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Title: Consensus Stereostructures for the Naphthoqui-nonopyrano-gamma-lactone Natural Products (–)-Arizonin B1 and (–)-Arizonin C1. Diastereocontrol of Oxa-Pictet-Spengler Cyclizations

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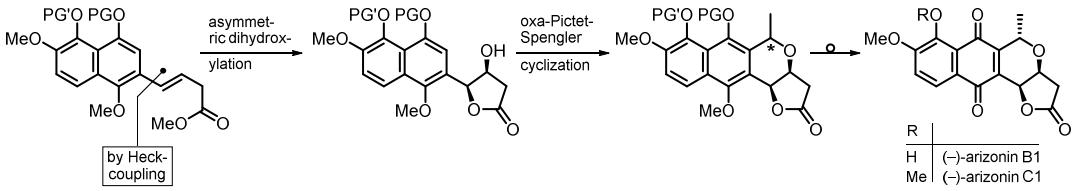
((For Table of Contents:)) Markus Neumeyer, Reinhard Brückner

Establishing Consensus Stereostructures for the Naphthoquinonopyrano-γ-lactone Natural Products (–)-Arizonin B1 and (–)-Arizonin C1 by Total Syntheses. Diastereocontrol of Oxa-Pictet-Spengler Cyclizations by Protective Group Optimization

((Short Title)) Total Syntheses of (–)-Arizonins B1 and C1



Previous total syntheses of the naphthoquinonopyrano-γ-lactone arizonin C1 led to opposite assignments of its absolute configuration. Here we disclose another total synthesis thereof and the first total synthesis of arizonin B1 different than via arizonin C1. The respective stereocenters stemmed from an asymmetric dihydroxylation and an ensuing oxa-Pictet-Spengler cyclization. The correctness of Fernandes´ configurational assignments of arizonin C1 and B1 was thereby ascertained.

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Establishing Consensus Stereostructures for the Naphthoquinonopyrano-γ-lactone Natural Products (–)-Arizonin B1 and (–)-Arizonin C1 by Total Syntheses. Diastereocontrol of Oxa-Pictet-Spengler Cyclizations by Protective Group Optimization

Markus Neumeyer[a] and Reinhard Brückner*[a]

Abstract: Previous total syntheses of arizonin C1 (**4**) led to opposite assignments of its absolute configuration. Here we report the fourth total synthesis thereof. In addition, we disclose the first total synthesis of arizonin B1 (**3**) proceeding differently than via arizonin C1. The stereocenters of the two targets stemmed from an asymmetric dihydroxylation and an ensuing oxa-Pictet-Spengler cyclization. Their configurations were in line with Fernandes' assignments. Protective group variation in the substrate modulated the diastereoselectivity of the Pictet-Spengler cyclization between 77:23 in favor of a *trans*-disubstitution at C-3a vs. C-5 – used for making the natural (–)-arizonins C1 and B1 – and 100:0 in favor of a *cis*-disubstitution – exploited for making the unnatural (+)-5-*epi*-arizonins C1 and B1. All naphthalenes of the present study were derived from the (benzyloxy)methoxynaphthalenediol **27**. It resulted from a Diels-Alder reaction of the aryne **26** with the siloxyfuran **18**.

Background

Naphthoquinonopyrano-γ-lactone natural products have been reviewed repeatedly with regard to their isolation, structure elucidation, biological activity, partial synthesis, and total synthesis.[1] The top line of Figure 1 exemplifies this familiy of compounds by the structures of six "monomers" and one "dimer". The monomers comprise (+)-kalafungin (**1**[2]), its naturally occurring antipode (–)-nanaomycin D (*ent*-**1**[3]), and (+)-frenolicin B (**2**[4]). These compounds are pentasubstituted naphthoquinones or naphthalenes.[5] The six arizonins[6] are "monomeric" naphthoquinonopyrano-γ-lactones from *Actinoplanes arizonaensis sp. nov.* They possess hexasubstituted naphthoquinone – or naphthalene[5] – cores. Figure 1 exemplifies the structures of four such arizonins:[6d] (1) this report's target molecule (–)-arizonin B1 (**3**[6a]), a lactone; (2) this report's target molecule (–)-arizonin C1 (**4**[6a]), another lactone; (3)-(4) the related seco-esters (–)-arizonin B2 (**5**[6a]) and (–)-arizonin C3(!) (**6**[6a]). Dimeric naphthoquinonopyrano-γ-lactone natural products are inherently more complex. Figure 1 illustrates them by (+)-γ-actinorhodin (**7**[7]); each naphthoquinone – or naphthalene[5] – moiety thereof is heptasubstituted.

The relative configurations of the arizonins were assumed to be identical in the entire family because of their common origin.[6a] Moreover, their relative configurations were equalled with that of (+)-kalafungin (**1**[2]).[6a] This was concluded[6a] from pronounced ^{1}H-NMR shift and H,H coupling constant similarities between (–)-arizonin B1 (**3**), (–)-arizonin C1 (**4**), and the reference compound (+)-kalafungin (**1**[2]). I. e., the pyrano-γ-lactone subunits are ^{3a,5}*trans*,^{3a,11b}*cis*-configured throughout. The latter insight was corroborated further[6a] by NOE experiments with (–)-arizonin B1 (**3**). In addition, the ORD spectrum of (–)-arizonin

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[1] 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**, DOI: 10.1002/ejoc.201600544; g) B. J. Naysmith, P. A. Hume, J. Sperry, M. A. Brimble, *Nat. Prod. Rep.* **2016**, DOI: 10.1039/C6NP00080K.

[2] 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 (**1**)].

[3] a) S. Omura, H. Tanaka, Y. Okada, H. Marumo, *J. Chem. Soc., Chem. Commun*. **1976**, 320-321; b) ref.[3a]: "The ORD curve of [(–)-nanaomycin D] shows a negative Cotton effect with a trough [ϕ] –450, at 355 nm and a peak, [ϕ] +640, at 292 nm (c 0.1, MeOH). The ORD curve of [(+)-kalafungin] is the exact reverse of this, with a peak at 355 nm and a trough at 292 nm, suggesting that the absolute configuration of nanaomycin D is as in ... the enantiomer of kalafungin."

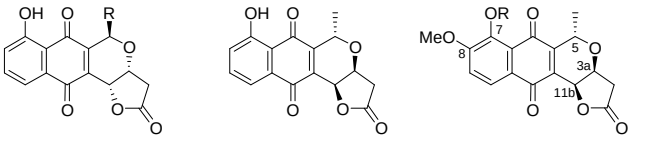
[4] a) Y. Iwai, A. Kora, Y. Takahashi, T. Hayashi, J. Awaya, R. Masuma, R. Oiwa, S. Omura, *J. Antibiot*. **1978**, *31*, 959-965 (without the sign of the specific rotation of natural **2**); b) ref.[4a] describes natural (+)-deoxyfrenolicin B, too; c) according to ref.[14b] synthetic (+)-deoxyfrenolicin B and "deoxyfrenolicin B methyl ester of natural origin" were converted into synthetic (+)-frenolicin B; combined with the finding from ref.[4b] this establishes the dextrorotation of natural **2**.

[5] "Naphthoquinonopyrano-γ-lactones" contain 1,4-naphthoquinone moieties. Unsubstituted 1,4-naphthoquinone has a higher oxidation state than unsubstituted naphthalene. Hence, it seems as if one could – and should – differentiate "naphthoquinones" and "naphthalenes" unambiguously. However, IUPAC nomenclature does not comply with this. In fact, certain substituted naphthoquinones are "dihydro(!)naphthalenes". For instance, (1,4-naphthoquinone-2-yl)–C(=O)–CH_2–O–CH_3 is named 2-(2-methoxyacetyl)-1,4-naphthoquinone while the isomer (1,4-naphthoquinone-2-yl)–C(=O)–O–CH_2–CH_3 is 1,4-dioxo-1,4-dihydronaphthalene-2-carboxylic acid ethyl ester. Accordingly, the present paper does not restrict the notion "naphthalene" to the strictest meaning but comprises naphthoquinone and naphthazarine (= 5,8-dihydroxy-1,4-naphthoquinone) motifs as well.

[6] a) J. E. Hochlowski, G. M. Brill, W. W. Andres, S. G. Spanton, J. B. McAlpine, *J. Antibiot.* **1987**, *40*, 401-407; b) the specific rotation of arizonin B2 (**5**) is not published in ref.[6a]; c) ref.[6a] lacks NMR data of arizonin B2 (**5**) and (–)-arizonin C3 (**6**), which leaves open on which grounds their relative configurations were published as shown in Figure 1; d) Figure 1 shows neither (–)-arizonin A1 nor (–)-arizonin A2. (–)-Arizonin A1 differs from (–)-arizonin B1 (**3**) by swapping OH and OMe, and so does (–)-arizonin A2 vs. (–)-arizonin B2 (**5**).

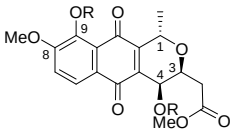
[7] a) Correct structure: A. Zeeck, H. Zähner, M. Mardin, *Liebigs Ann. Chem.* **1974**, 1100-1125; b) tautomeric structure: B. Krone, A. Zeeck, *Liebigs Ann. Chem.* **1987**, 751-758; c) the specific rotation was not determined at a single wavelength; its value at 589 nm can be interpolated from the ORD spectrum (P. Christiansen, *Ph. D. Thesis*, Universität Göttingen, Germany, **1970**; ref.[14b]).

B1 (**3**)[8] was compared[6a] with ORD data both of (+)-kalafungin (**1**)[2b] and (–)-nanaomycin D (*ent*-**1**).[3b] The inferrence was[6a] that their absolute configurations are the same.[9]

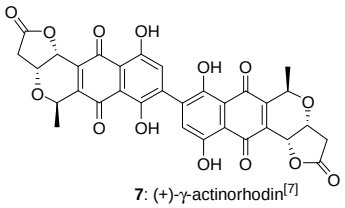


1, R = Me: (+)-kalafungin[2] *ent*-**1**: (–)-nanaomycin D[3]
2, R = *i*Pr: (+)-frenolicin B[4]

3, R = H: (–)-arizonin B1[6]
4, R = Me: (–)-arizonin C1[6]



5, $R_2 = H_2$: arizonin B2[6]
6, $R_2 = Me_2$: (–)-arizonin C3[6]



7: (+)-γ-actinorhodin[7]

Figure 1: Representative naphthoquinonopyrano-γ-lactone natural products: "monomers" (top and bottom left) and a "dimer" (bottom right). Except the arizonins B2 and C3 these compounds have been synthesized prior to the present study. *We* describe the first synthesis of (–)-arizonin B1 (**3**), which does not proceed via (–)-arizonin C1 (**4**), and another synthesis of (–)-arizonin C1 (**4**).

Five of the seven naphthoquinonopyrano-γ-lactone natural products shown in Figure 1 have been a synthetic target so far: kalafungin (**1**),[10,11] nanaomycin D (*ent*-**1**),[12] frenolicin B (**2**),[13,14] arizonin B1 (**3**),[15, 16] arizonin C1 (**4**),[15,16,17,18] and γ-actinorhodin (**7**).[19,20] The current paper contributes one synthesis both of (–)-arizonin B1 (**3**) and (–)-arizonin C1 (**4**).

The arizonin syntheses accomplished to date can be summarized as follows. In the mid-90s Brimble et al. synthesized racemic 5-*epi*-arizonin B1 (*rac*-5-*epi*-**3**),[15] racemic 5-*epi*-arizonin C1 (*rac*-5-*epi*-**4**),[15] and racemic arizonin C1 (*rac*-**4**).[17] In 2011, our group presented the first total synthesis of (–)-arizonin C1.[18] Supposedly it possessed the stereostructure **4** but, in truth, must have been the mirror image thereof. This became clear in 2013. Fernandes then was no longer a member of the earlier team[18a] but a researcher with his own group. He developed a different approach – and realized that the resulting structure *ent*-**4** was (+)-arizonin C1![16] Stunned about the discrepancy he had the key intermediate **4** of the earlier approach[18a] (Scheme 1) processed with AD-mix α (i. e., not, as published,[18a] with AD-mix β). Carrying the resulting product through the remainder of our sequence,[18a] they reached (–)-arizonin C1 (**4**).[16] This was the same enantiomer, which according to our report[18a] stemmed from dihydroxylating the intermediate **4** with AD-mix β. Obviously, we, too, must have converted **4** into (–)-arizonin C1 using AD-mix α. Thus, at some point we confounded a sample made for reaching the *desired* enantiomer **4** with an oppositely configured sample,[18b] which we carried through the identical sequence of steps for calibrating our HPLC analyses of the *ee*'s of the intermediates en route to **4**.

From our perspective making up for this flaw required designing another arizonin C1 synthesis from scratch. The access, which resulted allowed us to reach (–)-arizonin C1 anew. This confirms its stereostructure as **4**, just as deduced by Fernandes.[16] Moreover, our second generation synthesis of (–)-arizonin C1 was adopted to also making (–)-arizonin B1. The latter possesses stereostructure **3**. This is another confirmation of Fernandes' results.[16]

[8] Ref.[6a] neither substantiates this claim by revealing details of the ORD spectrum of (–)-arizonin B1 (**3**) nor details the origin of the "ORD spectrum of (+)-kalafungin" (cf. ref.[2b]!).

[9] Considering that both (–)-arizonin B1 (**3**) and (–)-arizonin C1 (**4**) are levorotatory (ref.[6a]) and (+)-kalafungin (**1**) is dextrorotatory (ref.[2a]) one wonders whether the absolute configurations should not rather be all opposite (cf. the respective deliberations in ref.[18a]).

[10] a) Total syntheses of *rac*-kalafungin (*rac*-**1**): T. Li, R. H. Ellison, *J. Am. Chem. Soc.* **1978**, *100*, 6263-6265; b) G. A. Kraus, H. Cho, S. Crowley, B. Roth, H. Sugimoto, S. Prugh, *J. Org. Chem.* **1983,** *48*, 3439-3444; c) G. A. Kraus, J. Li, M. S. Gordon, J. H. Jensen, *J. Org. Chem.* **1995**, *60*, 1154-1159.

[11] Total syntheses of (+)-kalafungin (**1**): a) K. Tatsuta, K. Akimoto, M. Annaka, Y. Ohno, M. Kinoshita, *Antibiot.* **1985**, 680-682; b) K. Tatsuta, K. Akimoto, M. Annaka, Y. Ohno, M. Kinoshita, *Bull. Chem. Soc. Jpn.* **1985**, *58*, 1699-1706; 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.

[12] Total syntheses of (–)-nanaomycin D (*ent*-**1**): a) Ref.[11a]; b) ref.[11b]; c) M. P.Winters, M. Stranberg, H. W. Moore, *J. Org. Chem.* **1994**, *59*, 7572-7574; d) ref.[11c]; e) N. P.S. Hassan, B. J. Naysmith, J. Sperry, M. A. Brimble, *Tetrahedron* **2015**, *71*, 7137-7143.

[13] Total syntheses of *rac*-frenolicin B (*rac*-**2**): a) A. Ichihara, M. Ubukata, H. Oikawa, K. Murakami, S. Sakamura, *Tetrahedron Lett.* **1980**, *21*, 4469-4472; b) ref.[10c]; c) P. Contant, M. Haess, J. Riegl, M. Scalone, M. Visnick, *Synthesis*, **1999**, 821-828; d) ref.[10c]; e) C. D. Donner, *Synthesis* **2010**, 415-420; f) C. D. Donner, M. I. Casana, *Tetrahedron Letters* **2012**, *53*, 1105-1107.

[14] Total syntheses of (+)-frenolicin B (**2**): a) G. A. Kraus, J. Li, *J. Am. Chem. Soc.* **1993**, *115*, 5859-5860; b) T. Masquelin, U. Hengartner, J. Streith, *Helv. Chim. Acta*, **1997**, *80*, 43-58; c) R. Fernandes, R. Brückner, unpublished; d) ref.[11e]; e) 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.

[15] Syntheses of racemic 5-*epi*-arizonin B1 (*rac*-5-*epi*-**3**) and of racemic 5-*epi*-arizonin C1 (*rac*-5-*epi*-**4**): M. A. Brimble, S. J. Phythian, *Tetrahedron Lett.* **1993**, *34*, 5813-5814.

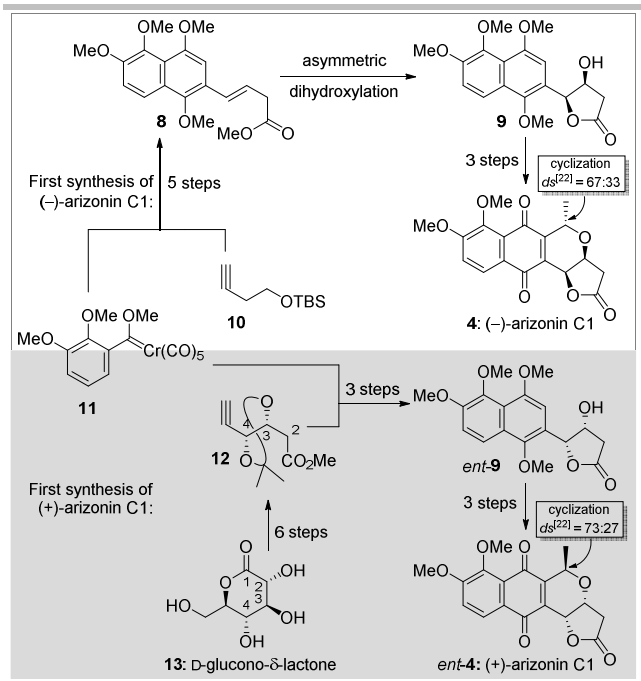
[16] Syntheses of (–)-arizonin C1 (**4**) and the unnatural antipodes (+)-*ent*-arizonin B1 (*ent*-**3**) and (+)-*ent*-arizonin C1 (*ent*-**4**): R. A. Fernandes, S. V. Mulay, V. P. Chavan, *Tetrahedron Asym.* **2013**, *24*, 1548-1555.

[17] First synthesis of *rac*-arizonin C1 (*rac*-**4**): M. A. Brimble, S. J. Phythian, H. Prabaharan, *J. Chem. Soc. Perkin Trans 1*, **1995**, 2855-2860.

[18] a) First synthesis of (–)-arizonin C1 (**4**): M. Mahlau, R. A. Fernandes, F Brückner, *Eur. J. Org. Chem.* **2011**, 4765-4772; b) regrettably, we confoun ded the enantiomers at some point. As a consequence thereof ref.[18a] depicts (–)-arizonin C1 (**4**) with the wrong absolute configuration. Fernandes corrected this mistake in [ref.16], we in footnote 133 of ref.[25].

[19] Synthetic approaches towards (+)-γ-actinorhodin (**7**): a) M. A. Brimble, L. J. Duncalf, S. J. Phythian, *Tetrahedron Lett.* **1995**, *36*, 9209-9210; b) M. A. Brimble, L. J. Duncalf, S. J. Phythian, *J. Chem. Soc., Perkin Trans. 1*, **1997**, 1399-1403; c) M. A. Brimble, L. J. Duncalf, D. Neville, *J. Chem. Soc., Perkin Trans. 1*, **1998**, 4165-4173; d) M. A. Brimble, F. Issa, *Aust. J. Chem.* **1999**, *52*, 1021-1028; e) S. V. Mulay, A. Bhowmik, R. A. Fernandes, *Eur. J. Org. Chem.* **2015**, 4931-4938; f) S. V. Mulay, R. A. Fernandes, *Chem. Eur. J.* **2015**, *21*, 4842-4852.

[20] Total synthesis of (+)-γ-actinorhodin (**7**): M. Neumeyer, R. Brückner, *Angew. Chem.* **2017**, DOI: 10.1002/anie.201611183, DOI: 10.1002/ange.201611183.

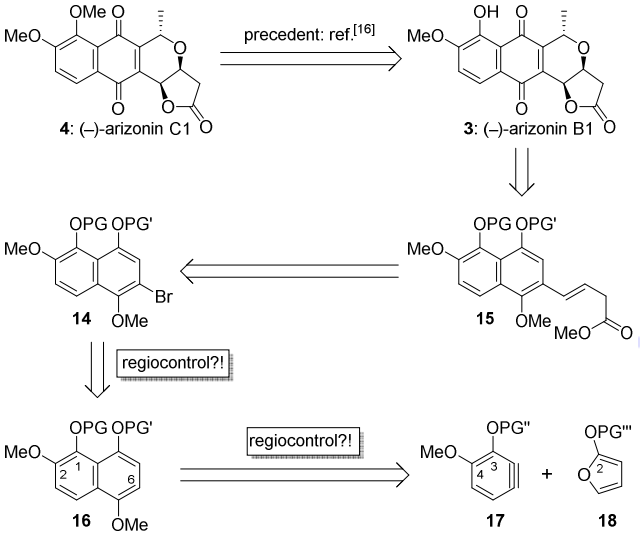


Scheme 1. Top (white background): Sketch of the first synthesis of (–)-arizonin C1 by our group.[18a] If we had performed the asymmetric dihydroxylation as published,[18a] i. e., using AD-mix β, we would have obtained the mirror images of the structures **9** and **4** shown here. Hindsight[18b] made clear that we used AD-mix α. Therefore, we must have obtained the molecules **9** and **4** depicted here. Fernandes re-synthesized **8** and deliberately dihydroxylated it with AD-mix α.[16] He thereby obtained **9** first and **4** in the sequel.[16] Bottom (grey background): Sketch of the first synthesis of (+)-arizonin C1 (*ent*-**4**) by Fernandes´ group.[16]

The arizonin C1 syntheses of ourselves[18a] (Scheme 1, at top) and Fernandes et al.[16] (Scheme 1, at bottom) share one key feature and differ with respect to a second one. The common feature is establishing a pentasubstituted naphthalene by de-novo syntheses of the aromatic nucleus[21] by Dötz reactions between the Fischer carbene **11** and the alkynes **10**[18a] or **12**.[16] The major difference between the arizonin C1 syntheses of Scheme 1 is the origin of the configurational homogeneity. In our approach,[18a] it stems from a highly enantioselective Sharpless dihydroxylation, in Fernandes' synthesis[16] from the incorporation of D-glucono-δ-lactone (**13**). Last but not least, both syntheses of Scheme 1 encountered the same selectivity problem: the methylated stereocenter of the dihydropyran moiety formed no better than with *ds*[22] = 67:33[18a] and 73:27[16], respectively. The syntheses, which we disclose in the following show how this selectivity can be modified by modifying the protective groups in the naphthalene moiety.[23]

An Aryne/Furan Diels-Alder Approach to the Cores of Arizonins B1 and C1

The interconvertibility of arizonin B1 (**3**) and arizonin C1 (**4**) through *O*-methylation[24] and mono-*O*-demethylation, respectively, is known.[16] The backward reaction made racemic 5-*epi*-arizonin C1 (*rac*-*epi*-**4**) a precursor of 5-*epi*-arizonin B1 (*rac*-*epi*-**3**)[15] and, likewise, (+)-arizonin C1 (*ent*-**4**) a precursor of (+)-arizonin B1 (*ent*-**3**).[16] In the forward sense, (–)-arizonin B1 (**3**) may be considered as a precursor of (–)-arizonin C1 (**4**). Indeed, in the present study we prepared (–)-arizonin B1 (**3**) first and continued to (–)-arizonin C1 (**4**) by an *O*-methylation. The second premise for the current approach to (–)-arizonin C1 (**4**) via (–)-arizonin B1 (**3**) was to establish the absolute configuration of arizonin B1 and C1 by an asymmetric *cis*,*vic*-dihydroxylation of a *trans*-configured β,γ-unsaturated ester **15** (Scheme 1). This kind of transformation suits well for accessing γ-lactones of high *ee* values.[25] Under the respective dihydroxylation conditions β-hydroxy-γ-lactones form in a single operation because the initially formed β,γ-dihydroxyesters lactonize spontaneously.



Scheme 2. Tracing back (–)-arizonin C1 (**4**) to arizonin (–)-B1 (**3**) retrosynthetically and simplifying the latter towards a de-novo synthesis of tetraoxygenated naphthalenes **16** by the Diels-Alder reaction of a 3,4-dioxygenated aryne **17** with a 2-oxygenated furan **18**.– PG-PG'" = protective groups

Starting from the mentioned presuppositions we continued our retrosynthetic analysis of (–)-arizonin C1 (**4**) – and arizonin B1 (**3**) – beyond the unsaturated ester **15** as shown in Scheme 2. Such esters are often reached by Heck coupling an aryl halide

[21] De-novo approaches to naphthalenes continue sparking synthetic interest. Selected recent examples: a) F. Wagner, K. Harms, U. Koert, *Org. Lett.* **2015**, *17*, 5670-5673; b) L. S. Kocsis, H. N. Kagalwala, S. Mutto, B. Godugu, S. Bernhard, D. J. Tantillo, K. M. Brummond, *J. Org. Chem.* **2015**, *80*, 11686-11698; c) T. A. Unzner, A. S. Grossmann, T. Magauer, *Angew. Chem.* **2016**, *128*, 9915-9919; *Angew. Chem. Int. Ed.* **2016**, *55*, 9763-9767; d) H. Takikawa, A. Nishii, K. Suzuki, *Synthesis* **2016**, *48*, 3331-3338; e) our approach in Scheme 4.

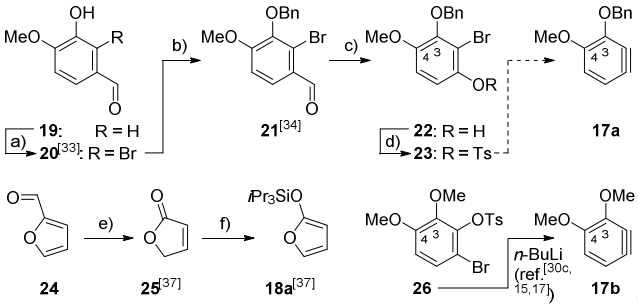
[22] We *distinguish* the terms „*ds*" and „*d.r.*" rather than use them as *synonyms*. „Diastereoselectivity" (*ds*) characterizes the selectivity, with which a stereogenic step generates a crude mixture of diastereomers. A „diastereomeric ratio" (*d.r.*) describes the compositions of chromatographed or recrystallized materials. In follow-up steps, the *d.r.* values of whatever substrate/-product pair may vary: to the extent, with which the respective purification procedure depletes or enriches the minor diastereomer. These variations do not alter, of course, the „diastereoselectivity" of the preceding diastereogenic step.

[23] We surmise that the responsible factor is a „steric relay effect". It exerted diasterocontrol in a total synthesis (ref.[20]) of γ-actinorhodin (**7**).

[24] Related *O*-methylations succeeded with natural (+)-kalafungin (**1**; ref.[2b]) or with a precursor of racemic arizonin C1 (*rac*-**4**; ref.17]).

[25] Nonracemic γ-lactone syntheses based on the asymmetric dihydroxylation of such esters were reviewed recently: M. Neumeyer, R. Brückner, *Eur. J. Org. Chem.* **2016**, 5060-5087.

to an alkyl but-3-enoate.[26] This approach defined type-**14** naphthyl halides as desirable precursors. While not described in the literature they looked accessible by brominating[27] or iodinating[28] type-**16** naphthalenes. An attractive way of getting hold of such substrates seemed to be the Diels-Alder reaction of an aryne **17** oxygenated at C-3 and C-4 (PG'' being a protective group) with a furan[29] oxygenated at C-2[30] (PG''' being another protective group). Eventually, we interpreted the aryne **17** as 3-(benzyloxy)-4-methoxybenz-1-yne (**17a**;[31] formula: Scheme 3) and the furan **18** as 2-(triisopropylsiloxy)furan (**18a**;[32] formula: Scheme 3).



Scheme 3. Starting material synthesis for this study's de-novo prepara tion of type-**16** naphthalenes. Striving for Diels-Alder reactions betwee 3,4-dioxygenated arynes **17** and 2-oxygenated furans **18**, we started b synthesizing the bromotosylate **23** as a precursor of aryne **17a** and th (triisopropylsiloxy)furan **18a** as the corresponding diene. Reagents an conditions: ***a)*** *Br_2 (1.0 equiv.), NaOAc (2.0 equiv.) Fe powder (8.0 mo %), HOAc, room temp., 5 h; 73% (ref.[33]: 70%);* ***b)*** *K_2CO_3 (3.0 equiv., BnCl (1.5 equiv.), EtOH, reflux, 1 d; 98% (ref.[34]: quant.);* ***c*** *mCPBA (1.5 equiv.), CH_2Cl_2, reflux, 14 h; aq. workup; aq. KOH (10% 4.0 equiv.), room temp., 3 h; 94%;* ***d)*** *TsCl (1.5 equiv.), NEt_3 (1. equiv.), CH_2Cl_2, 0°C → room temp., 16 h; 99%;* ***e)*** *N,N dimethylethanolamine (34 mol-%.), formic acid (2.0 equiv.), H_2O_2 (30% in H_2O, 2.0 equiv.), Na_2SO_4, room temp., 16 h; 59% (ref.[37]: 58%);* ***f)*** *iPr_3SiOTf[38] (1.2 equiv.), NEt_3 (1.3 equiv.), CH_2Cl_2, 0°C → room temp 1 h; 98% (ref.[37]: 94%).*

Giles et al. generated the aryne **17b** from the bromotosylate **2** by a Br/Li exchange reaction and an ensuing β-elimination o lithium *para*-toluenesulfinate (Scheme 3, bottom right).[30c] I the bromotosylate **23**, which we forsaw as a precursor of th differently protected aryne **17a**, the positions of Br and OT were swapped. This made the bromotosylate **23** accessible i fewer steps – namely four (Scheme 3, top) – than a benzy analog of the bromotosylate **26**. Step 1 was the bromination o isovanillin (**19**) giving 2-bromoisovanillin (**20**[33]). Step 2 was a *O*-benzylation (→ aldehyde **21**[34]). Step 3 was a Dakin oxidat on.[35] It turned the last-mentioned aldehyde into the phenol **2** –via a formate, which was hydrolyzed in situ.[36] Step 4, a tosy ation, accomplished the bromotosylate **23** in 67% overall yield The (triisopropylsiloxy)furan (**18a**) was gained from furfural (**24** by Pihko's 2-step synthesis (Scheme 3, bottom left).[37] Step was a Dakin-type oxidation. In-situ hydrolysis of the initiall formed formate and a subsequent tautomerization gave 59% o the butenolide **24**. Treatment of this compound with freshly pre pared *i*Pr_3SiOTf[38] provided 98% of the siloxyfuran **18a**.

[26] a) C. N. Eid, J. Shim, J. Bikker, M. Lin, *J. Org. Chem.* **2009**, *74*, 423-426; 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) S. Korwar, T. Nguyen, K. C. Ellis, *Bioorg. Med. Chem. Lett.* **2014**, *14*, 271-274; 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.

[27] 1-Substituted 2-oxygenated naphthalenes are brominated at C-6, i. e., "opposite" to the oxygen-containing substituent at C-2. Recent examples: a) C. Fehér, B. Urbán, L. Ürge, F. Darvas, J. Bakos, R. Skoda-Földes, *Tetrahedron* **2011**, *67*, 6327-6333; b) L. Feng, Y. Wang, F. Liang, M. Xu, X. Wang, *Tetrahedron*, **2011**, *67*, 3175-3180; c) J.-K. Ou-Yang, Y.-Y. Zhang, M.-L. He, J.-T. Li, X. Li, X.-L. Zhao, C.-H. Wang, Y. Yu, De-X. Wang, L. Xu, H.-B. Yang, *Org. Lett.* **2014**, *16*, 664-667; d) J. Yadav, G. R. Stanton, X. Fan, J. R. Robinson, E. J. Schelter, P. J. Walsh, M. A. Pericas, *Chem. Eur. J.* **2014**, *20*, 7122-7127; e) J. M. Wieting, T. J. Fisher, A. G. Schafer, M. D. Visco, J. C. Gallucci, A. E. Mattson, *Eur. J. Org. Chem.* **2015**, 525-533; f) Y. Zhao V. Snieckus, *Org. Lett.* **2015**, *17*, 4674-4677.

[28] 1-Substituted 2-oxygenated naphthalenes are iodinated at C-6, i. e., "opposite" to the oxygen-containing substituent at C-2, e. g.: a) ref.[27a]; b) T. Kamei, H. Shibaguchi, M. Sako, K. Toribatake, T. Shimada, *Tetrahedron Lett.* **2012**, *53*, 3894-3896.

