.65 and δ_B = 2.86, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.98 (s, 3H, 10-OMe), 4.00 (s, 3H, 9-OMe), 4.24 (dd, 1H, $J_{3a,B}$ = 5.3 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.33 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 6.02 (s, 1H, 5-H), 7.23 (d, 1H, $J_{7,8}$ = 8.7 Hz, 8-H), 7.38 (br,d, 2H, $J_{2',3'}$ = $J_{6',5'}$ = 8.5 Hz, 2'-H and 6'-H), 7.64 (br,d, 2H, $J_{3',2'}$ = $J_{5',6'}$ = 8.5 Hz, 3'-H and 6'-H), 7.91 (d, 1H, $J_{8,7}$ = 8.5 Hz, 7-H). 9-OMe was distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks (500.32 MHz, $CDCl_3$) [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.86 (3-H^B) ↔ δ = 5.33 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.38 (2'-H and 6'-H) ↔ δ = 4.24 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.38 (2'-H and 6'-H) ↔ δ = 6.02 (5-H), δ = 4.00 (9-OMe) ↔ δ = 7.23 (8-H). **^{19}F-NMR** (470.72 MHz, ^{1}H-decoupled, $CDCl_3$): δ = −62.83 ppm. **^{13}C-NMR** (125.82 MHz, $CDCl_3$): δ = 36.71 (C-3), 56.54 (9-OCH_3), 61.55 (10-OCH_3), 67.52 (C-3a), 68.91 (C-11b), 71.28 (C-5), 116.16 (C-8), 123.83 (q, 1C, $^1J_{C,F}$ = 272.5 Hz, 4'-CF_3), 125.03(C-10a), 125.17 (C-6a), 125.21 (C-7), 125.97 (q, 2C, $^3J_{C,F}$ = 3.7 Hz, C-3' and C-5'), 128.96 (C-2' and C-6'), 131.36 (q, 1C, $^2J_{C,F}$ = 32.8 Hz, C-4'), 137.89 (C-5a), 144.43 (C-11a), 140.39 (C-1'), 150.05 (C-10), 159.94 (C-9), 173.83 (C-2), 181.19 (C-11), 181.74 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 36.71 (C-3) ↔ δ_A = 2.68 and δ_B = 2.85 (3-H^A and 3-H^B), δ = 56.54 (9-OCH_3) ↔ δ = 4.00 (9-OMe), δ = 61.55 (10-OCH_3) ↔ δ = 3.98 (10-OMe), δ = 67.52 (C-3a) ↔ δ = 4.24 (3a-H), δ = 68.91 (C-11b) ↔ δ = 5.33 (11b-H), δ = 71.28 (C-5) ↔ δ = 6.02 (5-H), δ = 116.16 (C-8) ↔ δ = 7.23 (8-H), δ = 125.21 (C-7) ↔ δ = 7.91 (7-H), δ = 125.97 (q, 2C, $^3J_{C,F}$ = 3.7 Hz, C-3' and C-5') ↔ δ = 7.64 (3'-H and 5'-H), δ = 128.96 (C-2' and C-6') ↔ 7.38 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 125.03(C-10a) ↔ δ = 7.91(7-H), δ = 125.17 (C-6a) ↔ δ = 7.23 (8-H), δ = 131.36 (q, 1C, $^2J_{C,F}$ = 32.8 Hz, C-4') ↔ δ = 7.38 (2'-H and 6'-H), [δ = 137.89 and 144.43 (C-5a and C-11a) ↔ δ = 5.33 (11b-H), δ = 137.89 and 144.43 (C-5a and C-11a) ↔ δ = 6.02 (5-H) could not be assigned unambiguously], δ = 140.39 (C-1') ↔ δ = 7.64 (3'-H and 5'-H), δ = 140.39 (C-1') ↔ δ = 6.02 (5-H), δ = 150.05 (C-10) ↔ δ = 3.98 (10-OMe), δ = 150.05 (C-10) ↔ δ = 7.23 (8-H), δ = 159.94 (C-9) ↔ δ = 4.00 (9-OMe), δ = 159.94 (C-9) ↔ δ = 7.23 (8-H), δ = 159.94 (C-9) ↔ δ = 7.91 (7-H), δ = 173.83 (C-2) ↔ δ_A = 2.65 (3-H^A), δ = 173.83 (C-2) ↔ δ_B = 2.86 (3-H^B), δ = 173.83 (C-2) ↔ δ = 4.24 (3a-H), δ = 181.19 (C-11) ↔ δ = 5.33 (11b-H), δ = 181.74 (C-6) ↔ δ = 6.02 (5-H), δ = 181.74 (C-6) ↔ δ = 7.89 (7-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = −62.1 (c = 0.527, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{24}H_{17}F_3O_7$ $[M+H]^+$ = 475.09991; found 475.09976 (−0.32 ppm). **IR (film):** v = 2930, 2855, 1785, 1665, 1650, 1620, 1575, 1485, 1455, 1415, 1330, 1275, 1230, 1200, 110, 1125, 1095, 1030, 1020, 1000, 950, 905, 840 cm^{-1}.

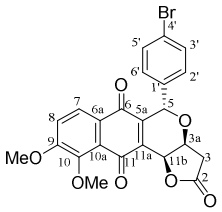
(3a*S*,5*S*,11b*S*)-9,10-Dimethoxy-5-(4-fluorophenyl)-3,3a-dihydro-2*H*-benzo[*g*]furo [3,2-*c*]isochromene-2,6-11(5*H*,11b*H*)-trione (14d)



Following the **General Procedure A** the title compound was prepared from **46d** (31.1 mg, 68.4 µmol) dissolved in MeCN (3 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (75.0 mg, 137 µmol, 2.0 equiv.) in H_2O (2 mL). Purification by flash chromatography [d = 1 cm, h = 12.5 cm, F = 8 mL; CH/EE 2:1 (F1-16)] afforded the pure product [F5-12, R_f (2:1) = 0.20, 20.2 mg, 70%] as a yellow oil.– **^{1}H-NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.64 and δ_B = 2.86, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.97 (s, 3H, 10-OMe), 4.00 (s, 3H, 9-OMe), 4.27 (dd, 1H, $J_{3a,B}$ = 5.3 Hz, $J_{3a,11b}$ = 3.1 Hz, 3a-H), 5.32 (d, 1H, $J_{11b,3a}$ = 3.1 Hz, 11b-H), 5.97 (s, 1H, 5-H), 7.06 (m_c, 2H, 3'-H and 5'-H), 7.22 (d, 1H, $J_{8,7}$ = 8.7 Hz, 8-H), 7.22 (m_c, 2H, 2'-H and 6'-H), 7.89 (d, 1H, $J_{7,8}$ = 8.7 Hz, 7-H). 9-OMe was distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.86 (3-H^B) ↔ δ = 5.33 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.22 (2'-H and 6'-H) ↔ δ = 4.27 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.22 (2'-H and 6'-H) ↔ δ = 5.97 (5-H), δ = 4.00 (9-OMe) ↔ δ = 7.89 (8-H). **^{19}F-NMR** (470.72 MHz, ^{1}H-decoupled, $CDCl_3$): δ = −112.12 ppm. **^{13}C-NMR** (125.82 MHz, $CDCl_3$): δ = 36.71 (C-3), 56.51 (9-OCH_3), 61.53 (10-OCH_3), 67.12 (C-3a), 69.05 (C-11b), 71.18 (C-5), 115.98 (d, 2C, $^2J_{C,F}$ = 21.7 Hz, C-3' and C-5'), 116.11 (C-8), 125.04(C-10a), 125.15 (C-7), 125.27 (C-6a), 130.40 (d, 2C, $^3J_{C,F}$ = 8.4 Hz, C-2' and C-6'), 132.34 (d, 1C, $^4J_{C,F}$ = 3.4 Hz, C-1'), 137.58 and 145.02 (C-5a and C-11a), 149.95 (C-10), 159.82 (C-9), 163.07 (d, 1C, $^1J_{C,F}$ = 249.2 Hz, C-4'), 174.04 (C-2), 181.34 (C-11), 181.70 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 36.71 (C-3) ↔ δ_A = 2.64 and δ_B = 2.86 (3-H^A and 3-H^B), δ = 56.51 (9-OCH_3) ↔ δ = 4.00 (9-OMe), δ = 61.53 (10-OCH_3) ↔ δ = 3.97 (10-OMe), δ = 67.12 (C-3a) ↔ δ = 4.27 (3a-H), δ = 69.05 (C-11b) ↔ δ = 5.32 (11b-H), δ = 71.18 (C-5) ↔ δ = 5.97 (5-H), δ = 115.98 (d, 2C, $^2J_{C,F}$ = 21.7 Hz, C-3' and C-5') ↔ δ = 7.06 (3'-H and 5'-H), δ = 116.11 (C-8) ↔ 7.22 (8-H), δ = 125.15 (C-7) ↔ 7.89 (7-H), δ = 130.40 (d, 2C, $^3J_{C,F}$ = 8.4 Hz, C-2' and C-6') ↔ δ = 7.22 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 125.04(C-10a) ↔ δ = 7.89 (7-H), δ = 125.27 (C-6a) ↔ δ = 7.22 (8-H), δ = 132.34 (d, 1C, $^4J_{C,F}$ = 3.4 Hz, C-1') ↔ δ = 7.09 (3'-H and 5'-H), δ = 132.34 (d, 1C, $^4J_{C,F}$ = 3.4 Hz, C-1') ↔ δ = 7.22 (2'-H and 6'-H), [δ = 137.58 and 145.02 (C-5a and C-11a) ↔ δ = 5.32 (11b-H), δ = δ = 137.58 and 145.02 (C-5a and C-11a) ↔ δ = 5.97 (5-H) could not be assigned unambiguously], δ = 149.95 (C-10) ↔ δ = 3.97 (10-OMe), δ = 149.95 (C-10) ↔ δ = 7.22 (8-H), δ = 149.95 (C-10) ↔ δ = 7.89 (7-H), δ = 159.82 (C-9) ↔ δ = 4.00 (9-OMe), δ = 159.82 (C-9) ↔ δ = 7.22 (8-H), δ = 159.82 (C-9) ↔ δ = 7.89 (7-H), δ = 163.07 (d, 1C, $^1J_{C,F}$ = 249.2 Hz, C-4') ↔ δ = 7.09 (3'-H and 5'-H), δ = 163.07 (d, 1C, $^1J_{C,F}$ = 249.2 Hz, C-4') ↔ δ = 7.22 (2'-H and 6'-H), δ = 174.04 (C-2) ↔ δ_A = 2.64 (3-H^A), δ = 174.04 (C-2) ↔ δ_B = 2.86 (3-H^B), δ = 174.04 (C-2) ↔ δ = 4.27 (3a-H), δ = 181.34 (C-11) ↔ δ = 5.32 (11b-H), δ = 181.70 (C-6) ↔ δ = 5.97 (5-H), δ = 181.70 (C-6) ↔ δ = 7.89 (7-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = −64.8 (c = 0.707, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{23}H_{17}FO_7$ $[M+H]^+$ = 425.10311; found 425.10291 (−0.48 ppm). **IR (film):**

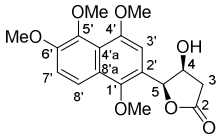
ν = 2930, 2850, 1785, 1665, 1645, 1605, 1575, 1510, 1485, 1455, 1415, 1335, 1275, 1230, 1200, 1155, 1095, 1060, 1030, 1015, 1000, 975, 905, 840 cm^{-1}.

(3a*S*,5*S*,11b*S*)-9,10-Dimethoxy-5-(4-bromophenyl)-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6-11(5*H*,11b*H*)-trione (14e)



Following the **General Procedure A** the title compound was prepared from **46e** (24.2 mg, 47.0 µmol) dissolved in MeCN (2 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (52.1 mg, 95.0 µmol, 2.0 equiv.) in H_2O (2 mL). Purification by flash chromatography [d = 1 cm, h = 14 cm, F = 8 mL; CH/EE 3:1 (F1-11), 2:1 (F12-28)] afforded the product [F11-24, R_f (2:1) = 0.20, 20.5 mg, 90%] as a yellow oil and as a 95:5 mixture of the two diastereomers.– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.63, δ_B = 2.85, J_{AB} = 17.8 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.3 Hz, 3-H^A and 3-H^B), 3.97 (s, 3H, 10-OMe), 4.00 (s, 3H, 9-OMe), 4.26 (dd, 1H, $J_{3a,B}$ = 5.3 Hz, $J_{3a,11b}$ = 3.0 Hz, 3a-H), 5.31 (d, 1H, $J_{11b,3a}$ = 3.0 Hz, 11b-H), 5.93 (s, 1H, 5-H), 7.12 (m_c, 2H, 2'-H and 6'-H), 7.22 (d, 1H, $J_{8,7}$ = 8.7 Hz, 8-H), 7.50 (m_c, 2H, 3'-H and 5'-H), 7.89 (d, 1H, $J_{7,8}$ = 8.6 Hz, 7-H). 9-OMe was distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.85 (3-H^B) ↔ δ = 5.31 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 4.26 (3a-H) ↔ δ = 5.31 (11b-H), δ = 7.12 (2'-H and 6'-H) ↔ δ = 4.26 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.12 (2'-H and 6'-H) ↔ δ = 5.93 (5-H), δ = 4.00 (9-OMe) ↔ δ = 7.22 (8-H). **^{13}C-NMR** (100.63 MHz, $CDCl_3$): δ = 36.71 (C-3), 56.52 (9-OCH_3), 61.53 (10-OCH_3), 67.30 (C-3a), 69.00 (C-11b), 71.30 (C-5), 116.15 (C-8), 123.46 (C-4'), 125.07 (C-10a), 125.14 (C-7), 125.28 (C-6a), 130.21 (C-2' and C-6'), 132.16 (C-3' and C-5'), 135.50 (C-1'), 137.71 and 144.74 (C-5a and C-11a), 150.02 (C-10), 159.87 (C-9), 173.93 (C-2), 181.27 (C-11), 181.68 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 100.63/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 36.71 (C-3) ↔ δ_A = 2.63 and δ_B = 2.85 (3-H^A and 3-H^B), δ = 56.52 (9-OCH_3) ↔ δ = 4.00 (9-OMe), δ = 61.53 (10-OCH_3) ↔ δ = 3.97 (10-OMe), δ = 67.30 (C-3a) ↔ δ = 4.26 (3a-H), δ = 69.00 (C-11b) ↔ δ = 5.31 (11b-H), δ = 71.30 (C-5) ↔ δ = 5.93 (5-H), δ = 116.15 (C-8) ↔ 7.22 (8-H), δ = 125.14 (C-7) ↔ 7.89 (7-H), δ = 130.21 (C-2' and C-6') ↔ δ = 7.12 (2'-H and 6'-H), δ = 132.16 (C-3' and C-5') ↔ δ = 7.50 (3'-H and 5'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 123.46 (C-4') ↔ δ = 7.12 (2'-H and 6'-H), δ = 123.46 (C-4') ↔ δ = 7.50 (3'-H and 5'-H), δ = 125.07 (C-10a) ↔ δ = 7.89 (7-H), δ = 125.28 (C-6a) ↔ δ = 7.22 (8-H), δ = 135.50 (C-1') ↔ δ = 5.93 (5-H), δ = 135.50 (C-1') ↔ δ = 7.50 (3'-H and 5'-H), [δ = 137.71 and 144.74 (C-5a and C-11a) ↔ δ = 5.31 (11b-H), δ = 137.71 and 144.74 (C-5a and C-11a) ↔ δ = 5.93 (5-H) could not be assigned unambiguously], δ = 150.02 (C-10) ↔ δ = 3.97 (10-OMe), δ = 150.02 (C-10) ↔ δ = 7.22 (8-H), δ = 159.87 (C-9) ↔ δ = 4.00 (9-OMe), δ = 159.87 (C-9) ↔ δ = 7.22 (8-H), δ = 159.87 (C-9) ↔ δ = 7.89 (7-H), δ = 173.93 (C-2) ↔ δ_A = 2.63 (3-H^A), δ = 173.93 (C-2) ↔ δ_B = 2.85 (3-H^B), δ = 173.93 (C-2) ↔ δ = 4.26 (3a-H), δ = 181.27 (C-11) ↔ δ = 5.31 (11b-H), δ = 181.68 (C-6) ↔ δ = 5.93 (5-H), δ = 181.68 (C-6) ↔ δ = 7.89 (7-H). **Melting point:** Oil. **HRMS** (pos. APCI): Calcd. for $C_{23}H_{17}BrO_7$ [M+H]$^+$ = 485.02304; found 485.02310 (+0.12 ppm), calcd. for $C_{23}H_{17}{}^{81}BrO_7$ [M+H]$^+$ = 487.02100; found 487.02087 (−0.25 ppm). **IR (film):** ν = 2925, 2850, 1785, 1735, 1665, 1645,1575, 1485, 1460, 1405, 1380, 1335, 1275, 1230, 1200, 1155, 1095, 1060, 1030, 1010, 975, 950, 905, 885 cm^{-1}.

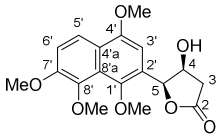
(4*S*,5*S*)-4-Hydroxy-5-(1,4,5,6-tetramethoxynaphthalen-2-yl)dihydrofuran-2(3*H*)-one (15)



A 86:14 isomeric mixture of (*E*)-methyl 4-(1,4,5,6-tetramethoxynaphthalen-2-yl)but-3-enoate (**17**) and its α,β-unsaturated carboxylic ester isomer (*iso*-**17**) (70.0 mg, 0.20 mmol) and $(DHQ)_2PHAL$ (1.6 mg, 2.1 µmol, 1.0 mol-%) were *dissolved* in *t*-BuOH (2 mL). $K_3Fe(CN)_6$ (0.20 g, 0.60 mmol, 3.0 equiv.), K_2CO_3 (82.9 mg, 0.60 mmol, 3.0 equiv.), $NaHCO_3$ (50.4 mg, 0.60 mmol, 3.0 equiv.) and $Me_2SO_2NH_2$ (19.0 mg, 0.20 mmol, 1.0 equiv.) were dissolved in H_2O (1.8 mL). The aqueous solution was added to the vigorously stirred organic reaction mixture. A solution of $K_2OsO_2(OH)_4$ (0.3 mg, 0.8 µmol, 0.4 mol-%) in H_2O (0.2 mL) was added in one portion to initiate the reaction. The reaction was vigorously stirred for 2 d. Afterwards it was quenched by the addition of solid Na_2SO_3 (0.20 g) and stirred for 30 min. EtOAc (10 mL) was added and the organic phase was separated. The aqueous phase was extracted with EtOAc (5 × 5 mL) and the combined organic extracts were washed with aqueous KOH solution (1 M, 2 × 5 mL) and brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash chromatography (d = 3 cm, h = 12 cm, F = 25 mL; CH/EE 1:1) to obtain the product [46.1 mg, 66% relative to the total of the substrate mixture = 77% relative to the fraction of **17** (ref.[7s]: 71% relative to the total of the substrate mixture = 79% relative to the fraction of the β,γ-unsaturated ester in the substrate mixture)] as a white solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 2.34 (br. s, 1H, 4-OH), AB signal (δ_A = 2.76, δ_B = 2.95, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,4}$ = 5.4 Hz, 3-H^A and 3-H^B), 3.81 (s, 3H, 5'-OMe), 3.85 (s, 3H, 1'-OMe), 3.94 (s, 3H, 4'-OMe), 3.97 (s, 3H, 6'-OMe), 4.82 (dd, 1H, $J_{4,B}$ = 5.0 Hz, $J_{4,5}$ = 3.8 Hz, $J_{4,4\text{-OH}}$ = 1.3 Hz, 4-H), 5.83 (d, 1H, $J_{5,4}$ = 3.8 Hz, 5-H), 6.83 (s, 1H, 3'-H), 7.25 (d, 1H, $J_{7',8'}$ = 9.2 Hz, 7'-H), 7.66 (d, 1H, $J_{8',7'}$ = 9.3 Hz, 8'-H). 1'-OMe, 4'-OMe and 8'-OMe were distinguished from 5'-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 2.34 (4-OH) ↔ δ = 4.82 (4-H), δ_B = 2.95 (3-H^B) ↔ δ = 5.83 (5-H, this cross-peak proves that 3-H^B and 5-H are oriented *cis* relative to one another), δ = 3.85 (1'-OMe) ↔ δ = 5.83 (5-H), δ = 3.85 (1'-OMe) ↔ δ = 7.66 (8'-H), δ = 3.94 (4'-OMe) ↔ δ = 6.83 (3'-H), δ = 3.97 (6'-OMe) ↔ δ = 7.25 (7'-H), δ = 6.83 (3'-H) ↔ δ = 5.83 (5-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 38.43 (C-3), 56.72 (4'-OCH_3), 57.21 (6'-OCH_3), 61.87 (5'-OCH_3), 62.37 (1'-OCH_3), 70.03 (C-4), 81.79 (C-5), 104.24 (C-3'), 115.86 (C-7'), 118.70 (C-8'), 119.46 (C-2'), 122.91 (C-4'a), 125.18 (C-8'a), 144.85 (C-5'), 146.53 (C-1'), 151.09 (C-6'), 152.71 (C-4'), 175.67 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 38.43 (C-3) ↔ [δ_A = 2.76 (3-H^A) and δ_B = 2.95 (3-H^B)], δ = 56.72 (4'-OCH_3) ↔ δ = 3.94 (4'-OMe), δ = 57.21 (6'-OCH_3) ↔ δ = 3.96 (6'-OMe), δ = 61.87 (5'-OCH_3) ↔ δ = 3.81 (5'-OMe), δ = 62.37 (1'-OCH_3) ↔ δ = 3.85 (1'-OMe), δ = 70.03 (C-4) ↔ δ = 4.82 (4-H), δ = 81.79 (C-5) ↔ δ = 5.83 (5-H), δ = 104.24 (C-3') ↔ δ = 6.83 (3'-H), δ = 115.86 (C-7') ↔ δ = 7.25 (7'-H), δ = 118.70 (C-8') ↔ δ = 7.66 (8'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 119.46 (C-2') ↔ δ = 5.83 (5-H), δ = 119.46 (C-2') ↔ δ = 6.83 (3'-H), δ = 122.91 (C-4'a) ↔ δ = 6.83 (3'-H), δ = 122.91 (C-4'a) ↔ δ = 7.66 (8'-H), δ = 125.18 (C-8'a) ↔ δ = 7.25 (7'-H), δ = 144.85 (C-5') ↔ δ = 3.81 (5'-OMe), δ = 144.85 (C-5') ↔ δ = 7.25 (7'-H), δ = 146.53 (C-1') ↔ δ = 3.85 (1'-OMe), δ = 146.53 (C-1') ↔ δ = 6.83 (3'-H), 146.53 (C-1') ↔ δ = 7.66 (8'-H), δ = 151.09 (C-6') ↔ δ = 3.97 (6'-OMe), δ = 151.09 (C-6') ↔ δ = 7.25 (7'-H), δ = 151.09 (C-6') ↔ δ

= 7.66 (8'-H), δ = 152.71 (C-4') ↔ δ = 3.94 (4'-OMe), δ = 152.71 (C-4') ↔ δ = 6.83 (3'-H), δ = 175.67 (C-2) ↔ [δ_A = 2.76 (3-H^A) and δ_B = 2.95 (3-H^B)]. **Melting point:** 74°C (decomp.). **Optical rotation of 15:** $[\alpha]_D^{20}$ = –5.2 (c = 1.04, $CHCl_3$) and $[\alpha]_D^{20}$ = –5.5 (c = 0.45, $CHCl_3$) {ref.[7s]: $[\alpha]_D^{20}$ = –3.5 (c = 0.46, $CHCl_3$); ref.[7t]: $[\alpha]_D^{25}$ = +5.2 (c = 0.4, $CHCl_3$)}. **HRMS** (neg. APCI): Calcd. for $C_{18}H_{20}O_7Cl$ $[M+Cl]^-$ = 383.09042; found: 383.09042 (+0.31 ppm). **Enantiomeric excess of 15: 98.5% *ee*** (ref.[7s]: 99.2% ee). The *ee* was determined by chiral HPLC (OD-H, heptane/EtOH = 60:40, λ = 230 nm, flow: 0.7 mL/min, t_R(*ent*-**15**) = 10.55 min, t_R(**15**) = 12.71 min). To develop a separation method for chiral HPLC a mixture of both enantiomers was measured (OD-H, heptane/EtOH = 60:40, λ = 230 nm, flow: 0.7 mL/min, t_R(*ent*-**15**) = 10.14 min, t_R(**15**) = 12.66 min). ***The optical antipode*** *ent*-**15** *was synthesized analogously by using the (DHQD)$_2$PHAL-ligand in the Sharpless asymmetric dihydroxylation procedure*. Yield: 58% (67% relative to the amount of **15**). **Optical rotation of *ent*-15:** $[\alpha]_D^{20}$ = +2.3 (c = 0.96, $CHCl_3$) and $[\alpha]_D^{20}$ = +3.1 (c = 0.45, $CHCl_3$) {ref.[7t]: $[\alpha]_D^{25}$ –4.6 (c = 0.5, $CHCl_3$)}. **Enantiomeric excess of *ent*-15: 96% *ee*.** The *ee* was determined by chiral HPLC (OD-H, heptane/EtOH = 60:40, λ = 230 nm, flow: 0.7 mL/min, t_R(*ent*-**15**) = 10.37 min, t_R(**15**) = 12.94 min).