[29] Diels-Alder reactions of arynes with furans devoid of an oxygen-substituent at C-2 render oxo-bridged 1,4-dihydronaphthalenes {= [2,3]benzo-(7-oxabicyclo[2.2.1]hepta-2,5-dienes)}. They were carried on to naphth-1-ols by acidic hydrolyses. First example: a) G. Wittig, L. Pohmer, *Angew. Chem*. **1955**, *13*, 348-348. b) G. Wittig, L. Pohmer, *Chem. Ber*. **1956**, *89*, 1334-1351; other early examples: c) E. Wolthuis, B. Bossenbroek, G. DeWall, E. Geels, A. Leegwater, *J. Org. Chem.* **1963**, *28*, 148-152; d) M. Nakata, M. Kinoshita, *Tetrahedron Lett.* **1984**, *25*, 1373-1376; e) K. Jung, M. Koreeda, *J. Org. Chem.* **1989**, *54*, 5667-5675; f) ref.[15] (used for making a naphthoquinonopyrano-γ-lactone); g) ref.[17] (used for making a naphthoquinonopyrano-γ-lactone); h) M. A. Brimble, L. J. Duncalf, S. J. Phythian, *Tetrahedron Lett.* **1995**, *36*, 9209-9210 (used for making a naphthoquinonopyrano-γ-lactone).

[30] Diels-Alder reactions of 3-oxygenated arynes with 2-oxygenated furans give oxa-bridged 1,4-dihydronaphthalenes {= [2,3]benzo-(7-oxabicyclo-[2.2.1]hepta-2,5-dienes)} with "orientational selectivity" (notion: ref.[40]; details: ref.[30]). These compounds inevitably hydrolyze during aqueous work-up and deliver mono-*O*-protected naphthohydroquinones thereby. Orientational selectivity starting from a 3,4-benzannulated lithium furan-2-olate: a) C. A. Townsend, S. G. Davis, S. B. Christensen, J. C. Link, C. P. Lewis, *J. Am. Chem. Soc.* **1981**, *103*, 6885-6888; orientational selectivity starting from 2-acetoxyfuran: b) R. G. F. Giles, M. V. Sargent, H. Sianipar, *J. Chem. Soc. Perkin Trans 1* **1991**, 1571-1579; orientational selectivities starting from 2-methoxyfuran: c) R. G. F. Giles, A. B. Hughes, M. V. Sargent, *J. Chem. Soc. Perkin Trans. 1* **1991**, 1581-1587; d) T. Matsumoto, T. Hosoya, M. Katsuki, K. Suzuki, *Tetrahedron Lett.* **1991**, *32*, 6735-6736; e) T. Matsumoto, T. Hosoya, K. Suzuki, *J. Am. Chem. Soc*. **1992**, *114*, 3568-3570; f) ref.[15]; g) T. Hosoya, E. Takashi, T. Matsumoto, K. Suzuki, *J. Am. Chem. Soc*. **1994**, *116*, 1004-1015; h) ref.[17]; i) M. A. Brimble, L. J. Duncalf, S. J. Phythian, *J. Chem. Soc., Perkin Trans. 1* **1997**, 1399-1403 (used for making a naphthoquinonopyrano-γ-lactone); j) S. Futagami, Y. Ohashi, K. Imura, T. Hosoya, K. Ohmori, T. Matsumoto, K. Suzuki, *Tetrahedron Lett.* **2000**, *41*, 1063-1067; k) M. A. Brimble, M. Y. H. Lai, *Org. Biomol. Chem.* **2003**, *1*, 2084-2095 (used for making a naphthoquinonopyrano-γ-lactone); orientational selectivity starting from a trisubstituted 2-ethoxyfuran: l) D. J. Pollart, B. Rickborn, *J. Org. Chem*. **1987**, *52*, 792-798; orientational selectivity starting from 2-(*tert*-butyldimethylsiloxy)furan: m) T. Matsumoto, H. Yamaguchi, M. Tanabe, Y. Yasui, K. Suzuki, *Tetrahedron* **1995**, *51*, 7347-7360.

[31] Aryne **17a** had not been described in the literature whereas aryne **17b** had {a) ref.[30c]; b) ref.[15]; c) ref.[17]}. However, if we had converted the latter to a type-**16** naphthalene by following the approach of Scheme 2 we would have reached (–)-arizonin C1 (**4**) first and, by demethylation, (–)-arizonin B1 (**3**) thereafter. However, we targeted (–)-arizonin B1 (**3**) first and, by deprotection and *O*-methylation, (–)-arizonin C1 (**4**) thereafter. This is why we'd rather employ the aryne **17a**.

[32] The only example of a Diels-Alder reaction of an aryne, albeit symmetri and 2-(triisopropylsiloxy)furan (**18a**), of which we are aware, is by S Narayan, W. R. Roush, *Org. Lett.* **2004**, *6*, 3789-3792.

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

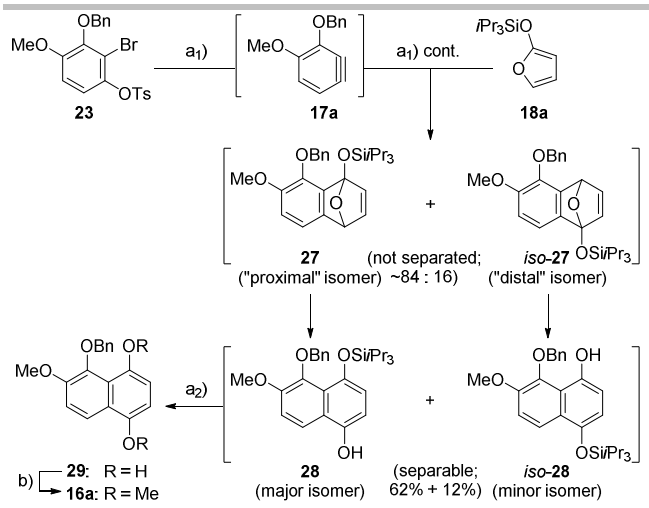
[34] B. Cheng, S. Zhang, L. Zhu, J. Zhang, Q. Li, A. Shan, L. He, *Synthesis* **2009**, *41*, 2501-2504.

[35] 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.

[36] A Dakin oxidation delivering **22** was unknown. We performed it by a procedure of M. Altemöller, T. Gehring, J. Cudaj, J. Podlech, H. Goesmann, C. Feldmann, A. Rothenberger, *Eur. J. Org. Chem.* **2009**, 2130-2140.

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

[38] We prepared *i*Pr_3SiOTf from *i*Pr_3SiH and TfOH (1.2 equiv.) directly prior to use, adopting conditions from two sources: 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.

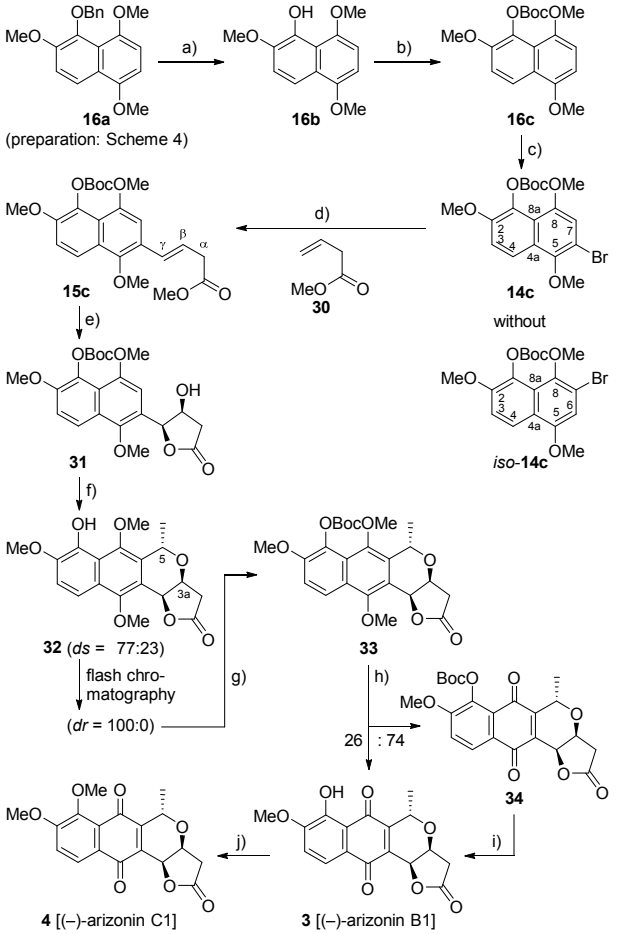


Scheme 4. The aryne / furan Diels-Alder reaction delivering the naphthalene core of the arizonins of this study. *Reagents and conditions:* ***a1) 18a*** *(1.5 equiv.), THF, –78°C; dropwise addition of BuLi (in hexane, 1.0 equiv.), THF, –78°C; 5 min; –78°C → room temp., 45 min;* ***a2)*** *cooling to 0°C; addition of Bu_4NF (in THF, 1.5 equiv.), 0°C → room temp., 8 min; 85%;* ***b)*** *Me_2SO_4 (10 equiv.) KOH (8 equiv.), Bu_4NBr (5.0 mol-%), THF/H_2O (2:1), 0°C → room temp., 14 h; 75%.*

With the bromotosylate **23** and the furan **18a** in our hands (Scheme 3), we dissolved a mixture thereof in THF and added 1.0 equiv. BuLi at –78°C.[39] This must have generated the aryne **17a** and therefrom mainly the Diels-Alder adduct **27** ("proximal" orientational isomer[40]) and subordinately the Diels-Alder adduct *iso*-**27** ("distal" orientational isomer[40]) (Scheme 4). This course of events followed from isolating, after hydrolyzing the crude product with aq. HCl, 62% of the naphthol **28** (as a 50:50 mixture with *i*Pr_3SiOH) and 12% of the isomeric naphthol *iso*-**28** (as a 78:22 mixture with *i*Pr_3SiOH). This is the result of an identical orientational preference as in all previously studied Diels-Alder reactions between 3-oxygenated arynes and 2-oxygenated furans.[30] When we treated the crude mixture of naphthols **28** and *iso*-**28** with a THF solution of tetrabutylammonium fluoride, it converged to 85% of one uncontaminated naphthohydroquinone **29**. Double *O*-methylation afforded the corresponding per-ether **16a** in 75% yield.

Synthetic (–)-Arizonin B1, Synthetic (–)-Arizonin C1, Synthetic (+)-5-*epi*-Arizonin B1, and Synthetic (+)-5-*epi*-Arizonin C1

NBS in DMF brominates 2-iodo-1,4,5,8-tetramethoxynaphthalene with perfect regioselectivity.[20] This suggested to brominate the naphthalene tetraether **16a** likewise. However, this compound decomposed. The same occurred when we treated the corresponding triether **16b** – obtained from **16a** hydrogenolytically (Scheme 5) – with NBS in DMF. Introducing an *O*-bound Boc group provided the carbonate **16c**. It was our first type-**16** substrate to react with NBS/DMF as expected.[27] The bromonaphthalene **14c** resulted in 94% yield as a single isomer, i. e., without a trace of the regioisomer *iso*-**14c**.[41]



Scheme 5. Total syntheses of (–)-arizonin B1 (**3**) and (–)-arizonin C1 (**4**). *Reagents and conditions:* ***a)*** *H_2, Pd (10 w-% on C, 1.5 mol-%), EtOAc, room temp., 16 h; 100%;* ***b)*** *Boc_2O (2.0 equiv.), NEt_3 (2.0 equiv.), DMAP (10 mol-%), CH_2Cl_2, 0°C → room temp., 16 h; 93%;* ***c)*** *NBS (1.0 equiv.), DMF, room temp., 16 h; 94%;* ***d) 30*** *(3.0 equiv), $Pd_2dba_3{\cdot}CHCl_3$ (2.0 mol-%), $P(tBu)_3$ (8.0 mol-%), Cy_2NMe (3.0 equiv.), toluene, reflux, 2 d; 82% of a 87:13 mixture of* ***15c*** *with the trans-configured α,β-unsaturated isomer;* ***e)*** *$K_2OsO_2(OH)_4$ (0.4 mol-%), $(DHQ)_2PHAL$ (1.0 mol-%), $K_3Fe(CN)_6$ (3.0 equiv.), K_2CO_3 (3.0 equiv.), $NaHCO_3$ (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), $tBuOH/H_2O$ (2:1), room temp., 2 d; 60% (98.6% ee);* ***f)*** *acetaldehyde (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min;* 75% *(ds = 77:23) and by re-purification thereof 51% (dr = 100:0);* ***g)*** *Boc_2O*

[39] These conditions resemble conditions for making another aryne for a Diels-Alder reaction with 2-methoxyfuran: ref.[15].

[40] Any Diels-Alder reaction between an unsymmetric dienophile and an unsymmetric diene may lead to "orientational isomers". The favored "orientational isomer" obtained from a dienophile with an electron-withdrawing group at C-1 and from diene oxygenated at C-1 is often called an "*ortho*"-adduct. Analogously, the respective disfavored "orientational isomer" would be a "*meta*"-adduct. In the case at hand, the orientationally isomeric Diels-Alder adducts from 3-oxygenated benz-1-ynes and 2-oxygenated furans have no established designations. The respectivé favored "orientational isomer" is a 1,4-dihydronaphthalene, which is dioxygenated at C-1 and monooxygenated at C-8, i. e., at a close-by position. Accordingly, this isomer may be called the "proximal"-adduct. The disfavored "orientational isomer" is a 1,1,5-triioxygenated naphhtalene. We refer to it as a "distal" product throughout the remainder of the text.

[41] NMR-analyses in $CDCl_3$ solution proved that we had obtained bromonaphthalene **14c** rather than its isomer *iso*-**14c** as follows: The ^{1}H-NMR spectrum (500 MHz) depicts an aromatic d (J_{ortho} = 9.3 Hz) as far down-field as δ = 7.96 ppm that it must be 4-H. Accordingly, the other aromatic d (δ = 7.35 ppm) is due to 3-H. Whether these locants reside in structure **14c** or structure *iso*-**14c** remains open. In this regard, the aromatic s at δ = 6.86 ppm is of no help, either: it may be caused by 7-H of structure **14c** or by 6-H of structure *iso*-**14c**. Distinguishing features: (1) In an HMBC spectrum (500 MHz / 126 MHz) 3-^{1}H showed a cross-peak to exactly 1 "bridgehead" ^{13}C nucleus (in **14c** and in *iso*-**14c** explicable by $^3J_{3\text{-H,C-4a}}$, $\delta_{\text{C-4a}}$ being 125.61 ppm). The same "bridgehead" ^{13}C nucleus showed no cross-peak to the aromatic singlet at 6.88 ppm (in **14c** explicable because $J_{\text{C-4a,7-H}}$ would be $^4J_{\text{C,H}}$; in *iso*-**14c** inexplicable because $J_{\text{C-4a,6-H}}$ would be $^3J_{\text{C,H}}$). (2) In the same HMBC spectrum (500 MHz / 126 MHz) 4-^{1}H displayed a cross-peak to exactly 1 "bridgehead" ^{13}C nucleus (in **14c** and in *iso*-**14c** explicable by $^3J_{\text{4-H,C-8a}}$, $\delta_{\text{C-8a}}$ being 120.87 ppm). The same "bridgehead" ^{13}C nucleus displayed a cross-peak to the aromatic singlet at 6.86 ppm (in **14c** explicable because $J_{\text{C-8a,7-H}}$ would be $^3J_{\text{C,H}}$; in *iso*-**14c** inexplicable because $J_{\text{C-8a,6-H}}$ would be $^4J_{\text{C,H}}$).

(2.0 equiv.), NEt_3 (2.0 equiv.), DMAP (10 mol-%), CH_2Cl_2, 0°C → room temp., 16 h; 85%; ***h)*** *$(NH_4)_2Ce(NO_3)_6$ (2.0 equiv.), MeCN/H_2O (1:1), room temp., 20 min; 39%* ***34*** *separated from 14%* ***3****;* ***i)*** *CF_3CO_2H/CH_2Cl_2 (1:1), room temp., 30 min; quant.;* ***j)*** *MeI (20 equiv.), Ag_2O (14 equiv.), CH_2Cl_2, room temp., 18 h; 34%* ***4****.*

The bromonaphthalene **14c** and methyl but-3-enoate (**30**) underwent a Heck-copuling in 82% yield (Scheme 5). It delivered a 87:13 mixture of the *trans*-isomers of the β,γ-unsaturated ester **15c** and the isomeric α,β-unsaturated ester.[26] An asymmetric Sharpless dihydroxylation of this mixture in the presence of $NaHCO_3$ ("buffered conditions[42]) furnished the hydroxylactone **31** (60% yield, 98.6% *ee*[43]).

The dihydropyran ring was annulated to the last-mentioned compound by what is often called an "oxa-Pictet-Spengler reaction[44]". It is a variant of the "classical Pictet-Spengler reaction[45]", i. e., an intramolecular Mannich reaction wherein an electron-rich aromatic is the nucleophile. In a classical Pictet-Spengler reaction the electrophile is an iminium-ion. However, it is an carboxoxonium-ion in oxa-Pictet-Spengler reactions. In Scheme 5, this carboxonium-ion was generated from the hydroxylactone **31**, acetaldehyde, and $BF_3{\cdot}OEt_2$. Nucleophilic attack by the electron-rich aromatic completed the oxa-Pictet-Spengler reaction. It provided a 77:23 mixture of tetracyclic diastereomers possessing a ^{3a,5}*trans*- and ^{3a,5}*cis*-configuration, respectively. Re-purification by flash-chromatography on silicagel[46] rendered 51% of the pure diastereomer ^{3a,5}*trans*-**32**.[47] It was deprived of the Boc group of its antecessor **31**, containing a phenolic proton instead [δ = 8.64 ppm (s), 400 MHz, $CDCl_3$]. This leaves open, however, whether Boc loss preceded dihydropyran formation or ensued.

Completing the arizonin B1 synthesis of Scheme 5 seemed to require no more than a $(NH_4)_2Ce(NO_3)_6$ oxidation of compound ^{3a,5}*trans*-**32**. Establishing the naphthoquinone motif thereby was a mandatory step in any previous arizonin[16,17,18] or 5-*epi*-arizonin synthesis.[15] However, substrate ^{3a,5}*trans*-**32** decomposed when treated with $(NH_4)_2Ce(NO_3)_6$. Suspecting the free OH group as responsible, we protected it with a Boc group. The resulting carbonate **33** was oxidizable with $(NH_4)_2Ce(NO_3)_6$. This gave the Boc-protected naphthoquinone **34** in 39% yield and the Boc-free naphthoquinone **3**, i. e.(–)-arizonin B1 [(–)-**3**] in 14% yield. The Boc-protected naphthoquinone **34** and trifluoroacetic acid delivered a second crop of (–)-arizonin B1 [(–)-**3**] in quantitative yield. Its *O*-methylation with MeI/Ag_2O provided synthetic (–)-arizonin C1 [(–)-**4**] in 34% yield.

Table 1. Specific rotations (589 nm) in methanol of both enantiomers of arizonin B1 (**3**) and arizonin C1 (**4**) published elsewhere or measured here.

Entry		**3** [(–)-arizonin B1]	*ent*-**3** [(+)-arizonin B1]
1	natural[6a]	–53.0 (*c* = 0.112)	
2	Fernandes et al.[18a]		+137.0 (*c* = 0.108) +168.0 (*c* = 0.024) +88.9 (*c* = 0.011) +166.6 (*c* = 0.108 in $CHCl_3$)
3	this work	–169.7 (*c* = 0.097)	

Entry		**4** [(–)-arizonin C1]	*ent*-**4** [(+)-arizonin C1]
4	natural[6a]	–84.3 (*c* = 1.017)	
5	Brückner et al.[16]	–86.5 (*c* = 0.7)	
6	Fernandes et al.[18a]	–72.4 (*c* = 0.84) –79.2 (*c* = 0.7) –76.6 (*c* = 0.35) –77.2 (*c* = 0.1) –68.0 (*c* = 0.01)	+75.3 (*c* = 0.7) +88.2 (*c* = 0.25) +93.9 (*c* = 0.04) +112.0 (*c* = 0.01)
7	this work	–159.2 (*c* = 0.34) –142.2 (*c* = 0.085)	

Our synthetic arizonins were levorotatory – like the respectiv natural products[6a] (Table 1, entries 1 and 4). However, the ab solute values of the specific rotations of our synthetic arizonin and the natural products differed markedly. For instance, th absolute value $[\alpha]_D$ of our synthetic (–)-arizonin B1 [(–)-3 (Table 1, entry 3) was more than 3 times that of natural (–)- (Table 1, entry 1[6a]). Similarly, the absolute value $|[\alpha]_D|$ of ou synthetic (–)-arizonin C1 [(–)-**4**] (Table 1, entry 7) was almos twice that of natural (–)-**4** (Table 1, entry 4[6a]). Moreover, ou newly obtained (–)-arizonin C1 [(–)-**4**] did not dissolve in MeOH in higher concentrations than about *c* = 0.35. Therefore, w could not confirm the respective rotation, which we had repor ed in 2011 (Table 1, entry 5[18a]). It should be recalled that Fer nandes' synthetic arizonins (+)-*ent*-**3**, (+)-*ent*-**4**, and [(–)-**4** als differed more non-negligibly from their natural role models re garding $|[\alpha]_D|$ values (Table 1, entries 2,[16] 6[16]). They eve seemed to show a concentration dependency.[16] Be this as ur satisfying as it may, the data of Table 1 reveal a 1:1 correlatio between the sign of the specific rotation and the absolute cor figuration. Accordingly, the levorotation of this work´s syntheti samples of (–)-arizonin B1 [(–)-**3**] and (–)-arizonin C1 [(–)-4 proves their (3a*S*,5*S*,11b*S*) rather than (3a*R*,5*R*,11b*R*) configu rations – and thereby the identical configurations of the respective natural products.

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

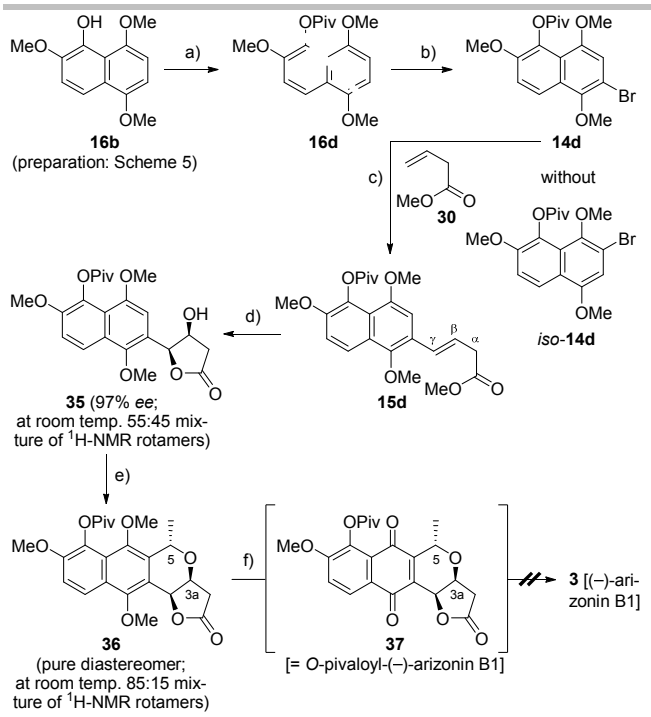
[43] This *ee* was determined by chiral HPLC (details: "Experimental Section").

[44] 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.[11e]; c) R. Bartholomäus, J. Bachmann, C. Mang, L. O. Haustedt, K. Harms, U. Koert, *Eur. J. Org. Chem*. **2013**, 180-190; d) ref.[19e]; e) ref. [20].

[45] First report: A. Pictet, T. Spengler, *Ber. dtsch. Chem. Ges.* **1911**, *44*, 2030-2036.

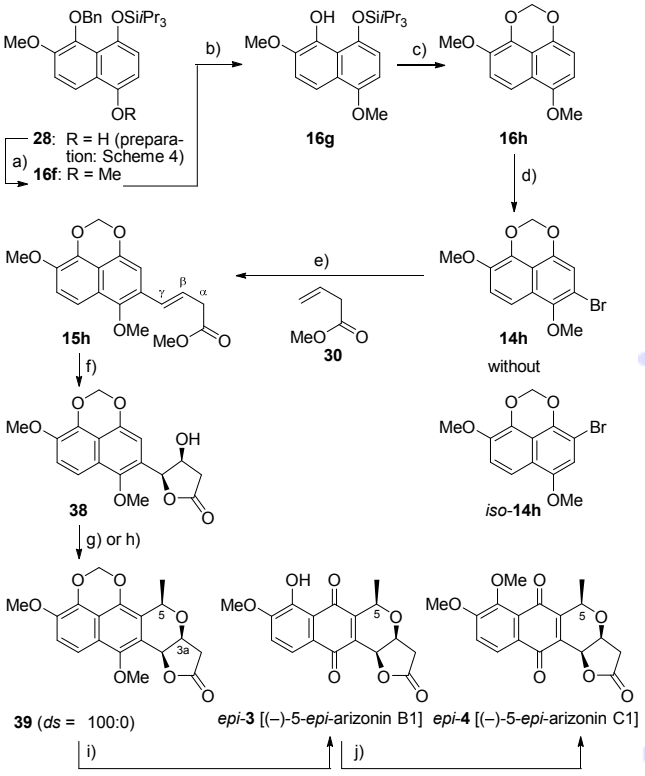
[46] W. C. Still, M. Kahn, A. Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923-2925.

[47] The *trans*-orientation of 5-CH_3 and 3a-C in the dihydropyran moiety of tetracycle ^{3a,5}*trans*-**32** implies a *cis*-orientation of 5-CH_3 and 3a-H. The latter followed from the occurrence of a respective cross-peak in the NOESY spectrum.



Scheme 6. Approaching (–)-arizonin B1 – in vain – with our most ^{3a,5}*trans*-selective oxa-Pictet-Spengler cyclization. *Reagents and conditions:* ***a)*** *Pivaloyl chloride (1.2 equiv.), NEt_3 (2.4 equiv.), DMAP (5 mol-%), CH_2Cl_2, 0°C → room temp., 16 h; 97%;* ***b)*** *NBS (1.0 equiv.), DMF, room temp., 16 h; 92%;* ***c)*** ***30*** *(3.0 equiv), $Pd_2dba_3{\cdot}CHCl_3$ (2.0 mol-%), $P(tBu)_3$ (8.0 mol-%), Cy_2NMe (3.0 equiv.), toluene, reflux, 2d; 60% (of a 87:13 mixture of* ***15d*** *with the trans-configured α,β-unsaturated isomer);* ***d)*** *$K_2OsO_2(OH)_4$ (0.4 mol-%), $(DHQ)_2PHAL$ (1.0 mol-%), $K_3Fe(CN)_6$ (3.0 equiv.), K_2CO_3 (3.0 equiv.), $NaHCO_3$ (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), tBuOH/H_2O (3:1), room temp., 2 d; 46% of a 55:45 mixture of rotamers (97% ee);* ***e)*** *acetaldehyde (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min; 58% (ds = 100:0);* ***f)*** *CAN (2.0 equiv.) MeCN/H_2O (1:1), room temp., 30 min; treatment of the crude product either with KOH (2.0 equiv.), MeOH, room temp., 30 min or: with conc. HCl/MeOH (1:1), room temp., 16 h.*

Scheme 6 shows what would have been a *highly* stereoselective total synthesis of (–)-arizonin B1 [(–)-**3**] – had we only been able to oxidize the oxa-Pictet-Spengler product **36** to the naphthoquinonopyrano-γ-lactone **37** and the latter, through depivaloylation, into (–)-arizonin B1. The route of Scheme 6 starts with a pivaloylation of the previously mentioned (Scheme 5) naphthol **16b**. It gave a 97% yield of the pivaloate **16d**. It was brominated with NBS in DMF in 92% yield to give the bromonaphthalene **14d** without any regioisomer *iso*-**14d**.[48] The bromonaphthalene **14d** was Heck-coupled with the β,γ-unsaturated ester **30**. The resulting 87:13 mixture of *trans*-configured β,γ-unsaturated ester **15d** and α,β-unsaturated isomer (not depicted) was Sharpless-dihydroxylated asymmetrically under "buffered conditions[42]". This gave the hydroxylactone **35**[49] in 46% yield with 97% *ee*. Subjecting this compound and acetaldehyde to an oxa-Pictet-Spengler cyclization[44] in the presence of BF_3-etherate, we obtained the ^{3a,5}*trans*-configured[50] dihydropyran diastereomer **36** *exclusively* (58% yield).[51] As indicated at the beginning of this paragraph, oxidations of compound **36** with $(NH_4)_2Ce(NO_3)_6$ failed. Obtaining a complex mixture of products, we tried to depivaloylate it under acidic and under basic conditions but got no identifiable material either.[52]



Scheme 7. Total syntheses of (+)-5-*epi*-arizonin B1 (*epi*-**3**) und (+)-5-*epi*-arizonin C1 (*epi*-**4**). *Reagents and conditions:* ***a)*** *Me_2SO_4 (10 equiv.) KOH (8 equiv.), Bu_4NBr (20 mol-%), THF/H_2O (2:1), 0°C → room temp., 19 h; 70%;* ***b)*** *H_2, Pd (10 w-% on C, 1.5 mol-%), EtOAc, room temp., 15 h; 99%;* ***c)*** *CH_2BrCl (1.2 equiv.), K_2CO_3 (1.2 equiv.), CsF (1.2 equiv.), DMF, 100°C, 16 h; 85%;* ***d)*** *NBS (1.0 equiv.), DMF, room temp., 16 h; 92%;* ***e)*** ***30*** *(3.0 equiv), $Pd_2dba_3{\cdot}CHCl_3$ (1.0 mol-%), $P(tBu)_3$ (4.0 mol-%), Cy_2NMe (3.0 equiv.), toluene, reflux, 2 d; 66% of a 93:7 mixture of* ***15h*** *with the trans-configured α,β-unsaturated isomer;* ***f)*** *$K_2OsO_2(OH)_4$ (0.4 mol-%), $(DHQ)_2PHAL$ (1.0 mol-%), $K_3Fe(CN)_6$ (3.0 equiv.), K_2CO_3 (3.0 equiv.), $NaHCO_3$ (3.0 equiv.), $MeSO_2NH_2$ (1.0 equiv.), tBuOH/H_2O (1:1), room temp., 2 d; 52% (> 99% ee);* ***g)*** *acetaldehyde (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min; 78% (ds = 100:0);* ***h)*** *acetaldehyde dimethyl acetal (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min; 78% (ds = 100:0);* ***i)*** *$(NH_4)_2Ce(NO_3)_6$ (2.0 equiv.), MeCN/H_2O (1:1), room temp., 30 min; 79% (dr = 100:0);* ***j)*** *MeI (20 equiv.), Ag_2O (14 equiv.), CH_2Cl_2, room temp., 18 h; 34%.*

Counting from isovanillin (**19**) our (–)-arizonin B1 [(–)-**3**] synthesis of Scheme 6 lasted 16 steps. This was partly due to three protective group *changes*: ① Si*i*Pr$_3$ → Me (**28** → **16a**); ② Bn → Boc (**16a** → **16c**); ③ H → Boc [**32** (wherein the Boc group had been lost) → **33**]. In order to obviate such unproductive steps we varied our protective group strategy once more (Scheme 7). We started by *O*-methylating the ring-opening product **28** of the Diels-Alder adduct **27** of Scheme 4. The resulting ether **16f** was debenzylated by hydrogenolysis (→**16g**). The silyl group was removed at 100°C by treatment with CsF in DMF in the presence of K_2CO_3 and CH_2BrCl. The latter two re-

[48] The bromonaphthalene **14d** was told apart from *iso*-**14d** analogously as decibed in footnote [41] for the diffentiation of the bromonaphthalene structures **14c** vs. *iso*-**14c**.

[49] Compound **35** was depicted as a 55:45 mixture of two rotamers in the ^{1}H-NMR spectrum (400 MHz, $CDCl_3$). However, chiral HPLC showed it to be one 98:5:1.5 mixture of two enantiomers.

[50] This configuration was proved analogously as detailed for the oxa-Pictet-Spengler product ^{3a,5}*trans*-**32** in footnote [47].

[51] The dihydropyran **36** was a 85:15 mixture of rotamers in a room temperature ^{1}H-NMR spectrum (500.4 MHz, $CDCl_3$) but a single species at +60°C.

[52] We tried to "save" our approach of Scheme 6 starting from the trichloroacetate analog **16i** of pivaloate **16d**. While it was brominated allright the resulting bromide **14i** did not Heck-couple with methyl 2-vinylacetate (**30**); instead, it was was reduced to the corresponding dichloroacetate **16j** (details: Supporting Information).

agents incorporated the available OH groups in the methylene acetal **16h** in 85% yield.[53] The four ensuing transformations of Scheme 7 equalled those in the syntheses of Scheme 5 and Scheme 6: 1) bromination with NBS/DMF (→ bromonaphthalene **14h** without any regioisomer *iso*-**14h**); 2) Heck coupling with ester **30** [method: ref.[26]; → β,γ-unsaturated ester **15h** contaminated by the α,β-unsaturated isomer (not depicted)]; 3) asymmetric Sharpless dihydroxylation in the presence of $NaHCO_3$[42] (→ hydroxylactone **38**; >99% *ee*); 4) oxa-Pictet-Spengler reaction[44] of the latter compound with acetaldehyde – or, giving the same result, with acetaldehyde dimethyl acetal – and BF_3 etherate. This step, however, proceeded with the opposite diastereoselectivity than the hydroxylactones **31** of Scheme 5 and **35** of Scheme 6. In fact, the hydroxylactone **38** of Scheme 7 was the only substrate favoring the ^{3a,5}*cis*-diastereomer: the respective dihydropyran **39** formed even with *ds* = 100:0[54] (78% yield)! An $(NH_4)_2Ce(NO_3)_6$ oxidation of the oxa-Pictet-Spengler product ^{3a,5}*cis*-**39** generated the naphthoquinone moiety. The concomitant loss of the methylene acetal moiety liberates the OH group of what was synthetic (+)-5-*epi*-arizonin B1 [(+)-5-*epi*-**3**]. *O*-methylation allowed to gain synthetic (+)-5-*epi*-arizonin C1 [(+)-5-*epi*-**4**], too. Previously, these two compounds were synthesized only as racemic mixtures.[15]

Protective Group Effects on the Induced Diastereoselectivity of Acetaldehyde-Incorporating oxa-Pictet-Spengler Cyclizations

The oxa-Pictet-Spengler cyclizations **35**→**36** (Scheme 6) and **38**→**39** (Scheme 7) disclosed in the preceding Section are unique in one regard: They proceed with perfect and complementary diastereoselectivities. Substrate **35** establishes a ^{3a,5}*trans*-substituted dihydropyran ring exclusively. Substrate **38** delivers a ^{3a,5}*cis*-substituted dihydropyran moiety selectively. Nonetheless, the oxygenation pattern of these oxa-Pictet-Spengler substrates is the same. It is just the differential *O*-protection, which makes these oxa-Pictet-Spengler reactions take opposite steric courses. We are unaware of literature precedents, where exactly that has been observed: the tunability – invertibility! – of the induced diastereoselectvity of such oxa-Pictet-Spengler reactions by protective group variations in the electron-rich aromatic nucleophile. These are remarkably remote substituent effects.

[53] F. Dallacker, J. Jacobs, W. Coerver, *Z. Naturforsch. B* **1983**, *38*, 1000-1007 treated naphthalene-1,4,5,8-tetraol likewise, i. e., with K_2CO_3 and CH_2BrCl in DMF at 100°C. This introduced *two* methylene acetal moieties.

[54] The *cis*-orientation of 5-CH_3 and 3a-C in the dihydropyran moiety of tetracycle ^{3a,5}*cis*-**39** implies a *cis*-orientation of 5-H and 3a-H [if numbered, for consistency, not according to IUPAC but as shown in Scheme 7; this numbering adheres to the numbering principle in the congeners **32** (Scheme 5) and **36** (Scheme 6)]. The latter followed from the occurrence of a respective cross-peak in the NOESY spectrum.

Table 2: Acetaldehyde-incorporating oxa-Pictet-Spengler cyclizations in naphthoquinonopyrano-γ-lactone synthesis. Juxtaposition of substitution patterns in the naphthalene moiety and the ^{3a,5}-*trans*- or ^{3a,5}-*cis*-selectivities, which they induce. For easier understanding, all lactones are depicted with the identical absolute configuration. However, at times, the respective formula represents the mirror image of the enantiomer actually employed/obtained. It should be noted that the span of reaction conditions is very wide. This concerns the reagent (acetaldehyde vs. acetaldehyde dimethyl acetal), the promotor (usually BF_3 etherate, once Me_3SiOTf), the solvent (usually CH_2Cl_2, else Et_2O/THF or CF_3CO_2H/THF), the temperature (between 0 and +70°C), and the allotted time (between 55 s and 1 d).– Gray backgrounds indicate a suspected remote substituent effect, which is conformationally relayed.

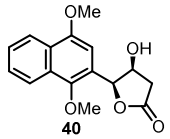
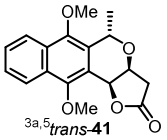
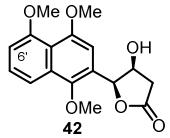
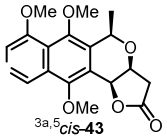
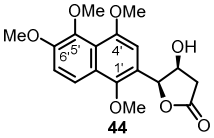
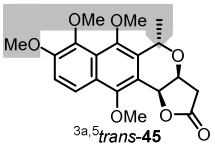
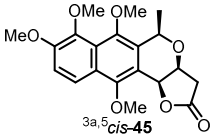
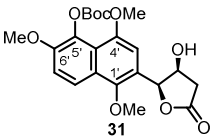
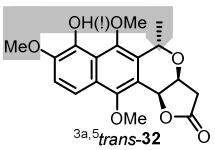
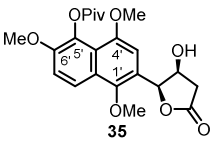
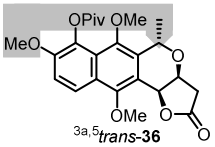
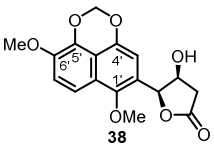
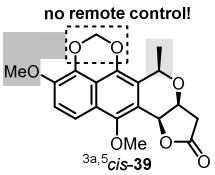
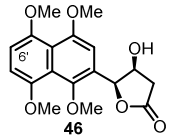
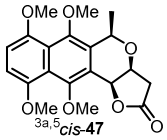
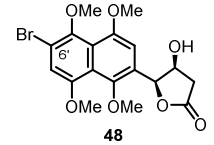
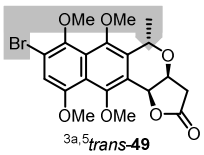
Entry		Reagents and conditions	Yield	Product	^{3a,5}*trans* : ^{3a,5}*cis*	
1[26a]		acetaldehyde (1.0 equiv.), $BF_3{\cdot}OEt_2$ (0.7 equiv.), CH_2Cl_2, 0°C → room temp., overnight	98%		>99:1	
2[55]	**40** (= mirror image of the enantiomer, which was actually used)	acetaldehyde (1.12 equiv.), $BF_3{\cdot}OEt_2$ (1.06 equiv.), CH_2Cl_2, 0°C → room temp., overnight	93%	^{3a,5}*trans*-**41**	>95:5	
3[10c]		acetaldehyde dimethyl acetal (2.0 equiv), $BF_3{\cdot}OEt_2$ (3.0 equiv), Et_2O/THF (4:1), room temp., 12 h	92%		0:100	
4[10e]	**42** (= mirror image of the enantiomer, which was actually used)	acetaldehyde dimethyl acetal (2.0 equiv), $BF_3{\cdot}OEt_2$ (1.1 equiv), CH_2Cl_2, 0 °C → room temp., 17 h	78%		0:100	^{3a,5}*cis*-**43**
5[18]		acetaldehyde (1.02 equiv.), $BF_3{\cdot}OEt_2$ (0.7 equiv.), CH_2Cl_2, 0°C → room temp., 1 d	86%		66:34	
6[16]		acetaldehyde dimethyl acetal (2.0 equiv.), $BF_3{\cdot}OEt_2$ (2.0 equiv.), CH_2Cl_2, 0°C → room temp., 12 h	71%	^{3a,5}*trans*-**45**	73:27	^{3a,5}*cis*-**45**
7[16]	**44** (= mirror image of the enantiomer, which was actually used)	acetaldehyde dimethyl acetal (4.0 equiv.), $BF_3{\cdot}OEt_2$ (10.0 equiv.), CF_3CO_2H/THF (4:1), 70°C, 55 s	45%		100:0	
8[16]		acetaldehyde dimethyl acetal (2.0 equiv.), Me_3SiOTf (1.5 equiv.), CH_2Cl_2, 0°C, 2 h	68%		35:65	
9[this work]		acetaldehyde (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min	75%		77:23	
10[this work]	**31**  **35**	acetaldehyde (1.02 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min	58	^{3a,5}*trans*-**32**  ^{3a,5}*trans*-**36**	100:0	
11[this work]		acetaldehyde (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min	78%		0:100	**no remote control!** 
12[this work]	**38**	acetaldehyde dimethyl acetal (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min	78%		0:100	^{3a,5}*cis*-**39**
13[20]		acetaldehyde (2.0 equiv.), $BF_3{\cdot}OEt_2$ (3.0 equiv.), CH_2Cl_2, 0°C → room temp., 1.5 h	86%		33:67	
14[19e]		acetaldehyde dimethyl acetal (2.0 equiv.), $BF_3{\cdot}OEt_2$ (2.0 equiv.), CH_2Cl_2, 0°C → room temp., 5 h	72%		0:100	
15[19e]	**46** (= mirror image of the enantiomer, which was actually used)	acetaldehyde dimethyl acetal (4.0 equiv.), $BF_3{\cdot}OEt_2$ (10.0 equiv.), CF_3CO_2H/THF (4:1), 70°C, 55 s	35%		0:100	^{3a,5}*cis*-**47**
16[20]	 **48** (= mirror image of the enantiomer, which was actually used)	acetaldehyde (7.5 equiv.), $BF_3{\cdot}OEt_2$ (10 equiv.), CH_2Cl_2, 0°C → room temp., 30 min	88%	 ^{3a,5}*trans*-**49**	90:10	

Table 2 represents the just-mentioned substituent/diastereoselectivity effects amidst a pertinent collection of literature data. They all are about acetaldehyde-incorporating oxa-Pictet-Spengler cyclizations for naphthoquinonopyrano-γ-lactone synthesis. Table 2 shows 8 differently γ-naphthylated β-hydroxy-γ-lactone substrates. It details, how they were carried on – with acetaldehyde or its dimethyl acetal – 8 different dihydropyrans and what the respective ^{3a,5}*trans*:^{3a,5}*cis*-selectivities were. Half of the substrate/product pairs stem from the current study (**31**/**32**, **35**/**36**, and **38**/**39**) or (**48**/**49**) from our total synthesis of γ-actinorhodin.[20] Three additional substrate/product pairs were studied by others and ourselves (**42**/**43**,[10c] **44**/**45**,[18a] and **46**/**47**[20]). The substrate/product pair **40**/**41** was investigated by others[26a,55] only. The substrates of Table 2 are ordered by the number of substituents – mostly methoxy group – in the naphthalene moiety. The entries into Table 2 begin with 2 substituents besides the omnipresent hydroxylactone group (in naphthyllactone **40**). The table continues with naphthyllactone **42**, which contains 3 extra-substituents. The five ensuing naphthyllactones contain 4 extra-substituents. They define two substitution patterns (**44**, **31**, **35**, and **38** vs. **46**). The last substrate of Table 2 (**48**) contains 5 substituents beyond the hydroxylactone group.

Table 2 displays oxa-Pictet-Spengler cyclizations, which are perfectly ^{3a,5}*trans*-selective (entries 1, 7, and 10), and others, which are as ^{3a,5}*cis*-selective (entries 3-4, 11-12, and 14-15). Moreover, Table 2 reveals that the substitution pattern of the naphthalene moiety influences the diastereoselectivity of the oxa-Pictet-Spengler cyclization, to which it is subjected. E. g., 2 methoxy groups let the naphthyllactone **40** cyclize ^{3a,5}*trans*-selectively (entries 1-2). In contrast, 3 methoxy groups make the naphthyllactone **42** cyclize ^{3a,5}*cis*-selectively entries 3-4). 4 methoxy groups may be distributed such that the corresponding cyclization is ^{3a,5}*trans*-selective (entries 5-7) or ^{3a,5}*cis*-selective (entries 13-15). We have no straightforward rationalization for these substituent effects. This is due to the widely varying reaction conditions (details: Table 2) and the incertitude whether the respective cyclization proceeds under kinetic or thermodynamic control.

Last but not least, Table 2 highlights a potential steering tool – and a way to "mute" it – for imposing the desired diastereoselectivity on an oxa-Pictet-Spengler cyclization: introducing a substituent at C-6' of the naphthalene core – or suppressing its effect by a suitable protective group:

- Diastereocontrol by a substituent at C-6' of oxa-Pictet-Spengler cyclizations as shown in Table 2: (a) The naphthalene moiety of lactone **42** contains 3 MeO groups. This compound oxa-Pictet-Spengler cyclizes ^{3a,5}*cis*-selectively (entries 3-4). With another MeO substituent at C-6', lactone **42** becomes lactone **44**. The latter oxa-Pictet-Spengler cyclizes oppositely, namely ^{3a,5}*trans*-selectively (entries 5-8). (b) The *trans*-inducing effect of the mentioned 6'-MeO group persists when the 5'-substituent MeO (in lactone **44**) is replaced by OBoc (in lactone **31**, entry 9) or OPiv (in lactone **35**, entry 10). (c) The naphthalene moiety of lactone **46** contains 4 MeO groups. This compound oxa-Pictet-Spengler cyclizes with a ^{3a,5}*cis*-preference (entry 13) or ^{3a,5}*cis*-selectively (entries 14-15). With another MeO substituent at C-6', lactone **46** becomes lactone **48**. It oxa-Pictet-Spengler cyclizes with an opposite 90:10 ^{3a,5}*trans*-preference (entry 16).[56]

- Suppressing diastereocontrol of oxa-Pictet-Spengler cyclizations as shown in Table 2 exertable by a substituent at C-6: The oxa-Pictet-Spengler cyclizations of lactones **44**, **31**, and **35** gave *trans*-dihydropyrans preferentially or exclusively (entries 5-7 and 9-10) – "due" (cf. above) to their 6'-bound MeO group. Although lactone **38** contains a 6'-bound MeO group, too, it cyclized to give a *cis*-dihydropyran with *ds* = 100:0 (entries 11-12). Lactone **38** differs from lactones **44**, **31**, and **35** by the installment of a *bridging* protective group between 5'-O and 4'-O.[57]

Controlling the diastereoselectivity of naphthoquinonopyranolactone-targeting oxa-Pictet-Spengler cyclizations by "remote substituent effects" as brought to light in Table 2 is a new synthetic handle. It complements the previous handle, i. e., promotor-control of diastereoselectivity.[58] The scope of either handle is still underexplored.

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 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 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.[59] **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:**[46] Macherey-Nagel silica gel 60® (230-400 mesh) was used for flash chromatography. All eluents were distilled prior to

[55] S. Korwar, T. Nguyen, K. C. Ellis, *Bioorg. Med. Chem. Lett.* **2014**, *14*, 271-274.

[56] a) One may speculate whether the 6'-substituent exerts its remote effect somehow (!) as a consequence of relaying steric hindrance from its own site (≡ C-'6) towards the site of attack (≡ C-3') of the oxa-Pictet-Spengler electrophile. This relay would be tantamount to the 6'-substituent shoving the oxygen-bound substituents "in between" – i. e., first OMe, OBoc or OPiv at C-5 and then OMe at C-4' towards C-3'. In order for this to be the case, these substituents at C-4' and C-3' would need to be conformationally mobile; b for a similar line of reasoning see ref.[20].

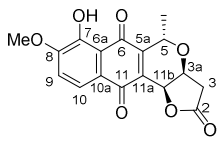
[57] Such a bridging protective group would be unable to relay the steric effect, which we contemplate in footnote [56] for rationalizing the remote effect of 6'-OMe and 6'-Br moieties.

[58] a) BF_3 etherate let lactone **44** (formula: Table 2) and acetaldehyde dimethyl acetal cyclize with a 73:27 *cis*-preference (Table 2, entry 6) or *cis*-selectively (Table 2, entry 7), while a 65:35 *trans*-preference results using TMS triflate (Table 2, entry 8); b) ref.[14e] varied the Lewis acid in aldehyde-incorporating oxa-Pictet-Spengler cyclizations of the mirror image of structure **42** (formula: Table 2). $Cu(OTf)_2$ in CH_2Cl_2 incorporated 11 aldehydes – among them 1 α-sustituted aldehyde and 2 aromatic aldehydes – in ^{3a,5}*cis*-configured dihydropyrans with *ds* ≥88:12 (only benzaldehyde gave a ^{3a,5}*trans*-configured dihydropyran under these conditions, *ds* = 75:25). $FeCl_3$ in THF incorporated butanal in a ^{3a,5}*trans*-configured dihydropyran with *ds* = 66:34.

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

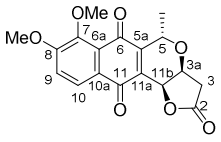
use. Chromatography conditions are documented as following: "[diameter d = y cm height h = x cm, eluent a/eluent b = v_a:v_b, fraction volume = e mL] furnished the product (Fx-y, yield in g and %)" example: "flash chromatography [d = 1.5 cm, h = 12 cm, CH/EE 5:1, F = 6 mL] furnished the product (F9-13, 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 doublet; 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.[60] **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.

(3a*S*,5*S*,11b*S*)-7-Hydroxy-8-methoxy-5-methyl-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene[5*H*,11b*H*]-trione = Arizonin B1 [(–)-3]



tert-Butyl (3a*S*,5*S*,11b*S*)-8-methoxy-5-methyl-2,6,11-trioxo-3,3a,5,6,11,11b-hexahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl carbonate (**34**, 12.2 mg, 28.3 µmol) was dissolved in CH_2Cl_2 (0.5 mL). At room temperature trifluoroacetic acid (0.5 mL) was added dropwise and the mixture was stirred for 30 min. The solvent was removed in vacuo. The title compound (9.8 mg, quant.) was obtained without further purification.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.56 (d, 3H, $J_{5\text{-}CH3,5}$ = 6.9 Hz, 5-CH_3), AB signal (δ_A = 2.69, δ_B = 2.96, J_{AB} = 18.0 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,3a}$ = 5.2 Hz, 3-H^A and 3-H^B), 4.00 (s, 3H, 8-OMe), 4.68 (dd, 1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.0 Hz, 3a-H), 5.07 (q, 1H, $J_{5,5\text{-}CH3}$ = 6.9 Hz, 5-H), 5.25 (d, 1H, $J_{11b,3a}$ = 2.9 Hz, 11b-H), 7.12 (d, 1H, $J_{9,10}$ = 8.2 Hz, 9-H), 7.74 (d, 1H, $J_{10,9}$ = 8.4 Hz, 10-H), 12.27 (s, 1H, 7-OH). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.56 (5-CH_3) ↔ δ = 4.68 (3a-H, this cross-peak proves that 5-CH_3 and 3a-H are oriented *cis* relative to one another), δ_B = 2.96 (3-H^B) ↔ δ = 5.25 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 4.00 (8-OMe) ↔ δ = 7.12 (9-H). **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 18.60 (5-CH_3), 37.00 (C-3), 56.57 (8-OCH_3), 66.32 (C-5), 66.54 (C-3a), 68.86 (C-11b), 114.88 (C-6a), 115.83 (C-9), 121.54 (C-10), 123.41 (C-10a), 135.86 (C-11a), 149.51 (C-5a), 152.54 (C-7), 154.46 (C-8), 174.13 (C-2), 180.48 (C-11), 188.56 (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 = 18.60 (5-CH_3) ↔ δ = 1.56 (5-CH_3), δ = 37.00 (C-3) ↔ [δ_A = 2.69 (3-H^A) and δ_B = 2.96 (3-H^B)], δ = 56.57 (8-OCH_3) ↔ δ = 4.00 (8-OMe), δ = 66.32 (C-5) ↔ δ = 5.07 (5-H), δ = 66.54 (C-3a) ↔ δ = 4.68 (3a-H), δ = 68.86 (C-11b) ↔ δ = 5.25 (11b-H), δ = 115.83 (C-9) ↔ δ = 7.12 (9-H), δ = 121.54 (C-10) ↔ δ = 7.74 (10-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 = 114.88 (C-6a) ↔ δ = 7.74 (10-H), δ = 123.41 (C-10a) ↔ δ = 7.12 (9-H), δ = 135.86 (C-11a) ↔ δ = 5.07 (5-H), δ = 135.86 (C-11a) ↔ δ = 5.25 (11b-H), δ = 149.51 (C-5a) ↔ δ = 1.56 (5-CH_3), δ = 149.51 (C-5a) ↔ δ = 5.07 (5-H), δ = 149.51 (C-5a) ↔ δ = 5.25 (11b-H), δ = 152.54 (C-7) ↔ δ = 7.12 (9-H), δ = 152.54 (C-7) ↔ δ = 12.27 (7-OH), δ = 154.46 (C-8) ↔ δ = 4.00 (8-OMe), δ = 154.46 (C-8) ↔ δ = 7.12 (9-H), δ = 154.46 (C-8) ↔ δ = 7.74 (10-H), δ = 154.46 (C-8) ↔ δ = 12.27 (7-OH), δ = 174.13 (C-2) ↔ [δ_A = 2.69 (3-H^A) and δ_B = 2.96 (3-H^B)], δ = 174.13 (C-2) ↔ 4.68(3a-H), δ = 180.48 (C-11) ↔ 5.25 (11b-H), δ = 180.48 (C-11) ↔ 7.74 (10-H), δ = 188.56 (C-6) ↔ 5.07 (5-H), δ = 188.56 (C-6) ↔ 7.74 (10-H). **Melting point:** 206°C (decomp.). **Optical rotation:** $[\alpha]_D^{20}$ = –169.7 (c = 0.094, MeOH). **HRMS** (pos. ESI, file: nebrc06s_hr1): calcd. for $C_{17}H_{14}O_7Na$ $[M+Na]^+$ = 353.06317; found 353.06351 (+0.94 ppm). **IR (film):** ν = 3060, 2935, 2850, 1790, 1775, 1650, 1620, 1590, 1460, 1440, 1410, 1365, 1340, 1270, 1240, 1200, 1155, 1100, 1085, 1070, 1035, 995, 955, 920, 905, 785, 765, 755, 735, 700, 680 cm^{-1}.

(3a*S*,5*S*,11b*S*)-7,8-Dimethoxy-5-methyl-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene[5*H*,11b*H*]-trione = Arizonin C1, [(–)-4]

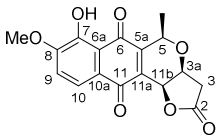


Under a nitrogen atmosphere arizonin B1 (**3**, 8.0 mg, 22.2 µmol) was dissolved in a freshly prepared solution of MeI (27.7 µL, 63.0 mg, 444 µmol, 20.0 equiv.) in CH_2Cl_2 (1 mL). Ag_2O (72.0 mg, 311 µmol, 14.0 equiv.) was added in one portion to initiate the reaction. The mixture was stirred at room temperature for 18 h. The reaction mixture was filtered over a small pipet (silica gel pad: h = 2 cm) and thoroughly rinsed with CH_2Cl_2 (10 mL). Afterwards the solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 8 cm, F = 8 mL; CH/EE 3:2 (F1-11), CH/EE 1:2 (F12-23)] afforded the title compound (F12-20, 3.2 mg, 41%, *dr* = 100:0)]. **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.54 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.9 Hz, 5-CH_3), AB signal (δ_A = 2.68, δ_B = 2.95, 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), 3.92 (s, 3H, 7-OMe), 3.98 (s, 3H, 8-OMe), 4.66 (dd, 1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.0 Hz, 3a-H), 5.06 (q, 1H, $J_{5,5\text{-}CH_3}$

[60] 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.

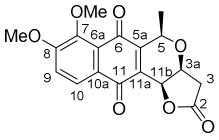
= 6.9 Hz, 5-H), 5.25 (d, 1H, $J_{11b,3a}$ = 3.0 Hz, 11b-H), 7.23 (d, 1H, $J_{9,10}$ = 8.7 Hz, 9-H), 7.98 (d, 1H, $J_{10,9}$ = 8.7 Hz, 10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks (500.32 MHz, $CDCl_3$) [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 1.54 (5-CH_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_B = 2.95 (3-H^B) ↔ δ = 5.25 (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 = 7.23 (9-H). δ = 3.92 (7-OMe) exhibited no cross-peak. **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 18.66 (5-CH_3), 37.06 (C-3), 56.45 (8-OCH_3), 61.27 (7-OCH_3), 66.47 (C-3a), 66.82 (C-5), 69.04 (C-11b), 116.27 (C-9), 124.97 (C-10), 124.97 (C-6a), 125.26 (C-10a), 133.20 (C-11a), 149.66 (C-7), 150.61 (C-5a), 159.29 (C-8), 174.23 (C-2), 181.46 (C-11), 182.47 (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 [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 18.66 (5-CH_3) ↔ δ = 1.54 (5-CH_3), δ = 37.06 (C-3) ↔ [δ_A = 2.68 (3-H^A) and δ_B = 2.95 (3-H^B)], δ = 56.45 (8-OCH_3) ↔ δ = 3.98 (8-OMe), δ = 61.27 (7-OCH_3) ↔ δ = 3.92 (7-OMe), δ = 66.47 (C-3a) ↔ δ = 4.66 (3a-H), δ = 66.82 (C-5) ↔ δ = 5.07 (5-H), δ = 69.04 (C-11b) ↔ δ = 5.25 (11b-H), δ = 116.27 (C-9) ↔ δ = 7.23 (9-H), δ = 124.97 (C-10) ↔ δ = 7.98 (10-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 = 124.97 (C-6a) ↔ δ = 7.98 (10-H), δ = 125.26 (C-10a) ↔ δ = 7.23 (9-H), δ = 133.20 (C-11a) ↔ δ = 5.06 (5-H), δ = 133.20 (C-11a) ↔ δ = 5.25 (11b-H), δ = 149.66 (C-7) ↔ δ = 3.92 (7-OMe), δ = 149.66 (C-7) ↔ δ = 7.23 (9-H), δ = 150.61 (C-5a) ↔ δ = 1.54 (5-CH_3), δ = 150.61 (C-5a) ↔ δ = 5.06 (5-H), δ = 150.61 (C-5a) ↔ δ = 5.25 (11b-H), δ = 159.29 (C-8) ↔ δ = 3.98 (8-OMe), δ = 159.29 (C-8) ↔ δ = 7.23 (9-H), δ = 159.29 (C-8) ↔ δ = 7.98 (10-H), δ = 174.23 (C-2) ↔ [δ_A = 2.68 (3-H^A) and δ_B = 2.95 (3-H^B)], δ = 174.23 (C-2) ↔ 4.66(3a-H), δ = 181.46 (C-11) ↔ 5.25 (11b-H), δ = 181.46 (C-11) ↔ 7.98 (10-H), δ = 182.47 (C-6) ↔ 5.06 (5-H), δ = 182.47 (C-6) ↔ 7.98 (10-H). **Melting point:** 126°C (decomp.); ref [6a]: 110-135°C (decomp.). **Optical rotation:** $[\alpha]_D^{20}$ = –159.2 (*c* = 0.34, MeOH). **HRMS** (pos. ESI): Calcd. for $C_{18}H_{16}O_7Na$ $[M+Na]^+$ = 367.07882; found 367.07898 (+0.42 ppm). **IR (film):** v = 3295, 2940, 2850, 1790, 1725, 1665, 1620, 1575, 1485, 1455, 1405, 1365, 1335, 1275, 1235, 1200, 1155, 1070, 1035, 995, 955, 905, 880, 845, 820, 785, 735, 700 cm^{-1}.

(3a*S*,5*R*,11b*S*)-7-Hydroxy-8-methoxy-5-methyl-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene[5*H*,11b*H*]-trione = (+)-5-*epi*-arizonin B1 [(+)-5-*epi*-3]



(7b*S*,10a*S*,12*R*)-4,7-Dimethoxy-12-methyl-7b,10,10a,12-tetrahydro-9*H*-furo[2'',3'':5',6']-pyrano[3',4':2,3]naphtho[1,8-*de*][1,3]dioxin-9-one (**39**, 15.5 mg, 43.3 µmol) was dissolved in acetonitrile (2 mL). A solution of CAN (47.4 mg, 86.5 µmol, 2.0 equiv.) in H_2O (1 mL) was added dropwise at room temperature. The reaction mixture was stirred for 30 min and afterwards diluted with EtOAc (5 mL). The organic phase was separated and the organic phase was extracted with EtOAc (2×5 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed in vacuo. Flash chromatography (d = 1.5 cm, h = 6 cm, F = 8 mL; CH/EE/HCO_2H 49:49:2) afforded the title compound [F7-13, R_f (49:49:2) = 0.2, 11.3 mg, 79%, *dr* = 100:0] as an orange solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$, spectrum contains 8 w-% MeOH with a singulet at δ = 3.49 ppm and 8 w-% water with a broad singulet at δ = 1.54 ppm): δ = 1.64 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.7 Hz, 5-CH_3), AB signal (δ_A = 2.74, δ_B = 2.88, J_{AB} = 17.4 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 4.6 Hz, 3-H^A and 3-H^B), 4.01 (s, 3H, 8-OMe), 4.33 (dd, 1H, $J_{3a,B}$ = 4.5 Hz, $J_{3a,11b}$ = 2.5 Hz, 3a-H), 4.78 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.6 Hz, $^5J_{5,11b}$ = 1.7 Hz, 5-H), 5.26 (d, 1H, $J_{11b,3a}$ = 2.4 Hz, $^5J_{11b,5}$ = 1.8 Hz, 11b-H), 7.14 (d*, 1H, $J_{9,10}$ = 8.4 Hz, 9-H), 7.73 (d, 1H, $J_{10,9}$ = 8.4 Hz, 10-H), 12.19 (d[Fehler! Textmarke nicht definiert.], 1H, $^5J_{7\text{-}OH,9}$ = 0.7 Hz**, 7-OH). * δ = 7.14 (9-H) is represented by a broad doublet that could also be interpreted as a dd. **A $^5J_{7\text{-}OH,9}$-coupling was not found in the DQF-COSY spectrum (500.32 MHz, $CDCl_3$). A **NOESY** spectrum allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks (500.32 MHz, $CDCl_3$) [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.88 (3-H^B) ↔ δ = 5.26 (11b-H, this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 4.01 (8-OMe) ↔ δ = 7.14 (9-H), δ = 4.78 (5-H) ↔ δ = 4.33 (3a-H, this cross-peak proves that 5-H and 3a-H are oriented *cis* relative to one another). **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 20.72 (5-CH_3), 37.40 (C-3), 56.59 (8-OCH_3), 68.68 (C-5), 69.94 (C-11b), 71.16 (C-3a), 115.84 (C-9), 121.40 (C-10), 115.25 (C-6a), 123.40 (C-10a), 136.44 (C-11a), 149.95 (C-5a), 152.4 (C-7), 154.53 (C-8), 174.33 (C-2), 180.59 (C-11), 189.28 (C-6). A **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 = 20.72 (5-CH_3) ↔ δ = 1.64 (5-CH_3), δ = 37.40 (C-3) ↔ [δ_A = 2.74 (3-H^A) and δ_B = 2.88 (3-H^B)], δ = 56.59 (8-OCH_3) ↔ δ 4.03 (8-OMe), δ = 68.68 (C-5) ↔ δ = 4.78 (5-H), δ = 69.94 (C-11b) ↔ = 5.26 (11b-H), δ = 71.16 (C-3a) ↔ δ = 4.33 (3a-H), δ = 115.84 (C-9) ↔ δ = 7.14 (9-H), δ = 121.40 (C-10) ↔ δ = 7.73 (10-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 = 115.25 (C 6a) ↔ δ = 7.73 (10-H), δ = 123.40 (C-10a) ↔ δ = 7.14 (9-H), δ = 136.4 (C-11a) ↔ δ = 4.78 (5-H), δ = 136.44 (C-11a) ↔ δ = 5.26 (11b-H), δ 149.95 (C-5a) ↔ δ = 1.64 (5-CH_3), δ = 149.95 (C-5a) ↔ δ = 4.78 (5-H δ = 149.95 (C-5a) ↔ δ = 5.26 (11b-H), δ = 152.41 (C-7) ↔ δ = 7.14 (9 H), δ = 154.53 (C-8) ↔ δ = 4.01 (8-OMe), δ = 154.53 (C-8) ↔ δ = 7.1 (9-H), δ = 154.53 (C-8) ↔ δ = 7.73 (10-H), δ = 174.33 (C-2) ↔ [δ_A 2.74 (3-H^A) and δ_B = 2.88 (3-H^B)], δ = 174.33 (C-2) ↔ 4.33(3a-H), δ 180.59 (C-11) ↔ 5.26 (11b-H). δ = 189.28 (C-6) exhibited no cross peak. **Melting point:** 206-210°C (decomp). **Optical rotation:** $[\alpha]^D_{20}$ +131.2 (*c* = 0.34, MeOH). **HRMS** (pos. APCI): Calcd. for $C_{17}H_{14}O$ $[M+NH_4]^+$ = 348.10778; found 348.10791 (+0.38 ppm). **IR (film):** *v* 2930, 2855, 1785, 1645, 1615, 1455, 1440, 1410, 1365, 1320, 127(1205, 1150, 1115, 1080, 1035, 995, 960, 930, 910, 880, 845, 795, 74(700, 670 cm^{-1}.