(4*S*,5*S*)-4-Hydroxy-5-(1,4,7,8-tetramethoxynaphthalen-2-yl)dihydrofuran-2(3*H*)-one (16)



A 92:8 isomeric mixture of (*E*)-methyl 4-(1,4,5,6-tetramethoxynaphthalen-2-yl)but-3-enoate (**18**) and its α,β-unsaturated carboxylic ester isomer *iso*-**18** (343.1 mg, 0.991 mmol) and $(DHQ)_2PHAL$ (7.8 mg, 10 µmol, 1.0 mol-%) were dissolved in *t*BuOH (10 mL). $K_3Fe(CN)_6$ (1.00 g, 3.04 mmol, 3.06 equiv.), K_2CO_3 (0.44 g, 3.17 mmol, 3.20 equiv.), $NaHCO_3$ (267 mg, 3.21 mmol, 3.24 equiv.) and $Me_2SO_2NH_2$ (103.3 mg, 1.076 mmol, 1.09 equiv.) were dissolved in H_2O (8 mL) and added dropwise to the vigorously stirred reaction mixture. $K_2OsO_2(OH)_4$ (1.6 mg, 4.3 µmol, 0.4 mol-%) was dissolved in H_2O (2 mL) and equally added to the solution. The reaction mixture was vigorously stirred for 15 h. Afterwards the reaction mixture was carefully quenched by adding solid sodium sulfite (0.99 g). The aqueous phase was extracted with EE (5 × 30 mL) and the combined organic extracts were washed with aqueous NaOH (1 M, 2 × 30 mL) and brine (30 mL) and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash chromatography [d = 3.5 cm, h = 13 cm, F = 20 mL; CH/EE 1:1 (F1-43)] to obtain a fraction containing impurities (R_f (1:1) = 0.25, F21-24 and 25-40, 205.3 mg, 60%).– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 1.68 (br.s, 1H, 4-OH), AB signal [δ_A = 2.76 and δ_B = 2.95, J_{AB} = 17.7 Hz, additionally splitted by $J_{B,4}$ = 5.5 Hz and $J_{A,4}$ = 0.9 Hz, 3-H^A and 3-H^B], 3.86 (s, 3H, 1`-OMe), 3.87 (s, 3H, 8`-OMe), 3.98 (s, 3H, 4`-OMe), 4.01 (s, 3H, 7`-OMe), 4.89 (ddd, 1H, $J_{4,B}$ = 5.4 Hz , $J_{4,5}$ = 3.8 Hz, $J_{4,A}$ = 0.8 Hz, 4-H), 5.96 (d, 1H, $J_{5,4}$ = 3.7 Hz, 5-H), 6.75 (s, 1H, 3`-H), 7.31 (d, 1H, $J_{6`,5`}$ = 9.3 Hz, 6`-H), 8.08 (d, 1H, $J_{5`,6`}$ = 9.3 Hz, 5`-H). 1`-OMe, 4`-OMe and 7`-OMe were distinguished from 8`-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$), that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.68 (4-OH) ↔ δ = 4.89 (4-H), δ_B = 2.95 (3-H^B) ↔ δ = 5.96 (5-H, this cross-peak proves that 3-H^B and 5-H are oriented *cis* relative to one another), δ = 3.86 (1`-OMe) ↔ $\delta$ = 5.96 (5-H), $\delta$ = 3.98 (4`-OMe) ↔ δ = 6.75 (3`-H), $\delta$ = 4.02 (7`-OMe) ↔ δ = 7.31 (6`-H). **$^{13}$C-NMR** (100.63 MHz, $CDCl_3$): $\delta$ = 38.33 (C-3), 56.04 (4`-OCH_3), 56.70 (7`-$OCH_3$), 62.05 (8`-OCH_3), 62.86 (1`-$OCH_3$), 70.12 (C-4), 82.19 (C-5), 100.10 (C-3`), 114.13 (C-6`), 119.62 (C-5`), 123.44 (C-2`), 123.55 (C-4`a), 123.86 (C-8`a), 142.50 (C-8`), 145.23 (C-1`), 151.37 (C-7`), 152.51 (C-4`), 175.56 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 38.33 (C-3) ↔ δ_A = 2.76 and δ_B = 2.95 (3-H^A and 3-H^B), δ = 56.04 (4`-$OCH_3$) ↔ $\delta$ = 3.98 (4`-OMe), δ = 56.70 (7`-$OCH_3$) ↔ $\delta$ = 4.01 (7`-OMe), δ = 62.05 (8`-$OCH_3$) ↔ $\delta$ = 3.87 (8`-OMe), δ = 62.86 (1`-$OCH_3$) ↔ $\delta$ = 3.86 (1`-OMe), δ = 70.12 (C-4) ↔ δ = 4.89 (4-H), δ = 82.19 (C-5) ↔ δ = 5.96 (5-H), δ = 100.10 (C-3`) ↔ $\delta$ = 6.75 (3`-H), δ = 114.13 (C-6`) ↔ $\delta$ = 7.31 (6`-H), δ = 119.62 (C-5`) ↔ $\delta$ = 8.08 (5`-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 123.44 (C-2`) ↔ $\delta$ = 5.96 (5-H), $\delta$ = 123.44 (C-2`) ↔ δ = 6.75 (3`-H), $\delta$ = 123.55 (C-4`a)↔ δ = 7.31 (6`-H), $\delta$ = 123.86 (C-8`a)↔ δ = 8.08 (5`-H), $\delta$ = 142.50 (C-8`)↔ δ = 3.87 (8`-OMe), $\delta$ = 142.50 (C-8`)↔ δ = 7.31 (6`-H), $\delta$ = 145.23 (C-1`)↔ δ = 3.86 (1`-OMe), $\delta$ = 145.23 (C-1`)↔ δ = 5.96 (5-H), δ = 145.23 (C-1`)↔ $\delta$ = 6.75 (3`-H), δ = 151.37 (C-7`)↔ $\delta$ = 4.01 (7`-OMe), δ = 151.37 (C-7`)↔ $\delta$ = 7.31 (6`-H), δ = 151.37 (C-7`)↔ $\delta$ = 8.08 (5`-H), δ = 152.51 (C-4`)↔ $\delta$ = 3.98 (4`-OMe), δ = 152.51 (C-4`)↔ $\delta$ = 6.75 (3`-H), δ = 152.51 (C-4`)↔ $\delta$ = 8.08 (5`-H), δ = 175.56 (C-2) ↔ δ_A = 2.76 (3-H^A), δ = 175.56 (C-2) ↔ δ_B = 2.95 (3-H^B), δ = 175.56 (C-2) ↔ δ = 4.89 (4-H). **Melting point:** 167-168°C. **Optical rotation of 22:** $[\alpha]_D^{20}$ = +36.4 (c = 0.623, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{18}H_{20}O_7$ $[M+Na]^+$ = 371.11012; found 371.11017 (+0.12 ppm). **IR (film):** ν = 2940, 2845, 1775, 1660, 1620, 1600, 1515, 1460, 1450, 1420, 1365, 1325, 1275, 1245, 1215, 1195, 1160, 1135, 1100, 1075, 1055, 1030, 1000, 975, 915, 895, 850, 820, 790, 735, 700, 665 cm^{-1}. **Enantiomeric excess of 22: > 99.5% *ee*.** The *ee* was determined by chiral HPLC [AD-3, heptane/EtOH = 40:60, λ = 230 nm, flow: 1.0 mL/min; t_R (**22**) = 4.33 min, t_R (*ent*-**22**) not detected]. To develop a separation method for chiral HPLC a mixture of both enantiomers was measured [AD-3, heptane/EtOH = 40:60, λ = 230 nm, flow: 1.0 mL/min; t_R (**22**) = 4.34 min, t_R (*ent*-**22**) = 7.81 min]. ***The optical antipode ent*-22** *was synthesized analogously by using the (DHQD)$_2$PHAL-ligand in the Sharpless asymmetric dihydroxylation procedure.* **Optical rotation of *ent*-22:** $[\alpha]_D^{20}$ = −48.2 (c = 0.330, $CHCl_3$).

(*E*)-Methyl 4-(1,4,5,6-tetramethoxynaphthalen-2-yl)but-3-enoate (17) and (*E*)-Methyl 4-(5-(*tert*-butoxycarbonyloxy)-1,4,6-trimethoxynaphthalen-2-yl)but-2-enoate (*iso*-17)[49]

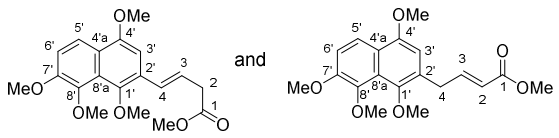
as an inseparable 86:14 mixture

2-Bromo-1,4,5,6-tetramethoxynaphthalene (**19**, 1.00 g, 3.06 mmol) and $Pd_2dba_3{\cdot}CHCl_3$ (63.2 mg, 0.06 mmol, 2.0 mol-%) were dissolved in freshly distilled toluene (30 mL). P(*t*Bu)$_3$ (49.6 mg, 0.24 mmol, 8.0 mol-%) was weighed out in a glove box and afterwards dissolved in freshly distilled toluene (2mL). The latter solution was transferred to the reaction mixture. *N,N*-dicyclohexylmethylamine (1.97 mL, 1.79 g, 9.17 mmol, 3.0 equiv.) and methyl 2-vinylacetate (0.98 mL, 0.92 g, 9.17 mmol, 3.0 equiv) were added at room temperature. The reaction mixture was refluxed for 2 d. The mixture was allowed to cool to room temperature and CH_2Cl_2 (40 mL) was added. The organic phase was washed with aqueous HCl (1M, 2 × 30 mL) and brine (30 ml) and dried over Na_2SO_4. The solvent was removed in vacuo and the oily residue was purified by flash chromatography (d = 4 cm, h = 15 cm, F = 50 mL; CH/EE 5:1) to obtain the product (0.88 g, 83%) as a yellow-brownish oil.− NMR characterization of **17**: **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 3.35 (dd, 2H, $J_{2,3}$ = 7.2 Hz, $^4J_{2,4}$ = 1.5 Hz, 2-H$_2$), 3.74 (s, 3H, 1-OMe), 3.84 (s, 3H, 1'-OMe), 3.88 (s, 3H, 5'-OMe), 3.98 (s, 3H, 6'-OMe), 3.99 (s, 3H, 4'-OMe), 6.35 (dt, 1H, $J_{3,4}$ = 16.0 Hz, $J_{3,2}$ = 7.2 Hz, 3-H), 6.90 (s, 1H, 3'-H), 6.93

[49] Note: This reaction needs to entirely be performed under inert gas. Every fluid reagent has to be degassed (freeze & pump technique) prior to use. It is mandatory to freshly distill toluene over potassium prior to use. P(*t*Bu)$_3$ has to be weighed out in a glove box.

(dt, 1H, $J_{4,3}$ = 16.0 Hz, $^4J_{4,2}$ = 1.5 Hz, 4-H), 7.28 (d, 1H, $J_{7',8'}$ = 9.2 Hz, 7'-H), 7.84 (d, 1H, $J_{8',7'}$ = 9.2 Hz, 8'-H). 1'-OMe, 4'-OMe and 6'-OMe were distinguished from 5'-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.84 (1'-OMe) ↔ δ = 6.93 (4-H), δ = 3.84 (1'-OMe) ↔ δ = 7.84 (8'-H), δ = 3.99 (4'-OMe) ↔ δ = 6.90 (3'-H), δ = 3.98 (6'-OMe) ↔ δ = 7.28 (7'-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 38.71 (C-2), 52.01 (1-OCH_3), 56.96 (4'-OCH_3), 57.26 (6'-OCH_3), 61.87 (5'-OCH_3), 62.51 (1'-OCH_3), 103.82 (C-3'), 115.70 (C-7'), 119.18 (C-8'), 121.96 (C-3), 127.81 (C-4), 126.21 (C-8'a), 144.94 (C-5'), 147.51 (C-1'), 150.93 (C-6'), 152.37 (C-4'), 172.23 (C-1). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 38.71 (C-2) ↔ δ = 3.35 (2-H_2), δ = 52.01 (1-OCH_3) ↔ δ = 3.74 (1-OMe), δ = 56.96 (4'-OCH_3) ↔ δ = 3.99 (4'-OMe), δ = 57.26 (6'-OCH_3) ↔ δ = 3.98 (6'-OMe), δ = 61.87 (5'-OCH_3) ↔ δ = 3.88 (5'-OMe), δ = 62.51 (1'-OCH_3) ↔ δ = 3.84 (1'-OMe), δ = 103.82 (C-3') ↔ δ = 6.90 (3'-H), δ = 115.70 (C-7') ↔ δ = 7.28 (7'-H), δ = 119.18 (C-8') ↔ δ = 7.84 (8'-H), δ = 121.96 (C-3) ↔ δ = 6.35 (3-H), δ = 127.81 (C-4) ↔ δ = 6.93 (4-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 122.59 and 122.73 (C-2' and C-4'a) ↔ δ = 6.90 (3'-H) and δ = 7.84 (8'-H) could not be assigned unambiguously], δ = 126.21 (C-8'a) ↔ δ = 7.28 (7'-H), δ = 144.94 (C-5') ↔ δ = 3.88 (5'-OMe), δ = 144.94 (C-5') ↔ δ = 7.28 (7'-H), δ = 147.51 (C-1') ↔ δ = 3.84 (1'-OMe), δ = 147.51 (C-1') ↔ δ = 6.90 (3'-H), δ = 147.51 (C-1') ↔ δ = 7.84 (8'-H), δ = 150.93 (C-6') ↔ δ = 3.98 (6'-OMe), δ = 150.93 (C-6') ↔ δ = 7.28 (7'-H), δ = 150.93 (C-6') ↔ δ = 7.84 (8'-H), δ = 152.37 (C-4') ↔ δ = 3.99 (4'-OMe), δ = 152.37 (C-4') ↔ δ = 6.90 (3'-H), δ = 172.23 (C-1) ↔ δ = 3.35 (2-H_2), δ = 172.23 (C-1) ↔ δ = 3.75 (1-OMe). NMR analysis of *iso*-**17**: **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 3.66 (dd, 2H, $J_{4,3}$ = 6.3 Hz, $^4J_{4,2}$ = 1.8 Hz, 4-H_2), 3.71, 3.83, 3.88, 3.94 and 3.98 (5×s, 5×3H, 1-OMe, 1'-OMe, 4'-OMe, 5'-OMe and 6'-OMe), 5.86 (dt, 1H, $J_{2,3}$ = 15.7 Hz, $^4J_{2,4}$ = 1.7 Hz, 2-H), 6.54 (s, 1H, 3'-H), 7.17 (dt, 1H, $J_{3,2}$ = 15.5 Hz, $J_{3,4}$ = 6.5 Hz, 3-H), 7.31 (d, 1H, $J_{7',8'}$ = 9.0 Hz, 7'-H), 7.81 (d, 1H, $J_{8',7'}$ = 9.2 Hz, 8'-H).

(*E*)-Methyl 4-(1,4,7,8-tetramethoxynaphthalen-2-yl)but-3-enoate (18) and (*E*)-Methyl 4-(1,4,7,8-tetramethoxynaphthalen-2-yl)but-2-enoate (*iso*-18)[49]



as an inseparable 91:9 mixture

3-Bromo-1,4,5,6-tetramethoxynaphthalene (**20**, 328 mg, 1.00 mmol) and Pd_2dba_3 (22.1 mg, 0.02 mmol, 2.0 mol-%) were dissolved in toluene (8mL). P(*t*Bu)$_3$ (16.8 mg, 0.08 mmol, 8 mol-%) was dissolved in toluene (2mL) and and transferred into the reaction mixture. *N,N*-dicyclohexylmethylamine (0.65 mL, 587 mg, 3.00 mmol, 3.0 equiv.) and methyl but-3-enoate (0.32 mL, 301 mg, 3.01 mmol, 3.0 equiv) were added dropwise at room temperature. The reaction mixture was refluxed for 2 d. The reaction was allowed to cool to room temperature and diluted with EE (15 mL). Afterwards it was washed with HCl (1M, 3 × 10 mL) and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash chromatography [d = 3.5 cm, h = 13 cm, F = 20 mL; CH/EE 5:1 (F1-23), 3:1 (F24-43)] to obtain the product (F25-30, R_f (5:1) = 0.20, 131.9 mg) as a pale-yellow oil and as 92:8 mixture with *iso*-**18**, as well as a second fraction containing impurities (F21-24 and F31). This second fraction was purified again by flash chromatography [d = 2.5 cm, h = 13 cm, F = 20 mL; CH/EE 5:1 (F1-26)], to obtain the product (F10-15, R_f (5:1) = 0.20, 80.3 mg) as a 91:9 mixture with *iso*-**18**. Combined yield: 212.2 mg, 61%.− NMR analysis of **18**: **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 3.37 (dd, 2H, $J_{2,3}$ = 7.1 Hz, $J_{2,4}$ = 1.5 Hz, 2-H_2), 3.75 (s, 3H, 1-OMe), 3.80 (s, 3H, 1`-OMe), 3.88 (s, 3H, 8`-OMe), 3.99 (s, 3H, 7`-OMe), 3.99 (s, 3H, 4`-OMe), 6.36 (dt, 1H, $J_{3,4}$ = 16.1 Hz, $J_{3,2}$ = 7.1 Hz, 3-H), 6.78 (s, 1H, 3`-H), 7.10 (dt, 1H, $J_{4,3}$ = 16.0 Hz, $J_{4,2}$ = 1.6 Hz, 4-H), 7.22 (d, 1H, $J_{6`,5`}$ = 9.3 Hz, 6`-H), 8.00 (d, 1H, $J_{5`,6`}$ = 9.2 Hz, 5`-H). 1'-OMe, 4'-OMe and 7'-OMe were distinguished from 8'-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.99 (7`-OMe) ↔ $\delta$ = 7.22 (6`-H), δ = 3.37 (2-H_2) ↔ δ = 7.10 (4-H), δ = 3.80 (1`-OMe) ↔ $\delta$ = 7.10 (4-H), $\delta$ = 3.99 (4`-OMe) ↔ δ = 6.78 (3`-H), $\delta$ = 6.36 (3-H) ↔ $\delta$ = 6.78 (3`-H). **^{13}C-NMR** (100.61 MHz, $CDCl_3$): δ = 38.75 (C-2), 52.00 (1-OCH_3), 55.75 and 56.63 (4`-$OCH_3$ and 7`-OCH_3), 62.05 (8`-$OCH_3$), 62.89 (1`-OCH_3), 98.81 (C-3`), 113.31 (C-6`), 119.21 (C-5`), 122.43 (C-3), 123.39 (C-4`a), 124.58 (C-8`a), 126.63 (C-2`), 128.44 (C-4), 143.11 (C-8`), 146.08 (C-1`), 151.33 (C-7`), 152.00 (C-4`), 172.30 (C-1). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 38.75 (C-2) ↔ δ =, 3.37 (2-H_2), δ = 52.00 (1-OCH_3) ↔ δ = 3.75 (1-OMe), [δ = 55.75 and 56.63 (4`-$OCH_3$ and 7`-OCH_3) ↔ δ = 3.99 (4`-OMe) and $\delta$ = 3.99 (7`-OMe) could not be assigned unambiguously], δ = 62.05 (8`-$OCH_3$) ↔ $\delta$ = 3.80 (8`-OMe), δ = 62.89 (1`-$OCH_3$) ↔ $\delta$ = 3.88 (1`-OMe), δ = 98.81 (C-3`) ↔ $\delta$ = 6.78 (3`-H), δ = 113.31 (C-6`) ↔ $\delta$ = 7.22 (6`-H), δ = 119.21 (C-5`) ↔ $\delta$ = 8.00 (5`-H), δ = 122.43 (C-3) ↔ δ = 6.36 (3-H), δ = 128.44 (C-4) ↔ δ = 7.10 (4-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 123.39 (C-4`a) ↔ $\delta$ = 6.78 (3`-H), δ = 123.39 (C-4`a) ↔ $\delta$ = 7.22 (6`-H), δ = 124.58 (C-8`a) ↔ $\delta$ = 8.00 (5`-H), δ = 126.63 (C-2`) ↔ $\delta$ = 6.36 (3-H), $\delta$ = 143.11 (C-8`) ↔ δ = 3.88 (8`-OMe), $\delta$ = 143.11 (C-8`) ↔ δ = 7.22 (6`-H), $\delta$ = 143.11 (C-8`) ↔ δ = 8.00 (5`-H), $\delta$ = 146.08 (C-1`) ↔ δ = 3.80 (1`-OMe), $\delta$ = 146.08 (C-1`) ↔ δ = 6.78 (3`-H), $\delta$ = 151.33 (C-7`) ↔ δ = 3.99 (7`-OMe), $\delta$ = 151.33 (C-7`) ↔ δ = 7.22 (6`-H), $\delta$ = 151.33 (C-7`) ↔ δ = 8.00 (5`-H), $\delta$ = 152.00 (C-4`) ↔ δ = 3.99 (4`-OMe), $\delta$ = 152.00 (C-4`) ↔ δ = 6.78 (3`-H), $\delta$ = 152.00 (C-4`) ↔ δ = 8.00 (5`-H), δ = 172.30 (C-1) ↔ δ = 3.37 (2-H_2), δ = 172.30 (C-1) ↔ δ = 3.75 (1-OMe), δ = 172.30 (C-1) ↔ δ = 6.36 (3-H). NMR analysis of *iso*-**18**: **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 3.65 (dd, 2H, $J_{4,3}$ = 6.4 Hz, $J_{4,2}$ = 1.8 Hz), 3.71, 3.79, 3.88, 3.93, 4.00 (s, 5 × OMe, 1-OMe, 1`-OMe, 4`-OMe, 7`-OMe, 8`-OMe), 5.87 (dt, 1H, $J_{2,3}$ = 15.5 Hz, $J_{2,4}$ = 1.8 Hz, 2-H), 6.40 (s, 1H, 3`-H), 7.20 (dt, 1H, $J_{3,2}$ = 15.6 Hz, $J_{3,4}$ = 6.5 Hz, 3-H), 7.17 (d, 1H, $J_{6`,5`}$ = 9.2 Hz, 6`-H), 8.02 (d, 1H, $J_{5`,6`}$ = 9.3 Hz, 5`-H). **Melting point:** Oil. **Elemental analysis:** Calculated: C: 65.88%, H: 6.40%; found: C: 65.58%, H: 6.04%; deviation: C: 0.30%, H: 0.36%. **HRMS** (pos. ESI): Calcd. for $C_{19}H_{22}O_6$ [M+Na]$^+$ = 369.13086; found 369.13123 (+0.99 ppm). **IR (film):** v = 2930, 2855, 1785, 1665, 1650, 1620, 1575, 1485, 1455, 1415, 1330, 1295, 1275, 1230, 1200, 1160, 1125, 1095, 1065, 1030, 1020, 1000, 905 cm^{-1}.