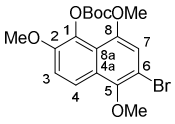
(3a*S*,5*R*,11b*S*)-7,8-Dimethoxy-5-methyl-3,3a-dihydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromene[5*H*,11b*H*]-trione = (+)-5-*ep* arizonin C1 [(+)-5-*epi*-4]



Under a nitrogen atmosphere 5-*epi*-arizonin B1 (5-*epi*-**3**, 9.5 mg 25.3 µmol) was dissolved in freshly prepared solution of MeI (31.6 µl 72.0 mg, 507µmol, 20.0 equiv.) in CH_2Cl_2 (1 mL). Ag_2O (82.1 mg 354 µmol, 14.0 equiv.) was added in one portion to initiate the reaction. The mixture was stirred at room temperature for 18 h. The reaction mixture was filtered over a small pipet (silica gel pad: h = 2 cm) and thoroughly rinsed with CH_2Cl_2 (10 mL). Afterwards the solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 8 cm, F = 8 mL; CH/EE 3:2 (F1-10), CH/EE 1:2 (F11-20)] afforded the title compound (F11-17, 3.2 mg, 34%, *dr* = 100:0)].– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.56 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.7 Hz, 5-CH_3), AB signal (δ_A = 2.73, δ_B = 2.88, J_{AB} = 17.5 Hz, A signal shows no further splitting, B signal further split by $J_{B,3a}$ = 4.8 Hz, 3-H^A and 3-H^B), 3.93 (s, 3H, 7-OMe), 3.99 (s, 3H, 8-OMe), 4.32 (dd, 1H, $J_{3a,B}$ = 4.7 Hz, $J_{3a,11b}$ = 2.6 Hz, 3a-H), 4.78 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.7 Hz, $^5J_{5,11b}$ = 1.7 Hz, 5-H), 5.28 (d, 1H, $J_{11b,3a}$ =

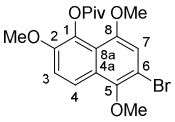
2.5 Hz, $^5J_{11b,5}$ = 1.7 Hz, 11b-H), 7.21 (d, 1H, $J_{9,10}$ = 8.7 Hz, 9-H), 7.95 (d, 1H, $J_{10,9}$ = 8.7 Hz, 10-H). 8-OMe was distinguished from 7-OMe by the occurrence of a cross-peak only for the former but not for the latter in the following **NOESY** spectrum (500.32 MHz, $CDCl_3$) that allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ_B = 2.88 (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 = 7.21 (9-H), δ = 4.78 (5-H) ↔ δ = 4.32 (3a-H, this cross-peak proves that 5-H and 3a-H are oriented *cis* relative to one another). δ = 3.92 (7-OMe) exhibited no cross-peak. **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 19.91 (5-CH_3), 37.34 (C-3), 56.45 (8-OCH_3), 61.27 (7-OCH_3), 69.01 (C-5), 69.79 (C-11b), 71.36 (C-3a), 116.08 (C-9), 124.75 (C-10), 125.31 (C-10a), 126.05 (C-6a), 133.19 (C-11a), 149.12 (C-7), 152.16 (C-5a), 159.09 (C-8), 174.45 (C-2), 181.39 (C-11), 184.10 (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 [$\delta(^{13}C) \leftrightarrow \delta(^1H)$]: δ = 19.91 (5-CH_3) ↔ δ = 1.56 (5-CH_3), δ = 37.34 (C-3) ↔ [δ_A = 2.73 (3-H^A) and δ_B = 2.88 (3-H^B)], δ = 56.45 (8-OCH_3) ↔ δ = 3.99 (8-OMe), δ = 61.27 (7-OCH_3) ↔ δ = 3.92 (7-OMe), δ = 69.01 (C-5) ↔ δ = 4.78 (5-H), δ = 69.79 (C-11b) ↔ δ = 5.28 (11b-H), δ = 71.36 (C-3a) ↔ δ = 4.32 (3a-H), δ = 116.08 (C-9) ↔ δ = 7.21 (9-H), δ = 124.75 (C-10) ↔ δ = 7.95 (10-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 = 125.31 (C-10a) ↔ δ = 7.21 (9-H), δ = 126.05 (C-6a) ↔ δ = 7.95 (10-H), δ = 133.19 (C-11a) ↔ δ = 4.78 (5-H), δ = 133.20 (C-11a) ↔ δ = 5.28 (11b-H), δ = 149.12 (C-7) ↔ δ = 3.93 (7-OMe), δ = 149.12 (C-7) ↔ δ = 7.21 (9-H), δ = 152.16 (C-5a) ↔ δ = 1.56 (5-CH_3), δ = 152.16 (C-5a) ↔ δ = 4.78 (5-H), δ = 152.16 (C-5a) ↔ δ = 5.28 (11b-H), δ = 159.09 (C-8) ↔ δ = 3.99 (8-OMe), δ = 159.09 (C-8) ↔ δ = 7.21 (9-H), δ = 159.09 (C-8) ↔ δ = 7.95 (10-H), δ = 174.45 (C-2) ↔ [δ_A = 2.73 (3-H^A) and δ_B = 2.88 (3-H^B)], δ = 174.45 (C-2) ↔ 4.32(3a-H), δ = 181.39 (C-11) ↔ 7.95 (10-H), δ = 184.10 (C-6) exhibited no cross-peak. **Optical rotation:** $[\alpha]_D^{20}$ = +143.1 (*c* = 0.32, MeOH). **HRMS** (pos. ESI): Calcd. for $C_{18}H_{17}O_7$ $[M+H]^+$ = 345.09688; found 345.09695 (+0.22 ppm). **IR (film):** ν = 3410, 3060, 2940, 2850, 1790, 1740, 1665, 1575, 1485, 1455, 1420, 1335, 1275, 1205, 1155, 1115, 1075, 1040, 995, 960, 905, 880, 845, 825, 785, 735, 700 cm^{-1}.

6-Bromo-2,5,8-trimethoxynaphthalen-1-yl *tert*-Butyl Carbonate (14c)



Under a nitrogen atmosphere 2,5,8-trimethoxynaphthalen-1-yl *tert*-butyl carbonate (**16c**, 2.79 g, 8.34 mmol) was dissolved in dry DMF (42 mL). Solid *N*-Bromosuccinimide (1.48 g, 8.34 mmol, 1.0 equiv.) was added 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 = 12, h = 12 cm, F = 100 ml; CH/EE 5:1) afforded the title compound (F9-14, R_f (5:1) = 0.25, 3.23 g, 94%) as a yellow solid.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.58 [s, 9H, C(CH_3)$_3$], 3.90 (s, 3H, 8-OMe), 3.91 (s, 3H, 5-OMe), 3.95 (s, 3H, 2-OMe), 6.86 (s, 1H, 7-H), 7.35 (d, 1H, $J_{3,4}$ = 9.3 Hz, 3-H), 7.96 (d, 1H, $J_{4,3}$ = 9.3 Hz, 4-H). 2-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 (400.13 MHz, $CDCl_3$) [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 3.90 (8-OMe) ↔ δ = 6.86 (7-H), δ = 3.95 (2-OMe) ↔ δ = 7.35 (3-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 27.89 [C(*C*H$_3$)$_3$], 56.60 (8-O*C*H$_3$), 57.03 (2-O*C*H$_3$), 61.47 (5-O*C*H$_3$), 110.60 (C-7), 115.28 (C-3), 121.22 (C-4), 82.86 [*C*(CH$_3$)$_3$], 109.60 (C-6), 120.87 (C-8a), 125.61 (C-4a), 134.65 (C-1), 147.03 (C-5), 149.73 (C-2), 151.74 (C-8), 151.90 (*carbonate*-C). 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 = 27.89 [C(*C*H$_3$)$_3$] ↔ δ = 1.58 [C(C*H*$_3$)$_3$], δ = 56.60 (8-O*C*H$_3$) ↔ δ = 3.90 (8-OMe), δ = 57.03 (2-O*C*H$_3$) ↔ δ = 3.95 (2-OMe), δ = 61.47 (5-O*C*H$_3$) ↔ δ = 3.91 (5-OMe), δ = 110.60 (C-7) ↔ δ = 6.86 (7-H), δ = 115.28 (C-3) ↔ δ = 7.35 (3-H), δ = 121.22 (C-4) ↔ δ = 7.96 (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 [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 82.86 [*C*(CH$_3$)$_3$] ↔ δ = 1.58 [C(C*H*$_3$)$_3$], δ = 109.60 (C-6) ↔ δ = 6.86 (7-H), δ = 120.87 (C-8a) ↔ δ = 6.86 (7-H), δ = 120.87 (C-8a) ↔ δ = 7.96 (4-H), δ = 125.61 (C-4a) ↔ δ = 7.35 (3-H), δ = 134.65 (C-1) ↔ δ = 6.86 (7-H), δ = 134.65 (C-1) ↔ δ = 7.35 (3-H), δ = 134.65 (C-1) ↔ δ = 7.96 (4-H), δ = 147.03 (C-5) ↔ δ = 3.91 (5-OMe), δ = 147.03 (C-5) ↔ δ = 6.86 (7-H), δ = 147.03 (C-5) ↔ δ = 7.96 (4-H), δ = 149.73 (C-2) ↔ δ = 3.96 (2-OMe), δ = 149.73 (C-2) ↔ δ = 7.35 (3-H), δ = 149.73 (C-2) ↔ δ = 7.96 (4-H), δ = 151.74 (C-8) ↔ δ = 3.90 (8-OMe), δ = 151.74 (C-8) ↔ δ = 6.86 (7-H). δ = 151.90 (*carbonate*-C) exhibited no cross-peak. **Melting point:** 90°C. **Elemental analysis:** Calculated: C: 52.31%, H: 5.12%; found: C: 51.94%, H: 5.00%; deviation: C:0.37%, H: 0.12%. **HRMS** (pos. ESI): calcd. for $C_{18}H_{21}{}^{79}BrO_6$: $[M+Na]^+$ = 435.04137; found: 435.04153 (0.37 ppm). **IR (film):** ν = 3005, 2980, 2935, 2845, 1760, 1625, 1585, 1510, 1465, 1440, 1380, 1370, 1320, 1285, 1255, 1160, 1145, 1075, 1050, 1030, 1005, 980, 930, 865, 820, 805, 790, 775, 735, 700 cm^{-1}.

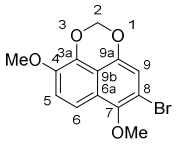
6-Bromo-2,5,8-trimethoxynaphthalen-1-yl Pivalate (14d)



Under a nitrogen atmosphere 2,5,8-trimethoxynaphthalen-1-yl pivalate (**16d**, 768 mg, 2.13 mmol) was dissolved in dry DMF (20 mL). Solid *N*-Bromosuccinimide (417 mg, 2.34 mmol, 1.1 equiv.) was added 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 = 4, h = 12 cm, F = 50 ml; CH/EE 5:1) afforded the title compound (F5-11, R_f (5:1) = 0.3, 780 mg, 92%) as a yellow solid.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.44 [s, 9H, C(CH_3)$_3$], 3.84 (s, 3H, 8-OMe), 3.90 (s, 3H, 2-OMe), 3.91 (s, 3H, 5-OMe), 6.82 (s, 1H, 7-H), 7.33 (d, 1H, $J_{3,4}$ = 9.2 Hz, 3-H), 7.96 (d, 1H, $J_{4,3}$ = 9.2 Hz, 4-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 3.84 (8-OMe) ↔ δ = 6.82 (7-H), δ = 3.90 (2-OMe) ↔ δ = 7.33 (3-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 27.41 [C(*C*H$_3$)$_3$], 39.24 [*C*(CH$_3$)$_3$], 55.90 (8-O*C*H$_3$), 56.88 (2-O*C*H$_3$), 61.40 (5-O*C*H$_3$), 109.42 (C-6), 110.03 (C-7), 114.96 (C-3), 120.87 (C-4), 120.96 (C-8a), 125.64 (C-4a), 135.01 (C-1), 146.83 (C-5), 149.12 (C-2), 151.94 (C-8), 176.75 (1-O$_2$*C*-C(CH$_3$)$_3$]. 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 = 27.41 [C(*C*H$_3$)$_3$] ↔ δ = 1.44 [C(C*H*$_3$)$_3$], δ = 55.90 (8-O*C*H$_3$) ↔ δ = 3.84 (8-OMe), δ = 56.88 (2-O*C*H$_3$) ↔ δ = 3.90 (2-OMe), δ = 61.40 (5-O*C*H$_3$) ↔ δ = 3.91 (5-OMe), δ = 110.03 (C-7) ↔ δ = 6.82 (7-H), δ = 114.96 (C-3) ↔ δ = 7.33 (3-H), δ = 120.87 (C-4) ↔ δ = 7.96 (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 [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 39.24 [*C*(CH$_3$)$_3$] ↔ δ = 1.44 [C(C*H*$_3$)$_3$], δ = 109.42 (C-6) ↔ δ = 6.82 (7-H), δ = 120.96 (C-8a) ↔ δ = 6.82 (7-H), δ = 120.96 (C-8a) ↔ δ = 7.96 (4-H), δ = 125.64 (C-4a) ↔ δ = 7.33 (3-H), δ = 135.01 (C-1) ↔ δ = 6.82 (7-H), δ = 135.01 (C-1) ↔ δ = 7.33 (3-H), δ = 135.01 (C-1) ↔ δ = 7.96 (4-H), δ =

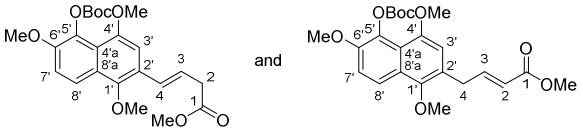
146.83 (C-5) ↔ *δ* = 3.91 (5-OMe), *δ* = 146.83 (C-5) ↔ *δ* = 6.82 (7-H), *δ* = 146.83 (C-5) ↔ *δ* = 7.96 (4-H), *δ* = 149.12 (C-2) ↔ *δ* = 3.90 (2-OMe), *δ* = 149.12 (C-2) ↔ *δ* = 7.33 (3-H), *δ* = 149.12 (C-2) ↔ *δ* = 7.96 (4-H), *δ* = 151.94 (C-8) ↔ *δ* = 3.84 (8-OMe), *δ* = 151.94 (C-8) ↔ *δ* = 6.82 (7-H), *δ* = 176.75 (1-O$_2$*C*-C(CH$_3$)$_3$] ↔ *δ* = 1.44 [C(*CH*$_3$)$_3$]. **Melting point:** 142-143°C. **HRMS** (pos. APCI): calcd. for $C_{18}H_{22}{}^{79}BrO_5$: $[M+H]^+$ = 397.06506; found: 397.06530 (+0.6 ppm), $C_{18}H_{22}{}^{81}BrO_5$: $[M+H]^+$ = 399.06301; found: 399.06320 (+0.5 ppm). **IR (film):** v = 2970, 1745, 1590, 1575, 1470, 1455, 1380, 1365, 1320, 1280, 1250, 1135, 1120, 1070, 1025, 1020, 815, 790 cm^{-1}.

8-Bromo-4,7-dimethoxynaphtho[1,8-*de*][1,3]dioxine (14h)



Under a nitrogen atmosphere 4,7-dimethoxynaphtho[1,8-*de*][1,3]dioxine (**16h**, 60.2 mg, 0.26 mmol) was dissolved in dry DMF (2 ml). Solid *N*-bromosuccinimide (46.3 mg, 0.26 mmol, 1.0 equiv.) was added 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 = 1.5 cm, h = 12 cm, F = 8 ml; CH/EE 9:1 (F1-12), CH/EE 5:1 (F13-25)] afforded the title compound (F10-15, R_f (9:1) = 0.2, R_f (5:1) = 0.4, 74.4 mg, 92%) as a pale-yellow solid. Note: An upscaling of this reaction was easily achieved: Bromination of **39** (2.06 g, 8.87 mmol) with *N*-bromosuccinimide (1.58 g, 8.87 mmol, 1.0 equiv.) in DMF (44 ml) furnished the title compound (2.48 g, 90%) in a slightly lower yield (Flash chromatography data: d = 12 cm, h = 12 cm, F = 100 ml; CH/EE 5:1, product: F9-13).– **^{1}H NMR** (400.13 MHz, $CDCl_3$): 3.94 (s, 3H, 7-OMe), 4.00 (s, 3H, 4-OMe), 5.53 (s, 2H, 2-H$_2$), 7.00 (s, 1H, 9-H), 7.30 (d, 1H, $J_{5,6}$ = 9.0 Hz, 5-H), 7.67 (d, 1H, $J_{6,5}$ = 9.0 Hz, 6-H). A **NOESY** spectrum allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks (400.13 MHz, $CDCl_3$) [*δ*(^{1}H) ↔ *δ*(^{1}H)]: *δ* = 3.94 (7-OMe) ↔ *δ* = 7.67 (6-H), *δ* = 4.00 (4-OMe) ↔ *δ* = 7.30 (5-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): *δ* = 57.32 (4-O*C*H$_3$), 61.57 (7-O*C*H$_3$), 91.35 (C-2), 112.72 (C-9), 110.47 (C-8), 116.11 (C-9b), 116.39 (C-6), 116.56 (C-5), 121.48 (C-6a), 137.62 (C-3a), 141.99 (C-4), 145.56 (C-9a), 147.90 (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 ^{1}H resonances [*δ*(^{13}C) ↔ *δ*(^{1}H)]: *δ* = 57.32 (4-O*C*H$_3$) ↔ *δ* = 4.00 (4-OMe), *δ* = 61.57 (7-O*C*H$_3$) ↔ *δ* = 3.94 (7-OMe), *δ* = 91.35 (C-2) ↔ *δ* = 5.53 (2-H$_2$), *δ* = 112.72 (C-9) ↔ *δ* = 7.00 (9-H), *δ* = 116.39 (C-6) ↔ *δ* = 7.67 (6-H), *δ* = 116.56 (C-5) ↔ *δ* = 7.30 (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* = 110.47 (C-8) ↔ *δ* = 7.00 (9-H), *δ* = 116.11 (C-9b) ↔ *δ* = 7.00 (9-H), *δ* = 116.11 (C-9b) ↔ *δ* = 7.67 (6-H), *δ* = 121.48 (C-6a) ↔ *δ* = 7.30 (5-H), *δ* = 137.62 (C-3a) ↔ *δ* = 5.53 (2-H$_2$), *δ* = 137.62 (C-3a) ↔ *δ* = 7.30 (5-H), *δ* = 141.99 (C-4) ↔ *δ* = 4.00 (4-OMe), *δ* = 141.99 (C-4) ↔ *δ* = 7.30 (5-H), *δ* = 141.99 (C-4) ↔ *δ* = 7.67 (6-H), *δ* = 145.56 (C-9a) ↔ *δ* = 5.53 (2-H$_2$), *δ* = 145.56 (C-9a) ↔ *δ* = 7.00 (9-H), *δ* = 147.90 (C-7) ↔ *δ* = 3.94 (7-OMe), *δ* = 147.90 (C-7) ↔ *δ* = 7.00 (9-H), *δ* = 147.90 (C-7) ↔ *δ* = 7.67 (6-H). **Melting point:** 98°C. **Elemental analysis:** Calculated: C: 65.45%, H: 5.49%; found: C: 65.32%, H: 5.83%; deviation: C: 0.13%, H: 0.34%. **HRMS** (pos. ESI): calcd. for $C_{13}H_{11}{}^{81}BrO_4$ $[M]^+$ = 311.98148; found 311.98154 (+0.19 ppm). **IR (film):** *v* = 3000, 2945, 2905, 2840, 1735, 1620, 1610, 1575, 1505, 1480, 1445, 1410, 1380, 1340, 1275, 1210, 1165, 1105, 1070, 1040, 1030, 1015, 995, 975, 935, 895, 855, 810, 785, 730, 710, 690 cm^{-1}.

(*E*)-Methyl 4-(5-(*tert*-butoxycarbonyloxy)-1,4,6-trimethoxynaphthalen-2-yl)but-3-enoate (15c) and (*E*)-Methyl 4-(5-(*tert*-butoxycarbonyloxy)-1,4,6-trimethoxynaphthalen-2-yl)but-2-enoate (*iso*-15c)[61]



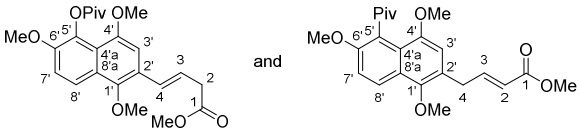
as an inseparable 87:13 mixture

6-Bromo-2,5,8-trimethoxynaphthalen-1-yl *tert*-butyl carbonate (**14c**, 1.38 g, 3.34 mmol) and $Pd_2dba_3{\cdot}CHCl_3$ (69.0 mg, 66.8 µmol, 2.0 mol-% were dissolved in freshly distilled toluene (34 mL). P(*t*-Bu)$_3$ (54.2 mg 267 µmol, 8.0 mol-%) was weighed out in a glove box and afterward dissolved in freshly distilled toluene (2mL). The latter solution wa transferred to the reaction mixture. *N,N*-dicyclohexylmethylamin (2.15 mL, 1.96 g, 10.0 mmol, 3.0 equiv.) and methyl vinylacetat (1.07 mL, 1.00 g, 10.0 mmol, 3.0 equiv) were added at roor temperature. The reaction mixture was refluxed for 2 d. The mixtur was allowed to cool to room temperature and EtOAc (40 mL) wa added. The organic phase was washed with aq. HCl (1M, 2×40 mL and brine (40 ml) and dried over Na_2SO_4. The solvent was removed i vacuo and the oily residue was purified by flash chromatograph [d = 4 cm, h = 12 cm, F = 50 mL; CH/EE 5:1 (F1-14), CH/EE 3:1 (F15 33)] to obtain the product [F15-23, R_f (5:1) = 0.1, R_f (3:1) = 0.25, 1.19 g 82%] as a yellow-brownish oil and as a 87:13 mixture of **15c** and it α,β-unsaturated carboxylic ester isomer *iso*-**15c**.– NMR analysis of **15c** **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.58 [s, 9H, C(CH$_3$)$_3$], 3.34 (dd, 2H $J_{2,3}$ = 7.1 Hz, $^4J_{2,4}$ = 1.5 Hz, 2-H$_2$), 3.74 (s, 3H, 1-OMe), 3.83 (s, 3H, 1 OMe), 3.93 (s, 3H, 4'-OMe), 3.95 (s, 3H, 6'-OMe), 6.32 (dt, 1H, $J_{3,4}$ 16.0 Hz, $J_{3,2}$ = 7.2 Hz, 3-H), 6.88 (s, 1H, 3'-H), 6.92 (dt, 1H, $J_{4,3}$ 16.1 Hz, $^4J_{4,2}$ = 1.5 Hz, 4-H), 7.30 (d, 1H, $J_{7',8'}$ = 9.3 Hz, 7'-H), 7.95 (d 1H, $J_{8',7'}$ = 9.3 Hz, 8'-H). A **NOESY** spectrum (400.13 MHz, CDCl allowed additional assignments of ^{1}H resonances by the occurrence c crosspeaks [*δ*(^{1}H) ↔ *δ*(^{1}H)]: *δ* = 1.58 [C(CH$_3$)$_3$] ↔ *δ* = 3.93 (4'-OMe), = 3.83 (1'-OMe) ↔ *δ* = 6.92 (4-H), *δ* = 3.83 (1'-OMe) ↔ *δ* = 7.95 (8'-H *δ* = 3.93 (4'-OMe) ↔ *δ* = 6.88 (3'-H), *δ* = 3.95 (6'-OMe) ↔ *δ* = 7.30 (7 H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): *δ* = 27.91 [C(*CH*$_3$)$_3$], 38.68 (C-2 52.00 (1-O*C*H$_3$), 56.46 (4'-O*C*H$_3$), 57.03 (6'-O*C*H$_3$), 62.55 (1'-O*C*H$_3$ 82.66 [*C*(CH$_3$)$_3$], 103.77 (C-3'), 114.72 (C-7'), 121.37 (C-4'a), 121.4 (C-8'), 122.14 (C-3), 122.96 (C-2'), 125.54 (C-8'a), 127.74 (C-4), 134.6 (C-5'), 147.29 (C-1'), 149.61 (C-6'), 151.48 (C-4'), 151.96 (5'-O*C*O$_2$tBu 172.17 (C-1). An **edHSQC** spectrum ("short-range C,H COSY 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of a nonquaternary ^{13}C atoms through their cross-peaks with th independently assigned ^{1}H resonances [*δ*(^{13}C) ↔ *δ*(^{1}H)]: *δ* = 27.9 [C(*CH*$_3$)$_3$] ↔ *δ* = 1.58 [C(*CH*$_3$)$_3$], *δ* = 38.68 (C-2) ↔ *δ* = 3.34 (2-H$_2$), *δ* 52.00 (1-O*C*H$_3$) ↔ *δ* = 3.74 (1-OMe), *δ* = 56.46 (4'-O*C*H$_3$) ↔ *δ* = 3.9 (4'-OMe), *δ* = 57.03 (6'-O*C*H$_3$) ↔ *δ* = 3.95 (6'-OMe), *δ* = 62.55 (1 O*C*H$_3$) ↔ *δ* = 3.83 (1'-OMe), *δ* = 103.77 (C-3') ↔ *δ* = 6.88 (3'-H), *δ* 114.72 (C-7') ↔ *δ* = 7.30 (7'-H), *δ* = 121.45 (C-8') ↔ *δ* = 7.95 (8'-H), = 122.14 (C-3) ↔ *δ* = 6.32 (3-H), *δ* = 127.74 (C-4) ↔ *δ* = 6.92 (4-H). A **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, CDCl 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* = 82.66 [*C*(CH$_3$)$_3$] ↔ *δ* = 1.58 [C(*CH*$_3$)$_3$], *δ* = 121.37 (C-4'a) ↔ *δ* = 6.88 (3'-H), *δ* = 121.37 (C-4'a) ↔ *δ* = 7.95 (8'-H), *δ* = 122.96 (C-2') ↔ *δ* = 6.32 (3-H), *δ* = 122.96 (C-2') ↔ *δ* = 6.88 (3'-H), *δ* = 125.54 (C-8'a) ↔ *δ* = 7.30 (7'-H), *δ* = 134.66 (C-5') ↔ *δ* = 7.30 (7'-H), *δ* = 134.66 (C-5') ↔ *δ* = 7.95 (8'-H), *δ* = 147.29 (C-1') ↔ *δ* = 3.83 (1'-OMe), *δ* = 147.29 (C-1') ↔ *δ* = 6.88 (3'-H), *δ* = 147.29 (C-1') ↔ *δ* = 7.95 (8'-H), *δ* = 149.61 (C-6') ↔ *δ*

[61] 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.

= 3.95 (6'-OMe), *δ* = 149.61 (C-6') ↔ *δ* = 7.30 (7'-H), **δ** = 149.61 (C-6') ↔ *δ* = 7.95 (8'-H), *δ* = 151.48 (C-4') ↔ *δ* = 3.93 (4'-OMe), *δ* = 151.48 (C-4') ↔ *δ* = 6.88 (3'-H), *δ* = 172.17 (C-1) ↔ *δ* = 3.34 (2-H_2), **δ** = 172.17 (C-1) ↔ *δ* = 3.74 (1-OMe). *δ* = 151.96 (5'-OCO_2tBu) exhibited no crosspeak. NMR analysis of *iso*-**15c**: Only an assignment of the **^{1}H NMR** (400.13 MHz, $CDCl_3$) resonances was possible: δ = 1.58 [s, 9H, $C(CH_3)_3$], 3.65 (dd, 2H, $J_{4,3}$ = 6.5 Hz, $^4J_{4,3}$ = 1.8 Hz, 4-H_2), 3.71, 3.81, 3.88, and 3.95 (4×s, 4×3H, 1-OMe, 1'-OMe, 4'-OMe, and 6'-OMe), 5.86 (dt, 1H, $J_{2,3}$ = 15.7 Hz, $^4J_{2,4}$ = 1.8 Hz, 2-H), 6.52 (s, 1H, 3'-H), 7.15 (dt, 1H, $J_{3,2}$ = 15.6 Hz, $J_{3,4}$ = 6.5 Hz, 3-H), 7.33 (d, 1H, $J_{7',8'}$ = 9.3 Hz, 7'-H), 7.92 (d, 1H, $J_{8',7'}$ = 9.3 Hz, 8'-H). **Melting point:** Oil. **HRMS** (pos. ESI): Calcd. for $C_{23}H_{28}O_8Na$ $[M+Na]^+$ = 455.16764; found 455.16757 (–0.15 ppm). **IR (film):** ν = 3450, 3055, 2980, 2945, 2845, 1745, 1660, 1605, 1510, 1480, 1460, 1440, 1375, 1340, 1280, 1255, 1200, 1155, 1140, 1070, 1010, 980, 895, 850, 820, 800, 775, 735, 705 cm^{-1}.