2-Bromo-1,4,5,6-tetramethoxynaphthalene (19) and 2-Bromo-1,4,7,8-tetramethoxynaphthalene (20)

84% 2%

Under a nitrogen atmosphere 1,2,5,8-tetramethoxynaphthalene (**27**, 1.36 g, 5.47 mmol) was dissolved in dry DMF (22 mL). Solid *N*-Bromosuccinimide (0.98 g, 5.51 mmol, 1.0 equiv.) was added in one portion and the solution was stirred at room temperature for 16 h. Silica gel was added and the solvent was removed in vacuo (60°C, 15 mbar, ~15 min, room temp., 1 mbar, ~15 min). Flash chromatography (d = 5,

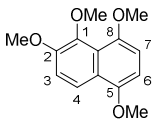
h = 12 cm, F = 50 ml; CH/EE 9:1) afforded the minor product **20** (F6-9, 38.0 mg, 2%) and the major product **19** (F10-18, 1.51 g, 84%) as a yellow solid.− Analysis of the major product **19**: **^{1}H NMR** (500.32 MHz, $CDCl_3$): 3.87 (s, 3H, 5-OMe), 3.92 (s, 3H, 1-OMe), 3.95 (s, 3H, 4-OMe), 3.98 (s, 3H, 6-OMe), 6.86 (s, 1H, 3-H), 7.32 (d, 1H, $J_{7,8}$ = 9.2 Hz, 7-H), 7.74 (d, 1H, $J_{8,7}$ = 9.2 Hz, 8-H). 1-OMe, 4-OMe and 6-OMe were distinguished from 5-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 3.92 (1-OMe) ↔ δ = 7.74 (8-H), δ = 3.95 (4-OMe) ↔ δ = 6.86 (3-H), δ = 3.98 (6-OMe) ↔ δ = 7.32 (7-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 56.89 (4-OCH_3), 57.18 (6-OCH_3), 61.40 (1-OCH_3), 61.91 (5-OCH_3), 110.25 (C-3), 116.13 (C-7), 118.86 (C-8), 109.39 (C-2), 121.99 (C-4a), 126.21 (C-8a), 144.93 (C-5), 147.02 (C-1), 150.01 (C-6), 152.65 (C-4). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 56.89 (4-OCH_3) ↔ δ = 3.95 (4-OMe), δ = 57.18 (6-OCH_3) ↔ δ = 3.98 (6-OMe), δ = 61.40 (1-OCH_3) ↔ δ = 3.92 (1-OMe), δ = 61.91 (5-OCH_3) ↔ δ = 3.89 (5-OMe), δ = 110.25 (C-3) ↔ δ = 6.86 (3-H), δ = 116.13 (C-7) ↔ δ = 7.32 (7-H), δ = 118.86 (C-8) ↔ δ = 7.74 (8-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 109.39 (C-2) ↔ δ = 6.86 (3-H), δ = 109.39 (C-2) ↔ δ = 7.74 (8-H), δ = 121.99 (C-4a) ↔ δ = 6.86 (3-H), δ = 121.99 (C-4a) ↔ δ = 7.74 (8-H), δ = 126.21 (C-8a) ↔ δ = 6.86 (3-H), δ = 126.21 (C-8a) ↔ δ = 7.32 (7-H), δ = 144.93 (C-5) ↔ δ = 3.87 (5-OMe), δ = 144.93 (C-5) ↔ δ = 6.86 (3-H), δ = 144.93 (C-5) ↔ δ = 7.32 (7-H), δ = 144.93 (C-5) ↔ δ = 7.74 (8-H), δ = 147.02 (C-1) ↔ δ = 3.92 (1-OMe), δ = 147.02 (C-1) ↔ δ = 6.86 (3-H), δ = 147.02 (C-1) ↔ δ = 7.74 (8-H), δ = 150.01 (C-6) ↔ δ = 3.98 (6-OMe), δ = 150.01 (C-6) ↔ δ = 7.32 (7-H), δ = 150.01 (C-6) ↔ δ = 7.74 (8-H), δ = 152.65 (C-4) ↔ δ = 3.95 (4-OMe), δ = 152.65 (C-4) ↔ δ = 6.86 (3-H), δ = 152.65 (C-4) ↔ δ = 7.74 (8-H). **Melting point:** 53°C. **Elemental analysis:** Calculated: C: 51.40%, H: 4.62%; found: C: 51.44%, H: 4.67%, deviation: C: 0.04%, H: 0.05%. **HRMS** (pos. ESI): Calcd. for $C_{14}H_{16}{}^{79}BrO_4$: $[M+H]^+$ = 327.02265; found: 327.02274 (+0.27 ppm); calcd. for $C_{14}H_{16}{}^{79}BrO_4$: $[M+NH_4]^+$ = 344.04920; found: 344.04935 (+0.44 ppm). **IR (film):** v = 2955, 2935, 2835, 1585, 1575, 1510, 1465, 1375, 1365, 1315, 1275, 1245, 1130, 1075, 1035, 1005, 975, 920, 815, 790 cm^{-1}. Analysis of the minor product **20**: **^{1}H NMR** (400.13 MHz, $CDCl_3$): 3.88 (s, 3H, 1-OMe), 3.89 (s, 3H, 8-OMe), 3.94 (s, 3H, 4-OMe), 3.99 (s, 3H, 7-OMe), 6.78 (s, 1H, 3-H), 7.26 (d, 1H, $J_{6,5}$ = 9.2 Hz, 6-H), 8.00 (d, 1H, $J_{5,6}$ = 9.2 Hz, 5-H). 4-OMe and 7-OMe were distinguished from 1-OMe and 8-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 3.94 (4-OMe) ↔ δ = 6.78 (3-H), δ = 3.99 (7-OMe) ↔ δ = 7.26 (6-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 55.96 (4-OCH_3), 56.60 (7-OCH_3), 61.87 (1-OCH_3), 62.09 (8-OCH_3), 106.39 (C-3), 113.56 (C-6), 119.50 (C-5), 109.39 (C-2), 121.61 (C-4a), 125.02 (C-8a), 142.28 (C-8), 145.37 (C-1), 151.57 (C-7), 152.17 (C-4). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 55.96 (4-OCH_3) ↔ δ = 3.94 (4-OMe), δ = 56.60 (7-OCH_3) ↔ δ = 3.99 (7-OMe), δ = 61.87 (1-OCH_3) ↔ δ = 3.88 (1-OMe), δ = 62.09 (8-OCH_3) ↔ δ = 3.89 (8-OMe), δ = 106.39 (C-3) ↔ δ = 6.78 (3-H), δ = 113.56 (C-6) ↔ δ = 7.26 (6-H), δ = 119.50 (C-5) ↔ δ = 8.00 (5-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 109.39 (C-2) ↔ δ = 6.78 (3-H), δ = 121.61 (C-4a) ↔ δ = 6.78 (3-H), δ = 121.61 (C-4a) ↔ δ = 7.26 (6-H), δ = 125.02 (C-8a) ↔ δ = 8.00 (5-H), δ = 142.28 (C-8) ↔ δ = 3.89 (8-OMe), δ = 142.28 (C-8) ↔ δ = 7.26 (6-H), δ = 142.28 (C-8) ↔ δ = 8.00 (5-H), δ = 145.37 (C-1) ↔ δ = 3.88 (1-OMe), δ = 145.37 (C-1) ↔ δ = 6.78 (3-H), δ = 151.57 (C-7) ↔ δ = 3.99 (7-OMe), δ = 151.57 (C-7) ↔ δ = 7.26 (6-H), δ = 151.57 (C-7) ↔ δ = 8.00 (5-H), δ = 152.17 (C-4) ↔ δ = 3.94 (4-OMe), δ = 152.17 (C-4) ↔ δ = 6.78 (3-H). **Melting point:** 68-71°C. **Elemental analysis:** Calculated: C: 51.40%, H: 4.62%; found: C: 51.33%, H: 4.65%; deviation: C: 0.07%, H: 0.03%. **HRMS** (pos. ESI): Calcd. for $C_{14}H_{15}{}^{79}BrO_4Na$: $[M+Na]^+$ = 349.00459; found: 349.00476 (+0.48 ppm). **IR (film):** v = 2995, 2960, 2935, 2835, 1610, 1595, 1515, 1460, 1450, 1410, 1370, 1325, 1275, 1240, 1210, 1190, 1180, 1130, 1060, 1005, 980, 925, 880, 815, 795, 760, 725, 715, 680, 665 cm^{-1}.

Alternative Preparation of 19 from *iso*-23: 3-Bromo-7,8-dimethoxy-4-(triisopropylsilyloxy)naphthalen-1-ol (*iso*-**23**, 132.0 mg, 0.289 mmol) was dissolved in THF (3 mL) and Bu_4NF (1.0 M in THF, 0.30 mL, 0.30 mmol, 1.10 equiv.) was added dropwise at 0°C and the solution was allowed to warm up to room temperature for 15 min. KOH (85 w-%, 136.6 g, 2.069 mmol, 7.16 equiv.) was dissolved in H_2O (1.5 mL, degassed with N_2) and the solution was transferred dropwise at 0°C. Me_2SO_4 (0.30 mL, 0.36 g, 2.89 mmol, 10.0 equiv.) was added dropwise at 0°C and the solution was allowed to warm to room temperature and stirred for 16 h. Afterwards the reaction mixture was carefully quenched by adding conc. NH_3 (2 mL) and the solution was stirred for 30 min. THF was removed under reduced pressure and the aqueous phase was extracted with EE (4 × 10 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash chromatography [d = 2 cm, h = 14 cm, F = 20 mL; CH/EE 5:1 (F1-17)] to obtain the pure product [F5-7, R_f (5:1) = 0.25, 68.1 mg, 72%] as pale-yellow solid.

Alternative Preparation of 20 from 23:

3-Bromo-5,6-dimethoxy-4-(triisopropylsilyloxy)naphthalen-1-ol (**23**, 2.28 g, 5.01 mmol) was dissolved in THF (50 mL), tetrabutylammonium fluoride (1.0 M in THF, 5.5 mL, 5.5 mmol, 1.1 equiv.) was added dropwise at 0°C and the solution was stirred at room temperature for 45 min. Afterwards the mixture was quenched with aqueous HCl (1 M, 10 mL, 10 mmol, 2.0 equiv.) and stirred for 15 min. EE (150 mL) was added, the organic phase was separated and the aqueous phase was extracted with EE (4 × 50 mL). The combined organic extracts were washed with aqueous $CaCl_2$ (5%, 50 mL) and brine (50 mL) and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash chromatography [d = 7.5 cm, h = 12 cm, F = 100 mL; CH/EE 3:1 (contained 1% formic acid, F1-24), 1:1 (contained 2% formic acid, F25-34)] to obtain the desilylated product (F12-20, R_f (3:1) = 0.20, 427.5 mg, 29%) as a pale-yellow oil that was used in the following step without further purification. Crude 2-bromo-7,8-dimethoxynaphthalene-1,4-diol (387.5 mg, 1.295 mmol), sodium dithionite (22.1 mg, 0.13 mmol, 9.0 mol-%), Bu_4NBr (35.0 mg, 0.11 mmol, 8.0 mol-%) and KOH (85 w-%, 796 mg, 12.1 mmol, 9.3 equiv) were dissolved in THF (8.7 mL) and H_2O (4.3 mL) at 0°C. Dimethyl sulfate (1.23 mL, 1.64 g, 13.0 mmol, 10.0 equiv.) was added dropwise at 0°C and the solution was stirred at room temperature for 16 h. Afterwards the reaction mixture was carefully quenched by adding conc. NH_3 (10 mL). After stirring for 45 min, the organic phase was separated and the aqueous phase was extracted with EE (5 × 10 mL). The combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by flash chromatography [d = 3 cm, h = 12 cm, F = 20 mL; CH/EE 9:1 (F1-16), 5:1 (F17-28)] to obtain the pure product [F6-15, R_f (5:1) = 0.50, 358.1 mg, 85% (25% over these 2 steps)] as a white solid.

1,2,5,8-Tetramethoxynaphthalene (21)



One-pot procedure from 2-bromo-3,4-dimethoxyphenyl 4-methylbenzenesulfonate (29): 2-Bromo-3,4-dimethoxyphenyl 4-methylbenzenesulfonate (**29**, 5.81 g, 15.0 mmol) and (furan-2-yloxy)triisopropylsilane (**27**, 5.40 g, 22.5 mmol, 1.5 equiv.) were dissolved in freshly distilled THF (40 ml).[50] At –78°C *n*BuLi (2.37 M in hexane, 6.33 ml, 15.0 mmol, 1.0 equiv.) was added dropwise and the solution was stirred at this temperature for 5 min. Afterwards the cooling bath was removed and by continuous stirring the reaction was allowed to warm to room temperature for 45 min. The solution was cooled to 0°C and TBAF (1 M in THF, 22.5 ml, 22.5 mmol, 1.5 equiv.) was added dropwise. The ice-bath was removed and the reaction mixture was stirred at room temperature for 15 min. Solid *n*Bu$_4$NBr (0.24 g, 0.75mmol, 5.0 mol-%) was added, the mixture was cooled to 0°C and a solution of KOH [85%, technical grade, 7.92 g, (≙6.73 g), 120 mmol, 8.0 equiv.] in degassed H_2O (20 ml) was added dropwise. The methylation reaction was started by the dropwise addition of Me_2SO_4 (14.23 ml, 18.92 g, 150 mmol, 10 equiv.) at 0°C. The ice-bath was removed and the reaction mixture was stirred for 17 h at room temperature. The reaction was quenched with conc. ammonium hydroxide solution (12 ml) and stirred for 1.5 h at room temperature. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 50 ml). The combined organic extracts were washed with brine (50 ml) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 5 cm, h = 12 cm, F = 100 ml; CH/EE 5:1 (F1-12), CH/EE 3:1 (F13-27)] afforded the title compound (F14-21, R_f (5:1) = 0.15, R_f (3:1) = 0.5, 2.95 g, 79%) as a pale-yellow solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): 3.89 (s, 3H, 1-OMe), 3.93 (s, 3H, 5-OMe), 3.94 (s, 3H, 8-OMe), 3.98 (s, 3H, 2-OMe), AB signal (δ_A = 6.57, δ_B = 6.76, J_{AB} = 8.4 Hz, A and B signal show no further splitting, 6-H and 7-H), 7.27 (d, 1H, $J_{3,4}$ = 9.2 Hz, 3-H), 8.02 (d, 1H, $J_{4,3}$ = 9.2 Hz, 4-H). 2-OMe, 5-OMe and 8-OMe were distinguished from 1-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.93 (5-OMe) ↔ δ_A = 6.57 (6-H), δ = 3.93 (5-OMe) ↔ δ = 8.02 (4-H), δ = 3.94 (8-OMe) ↔ δ_B = 6.76 (7-H), δ = 3.98 (2-OMe) ↔ δ = 7.28 (3-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 55.74 (8-OCH_3), 57.13 (2-OCH_3), 57.58 (5-OCH_3), 61.86 (1-OCH_3), 101.52 (C-6), 107.58 (C-7), 114.53 (C-3), 118.81 (C-4), 122.71 (C-8a), 123.56 (C-4a), 144.02 (C-1), 149.72 and 149.97 (C-5 and C-8), 150.94 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 55.74 (8-OCH_3) ↔ δ = 3.94 (8-OMe), δ = 57.13 (2-OCH_3) ↔ δ = 3.98 (2-OMe), δ = 57.58 (5-OCH_3) ↔ δ = 3.93 (5-OMe), δ = 61.86 (1-OCH_3) ↔ δ = 3.89 (1-OMe), δ = 101.52 (C-6) ↔ δ_A = 6.57 (6-H), δ = 107.58 (C-7) ↔ δ_B = 6.76 (7-H), δ = 114.53 (C-3) ↔ δ = 7.27 (3-H), δ = 118.81 (C-4) ↔ δ = 8.02 (4-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 122.71 (C-8a) ↔ δ_B = 6.76 (7-H),, δ = 122.71 (C-8a) ↔ δ = 8.02 (4-H), δ = 123.56 (C-4a) ↔ δ_A = 6.57 (6-H), δ = 123.56 (C-4a) ↔ δ = 7.27 (3-H), δ = 144.02 (C-1) ↔ δ = 3.89 (1-OMe), δ = 144.02 (C-1) ↔ δ = 6.76 (7-H), δ = 144.02 (C-1) ↔ δ = 7.27 (3-H), δ = 144.02 (C-1) ↔ δ = 8.02 (4-H), [δ = 149.72 and 149.97 (C-5 and C-8) ↔ δ = 3.93 and 3.94 (5-OMe and 8-OMe), δ = 149.72 and 149.97 (C-5 and C-8) ↔ δ = 6.57 (6-H), δ = 149.72 and 149.97 (C-5 and C-8) ↔ δ = 6.76 (7-H) and δ = 149.72 and 149.97 (C-5 and C-8) ↔ δ = 8.02 (4-H) could not be assigned unambiguously.], δ = 150.94 (C-2) ↔ δ = 3.98 (2-OMe), δ = 150.94 (C-2) ↔ δ = 7.27 (3-H), δ = 150.94 (C-2) ↔ δ = 8.02 (4-H). **Melting point:** 64°C. **Elemental analysis:** Calculated: C: 67.73%, H: 6.50%; found: C: 67.64%, H: 6.30%; deviation: C: 0.09%, H: 0.20%. **HRMS** (pos. ESI): Calcd. for $C_{14}H_{17}O_4$: $[M+H]^+$ = 249.11214; found: 249.11230 (+0.68 ppm). **IR (film):** ν = 2935, 2835, 1620, 1600, 1465, 1450, 1425, 1410, 1360, 1275, 1260, 1080, 1050, 1010, 815, 805, 790, 730 cm^{-1}.

Preparation of 21 from 5,6-Dimethoxynaphthalene-1,4-diol (39): In a 100 ml round-bottomed flask 5,6-dimethoxynaphthalene-1,4-diol (**39**, 0.98 g, 4.45 mmol,) and Bu$_4$NBr (72 mg, 0.23mmol, 5.0 mol-%) were suspended in freshly distilled THF (30 ml) under N_2 atmosphere. At 0°C a solution of KOH [85%, technical grade, 2.35g (≙2.00 g), 35.6 mmol, 8.0 equiv.] in degassed H_2O (15 ml) was added dropwise. The methylation reaction was started by the dropwise addition of Me_2SO_4 (4.22 ml, 5.61 g, 44.5 mmol, 10 equiv.) at 0°C. The ice-bath was removed and the reaction mixture was stirred for 14 h at room temperature. The reaction was quenched with conc. ammonium hydroxide solution (5 ml) and stirred for 1.5 h at room temperature. CH_2Cl_2 (20 ml) was added, the organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 20 ml). The combined organic extracts were washed with brine (20 ml) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography (d = 4 cm, h = 12 cm, F = 50 mL; CH/EE 3:1) afforded the title compound [F4-7, R_f (3:1) = 0.5, 1.06 g, 96%] as a pale-yellow solid.

5,6-Dimethoxy-4-[(triisopropylsilyl)oxy]naphthalen-1-ol (22) and 7,8-Dimethoxy-4-((triisopropylsilyl)oxy)naphthalen-1-ol (*iso*-22)

62% 12% (as a 10:90 mixture with iPr$_3$SiOH)

2-bromo-3,4-dimethoxyphenyl 4-methylbenzenesulfonate (**29**, 3.10 g, 8.0 mmol) and (furan-2-yloxy)triisopropylsilane (**27**, 2.89 g, 12.0 mmol, 1.5 equiv.) were dissolved in freshly distilled THF (16 ml).[50] At –78°C *n*BuLi (2.60 M in hexane, 3.1 ml, 8.0 mmol, 1.0 equiv.) was added dropwise and the solution was stirred at this temperature for 5 min. Afterwards the cooling bath was removed and by continuous stirring the reaction was allowed to warm to room temperature for 45 min. The reaction was quenched with aqueous HCl (1 M, 12 ml) and stirred for 5 min at room temperature. CH_2Cl_2 (30 ml) was added and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 50 ml). The combined organic extracts were washed with brine (30 ml) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 5 cm, h = 15 cm, F = 100 ml; CH/EE 9:1] afforded the minor isomer *iso*-**22** [F6-8, 1.05 g of a 10:90 mixture with iPr$_3$SiOH (≙ 0.20 g, 7% of pure *iso*-**22**)] and in a second fraction the major isomer **22** (F9-17, 1.87 g, 62%) as a dark green oil.– Analysis of **22**: **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.12 {d, 18H, $J_{silyl\text{-}CH,silyl\text{-}CH_3}$ = 7.4 Hz, 4-OSi[CH(CH_3)$_2$]$_3$}, 1.39 {sept, 3H, $J_{silyl\text{-}CH_3,silyl\text{-}CH}$ = 7.5 Hz, 4-OSi[CH(CH_3)$_2$]$_3$}, 3.85 (s, 3H, 5-OMe), 3.98 (s, 3H, 6-OMe), 4.95 (br. s, 1H, 1-OH), AB signal (δ_A = 6.50, δ_B = 6.64, J_{AB} = 8.1 Hz, A and B signal show no further splitting, 2-H and 3-H), 7.27 (d, 1H, $J_{7,8}$ = 9.3 Hz, 7-H), 7.93 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H). 6-OMe was distinguished from 5-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.98 (6-OMe) ↔ δ = 7.27 (7-H), δ = 4.95 (1-OH) ↔ δ = 7.93 (8-H), δ_B = 6.64 (3-H) ↔ δ = 4.95 (1-OH), δ_B = 6.64 (3-H) ↔ δ = 1.12 {4-OSi[CH(CH_3)$_2$]$_3$}, δ_B = 6.64 (3-H) ↔ δ = 1.39 {4-OSi[CH(CH_3)$_2$]$_3$}. **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 13.55 {4-OSi[CH(CH_3)$_2$]$_3$}, 18.03 {4-OSi[CH(CH_3)$_2$]$_3$}, 56.83 (6-OCH_3), 62.11 (5-OCH_3), 106.33 (C-2), 113.96 (C-7), 114.07 (C-3), 118.55 (C-8), 122.74 (C-8a), 123.95 (C-4a), 144.36 (C-5), 145.37 (C-1), 145.77 (C-4), 150.31 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 13.55 {4-OSi[CH(CH_3)$_2$]$_3$} ↔ δ = 1.39 {4-OSi[CH(CH_3)$_2$]$_3$}, δ = 18.03 {4-OSi[CH(CH_3)$_2$]$_3$} ↔ δ = 1.17 {4-OSi[CH(CH_3)$_2$]$_3$}, δ = 56.83 (6-OCH_3) ↔ δ = 3.98 (6-OMe), δ = 62.11 (5-OCH_3) ↔ δ = 3.85 (5-OMe), δ = 106.33 (C-2) ↔ δ_A = 6.50 (2-H), δ =

[50] It is absolutely neccessary, that 2-bromo-3,4-dimethoxyphenyl 4-methylbenzenesulfonate (**29**) is entirely dissolved at room temperature.