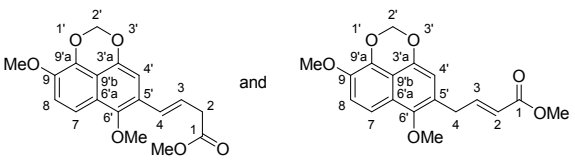
(*E*)-Methyl 4-[1,4,6-trimethoxy-5-(pivaloyloxy)-naphthalen-2-yl]but-3-enoate (15d) and (*E*)-Methyl 4-(1,4,6-trimethoxy-5-pivaloyloxynaphthalen-2-yl)but-2-enoate (*iso*-15d)[61]



as an inseparable 87:13 mixture

6-Bromo-2,5,8-trimethoxynaphthalen-1-yl pivalate (**14d**, 280 mg, 0.70 mmol) and $Pd_2dba_3{\cdot}CHCl_3$ (14.5 mg, 14.0 µmol, 2.0 mol-%) were dissolved in freshly distilled toluene (7 mL). P(*t*-Bu)$_3$ (11.3 mg, 56 µmol, 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 (0.45 mL, 0.41 g, 2.1 mmol, 3.0 equiv.) and methyl vinylacetate (0.22 mL, 0.21 g, 2.1 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 (25 mL) was added. The organic phase was washed with aq. HCl (1M, 2×25 mL) and brine (25 ml) and dried over Na_2SO_4. The solvent was removed in vacuo and the oily residue was purified by flash chromatography [d = 3 cm, h = 12 cm, F = 25 mL; CH/EE 5:1] to obtain the product [F19-22, R_f (5:1) = 0.15, 175 mg, 60%] as a yellow-brownish oil and as a 87:13 mixture of **15d** and its α,β-unsaturated carboxylic ester isomer *iso*-**15d**.– NMR analysis of **15d**: **^{1}H NMR** (500.42 MHz, $CDCl_3$): *δ* = 1.44 [s, 9H, $C(CH_3)_3$], 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), 3.83 (s, 3H, 1'-OMe), 3.88 (s, 3H, 4'-OMe), 3.89 (s, 3H, 6'-OMe), 6.31 (dt, 1H, $J_{3,4}$ = 16.0 Hz, $J_{3,2}$ = 7.2 Hz, 3-H), 6.83 (s, 1H, 3'-H), 6.92 (dt, 1H, $J_{4,3}$ = 16.0 Hz, $^4J_{4,2}$ = 1.5 Hz, 4-H), 7.29 (d, 1H, $J_{7',8'}$ = 9.2 Hz, 7'-H), 7.95 (d, 1H, $J_{8',7'}$ = 9.2 Hz, 8'-H). A **NOESY** spectrum (500.42 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [*δ*(^{1}H) ↔ *δ*(^{1}H)]: *δ* = 3.83 (1'-OMe) ↔ *δ* = 6.92 (4-H), *δ* = 3.88 (4'-OMe) ↔ *δ* = 6.83 (3'-H), *δ* = 3.89 (6'-OMe) ↔ *δ* = 7.29 (7'-H), *δ* = 6.83 (3'-H) ↔ *δ* = 6.31 (3-H). **^{13}C NMR** (125.83 MHz, $CDCl_3$): *δ* = 27.50 [$C(CH_3)_3$], 38.69 (C-2), 39.30 [*C*$(CH_3)_3$], 52.03 (1-OCH_3), 55.73 (4'-OCH_3), 56.94 (6'-OCH_3), 62.58 (1'-OCH_3), 102.97 (C-3'), 114.43 (C-7'), 121.18 (C-8'), 121.95 (C-3), 121.48 (C-4'a), 122.76 (C-2'), 125.59 (C-8'a), 127.80 (C-4), 134.99 (C-5'), 147.13 (C-1'), 149.06 (C-6'), 151.72 (C-4'), 172.26 (C-1), 176.86 (5'-O_2*C*tBu). An **edHSQC** spectrum ("short-range C,H COSY"; 125.83/500.42 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* = 27.50 [$C(CH_3)_3$] ↔ *δ* = 1.44 [$C(CH_3)_3$], *δ* = 38.69 (C-2) ↔ *δ* = 3.35 (2-H_2), *δ* = 52.03 (1-OCH_3) ↔ *δ* = 3.74 (1-OMe), *δ* = 55.73 (4'-OCH_3) ↔ *δ* = 3.88 (4'-OMe), *δ* = 56.94 (6'-OCH_3) ↔ *δ* = 3.89 (6'-OMe), *δ* = 62.58 (1'-OCH_3) ↔ *δ* = 3.83 (1'-OMe), *δ* = 102.97 (C-3') ↔ *δ* = 6.83 (3'-H), *δ* = 114.43 (C-7') ↔ *δ* = 7.29 (7'-H), *δ* = 121.18 (C-8') ↔ *δ* = 7.95 (8'-H), *δ* = 121.95 (C-3) ↔ *δ* = 6.31 (3-H), *δ* = 127.80 (C-4) ↔ *δ* = 6.92 (4-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.83/500.42 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* = 39.30 [*C*$(CH_3)_3$] ↔ *δ* = 1.44 [$C(CH_3)_3$], *δ* = 121.48 (C-4'a) ↔ *δ* = 6.83 (3'-H), *δ* = 121.48 (C-4'a) ↔ *δ* = 7.95 (8'-H), *δ* = 122.76 (C-2') ↔ *δ* = 6.31 (3-H), *δ* = 122.76 (C-2') ↔ *δ* = 6.83 (3'-H), *δ* = 125.59 (C-8'a) ↔ *δ* = 6.83 (3'-H), *δ* = 125.59 (C-8'a) ↔ *δ* = 7.29 (7'-H), *δ* = 134.99 (C-5') ↔ *δ* = 6.83 (3'-H), *δ* = 134.99 (C-5') ↔ *δ* = 7.29 (7'-H), *δ* = 134.99 (C-5') ↔ *δ* = 7.95 (8'-H), *δ* = 147.13 (C-1') ↔ *δ* = 3.83 (1'-OMe), *δ* = 147.13 (C-1') ↔ *δ* = 6.83 (3'-H), *δ* = 147.13 (C-1') ↔ *δ* = 6.92 (4-H), *δ* = 149.06 (C-6') ↔ *δ* = 3.95 (6'-OMe), *δ* = 149.06 (C-6') ↔ *δ* = 7.29 (7'-H), *δ* = 149.06 (C-6') ↔ *δ* = 7.95 (8'-H), *δ* = 151.72 (C-4') ↔ *δ* = 3.88 (4'-OMe), *δ* = 151.72 (C-4') ↔ *δ* = 6.83 (3'-H), *δ* = 172.26 (C-1) ↔ *δ* = 3.35 (2-H_2), *δ* = 172.26 (C-1) ↔ *δ* = 3.74 (1-OMe), *δ* = 172.26 (C-1) ↔ *δ* = 6.31 (3-H), *δ* = 176.86 (5'-O_2*C*tBu) ↔ *δ* = 1.44 [$C(CH_3)_3$]. NMR analysis of *iso*-**15d**: Due to the small amount of the minor product structural assignments in the NOESY and HMBC spectra were impossible. **^{1}H NMR** (500.42 MHz, $CDCl_3$): δ = 1.44 [s, 9H, $C(CH_3)_3$], 3.65 (ddd, 2H, $J_{4,3}$ = 7.2 Hz, $^4J_{4,2}$ = 1.5 Hz, $^4J_{4,3'}$ = 1.5 Hz, 4-H_2,), 3.71, 3.82, 3.83, and 3.90 (4×s, 4×3H, 1-OMe, 1'-OMe, 4'-OMe, and 6'-OMe), 5.82 (dt, 1H, $J_{2,3}$ = 15.5 Hz, $^4J_{2,4}$ = 1.7 Hz, 2-H), 6.48 (br. s, 1H, $^4J_{3',4}$ not observed 3'-H,), 7.15 (dt, 1H, $J_{3,2}$ = 15.5 Hz, $J_{3,4}$ = 6.4 Hz, 3-H), 7.33 (d, 1H, $J_{7',8'}$ = 9.1 Hz, 7'-H), 7.92 (d, 1H, $J_{8',7'}$ = 9.1 Hz, 8'-H). **^{13}C NMR** (125.83 MHz, $CDCl_3$):*δ* = 27.50 [$C(CH_3)_3$], 32.58 (C-4), 39.30 [*C*$(CH_3)_3$], 51.53, 55.77, 57.02, and 62.41 (1-OCH_3, 1'-OCH_3, 4'-OCH_3, and 6'-OCH_3,) could not be assigned unambiguously, 107.70 (C-3'), 114.59 (C-7'), 120.83, 123.27, and 125.53 (C-2', C-4'a, and C-8'a) could not be assigned unambiguously, 120.98 (C-8'), 122.06 (C-2), 134.99 (C-5'), 147.33 (C-3), 147.61, 148.71, and 151.76 (C1', C-4', and C-6') could not be assigned unambiguously, 166.99 (C-1), 176.92 (5'-O_2*C*tBu). An **edHSQC** spectrum ("short-range C,H COSY"; 125.83/500.42 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* = 27.50 [$C(CH_3)_3$] ↔ *δ* = 1.44 [$C(CH_3)_3$], *δ* = 32.58 (C-4) ↔ *δ* = 3.65 (4-H_2), *δ* = 51.53, 55.77, 57.02, and 62.41 (1-OCH_3, 1'-OCH_3, 4'-OCH_3, and 6'-OCH_3,) could not be assigned unambiguously, *δ* = 107.70 (C-3') ↔ *δ* = 6.48 (3'-H), *δ* = 114.59 (C-7') ↔ *δ* = 7.32 (7'-H), *δ* = 120.98 (C-8') ↔ *δ* = 7.92 (8'-H), *δ* = 122.06 (C-2) ↔ *δ* = 5.82 (2-H), *δ* = 147.33 (C-3) ↔ *δ* = 7.15 (3-H). **Melting point:** Oil. **HRMS** (pos. APCI): calcd. for $C_{23}H_{29}O_7$ $[M+H]^+$ = 417.19133; found 417.19090 (–1.0 ppm). **IR (film):** ν = 3325, 2975, 2875, 1750, 1665, 1605, 1590, 1480, 1460, 1440, 1395, 1365, 1335, 1280, 1200, 1105, 1075, 1030, 890, 825, 780, 750 cm^{-1}.

(*E*)-Methyl 4-(6,9-dimethoxynaphtho[1,8-*de*][1,3 dioxine-5-yl]but-3-enoate (15h) and (*E*)-Methyl 4-(6,9-dimethoxynaphtho[1,8-*de*][1,3 dioxine-5-yl]but-2-enoate (*iso*-15h)[61]

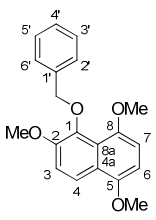


as an inseparable 93:7 mixture

8-Bromo-4,7-dimethoxynaphtho[1,8-*de*][1,3]dioxine (**14h**, 1.56 g, 5.01 mmol) and $Pd_2dba_3{\cdot}CHCl_3$ (51.8 mg, 0.05 mmol, 1.0 mol-%) were dissolved in freshly distilled toluene (50mL). P(*t*-Bu)$_3$ (40.6 mg, 0.20 mmol, 4.0 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 (3.23 mL, 2.94 g, 15.0 mmol, 3.0 equiv.) and methyl vinylacetate (1.60 mL, 1.50 g, 15.0 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 EtOAc (100 mL) was added. The organic phase was washed with aq. HCl (1M, 2×50 mL) and brine (50 ml) and dried over Na_2SO_4. The solvent was removed in

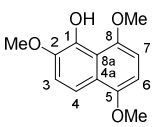
vacuo and the oily residue was purified by flash chromatography (d = 5 cm, h = 12 cm, F = 50 mL; CH/EE 5:1) to obtain the product [F16-20, R_f (5:1) = 0.2, 571.7 mg] as pale-yellow oil and a second fraction (F11-15, 620.7 mg) containing unidentified impurities This second fraction was purified again by a second flash chromatography (d = 4 cm, h = 12 cm, F = 50 mL; CH/EE 7:1) to obtain the product (F16-22, 527.0 mg). Combined yield: 1.099 g, 66%, obtained as a 93:7 mixture of the title compound with its α,β-unsaturated ester isomer ***iso*-15h**.– NMR-analysis of **15h**: **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 3.33 (dd, 2H, $J_{2,3}$ = 7.2 Hz, $^4J_{2,4}$ = 1.6 Hz, 2-H$_2$), 3.73 (s, 3H, 1-OMe), 3.87 (s, 3H, 6'-OMe), 4.00 (s, 3H, 9'-OMe), 5.55 (s, 2H, 2'-H$_2$), 6.32 (dt, 1H, $J_{3,4}$ = 16.0 Hz, $J_{3,2}$ = 7.2 Hz, 3-H), 6.93 (dt, 1H, $J_{4,3}$ = 16.0 Hz, $^4J_{4,2}$ = 1.6 Hz, 4-H), 7.02 (s, 1H, 4'-H), 7.28 (d, 1H, $J_{8',7'}$ = 9.2 Hz, 8'-H), 7.67 (d, 1H, $J_{7',8'}$ = 9.2 Hz, 7'-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 4.00 (9'-OMe) ↔ δ = 7.28 (8'-H), δ = 7.02 (4'-H) ↔ δ = 6.32 (3-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 38.68 (C-2), 52.00 (1-O*C*H$_3$), 57.31 (9'-O*C*H$_3$), 62.62 (6'-O*C*H$_3$), 91.37 (C-2'), 105.65 (C-4'), 115.89 (C-8'), 116.45 (C-9'b), 116.59 (C-7'), 122.78 (C-3), 124.08 (C-6'a), 124.38 (C-5'), 127.54 (C-4), 137.69 (C-9'a), 141.91 (C-9'), 145.36 (C-3'a), 147.96 (C-6'), 172.03 (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 = 38.68 (C-2) ↔ δ = 3.33 (2-H$_2$), δ = 52.00 (1-O*C*H$_3$) ↔ δ = 3.73 (1-OMe), δ = 57.31 (9'-O*C*H$_3$) ↔ δ = 4.00 (9'-OMe), δ = 62.62 (6'-O*C*H$_3$) ↔ δ = 3.87 (6'-OMe), δ = 91.37 (C-2') ↔ δ = 5.55 (*2'*-H$_2$), δ = 105.65 (C-4') ↔ δ = 7.02 (4'-H), δ = 115.89 (C-8') ↔ δ = 7.28 (8'-H), δ = 116.59 (C-7') ↔ δ = 7.67 (7'-H), δ = 122.78 (C-3) ↔ δ = 6.32 (3-H), δ = 127.54 (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 = 116.45 (C-9'b) ↔ δ = 7.02 (4'-H), δ = 116.45 (C-9'b) ↔ δ = 7.67 (7'-H), δ = 124.08 (C-6'a) ↔ δ = 7.28 (8'-H), δ = 124.38 (C-5') ↔ δ = 6.32 (3-H), δ = 137.69 (C-9'a) ↔ δ = 5.55 (2'-H$_2$), δ = 137.69 (C-9'a) ↔ δ = 7.28 (8'-H), δ = 141.91 (C-9') ↔ δ = 4.00 (9'-OMe), δ = 141.91 (C-9') ↔ δ = 7.28 (8'-H), δ = 141.91 (C-9') ↔ δ = 7.67 (7'-H), δ = 145.36 (C-3'a) ↔ δ = 5.55 (2'-H$_2$), δ = 145.36 (C-3'a) ↔ δ = 7.02 (4'-H), δ = 147.96 (C-6') ↔ δ = 3.87 (6'-OMe), δ = 147.96 (C-6') ↔ δ = 7.02 (4'-H), δ = 147.96 (C-6') ↔ δ = 7.67 (7'-H), δ = 172.03 (C-1) ↔ δ = 3.33 (2-H$_2$), δ = 172.03 (C-1) ↔ δ = 3.73 (1-OMe), δ = 172.03 (C-1) ↔ δ = 6.32 (3-H). NMR analysis of ***iso*-15h**: Only an assignment of the **^{1}H NMR** (400.13 MHz, $CDCl_3$) resonances was possible: 3.66 (dd, 2H, $J_{4,3}$ = 6.7 Hz, $^4J_{4,3}$ = 1.6 Hz, 4-H$_2$), 3.71, 3.89, 4.01 (3×s, 3×3H, 1-OMe, 6'-OMe, and 9'-OMe), 5.55 (s, 2H, 2'-H$_2$), 5.84 (dt, 1H, $J_{2,3}$ = 15.6 Hz, $^4J_{2,4}$ = 1.7 Hz, 2-H), 6.65 (s, 1H, 4'-H), 7.13 (dt, 1H, $J_{3,2}$ = 15.6 Hz, $J_{3,4}$ = 6.5 Hz, 3-H), 7.30 (d, 1H, $J_{8',7'}$ = 9.2 Hz, 8'-H), 7.64 (d, 1H, $J_{7',8'}$ = 9.2 Hz, 7'-H). **Melting point:** 105°C. **Elemental analysis:** Calculated: C: 65.45%, H: 5.49%; found: C: 65.06%, H: 5.53%; deviation: C: 0.39%, H: 0.04%. **HRMS** (pos. ESI): calcd. for $C_{18}H_{18}O_6$ $[M+Na]^+$ = 353.09956; found 353.09988 (+0.92 ppm). **IR (film):** *v* = 3055, 2985, 2950, 2845, 2305, 1735, 1620, 1575, 1505, 1485, 1440, 1405, 1385, 1340, 1275, 1265, 1205, 1165, 1105, 1070, 1035, 1015, 995, 970, 895, 860, 815, 740, 705 cm^{-1}.

1-(Benzyloxy)-2,5,8-trimethoxynaphthalene (16a)



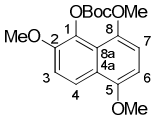
In a 50 ml round-bottomed flask 5-(benzyloxy)-6-methoxynaphthalene-1,4-diol (**29**, 1.89 g, 6.38 mmol) and *n*Bu$_4$NBr (103 mg, 0.32mmol, 5.0 mol-%) were suspended in freshly distilled THF (12 ml) under a N_2 atmosphere. At 0°C a solution of KOH [85%, technical grade, 3.37g (≙2.86 g), 51.0 mmol, 8.0 equiv.] in degassed H_2O (6 ml) was added dropwise. The methylation reaction was started by the dropwise addition of Me_2SO_4 (6.05 ml, 8.05 g, 63.8 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 (10 ml) and stirred for 1 h at room temperature. CH_2Cl_2 (30 ml) was added, the organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (3×30 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 = 12 cm, F = 50 mL; CH/EE 5:1) afforded the title compound [F5-8, R_f (5:1) = 0.5, 1.55 g, 75%] as a white solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 3.84 (s, 3H, 8-OMe), 3.95 (s, 3H, 5-OMe), 3.96 (s, 3H, 2-OMe), 5.03 (s, 2H, 1-OCH$_2$), AB signal (δ_A = 6.59, δ_B = 6.76, J_{AB} = 8.4 Hz, A and B signal show no further splitting, 6-H and 7-H), 7.30 (d, 1H, $J_{3,4}$ = 9.3 Hz, 3-H), 7.32-7.35 (m, 1H, 4'-H), 7.39-7.43 (m, 2H, 3'-H and 5'-H), 7.59-7.62 (m, 2H, 2'-H, and 6'-H), 8.06 (d, 1H, $J_{4,3}$ = 9.2 Hz, 4-H). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H ↔ δ(^{1}H)]: δ = 3.84 (8-OMe) ↔ δ_B = 6.76 (7-H), δ = 3.95 (5-OMe) ↔ δ = 6.59 (6-H), δ = 3.96 (2-OMe) ↔ δ = 7.30 (3-H), δ = 5.03 (1-OCH$_2$) ↔ δ = 7.59-7.62 (m, 2H, 2'-H, and 6'-H). **^{13}C NMR** (125.81 MHz, $CDCl_3$): = 55.78 (5-O*C*H$_3$), 57.22 (2-O*C*H$_3$), 57.30 (8-O*C*H$_3$), 76.12 (5-O*C*H$_2$), 101.55 (C-6), 107.33 (C-7), 114.67 (C-3), 119.03 (C-4), 122.94 (C-8a), 123.62 (C-4a), 127.63 (C-4'), 128.28 (C-3' and C-5'), 128.39 (C-2' and C-6'), 138.60 (C-1'), 142.86 (C-1), 149.82 (C-8), 149.94 (C-5), 151.2 (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 = 55.78 (5-O*C*H$_3$) ↔ δ = 3.95 (5-OMe), δ = 57.22 (2-O*C*H$_3$) ↔ δ = 3.96 (2-OMe), = 57.30 (8-O*C*H$_3$) ↔ δ = 3.84 (8-OMe), δ = 76.12 (5-O*C*H$_2$) ↔ δ = 5.0 (5-O*C*H$_2$), δ = 101.55 (C-6) ↔ δ_A = 6.59 (6-H), δ = 107.33 (C-7) ↔ δ_B 6.76 (7-H), δ = 114.67 (C-3) ↔ δ = 7.30 (3-H), δ = 119.03 (C-4) ↔ δ 8.06 (4-H), δ = 127.63 (C-4') ↔ δ = 7.32-7.35 (m, 1H, 4'-H), δ = 128.2 (C-3' and C-5') ↔ δ = 7.39-7.43 (m, 2H, 3'-H and 5'-H), δ = 128.39 (C 2' and C-6') ↔ δ = 7.59-7.62 (m, 2H, 2'-H, and 6'-H). An **HMB** 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 = 122.94 (C 8a) ↔ δ_B = 6.76 (7-H), δ = 122.94 (C-8a) ↔ δ = 8.06 (4-H), δ = 123.6 (C-4a) ↔ δ_A = 6.59 (6-H), δ = 123.62 (C-4a) ↔ δ = 7.30 (3-H), δ 138.60 (C-1') ↔ δ = 5.03 (1-OCH$_2$), δ = 138.60 (C-1') ↔ δ = 7.39-7.4 (m, 2H, 3'-H and 5'-H), δ = 142.86 (C-1) ↔ δ = 5.03 (1-OCH$_2$), δ 142.86 (C-1) ↔ δ = 7.30 (3-H), δ = 149.82 (C-8) ↔ δ = 3.84 (8-OMe), = 149.82 (C-8) ↔ δ_A = 6.59 (6-H), δ = 149.82 (C-8) ↔ δ_B = 6.76 (7-H δ = 149.94 (C-5) ↔ δ = 3.95 (5-OMe), δ = 149.94 (C-5) ↔ δ_A = 6.51 (6 H), δ = 149.94 (C-5) ↔ δ_B = 6.76 (7-H), δ = 149.94 (C-5) ↔ δ = 8.06 (4 H), δ = 151.24 (C-2) ↔ δ = 3.96 (2-OMe), δ = 151.24 (C-2) ↔ δ = 7.3 (3-H), δ = 151.24 (C-2) ↔ δ = 8.06 (4-H). **Melting point:** 65-68°C **Elemental analysis:** Calculated: C: 74.06%, H: 6.21%; found: C 74.17%, H: 6.24%; deviation: C:0.11%, H: 0.03%. **HRMS** (pos. ESI calcd. for $C_{20}H_{21}O_4$: $[M+H]^+$ = 325.14344; found: 325.14340 (–0.1 ppm). **IR (film):** v = 3335, 3065, 3030, 3000, 2940, 2835, 1735, 166(1620, 1595, 1520, 1495, 1455, 1440, 1410, 1380, 1350, 1320, 1275, 1260, 1180, 1075, 1050, 995, 910, 875, 805, 785, 735, 700 cm^{-1}.

***rel*-(*S*)- 2,5,8-Trimethoxynaphthalen-1-ol (16b)**



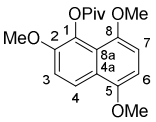
In a 250 mL round-bottomed flask und a nitrogen atmospher 1-(benzyloxy)-2,5,8-trimethoxynaphthalene (**16a**, 4.00 g, 12.33 mmol) and Pd/C (containing 10 w-% of Pd, 0.20 g, 0.19 mmol Pd, 1.5 mol-%) were dissolved in EE (120 mL) and the mixture was frozen to –196°C with gentle stirring. At this temperature the flask was evacuated and flushed with hydrogen (hydrogen balloon) three times ("freeze & pump technique"). Afterwards the mixture was allowed to warm to room temperature and stirred under the hydrogen atmosphere at room temperature for 16 h. After removing the hydrogen balloon the resulting suspension was filtered over a pad of silica gel (d = 1.5 cm, h = 4 cm) and the silica gel pad was washed carefully with CH_2Cl_2 (100 mL) in portions. Removal of the solvent under reduced pressure furnished the title compound (2.89 g, 100%) without further purification. Note: If the reaction was performed in THF, it yielded the title compound in only 58%.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 3.93 (s, 3H, 5-OMe), 3.99 (s, 3H, 2-OMe), 4.05 (s, 3H, 8-OMe), AB signal (δ_A = 6.51, δ_B = 6.64, J_{AB} = 8.4 Hz, A and B signal show no further splitting, 6-H and 7-H), 7.25 (d, 1H, $J_{3,4}$ = 9.1 Hz, 3-H)*, 7.71 (d, 1H, $J_{4,3}$ = 9.1 Hz, 4-H), 9.46 (d, 1H, $J_{1\text{-}OH,3}$ = 0.5 Hz, 1-OH). *Broad doublet of 3-H does not show $J_{3,1\text{-}OH}$ coupling due to insufficient resolution. A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 4.01 (8-OMe) ↔ δ_B = 6.64 (7-H), δ = 3.93 (5-OMe) ↔ δ_A = 6.51 (6-H), δ = 3.99 (2-OMe) ↔ δ = 7.25 (3-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 55.75 (5-O*C*H$_3$), 56.58 (8-O*C*H$_3$), 57.16 (2-O*C*H$_3$), 100.75 (C-6), 103.88 (C-7), 113.25 (C-4), 115.04 (C-3), 116.47 (C-8a), 123.11 (C-4a), 142.38 (C-1), 144.14 (C-2), 149.73 (C-8), 150.46 (C-5). 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 = 55.75 (5-O*C*H$_3$) ↔ δ = 3.93 (5-OMe), δ = 56.58 (8-O*C*H$_3$) ↔ δ = 4.01 (8-OMe), δ = 57.16 (2-O*C*H$_3$) ↔ δ = 3.99 (2-OMe), δ = 100.75 (C-6) ↔ δ_A = 6.51 (6-H), δ = 103.88 (C-7) ↔ δ_B = 6.64 (7-H), δ = 113.25 (C-4) ↔ δ = 7.71 (4-H), δ = 115.04 (C-3) ↔ δ = 7.25 (3-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 = 116.47 (C-8a) ↔ δ_B = 6.64 (7-H), δ = 116.47 (C-8a) ↔ δ = 7.71 (4-H), δ = 116.47 (C-8a) ↔ δ = 9.46 (1-OH), δ = 123.11 (C-4a) ↔ δ_A = 6.51 (6-H), δ = 123.11 (C-4a) ↔ δ = 7.25 (3-H), δ = 142.38 (C-1) ↔ δ = 7.25 (3-H), δ = 142.38 (C-1) ↔ δ = 7.71 (4-H), δ = 142.38 (C-1) ↔ δ = 9.46 (1-OH), δ = 144.14 (C-2) ↔ δ = 3.99 (2-OMe), δ = 144.14 (C-2) ↔ δ = 7.25 (3-H), δ = 144.14 (C-2) ↔ δ = 7.71 (4-H), δ = 144.14 (C-2) ↔ δ = 9.46 (1-OH), δ = 149.73 (C-8) ↔ δ = 4.01 (8-OMe), δ = 149.73 (C-8) ↔ δ_A = 6.51 (6-H), δ = 149.73 (C-8) ↔ δ_B = 6.64 (7-H), δ = 150.46 (C-5) ↔ δ = 3.93 (5-OMe), δ = 150.46 (C-5) ↔ δ_A = 6.51 (6-H), δ = 150.46 (C-5) ↔ δ_B = 6.64 (7-H), δ = 150.46 (C-5) ↔ δ = 7.71 (4-H). **Melting point:** 161°C. **Elemental analysis:** Calculated: C: 66.66%, H: 6.02%; found: C: 66.74%, H: 5.99%; deviation: C: 0.08%, H: 0.03%. **IR (film):** v = 3315, 2985, 2935, 2835, 1620, 1590, 1520, 1465, 1455, 1440, 1390, 1310, 1275, 1245, 1215, 1180, 1160, 1100, 1075, 1045, 980, 800, 780, 725, 685, 670 cm^{-1}.

2,5,8-Trimethoxynaphthalen-1-yl *tert*-Butyl Carbonate (16c)



2,5,8-Trimethoxynaphthalen-1-ol(**16b**, 100 mg, 0.43 mmol) and DMAP (5.2 mg, 43 µmol, 10 mol-%) were suspended in CH_2Cl_2 (4 mL). At 0°C di-*t*-butyl dicarbonate (0.18 mL, 0.19 g, 0.85 mmol, 2.0 equiv.) was added and the reaction was started by slow addition of NEt_3 (0.12 mL, 86 mg, 0.85 mmol, 2.0 equiv.). The ice-bath was removed, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The mixture was diluted with CH_2Cl_2 (15 mL) and washed with aq. saturated $NaHCO_3$ solution (10 mL). After drying over Na_2SO_4 the solvent was removed in vacuo. Flash chromatography (d = 1.5 cm, h = 12 cm, F = 8 ml; CH/EE 5:1) afforded the title compound (F8-15, R_f (5:1) = 0.25, 133.4 mg, 93%) as a colorless solid. Note: An upscaling of this reaction was easily achieved: Boc protection of **16b** (949 mg, 4.05 mmol) with DMAP (49.5 mg, 0.41 mmol, 10 mol-%), di-*t*-butyl dicarbonate (1.74 mL, 1.77 g, 8.11 mmol, 2.0 equiv.), and NEt_3 (1.12 mL, 0.82 g, 8.11 mmol, 2.0 equiv.). in CH_2Cl_2 (40 mL) furnished the title compound (1.187 g, 88%) in a slightly lower yield (Flash chromatography data: d = 4 cm, h = 12 cm, F = 50 ml; CH/EE 5:1, product: F11-21).– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.58 [s, 9H, C(C*H*$_3$)$_3$], 3.88 (s, 3H, 8-OMe), 3.93 (s, 3H, 5-OMe), 3.95 (s, 3H, 2-OMe), AB signal (δ_A = 6.56, δ_B = 6.72, J_{AB} = 8.4 Hz, A and B signal show no further splitting, 6-H and 7-H), 7.28 (d, 1H, $J_{3,4}$ = 9.3 Hz, 3-H), 8.12 (d, 1H, $J_{4,3}$ = 9.3 Hz, 4-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.88 (8-OMe) ↔ δ_B = 6.72 (7-H), δ = 3.93 (5-OMe) ↔ δ_A = 6.56 (6-H), δ = 3.95 (2-OMe) ↔ δ = 7.28 (3-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 27.92 [C(*C*H$_3$)$_3$], 55.84 (5-O*C*H$_3$), 56.84 (8-O*C*H$_3$), 56.99 (2-O*C*H$_3$), 101.78 (C-6), 107.05 (C-7), 113.66 (C-3), 121.12 (C-4), 121.48 (C-8a), 123.00 (C-4a), 133.98 (C-1), 148.99 (C-8), 149.70 and 149.77 (C-2 and C-5), 152.01 (*carbonate*-C). 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 = 27.92 [C(*C*H$_3$)$_3$] ↔ δ = 1.58 [C(C*H*$_3$)$_3$], δ = 55.84 (5-O*C*H$_3$) ↔ δ = 3.93 (5-OMe), δ = 56.84 (8-O*C*H$_3$) ↔ δ = 3.88 (8-OMe), δ = 56.99 (2-O*C*H$_3$) ↔ δ = 3.95 (2-OMe), δ = 101.78 (C-6) ↔ δ_A = 6.56 (6-H), δ = 107.05 (C-7) ↔ δ_B = 6.72 (7-H), δ = 113.66 (C-3) ↔ δ = 7.28 (3-H), δ = 121.12 (C-4) ↔ δ = 8.12 (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 = 82.48 [*C*(CH$_3$)$_3$] ↔ δ = 1.58 [C(C*H*$_3$)$_3$], δ = 121.48 (C-8a) ↔ δ_B = 6.72 (7-H),, δ = 121.48 (C-8a) ↔ δ = 8.12 (4-H), δ = 123.00 (C-4a) ↔ δ_A = 6.56 (6-H), δ = 123.00 (C-4a) ↔ δ = 7.28 (3-H), δ = 133.98 (C-1) ↔ δ = 7.28 (3-H), δ = 133.98 (C-1) ↔ δ = 8.12 (4-H), δ = 148.99 (C-8) ↔ δ = 3.88 (8-OMe), [δ = 149.70 and 149.77 (C-2 and C-5)] ↔ [δ = 3.93 and 3.94 (2-OMe and 5-OMe)]. δ = 152.01 (*carbonate*-C) exhibited no cross-peak. **Melting point:** 86°C. **Elemental analysis:** Calculated: C: 64.66%, H: 6.63%; found: C: 64.62%, H: 6.56%, deviation: C: 0.04%, H: 0.07%. **HRMS** (pos. ESI): calcd. for $C_{18}H_{22}O_6$: [M+Na]$^+$ = 357.13086; found: 357.13095 (0.26 ppm). **IR (film):** v = 2980, 2940, 2840, 1760, 1665, 1630, 1605, 1520, 1460, 1415, 1395, 1370, 1330, 1285, 2160, 1200, 1160, 1145, 1080, 1055, 1015, 980, 920, 895, 855, 805, 775, 730, 705, 685 cm^{-1}.

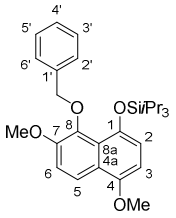
2,5,8-Trimethoxynaphthalen-1-yl Pivalate (16d)



2,5,8-Trimethoxynaphthalen-1-ol(**16b**, 504 mg, 2.19 mmol) and DMAP (13.4 mg, 0.11 mol, 5 mol-%) were suspended in CH_2Cl_2 (20 mL). At 0°C pivaloyl chloride (0.32 mL, 0.32 g, 2.63 mmol, 1.2 equiv.) was added and the reaction was started by slow addition of NEt_3 (0.73 mL, 0.53 g, 5.26 mmol, 2.4 equiv.). The ice-bath was removed, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The mixture was quenched with MeOH (5 mL) and stirred for 30 min. Afterwards the solution was washed with aq. HCl (1M, 20 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the obtained white solid (678 mg, 97%) was dried in a Schlenk vacuum overnight.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.45 [s, 9H, C(C*H*$_3$)$_3$], 3.83 (s, 3H, 8-OMe), 3.89 (s, 3H, 2-OMe), 3.93 (s, 3H, 5-OMe), AB signal (δ_A = 6.55, δ_B = 6.67, J_{AB} = 8.4 Hz, A and B signal show no further splitting, 6-H and 7-H), 7.27 (d, 1H, $J_{3,4}$ = 9.3 Hz, 3-H), 8.12 (d, 1H, $J_{4,3}$ = 9.3 Hz, 4-H). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 3.83 (8-OMe) ↔ δ_B = 6.67 (7-H), δ = 3.89 (2-OMe) ↔ δ =

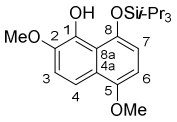
7.27 (3-H), δ = 3.93 (5-OMe) ↔ δ_A = 6.55 (6-H). **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 27.52 [C(CH_3)$_3$], 39.29 [C(CH$_3$)$_3$], 55.80 (5-OCH_3), 55.93 (8-OCH_3), 56.91 (2-OCH_3), 101.60 (C-6), 106.00 (C-7), 113.42 (C-3), 120.81 (C-4), 121.51 (C-8a), 123.06 (C-4a), 134.32 (C-1), 149.13 (C-2), 149.22 (C-8), 149.77 (C-5), 176.94 [1-O2C-C(CH$_3$)$_3$]. 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 = 27.52 [C(CH_3)$_3$] ↔ δ = 1.45 [C(CH_3)$_3$], δ = 55.80 (5-OCH_3) ↔ δ = 3.93 (5-OMe), δ = 55.93 (8-OCH_3) ↔ δ = 3.83 (8-OMe), δ = 56.91 (2-OCH_3) ↔ δ = 3.89 (2-OMe), δ = 101.60 (C-6) ↔ δ_A = 6.55 (6-H), δ = 106.00 (C-7) ↔ δ_B = 6.67 (7-H), δ = 113.42 (C-3) ↔ δ = 7.27 (3-H), δ = 120.81 (C-4) ↔ δ = 8.12 (4-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 = 39.29 [C(CH$_3$)$_3$] ↔ δ = 1.45 [C(CH_3)$_3$], δ = 121.51 (C-8a) ↔ δ_B = 6.67 (7-H), δ = 121.51 (C-8a) ↔ δ = 8.12 (4-H), δ = 123.06 (C-4a) ↔ δ_A = 6.55 (6-H), δ = 123.06 (C-4a) ↔ δ = 7.27 (3-H), δ = 134.32 (C-1) ↔ δ = 7.27 (3-H), δ = 134.32 (C-1) ↔ δ = 8.12 (4-H), δ = 149.13 (C-2) ↔ δ = 3.89 (2-OMe), δ = 149.22 (C-8) ↔ δ = 3.83 (8-OMe), δ = 149.77 (C-5) ↔ δ = 3.93 (5-OMe), δ = 176.94 [1-O2C-C(CH$_3$)$_3$] ↔ δ = 1.45 [C(CH_3)$_3$]. **Melting point:** 114°C. **HRMS** (pos. APCI): calcd. for $C_{18}H_{26}O_5N$: [M+NH$_4$]$^+$ = 336.18055; found: 336.18054 (–0.02 ppm). **IR (film):** ν = 2975, 2940, 2840, 1750, 1630, 1605, 1520, 1465, 1440, 1415, 1365, 1285, 1260, 1235, 1175, 1135, 1115, 1070, 1040, 980, 875, 815, 800, 770, 755 730, 705 cm^{-1}.

(8-(Benzyloxy)-4,7-dimethoxynapthalen-1-yloxy)triisopropylsilane (16f)



5-(Benzyloxy)-6-methoxy-4-((triisopropylsilyl)oxy)naphthalen-1-ol (**28**, 7.60 g, 16.8 mmol) and Bu$_4$NBr (1.08 g, 3.35mmol, 20 mol-%) were suspended in THF (60 ml). The solution was cooled to 0°C and Me_2SO_4 (15.9 ml, 21.2 g, 168 mmol, 10 equiv.) was added. The reaction was started by dropwise addition of a solution of KOH [85%, technical grade, 8.87 g, (≙7.85 g), 134 mmol, 8.0 equiv.] in degassed H_2O (15 ml) at 0°C. Afterwards the ice-bath was removed and the reaction mixture was stirred at room temperature for 19 h. The reaction was quenched with conc. ammonium hydroxide solution (30 ml) and stirred at room temperature for 1 h. The organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (2×50 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 = 12 cm, h = 12 cm, F = 100 ml; CH/EE 95:5) afforded the title compound (F5-11, R_f (9:1) = 0.7, 5.46 g, 70%) as a colorless solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.05 (d, 18H, $J_{Silyl\text{-}CH,Silyl\text{-}CH_3}$ = 7.5 Hz, Si[CH(CH_3)$_2$]$_3$), 1.31 (septett, 3H, $J_{Silyl\text{-}CH_3,Silyl\text{-}CH,}$ = 7.5 Hz, Si[CH(CH$_3$)$_2$]$_3$), 3.73 (s, 3H, 7-OMe), 3.94 (s, 3H, 4-OMe), 5.05 (s, 2H, 8-OCH$_2$), 6.51 (d, 1H, $J_{3,2}$ = 8.3 Hz, 3-H), 6.75 (d, 1H, $J_{2,3}$ = 8.3 Hz, 2-H), 7.16 (d, 1H, $J_{6,5}$ = 9.2 Hz, 6-H), 7.22-7.30 (m, 3H, 3'-H, 4'-H, and 5'-H), 7.38-7.42 (m, 2H, 2'-H and 6'-H), 7.99 (d, 1H, $J_{5,6}$ = 9.2 Hz, 5-H). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.05 (Si[CH(CH_3)$_2$]$_3$) ↔ δ = 5.05 (8-OCH$_2$), δ = 1.05 (Si[CH(CH_3)$_2$]$_3$) ↔ δ = 6.75 (2-H), δ = 1.31 (Si[CH(CH$_3$)$_2$]$_3$) ↔ δ = 5.05 (8-OCH$_2$), δ = 1.31 (Si[CH(CH$_3$)$_2$]$_3$) ↔ δ = 6.75 (2-H), δ = 3.94 (4-OMe) ↔ δ = 6.51 (3-H), δ = 3.73 (7-OMe) ↔ δ = 7.16 (6-H), δ = 7.38-7.42 (2'-H and 6'-H), ↔ δ = 5.05 (8-OCH$_2$). **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 13.44 (Si[CH(CH$_3$)$_2$]$_3$), 18.18 (Si[CH(CH_3)$_2$]$_3$), 55.72 (4-OCH_3), 56.70 (7-OCH_3), 76.76 (8-OCH_2), 101.65 (C-3), 113.87 (C-2), 113.94 (C-6), 118.61 (C-5), 123.62 (C-4a), 124.24 (C-8a), 127.33 and 127.77 (C-3', C-4', and C-5'), 128.22 (C-2' and C-6'), 138.61 (C-1'), 142.87 (C-8), 145.38 (C-1), 149.74 (C-4), 150.63 (C-7). 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 = 13.44 (Si[CH(CH$_3$)$_2$]$_3$) ↔ δ = 1.31 (Si[CH(CH$_3$)$_2$]$_3$), δ = 18.18 (Si[CH(CH_3)$_2$]$_3$) ↔ δ = 1.05 (Si[CH(CH_3)$_2$]$_3$), δ = 55.72 (4-OCH_3) ↔ δ = 3.94 (4-OMe), δ = 56.70 (7-OCH_3) ↔ δ = 3.73 (7-OMe), δ = 76.76 (8-OCH_2) ↔ δ = 5.05 (8-O CH_2), δ = 101.65 (C-3) ↔ δ = 6.51 (3-H), δ = 113.87 (C-2) ↔ δ = 6.75 (2-H), δ = 113.94 (C-6) ↔ δ = 7.16 (6-H), δ = 118.61 (C-5) ↔ δ = 7.99 (5-H), δ = 127.33 and δ = 127.77 (C-3', C-4', and C-5') ↔ δ = 7.22-7.30 (3'-H, 4'-H, and 5'-H), δ = 128.22 (C-2' and C-6') ↔ δ = 7.38-7.42 (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 covalent bonds]: δ = 123.62 (C-4a) ↔ δ = 6.51 (3-H), δ = 123.62 (C-4a ↔ δ = 7.16 (6-H), δ = 124.24 (C-8a) ↔ δ = 6.75 (2-H), δ = 124.24 (C 8a) ↔ δ = 7.99 (5-H), δ = 138.61 (C-1') ↔ δ = 5.05 (8-OCH$_2$), δ 142.87 (C-8) ↔ δ = 5.05 (8-OCH$_2$), δ = 142.87 (C-8) ↔ δ = 7.16 (6-H δ = 145.38 (C-1) ↔ δ = 6.51 (3-H), δ = 145.38 (C-1) ↔ δ = 6.75 (2-H), = 149.74 (C-4) ↔ δ = 3.94 (4-OMe), δ = 149.74 (C-4) ↔ δ = 6.51 (3-H δ = 149.74 (C-4) ↔ δ = 6.75 (2-H), δ = 149.74 (C-4) ↔ δ = 7.99 (5-H), = 150.63 (C-7) ↔ δ = 3.73 (7-OMe), δ = 150.63 (C-7) ↔ δ = 7.99 (5-H **Melting point:** 85°C. **Elemental analysis:** Calculated: C: 72.06%, H 8.21%; found: C: 71.94%, H: 8.21%; deviation: C: 0.12%, H: 0.00% **IR (film):** v = 698, 810, 831, 883, 1016, 1029, 1055, 1274, 1348, 1383 1414, 1448, 1462, 1598, 2838, 2865, 2892, 2943 cm^{-1}.

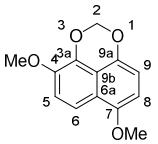
2,5-Dimethoxy-8-(triisopropylsilyloxy)napthalene-1-ol (16g)



(8-(Benzyloxy)-4,7-dimethoxynapthalen-1-yloxy)triisopropylsilane (**16** 1.52 g, 3.26 mmol) and Pd/C [10 w-%, 53.0 mg (≙5.3 mg pure Pd 49.8 μmol, 1.5 mol-%] were suspended in EtOAc (35 ml). The mixtur was flash-frozen with liquid nitrogen, evacuated and flushed wit hydrogen (hydrogen-balloon, freeze & pump technique, 3 times). Th mixture was allowed to warm to room temperature and vigorousl stirred at room temperature for 15 h. Afterwards the mixture was filtere over silica gel (glass frit, d = 1.5 cm, h = 4 cm) and additional EtOA (100 ml) was passed through to remove residual product from the silic gel phase. The solvent was removed in vacuo and the title compoun (1.26 g, 99%) was obtained without further purification.– **^{1}H NM** (400.13 MHz, $CDCl_3$): δ = 1.17 (d, 18H, $J_{silyl\text{-}CH,silyl\text{-}CH3}$ = 7.3 Hz Si[CH(CH_3)$_2$]$_3$), 1.30-1.50 (m, 3H, Si[CH(CH$_3$)$_2$]$_3$), 3.92 (s, 3H, 5-OMe 3.99 (s, 3H, 2-OMe), AB signal (δ_A = 6.42, δ_B = 6.59, J_{AB} = 8.3 Hz, A and B signal show no further splitting, 6-H and 7-H), 7.24 (d, 1H $J_{3,4}$ = 9.3 Hz, 3-H), 7.69 (d, 1H, $J_{4,3}$ = 9.3 Hz, 4-H), 9.93 (s, 1H, 1-OH A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additiona assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H ↔ δ(^{1}H)]: δ = 3.92 (5-OMe) ↔ δ = 6.42 (6-H), δ = 3.99 (2-OMe) ↔ δ 7.24 (3-H), δ = 6.59 (7-H) ↔ δ = 1.38-1.50 {Si[CH(CH$_3$)$_2$]$_3$}. **^{13}C NM** (100.61 MHz, $CDCl_3$): δ = 13.37 {Si[CH(CH$_3$)$_2$]$_3$}, 18.03 {Si[CH(CH_3)$_2$]$_3$ 55.67 (5-OCH_3), 56.92 (2-OCH_3), 100.88 (C-6), 110.24 (C-7), 113.10 (C-4), 114.43 (C-3), 117.50 (C-8a), 123.34 (C-4a), 142.44 (C-1), 143.63 (C-2), 145.32 (C-8), 150.36 (C-5). 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 = 13.37 {Si[CH(CH$_3$)$_2$]$_3$} ↔ δ = 1.38-1.50 {Si[CH(CH$_3$)$_2$]$_3$}, δ = 18.03 {Si[CH(CH_3)$_2$]$_3$} ↔ δ = 1.17 {Si[CH(CH_3)$_2$]$_3$}, δ = 55.67 (5-OCH_3) ↔ δ = 3.92 (5-OMe), δ = 56.92 (2-OCH_3) ↔ δ = 3.99 (2-OMe), δ = 100.88 (C-6) ↔ δ_A = 6.42 (6-H), δ = 110.24 (C-7) ↔ δ_B = 6.59 (7-H), δ = 113.10 (C-4) ↔ δ = 7.69 (4-H), δ = 114.43 (C-3) ↔ δ = 7.24 (3-H).An **HMBC** spectrum ("long-range C,H COSY"; 100.61/400.13 MHz, $CDCl_3$)

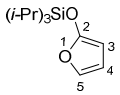
allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^{1}H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 117.50 (C-8a) ↔ δ_B = 6.59 (7-H), δ = 117.50 (C-8a) ↔ δ = 7.69 (4-H), δ = 117.50 (C-8a) ↔ δ = 9.93 (1-OH), δ = 123.34 (C-4a) ↔ δ_A = 6.42 (6-H), δ = 123.34 (C-4a) ↔ δ = 7.24 (3-H), δ = 142.44 (C-1) ↔ δ = 7.24 (3-H), δ = 142.44 (C-1) ↔ δ = 9.93 (1-OH), δ = 143.63 (C-2) ↔ δ = 3.99 (2-OMe), δ = 143.63 (C-2) ↔ δ = 7.69 (4-H), δ = 143.63 (C-2) ↔ δ = 9.93 (1-OH), δ = 145.32 (C-8) ↔ δ_A = 6.42 (6-H), δ = 145.32 (C-8) ↔ δ_B = 6.59 (7-H), δ = 150.36 (C-5) ↔ δ = 3.92 (5-OMe), δ = 150.36 (C-5) ↔ δ_A = 6.42 (6-H), δ = 150.36 (C-5) ↔ δ_B = 6.59 (7-H), δ = 150.36 (C-5) ↔ δ = 7.69 (4-H). **Melting point:** oil. **Elemental analysis:** Calculated: C: 66.98%, H: 8.57%; found: C: 66.56%, H: 8.83%; deviation: C: 0.42%, H: 0.26%. **HRMS** (pos. ESI): calcd. for $C_{21}H_{32}O_4Si$ $[M+Na]^+$ = 399.19621; found 399.19638 (+0.43 ppm). **IR (film):** ν = 3345, 2950, 2895, 2870, 1610, 1590, 1520, 1460, 1400, 1365, 1350, 1310, 1275, 1255, 1210, 1190, 1180, 1150, 1100, 1050, 1000, 945, 925, 885, 870, 810, 775, 735, 690, cm^{-1}.

4,7-Dimethoxynaphtho[1,8-*de*][1,3]dioxine (16h)



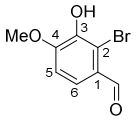
In a Schlenk flask under a nitrogen atmosphere 2,5-dimethoxy-8-(triisopropylsilyloxy)napthalene-1-ol (**16g**, 0.98 g, 2.60 mmol), K_2CO_3 (0.40 g, 3.12 mmol, 1.2 equiv.) and CsF (0.47 g, 3.12 mmol, 1.2 equiv.) were suspended in dry DMF (5 ml). CH_2BrCl (0.21 mL, 0.40 g, 3.12 mmol, 1.2 equiv.) was added and the mixture was stirred at 100°C (oil-bath temperature) for 16 h. Afterwards the mixture was allowed to cool to room temperature and silica gel was added. The DMF was removed in vacuo (60°C, 15 mbar, ~15 min, room temp., 1 mbar, ~15 min). Flash chromatography [d = 3 cm, h = 12 cm, F = 25 ml; CH/EE 5:1] afforded the title compound (F6-12, R_f (5:1) = 0.4, 513.7 mg, 85%) as a colorless solid.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 3.95 (s, 3H, 7-OMe), 4.01 (s, 3H, 4-OMe), 5.54 (s, 2H, 2-H_2), 6.57 (d, 1H, $J_{8,9}$ = 8.2 Hz, 8-H), 6.78 (d, 1H, $J_{9,8}$ = 8.2 Hz, 9-H), 7.24 (d, 1H, $J_{5,6}$ = 9.2 Hz, 5-H), 7.69 (d, 1H, $J_{6,5}$ = 9.2 Hz, 6-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [$\delta(^{1}H) \leftrightarrow \delta(^{1}H)$]: δ = 3.95 (7-OMe) ↔ δ = 6.57 (8-H), δ = 4.01 (4-OMe) ↔ δ = 7.26 (5-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 55.76 (7-OCH_3), 57.23 (4-OCH_3), 91.40 (C-2), 102.18 (C-8), 107.90 (C-9), 114.75 (C-5), 116.29 (C-6), 116.72 (C-9b), 121.48 (C-6a), 137.08 (C-3a), 142.08 (C-4), 142.67 (C-9a), 150.50 (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 ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^{1}H)$]: δ = 55.76 (7-OCH_3) ↔ δ = 3.95 (7-OMe), δ = 57.23 (4-OCH_3) ↔ δ = 4.01 (4-OMe), δ = 91.40 (C-2) ↔ δ = 5.54 (2-H_2), δ = 102.18 (C-8) ↔ δ = 6.57 (8-H), δ = 107.90 (C-9) ↔ δ_B = 6.78 (9-H), δ = 114.75 (C-5) ↔ δ = 7.26 (5-H), δ = 116.29 (C-6) ↔ δ = 7.80 (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 ^{1}H resonances [$\delta(^{13}C) \leftrightarrow \delta(^{1}H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 116.72 (C-9b) ↔ δ = 6.78 (9-H), δ = 116.72 (C-9b) ↔ δ = 7.80 (6-H), δ = 121.48 (C-6a) ↔ δ = 6.57 (8-H), δ = 121.48 (C-6a) ↔ δ = 7.26 (5-H), δ = 137.08 (C-3a) ↔ δ = 5.54 (2-H_2), δ = 137.08 (C-3a) ↔ δ = 7.26 (5-H), δ = 137.08 (C-3a) ↔ δ = 7.80 (6-H), δ = 142.08 (C-4) ↔ δ = 4.01 (4-OMe), δ = 142.08 (C-4) ↔ δ = 7.26 (5-H), δ = 142.08 (C-4) ↔ δ = 7.80 (6-H), δ = 142.67 (C-9a) ↔ δ = 5.54 (2-H_2), δ = 142.67 (C-9a) ↔ δ = 6.57 (8-H), δ = 142.67 (C-9a) ↔ δ = 6.78 (9-H), δ = 150.50 (C-7) ↔ δ = 3.95 (7-OMe), δ = 150. 50 (C-7) ↔ δ = 6.57 (8-H), δ = 150. 50 (C-7) ↔ δ = 6.78 (9-H), δ = 150. 50 (C-7) ↔ δ = 7.80 (6-H). **Melting point:** 70°C. **Elemental analysis:** Calculated: C: 67.23%, H: 5.21%; found: C: 67.21%, H: 5.18%; deviation: C: 0.02%, H: 0.03%. **HRMS** (pos. ESI): calcd. for $C_{13}H_{12}O_4$ $[M]^+$ = 232.07301; found 232.07321 (+0.87 ppm). **IR (film):** ν = 3000, 2940, 2905, 2840, 1740, 1620, 1590, 1515, 1450, 1415, 1375, 1335, 1275, 1255, 1210, 1185, 1160, 1130, 1095, 1065, 1045, 1000, 980, 920, 880, 810, 780, 730, 700, 670 cm^{-1}.

2-(Triisopropylsiloxy)furan (18a)



According to a general procedure for the preparation of silyltriflates from ref.[38] triisopropylsilane (25.9 mL, 20.0 g, 126 mmol) was suspended in a 50 mL flask and trifluoromethanesulfonic acid (12.3 mL, 20.8 g, 139 mmol, 1.10 equiv.) was added dropwise at 0°C by a dropping funnel. The solution was stirred for 1 h at 0°C, then was allowed to warm to room temperature and stirred for 20 h at room temperature. The resulting product was used as following without further purification. Furan-2(5*H*)-one[62] (**25**, 7.44 ml, 8.85 g, 105 mmol) was suspended in dry CH_2Cl_2 (90 mL). The freshly prepared triisopropylsilyl trifluoromethanesulfonate (see above, 73.6 mmol, 1.2 equiv.) was transferred via cannula at 0°C. At the same temperature NEt_3 (11.1 mL, 8.08 g, 79.8 mmol, 1.30 equiv.) was added dropwise to initiate the silylation reaction. The mixture was allowed to warm to room temperature and stirred for 1 h. Afterwards the mixture was quenched with saturated aq. $NaHCO_3$ solution (50 mL). The organic phase was separated and the organic phase was extracted with dichloromethane (3×30 mL). The combined organic extracts were washed with brine (30 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by distillation (0.1 mbar, 83°C) to furnish the title compound (5.63 g, 98%, ref.[37]: 94%) as a colorless fluid. .– **^{1}H-NMR** (300.13 MHz, $CDCl_3$, spectrum contains 5 w-% iPr_3SiOH): δ = 1.10 (d, 18H, $J_{2\text{-}OSi(CH(CH_3)_2)_3,2\text{-}OSi(CH(CH_3)_2)_3}$ = 7.5 Hz, 2-OSi(CH(CH_3)$_2$)$_3$), 1.19-1.32 (m, 3H,2-OSi(CH(CH$_3$)$_2$)$_3$), 5.12 (dd, 1H, $J_{3,4}$ = 3.2 Hz, $^4J_{3,5}$ = 1.1 Hz, 3-H), 6.20 (dd, 1H, $J_{4,3}$ = 3.2 Hz, $J_{4,5}$ = 2.2 Hz, 4-H), 6.80 (dd, 1H, $J_{5,4}$ = 2.2 Hz, $^4J_{5,3}$ = 1.1 Hz, 5-H). The NMR data is in consistent with the one reported in literature.[37]

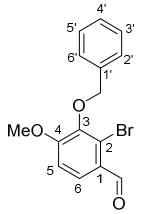
2-Bromo-3-hydroxy-4-methoxybenzaldehyde (20)



Isovanillin (**19**) (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). It was 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 (**20**) (55.50 g, 73%; Lit.[33]: 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).

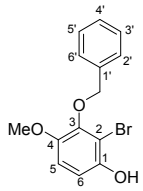
[62] Preparation: Experimental details of ref.[37]

3-Benzyloxy-2-bromo-4-methoxybenzaldehyde (21)



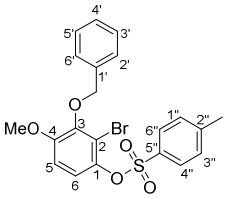
To a suspension of 2-bromo-3-hydroxy-4-methoxybenzaldehyde (**20**) (20.71 g, 89.63 mmol) and potassium carbonate (37.35 g, 270.3 mmol, 3.02 equiv.) in abs. ethanol (360 mL), benzyl chloride (15.6 mL, 17.2 g, 136 mmol, 1.52 equiv.) was added and the reaction mixture was heated to reflux for 24 h. After cooling to room temperature, the solvent was removed in vacuo, the residue was dissolved in EE (200 mL) and H_2O (100 mL) and vigorously stirred for 5 min. The organic phase was separated and the aq. phase was extracted with EE (3×100 mL). The combined organic extracts were washed with aq. NaOH (1 M, 2×100 mL), aq. HCl (1 M, 100 mL), brine (100 mL), and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography [d = 10 cm, h = 12 cm, F = 100 mL; CH/EE 9:1 (F1-15), 5:1 (F16-25), 3:1 (F26-35)], to obtain the product (F12-30, R_f (5:1) = 0.25, 28.08 g, 98%, ref.[34]: quant.) as a colorless solid.– **^{1}H-NMR** (300.13 MHz, $CDCl_3$): δ = 3.96 (s, 3H, 4-OMe), 5.05 (s, 2H, 3-OCH_2), 6.98 (dd, 1H, $J_{6,5}$ = 8.7 Hz, $^4J_{6,1\text{-CHO}}$ = 0.9 Hz, 6-H), 7.31-7.58 (m, 5H, 2`-H, 3`-H, 4`-H, 5`-H, and 6`-H), 7.76 (d, 1H, $J_{5,6}$ = 8.7 Hz, 5-H), 10.26 (d, 1H, $^4J_{1\text{-CHO},6}$ = 0.8 Hz, 1-CHO) ppm. The ^{1}H-NMR data is in a good agreement with that reported in literature.[34]

3-Benzyloxy-2-bromo-4-methoxyphenol (22)



3-Benzyloxy-2-bromo-4-methoxybenzaldehyde (**21**, 20.67 g, 64.36 mmol) and *m*CPBA (77 w-%, 16.66 g, 96.54 mmol, 1.50 equiv.) were suspended in CH_2Cl_2 (300 mL) and the mixture was refluxed for 14 h. Saturated aq. Na_2SO_3 solution (200 mL) was added carefully and the mixture was stirred for 15 min. The aq. phase was separated and the organic phase was washed with saturated aq. $NaHCO_3$ solution (3×100 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed in vacuo. The oily residue was taken up in aq. KOH solution (10%, 150 mL, 4.0 equiv., degassed with N_2). After stirring at room temperature for 3 h, the reaction mixture was acidified with HCl (conc., 25 mL) to pH 1. CH_2Cl_2 (200 mL) was added and the mixture was vigorously stirred for 5 min. The organic phase was separated and the aq. 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 to furnish the title compound (18.78 g, 94%) as a brown oil that could be used in the following tosylation step without further purification.– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 3.84 (s, 3H, 4-OMe), 5.08 (s, 2H, 3-OCH_2), 5.23 (s, 1H, 1-OH), AB signal (δ_A = 6.77 and δ_B = 6.85, J_{AB} = 9.0 Hz, A- and B-signal show no further splitting, 6-H and 5-H), 7.31-7.42 (m, 3H, 3`-H, 4`-H and 5`-H), 7.52-7.56 (m, 2H, 2`-H and 6`-H) ppm. A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of $^1$H resonances by the occurrence of crosspeaks [$\delta$($^1$H) ↔ $\delta$($^1$H)]: $\delta$ = 3.84 (4-OMe) ↔ $\delta_B$ = 6.84 (5-H), $\delta$ = 7.52-7.56 (2`-H and 6`-H) ↔ δ = 5.08 (3-OCH_2). **^{13}C-NMR** (100.63 MHz, $CDCl_3$): δ = 57.11 (4-OCH_3), 74.97 (3-OCH_2), 110.14 (C-6), 113.51 (C-5), 128.21, 128.42, and 128.56 (C-2', C-3', C-4', C-5', and C-6'), 107.23 (C-2), 137.14 (C-1'), 145.77, 147.36 and 147.53 (C-1, C-3, and 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 = 57.11 (4-OCH_3) ↔ δ = 3.84 (4-OMe), δ = 74.97 (3-OCH_2) ↔ δ = 5.08 (3-OCH_2), δ = 110.14 (C-6) ↔ δ_A = 6.77 (6-H), δ = 113.51 (C-5) ↔ δ_B = 6.85 (5-H), [δ = 128.21, 128.42, and 128.56 (C-2', C-3', C-4', C-5', and C-6') ↔ δ = 7.31-7.42 (3`-H, 4`-H, and 5`-H) and $\delta$ = 7.52-7.56 (2`-H and 6`-H) could not be assigned unambiguously]. 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 = 107.23 (C-2) ↔ δ = 5.23 (1-OH), δ = 106.82 (C-2) ↔ δ_A = 6.77 (6-H), δ = 106.82 (C-2) ↔ δ_B = 6.85 (5-H), δ = 137.14 (C-1') ↔ δ = 5.08 (3-OCH_2). Note: δ = 145.77, 147.36, and 147.53 (C-1, C-3, and C-4) could not be assigned unambiguously. **Melting point:** Oil. **Elemental analysis:** Calculated: C 54.39% , H: 4.24%; found: C: 54.14%, H: 4.35%; deviation: C: 0.25% H: 0.11%. **HRMS** (pos. ESI): calcd. for $C_{14}H_{13}{}^{79}BrO_3Na$ $[M+Na]^+$ 330.99403; found 330.99426 (+0.71 ppm); calcd. for $C_{14}H_{13}{}^{81}BrO_3N$ $[M+Na]^+$ = 332.99198; found 332.99213 (+0.44 ppm). **IR (film)** v = 3090, 3065, 3030, 3005, 2945, 2880, 2835, 2605, 2555, 1955, 1875, 1815, 1745, 1600, 1585, 1485, 1455, 1440, 1375, 1330, 1305, 1270, 1200, 1170, 1140, 1130, 1080, 1030, 960, 910, 845, 820, 800, 750, 730, 700, 665 cm^{-1}.

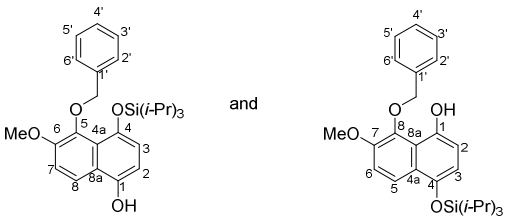
3-(Benzyloxy)-2-bromo-4-methoxyphenyl 4-Methylbenzenesulfonate (23)



3-Benzyloxy-2-bromo-4-methoxyphenol (**22**, 18.78 g, 60.75 mmol) and TsCl (17.37 g, 91.13 mmol, 1.50 equiv.) were dissolved in CH_2Cl (120 mL). The solution was cooled to 0°C and NEt_3 (12.62 mL, 9.22 g, 91.13 mmol, 1.50 equiv.) was added successively. After stirring for 16 at room temperature, the reaction mixture was diluted with CH_2Cl (200 mL), washed with saturated aq. $NaHCO_3$ (2 × 100 mL), H_2O (100 mL), and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography [d = 12 cm, h = 12 cm, F = 100 mL; CH/EE 5:1 (F1-15), 3:1 (F16-24), 1:1 (F25-35 to obtain the pure product (F15-28, R_f (5:1) = 0.2, 27.75 g, 99%) as white solid.– **^{1}H-NMR** (400.13 MHz, $CDCl_3$): δ = 2.44 (s, 3H, 4''-CH_3), 3.86 (s, 3H, 4-OMe), 4.97 (s, 2H, 3-OCH_2), AB signal [δ_A = 6.84 and δ_B = 7.13, J_{AB} = 9.2 Hz, A and B signal show no further splitting, 5-H and 6-H], 7.28-7.31 (m, 2H, 3''-H and 5''-H), 7.31-7.38 (m, 3H, 3'-H, 4-H, and 5'-H), 7.46-7.50 (m, 2H, 2'-H and 6'-H), 7.75-7.79 (m, 2H, 2''-H and 6''-H) ppm. **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 21.74 (4''-CH_3), 56.32 (4-OCH_3), 74.80 (3-OCH_2), 110.89 (C-5), 113.70 (C-2), 118.9 (C-6), 128.21 (C-4'), 128.34 (C-3' and C-5'), 128.47 (C-2' and C-6'), 128.79 (C-2'' and C-6''), 129.71 (C-3'' and C-5''), 132.78 (C-1''), 136.7 (C-1'), 140.91 (C-1), 145.56 (C-4''), 146.24 (C-3), 152.50 (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 = 21.74 (4''-CH_3) ↔ δ = 2.44 (4''- CH_3), δ = 56.32 (4-OCH_3) ↔ δ = 3.86 (4-OMe), δ = 74.80 (3-OCH_2) ↔ δ = 4.97 (3-OCH_2), δ = 110.89 (C-5) ↔ δ_A = 6.84 (5-H), δ = 118.96 (C-6) ↔ δ_B = 7.13 (6-H), δ = 128.21 (C-4') ↔ δ = 7.31-7.38 (3'-H, 4'-H, and 5'-H), δ = 128.34 (C-3' and C-5') ↔ δ = 7.31-7.38 (3'-H, 4'-H, and 5'-H), δ = 128.47 (C-2' and C-6') ↔ δ = 7.46-7.50 (2'-H and 6'-H), δ = 128.79 (C-2'' and C-6'') ↔ δ = 7.75-7.79 (2''-H and 6''-H), δ = 129.71 (C-3'' and C-5'') ↔ δ = 7.28-7.31 (3''-H and 5''-H). An **HMBC** spectrum ("long-range C,H

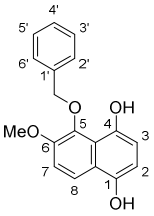
COSY"; 100.61/400.13 MHz, $CDCl_3$) allowed the assignment of all quaternary ^{13}C atoms through their cross-peaks with the independently assigned ^1H resonances [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 113.70 (C-2) $\leftrightarrow \delta_A$ = 6.84 (5-H), δ = 113.70 (C-2) $\leftrightarrow \delta_B$ = 7.13 (6-H), δ = 132.78 (C-1'') $\leftrightarrow \delta$ = 7.28-7.31 (3''-H and 5''-H), δ = 136.76 (C-1') $\leftrightarrow \delta$ = 4.97 (3-OC*H*$_2$), δ = 136.76 (C-1') $\leftrightarrow \delta$ = 7.31-7.38 (3'-H, 4'-H, and 5'-H), δ = 140.91 (C-1) $\leftrightarrow \delta_A$ = 6.84 (5-H), δ = 140.91 (C-1) $\leftrightarrow \delta_B$ = 7.13 (6-H), δ = 145.56 (C-4'') $\leftrightarrow \delta$ = 2.44 (4''- CH_3), δ = 145.56 (C-4'') $\leftrightarrow \delta$ = 7.75-7.79 (2''-H and 6''-H), δ = 146.24 (C-3) $\leftrightarrow \delta$ = 4.97 (3-OC*H*$_2$), δ = 146.24 (C-3) $\leftrightarrow \delta_A$ = 6.84 (5-H), δ = 146.24 (C-3) $\leftrightarrow \delta_B$ = 7.13 (6-H), δ = 152.50 (C-4) $\leftrightarrow \delta$ = 3.86 (4-OMe), δ = 152.50 (C-4) $\leftrightarrow \delta_A$ = 6.84 (5-H), δ = 152.50 (C-4) $\leftrightarrow \delta_B$ = 7.13 (6-H). **Melting point:** 88-90°C. **Elemental analysis:** Calculated: C: 54.44%, H: 4.13%, S: 6.92%; found: C: 54.39%, H: 4.11%, S: 6.86%; deviation: C: 0.05%, H: 0.02%, S: 0.06%. **IR (film):** v = 3090, 3065, 3030, 2940, 2840, 1595, 1495, 1480, 1440, 1425, 1375, 1300, 1270, 1240, 1190, 1175, 1140, 1120, 1095, 1035, 1015, 960, 910, 835, 815, 790, 755, 745, 715, 700, 685, 670, 660 cm^{-1}.