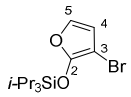
113.96 (C-7) ↔ δ = 7.27 (7-H), δ = 114.07 (C-3) ↔ δ_B = 6.64 (3-H), δ = 118.55 (C-8) ↔ δ = 7.93 (8-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 122.74 (C-8a) ↔ δ_A = 6.50 (2-H), δ = 122.74 (C-8a) ↔ δ = 7.27 (7-H), δ = 123.95 (C-4a) ↔ δ_B = 6.64 (3-H), δ = 123.95 (C-4a) ↔ δ = 7.93 (8-H), δ = 144.36 (C-5) ↔ δ = 3.85 (5-OMe), δ = 144.36 (C-5) ↔ δ = 7.27 (7-H), δ = 145.37 (C-1) ↔ δ_A = 6.50 (2-H), 145.37 (C-1) ↔ δ_B = 6.64 (3-H), δ = 145.37 (C-1) ↔ δ = 7.93 (8-H), δ = 145.77 (C-4) ↔ δ_A = 6.50 (2-H), δ = 145.77 (C-4) ↔ δ_B = 6.64 (3-H), δ = 150.31 (C-6) ↔ δ = 3.98 (6-OMe), δ = 150.31 (C-6) ↔ δ = 7.27 (7-H), δ = 150.31 (C-6) ↔ δ = 7.93 (8-H). **Melting point:** Oil. **Elemental analysis:** Calculated: C: 66.98%, H: 8.57%; found: C: 67.02%, H: 8.13%; deviation: C: 0.04%, H: 0.44%. **HRMS** (pos. APCI): Calcd. for $C_{21}H_{33}O_4Si$: $[M+H]^+$ = 377.21426; found: 377.21436 (+0.25 ppm). **IR (film):** ν = 3430, 2945, 2890, 2845, 2345 1620, 1595, 1520, 1460, 1425, 1385, 1350, 1270, 1165, 1145, 1095, 1055, 1010, 930, 880, 840, 810, 790, 735, 700, 680 cm^{-1}. *iso*-**22** could not be freed from its byproduct *i*Pr_3SiOH and therefore was not characterized.

3-Bromo-5,6-dimethoxy-4-(triisopropylsilyloxy)naphthalen-1-ol (23) and 3-Bromo-7,8-dimethoxy-4-(triisopropylsilyloxy)naphthalen-1-ol (*iso*-23)

48% 14% (as a 93:7 mixture with *i*Pr_3SiOH)

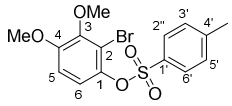
2-Bromo-3,4-dimethoxy-((1-methylphenylsulfonyl)oxy)benzene (**29**, 194.9 mg, 0.510 mmol) and 3-bromo-2-(triisopropylsilyloxy)furan (**28**, 250.9 g, 0.786 mmol, 1.56 equiv.) were dissolved in THF (2 mL) and the solution was cooled to −78°C. Then *n*BuLi (2.34 M in hexane, 0.21 mL, 0.49 mmol, 0.98 equiv.) was added dropwise and the reaction mixture was allowed to warm to room temperature and stirred for 45 min. Aqueous HCl (1M, 5 mL) was added, the mixture was stirred over a period of 20 min and the organic phase was separated. The aqueous phase was extracted with EE (4 × 10 mL), the combined organic extracts were washed with brine (10 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography [d = 3 cm, h = 17 cm, F = 20 mL; CH/EE 95:5 (1-16), 9:1 (17-30), 5:1 (30-40)], to obtain *iso*-**23** [F7-11, R_f (9:1) = 0.30, 33.7 mg] as a 93:7 mixture with triisopropylsilyl alcohol. This corresponds to 97 w-% of *iso*-**23** (32.7 mg, 14%). Another fraction furnished **23** (F18-26, R_f (9:1) = 0.10, 108.8 mg, 48%) as a 94:6 mixture with debrominated product. An analytical sample of **23** was prepared as follows: The obtained product was completely dissolved in CH_2Cl_2 (7 mL) and heptane (3 mL) was added. CH_2Cl_2 was removed under reduced pressure and the solution was cooled to 0°C. The heptane phase was removed with a pipet and the yellow oil (**23**) was dried in vacuo. **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 1.03 (d, 18-H, $J_{4\text{-OSi[CH(CH}_3)_2]_3,4\text{-OSi[CH(CH}_3)_2]_3}$ = 7.6 Hz, 4-OSi[CH(CH_3)$_2$]$_3$), 1.56 (sept, 3H, $J_{4\text{-OSi[CH(CH}_3)_2]_3,4\text{-OSi[CH(CH}_3)_2]_3}$ = 7.6 Hz, 4-OSi[CH(CH$_3$)$_2$]$_3$), 3.74 (s, 3H, 5-OMe), 3.99 (s, 3H, 6-OMe), 5.12 (s, 1H, 1-OH), 6.82 (s, 1H, 2-H), 7.26 (d, 1H, $J_{7,8}$ = 9.2 Hz, 7-H), 7.87 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H). 6-OMe was distinguished from 5-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 3.99 (6-OMe) ↔ δ = 7.26 (7-H). **^{13}C-NMR** (100.61 MHz, $CDCl_3$): δ = 14.33 (4-OSi[CH(CH$_3$)$_2$]$_3$), 18.39 (4-OSi[CH(CH_3)$_2$]$_3$), 57.11 (6-OCH$_3$), 62.16 (5-OCH$_3$), 110.96 (C-3), 111.38 (C-2), 114.33 (C-7), 118.70 (C-8), 121.75 (C-8a), 124.99 (C-4a), 142.88 (C-4), 144.07 (C-5), 145.70 (C-1), 150.65 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 14.33 (4-OSi[CH(CH$_3$)$_2$]$_3$) ↔ δ = 1.56 (4- Si[CH(CH$_3$)$_2$]$_3$), δ = 18.39 (4-OSi[CH(CH_3)$_2$]$_3$) ↔ δ = 1.03 (4-OSi[CH(CH_3)$_2$]$_3$), δ = 57.11 (6-OCH$_3$) ↔ δ = 3.99 (6-OMe), δ = 62.16 (5-OCH$_3$) ↔ δ = 3.74 (5-OMe), δ = 111.38 (C-2) ↔ δ = 6.82 (2-H), δ = 114.33 (C-7) ↔ δ = 7.26 (7-H), δ = 118.70 (C-8) ↔ δ = 7.87 (8-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 110.96 (C-3) ↔ δ = 6.82 (2-H), δ = 121.75 (C-8a) ↔ δ = 6.82 (2-H), δ = 121.75 (C-8a) ↔ δ = 7.26 (7-H), δ = 124.99 (C-4a) ↔ δ = 7.87 (8-H), δ = 142.88 (C-4) ↔ δ = 6.82 (2-H), δ = 144.07 (C-5) ↔ δ = 3.74 (5-OMe), δ = 144.07 (C-5) ↔ δ = 7.26 (7-H), δ = 145.70 (C-1) ↔ δ = 6.82 (2-H), δ = 145.70 (C-1) ↔ δ = 7.87 (8-H), δ = 150.65 (C-6) ↔ δ = 3.99 (6-OMe), δ = 150.65 (C-6) ↔ δ = 7.26 (7-H), δ = 150.65 (C-6) ↔ δ = 7.87 (8-H). **Melting point:** 152-154°C. **Elemental analysis:** Calculated: C: 55.38%, H: 6.86%; found: C: 55.00%, H: 6.43%; deviation: C: 0.38%, H: 0.43%. **HRMS** (neg. ESI): Calcd. for $C_{21}H_{31}{}^{79}BrO_4Si$ $[M-H]^-$ = 453.11022; found 453.11108 (+1.90 ppm), calcd. for $C_{21}H_{31}{}^{81}BrO_4Si$ $[M-H]^-$ = 455.10818; found 455.10907 (+1.97 ppm). **IR (film):** ν = 2945, 2895, 2865, 1680, 1650, 1575, 1490, 1465, 1455, 1440, 1415, 1385, 1335, 1280, 1255, 1215, 1190 1170, 1140, 1115, 1050, 1015, 920, 885, 830, 750, 720, 680 cm^{-1}. An analytical sample of *iso*-**23** was prepared as follows: *iso*-**23** was purified again by flash chromatography [d = 1.5 cm, h = 14 cm, F = 8 mL; PE/CH_2Cl_2 3:1 (F1-21), 1:1 (F22-44)], to obtain the product (F28-33, R_f (PE/CH_2Cl_2 3:1) = 0.20, 16.4 mg, 7%) as a light-brown oil. **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 1.12 (d, 18-H, $J_{4\text{-OSi[CH(CH}_3)_2]_3,4\text{-OSi[CH(CH}_3)_2]_3}$ = 7.6 Hz, 4-OSi[CH(CH_3)$_2$]$_3$), 1.49 (sept, 3H, $J_{4\text{-OSi[CH(CH}_3)_2]_3,4\text{-OSi[CH(CH}_3)_2]_3}$ = 7.6 Hz, 4-OSi[CH(CH$_3$)$_2$]$_3$), 3.99 (s, 3H, 7-OMe), 4.06 (s, 3H, 8-OMe), 6.93 (s, 1H, 2-H), 7.24 (d, 1H, $J_{6,5}$ = 9.3 Hz, 6-H), 7.84 (d, 1H, $J_{5,6}$ = 9.3 Hz, 5-H), 9.32 (s, 1H, 1-OH). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 7.23 (6-H) ↔ δ = 3.98 (7-OMe), δ = 7.84 (5-H) ↔ δ = 1.12 (4-OSi[CH(CH_3)$_2$]$_3$), δ = 7.84 (5-H) ↔ δ = 1.49 (4-OSi[CH(CH$_3$)$_2$]$_3$), δ = 9.32 (1-OH) ↔ δ = 4.06 (8-OMe). **^{13}C-NMR** (100.61 MHz, $CDCl_3$): δ = 14.49 (4-OSi[CH(CH$_3$)$_2$]$_3$), 18.18 (4-OSi[CH(CH_3)$_2$]$_3$), 56.73 (7-OCH$_3$), 62.18 (8-OCH$_3$), 107.54 (C-3), 114.19 (C-2), 114.57 (C-6), 118.28 (C-8a), 120.45 (C-5), 125.52 (C-4a), 142.66 (C-4), 142.93(C-8), 147.50 (C-1), 147.81 (C-7). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 14.49 (4-OSi[CH(CH$_3$)$_2$]$_3$) ↔ δ = 1.49 (4- Si[CH(CH$_3$)$_2$]$_3$), δ = 18.18 (4-OSi[CH(CH_3)$_2$]$_3$) ↔ δ = 1.12 (4-OSi[CH(CH_3)$_2$]$_3$), δ = 56.73 (7-OCH$_3$) ↔ δ = 3.99 (7-OMe), δ = 62.18 (8-OCH$_3$) ↔ δ = 4.06 (8-OMe), δ = 114.19 (C-2) ↔ δ = 6.93 (2-H), δ = 114.57 (C-6) ↔ δ = 7.24 (6-H), δ = 120.45 (C-5) ↔ δ = 7.84 (5-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]:δ = 107.54 (C-3) ↔ δ = 6.93 (2-H), δ = 107.54 (C-3) ↔ δ = 9.32 (1-OH), δ = 114.19 (C-2) ↔ δ = 9.32 (1-OH), δ = 118.28 (C-8a) ↔ δ = 6.93 (2-H), δ = 118.28 (C-8a) ↔ δ = 7.84 (5-H), δ = 118.28 (C-8a) ↔ δ = 9.32 (1-OH), δ = 125.52 (C-4a) ↔ δ = 7.24 (6-H), δ = 142.66 (C-4) ↔ δ = 6.93 (2-H), δ = 142.66 (C-4) ↔ δ = 7.84 (5-H), δ = 142.93(C-8) ↔ δ = 4.06 (8-OMe), δ = 142.93(C-8) ↔ δ = 7.24 (6-H), δ = 147.50 (C-1) ↔ δ = 6.93 (2-H), δ = 147.50 (C-1) ↔ δ = 9.32 (1-OH), δ = 147.81 (C-7) ↔ δ = 3.99 (7-OMe), δ = 147.81 (C-7) ↔ δ = 7.24 (6-H), δ = 147.81 (C-7) ↔ δ = 7.84 (5-H). **Melting point:** Oil. **HRMS** (pos. ESI): Calcd. for $C_{21}H_{31}{}^{79}BrO_4Si$ $[M+H]^+$ = 455.12478; found 455.12476 (−0.04 ppm), calcd. for $C_{21}H_{31}{}^{81}BrO_4Si$ $[M+H]^+$ = 457.12273; found 457.12268 (−0.10 ppm). **IR (film):** ν = 2945, 2895, 2865, 1665, 1610, 1575, 1505, 1485, 1465, 1435, 1415, 1390, 1350, 1270, 1220, 1200, 1165, 1145, 1110, 1055, 1015, 945, 920, 885, 845, 825, 810, 785, 765, 680 cm^{-1}.

[(3-bromofuran-2-yl)oxy]triisopropylsilane (28)



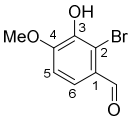
According to a general procedure for the preparation of silyltriflates (ref.[35]) triisopropylsilane (44.0 mL, 34.0 g, 215 mmol) was suspended in a 100 mL Schlenk flask and trifluoromethanesulfonic acid (21.0 mL, 35.6 g, 237 mmol, 1.10 equiv.) was added dropwise at 0°C. The solution was stirred for 1 h at 0°C, allowed to warm to room temperature and stirred for further 17 h. The crude product was used in the following step without further purification. 3-Bromofuran-2(5*H*)-one (**38**, 29.2 g, 179 mmol) was dissolved in CH_2Cl_2 (200 mL). *i*Pr_3SiOTf (57.8 mL, 65.8 g, 215 mmol, 1.20 equiv.) was transferred via cannula into this solution at 0°C and NEt_3 (34.5 mL, 25.2 g, 249 mmol, 1.40 equiv.) was added at 0°C to initiate the reaction. The ice-bath was removed and the solution was stirred for 2.5 h at room temperature. Afterwards the mixture was quenched with saturated aqueous $NaHCO_3$ (200 mL). The organic phase was separated and the aqueous phase was extracted with dichloromethane (3 × 100 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography [d = 8.5 cm, h = 12 cm, F = 100 mL; PE/CH_2Cl_2 90:10 containing 1% NEt_3 (F1-20)], to obtain the pure product [F8-15, R_f (PE/CH_2Cl_2 90:10, containing 1% NEt_3) = 0.8, 47.16 g, 79%; ref.[37]: 90%, Lit.34:54%) as a yellow liquid.– **^{1}H-NMR** (300.13 MHz, $CDCl_3$, product contained 5 w-% CH_2Cl_2): δ = 1.11 {d, 18H, $J_{silyl\text{-}CH_3,silyl\text{-}CH}$ = 7.0 Hz, 2-OSi[CH(C*H*$_3$)$_2$]$_3$}, 1.20-1.38 {m, 3H, 2-OSi[C*H*(CH$_3$)$_2$]$_3$}, 6.27 (d, 1H, $J_{5,4}$ = 2.4 Hz, 5-H), 6.79 (d, 1H, $J_{4,5}$ = 2.4 Hz, 4-H).

2-Bromo-3,4-dimethoxyphenyl 4-Methylbenzenesulfonate (29)



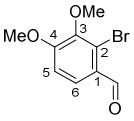
2-Bromo-3,4-dimethoxyphenol (**33**,13.99 g, 60.01 mmol) and TsCl (17.20 g, 90.01 mmol, 1.50 equiv.) were dissolved in CH_2Cl_2 (100 mL). The solution was cooled to 0°C and NEt_3 (12.5 mL, 9.13 g, 90.0 mmol, 1.50 equiv.) was added successively. After stirring for 4 d at room temperature, the reaction mixture was diluted with CH_2Cl_2 (200 mL), washed with saturated aqueous $NaHCO_3$ (2 × 100 mL), H_2O (100 mL) and brine (100 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography [d = 8.5 cm, h = 10 cm, F = 100 mL; CH/EE 5:1 (F1-11), 3:1 (F12-44), 1:1 (F45-55), 1:3 (F55-75)] to obtain the title compound (F21-64, $R_{f,\ 3:1}$ = 0.27, 22.58 g) as a 96:4 mixture with TsCl. A second flash chromatography [d = 8.5 cm, h = 12 cm, F = 100 mL; CH:EE 5:1 (F1-16), 3:1 (F17-36), 1:1 (F37-56)] furnished the product (F19-45, $R_{f,\ 3:1}$ = 0.30, 19.88 g, 85%) as a white solid.– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 2.44 (s, 3H, 4`-$CH_3$), 3.79 (s, 3H, 3-OMe), 3.86 (s, 3H, 4-OMe), AB signal [$\delta_A$ = 6.82 and $\delta_B$ = 7.09, $J_{AB}$ = 9.1 Hz, A and B signal show no further splitting, 5-H and 6-H], 7.29-7.32 (m, 2H, 3`-H and 5`-H), 7.76-7.79 (m, 2H, 2`-H and 6`-H) ppm. 4-OMe was distinguished from 3-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.86 (4-OMe) ↔ δ_A = 6.82 (5-H), δ = 7.29-7.32 (3`-H and 5`-H) ↔ δ = 2.44 (4'-CH_3). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 21.81 (4'-CH_3), 56.36 (4-OCH_3), 60.68 (3-OCH_3), 110.94 (C-5), 118.85 (C-6), 128.85 (C-2' and C-6'), 129.78 (C-3' and C-5'), 113.41 (C-2), 132.88 (C-1'), 140.92 (C-1), 145.64 (C-1'), 147.55 (C-3), 152.42 (C-4). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 21.81 (4'-CH_3) ↔ δ = 2.44 (4'- CH_3), δ = 56.36 (4-OCH_3) ↔ δ = 3.86 (4-OMe), δ = 60.68 (3-OCH_3) ↔ δ = 3.79 (3-OMe), δ = 110.94 (C-5) ↔ δ_A = 6.82 (5-H), δ = 118.85 (C-6) ↔ δ_B = 7.09 (6-H), δ = 128.85 (C-2' and C-6') ↔ δ = 7.76-7.79 (2'-H and 6'-H), δ = 129.78 (C-3' and C-5') ↔ δ = 7.29-7.32 (3'-H and 5'-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 113.41 (C-2) ↔ δ_A = 6.82 (5-H), δ = 113.41 (C-2) ↔ δ_B = 7.09 (6-H), δ = 132.88 (C-1') ↔ δ = 7.29-7.32 (3'-H and 5'-H), δ = 140.92 (C-1) ↔ δ_A = 6.82 (5-H), δ = 140.92 (C-1) ↔ δ_B = 7.09 (6-H), δ = 145.64 (C-4') ↔ δ = 2.44 (4'- CH_3), δ = 145.64 (C-4') ↔ δ = 7.76-7.79 (2'-H and 6'-H), δ = 147.55 (C-3) ↔ δ = 3.79 (3-OMe), δ = 147.55 (C-3) ↔ δ_A = 6.82 (5-H), δ = 152.42 (C-4) ↔ δ_A = 6.82 (5-H), δ = 152.42 (C-4) ↔ δ_B = 7.09 (6-H), δ = 152.42 (C-4) ↔ δ = 3.86 (4-OMe). **Melting point:** 99-100°C. **Elemental analysis:** Calculated: C: 46.52%, H: 3.90%, S: 8.28%; found: C: 46.41%, H: 3.88%, S: 8.28%; deviation: C: 0.11%, H: 0.02%, S: 0.00%. **IR (film):** v = 3005, 2970, 2940, 2840, 1595, 1585, 1480, 1450, 1435, 1405, 1375, 1300, 1270, 1240, 1210, 1190, 1175, 1140, 1120, 1095, 1035, 945, 835, 815, 785, 755, 715, 685, 665 cm^{-1}.

2-Bromo-3-hydroxy-4-methoxybenzaldehyde (31)



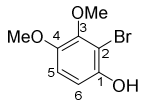
Isovanillin (**30**) (50.0 g, 329 mmol), anhydrous sodium acetate (54.2 g, 658 mmol, 2.0 equiv.) and iron powder (1.47 g, 26.3 mmol, 8.0 mol%) were suspended in glacial acetic acid (300 mL). At room temperature a solution of bromine (16.8 mL, 52.5 g, 329 mmol, 1.0 equiv.) in glacial acetic acid (70 mL) was added dropwise over a period of 20 min. The reaction mixture was stirred at room temperature for 5 h (KPG stirrer) and afterwards poured into ice-cold water (2 L). The precipitate was filtered and washed with ice-cold water (3 × 200 mL) and dried in vacuo at 60°C (drying pistol, KOH) for 6 h and at room temperature for 3 d ($p < 1$ mbar). The product 2-bromo-3-hydroxy-4-methoxybenzaldehyde (**31**) (55.50 g, 73%; Lit.[31]: 70%) was received as a white-brown solid.– **^{1}H NMR** (300.07 MHz, DMSO-d^6): δ = 3.91 (s, 3H, 4-OMe), 7.12 (d, 1H, $J_{5,6}$ = 6.9 Hz, 5-H), 7.39 (d, 1H, $J_{6,5}$ = 7.0 Hz, 6-H), 9.87 (br. s, 1H, 3-OH), 10.09 (s, 1H, 1-CHO).

2-Bromo-3,4-dimethoxybenzaldehyde (32)



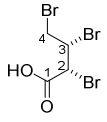
2-Bromoisovanillin (**31**, 16.00 g, 69.25 mmol) and KOH (85w-%, 7.31 g, 111 mmol, 1.60 equiv.) were dissolved in H_2O (100 mL). After heating the mixture to 60°C, dimethyl sulfate (10.5 mL, 14.0 g, 111 mmol, 1.60 equiv.) was added dropwise over a period of 30 min and the reaction mixture was stirred at 60°C for 30 min (KPG-stirrer). After cooling to room temperature, the suspension was filtered (Büchner funnel) and the precipitate was subsequently washed with aqueous NaOH (1 M, 2×50 mL) and H_2O (2 × 50 mL). The solid was dissolved in CH_2Cl_2 (300 mL), washed with brine (100 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the title compound was received as light-brown solid (12.51 g, 74%; (Lit.[31]: 96%) and used in the following step without further purification.– **^{1}H-NMR** (300.13 MHz, $CDCl_3$): δ = 3.90 (s, 3H, 3-OMe*), 3.97 (s, 3H, 4-OMe*), 6.97 (d, 1H, $J_{6,5}$ = 8.7 Hz, 6-H), 7.75 (d, 1H, $J_{5,6}$ = 8.7 Hz, 5-H), 10.27 (s, 1H, 1-CHO) ppm. *Assignment interchangeable.

2-Bromo-3,4-dimethoxyphenol (33)



2-Bromo-3,4-dimethoxybenzaldehyde (**32**, 12.46 g, 50.84 mmol) and *m*CPBA [77%, 17.55g (≙ 13.15 g), 76.26 mmol, 1.5 equiv.] were dissolved in CH_2Cl_2 (250 mL) and the mixture was refluxed for 20 h. After cooling to room temperature saturated aqueous Na_2SO_3 solution (100 mL) was added and the mixture was stirred vigorously for 10 min. The aqueous phase was separated and the organic phase was subsequently washed with saturated aqueous $NaHCO_3$ solution (3×100 mL) and brine (100 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the oily residue was taken up in aqueous KOH (10% in H_2O, 120 mL, 4.0 equiv., degassed with N_2). After vigorous stirring at room temperature for 3 h, the reaction mixture was acidified with conc. HCl (25 mL) to pH 1. CH_2Cl_2 (300 mL) was added and the solution was vigorously stirred for 5 min. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (2 × 100 mL). The combined organic extracts were washed with brine (100 mL) and dried over Na_2SO_4. The solvent was removed in vacuo. The title compound (10.89 g, 92%) was obtained as a colorless solid.– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 3.83 (s, 3H, 4-OMe), 3.88 (s, 3H, 3-OMe), 5.22 (s, 1H, 1-OH), AB signal (δ_A = 6.75 and δ_B = 6.82, J_{AB} = 9.0 Hz, A and B signal show no further splitting, 6-H and 5-H). 4-OMe was distinguished from 3-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.83 (4-OMe) ↔ δ_B = 6.82 (5-H). **^{13}C-NMR** (100.63 MHz, $CDCl_3$): δ = 57.02 (4-OMe), 60.75 (3-OMe), 106.82 (C-2), 110.04 (C-6), 113.40 (C-5), 146.97, 147.32 and 147.38 (C-1, C-3 and C-4). An **edHSQC** spectrum ("short-range C,H COSY"; 100.63/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 57.11 (4-OCH_3) ↔ δ = 3.84 (4-OMe), δ = 60.75 (3-OCH_3) ↔ δ = 3.88 (3-OMe), δ = 110.04 (C-6) ↔ δ_A = 6.75 (6-H), δ = 113.40 (C-5) ↔ δ_B = 6.82 (5-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.63/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 106.82 (C-2) ↔ δ = 5.22 (1-OH), δ = 106.82 (C-2) ↔ δ_A = 6.75 (6-H), δ = 106.82 (C-2) ↔ δ_B = 6.82 (5-H). δ = 146.97, 147.32 and 147.38 (C-1, C-3 and C-4) could not be assigned unambiguously. **Melting point:** 98-99°C (ref.[51]: 103-104°C, ref.[52]:113-115°C). **Elemental analysis:** Calculated: C: 41.23%, H: 3.89%; found: C: 41.11%, H: 3.80%; deviation: C: 0.12%, H: 0.09%. **HRMS** (neg. ESI): Calcd. for $C_8H_9{}^{79}BrO_3$ $[M-H]^-$ = 230.96623; found 230.96631 (+0.34 ppm), calcd. for $C_8H_9{}^{81}BrO_3$ $[M-H]^-$ = 232.96418; found 232.96426 (+0.34 ppm). **IR (film):** ν = 3005, 2975, 2945, 2925, 2850, 2830, 1495, 1460, 1425, 1320, 1305, 1270, 1230, 1170, 1140, 1035, 950, 820, 795, 750, 730 cm^{-1}.