5-Benzyloxy-6-methoxy-4-(triisopropylsilyloxy)naphthalen-1-ol (28) and 8-Benzyloxy -7-methoxy-4-(triisopropylsilyloxy)naphthalen-1-ol (*iso*-28)



Under a nitrogen atmosphere 3-benzyloxy-4-methoxy-[(1-methylphenylsulfonyl)oxy]benzene (**23**, 9.26 g, 20.0 mmol) and 2-(triisopropylsiloxy)furan (**18a**, 7.2 mL, 7.2 g, 30 mmol, 1.5 equiv.) were dissolved in freshly distilled THF (40 mL) and the solution was cooled to −78°C. Then BuLi (2.55 M in hexane, 7.84 mL, 20.0 mmol, 1.0 equiv.) was added dropwise and the solution was stirred at −78°C for 5 min. Afterwards the reaction mixture was allowed to warm to room temperature and stirred for 45 min. Aq. HCl (1M, 50 mL) was added and the mixture was stirred over a period of 5 min. The organic phase was separated. The aq. phase was extracted with CH_2Cl_2 (2×50 ml), the combined organic extracts were washed with brine (50 mL) and dried over Na_2SO_4. The solvent was removed in vacuo and the residue was purified by flash chromatography (d = 12 cm, h = 12 cm, F = 100 mL; CH/EE 9:1) to obtain *iso*-**28** (F5-8, R_f (9:1) = 0.6, 1.215 g) as a 78:22 mixture with *i*Pr_3SiOH and containing an unidentifiable impurity. This corresponds to 90 w-% of *iso*-**28** (1.094 g, 12%). Another fraction furnished **28** (F9-18, R_f (9:1) = 0.2, 7.74 g) as a 50:50 mixture with *i*Pr_3SiOH. This corresponds to 72 w-% of **29** (5.57 g, 62%). Side product *iso*-**28** contained an unidentifiable impurity. The product mixture was not air-stable and therefore not characterized. If this mixture was treated with Bu_4NF (1M in THF, 1.5 equiv.) in THF naphthohydroquinone 28 was obtained. A second flash chromatography of the **28** fraction allowed to diminish the content of triisopropylsilyl alcohol to 9 w-%. The compound was characterized as follows: **^{1}H-NMR** (500.32 MHz, $CDCl_3$, product contains 9 w-% *i*Pr_3SiOH with a s at δ = 1.06 and a m at δ = 1.30 ppm, NMR-file: 2016: NeBrMi25-5050): δ = 1.05 (d, 18H, $J_{4\text{-}OSi(CH(CH_3)_2)_3;4\text{-}OSi(CH(CH_3)_2)_3}$ = 7.5 Hz, 4-OSi(CH(C*H*$_3$)$_2$)$_3$), 1.30 (sept, 3H, $J_{4\text{-}OSi(CH(CH_3)_2)_3;4\text{-}OSi(CH(CH_3)_2)_3}$ = 7.5 Hz, 4-OSi(C*H*(CH$_3$)$_2$)$_3$), 3.74 (s, 3H, 6-OCH$_3$), 5.06 (s, 2H, 5-OCH$_2$), AB signal (δ_A = 6.52, δ_B = 6.68, J_{AB} = 8.1 Hz, A and B signal show no further splitting, 2-H and 3-H), 7.19 (d, 1H, $J_{7,8}$ = 9.2 Hz, 7-H), 7.22-7.31 (m, 3H, 3`-H, 4`-H, and 5`-H), 7.38-7.42 (m, 2H, 2`-H and 6`-H), 7.91 (d, 1H, $J_{8,7}$ = 9.2 Hz, 8-H). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^1H resonances by the occurrence of crosspeaks [$\delta(^1H) \leftrightarrow \delta(^1H)$]: δ = 1.05 (4-OSi[CH(C*H*$_3$)$_2$]$_3$) $\leftrightarrow \delta_B$ = 6.68 (3-H), δ = 1.05 (4-OSi[CH(C*H*$_3$)$_2$]$_3$) $\leftrightarrow$ δ = 7.38-7.42 (m, 2H, 2`-H and 6`-H), δ = 1.30 (4-OSi[C*H*(CH$_3$)$_2$]$_3$) $\leftrightarrow \delta_B$ = 6.68 (3-H), δ = 5.06 (8-OCH$_2$) $\leftrightarrow \delta$ = 7.38-7.42 (2`-H and 6`-H), δ = 7.19 (7-H) $\leftrightarrow \delta$ = 3.74 (6-OMe). **^{13}C-NMR** (125.81 MHz, $CDCl_3$): δ = 13.44 (4-OSi[*C*H(CH$_3$)$_2$]$_3$), 18.17 (4-OSi[CH(*C*H$_3$)$_2$]$_3$), 56.76 (6-O*C*H$_3$), 76.77 (5-O*C*H$_2$), 106.29 (C-2), 114.12 (C-3), 114.13 (C-7), 118.49 (C-8), 122.71 (C-8a), 124.30 (C-4a), 127.37 (C-4'), 127.79 (C-3`and C-5`), 128.25 (C-2` and C-6`), 138.52 (C-1`), 142.97 (C-5), 145.43 (C-1), 145.76 (C-4), 150.55 (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 = 13.44 (4-OSi[*C*H(CH$_3$)$_2$]$_3$) $\leftrightarrow \delta$ = 1.30 (4- Si[C*H*(CH$_3$)$_2$]$_3$), δ = 18.17 (4-OSi[CH(*C*H$_3$)$_2$]$_3$) $\leftrightarrow \delta$ = 1.05 (4-OSi[CH(C*H*$_3$)$_2$]$_3$), δ = 56.76 (6-O*C*H$_3$) $\leftrightarrow \delta$ = 3.74 (6-OMe), δ = 76.77 (5-O*C*H$_2$) $\leftrightarrow \delta$ = 5.06 (5-OC*H*$_2$), δ = 106.29 (C-2) $\leftrightarrow \delta_A$ = 6.52 (2-H), δ = 114.12 (C-3) $\leftrightarrow \delta_B$ = 6.68 (3-H), δ = 114.13 (C-7) $\leftrightarrow \delta$ = 7.19 (7-H), δ = 118.49 (C-8) $\leftrightarrow \delta$ = 7.91 (8-H), [δ = 127.37 (C-4') and 127.79(C-3`and C-5`)] $\leftrightarrow \delta$ = 7.22-7.31 (3`-H, 4`-H, and 5`-H), $\delta$ = 128.25 (C-2` and C-6`) $\leftrightarrow \delta$ = 7.38-7.42 (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 [$\delta(^{13}C) \leftrightarrow \delta(^1H)$; in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 122.71 (C-8a) $\leftrightarrow \delta_A$ = 6.52 (2-H), δ = 122.71 (C-8a) $\leftrightarrow \delta$ = 7.19 (7-H), δ = 124.30 (C-4a) $\leftrightarrow \delta_B$ = 6.68 (3-H), δ = 124.30 (C-4a) $\leftrightarrow \delta$ = 7.91 (8-H), δ = 138.52 (C-1`) $\leftrightarrow \delta$ = 5.06 (5-OCH$_2$), $\delta$ = 138.52 (C-1`) $\leftrightarrow \delta$ = 7.22-7.31 (3`-H, 4`-H, and 5`-H), δ = 142.97 (C-5) $\leftrightarrow \delta$ = 5.06 (5-OCH$_2$), δ = 142.97 (C-8) $\leftrightarrow \delta$ = 7.19 (7-H), δ = 145.43 (C-1) $\leftrightarrow \delta_B$ = 6.68 (3-H), δ = 145.43 (C-1) $\leftrightarrow \delta$ = 7.91 (8-H), δ = 145.76 (C-4) $\leftrightarrow \delta_A$ = 6.52 (2-H), δ = 150.55 (C-6) $\leftrightarrow \delta$ = 3.74 (6-OCH$_3$), δ = 150.55 (C-6) $\leftrightarrow \delta$ = 7.19 (7-H), δ = 150.55 (C-6) $\leftrightarrow \delta$ = 7.91 (8-H). **Melting point:** Oil. **HRMS** (pos. APCI): calcd. for $C_{27}H_{37}O_4Si$ $[M+H]^+$ = 453.24556; found 453.24536 (–0.44 ppm). **IR (film):** v = 3428, 3155, 2980, 2940, 2870, 2255, 1795, 1650, 1600, 1570, 1465, 1385, 1350, 1275, 1150, 1110, 1065, 995, 915, 845, 745 cm^{-1}.

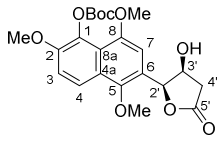
5-(Benzyloxy)-6-methoxynaphthalene-1,4-diol (29)



In a dry round bottomed flask under a nitrogen atmosphere 3-Benzyloxy-2-bromo-4-methoxy-[(1-methylphenylsulfonyl)oxy]benzene (**23**, 9.26 g, 20.0 mmol) and 2-(triisopropylsiloxy)furan (**18a**, 7.20 g, 30.0 mmol, 1.5 equiv.) were dissolved in freshly distilled THF (40 mL). At –78°C *n*BuLi (2.55 M in hexane, 7.84 mL, 20.0 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, 30 mL, 30 mmol, 1.5 equiv.) was added. The ice-bath was removed and the reaction mixture was stirred at room temperature for 8 min. The reaction was quenched with aq. HCl (1 M, 50 mL) and stirred for 5 min at room temperature. CH_2Cl_2 (50 mL) was added and the organic phase was separated. The aq. phase was extracted with CH_2Cl_2 (2×50 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 = 12 cm, h = 12 cm, F = 100 mL; CH/EE 3:1 (contained 1% HCOOH, F1-14), CH/EE 1:1 (contained 1% HCOOH, F15-26)] afforded the title compound [F9-22, R_f (3:1) = 0.25, 5.02 g, 85%] as a yellow-orange solid. Note: Product is moderately air-stable as solid but decomposes slowly in solution. Therefore the NMR spectra contain signals of degradation products.– **^{1}H NMR** (400.13 MHz, $CDCl_3$,

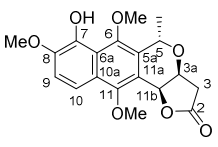
spectrum contains degradation products): 4.03 (s, 3H, 6-OMe), 5.09 (br. s, 1H, 1-OH), 5.25 (s, 2H, 5-OCH_2), AB signal (δ_A = 6.58, δ_B = 6.65, J_{AB} = 8.1 Hz, A and B signal show no further splitting, 2-H and 3-H), 7.28 (d, 1H, $J_{7,8}$ = 9.3 Hz, 7-H), 7.37-7.43 (m, 3H, 3'-H, 4'-H, and 5'-H), 7.51-7.55 (m, 2H, 2'-H and 6'-H), 7.96 (d, 1H, $J_{8,7}$ = 9.3 Hz, 8-H), 9.22 (s, 1H, 4-OH). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 4.03 (6-OMe) ↔ δ = 7.28 (7-H), δ = 5.25 (5-OCH_2) ↔ δ =7.51-7.55 (2'-H and 6'-H).**^{13}C NMR** (100.61 MHz, $CDCl_3$, spectrum contains degradation products): δ = 57.00 (6-O*C*H$_3$), 76.93 (5-O*C*H$_2$), 107.91 (C-2), 109.55 (C-3), 114.37 (C-7), 119.71 (C-8), 128.86, 128.92, and 129.07 (C-2', C-3', C-4', C-5', and C-6'), δ = 119.26 (C-4a), δ = 122.01 (C-8a), δ = 135.97 (C-1'), δ = 141.67 (C-5), δ = 144.11 (C-1), δ = 147.08 (C-4), δ = 148.15 (C-6). **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 = 57.00 (6-OC*H*$_3$) ↔ δ = 4.03 (6-OMe), δ = 76.93 (5-OC*H*$_2$) ↔ δ = 5.25 (5-OC*H*$_2$), δ = 107.91 (C-2) ↔ δ_A = 6.58 (2-H), δ = 109.55 (C-3) ↔ δ_B = 6.65 (3-H), δ = 114.37 (C-7) ↔ δ = 7.28 (7-H), δ = 119.71 (C-8) ↔ δ = 7.96 (8-H), δ = 128.86, 128.92, and 129.07 (C-2', C-3', C-4', C-5', and C-6') ↔ 7.37-7.43 (3'-H, 4'-H, and 5'-H) and 7.51-7.55 (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 ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds]: δ = 119.26 (C-4a) ↔ δ_B = 6.65 (3-H), δ = 119.26 (C-4a) ↔ δ = 7.96 (8-H), δ = 119.26 (C-4a) ↔ δ = 9.22 (4-OH), δ = 122.01 (C-8a) ↔ δ_A = 6.58 (2-H),, δ = 122.01 (C-8a) ↔ δ = 7.28 (7-H), δ = 135.97 (C-1') ↔ δ = 5.25 (5-OCH_2), δ = 141.67 (C-5) ↔ δ = 5.25 (5-OCH_2), δ = 141.67 (C-5) ↔ δ = 7.28 (7-H), δ = 141.67 (C-5) ↔ δ = 7.96 (8-H), δ = 144.11 (C-1) ↔ δ_A = 6.58 (2-H), δ = 144.11 (C-1) ↔ δ_B = 6.65 (3-H), δ = 144.11 (C-1) ↔ δ = 7.96 (8-H), δ = 147.08 (C-4) ↔ δ_A = 6.58 (2-H), δ = 147.08 (C-4) ↔ δ_B = 6.65 (3-H), δ = 147.08 (C-4) ↔ δ = 9.22 (4-OH), δ = 148.15 (C-6) ↔ δ = 4.03 (6-OMe), δ = 148.15 (C-6) ↔ δ = 7.28 (7-H), δ = 148.15 (C-6) ↔ δ = 7.96 (8-H). **Melting point:** 130-140°C (decomp.). **HRMS** (neg. APCI): calcd. for $C_{18}H_{16}O_4Cl$: $[M+Cl]^-$ = 331.07426; found: 331.07437 (+0.34 ppm). **IR (film):** v = 3370, 1660, 1610, 1570, 1470, 1455, 1440, 1410, 1365, 1335, 1320, 1270, 1215, 1175, 1035, 970, 750, 700 cm^{-1}.

***tert*-Butyl 6((2*S*,3*S*)-3-Hydroxy-5-oxotetrahydrofuran-2-yl)-2,5,8-trimethoxynaphthalen-1-yl Carbonate (31)**



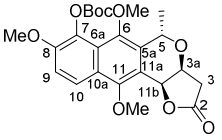
A 87:13 isomeric mixture of (*E*)-methyl 4-(5-(*tert*-butoxycarbonyloxy)-1,4,6-trimethoxynaphthalen-2-yl)but-3-enoate (**15c**) and its α,β-unsaturated carboxylic ester isomer (*iso*-**15c**) (357.8 mg, 0.826 mmol) and $(DHQ)_2PHAL$ (6.4 mg, 8.3 µmol, 1.0 mol-%) were *dissolved* in *t*-BuOH (26 mL). $K_3Fe(CN)_6$ (817 mg, 2.48 mmol, 3.0 equiv.), K_2CO_3 (343 mg, 2.48 mmol, 3.0 equiv.), $NaHCO_3$ (209 mg, 2.48 mmol, 3.0 equiv.), and $Me_2SO_2NH_2$ (79.3 mg, 0.826 mmol, 1.0 equiv.) were dissolved in H_2O (13 mL). The aq. solution was added to the vigorously stirred organic reaction mixture. Solid $K_2OsO_2(OH)_4$ (1.2 mg, 3.3 µmol, 0.4 mol-%) 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 (0.83 g) and stirred for 30 min. EtOAc (20 mL) was added and the organic phase was separated. The aq. phase was extracted with EtOAc (5×10 mL) and the combined organic extracts were washed with aq. KOH solution (1 M, 2×10 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 (F14-26, R_f (1:1) = 0.2, 213.9 mg, 60%) as a white solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.58 [s, 9H, $C(CH_3)_3$], 1.86 (br. s, 1H, 3'-OH), AB signal (δ_A = 2.72, δ_B = 2.92, J_{AB} = 17.6 Hz, A signal shows no further splitting, B signal further split by $J_{B,3'}$ = 5.4 Hz, 4'-H^A and 4'-H^B), 3.87 (s, 3H, 5-OMe), 3.92 (s, 3H, 8-OMe), 3.96 (s, 3H, 2-OMe), 4.78 (dd, 1H, $J_{3',B}$ = 5.0 Hz, $J_{3',2'}$ = 3.8 Hz, 3'-H), 5.82 (d, 1H, $J_{4',3'}$ = 3.6 Hz, 2'-H), 6.85 (s, 1H, 7-H), 7.36 (d, 1H, $J_{3,4}$ = 9.3 Hz, 3-H), 7.89 (d, 1H, $J_{4,3}$ = 9.3 Hz, 4-H). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.92 (4'-H^B) ↔ δ = 5.82 (2'-H; this cross-peak proves that 4'-H^B and 2'-H are oriented *cis* relative to one another), δ = 3.87 (5-OMe) ↔ δ = 5.82 (2'-H), δ = 3.87 (5-OMe) ↔ δ = 7.89 (4-H), δ = 3.92 (8-OMe) ↔ δ = 1.58 [$C(CH_3)_3$], δ = 3.92 (8-OMe) ↔ δ = 6.85 (7-H), δ = 3.96 (2-OMe) ↔ δ = 7.36 (3-H), δ = 6.85 (7-H) ↔ δ = 5.82 (2'-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 27.88 [$C(CH_3)_3$], 38.36 (C-4'), 56.52 (8-O*C*H$_3$), 57.02 (2-O*C*H$_3$), 62.48 (5-O*C*H$_3$), 70.00 (C-3'), 81.63 (C-2'), 82.99 [*C*$(CH_3)_3$], 104.65 (C-7), 114.98 (C-3), 119.83 (C-6), 121.04 (C-4), 121.79 (C-8a), 124.61 (C-4a), 134.56 (C-1), 146.45 (C-5), 149.9 (C-2), 151.86 (C-8), 152.04 (1-O*C*O$_2$*t*Bu), 175.29 (C-5'). An **edHSQ** spectrum ("short-range C,H COSY"; 125.82/500.32 MHz, $CDCl_3$) allowed the assignment of all nonquaternary ^{13}C atoms through the cross-peaks with the independently assigned ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H)]: δ = 27.88 [$C(CH_3)_3$] ↔ δ = 1.58 [$C(CH_3)_3$], δ = 38.36 (C-4') ↔ [δ = 2.72 (4'-H^A) and δ_B = 2.92 (4'-H^B)], δ = 56.52 (8-O*C*H$_3$) ↔ δ = 3.92 (8-OMe), δ = 57.02 (2-O*C*H$_3$) ↔ δ = 3.96 (2-OMe), δ = 62.48 (5-O*C*H$_3$) ↔ δ = 3.87 (5-OMe), δ = 70.00 (C-3') ↔ δ = 4.78 (3'-H), δ = 81.63 (C-2' ↔ δ = 5.82 (2'-H), δ = 104.65 (C-7) ↔ δ = 6.85 (7-H), δ = 114.98 (C-3 ↔ δ = 7.36 (3-H), δ = 121.04 (C-4) ↔ δ = 7.89 (4-H). An **HMB** 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 = 82.9 [$C(CH_3)_3$] ↔ δ = 1.58 [$C(CH_3)_3$], δ = 119.83 (C-6) ↔ δ = 5.82 (2'-H), δ 119.83 (C-6) ↔ δ = 6.85 (7-H), δ = 121.79 (C-8a) ↔ δ = 6.85 (7-H), δ 121.79 (C-8a) ↔ δ = 7.89 (4-H), δ = 124.61 (C-4a) ↔ δ = 7.36 (3-H), = 134.56 (C-1) ↔ δ = 7.36 (3-H), δ = 134.56 (C-1) ↔ δ = 7.89 (4-H), δ 146.45 (C-5) ↔ δ = 3.87 (5-OMe), 146.45 (C-5) ↔ δ = 5.82 (2'-H 146.45 (C-5) ↔ δ = 6.85 (7-H), 146.45 (C-5) ↔ δ = 7.89 (4-H), δ 149.92 (C-2) ↔ δ = 3.96 (2-OMe), δ = 149.92 (C-2) ↔ δ = 7.36 (3-H), = 149.92 (C-2) ↔ δ = 7.89 (4-H), δ = 151.86 (C-8) ↔ δ = 3.92 (8-OMe δ = 151.86 (C-8) ↔ δ = 6.85 (7-H), δ = 175.29 (C-5') ↔ [δ_A = 2.72 (4 H^A) and δ_B = 2.92 (4'-H^B)], δ = 175.29 (C-5') ↔ 4.72(3'-H). δ = 152.0 (1-O*C*O$_2$*t*Bu) exhibited no cross-peak. **Melting point:** 90-95°C (decomposition). **Optical rotation:** $[\alpha]_D^{20}$ = +12.4 (*c* = 0.755, $CHCl_3$ **HRMS** (pos. APCI): Calcd. for $C_{22}H_{26}O_9$ $[M+Na]^+$ = 457.14690; foun 457.14682 (–0.18 ppm). **IR (film):** v = 3475, 3055, 2980, 2940, 284 2305, 1760, 1660, 1630, 1610, 1515, 1480, 1465, 1385, 1370, 128 1255, 1155, 1080, 1045, 1030, 1010, 980, 905, 860, 820, 800, 77 735, 705 cm^{-1}. **Enantiomeric excess: 98.6%** ***ee.*** The *ee* wa determined by chiral HPLC (OD-3, heptane:EtOH = 75:25, λ = 230 nm flow: 0.5 mL/min, t_R(**31**) = 9.40 min, t_R(*ent*-**31**) = 11.12 min). To develo a separation method for chiral HPLC a mixture of both enantiomers wa measured (OD-3, heptane:EtOH = 75:25, λ = 230 nm, flow: 0.5 mL/mir t_R(**31**) = 9.41 min, t_R(*ent*-**31**) = 11.37 min). The optical antipode *ent*-**3** was synthesized analogously by using the $(DHQD)_2PHAL$-ligand in th Sharpless asymmetric dihydroxylation procedure. Yield: 49%. **Optica rotation:** $[\alpha]_D^{20}$ = –13.5 (*c* = 0.755, $CHCl_3$). **Enantiomeric excess 97.9%** ***ee.*** The *ee* was determined by chiral HPLC (OD-3 heptane:EtOH = 75:25, λ = 230 nm, flow: 0.5 mL/min, t_R(**31**) = 9.07 mir t_R(*ent*-**31**) = 11.35 min).

(3a*S*,5*S*,11b*S*)-7-Hydroxy-6,8,11-trimethoxy-5-methyl-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2-one (32)



tert-Butyl 6((2*S*,3*S*)-3-hydroxy-5-oxotetrahydrofuran-2-yl)-2,5,8-trimethoxynaphthalen-1-yl carbonate (**31**, 201.1 mg, 0.463 mmol) was suspended in CH_2Cl_2 (5 mL). At 0°C acetaldehyde (0.19 mL, 0.15 g, 3.47 mmol, 7.5 equiv.) was added and the reaction was started by the addition of $BF_3{\cdot}OEt_2$ (0.59 mL, 0.66 g, 4.63 mmol, 10 equiv.). Afterwards the ice-bath was removed. The reaction mixture was allowed to warm to room temperature and stirred for 20 min. Afterwards the reaction mixture was quenched by the addition of H_2O (5 mL) and stirred for 5 min. The organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (3× 10mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed in vacuo. Flash chromatography [d = 3 cm, h = 12 cm, F = 25 mL; CH/EE 2:1 (F1-14), CH/EE 1:1 (F15-40)] afforded the title compound (F16-23, 84.8 mg, 51%, *ds* = 100:0) as single diastereomer and two additional fractions containing diastereomeric mixtures (F24-25, 22.8 mg, 14%, *ds* = 55:45 and F26-30, 17.0 mg, 10%, *ds* = 16:84) as colorless solids. Combined yield: 126.6 mg, 75%, *ds* = 77:23, R_f (major diastereomer, 1:1) = 0.3, R_f (minor diastereomer, 1:1) = 0.25.– **^{1}H NMR** (400.13 MHz, $CDCl_3$, substance contains 3 w-% EtOAc with resonances at δ = 1.25, 2.05, and 4.12): δ = 1.56 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.7 Hz, 5-CH_3), AB signal (δ_A = 2.71, δ_B = 2.97, J_{AB} = 17.5 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,3a}$ = 4.9 Hz, 3-H^A and 3-H^B), 3.95 (s, 3H, 6-OMe), 4.03 (s, 3H, 8-OMe), 4.07 (s, 3H, 11-OMe), 4.72 (dd, 1H, $J_{3a,B}$ = 4.9 Hz, $J_{3a,11b}$ = 2.7 Hz, 3a-H), 5.36 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.8 Hz, 5-H), 5.56 (d, 1H, $J_{11b,3a}$ = 2.7 Hz, 11b-H), 7.32 (d, 1H, $J_{9,10}$ = 9.2 Hz, 9-H), 7.64 (d, 1H, $J_{10,9}$ = 9.2 Hz, 10-H), 8.64 (s, 1H, 7-OH). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.56 (5-CH_3) ↔ δ = 4.72 (3a-H; this cross-peak proves that 5-CH_3 and 3a-H are oriented *cis* relative to one another), δ_B = 2.97 (3-H^B) ↔ δ = 5.56 (11b-H; this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.95 (6-OMe) ↔ δ = 5.36 (5-H), δ = 3.95 (6-OMe) ↔ δ = 8.64 (7-OH), δ = 4.03 (8-OMe) ↔ δ = 7.32 (9-H), δ = 4.07 (11-OMe) ↔ δ = 5.56 (11b-H), δ = 4.07 (11-OMe) ↔ δ = 7.64 (10-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 19.66 (5-*C*H_3), 37.96 (C-3), 57.11 (8-O*C*H_3), 63.31 (6-O*C*H_3), 64.17 (11-O*C*H_3), 66.29 (C-3a), 67.61 (C-5), 72.00 (C-11b), 114.66 (C-10), 115.13 (C-9), 115.72 (C-11a), 119.45 (C-6a), 124.33 (C-10a), 127.51 (C-5a), 140.92 (C-7), 144.43 (C-8), 146.11 (C-6), 154.40 (C-11), 175.29 (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 = 19.66 (5-*C*H_3) ↔ δ = 1.51 (5-C*H*$_3$), δ = 37.96 (C-3) ↔ [δ_A = 2.71 (3-H^A) and δ_B = 2.97 (3-H^B)], δ = 57.11 (8-O*C*H_3) ↔ δ = 4.03 (8-OMe), δ = 63.31 (6-O*C*H_3) ↔ δ = 3.95 (6-OMe), δ = 64.17 (11-O*C*H_3) ↔ δ = 4.07 (11-OMe), δ = 66.29 (C-3a) ↔ δ = 4.72 (3a-H), δ = 67.61 (C-5) ↔ δ = 5.36 (5-H), δ = 72.00 (C-11b) ↔ δ = 5.56 (11b-H), δ = 114.66 (C-10) ↔ δ = 7.64 (10-H), δ = 115.13 (C-9) ↔ δ = 7.32 (9-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 = 115.72 (C-11a) ↔ δ = 5.36 (5-H), δ = 115.72 (C-11a) ↔ δ = 5.56 (11b-H), δ = 119.45 (C-6a) ↔ δ = 7.64 (10-H), δ = 119.45 (C-6a) ↔ δ = 8.64 (7-OH), δ = 124.33 (C-10a) ↔ δ = 7.32 (9-H), δ = 127.51 (C-5a) ↔ δ = 1.56 (5-CH_3), δ = 127.51 (C-5a) ↔ δ = 5.36 (5-H), δ = 125.51 (C-5a) ↔ δ = 5.56 (11b-H), δ = 140.92 (C-7) ↔ δ = 7.32 (9-H), δ = 140.92 (C-7) ↔ δ = 8.64 (7-OH), δ = 144.43 (C-8) ↔ δ = 4.03 (8-OMe), δ = 144.43 (C-8) ↔ δ = 7.32 (9-H), δ = 144.43 (C-8) ↔ δ = 7.64 (10-H), δ = 144.43 (C-8) ↔ δ = 8.64 (7-OH), δ = 146.11 (C-6) ↔ δ = 3.95 (6-OMe), δ = 146.11 (C-6) ↔ δ = 5.36 (5-H), δ = 154.40 (C-11) ↔ δ = 4.07 (11-OMe), δ = 154.40 (C-11) ↔ δ = 5.56 (11b-H), δ = 154.40 (C-11) ↔ δ = 7.64 (10-H), δ = 175.29 (C-2) ↔ [δ_A = 2.71 (3-H^A) and δ_B = 2.97 (3-H^B)], δ = 175.29 (C-2) ↔ 4.72(3a-H). **Optical rotation:** $[\alpha]_D^{20}$ = –218.7 (*c* = 1.158, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{19}H_{21}O_7$ $[M+H]^+$ = 361.12818; found 361.12817 (–0.01 ppm). **IR (film):** v = 3365, 2980, 2945, 2845, 1770, 1630, 1455, 1415, 1365, 1345, 1305, 1270, 1200, 1145, 1090, 1065, 1035, 1010, 990, 905, 875, 825, 735, 700 cm^{-1}.