***rac*-2,3,4-Tribromobutyric Acid (*rac*-37)**

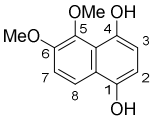


Crotonic acid (30.02 g, 348.7 mmol) and NBS (62.16 g, 349.2 mmol, 1.00 equiv.) were suspended in CCl_4 (240 mL). The solution was heated to reflux and AIBN (350 mg, 2.13 mmol, 0.6 mol%) was added in three steps. For initiation of the reaction: 117 mg, 0.71 mmol, 0.20 mol%. After 50 min (102 mg, 0.62 mmol, 0.17 mol-%) and after 1h 45 min (131 mg, 0.80 mmol, 0.23 mol%). The reaction mixture was refluxed for 3.5 h. After cooling to room temperature, the mixture was stored in a refrigerator overnight. The resulting precipitate was filtered and bromine (22.0 mL, 68.6 g, 428 mmol, 1.23 equiv.) was added dropwise to the filtrate. The solution was stirred at 40°C for 5 hours and kept at room temperature overnight. Afterwards the reaction mixture was carefully quenched by slow addition of saturated aqueous $NaHSO_3$ (100 mL). A violent reaction was observed. The organic phase was separated dried over $NaSO_4$ and kept at room temperature overnight. The crystallized product was filtered off and dried in vacuo (batch 1: 4.28 g). The solvent of the filtrate was evaporated in vacuo to furnish a yellow-brown oil (batch 2: 42.58 g). Combined yield: 46.86 g, 41% (ref.[36]: 35%) over the two steps. The product was used in the following step without further purification.– **^{1}H-NMR** (300.13 MHz, $CDCl_3$; raw material, additional resonances at δ = 1.91, 4.40 ppm): δ = AB signal [δ_A = 3.93 and δ_B = 4.15, J_{AB} = 11.9 Hz, additionally splitted by $J_{A,3}$ = 2.7 Hz and $J_{B,3}$ = 3.7 Hz, 4-H_2], 4.60 (ddd, $J_{3,2}$ = 10.5 Hz, $J_{3,B}$ = 3.7 Hz, $J_{3,A}$ = 2.8 Hz, 3-H), 4.67 (d, $J_{2,3}$ = 10.5 Hz, 2-H), 11.37 (br. s., CO_2H).

3-Bromofuran-2-one (38)

rac-2,3,4-Tribromobutyric acid (*rac*-**37**) (46.86 g, 144.3 mmol) was suspended in H_2O (150 mL) and heated to reflux under vigourous stirring for 4h 20 min. The aqueous phase was adjusted to pH 7 with an aqueous solution of Na_2CO_3 (2 M, 80 mL). The mixture was extracted with TBME (3 × 180 mL), washed with brine (140 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the title compound (10.00 g, 43%; ref.[36]: 31%) received as light brown solid.– **^{1}H-NMR** (300.13 MHz, $CDCl_3$): δ = 4.85 (d, 2H, $J_{5,4}$ = 2.0 Hz, 5-H_2), 7.61 (t, 1H, $J_{4,5}$ = 1.9 Hz, 4-H) ppm.

5,6-Dimethoxynaphthalene-1,4-diol (39)



One-pot procedure from 2-bromo-3,4-dimethoxyphenyl 4-methylbenzenesulfonate (29)]: 2-Bromo-3,4-dimethoxyphenyl 4-methylbenzenesulfonate (**29**, 3.87 g, 10.0 mmol) and (furan-2-yloxy)triisopropylsilane (**27**, 3.60 g, 15.0 mmol, 1.5 equiv.) were dissolved in freshly distilled THF (20 mL).[50] At –78°C *n*BuLi (2.56 M in hexane, 3.91 mL, 10.0 mmol, 1.0 equiv.) was added dropwise and the solution was stirred at this temperature for 5 min. Afterwards the cooling bath was removed and by continuous stirring the reaction was allowed to warm to room temperature for 45 min. The solution was cooled to 0°C and TBAF (1 M in THF, 15 mL, 15 mmol, 1.5 equiv.) was added dropwise. The ice-bath was removed and the reaction mixture was stirred at room temperature for 8 min. The reaction was quenched with aqueous HCl (1 M, 25 mL) and stirred for 5 min at room temperature. CH_2Cl_2 (25 mL) was added and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 mL). The combined organic extracts were washed with brine (25 mL) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 5 cm, h = 12 cm, F = 100 mL; CH/EE 3:1 (F1-20), CH/EE 1:1 (F21-45)] afforded the title compound (F10-40, 1.81 g, 82%) as a yellow-orange solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 3.93 (s, 3H, 5-OMe), 3.94 (s, 3H, 6-OMe), 5.09 (br. s, 1H, 1-OH), AB signal (δ_A = 6.60, δ_B = 6.68, J_{AB} = 8.1 Hz, A and B signal show no further splitting, 3-H and 2-H), 7.25 (d, 1H, $J_{7,8}$ = 9.3 Hz, 7-H), 7.94 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H), 9.23 (s, 1H, 4-OH). A **NOESY** spectrum (500.32

[51] T. Katoh, M. Nakatani, S. Shikita, R. Sampe, A. Ishiwata, O. Ohmori, M. Nakamura, S. Terashima, *Org. Lett.* **2001**, *3*, 2701-2704.

[52] H. A. Anderson, R. H. Thomson, *J. Chem. Soc., C* **1967**, 2152-2155.

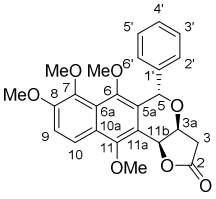
MHz, $CDCl_3$) allowed additional assignments of ^1H resonances by the occurrence of cross-peaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 3.99 (6-OMe) ↔ δ = 7.25 (7-H), δ = 4.07 (5-OMe) ↔ δ = 9.23 (4-OH). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 56.87 (6-OCH_3), 62.12 (5-OCH_3), 107.82 (C-3), 109.48 (C-2), 114.31 (C-7), 119.67 (C-8), 118.87 (C-4a), 121.88 (C-8a), 142.80 (C-5), 144.15 (C-1), 147.05 (C-4), 148.06 (C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 56.87 (6-OCH_3) ↔ δ = 3.99 (6-OMe), δ = 62.12 (5-OCH_3) ↔ δ = 4.07 (5-OMe), δ = 107.82 (C-3) ↔ δ_A = 6.60 (3-H), δ = 109.48 (C-2) ↔ δ_B = 6.67 (2-H), δ = 114.31 (C-7) ↔ δ = 7.25 (7-H), δ = 119.67 (C-8) ↔ δ = 7.94 (8-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 118.87 (C-4a) ↔ δ_B = 6.67 (2-H), δ = 118.87 (C-4a) ↔ δ = 7.94 (8-H), δ = 118.87 (C-4a) ↔ δ = 9.23 (4-OH), δ = 121.88 (C-8a) ↔ δ_A = 6.60 (3-H),, δ = 121.88 (C-8a) ↔ δ = 7.25 (7-H), δ = 142.80 (C-5) ↔ δ = 4.07 (5-OMe), δ = 142.80 (C-5) ↔ δ = 7.25 (7-H), δ = 142.80 (C-5) ↔ δ = 7.94 (8-H), δ = 144.15 (C-1) ↔ δ_A = 6.60 (3-H), δ = 144.15 (C-1) ↔ δ_B = 6.67 (2-H), δ = 147.05 (C-4) ↔ δ_A = 6.60 (3-H), δ = 147.05 (C-4) ↔ δ_B = 6.67 (2-H), δ = 147.05 (C-4) ↔ δ = 9.23 (4-OH), δ = 148.06 (C-6) ↔ δ = 3.99 (6-OMe), δ = 148.06 (C-6) ↔ δ = 7.25 (7-H), δ = 148.06 (C-6) ↔ δ = 7.94 (8-H). **Melting point:** 119°C. **Elemental analysis:** Calculated: C: 65.45%, H: 5.49%; found: C: 65.43%, H: 5.45%; deviation: C: 0.02%, H: 0.04%. **HRMS** (pos. ESI, 70 eV, file: nebrb48s_hr2): Calcd. for $C_{12}H_{10}O_4Na$: $[M+Na]^+$ = 241.04713; found: 241.04720 (+0.27 ppm). **IR (film):** ν = 3320, 3010, 2935, 2830, 1635, 1610, 1590, 1525, 1465, 1435, 1405, 1370, 1355, 1315, 1270, 1230, 1205, 1175, 1140, 1090, 1035, 995, 870, 805, 780, 750, 690, 665 cm^{-1}.

Alternative Preparation from 22 or *iso*-22: 5,6-dimethoxy-4-((triisopropylsilyl)oxy)naphthalen-1-ol (**22**, 1.41 g, 3.74 mmol) was suspended in freshly distilled THF (15 ml) and TBAF (1 M in THF, 3.8 ml, 3.8 mmol, 1.0 equiv.) was added dropwise at room temperature. The reaction mixture was stirred for 15 min at room temperature. Afterwards the reaction was quenched with HCl (1 M, 10 ml) and the organic phase was separated. The aqueous phase was extracted with CH_2Cl_2 (3 × 30 ml). The combined organic extracts were washed with aqueous $CaCl_2$ (10%, 30 ml) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 4 cm, h = 12 cm, F = 50 ml; CH/EE 3:1 (F1-11), CH/EE 1:1 (F12-25)] afforded the title compound (F5-18, 0.74 g, 90%) as a yellow-orange solid. *Note:* In an analogous procedure the isomer 7,8-dimethoxy-4-((triisopropylsilyl)oxy)naphthalen-1-ol [*iso*-**22**, as a 10:90 mixture with iPr$_3$SiOH, 1.04 g (≙0.20 g, 0.53 mmol of pure *iso*-**22**)] was desilylated to furnish the title compound (0.10 g, 86%) as a yellow-orange solid.

General Procedure B: Representative oxa-Pictet Spengler Cyclization of β-Hydroxy-γ-lactone 15 and Benzaldehyde to Dihydropyran 43b.

(4*S*,5*S*)-4-Hydroxy-5-(1,4,5,6-tetramethoxynaphthalen-2-yl)dihydrofuran-2(3*H*)-one (**15**, 52.3 mg, 0.15 mmol) was suspended in CH_2Cl_2 (1.5 ml). At 0°C benzaldehyde (45.9 µl, 47.8 mg, 0.45 mmol, 3.0 equiv.) was added and the reaction was started by the addition of $BF_3{\cdot}OEt_2$ (76.0 µl, 85.2 mg, 0.60 mmol, 4.0 equiv.). Afterwards the ice-bath was removed. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. Afterwards the reaction mixture was quenched by the addition of aqueous saturated $NaHCO_3$ (2 ml) and stirred for 5 min. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3× 8ml). The combined organic extracts were washed with brine (8 ml) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 ml; CH/EE 3:1 (F1-10), CH/EE 2:1 (F11-26)] afforded **43b** (F10-18, R_f (3:1) = 0.1, R_f (2:1) = 0.4, 58.1 mg, 89%, *ds* = 100:0) as a colorless oil.

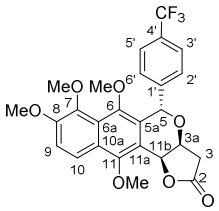
(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-5-phenyl-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (43b)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **15** (52.3 mg, 0.15 mmol), benzaldehyde (45.9 µL, 47.8 mg, 0.45 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (76.0 µL, 85.2 mg, 0.60 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 ml; CH/EE 3:1 (F1-10), CH/EE 2:1 (F11-26)] afforded the title compound (F10-18, R_f (3:1) = 0.1, R_f (2:1) = 0.4, 58.1 mg, 89%, *ds* = 100:0) as a colorless oil.− Note: The optical antipode *ent*-**43b** was synthesized analogously from *ent*-**15** in 67% yield (*ds* = 100:0).− **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.66, δ_B = 2.83, J_{AB} = 17.7 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.1 Hz, 3-H^A and 3-H^B), 3.52 (s, 3H, 6-OMe), 3.81 (s, 3H, 7-OMe, exclusion principle), 4.03 (s, 3H, 8-OMe), 4.12 (s, 3H, 11-OMe), 4.31 (dd, 1H, $J_{3a,B}$ = 5.1 Hz, $J_{3a,11b}$ = 2.9 Hz, 3a-H), 5.57 (d, 1H, $J_{11b,3a}$ = 2.9 Hz, 11b-H), 6.41 (s, 1H, 5-H), 7.10-7.15 (m, 2H, 2'-H and 6'-H), 7.26-7.31 (m, 3H, 3'-H, 4'-H and 5'-H), 7.39 (d, 1H, $J_{9,10}$ = 9.3 Hz, 9-H), 7.98 (d, 1H, $J_{10,9}$ = 9.3 Hz, 10-H). 6-OMe, 8-OMe and 11-OMe were distinguished from 7-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of cross-peaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.83 (3-H^B) ↔ δ = 5.57 (11b-H this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.52 (6-OMe) ↔ δ = 6.41 (5-H), δ = 4.03 (8-OMe) ↔ δ = 7.39 (9-H), δ = 4.12 (11-OMe) ↔ δ = 5.57 (11b-H), δ = 4.12 (11-OMe) ↔ δ = 7.98 (10-H), δ = 7.10-7.15 (2'-H and 6'-H) ↔ δ = 4.31 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.10-7.15 (2'-H and 6'-H) ↔ δ = 6.41 (5-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 37.55 (C-3), 56.82 (8-OCH_3), 62.25 (7-OCH_3), 62.40 (6-OCH_3), 64.43 (11-OCH_3), 66.83 (C-3a), 72.47 (C-11b), 73.26 (C-5), 114.88 (C-9), 116.91 and 125.56 (C-5a and C-11a could not be assigned unambiguously), 120.08 (C-10), 125.06 and 125.26 (C-6a and C-10a could not be assigned unambiguously), 128.39 (C-4'), 128.45 (C-3' and C-5'), 128.89 (C-2' and C-6'), 139.64 (C-1'), 143.12 (C-7), 147.13 (C-6), 151.48 (C-8), 153.65 (C-11), 175.28 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 37.55 (C-3) ↔ [δ_A = 2.66 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 56.82 (8-OCH_3) ↔ δ = 4.03 (8-OMe), δ = 62.25 (7-OCH_3) ↔ δ = 3.81 (7-OMe), δ = 62.40 (6-OCH_3) ↔ δ = 3.52 (6-OMe), δ = 64.43 (11-OCH_3) ↔ δ = 4.12 (11-OMe), δ = 66.83 (C-3a) ↔ δ = 4.31 (3a-H), δ = 72.47 (C-11b) ↔ δ = 5.57 (11b-H), δ = 73.26 (C-5) ↔ δ = 6.41 (5-H), δ = 114.88 (C-9) ↔ δ = 7.39 (9-H), δ = 120.08 (C-10) ↔ δ = 7.98 (10-H), δ = 128.39 (C-4') ↔ δ = 7.26-7.31 (3'-H, 4'-H and 5'-H), δ = 128.45 (C-3' and C-5') ↔ δ = 7.26-7.31 (3'-H, 4'-H and 5'-H), δ = 128.89 (C-2' and C-6') ↔ δ = 7.10-7.15 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 116.91 and 125.56 (C-5a and C-11a) ↔ δ = 5.56 (11b-H), δ = 116.91 and 125.56 (C-5a and C-11a) ↔ δ = 6.41 (5-H), δ = 125.06 and 125.26 (C-6a and C-10a) ↔ δ = 7.36 and 7.98 (9-H and 10-H), δ = 139.64 (C-1') ↔ δ = 6.41 (5-H), δ = 139.64 (C-1') ↔ δ = 7.26-7.31 (3'-H and 5'H), δ = 143.12 (C-7) ↔ δ = 3.81 (7-OMe), δ = 143.12 (C-7) ↔ δ = 7.39 (9-H), δ = 143.12 (C-7) ↔ δ = 7.98 (10-H), δ = 147.13 (C-6) ↔ δ = 3.52 (6-OMe), δ = 147.13 (C-6) ↔ δ = 6.41 (5-H), δ = 151.48 (C-8) ↔ δ = 4.03 (8-OMe), δ = 151.48 (C-8) ↔ δ = 7.39 (9-H), δ = 151.48 (C-8) ↔ δ = 7.98 (10-H), δ = 153.65 (C-11) ↔ δ = 4.12 (11-OMe), δ = 153.65 (C-11) ↔ δ = 5.57 (11b-H), δ = 153.65 (C-11) ↔ δ = 7.98 (10-H), δ = 175.28

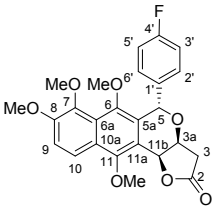
(C-2) ↔ [δ_A = 2.66 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 175.28 (C-2) ↔ 4.31(3a-H). **Melting point:** Oil. **Optical rotation of 43b:** $[\alpha]_D^{20}$ = –437.2 (*c* = 1.162, $CHCl_3$). **Optical rotation of *ent*-43b:** $[\alpha]_D^{20}$ = +411.5 (*c* = 0.686, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{25}H_{25}O_7$ $[M+H]^+$ = 437.15948; found 437.15961 (0.29 ppm). **IR (film):** *v* = 2940, 2845, 1780, 1665, 1615, 1600, 1505, 1455, 1425, 1405, 1360, 1335, 1275, 1200, 1155, 1110, 1065, 1045, 990, 955, 905, 885, 845, 805, 735, 700 cm^{-1}.

(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-5-(4-(trifluoromethyl)phenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (43c)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **15** (52.3 mg, 0.15 mmol), 4-(trifluoromethyl)benzaldehyde (61.5 µL, 78.4 mg, 0.45 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (76.0 µL, 85.2 mg, 0.60 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 3:1 (F1-11), CH/EE 2:1 (F12-30)] afforded the title compound (F13-19, R_f (3:1) = 0.1, R_f (2:1) = 0.5, 68.6 mg, 91%, *ds* = 100:0) as a colorless oil.– Note: The optical antipode *ent*-**43c** was synthesized analogously from *ent*-**15** in 70% yield (*ds* = 100:0). – **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.68, δ_B = 2.85, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.1 Hz, 3-H^A and 3-H^B), 3.61 (s, 3H, 6-OMe), 3.81 (s, 3H, 7-OMe), 4.04 (s, 3H, 8-OMe), 4.12 (s, 3H, 11-OMe), 4.22 (dd, 1H, $J_{3a,B}$ = 5.1 Hz, $J_{3a,11b}$ = 2.8 Hz, 3a-H), 5.56 (d, 1H, $J_{11b,3a}$ = 2.8 Hz, 11b-H), 6.40 (s, 1H, 5-H), 7.26 (br. d, 2H, $J_{2',3'} = J_{6',5'}$ = 8.0 Hz, 2'-H and 6'-H), 7.41 (d, 1H, $J_{9,10}$ = 9.3 Hz, 9-H), 7.56 (br. d, 2H, $J_{3',2'} = J_{5',6'}$ = 8.0 Hz, 3'-H and 5'-H), 7.99 (d, 1H, $J_{10,9}$ = 9.3 Hz, 10-H). 6-OMe, 8-OMe and 11-OMe were distinguished from 7-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.61 (6-OMe) ↔ δ = 6.40 (5-H), δ = 4.04 (8-OMe) ↔ δ = 7.41 (9-H), δ = 4.12 (11-OMe) ↔ δ = 5.56 (11b-H), δ = 4.12 (11-OMe) ↔ δ = 7.99 (10-H). δ = 7.26 (2'-H and 6'-H) ↔ δ = 4.22 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another). **^{19}F NMR** (470.77 MHz, $CDCl_3$): δ = –62.64 (s, 3F, CF_3). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 37.53 (C-3), 56.77 (8-OCH_3), 62.25 (7-OCH_3), 62.49 (6-OCH_3), 64.47 (11-OCH_3), 67.22 (C-3a), 72.18 (C-11b), 72.57 (C-5), 115.03 (C-9), 116.46 and 124.37 (C-5a and C-11a), 120.15 (C-10), 124.01 (q, 1C, $^1J_{C,F}$ = 272.0 Hz, 4'-CF_3), 125.05 and 125.33 (C-6a and C-10a), 125.45 (q, 2C, $^3J_{C,F}$ = 3.6 Hz, C-3' and C-5'), 129.01 (C-2' and C-6'), 130.58 (q, 1C, $^2J_{C,F}$ = 32.4 Hz, C-4'), 143.00 (C-7), 143.36 (C-1'), 147.17 (C-6), 151.63 (C-8), 153.90 (C-11), 175.04 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 37.53 (C-3) ↔ [δ_A = 2.68 (3-H^A) and δ_B = 2.85 (3-H^B)], δ = 56.77 (8-OCH_3) ↔ δ = 4.04 (8-OMe), δ = 62.25 (7-OCH_3) ↔ δ = 3.81 (7-OMe), δ = 62.49 (6-OCH_3) ↔ δ = 3.61 (6-OMe), δ = 64.47 (11-OCH_3) ↔ δ = 4.12 (11-OMe), δ = 67.22 (C-3a) ↔ δ = 4.22 (3a-H), δ = 72.18 (C-11b) ↔ δ = 5.56 (11b-H), δ = 72.57 (C-5) ↔ δ = 6.40 (5-H), δ = 115.03 (C-9) ↔ δ = 7.41 (9-H), δ = 120.15 (C-10) ↔ δ = 7.99 (10-H), δ = 125.45 (C-3' and C-5') ↔ δ = 7.56 (3'-H and 5'-H), δ = 129.01 (C-2' and C-6') ↔ δ = 7.26 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 116.46 and 124.37 (C-5a and C-11a) ↔ δ = 5.56 (11b-H), δ = 116.46 and 124.37 (C-5a and C-11a) ↔ δ = 6.40 (5-H) could not be assigned unambiguously], [δ = 125.05 and 125.33 (C-6a and C-10a) ↔ δ = 7.41 (9-H), δ = 125.05 and 125.33 (C-6a and C-10a) ↔ δ = 7.99 (10-H) could not be assigned unambiguously], δ = 143.00 (C-7) ↔ δ = 3.81 (7-OMe), δ = 143.00 (C-7) ↔ δ = 7.41 (9-H), δ = 143.00 (C-7) ↔ δ = 7.99 (10-H), δ = 143.36 (C-1') ↔ δ = 6.40 (5-H), δ = 143.36 (C-1') ↔ δ = 7.56 (3'-H and 5'H), δ = 147.17 (C-6) ↔ δ = 3.61 (6-OMe), δ = 147.17 (C-6) ↔ δ = 6.40 (5-H), δ = 151.63 (C-8) ↔ δ = 4.04 (8-OMe), δ = 151.63 (C-8) ↔ δ = 7.41 (9-H), δ = 151.63 (C-8) ↔ δ = 7.99 (10-H), δ = 153.90 (C-11) ↔ δ = 4.12 (11-OMe), δ = 153.90 (C-11) ↔ δ = 5.56 (11b-H), δ = 153.90 (C-11) ↔ δ = 7.99 (10-H), δ = 175.04 (C-2) ↔ [δ_A = 2.68 (3-H^A) and δ_B = 2.85 (3-H^B)], δ = 175.04 (C-2) ↔ 4.22 (3a-H). **Melting point:** 68-72°C. **Optical rotation of 43c:** $[\alpha]_D^{20}$ = –354.8 (*c* = 1.372, $CHCl_3$). **Optical rotation of *ent*-43c:** $[\alpha]_D^{20}$ = +308.8 (*c* = 0.96, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{26}H_{24}O_7F_3$ $[M+H]^+$ = 505.14686; found 505.14658 (–0.57 ppm). **IR (film):** *v* = 2945, 2845, 1785, 1665, 1620, 1580, 1460, 1415, 1365, 1325, 1275, 1200, 1165, 1065, 1015, 995, 905, 885, 830, 780, 735, 700 cm^{-1}.

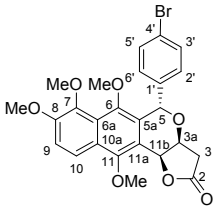
(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-5-(4-fluorophenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (43d)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **15** (52.3 mg, 0.15 mmol), 4-fluorobenzaldehyde (48.1 µL, 55.8 mg, 0.45 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (76.0 µL, 85.2 mg, 0.60 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 3:1 (F1-12), CH/EE 2:1 (F13-28)] afforded the title compound (F14-21, R_f (3:1) = 0.1, R_f (2:1) = 0.5, 62.2 mg, 91%, *ds* = 100:0) as a colorless oil.– Note: The optical antipode *ent*-**43d** was synthesized analogously from *ent*-**15** in 62% yield (*ds* = 95:5).– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.66, δ_B = 2.85, J_{AB} = 17.7 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.2 Hz, 3-H^A and 3-H^B), 3.55 (s, 3H, 6-OMe), 3.80 (s, 3H, 7-OMe), 4.03 (s, 3H, 8-OMe), 4.12 (s, 3H, 11-OMe), 4.28 (dd, 1H, $J_{3a,B}$ = 5.1 Hz, $J_{3a,11b}$ = 2.9 Hz, 3a-H), 5.57 (d, 1H, $J_{11b,3a}$ = 2.9 Hz, 11b-H), 6.37 (s, 1H, 5-H), 6.98 (m_c, 2H, 3'-H and 5'-H), 7.09 (m_c, 2H, 2'-H and 6'-H), 7.39 (d, 1H, $J_{9,10}$ = 9.3 Hz, 9-H), 7.98 (d, 1H, $J_{10,9}$ = 9.3 Hz, 10-H). 6-OMe, 8-OMe and 11-OMe were distinguished from 7-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.85 (3-H^B) ↔ δ = 5.57 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.60 (6-OMe) ↔ δ = 4.28 (3a-H), δ = 3.60 (6-OMe) ↔ δ = 6.37 (5-H), δ = 4.03 (8-OMe) ↔ δ = 7.39 (9-H), δ = 4.12 (11-OMe) ↔ δ = 5.57 (11b-H), δ = 4.12 (11-OMe) ↔ δ = 7.98 (10-H), δ = 7.09 (2'-H and 6'-H) ↔ δ = 4.28 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.09 (2'-H and 6'-H) ↔ δ = 5.57 (11b-H). **^{19}F NMR** (470.77 MHz, $CDCl_3$): δ = –113.63 (s, 1F, 4'-F). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 37.51 (C-3), 56.76 (8-OCH_3), 62.24 (7-OCH_3), 62.45 (6-OCH_3), 64.45 (11-OCH_3), 66.76 (C-3a), 72.32 (C-11b), 72.49 (C-5), 114.88 (C-9), 116.63, 125.03, 125.22 and 125.24 (C-5a, C-6a, C-10a and C-11a could not be assigned unambiguously), 120.10 (C-10), 115.35 (d, 2C, $^2J_{C,F}$ = 21.5 Hz, C-3' and C-5'), 130.50 (d, 2C, $^3J_{C,F}$ = 8.4 Hz, C-2' and C-6'), 135.47 (d, 1C, $^4J_{C,F}$ = 3.2 Hz, C-1'), 142.99 (C-7), 147.05 (C-6), 151.52 (C-8), 153.73 (C-11), 162.64 (d, 1C, $^1J_{C,F}$ = 247.5 Hz, C-4'), 175.21 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 37.51 (C-3) ↔ [δ_A = 2.66 (3-H^A) and δ_B = 2.85 (3-H^B)], δ = 56.76 (8-OCH_3) ↔ δ = 4.03 (8-OMe), δ = 62.24 (7-OCH_3) ↔ δ = 3.80 (7-OMe), δ = 62.45 (6-

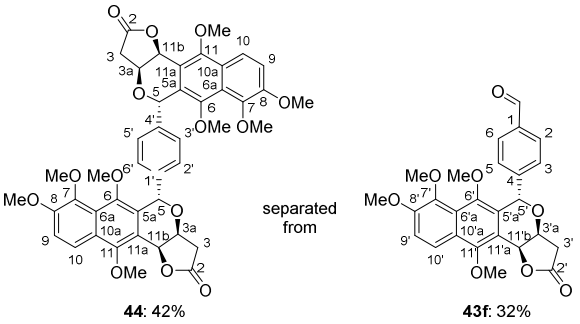
OCH_3) ↔ *δ* = 3.55 (6-OMe), *δ* = 64.45 (11-OCH_3) ↔ *δ* = 4.12 (11-OMe), *δ* = 66.76 (C-3a) ↔ *δ* = 4.28 (3a-H), *δ* = 72.32 (C-11b) ↔ *δ* = 5.57 (11b-H), *δ* = 72.49 (C-5) ↔ *δ* = 6.37 (5-H), *δ* = 114.88 (C-9) ↔ *δ* = 7.39 (9-H), *δ* = 120.10 (C-10) ↔ *δ* = 7.98 (10-H), *δ* = 115.35 (C-3' and C-5') ↔ *δ* = 6.98 (3'-H and 5'-H), *δ* = 130.50 (C-2' and C-6') ↔ *δ* = 7.09 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [*δ*(^{13}C) ↔ *δ*(^1H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: *δ* = 135.47 (C-1') ↔ *δ* = 6.37 (5-H), *δ* = 135.47 (C-1') ↔ *δ* = 6.98 (3'-H and 5'H), *δ* = 142.99 (C-7) ↔ *δ* = 3.80 (7-OMe), *δ* = 142.99 (C-7) ↔ *δ* = 7.39 (9-H), *δ* = 147.05 (C-6) ↔ *δ* = 3.55 (6-OMe), *δ* = 147.05 (C-6) ↔ *δ* = 6.37 (5-H), *δ* = 151.52 (C-8) ↔ *δ* = 4.03 (8-OMe), *δ* = 151.52 (C-8) ↔ *δ* = 7.98 (10-H), *δ* = 153.73 (C-11) ↔ *δ* = 4.12 (11-OMe), *δ* = 153.73 (C-11) ↔ *δ* = 7.98 (10-H), *δ* = 162.64 (C-4') ↔ *δ* = 6.98 (3'-H and 5'H), *δ* = 162.64 (C-4') ↔ *δ* = 7.09 (2'-H and 6'H), *δ* = 175.21 (C-2) ↔ [δ_A = 2.66 (3-H^A) and δ_B = 2.85 (3-H^B)], *δ* = 175.21 (C-2) ↔ 4.28 (3a-H). **Melting point:** 76-77°C. **Optical rotation of 43d:** $[\alpha]_D^{20}$ = –336.7 (*c* = 1.39, $CHCl_3$). **Optical rotation of *ent*-43d:** $[\alpha]_D^{20}$ = +333.2 (*c* = 0.73, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{25}H_{24}O_7F$ $[M+H]^+$ = 455.15006; found 455.14978 (–0.61 ppm). **IR (film):** *v* = 3365, 3055, 2985, 2945, 2845, 2305, 1775, 1665, 1625, 1605, 1575, 1510, 1460, 1415, 1360, 1335, 1275, 1225, 1200, 1155, 1080, 1050, 1000, 910, 885, 835, 800, 730, 705 cm^{-1}.

(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-5-(4-bromophenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (43e)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **15** (52.3 mg, 0.15 mmol), 4-bromobenzaldehyde (82.3 mg, 0.45 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (76.0 µL, 85.2 mg, 0.60 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 3:1 (F1-11), CH/EE 2:1 (F12-29)] afforded the title compound (F9-17, R_f (3:1) = 0.1, R_f (2:1) = 0.5, 74.2 mg, 96%, *ds* = 100:0) as a colorless solid.– Note: The optical antipode *ent*-**43e** was synthesized analogously from *ent*-**15** in 68% yield (*ds* = 100:0).– **^{1}H NMR** (400.13 MHz, $CDCl_3$): *δ* = AB signal (δ_A = 2.66, δ_B = 2.84, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.1 Hz, 3-H^A and 3-H^B), 3.58 (s, 3H, 6-OMe), 3.81 (s, 3H, 7-OMe), 4.03 (s, 3H, 8-OMe), 4.12 (s, 3H, 11-OMe), 4.26 (dd, 1H, $J_{3a,B}$ = 5.1 Hz, $J_{3a,11b}$ = 2.8 Hz, 3a-H), 5.55 (d, 1H, $J_{11b,3a}$ = 2.9 Hz, 11b-H), 6.34 (s, 1H, 5-H), 6.98-7.02 (m, 2H, 2'-H and 6'-H), 7.40 (d, 1H, $J_{9,10}$ = 9.4 Hz, 9-H), 7.40-7.44 (m, 2H, 3'-H and 5'-H), 7.98 (d, 1H, $J_{10,9}$ = 9.2 Hz, 10-H). 6-OMe, 8-OMe and 11-OMe were distinguished from 7-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^1H resonances by the occurrence of cross-peaks [*δ*(^1H) ↔ *δ*(^1H)]: *δ* = 2.84 (3-H^B) *δ* = 5.55 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), *δ* = 3.58 (6-OMe) ↔ *δ* = 6.34 (5-H), *δ* = 4.03 (8-OMe) ↔ *δ* = 7.40 (9-H), *δ* = 4.12 (11-OMe) ↔ *δ* = 7.99 (10-H), *δ* = 7.26 (2'-H and 6'-H) ↔ *δ* = 4.22 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), *δ* = 7.26 (2'-H and 6'-H) ↔ *δ* =6.34 (5-H). **^{13}C NMR** (100.63 MHz, $CDCl_3$): *δ* = 37.53 (C-3), 56.82 (8-OCH_3), 62.25 (7-OCH_3), 62.49 (6-OCH_3), 64.47 (11-OCH_3), 66.97 (C-3a), 72.27 (C-11b), 72.60 (C-5), 115.04 (C-9), 116.63 and 124.83 (C-5a and C-11a), 120.12 (C-10), 122.54 (C-4'), 125.07 (C-6a), 125.33 (C-10a), 130.46 (C-2' and C-6'), 131.64 (C-3' and C-5'), 138.67 (C-1'), 143.10 (C-7), 147.14 (C-6), 151.59 (C-8), 153.81 (C-11), 175.09 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 100.63/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [*δ*(^{13}C) ↔ *δ*(^1H)]: *δ* = 37.53 (C-3) ↔ [δ_A = 2.66 (3-H^A) and δ_B = 2.84 (3-H^B)], *δ* = 56.82 (8-OCH_3) ↔ *δ* = 4.03 (8-OMe), *δ* = 62.25 (7-OCH_3) ↔ *δ* = 3.81 (7-OMe), *δ* = 62.49 (6-OCH_3) ↔ *δ* = 3.58 (6-OMe), *δ* = 64.47 (11-OCH_3) ↔ *δ* = 4.12 (11-OMe), *δ* = 66.97 (C-3a) ↔ *δ* = 4.26 (3a-H), *δ* = 72.27 (C-11b) ↔ *δ* = 5.55 (11b-H), *δ* = 72.60 (C-5) ↔ *δ* = 6.34 (5-H), *δ* = 115.04 (C-9) ↔ *δ* = 7.40 (9-H), *δ* = 120.12 (C-10) ↔ *δ* = 7.98 (10-H), *δ* = 130.46 (C-2' and C-6') ↔ *δ* = 6.98-7.02 (2'-H and 6'-H), *δ* = 131.64 (C-3' and C-5') ↔ *δ* = 7.40-7.44 (3'-H and 5'-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.63/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [*δ*(^{13}C) ↔ *δ*(^1H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [*δ* = 116.63 and 124.83 (C-5a and C-11a) ↔ *δ* = 5.55 (11b-H), *δ* = 116.63 and 124.83 (C-5a and C-11a) ↔ *δ* = 6.34 (5-H) could not be assigned unambiguously] , *δ* = 122.54 (C-4') ↔ *δ* = 6.98-7.02 (2'-H and 6'-H), *δ* = 122.54 (C-4') ↔ 7.40-7.44 (3'-H and 5'-H), *δ* = 125.07 (C-6a) ↔ *δ* = 7.98 (10-H), *δ* = 125.33 (C-10a) ↔ *δ* = 7.40 (9-H), *δ* = 138.67 (C-1') ↔ *δ* = 6.34 (5-H), *δ* = 138.67 (C-1') ↔ *δ* = 7.40-7.44 (3'-H and 5'H), *δ* = 143.10 (C-7) ↔ *δ* = 3.81 (7-OMe), *δ* = 143.10 (C-7) ↔ *δ* = 7.40 (9-H), *δ* = 143.10 (C-7) ↔ *δ* = 7.98 (10-H), *δ* = 147.14 (C-6) ↔ *δ* = 3.58 (6-OMe), *δ* = 147.14 (C-6) ↔ *δ* = 6.34 (5-H), *δ* = 151.59 (C-8) ↔ *δ* = 4.03 (8-OMe), *δ* = 151.59 (C-8) ↔ *δ* = 7.40 (9-H), *δ* = 151.59 (C-8) ↔ *δ* = 7.98 (10-H), *δ* = 153.81 (C-11) ↔ *δ* = 4.12 (11-OMe), *δ* = 153.81 (C-11) ↔ *δ* = 5.55 (11b-H), *δ* = 153.81 (C-11) ↔ *δ* = 7.98 (10-H), *δ* = 175.09 (C-2) ↔ [δ_A = 2.66 (3-H^A) and δ_B = 2.84 (3-H^B)], *δ* = 175.09 (C-2) ↔ 4.26 (3a-H). **Melting point:** 70-73°C. **Optical rotation of 43e:** $[\alpha]_D^{20}$ = –311.8 (*c* = 1.484, $CHCl_3$). **Optical rotation of *ent*-43e:** $[\alpha]_D^{20}$ = +360.4 (*c* = 0.74, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{25}H_{23}{}^{79}BrO_7Na$ $[M+Na]^+$ = 537.05194; found 537.05164 (–0.56 ppm) and calcd. for $C_{25}H_{23}{}^{81}BrO_7Na$ $[M+Na]^+$ = 539.04989; found 539.04950 (–0.72 ppm). **IR (film):** *v* = 2935, 2840, 1780, 1615, 1600, 1505, 1485, 1465, 1450, 1425, 1380, 1360, 1335, 1275, 1250, 1200, 1150, 1130, 1100, 1070, 1050, 1010, 990, 905, 885, 850, 820, 730 cm^{-1}.

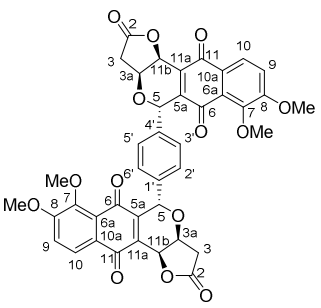
(3a*S*,3a'*S*,5*S*,5'*S*,11b*S*,11b'*S*)-5,5'-(1,4-Phenylene)bis(6,7,8,11-tetramethoxy-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one) (44) and 4-{(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-2-oxo-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-5-yl}benzaldehyde (43f)



(4*S*,5*S*)-4-Hydroxy-5-(1,4,5,6-tetramethoxynaphthalen-2-yl)dihydrofuran-2(3*H*)-one (**15**, 33.8 mg, 97.0 µmol) and terephthaldehyde (6.7 mg, 50 µmol, 0.52 equiv.) were suspended in CH_2Cl_2 (1.0 mL). At 0°C the reaction was started by the addition of $BF_3{\cdot}OEt_2$ (25.3 µL, 28.4 mg, 0.20 mmol, 2.06 equiv.). Afterwards the ice-bath was removed. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. Afterwards the reaction mixture was quenched by the addition of H_2O (3 mL) and stirred for 5 min. The organic phase was separated and the aqueous phase was extracted with CH_2Cl_2 (3 × 5mL). The combined organic extracts were washed with brine (5 mL) and dried over Na_2SO_4. The solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 2:1 (F1-11), CH/EE 1:1 (F12-26), CH/EE 1:3 (F27-46)] afforded the aldehyde **43f** (F9-16, R_f (1:1) = 0.4, 14.5 mg, 32%, *ds* = 100:0) as a colorless oil and the dimeric compound **40** (F20-38, R_f (1:1) = 0.2, 16.2 mg, 42%, *ds* = 100:0) as a colorless oil.– **Analysis of**

dimer 44: ^{1}H NMR (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.65, δ_B = 2.83, J_{AB} = 17.7 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.2 Hz, 2×3-H^A and 2×3-H^B), 3.53 (s, 2×3H, 2×6-OMe), 3.79 (s, 2×3H, 2×7-OMe), 4.02 (s, 2×3H, 2×8-OMe), 4.09 (s, 2×3H, 2×11-OMe), 4.28 (dd, 2×1H, $J_{3a,B}$ = 5.0 Hz, $J_{3a,11b}$ = 2.9 Hz, 2×3a-H), 5.53 (d, 2×1H, $J_{11b,3a}$ = 2.9 Hz, 2×11b-H), 6.34 (s, 2×1H, 2×5-H), 7.05 (br. s, 4H, 2'-H, 3'-H, 5'-H and 6'-H), 7.37 (d, 2×1H, $J_{9,10}$ = 9.3 Hz, 2×9-H), 7.95 (d, 2×1H, $J_{10,9}$ = 9.3 Hz, 2×10-H). 6-OMe, 8-OMe and 11-OMe were distinguished from 7-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_A = 2.83 (3-H^B) ↔ δ = 5.53 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.53 (6-OMe) ↔ δ = 6.34 (5-H), δ = 3.53 (6-OMe) ↔ δ = 7.05 (2'-H, 3'-H, 5'-H and 6'-H), δ = 4.02 (8-OMe) ↔ δ = 7.37 (9-H), δ = 4.09 (11-OMe) ↔ δ = 5.53 (11b-H), δ = 4.09 (11-OMe) ↔ δ = 7.95 (10-H), δ = 7.05 (2'-H, 3'-H, 5'-H and 6'-H) ↔ δ = 4.28 (3a-H, this cross-peak proves that the phenyl ring and both 3a-H are oriented *cis* relative to one another). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 37.59 (2×C-3), 56.78 (2×8-OCH_3), 62.23 (2×7-OCH_3), 62.38 (2×6-OCH_3), 64.44 (2×11-OCH_3), 66.96 (2×C-3a), 72.34 (2×C-11b), 72.75 (2×C-5), 114.88 (2×C-9), 116.59 and 125.19 (2×C-5a and 2×C-11a), 120.09 (2×C-10), 124.96 (2×C-6a), 125.19 (2×C-10a), 128.74 (C-2', C-3', C-5' and C-6'), 139.55 (C-1' and C-4'), 142.97 (2×C-7), 147.05 (2×C-6), 151.50 (2×C-8), 153.72 (2×C-11), 175.18 (2×C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 37.59 (C-3) ↔ [δ_A = 2.65 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 56.78 (8-OCH_3) ↔ δ = 4.02 (8-OMe), δ = 62.23 (7-OCH_3) ↔ δ = 3.79 (7-OMe), δ = 62.38 (6-OCH_3) ↔ δ = 3.53 (6-OMe), δ = 64.44 (11-OCH_3) ↔ δ = 4.09 (11-OMe), δ = 66.96 (C-3a) ↔ δ = 4.28 (3a-H), δ = 72.34 (C-11b) ↔ δ = 5.53 (11b-H), δ = 72.75 (C-5) ↔ δ = 6.34 (5-H), δ = 114.88 (C-9) ↔ δ = 7.37 (9-H), δ = 120.09 (C-10) ↔ δ = 7.95 (10-H), δ = 128.74 (C-2', C-3', C-5' and C-6') ↔ δ = 7.05 (2'-H, 3'-H, 5'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 116.59 and 125.19 (C-5a and C-11a) ↔ δ = 5.53 (11b-H), δ = 116.59 and 125.19 (C-5a and C-11a) ↔ δ = 6.34 (5-H) could not be assigned unambiguously], δ = 124.96 (C-6a) ↔ δ = 7.95 (10-H), δ = 125.19 (C-10a) ↔ δ = 7.37 (9-H), δ = 139.55 (C-1' and C-4') ↔ δ = 6.34 (5-H), δ = 139.55 (C-1' and C-4') ↔ δ = 7.05 (2'-H, 3'-H, 5'-H and 6'-H), δ = 142.97 (C-7) ↔ δ = 3.79 (7-OMe), δ = 142.97 (C-7) ↔ δ = 7.37 (9-H), δ = 142.97 (C-7) ↔ δ = 7.95 (10-H), δ = 147.05 (C-6) ↔ δ = 3.53 (6-OMe), δ = 147.05 (C-6) ↔ δ = 6.34 (5-H), δ = 151.50 (C-8) ↔ δ = 4.02 (8-OMe), δ = 151.50 (C-8) ↔ δ = 7.37 (9-H), δ = 151.50 (C-8) ↔ δ = 7.95 (10-H), δ = 153.72 (C-11) ↔ δ = 4.09 (11-OMe), δ = 153.72 (C-11) ↔ δ = 7.95 (10-H), δ = 175.18 (C-2) ↔ [δ_A = 2.65 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 175.18 (C-2) ↔ 4.28 (3a-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = –474.3 (*c* = 0.527, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{44}H_{43}O_{14}$ $[M+H]^+$ = 795.26473; found 795.26398 (–0.95 ppm). **IR (film):** *v* = 2935, 1780, 1615, 1600, 1510, 1465, 1450, 1425, 1400, 1380, 1360, 1335, 1275, 1200, 1155, 1130, 1105, 1085, 1065, 1050, 1020, 990, 955, 920, 905, 885, 815, 805, 735, 700 cm^{-1}.– **Analysis of 43f: ^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.68, δ_B = 2.85, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3'a}$ = 5.0 Hz, 3'-H^A and 3'-H^B), 3.60 (s, 3H, 6'-OMe), 3.81 (s, 3H, 7'-OMe, exclusion principle), 4.04 (s, 3H, 8'-OMe), 4.13 (s, 3H, 11'-OMe), 4.24 (dd, 1H, $J_{3'a,B}$ = 5.0 Hz, $J_{3'a,11'b}$ = 2.8 Hz, 3'a-H), 5.57 (d, 1H, $J_{11'b,3'a}$ = 2.8 Hz, 11'b-H), 6.41 (s, 1H, 5'-H), 7.32 (m_c, 2H, 3-H and 5-H), 7.41 (d, 1H, $J_{9',10'}$ = 9.4 Hz, 9'-H), 7.82 (m_c, 2H, 2-H, and 6-H), 8.00 (d, 1H, $J_{10',9'}$ = 9.2 Hz, 10'-H), 9.99 (s, 1H, 1-CHO). 6'-OMe, 8'-OMe and 11'-OMe were distinguished from 7'-OMe by the occurrence of cross-peaks only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.60 (6'-OMe) ↔ δ = 6.41 (5'-H), δ = 4.04 (8'-OMe) ↔ δ = 7.41 (9'-H), δ = 4.13 (11'-OMe) ↔ δ = 5.57 (11'b-H), δ = 4.13 (11'-OMe) ↔ δ = 8.00 (10'-H), δ = 7.32 (3-H and 5-H) ↔ δ = 4.24 (3'a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.32 (3-H and 5-H) ↔ δ = 6.41 (5'-H), δ = 7.82 (2-H and 6-H) ↔ δ = 9.99 (1-CHO). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 37.57 (C-3'), 56.82 (8'-OCH_3), 62.24 (7'-OCH_3), 62.46 (6'-OCH_3), 64.49 (11'-OCH_3), 67.33 (C-3'a), 72.19 (C-11'b), 72.82 (C-5'), 115.14 (C-9'), 116.48 and 124.39 (C-5'a and C-11'a), 120.16 (C-10'), 125.09 (C-6'a), 125.40 (C-10'a), 129.38 (C-3 and C-5), 129.83 (C-2 and C-6), 136.36 (C-1), 143.08 (C-7'), 146.21 (C-4), 147.23 (C-6'), 151.66 (C-8'), 153.92 (C-11'), 174.97 (C-2'), 191.68 (1-CHO). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 37.57 (C-3') ↔ [δ_A = 2.68 (3'-H^A) and δ_B = 2.85 (3'-H^B)], δ = 56.82 (8'-OCH_3) ↔ δ = 4.04 (8'-OMe), δ = 62.24 (7'-OCH_3) ↔ δ = 3.81 (7'-OMe), δ = 62.46 (6'-OCH_3) ↔ δ = 3.60 (6'-OMe), δ = 64.49 (11'-OCH_3) ↔ δ = 4.13 (11'-OMe), δ = 67.33 (C-3'a) ↔ δ = 4.24 (3'a-H), δ = 72.19 (C-11'b) ↔ δ = 5.57 (11'b-H), δ = 72.82 (C-5') ↔ δ = 6.41 (5'-H), δ = 115.14 (C-9') ↔ δ = 7.41 (9'-H), δ = 120.16 (C-10') ↔ δ = 8.00 (10'-H), δ = 129.38 (C-3 and C-5) ↔ δ = 7.32 (3-H and 5-H), δ = 129.83 (C-2 and C-6) ↔ δ = 7.82 (2-H and 6-H), δ = 191.68 (1-CHO) ↔ δ = 9.99 (1-CHO). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 116.48 and 124.39 (C-5'a and C-11'a) ↔ δ = 5.57 (11'b-H), δ = 116.48 and 124.39 (C-5'a and C-11'a) ↔ δ = 6.41 (5'-H) could not be assigned unambiguously], δ = 125.09 (C-6'a) ↔ δ = 8.00 (10'-H), δ = 125.40 (C-10'a) ↔ δ = 7.41 (9'-H), δ = 136.36 (C-1) ↔ δ = 7.32 (3-H and 5-H), δ = 136.36 (C-1) ↔ δ = 9.99 (1-C*H*O), δ = 143.08 (C-7') ↔ δ = 3.81 (7'-OMe), δ = 143.08 (C-7') ↔ δ = 7.41 (9'-H), δ = 143.08 (C-7') ↔ δ = 8.00 (10'-H), δ = 146.21 (C-4) ↔ δ = 6.41 (5'-H), δ = 146.21 (C-4) ↔ δ = 7.82 (2-H and 6-H), δ = 147.23 (C-6') ↔ δ = 3.60 (6'-OMe), δ = 147.23 (C-6') ↔ δ = 6.41 (5'-H), δ = 151.66 (C-8') ↔ δ = 4.04 (8'-OMe), δ = 151.66 (C-8') ↔ δ = 7.41 (9'-H), δ = 151.66 (C-8') ↔ δ = 8.00 (10'-H), δ = 153.92 (C-11') ↔ δ = 4.13 (11'-OMe), δ = 153.92 (C-11') ↔ δ = 5.57 (11'b-H), δ = 153.92 (C-11') ↔ δ = 8.00 (10'-H), δ = 174.97 (C-2') ↔ [δ_A = 2.68 (3'-H^A) and δ_B = 2.85 (3'-H^B)], δ = 174.97 (C-2') ↔ 4.24 (3'a-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = –318.5 (*c* = 0.483, $CHCl_3$). **HRMS** (pos. APCI): calcd. for $C_{26}H_{25}O_8$ $[M+H]^+$ = 465.15439; found 465.15408 (–0.66 ppm). **IR (film):** *v* = 2940, 2845, 1785, 1700, 1665, 1605, 1575, 1505, 1455, 1425, 1360, 1335, 1275, 1205, 1155, 1085, 1065, 1050, 990, 905, 885 840, 810, 735 cm^{-1}.

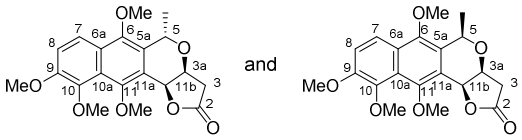
(3a*S*,3a'*S*,5*S*,5'*S*,11b*S*,11b'*S*)-5,5'-(1,4-Phenylene)bis(7,8-dimethoxy-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene-2,6,11-trione) (45)



Following the **General Procedure A** the title compound was prepared from **44** (15.8 mg, 19.9 µmol) suspended in MeCN (1 mL) and a solution of $(NH_4)_2Ce(NO_3)_6$ (43.6 mg, 79.6 µmol, 4.0 equiv.) in H_2O (1 mL). Purification by flash chromatography (d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 1:1) afforded the title compound [F15-26, R_f (1:1) = 0.2, 10.8 mg, 74%, *dr* = 100:0] as an orange solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.62, δ_B = 2.83, J_{AB} = 17.9 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.3 Hz, 2×3-H^A and 2×3-H^B), 3.86 (s, 2×3H, 2×7-OMe), 3.98 (s, 2×3H, 2×8-OMe), 4.26 (dd, 2×1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.1 Hz, 2×3a-H), 5.23 (d, 2×1H, $J_{11b,3a}$ = 3.1 Hz, 2×11b-

H), 6.01 (s, 2×1H, 2×5-H), 7.24 (br. s, 4H, 2'-H, 3'-H, 5'-H and 6'-H), 7.24 (d, 2×1H, $J_{9,10}$ = 8.7 Hz, 2×9-H), 8.02 (d, 2×1H, $J_{10,9}$ = 8.9 Hz, 2×10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.83 (3-H^B) ↔ δ = 5.23 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.98 (8-OMe) ↔ δ = 7.24 (9-H), δ = 7.24 (2'-H, 3'-H, 5'-H and 6'-H) ↔ δ = 4.26 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.24 (2'-H, 3'-H, 5'-H and 6'-H) ↔ δ = 6.01 (5-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 36.63 (2×C-3), 56.48 (2×8-O*C*H$_3$), 61.30 (2×7-O*C*H$_3$), 67.15 (2×C-3a), 69.01 (2×C-11b), 71.60 (2×C-5), 116.45 (2×C-9), 124.21 (2×C-6a), 125.21 (2×C-10), 125.39 (2×C-10a), 129.11 (C-2', C-3', C-5' and C-6'), 135.66 and 147.09 (2×C-5a and 2×C-11a), 137.28 (C-1' and C-4'), 149.77 (2×C-7), 159.42 (2×C-8), 173.97 (2×C-2), 181.13 (2×C-11), 182.04 (2×C-6). An **edHSQC** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 36.63 (C-3) ↔ [δ_A = 2.65 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 56.48 (8-O*C*H$_3$) ↔ δ = 3.98 (8-OMe), δ = 61.30 (7-O*C*H$_3$) ↔ δ = 3.86 (7-OMe), δ = 67.15 (C-3a) ↔ δ = 4.26 (3a-H), δ = 69.01 (C-11b) ↔ δ = 5.23 (11b-H), δ = 71.60 (C-5) ↔ δ = 6.01 (5-H), δ = 116.45 (C-9) ↔ δ = 7.24 (9-H), δ = 125.21 (C-10) ↔ δ = 8.02 (10-H), δ = 129.11 (C-2', C-3', C-5' and C-6') ↔ δ = 7.24 (2'-H, 3'-H, 5'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 124.21 (C-6a) ↔ δ = 8.02 (10-H), δ = 125.39 (C-10a) ↔ δ = 7.24 (9-H), [δ = 135.66 and 147.09 (C-5a and C-11a) ↔ δ = 5.23 (11b-H), δ = 135.66 and 147.09 (C-5a and C-11a) ↔ δ = 6.01 (5-H), δ = 137.28 (C-1' and C-4') ↔ δ = 7.24 (2'-H, 3'-H, 5'-H and 6'-H), δ = 149.77 (C-7) ↔ δ = 3.86 (7-OMe), δ = 149.77 (C-7) ↔ δ = 7.24 (9-H), δ = 159.42 (C-8) ↔ δ = 3.98 (8-OMe), δ = 159.42 (C-8) ↔ δ = 7.24 (9-H), δ = 159.42 (C-8) ↔ δ = 8.02 (10-H), δ = 173.97 (C-2) ↔ [δ_A = 2.62 (3-H^A) and δ_B = 2.83 (3-H^B)], δ = 173.97 (C-2) ↔ 4.26 (3a-H). δ = 181.13 (C-11) ↔ δ = 8.02 (10-H), δ = 182.04 (C-6) ↔ δ = 6.01 (5-H). **Optical rotation:** $[\alpha]_D^{20}$ = –303.0 (*c* = 0.3, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{40}H_{30}O_{14}Na$ $[M+Na]^+$ = 757.15278; found 757.15216 (–0.81 ppm). **IR (film):** *v* = 2935, 2850, 1785, 1665, 1575, 1485, 1455, 1400, 1335, 1275, 1230, 1200, 1155, 1095, 1080, 1050, 1020, 1000, 975, 945, 910, 885, 820, 680 cm^{-1}.

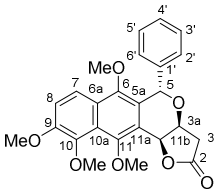
(3a*S*,5*S*,11b*S*)-6,7,8,11-Tetramethoxy-5-methyl-3,3a,5,11b-tetrahydro2*H*-benzo[*g*]furo[3,2-*c*]isochomen-2-one (46a) and (3a*S*,5*R*,11b*S*)-6,7,8,11-Tetramethoxy-5-methyl-3,3a,5,11b-tetrahydro2*H*-benzo[*g*]furo[3,2-*c*]isochomen-2-one (5-*epi*-46a)



Procedure 1) Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **16** (38.1 mg, 109 µmol), acetaldehyde (50 µL, 39 mg, 0.89 mmol, 8.0 equiv.) and $BF_3{\cdot}OEt_2$ (140 µL, 161 mg, 1.13 mmol, 10 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 13.5 cm, F = 8 mL; CH/EE 2:1 (F1-20), 1:1 (21-30)] afforded the title compounds [F9-11, R_f (CH/EE 1:1) = 0.50, 11.1 mg, 27%, *dr* = 96:4] as a pale-yellow oil as well as a second fraction [F12-19, 14.7 mg, 36%, *dr* = 69:31]. Combined yield: 25.8 mg, 63%, *ds* = 81:19. Procedure 2) Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **16** (19.7 mg, 56.6 µmol), acetaldehyde dimethyl acetal (48 µL, 41 mg, 0.45 mmol, 8.0 equiv.)and $BF_3{\cdot}OEt_2$ (70 µL, 81 mg, 0.57 mmol, 10 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 13 cm, F = 8 mL; CH_2Cl_2/TBME 20:1 (F1-28), 9:1 (29-36)] afforded the title compounds [F9-15, R_f (CH_2Cl_2/TBME 20:1) = 0.50, 16.0 mg, 75%] as a pale-yellow oil and as a 52:48 diastereomeric mixture of **46a** and 5-*epi*-**46a**.– NMR analysis of **46a**: **^{1}H-NMR** (500.32 MHz, $CDCl_3$): δ = 1.55 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.8 Hz, 5-CH_3), AB signal [δ_A = 2.71 and δ_B = 2.98, J_{AB} = 17.4 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 4.9 Hz, 3-H^A and 3-H^B), 3.89 (s, 3H, 10-OMe), 3.91 (s, 3H, 6-OMe), 4.00 (s, 3H, 11-OMe), 4.02 (s, 3H, 9-OMe), 4.74 (dd, 1H, $J_{3a,B}$ = 4.9 Hz, $J_{3a,11b}$ = 2.7 Hz, 3a-H), 5.32 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.8 Hz, 5-H), 5.62 (d, 1H, $J_{11b,3a}$ = 2.6 Hz, 11b-H), 7.39 (d, 1H, $J_{8,7}$ = 9.2 Hz, 8-H), 7.84 (d, 1H, $J_{7,8}$ = 9.2 Hz, 7-H). 6-OMe, 9-OMe and 11-OMe were distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 1.55 (5-CH_3) ↔ δ = 4.74 (3a-H, this cross-peak proves that 5-CH_3 and 3a-H are oriented *cis* relative to one another), δ = 3.91 (6-OMe) ↔ δ = 5.32 (5-H), δ = 3.91 (6-OMe) ↔ δ = 7.84 (7-H), δ = 4.02 (9-OMe) ↔ δ = 7.39 (8-H), δ = 4.00 (11-OMe) ↔ δ = 5.62 (11b-H). **^{13}C-NMR** (125.81 MHz, $CDCl_3$): δ = 19.86 (5-CH_3), 38.07 (C-3), 56.88 (9-OCH_3), 61.92 (6-OCH_3), 62.14 (10-OCH_3), 64.60 (11-OCH_3), 66.54 (C-3a), 67.77 (C-5), 72.40 (C-11b), 115.90 or 115.91 (C-8)*, 119.09 (C-11a), 119.16 (C-7), 123.73 (C-10a), 125.57 (C-5a), 126.25 (C-6a), 143.44 (C-10), 147.14 (C-6), 150.51 (C-9), 152.55 or 152.59 (C-11)*, 175.50 (C-2). *Assignment to the appropriate diastereomer impossible. An **edHSQC** spectrum ("short-range C,H, COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 19.86 (5-CH_3) ↔ δ = 1.55 (5-C*H*$_3$), δ = 38.07 (C-3) ↔ δ_A = 2.71 and δ_B = 2.98 (3-H^A and 3-H^B), δ = 56.88 (9-OCH_3) ↔ δ = 4.02 (9-OMe), δ = 61.92 (6-OCH_3) ↔ δ = 3.91 (6-OMe), δ = 62.14 (10-OCH_3) ↔ δ = 3.89 (10-OMe), δ = 64.60 (11-OCH_3) ↔ δ = 4.00 (11-OMe), δ = 66.54 (C-3a) ↔ δ = 4.74 (3a-H), δ = 67.77 (C-5) ↔ δ = 5.32 (5-H), δ = 72.40 (C-11b) ↔ δ = 5.62 (11b-H), δ = 115.90 or 115.91 (C-8) *↔ δ = 7.39 (8-H), δ = 119.16 (C-7) ↔ δ = 7.84 (7-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 119.09 (C-11a) ↔ δ = 5.32 (5-H), δ = 119.09 (C-11a) ↔ δ = 5.62 (11b-H), δ = 123.73 (C-10a) ↔ δ = 7.84 (7-H), δ = 125.57 (C-5a) ↔ δ = 1.55 (5-C*H*$_3$), δ = 125.57 (C-5a) ↔ δ = 5.32 (5-H), δ = 125.57 (C-5a) ↔ δ = 5.62 (11b-H), δ = 126.25 (C-6a) ↔ δ = 7.39 (8-H), δ = 143.44 (C-10) ↔ δ = 3.89 (10-OMe), δ = 143.44 (C-10) ↔ δ = 7.39 (8-H), δ = 147.14 (C-6) ↔ δ = 3.91 (6-OMe), δ = 147.14 (C-6) ↔ δ = 5.32 (5-H), δ = 147.14 (C-6) ↔ δ = 7.84 (7-H), δ = 150.51 (C-9) ↔ δ = 4.02 (9-OMe), δ = 150.51 (C-9) ↔ δ = 7.39 (8-H), δ = 150.51 (C-9) ↔ δ = 7.84 (7-H), δ = 152.55 or 152.59 (C-11)* ↔ δ = 4.00 (11-OMe), δ = 152.55 or 152.59 (C-11)* ↔ δ = 5.62 (11b-H), δ = 175.50 (C-2) ↔ δ_A = 2.71 (3-H^A), δ = 175.50 (C-2) ↔ δ_B = 2.98 (3-H^B), δ = 175.50 (C-2) ↔ δ = 4.74 (3a-H) .– NMR analysis of 5-*epi*-**46a**: **^{1}H-NMR** (500.32 MHz, $CDCl_3$): δ = 1.73 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.3 Hz, 5-CH_3), AB signal (δ_A = 2.77 and δ_B = 2.91, J_{AB} = 17.3 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,3a}$ = 4.5 Hz, 3-H^A and 3-H^B), 3.80 (s, 3H, 6-OMe), 3.91 (s, 3H, 10-OMe), 4.01 (s, 3H, 9-OMe), 4.02 (s, 3H, 11-OMe), 4.38 (dd, 1H, $J_{3a,B}$ = 4.3 Hz, $J_{3a,11b}$ = 2.4 Hz, 3a-H), 5.01 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.3 Hz, 5-H), 5.61 (d, 1H, $J_{11b,3a}$ = 2.3 Hz, 11b-H), 7.39 (d, 1H, $J_{8,7}$ = 9.2 Hz, 8-H), 7.89 (d, 1H, $J_{7,8}$ = 9.2 Hz, 7-H). 6-OMe, 9-OMe and 11-OMe were distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 5.01 (5-H) ↔ δ = 4.38 (3a-H, this cross-peak proves that 5-H and 3a-H are oriented *cis* relative to one another), δ = 3.80 (6-OMe) ↔ δ = 5.01 (5-H), δ = 3.80 (6-OMe) ↔ δ = 7.89 (7-H), δ = 4.01 (9-OMe) ↔ δ = 7.39 (8-H), δ = 4.02 (11-OMe) ↔ δ = 5.61 (11b-H). **^{13}C-NMR** (125.81 MHz, $CDCl_3$): δ = 21.52 (5-CH_3), 38.43 (C-3), 56.84 (9-OCH_3), 61.04 (6-OCH_3), 62.14 (10-OCH_3), 64.73 (11-OCH_3), 70.12 (C-5), 72.07 (C-3a), 73.56 (C-11b), 115.90 or 115.91 (C-8) *, 119.29 (C-7), 120.31 (C-11a), 123.86 (C-10a), 125.76 (C-5a) 126.70 (C-6a) 143.24 (C-10) 148.46 (C-6) 150.65 (C-9), 152.55 or 152.59 (C-11)*, 175.68 (C-2). *Assignment to the appropriate diastereomer impossible. An **edHSQC** spectrum ("short-range C,H, COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 21.52 (5-CH_3) ↔ δ = 1.73 (5-C*H*$_3$), δ = 38.43 (C-3) ↔ δ_A = 2.77 and δ_B = 2.91 (3-H^A and 3-H^B), δ = 56.84 (9-OCH_3) ↔ δ = 4.02 (9-OMe), δ = 61.04 (6-OCH_3) ↔ δ = 3.80 (6-OMe), δ = 62.14 (10-OCH_3) ↔ δ = 3.91 (10-OMe), δ = 64.73 (11-OCH_3) ↔ δ = 4.01 (11-OMe), δ = 70.12 (C-5) ↔ δ = 5.01 (5-H), δ = 72.07 (C-3a) ↔ δ = 4.38 (3a-H), δ = 73.56 (C-11b) ↔ δ = 5.61 (11b-H), δ = 115.90 or 115.91 (C-8) *↔ δ = 7.39 (8-H), δ = 119.29 (C-7) ↔ δ = 7.89 (7-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 120.31 (C-11a) ↔ δ = 5.01 (5-H), δ = 120.31 (C-11a) ↔ δ = 5.61 (11b-H), δ = 123.86 (C-10a) ↔ δ = 7.89 (7-H), δ = 125.76 (C-5a) ↔ δ = 1.73 (5-C*H*$_3$), δ = 125.76 (C-5a) ↔ δ = 5.01 (5-

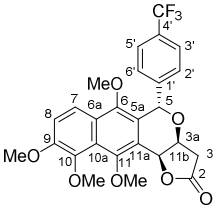
H), δ = 125.76 (C-5a) ↔ δ = 5.61 (11b-H), δ = 126.70 (C-6a) ↔ δ = 7.39 (8-H), δ = 143.24 (C-10) ↔ δ = 3.91 (10-OMe), δ = 143.24 (C-10) ↔ δ = 7.39 (8-H), δ = 148.46 (C-6) ↔ δ = 3.80 (6-OMe), δ = 148.46 (C-6) ↔ δ = 5.01 (5-H), δ = 148.46 (C-6) ↔ δ = 7.89 (7-H), δ = 150.65 (C-9) ↔ δ = 4.01 (9-OMe), δ = 150.65 (C-9) ↔ δ = 7.39 (8-H), δ = 150.65 (C-9) ↔ δ = 7.89 (7-H), δ = 152.55 or 152.59 (C-11)* ↔ δ = 4.02 (11-OMe), δ = 152.55 or 152.59 (C-11)* ↔ δ = 5.61 (11b-H), δ = 175.68 (C-2) ↔ δ_A = 2.77 (3-H^A), δ = 175.68 (C-2) ↔ δ_B = 2.91 (3-H^B), δ = 175.68 (C-2) ↔ δ = 4.38 (3a-H). **Melting point:** Oil. **HRMS** (pos. ESI): Calcd. for $C_{20}H_{22}O_7$ $[M+H]^+$ = 375.14383; found 375.14389 (+0.16 ppm).

(3a*S*,5*S*,11b*S*)-5-Phenyl-6,9,10,11-tetramethoxy-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (46b)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **16** (30.0 mg, 86.1 µmol), benzaldehyde (27 µL, 27 mg, 0.26 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (42 µL, 49 mg, 0.34 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 13.5 cm, F = 8 mL; CH/EE 3:1 (F1-18), 1:1 (19-24)] afforded the pure product [F11-21, R_f (1:1) = 0.65, 32.2 mg, 86%, *ds* = 100:0] as yellow oil.– **^{1}H-NMR** (500.32 MHz, $CDCl_3$, spectrum contains water with br. s at δ = 1.57 ppm and grease with resonances at δ = 0.85 and 1.25 ppm): AB signal (δ_A = 2.66 and δ_B = 2.84, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.0 Hz, 3-H$^{A`}$ and 3-H^B), 3.67 (s, 3H, 6-OMe), 3.95 (s, 3H, 10-OMe), 4.03 (s, 3H, 9-OMe), 4.05 (s, 3H, 11-OMe), 4.33 (dd, 1H, $J_{3a,B}$ = 5.0 Hz, $J_{3a,11b}$ = 2.8 Hz, 3a-H), 5.61 (d, 1H, $J_{11b,3a}$ = 2.8 Hz, 11b-H), 6.30 (s, 1H, 5-H), 7.10-7.15 (m, 2H, 2'-H and 6'-H), 7.28-7.32 (m, 3H, 3'-H, 4'-H and 5'-H), 7.41 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H), 7.84 (d, 1H, $J_{7,8}$ = 9.3 Hz, 7-H). 6-OMe, 9-OMe and 11-OMe were distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 2.84 (3-H^B) ↔ δ = 5.61 (11b-H, this cross-peak proves that the 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.10-7.15 (2'-H and 6'-H) ↔ δ = 4.33 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.10-7.15 (2'-H and 6'-H) ↔ δ = 6.30 (5-H), δ = 3.67 (6-OMe) ↔ δ = 6.30 (5-H), δ = 3.67 (6-OMe) ↔ δ = 7.84 (7-H), δ = 4.03 (9-OMe) ↔ δ = 7.41 (8-H), δ = 4.05 (11-OMe) ↔ δ = 5.61 (11b-H). **^{13}C-NMR** (125.81 MHz, $CDCl_3$): δ = 37.68 (C-3), 56.89 (9-OCH_3), 61.88 (6-OCH_3), 62.22 (10-OCH_3), 64.75 (11-OCH_3), 67.19 (C-3a), 72.65 (C-11b), 72.98 (C-5), 115.92 (C-8), 119.48 (C-7), 120.27 and 121.81 (C-5a and C-11a), 124.26 (C-10a), 126.02 (C-6a), 128.46 and 128.53 (C-3', C-4' and C-5'), 128.72 (C-2' and C-6'), 139.22 (C-1'), 143.53 (C-10), 148.11 (C-6), 150.78 (C-9), 152.66 (C-11),175.38 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 37.68 (C-3) ↔ δ_A = 2.66 and δ_B = 2.84 (3-H^A and 3-H^B), δ = 56.89 (9-OCH_3) ↔ δ = 4.03 (9-OMe), δ = 61.88 (6-OCH_3) ↔ δ = 3.67 (6-OMe), δ = 62.22 (10-OCH_3) ↔ δ = 3.95 (10-OMe), δ = 64.75 (11-OCH_3) ↔ δ = 4.05 (11-OMe), δ = 67.19 (C-3a) ↔ δ = 4.33 (3a-H), δ = 72.65 (C-11b) ↔ δ = 5.61 (11b-H), δ = 72.98 (C-5) ↔ δ = 6.30 (5-H), δ = 115.92 (C-8) ↔ δ = 7.41 (8-H), δ = 119.48 (C-7) ↔ δ = 7.84 (7-H), δ = 128.46 and 128.53 (C-3', C-4' and C-5') ↔ δ = 7.28-7.35 (3'-H, 4'-H and 5'-H), δ = 128.72 (C-2' and C-6') ↔ δ = 7.10-7.15 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 120.27 and 121.81 (C-5a and C-11a) ↔ δ = 5.61 (11b-H), δ = 120.27 and 121.81 (C-5a and C-11a) ↔ δ = 6.30 (5-H) could not be assigned unambiguously], δ = 124.26 (C-10a) ↔ δ = 7.81 (7-H), δ = 126.02 (C-6a) ↔ δ = 7.41 (8-H), δ = 139.22 (C-1') ↔ δ = 6.30 (5-H), δ = 139.22 (C-1') ↔ δ = 7.28-7.35 (3'-H, 4'-H and 5'-H), δ = 143.53 (C-10) ↔ δ = 3.95 (10-OMe), δ = 143.53 (C-10) ↔ δ = 7.41 (8-H), δ = 143.53 (C-10) ↔ δ = 7.84 (7-H), δ = 148.11 (C-6) ↔ δ = 3.67 (6-OMe), δ = 148.11 (C-6) ↔ δ = 6.30 (5-H), δ = 148.11 (C-6) ↔ δ = 7.84 (7-H), δ = 150.78 (C-9) ↔ δ = 4.03 (9-OMe), δ = 150.78 (C-9) ↔ δ = 7.41 (8-H), δ = 150.78 (C-9) ↔ δ = 7.84 (7-H), δ = 152.66 (C-11) ↔ δ = 4.05 (11-OMe), δ = 152.66 (C-11) ↔ δ = 5.61 (11b-H), δ = 175.38 (C-2) ↔ δ_A = 2.66 (3-H^A), δ = 175.38 (C-2) ↔ δ_B = 2.84 (3-H^B), δ = 175.38 (C-2) ↔ δ = 4.33 (3a-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = −311.7 (c = 0.870, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{25}H_{24}O_7$ $[M+NH_4]^+$ = 454.18603; found 454.18570 (−0.72 ppm). **IR (film):** v = 2930, 2845, 1780, 1615, 1595, 1505, 1495, 1465, 1450, 1425, 1410, 1365, 1340, 1295, 1275, 1225, 1200, 1155, 1130, 1110, 1085, 1065, 1050, 1040, 990, 950, 915, 905, 885, 810, 735, 700 cm^{-1}.

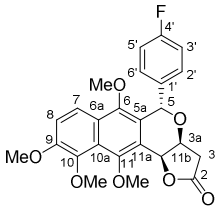
(3a*S*,5*S*,11b*S*)-6,9,10,11-Tetramethoxy-5-(4-(trifluoromethyl)phenyl)-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3, 2-*c*]isochromen-2-one (46c)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **16** (28.2 mg, 81.0 µmol), 4-(trifluoromethyl)benzaldehyde (33 µL, 42 mg, 0.24 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (41 µL, 46 mg, 0.32 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 13.5 cm, F = 8 mL; CH/EE 5:1 (F1-12), 3:1 (13-34)] afforded the pure title compound [F16-20, R_f (2:1) = 0.40, 24.1 mg, 60%] as a colorless oil.– **^{1}H-NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.68 and δ_B = 2.86, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.0 Hz, 3-H^A and 3-H^B), 3.75 (s, 3H, 6-OMe), 3.95 (s, 3H, 10-OMe), 4.04 (s, 3H, 9-OMe), 4.05 (s, 3H, 11-OMe), 4.25 (dd, 1H, $J_{3a,B}$ = 4.9 Hz, $J_{3a,11b}$ = 2.7 Hz, 3a-H), 5.60 (d, 1H, $J_{11b,3a}$ = 2.7 Hz, 11b-H), 6.30 (s, 1H, 5-H), 7.26 (br.d, 2H, $J_{3',2'}$ = $J_{5',6'}$ = 7.9 Hz, 2'-H and 6'-H), 7.43 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H), 7.56 (br.d, 2H, $J_{2',3'}$ = $J_{6',5'}$ = 8.1 Hz, 3'-H and 5'-H), 7.85 (d, 1H, $J_{7,8}$ = 9.3 Hz, 7-H). 6-OMe, 9-OMe and 11-OMe were distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 2.86 (3-H^B) ↔ δ = 5.60 (11b-H, this cross-peak proves that the 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.26 (2'-H and 6'-H) ↔ δ = 4.25 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.26 (2'-H and 6'-H) ↔ δ = 6.30 (5-H), δ = 3.75 (6-OMe) ↔ δ = 6.30 (5-H), δ = 3.75 (6-OMe) ↔ δ = 7.85 (7-H), δ = 4.04 (9-OMe) ↔ δ = 7.43 (8-H), δ = 4.05 (11-OMe) ↔ δ = 5.60 (11b-H). **^{19}F-NMR** (470.77 MHz, $CDCl_3$): δ = −62.68 (s, 3F, CF_3). **^{13}C-NMR** (125.81 MHz, $CDCl_3$): δ = 36.67 (C-3), 56.88 (9-OCH_3), 61.98 (6-OCH_3), 62.21 (10-OCH_3), 64.80 (11-OCH_3), 67.59 (C-3a), 72.35 and 72.37 (C-5 and C-11b), 116.10 (C-8), 119.46 (C-7), 119.87 and 120.66 (C-5a and C-11a), 124.00 (q, 1C.$^1J_{C,F}$ = 272.2 Hz, CF_3), 124.51 (C-10a), 125.53 (q, 2C.$^3J_{C,F}$ = 3.6 Hz, C-3' and C-5'), 125.90 (C-6a), 128.91 (C-2' and C-6'), 130.63 (q, 1C.$^2J_{C,F}$ = 32.5 Hz, C-4'), 143.11 (C-1'), 143.58 (C-10), 148.19 (C-6), 151.01 (C-9), 152.94 (C-11), 175.08 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 36.67 (C-3) ↔ δ_A = 2.68 and δ_B = 2.86 (3-H^A and 3-H^B), δ = 56.88 (9-OCH_3) ↔ δ = 4.04 (9-OMe), δ = 61.98 (6-OCH_3) ↔ δ = 3.75 (6-OMe), δ = 62.21 (10-OCH_3) ↔ δ = 3.95 (10-OMe), δ = 64.80 (11-OCH_3) ↔ δ = 4.05 (11-OMe), δ = 67.59 (C-3a) ↔ δ = 4.25 (3a-H), [δ = 72.35 and

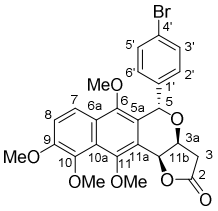
72.37 (C-5 and C-11b) ↔ δ = 5.60 (11b-H) and δ = 6.30 (5-H) could not be assigned unambiguously], δ = 116.10 (C-8) ↔ δ = 7.43 (8-H), δ = 119.46 (C-7) ↔ δ = 7.85 (7-H), δ = 125.53 (q, 2C. $^3J_{C,F}$ = 3.6 Hz, C-3' and C-5') ↔ δ = 7.56 (3'-H and 5'-H), δ = 128.91 (C-2' and C-6') ↔ δ = 7.26 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C)$ ↔ $\delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 119.87 and 120.66 (C-5a and C-11a) ↔ δ = 5.60 (11b-H), δ = 119.87 and 120.66 (C-5a and C-11a) ↔ δ = 6.30 (5-H) could not be assigned unambiguously], δ = 124.51 (C-10a) ↔ δ = 7.85(7-H), δ = 125.90 (C-6a) ↔ δ = 7.43 (8-H), δ = 143.11 (C-1') ↔ δ = 6.30 (5-H), δ = 143.11 (C-1') ↔ δ = 7.56 (3'-H and 5'-H), δ = 143.58 (C-10) ↔ δ = 3.95 (10-OMe), δ = 143.58 (C-10) ↔ δ = 7.43 (8-H), δ = 143.58 (C-10) ↔ δ = 7.85 (7-H), δ = 148.19 (C-6) ↔ δ = 3.75 (6-OMe), δ = 148.19 (C-6) ↔ δ = 6.30 (5-H), δ = 148.19 (C-6) ↔ δ = 7.85 (7-H), δ = 151.01 (C-9) ↔ δ = 4.04 (9-OMe), δ = 151.01 (C-9) ↔ δ = 7.43 (8-H), δ = 151.01 (C-9) ↔ δ = 7.85 (7-H), δ = 152.94 (C-11) ↔ δ = 5.60 (11b-H), δ = 152.94 (C-11) ↔ δ = 4.05 (11-OMe), δ = 175.08 (C-2) ↔ δ_A = 2.68 (3-H^A), δ = 175.08 (C-2) ↔ δ_B = 2.86 (3-H^B), δ = 175.08 (C-2) ↔ δ = 4.25 (3a-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = −304.5 (c = 0.787, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{26}H_{23}F_3O_7$ $[M+Na]^+$ = 527.12881; found 527.12891 (+0.18 ppm). **IR (film):** v = 2935, 2845, 1785, 1600, 1465, 1450, 1425, 1410, 1365, 1340, 1325, 1295, 1275, 1200, 1160, 1130, 1115, 1090, 1065, 1055, 1040, 1020, 990, 905 cm^{-1}.

(3a*S*,5*S*,11b*S*)-5-(4-Fluorophenyl)-6,9,10,11-tetramethoxy-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (46d)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **16** (29.6 mg, 85.0 μmol), 4-fluorobenzaldehyde (27 μL, 32 mg, 0.26 mmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (42 μL, 49 mg, 0.34 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 5:1 (F1-12), 3:1 (13-40)] afforded the pure title compound [F21-28, R_f (3:1) = 0.15, 33.2 mg, 86%, *ds* = 100:0] as white solid.– **^{1}H-NMR** (500.32 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.66 and δ_B = 2.86, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.0 Hz, 3-H^A and 3-H^B), 3.70 (s, 3H, 6-OMe), 3.94 (s, 3H, 10-OMe), 4.04 (s, 3H, 9-OMe), 4.05 (s, 3H, 11-OMe), 4.29 (dd, 1H, $J_{3a,B}$ = 5.0 Hz, $J_{3a,11b}$ = 2.8 Hz, 3a-H), 5.60 (d, 1H, $J_{11b,3a}$ = 2.7 Hz, 11b-H), 6.27 (s, 1H, 5-H), 6.99 (m_c, 2H, 3'-H and 5'-H), 7.09 (m_c, 2H, 3'-H and 6'-H), 7.41 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H), 7.83 (d, 1H, $J_{7,8}$ = 9.3 Hz, 7-H). 6-OMe, 9-OMe and 11-OMe were distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$), that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H)$ ↔ $\delta(^1H)$]: δ = 2.86 (3-H^B) ↔ δ = 5.60 (11b-H, this cross-peak proves that the 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.09 (2'-H and 6'-H) ↔ δ = 4.29 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.09 (2'-H and 6'-H) ↔ δ = 6.27 (5-H), δ = 3.70 (6-OMe) ↔ δ = 6.27 (5-H), δ = 3.70 (6-OMe) ↔ δ = 7.83 (7-H), δ = 4.04 (9-OMe) ↔ δ = 7.41 (8-H), δ = 4.05 (11-OMe) ↔ δ = 5.60 (11b-H). **^{19}F-NMR** (470.77 MHz, $CDCl_3$): δ = −113.56 (m, 1F, 4'-F). **^{13}C-NMR** (125.81 MHz, $CDCl_3$): δ = 37.65 (C-3), 56.88 (9-OCH_3), 61.92 (6-OCH_3), 62.20 (10-OCH_3), 64.78 (11-OCH_3), 67.13 (C-3a), 72.26 (C-5), 72.51 (C-11b), 115.44 (d, 2C, $^2J_{C,F}$ = 21.6 Hz, C-3' and C-5'), 116.00 (C-8), 119.45 (C-7), 120.06 and 121.52 (C-5a and C-11a), 124.35 (C-10a), 125.96 (C-6a), 130.39 (d, 2C, $^3J_{C,F}$ = 8.7 Hz, C-2' and C-6'), 135.10 (d, 1C, $^4J_{C,F}$ = 3.3 Hz, C-1'), 143.54 (C-10), 148.06 (C-6), 150.87 (C-9), 152.78 (C-11), 162.68 (d, 1C, $^1J_{C,F}$ = 247.5 Hz, C-4'), 175.26 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C)$ ↔ $\delta(^1H)$]: δ = 37.65 (C-3) ↔ δ_A = 2.66 and δ_B = 2.85 (3-H^A and 3-H^B), δ = 56.88 (9-OCH_3) ↔ δ = 4.04 (9-OMe), δ = 61.92 (6-OCH_3) ↔ δ = 3.70 (6-OMe), δ = 62.20 (10-OCH_3) ↔ δ = 3.94 (10-OMe), δ = 64.78 (11-OCH_3) ↔ δ = 4.05 (11-OMe), δ = 67.13 (C-3a) ↔ δ = 4.29 (3a-H), δ = 72.26 (C-5) ↔ δ = 6.27 (5-H), δ = 72.51 (C-11b) ↔ δ = 5.60 (11b-H), δ = 115.44 (d, 2C, $^2J_{C,F}$ = 21.6 Hz, C-3' and C-5') ↔ δ = 6.99 (3'-H and 5'-H), δ = 116.00 (C-8) ↔ δ = 7.41 (8-H), δ = 119.45 (C-7) ↔ δ = 7.83 (7-H), δ = 130.39 (d, 2C, $^3J_{C,F}$ = 8.7 Hz, C-2' and C-6') ↔ δ = 7.09 (2'-H and 6'-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.32 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C)$ ↔ $\delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 120.06 and 121.52 (C-5a and C-11a) ↔ δ = 5.60 (11b-H), δ = 120.06 and 121.52 (C-5a and C-11a) ↔ δ = 6.27 (5-H) could not be assigned unambiguously], δ = 124.35 (C-10a) ↔ δ = 7.83(7-H), δ = 125.96 (C-6a) ↔ δ = 7.41 (8-H), δ = 143.54 (C-10) ↔ δ = 3.94 (10-OMe), δ = 143.54 (C-10) ↔ δ = 7.41 (8-H), δ = 143.54 (C-10) ↔ δ = 7.83 (7-H), δ = 148.06 (C-6) ↔ δ = 3.70 (6-OMe), δ = 148.06 (C-6) ↔ δ = 6.27 (5-H), δ = 148.06 (C-6) ↔ δ = 7.83 (7-H), δ = 150.87 (C-9) ↔ δ = 4.04 (9-OMe), δ = 150.87 (C-9) ↔ δ = 7.41 (8-H), δ = 150.87 (C-9) ↔ δ = 7.83 (7-H), δ = 152.78 (C-11) ↔ δ = 4.05 (11-OMe), δ = 152.78 (C-11) ↔ δ = 5.60 (11b-H), δ = 162.68 (d, 1C, $^1J_{C,F}$ = 247.5 Hz, C-4') ↔ δ = 6.98 (3'-H and 5'-H), δ = 162.68 (d, 1C, $^1J_{C,F}$ = 247.5 Hz, C-4') ↔ δ = 7.09 (2'-H and 6'-H), δ = 175.26 (C-2) ↔ δ_A = 2.66 (3-H^A), δ = 175.26 (C-2) ↔ δ_B = 2.86 (3-H^B), δ = 175.26 (C-2) ↔ δ = 4.29 (3a-H). **Melting point:** 111°C. **Optical rotation:** $[\alpha]_D^{20}$ = −260.7 (c = 1.103, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{25}H_{23}FO_7$ $[M+Na]^+$ = 477.13200; found 477.13208 (+0.16 ppm). **IR (film):** v = 1930, 2850, 1780, 1600, 1565, 1505, 1465, 1450, 1425, 1410, 1365, 1340, 1295, 1275, 1225, 1200, 1135, 1110, 1085, 1065, 1050, 1040, 990, 955, 905, 885, 835, 820, 805, 790, 735, 695 cm^{-1}.

(3a*S*,5*S*,11b*S*)-5-(4-Bromophenyl)-6,9,10,11-tetramethoxy-3,3a,5,11b-tetrahydro-2*H*-benzo[g]furo[3,2-*c*]isochromen-2-one (46e)



Following the **General Procedure B** the title compound was prepared from β-hydroxy-γ-lactone **16** (24.8 mg, 71.2 μmol), 4-bromobenzaldehyde (39.5 mg, 213 μmol, 3.0 equiv.) and $BF_3{\cdot}OEt_2$ (36 μL, 40 mg, 0.28 mmol, 4.0 equiv.). Purification by flash chromatography [d = 1.5 cm, h = 13 cm, F = 8 mL; CH/EE 3:1 (F1-20), 2:1 (21-41)] afforded the product [F8-15, R_f (2:1) = 0.25, 26.5 mg, 73%] as pale-yellow oil and as 95:5 diastereomeric mixture of **46e** and 5-*epi*-**46e**.– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = AB signal (δ_A = 2.66 and δ_B = 2.85, J_{AB} = 17.5 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 5.0 Hz, 3-H^A and 3-H^B), 3.71 (s, 3H, 6-OMe), 3.94 (s, 3H, 10-OMe), 4.04 (s, 3H, 9-OMe), 4.05 (s, 3H, 11-OMe), 4.27 (dd, 1H, $J_{3a,B}$ = 4.9 Hz, $J_{3a,11b}$ = 2.7 Hz, 3a-H), 5.59 (d, 1H, $J_{11b,3a}$ = 2.8 Hz, 11b-H), 6.23 (s, 1H, 5-H), 7.00 (m_c, 2H, 2`-H and 6`-H), 7.41 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H), 7.43 (m_c, 2H, 3`-H and 5`-H), 7.83 (d, 1H, $J_{7,8}$ = 9.2 Hz, 7-H). 6-OMe, 9-OMe and 11-OMe were distinguished from 10-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (400.13 MHz, $CDCl_3$), that allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H)$ ↔ $\delta(^1H)$]: δ_B = 2.85 (3-H^B) ↔ δ = 5.59 (11b-H, this cross-peak proves that the 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 7.00 (2`-H and 6`-H) ↔ δ = 4.27 (3a-H, this cross-peak proves that the phenyl ring and 3a-H are oriented *cis* relative to one another), δ = 7.00 (2`-H and 6`-H) ↔ δ = 6.23

(5-H), δ = 3.71 (6-OMe) ↔ δ = 6.23 (5-H), δ = 3.71 (6-OMe) ↔ δ = 7.83 (7-H), δ = 4.04 (9-OMe) ↔ δ = 7.41 (8-H), δ = 4.05 (11-OMe) ↔ δ = 5.59 (11b-H). **^{13}C-NMR** (100.61 MHz, $CDCl_3$): δ = 37.64 (C-3), 56.92 (9-OCH_3), 61.93 (6-OCH_3), 62.19 (10-OCH_3), 64.78 (11-OCH_3), 67.33 (C-3a), 72.36 (C-5), 72.45 (C-11b), 116.13 (C-8), 119.45 (C-7), 120.01 and 121.12 (C-5a and C-11a), 122.62 (C-4`), 124.43 (C-10a), 125.98 (C-6a), 130.33 (C-2` and C-6`), 131.71 (C-3` and C-5`), 138.29 (C-1`), 143.64 (C-10), 148.13 (C-6), 150.94 (C-9), 152.86 (C-11), 175.14 (C-2). An **edHSQC** spectrum ("short-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 37.64 (C-3) ↔ δ_A = 2.66 and δ_B = 2.85 (3-H^A and 3-H^B), δ = 56.92 (9-OCH_3) ↔ δ = 4.04 (9-OMe), δ = 61.93 (6-OCH_3) ↔ δ = 3.71 (6-OMe), δ = 62.19 (10-OCH_3) ↔ δ = 3.94 (10-OMe), δ = 64.78 (11-OCH_3) ↔ δ = 4.05 (11-OMe), δ = 67.33 (C-3a) ↔ δ = 4.27 (3a-H), δ = 72.36 (C-5) ↔ δ = 6.23 (5-H), δ = 72.45 (C-11b) ↔ δ = 5.59 (11b-H), δ = 116.13 (C-8) ↔ δ = 7.41 (8-H), δ = 119.45 (C-7) ↔ δ = 7.83 (7-H), δ = 130.33 (C-2` and C-6`) ↔ δ = 7.00 (2`-H and 6`-H), δ = 131.71 (C-3` and C-5`) ↔ δ = 7.43 (3`-H and 5`-H). An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: [δ = 120.01 and 121.12 (C-5a and C-11a) ↔ δ = 5.59 (11b-H), δ = 120.01 and 121.12 (C-5a and C-11a) ↔ δ = 6.23 (5-H) could not be assigned unambiguously], δ = 122.62 (C-4`) ↔ $\delta$ = 7.00 (2`-H and 6`-H), $\delta$ = 122.62 (C-4`) ↔ δ = 7.43 (3`-H and 5`-H), δ = 124.43 (C-10a) ↔ δ = 7.83 (7-H), δ = 125.98 (C-6a) ↔ δ = 7.41 (8-H), δ = 138.29 (C-1`) ↔ $\delta$ = 6.23 (5-H), $\delta$ = 138.29 (C-1`) ↔ δ = 7.43 (3`-H and 5`-H), δ = 143.64 (C-10) ↔ δ = 3.94 (10-OMe), δ = 143.64 (C-10) ↔ δ = 7.41 (8-H), δ = 143.64 (C-10) ↔ δ = 7.83 (7-H), δ = 148.13 (C-6) ↔ δ = 3.75 (6-OMe), δ = 148.13 (C-6) ↔ δ = 6.23 (5-H), δ = 148.13 (C-6) ↔ δ = 7.83 (7-H), δ = 150.94 (C-9) ↔ δ = 4.04 (9-OMe), δ = 150.94 (C-9) ↔ δ = 7.41 (8-H), δ = 150.94 (C-9) ↔ δ = 7.83 (7-H), δ = 152.86 (C-11) ↔ δ = 4.05 (11-OMe), δ = 152.86 (C-11) ↔ δ = 5.59 (11b-H), δ = 175.14 (C-2) ↔ δ_A = 2.66 (3-H^A), δ = 175.14 (C-2) ↔ δ_B = 2.85 (3-H^B), δ = 175.14 (C-2) ↔ δ = 4.27 (3a-H). **Melting point:** Oil. **Optical rotation:** $[\alpha]_D^{20}$ = −302.9 (c = 0.813, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{25}H_{23}BrO_7$ $[M+H]^+$ = 515.06999; found 515.07007 (+0.15 ppm). **IR (film):** v = 2925, 2850, 1780, 1655, 1595, 1505, 1485, 1460, 1410, 1365, 1340, 1275, 1200, 1155, 1090, 1065, 1055, 1010, 995, 905, 825 cm^{-1}.

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Keywords: arynes • asymmetric dihydroxylation • Diels-Alder addition • naphthalenes • naphthoquinonopyrano-γ-lactones • oxa-Pictet-Spengler cyclization