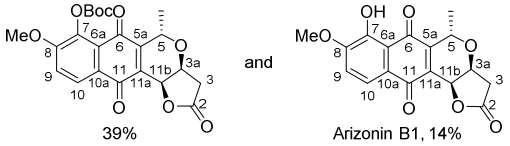
***tert*-Butyl (3a*S*,5*S*,11b*S*)-6,8,11-trimethoxy-5-methyl-2-trioxo-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl Carbonate *tert*-Butyl (3a*S*,5*S*,11b*S*)-6,8,11-trimethoxy-5-methyl-2-trioxo-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl Carbonate (33)**



(3a*S*,5*S*,11b*S*)-6,8,11-Trimethoxy-5-methyl-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-2- one (**32**, 43.5 mg, 121 µmol) and DMAP (1.5 mg, 12 µmol, 10 mol-%) were suspended in CH_2Cl_2 (1 mL). At 0°C di-*t*-butyl dicarbonate (51.8 µL, 52.8 mg, 242 µmol, 2.0 equiv.) was added and the reaction was started by slow addition of NEt_3 (33.5 µL, 24.5 mg, 242 µmol, 2.0 equiv.). The ice-bath was removed, the reaction mixture was allowed to warm to room temperature and stirred for 16 h. The mixture was diluted with CH_2Cl_2 (10 mL) and washed with aq. saturated $NaHCO_3$ solution (5 mL) and brine (5 mL. After drying over Na_2SO_4 the solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 ml; CH/EE 2:1 (F1-20), CH/EE 1:1 (F21-36)] afforded the title compound [F12-26, R_f (2:1) = 0.25, 47.5 mg, 85%] as a colorless oil.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.51 (d, 3H, $J_{5\text{-}CH3,5}$ = 6.8 Hz, 5-CH_3), 1.55 [s, 9H, C(CH_3)$_3$], AB signal (δ_A = 2.69, δ_B = 2.96, J_{AB} = 17.5 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,3a}$ = 5.0 Hz, 3-H^A and 3-H^B), 3.83 (s, 3H, 6-OMe), 3.99 (s, 3H, 8-OMe), 4.06 (s, 3H, 11-OMe), 4.71 (dd, 1H, $J_{3a,B}$ = 4.9 Hz, $J_{3a,11b}$ = 2.8 Hz, 3a-H), 5.33 (q, 1H, $J_{5,5\text{-}CH3}$ = 6.7 Hz, 5-H), 5.53 (d, 1H, $J_{11b,3a}$ = 2.8 Hz, 11b-H), 7.35 (d, 1H, $J_{9,10}$ = 9.3 Hz, 9-H), 8.01 (d, 1H, $J_{10,9}$ = 9.3 Hz, 10-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.55 (5-CH_3) ↔ δ = 4.71 (3a-H, this cross-peak proves that 5-CH_3 and 3a-H are oriented *cis* relative to one another), δ_B = 2.96 (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 = 3.83 (6-OMe) ↔ δ = 5.33 (5-H), δ = 3.99 (8-OMe) ↔ δ = 7.35 (9-H), δ = 4.06 (11-OMe) ↔ δ = 5.53 (11b-H), δ = 4.06 (11-OMe) ↔ δ = 8.01 (10-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 19.66 (5-*C*H_3), 27.76 [C(*C*H_3)$_3$], 37.93 (C-3), 56.90 (8-O*C*H_3), 62.34 (6-O*C*H_3), 64.34 (11-O*C*H_3), 66.23 (C-3a), 68.00 (C-5), 72.05 (C-11b), 83.13 [*C*(CH$_3$)$_3$], 114.27 (C-9), 115.97 (C-11a), 122.20 (C-10), 124.24 (C-6a), 124.24 (C-10a), 130.14 (C-5a), 133.00 (C-7), 145.45 (C-6), 150.43 (C-8), 151.47 (7-O*C*O$_2$tBu, exclusion principle), 153.82 (C-11), 175.32 (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 = 19.66 (5-*C*H_3) ↔ δ = 1.51 (5-C*H*$_3$), δ = 27.76 [C(*C*H_3)$_3$] ↔ δ = 1.55 [C(C*H*$_3$)$_3$], δ = 37.93 (C-3) ↔ [δ_A = 2.69 (3-H^A) and δ_B = 2.96 (3-H^B)], δ = 56.90 (8-O*C*H_3) ↔ δ = 3.99 (8-OMe), δ = 62.34 (6-O*C*H_3) ↔ δ = 3.83 (6-OMe), δ = 64.34 (11-O*C*H_3) ↔ δ = 4.06 (11-OMe), δ = 66.23 (C-3a) ↔ δ = 4.71 (3a-H), δ = 68.00 (C-5) ↔ δ = 5.33 (5-H), δ = 72.05 (C-11b) ↔ δ = 5.53 (11b-H), δ = 114.27 (C-9) ↔ δ = 7.35 (9-H), δ = 122.20 (C-10) ↔ δ = 8.01 (10-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 =83.13 [*C*(CH$_3$)$_3$] ↔ δ = 1.55 [C(C*H*$_3$)$_3$], δ = 115.97 (C-11a) ↔ δ = 5.33 (5-H), δ = 115.97 (C-11a) ↔ δ = 5.53 (11b-H),δ = 124.24 (C-6a*) ↔ δ = 8.01 (10-H), δ = 124.24 (C-10a*) ↔ δ = 7.35 (9-H), δ = 130.14 (C-5a) ↔ δ = 1.51 (5-CH_3), δ = 130.14 (C-5a) ↔ δ = 5.33 (5-H), δ = 130.14 (C-5a) ↔ δ = 5.53 (11b-H), δ = 133.00 (C-7) ↔ δ = 7.35 (9-H), δ = 133.00 (C-7) ↔ δ = 8.01 (10-H), δ = 145.45 (C-6) ↔ δ = 3.83 (6-OMe), δ = 145.45 (C-6) ↔ δ = 5.33 (5-H), δ = 145.45 (C-6) ↔ δ = 8.01 (10-H), δ = 150.43 (C-8) ↔ δ = 3.99 (8-OMe), δ = 150.43 (C-8) ↔ δ = 7.35 (9-H), δ = 150.43 (C-8) ↔ δ = 8.01 (10-H), δ = 153.82 (C-11) ↔ δ = 4.06 (11-OMe), δ =

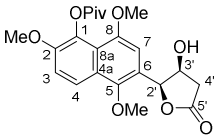
153.82 (C-11) ↔ δ = 5.53 (11b-H), δ = 153.82 (C-11) ↔ δ = 8.01 (10-H), δ = 175.32 (C-2) ↔ [δ_A = 2.69 (3-H^A) and δ_B = 2.96 (3-H^B)], δ = 175.32 (C-2) ↔ 4.71(3a-H). δ = 151.47 (7-O*C*O2tBu) exhibited no cross-peak. *both resonances have the same chemical chift. **Melting point:** Oil. **Optical rotation:** $[\alpha]^D_{20}$ = –146.3 (*c* = 0.7, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{24}H_{28}O_9$ $[M+H]^+$ = 461.18061; found 461.18054 (–0.15 ppm). **IR (film):** v = 3430, 3060, 2980, 2940, 2850, 1765, 1670, 1625, 1605, 1505, 1495, 1455, 1405, 1395, 1370, 1355, 1340, 1280, 1255, 1200, 1150, 1090, 1065, 1035, 1005, 980, 955, 915, 900, 875, 840, 810, 770, 755, 735, 700, 670 cm^{-1}.

tert-Butyl (3a*S*,5*S*,11b*S*)-8-methoxy-5-methyl-2,6,11-trioxo-3,3a,5,6,11,11b-hexahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl Carbonate (34) and (3a*S*,5*S*,11b*S*)-7-Hydroxy-8-methoxy-5-methyl-3,3a-dihydro-2*H*-benzo[g]furo[3,2-*c*]isochromene[5*H*,11b*H*]-trione (Arizonin B1, 3)



tert-Butyl (3a*S*,5*S*,11b*S*)-6,8,11-trimethoxy-5-methyl-2-trioxo-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl carbonate (**33**, 48.5 mg, 105 µmol) was dissolved in acetonitrile (2 mL). At room temperature a freshly prepared solution of CAN (115.5 mg, 210 µmol, 2.0 equiv.) in H_2O (2 mL) was added dropwise. The reaction mixture was stirred for 20 min and afterwards diluted with EE (10 mL). The organic phase was separated and the aq. phase was extracted with EE (4×10 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 8 cm, F = 8 mL; CH/EE 2:1 (F1-16), CH/EE 1:1 (F17-30), CH/EE/HCO_2H 49:49:2 (F31-45)] afforded the major product [**34**, F19-25, R_f (2:1) = 0.1, 17.7 mg, 39%, *dr* = 100:0] as an orange solid as well as the minor product arizonin B1 [**3**, F33-37, 5.0 mg, 14%, *dr* = 100:0] as an orange solid.– Analysis of *tert*-butyl (3a*S*,5*S*,11b*S*)-8-methoxy-5-methyl-2,6,11-trioxo-3,3a,5,6,11,11b-hexahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl carbonate (**34**): **^{1}H NMR** (400.13 MHz, $CDCl_3$, NMR-file: 2015: NeBrMi19-4060): δ = 1.51 (d, 3H, $J_{5\text{-}CH3,5}$ = 6.9 Hz, 5-CH_3), 1.60 [s, 9H, C(CH_3)$_3$], AB signal (δ_A = 2.67, δ_B = 2.94, 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), 3.97 (s, 3H, 8-OMe), 4.66 (dd, 1H, $J_{3a,B}$ = 5.2 Hz, $J_{3a,11b}$ = 3.0 Hz, 3a-H), 5.02 (q, 1H, $J_{5,5\text{-}CH3}$ = 6.9 Hz, 5-H), 5.24 (d, 1H, $J_{11b,3a}$ = 3.0 Hz, 11b-H), 7.30 (d, 1H, $J_{9,10}$ = 8.8 Hz, 9-H), 8.09 (d, 1H, $J_{10,9}$ = 8.8 Hz, 10-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.51 (5-CH_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 = 3.97 (8-OMe) ↔ δ = 7.30 (9-H). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 18.56 (5-CH_3), 27.76 [C(CH_3)$_3$], 37.00 (C-3), 56.69 (8-OCH_3), 66.48 (C-3a), 66.71 (C-5), 68.93 (C-11b), 84.60 [*C*(CH_3)$_3$], 116.68 (C-9), 124.52 (C-6a), 124.94 (C-10a), 126.89 (C-10), 133.60 (C-11a), 138.99 (C-7), 150.25 (C-5a), 150.54 (7-O*C*O$_2$tBu), 157.51 (C-8), 174.09 (C-2), 180.96 (C-11), 182.12 (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 = 18.56 (5-CH_3) ↔ δ = 1.51 (5-CH_3), δ = 27.76 [C(CH_3)$_3$] ↔ δ = 1.60 [C(*C*H_3)$_3$], δ = 37.00 (C-3) ↔ [δ_A = 2.67 (3-H^A) and δ_B = 2.94 (3-H^B)], δ = 56.69 (8-OCH_3) ↔ δ = 3.97 (8-OMe), δ = 66.48 (C-3a) ↔ δ = 4.66 (3a-H), δ = 66.71 (C-5) ↔ δ = 5.02 (5-H), δ = 68.93 (C-11b) ↔ δ = 5.24 (11b-H), δ = 116.68 (C-9) ↔ δ = 7.30 (9-H), δ = 126.89 (C-10) ↔ δ = 8.09 (10-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 =84.60 [*C*(CH_3)$_3$] ↔ δ = 1.60 [C(*C*H_3)$_3$], δ = 124.52 (C-6a) ↔ δ = 8.09 (10-H), δ = 124.94 (C-10a) ↔ δ = 7.30 (9-H), δ = 133.60 (C-11a) ↔ δ = 5.02 (5-H), δ = 133.60 (C-11a) ↔ δ = 5.24 (11b-H), δ = 138.99 (C-7) ↔ δ = 7.30 (9-H), δ = 138.99 (C-7) ↔ δ = 8.09 (10-H), δ = 150.25 (C-5a) ↔ δ = 1.51 (5-CH_3), δ = 150.25 (C-5a) ↔ δ = 5.02 (5-H), δ = 150.25 (C-5a) ↔ δ = 5.24 (11b-H), δ = 157.51 (C-8) ↔ δ = 3.97 (8-OMe), δ = 157.51 (C-8) ↔ δ = 7.30 (9-H), δ = 157.51 (C-8) ↔ δ = 8.09 (10-H), δ = 174.09 (C-2) ↔ [δ_A = 2.67 (3-H^A) and δ_B = 2.94 (3-H^B)], δ = 174.09 (C-2) ↔ 4.66(3a-H), δ = 180.96 (C-11) ↔ 5.24 (11b-H), δ = 180.96 (C-11) ↔ 8.09 (10-H), δ = 182.12 (C-6) ↔ 5.02 (5-H). δ = 150.54 (7-O*C*O2tBu) exhibited no cross-peak. **Melting point:** 102-106°C. **Optical rotation:** $[\alpha]^D_{20}$ = –48.1 (*c* = 0.58, $CHCl_3$). **HRMS** (pos. APCI): calcd. for $C_{22}H_{22}O_9$ $[M+H]^+$ = 431.13366; found 431.13409 (+1.01 ppm). **IR (film):** v = 2980, 2940, 2850, 1775, 1665, 1590, 1490, 1445, 1400, 1370, 1335, 1290, 1270, 1255, 1220, 1200, 1150, 1100, 1085, 1070, 1035, 995, 950, 905, 875, 845, 825, 740, 700 cm^{-1}. Warum steht hier nichts über Arizonin B1

6-[(2*S*,3*S*)-3-Hydroxy-5-oxotetrahydrofuran-2-yl]-2,5,8-trimethoxynaphthalen-1-yl Pivalate (35)

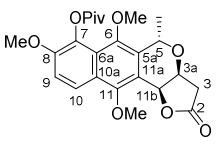


as a 55:45 mixture of rotamers

A 87:13 isomeric mixture of (*E*)-methyl 4-(5-(pivaloyloxy)-1,4,6 trimethoxynaphthalen-2-yl)but-3-enoate (**15d**) and its α,β-unsaturate carboxylic ester isomer (*iso*-**15d**) (96.0 mg, 0.23 mmol) an (DHQ)$_2$PHAL (1.8 mg, 2.3 µmol, 1.0 mol-%) were *dissolved* in *t*-BuO (7 mL). $K_3Fe(CN)_6$ (227.2 mg, 0.69 mmol, 3.0 equiv.), K_2CO_3 (95.4 mg 0.69 mmol, 3.0 equiv.), $NaHCO_3$ (58.0 mg, 0.69 mmol, 3.0 equiv.) an $Me_2SO_2NH_2$ (22.1 mg, 0.23 mmol, 1.0 equiv.) were dissolved in H_2 (1.0 mL). The aq. solution was added to the vigorously stirred organi reaction mixture. An solution of $K_2OsO_2(OH)_4$ (0.34 mg, 0.9 µmo 0.4 mol-%) in H_2O (0.2 mL) was added in one portion to initiate th reaction. The reaction was vigorously stirred for 2 d. Afterwards it wa quenched by the addition of solid Na_2SO_3 (0.23 g) and stirred fo 30 min. EtOAc (8 mL) was added and the organic phase wa separated. The aq. phase was extracted with EtOAc (5×8 mL) and th combined organic extracts were washed with aq. KOH solution (1 M 2×8 mL) and brine (8 mL) and dried over Na_2SO_4. The solvent wa evaporated in vacuo and the residue was purified by flas chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 1:1] to obtai the product (F12-22, R_f (1:1) = 0.2, 44.1 mg, 46%) as a white solid.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): ***Rotamer 1*:*** δ = 1.45 [s, 9H, C(CH_3)$_3$], 1.7 (br. s, 1H, 3'-OH), AB signal (δ_A = 2.74, δ_B = 2.93, J_{AB} = 17.6 Hz, A pa shows no further splitting, B part further split by $J_{B,3'}$ = 5.3 Hz, 4'-H^A an 4'-H^B), 3.88 (s, 3H, 5-OMe), 3.89 (s, 3H, 8-OMe), 3.92 (s, 3H, 2-OMe 4.77 (br. s, 1H, 3'-H), 5.86 (d, 1H, $J_{4',3'}$ = 3.5 Hz, 2'-H), 6.82** (s, 1H, 7 H), 7.36 (d, 1H, $J_{3,4}$ = 9.2 Hz, 3-H), 7.91 (d, 1H, $J_{4,3}$ = 9.2 Hz, 4-H ***Rotamer 2*:*** δ = 1.45 [s, 9H, C(CH_3)$_3$], 1.65 (br. s, 1H, 3'-OH), A signal (δ_A = 2.74, δ_B = 2.93, J_{AB} = 17.6 Hz, A part shows no furthe splitting, B part further split by $J_{B,3'}$ = 5.3 Hz, 4'-H^A and 4'-H^B), 3.88 (s 3H, 5-OMe), 3.89 (s, 3H, 8-OMe), 3.92 (s, 3H, 2-OMe), 4.82 (br. s, 1H 3'-H), 5.82 (d, 1H, $J_{4',3'}$ = 3.6 Hz, 2'-H), 6.83** (s, 1H, 7-H), 7.36 (d, 1H, $J_{3,4}$ = 9.2 Hz, 3-H), 7.91 (d, 1H, $J_{4,3}$ = 9.2 Hz, 4-H). * If the rotamer resonances were not identical they were distinguished from each other by the assignment of their cross-peaks in a DQF-COSY spectrum (400.13 MHz, $CDCl_3$). **For δ = 6.82 and 6.83 (7-H) an unambiguous assignment was impossible, therefore these signals are interchangeable. In the following spectra (NOESY, ^{13}C NMR, edHSQC and HMBC) the rotamer resonances could not be distinguished from each other. Thus, if the resonances were not identical, their δ values are connected by the word "and". A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.93 (4'-H^B) ↔ δ = 5.85

and 5.86 (2'-H; this cross-peak proves that 4'-H^B and 2'-H are oriented *cis* relative to one another), δ = 3.88 (8-OMe) ↔ δ = 1.45 [C(CH_3)$_3$], δ = 3.88 (8-OMe) ↔ δ = 6.82 and 6.83 (7-H), δ = 3.89 (5-OMe) ↔ δ = 5.82 (2'-H), δ = 3.89 (5-OMe) ↔ δ = 7.91 (4-H), δ = 3.92 (2-OMe) ↔ δ = 7.36 (3-H), δ = 6.82 and 6.83 (7-H) ↔ δ = 5.85 and 5.86 (2'-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 27.49 [C(CH_3)$_3$], 38.30 and 38.40 (C-4'), 39.35 [C(CH_3)$_3$], 55.99 (8-OCH_3), 57.02 (2-OCH_3), 62.35 and 62.59 (5-OCH_3), 69.92 (C-3', *rotamer 2*), 70.13 (C-3', *rotamer 1*), 81.54 (C-2', *rotamer 1*), 81.83 (C-2', *rotamer 2*), 104.06 and 104.23 (C-7), 114.86 and 114.92 (C-3), 119.58 and 119.66 (C-6),120.71 and 120.83 (C-4), 122.08 (broad resonance, C-8a), 124.80 (C-4a), 135.19 (C-1), 146.16 and 146.58 (C-5), 149.47 (C-2), 152.21 and 152.34 (C-8), 175.46 and 175.60 (C-5'), 176.88 and 177.08. 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 = 27.49 [C(CH_3)$_3$] ↔ δ = 1.45 [C(CH_3)$_3$], δ = 38.30 and 38.40 (C-4') ↔ [δ_A = 2.74 (4'-H^A) and δ_B = 2.93 (4'-H^B)], δ = 55.99 (8-OCH_3) ↔ δ = 3.88 (8-OMe), δ = 57.02 (2-OCH_3) ↔ δ = 3.92 (2-OMe), δ = 62.35 and 62.59 (5-OCH_3) ↔ δ = 3.89 (5-OMe), δ = 69.92 (C-3', *rotamer 2*) ↔ δ = 4.82 (3'-H, *rotamer 2*), δ = 70.13 (C-3', *rotamer 1*) ↔ δ = 4.77 (3'-H, *rotamer 1*), δ = 81.54 (C-2', *rotamer 1*) ↔ δ = 5.86 (2'-H, *rotamer 1*), δ = 81.83 (C-2', *rotamer 2*) ↔ δ = 5.82 (2'-H, *rotamer 2*), δ = 104.06 and 104.23 (C-7) ↔ δ = 6.82 and 6.83 (7-H), δ = 114.86 and 114.92 (C-3) ↔ δ = 7.36 (3-H), δ = 120.71 and 120.83 (C-4) ↔ δ = 7.91 (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 = 39.35 [C(CH_3)$_3$] ↔ δ = 1.45 [C(CH_3)$_3$], δ = 119.58 and 119.66 (C-6) ↔ δ = 6.82 and 6.83 (7-H), δ = 122.08 (broad signal, C-8a) ↔ δ = 6.82 and 6.83 (7-H), δ = 122.08 (broad signal, C-8a) ↔ δ = 7.91 (4-H), δ = 124.80 (C-4a) ↔ δ = 7.36 (3-H), δ = 135.19 (C-1) ↔ δ = 7.36 (3-H), δ = 135.19 (C-1) ↔ δ = 7.91 (4-H), δ = 146.16 and 146.58 (C-5) ↔ δ = 3.89 (5-OMe), 146.16 and 146.58 (C-5) ↔ δ = 6.82 and 6.83 (7-H), 146.16 and 146.58 (C-5) ↔ δ = 7.91 (4-H), δ = 149.47 (C-2) ↔ δ = 3.96 (2-OMe), δ = 149.47 (C-2) ↔ δ = 7.36 (3-H), δ = 149.47 (C-2) ↔ δ = 7.91 (4-H), δ = 152.21 and 152.34 (C-8) ↔ δ = 3.88 (8-OMe), δ = 152.21 and 152.34(C-8) ↔ δ = 6.82 and 6.83 (7-H), δ = 175.46 and 175.60 (C-5') ↔ [δ_A = 2.74 (4'-H^A) and δ_B = 2.93 (4'-H^B)], δ = 176.88 and 177.08 (5'-O_2C*t*Bu) ↔ δ = 1.45[C(CH_3)$_3$]. **Optical rotation (35):** [α]$_D^{20}$ = +21.4 (*c* = 0.725, $CHCl_3$). **HRMS** (pos. APCI, 70 eV, file: nebrc62t_hr4): Calcd. for $C_{22}H_{30}O_8N$ $[M+NH_4]^+$ = 436.1966; found 436.1965 (–0.28 ppm). **IR (film):** v = 3470, 2970, 2935, 2845, 1750, 1665, 1630, 1610, 1515, 1480, 1465, 1385, 1370, 1340, 1280, 1255, 1235, 1200, 1150, 1120, 1075, 1045, 1015, 980, 920, 900, 875, 820, 800, 750 cm^{-1}. **Enantiomeric excess (35): >97% *ee*.** The *ee* was determined by chiral HPLC (OD-3, heptane:EtOH = 75:25, λ = 230 nm, flow: 0.5 mL/min, t_R(**35**) = 8.53 min, t_R(*ent*-**35**) not detected. To develop a separation method for chiral HPLC a mixture of both enantiomers was measured (OD-3, heptane:EtOH = 75:25, λ = 230 nm, flow: 0.5 mL/min, t_R(**35**) = 8.40 min, t_R(*ent*-**35**) = 9.47 min). The optical antipode **35** was synthesized analogously by using the $(DHQD)_2PHAL$-ligand in the Sharpless' asymmetric dihydroxylation procedure. **Optical rotation (*ent*-35):** [α]$_D^{20}$ = –19.3 (*c* = 0.87, $CHCl_3$). **Enantiomeric excess (*ent*-35): 97% *ee.*** The *ee* was determined by chiral HPLC (OD-3, heptane:EtOH = 75:25, λ = 230 nm, flow: 0.5 mL/min, t_R(**35**) = 8.00 min, t_R(*ent*-**35**) = 9.52 min).

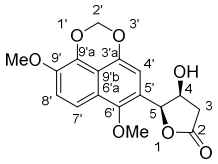
(3a*S*,5*S*,11b*S*)-6,8,11-Trimethoxy-5-methyl-2-oxo-3,3a,5,11b-tetrahydro-2*H*-benzo[*g*]furo[3,2-*c*]isochromen-7-yl Pivalate (36)



6-[(2*S*,3*S*)-3-Hydroxy-5-oxotetrahydrofuran-2-yl]-2,5,8-trimethoxynaphthalen-1-yl pivalate (**35,** 11.2 mg, 26.7 μmol) was suspended in CH_2Cl_2 (0.5 mL). At 0°C acetaldehyde (11.2 μL, 8.9 mg, 0.20 mmol, 7.5 equiv.) was added and the reaction was started by the addition of $BF_3{\cdot}OEt_2$ (34 μL, 38 mg, 0.27 mmol, 10 equiv.). The ice-bath was removed. The reaction mixture was allowed to warm to room temperature and stirred for 30 min. It was quenched by the addition of aq. saturated $NaHCO_3$ (5 mL) and vigorously stirred for 5 min. The organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (4× 5mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed in vacuo. Flash chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 1:1] afforded the title compound [R_f(1:1) = 0.5, F5-10, 6.9 mg, 58%] as a colorless solid. The product came up as a 85:15 rotameric mixture at room temperature (proved by ^{1}H NMR spectroscopy (500.42 MHz, $CDCl_3$, see below). A ^{1}H-NMR spectrum (500.32 MHz, $CDCl_3$) recorded at 333 K proved the mixture to be a single diastereomer.– **^{1}H NMR** (500.32 MHz, $CDCl_3$, 333K): δ = 1.46 [s, 9H, C(CH_3)$_3$], 1.53 (d, 3H, $J_{5\text{-}CH3,5}$ = 6.7 Hz, 5-CH_3), AB signal (δ_A = 2.68, δ_B = 2.93, 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), 3.78 (br. s, 3H, 6-OMe), 3.93 (s, 3H, 8-OMe), 4.08 (s, 3H, 11-OMe), 4.70 (dd, 1H, $J_{3a,B}$ = 4.9 Hz, $J_{3a,11b}$ = 2.8 Hz, 3a-H), 5.31 (q, 1H, $J_{5,5\text{-}CH3}$ = 6.5 Hz, 5-H), 5.52 (d, 1H, $J_{11b,3a}$ = 2.8 Hz, 11b-H), 7.33 (d, 1H, $J_{9,10}$ = 9.3 Hz, 9-H), 8.02 (d, 1H, $J_{10,9}$ = 9.2 Hz, 10-H). The NMR analysis (room temperature) only contains the resonances of the main rotamer. The minor rotamer's resonances were too broad to be determined. **^{1}H NMR** (500.42 MHz, $CDCl_3$, room temperature,): δ = 1.44 [s, 9H, C(CH_3)$_3$], 1.51 (d, 3H, $J_{5\text{-}CH_3,5}$ = 6.7 Hz, 5-CH_3), AB signal (δ_A = 2.70, δ_B = 2.97, J_{AB} = 17.5 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), 3.78 (br. s, 3H, 6-OMe), 3.93 (s, 3H, 8-OMe), 4.07 (s, 3H, 11-OMe), 4.71 (br. s, 1H, 3a-H), 5.28 (q, 1H, $J_{5,5\text{-}CH_3}$ = 6.6 Hz, 5-H), 5.54 (br. s, 1H, 11b-H), 7.34 (d, 1H, $J_{9,10}$ = 9.3 Hz, 9-H), 8.02 (d, 1H, $J_{10,9}$ = 9.3 Hz, 10-H). A **NOESY** spectrum (500.42 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of cross-peaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 1.51 (5-CH_3) ↔ δ = 4.71 (3a-H, this cross-peak proves that 5-CH_3 and 3a-H are oriented *cis* relative to one another), δ_B = 2.97 (3-H^B) ↔ δ = 5.54 (11b-H this cross-peak proves that 3-H^B and 11b-H are oriented *cis* relative to one another), δ = 3.78 (6-OMe) ↔ δ = 1.44 [C(CH_3)$_3$], δ = 3.78 (6-OMe) ↔ δ = 5.28 (5-H), δ = 3.93 (8-OMe) ↔ δ = 1.44 [C(CH_3)$_3$], δ = 3.93 (8-OMe) ↔ δ = 7.34 (9-H), δ = 4.07 (11-OMe) ↔ δ = 5.54 (11b-H), δ = 4.07 (11-OMe) ↔ δ = 8.02 (10-H). **^{13}C NMR** (125.81 MHz, $CDCl_3$): δ = 19.8 (5-CH_3), 27.5 [C(CH_3)$_3$], 38.0 (C-3), 39.4 [C(CH_3)$_3$], 56.8 (8-OCH_3), 62.6 (6-OCH_3), 64.3 (11-OCH_3), 66.2 (C-3a), 68.1 (C-5), 72.2 (C-11b), 114.0 (C-9), 115.9 (C-11a), 122.1 (C-10), 124.3, 124.6, and 133.5 (C-6a, C-7, and C-10a), 129.8 (C-5a), 146.0 (C-6), 149.9 (C-8), 153.7 (C-11), 175.5 (C-2), 176.7 (7-O_2CtBu). An **edHSQC** spectrum ("short-range C,H COSY"; 125.81/500.42 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 = 19.8 (5-CH_3) ↔ δ = 1.51 (5-CH_3), δ = 27.5 [C(CH_3)$_3$] ↔ δ = 1.44 [C(CH_3)$_3$], δ = 38.0 (C-3) ↔ [δ_A = 2.70 (3-H^A) and δ_B = 2.97 (3-H^B)], δ = 56.8 (8-OCH_3) ↔ δ = 3.93 (8-OMe), δ = 62.6 (6-OCH_3) ↔ δ = 3.78 (6-OMe), δ = 64.3 (11-OCH_3) ↔ δ = 4.07 (11-OMe), δ = 66.2 (C-3a) ↔ δ = 4.71 (3a-H), δ = 68.1 (C-5) ↔ δ = 5.28 (5-H), δ = 72.2 (C-11b) ↔ δ = 5.54 (11b-H), δ = 114.0 (C-9) ↔ δ = 7.34 (9-H), δ = 122.1 (C-10) ↔ δ = 8.02 (10-H). An **HMBC** spectrum ("long-range C,H COSY"; 125.81/500.42 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 =39.4 [C(CH_3)$_3$] ↔ δ = 1.44 [C(CH_3)$_3$], δ = 115.9 (C-11a) ↔ δ_A = 2.70 (3-H^A), δ = 115.9 (C-11a) ↔ δ = 5.28 (5-H), δ = 115.9 (C-11a) ↔ δ = 5.54 (11b-H), δ = 124.3, 124.6, and 133.5 (C-6a, C-7, and C-10a) ↔ [δ = 7.32 (9-H) and δ = 8.02 (10-H) could not be assigned unambiguously], δ = 129.8 (C-5a) ↔ δ = 1.51 (5-CH_3), δ = 129.8 (C-5a) ↔ δ = 5.28 (5-H), δ = 129.8 (C-5a) ↔ δ = 5.54 (11b-H), δ = 146.0 (C-6) ↔ δ = 3.78 (6-OMe), δ = 146.0 (C-6) ↔ δ = 5.28 (5-H), δ = 149.9 (C-8) ↔ δ = 3.93 (8-OMe), δ = 149.9 (C-8) ↔ δ = 7.34 (9-H), δ = 149.9 (C-8) ↔ δ = 8.02 (10-H), δ = 153.7 (C-11) ↔ δ = 4.07 (11-OMe), δ = 153.7 (C-11) ↔ δ = 5.54 (11b-

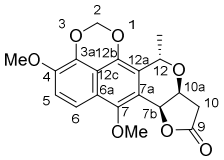
H), δ = 153.7 (C-11) ↔ δ = 8.02 (10-H), δ = 175.5 (C-2) ↔ [δ_A = 2.70 (3-H^A) and δ_B = 2.97 (3-H^B)], δ = 175.5 (C-2) ↔ 4.71(3a-H), δ = 176. 7 (7-O$_2$CtBu) exhibited no cross-peak. **Optical rotation:** $[\alpha]^{D}_{20}$ = –132.9 (*c* = 0.62, $CHCl_3$). **HRMS** (pos. APCI): Calcd. for $C_{24}H_{32}O_8N$ $[M+NH_4]^+$ = 462.2122; found 462.2122 (–0.05 ppm). **IR (film):** ν = 2975, 2935, 2875, 2850, 1785, 1625, 1600, 1505, 1480, 1465, 1405, 1365, 1355, 1340, 1280, 1200, 1130, 1065, 1035, 1010, 980, 955, 915, 900, 820, 795, 760, 735 cm^{-1}.

(4*S*,5*S*)-5-(6,9-dimethoxynaphtho[1,8-*de*][1,3-dioxin-5-yl]-4-hydroxydihydrofuran-2(3*H*)-one (38)



A 93:7 isomeric mixture of (*E*)-methyl 4-(6,9-dimethoxynaphtho[1,8-*de*][1,3 dioxine-5-yl]but-3-enoate (**15h**) and its α,β-unsaturated carboxylic ester isomer (*iso*-**15h**) (197.8 mg, 0.60 mmol) and $(DHQ)_2PHAL$ (4.7 mg, 6.0 µmol, 1.0 mol-%) were *dissolved* in *t*-BuOH (48 mL). $K_3Fe(CN)_6$ (0.59 g, 1.79 mmol, 2.99 equiv.), K_2CO_3 (0.25 g, 1.81 mmol, 3.01 equiv.), $NaHCO_3$ (0.15 g, 1.79 mmol, 2.99 equiv.), and $Me_2SO_2NH_2$ (57.6 mg, 0.60 mmol, 1.00 equiv.) were dissolved in H_2O (12 mL). The aq. solution was added to the vigorously stirred organic reaction mixture. Solid $K_2OsO_2(OH)_4$ (0.9 mg, 2.4 µmol, 0.4 mol-%) 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 (0.60 g) and stirred for 30 min. EtOAc (50 mL) was added and the organic phase was separated. The aq. phase was extracted with EtOAc (4×20 mL) and the combined organic extracts were washed with aq. KOH solution (1 M, 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 cm, h = 12 cm, F = 25 mL; CH/EE 1:1] to obtain the product (F18-28, R_f (1:1) = 0.2, 102.8 mg, 52%) as a pale-yellow solid.– **^{1}H NMR** (500.32 MHz, $CDCl_3$): δ = 1.84 (br. s, 1H, 4-OH), AB signal (δ_A = 2.74, δ_B = 2.94, J_{AB} = 17.7 Hz, A signal further splitted by $J_{A,4}$ = 0.9 Hz, B signal further split by $J_{B,4}$ = 5.6 Hz, 3-H^A and 3-H^B), 3.95 (s, 3H, 6'-OMe), 4.01 (s, 3H, 9'-OMe), 4.81 (m, 1H, 4-H), AB signal (δ_A = 5.52, δ_B = 5.58, J_{AB} = 5.0 Hz, A and B signal show no further splitting, 2'-H^A and 2'-H^B), 5.84 (d, 1H, $J_{5,4}$ = 3.8 Hz, 5-H), 6.98 (s, 1H, 4'-H), 7.33 (d, 1H, $J_{8',7'}$ = 9.2 Hz, 8'-H), 7.63 (d, 1H, $J_{7',8'}$ = 9.2 Hz, 7'-H). A **NOESY** spectrum (500.32 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ_B = 2.94 (3-H^B) ↔ δ = 5.84 (5-H, this cross-peak proves that 3-H^B and 5-H are oriented *cis* relative to one another), δ = 3.95 (6'-OMe) ↔ δ = 5.84 (5-H), δ = 3.95 (6'-OMe) ↔ δ = 7.63 (7'-H), δ = 4.01 (9'-OMe) ↔ δ = 7.33 (8'-H), δ = 6.98 (4-H) ↔ δ = 5.84 (5-H). **^{13}C NMR** (125.82 MHz, $CDCl_3$): δ = 38.42 (C-3), 57.34 (9'-OCH_3), 62.55 (6'-OCH_3), 69.96 (C-4), 81.65 (C-5), 91.28 (C-2'), 107.33 (C-4'), 116.17 (C-7'), 116.25 (C-8'), 117.14 (C-9'b), 121.05 (C-5'), 123.15 (C-6'a), 137.64 (C-9'a), 142.05 (C-9'), 145.76 (C-3'a), 147.38 (C-6'), 175.25 (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 = 38.42 (C-3) ↔ δ_A = 2.74 (3-H^A) and δ_B = 2.94 (3-H^B), δ = 57.34 (9'-OCH_3) ↔ δ = 4.01 (9'-OMe), δ = 62.55 (6'-OCH_3) ↔ δ = 3.95 (6'-OMe), δ = 69.96 (C-4) ↔ δ = 4.81 (4-H), δ = 81.65 (C-5) ↔ δ = 5.84 (5-H), δ = 91.28 (C-2') ↔ δ_A = 5.52 (2'-H^A) and δ_B = 5.58 (2'-H^B), δ = 107.33 (C-4') ↔ δ = 6.98 (4'-H), δ = 116.17 (C-7') ↔ δ = 7.63 (7'-H), δ = 116.25 (C-8') ↔ δ = 7.33 (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 = 117.14 (C-9'b) ↔ δ = 6.98 (4'-H), δ = 117.14 (C-9'b) ↔ δ = 7.63 (7'-H), δ = 121.05 (C-5') ↔ δ = 5.84 (5-H), δ = 121.05 (C-5') ↔ δ = 6.98 (4'-H), δ = 123.15 (C-6'a) ↔ δ = 7.33 (8'-H), δ = 137.64 (C-9'a) ↔ δ_A = 5.52 (2'-H^A) and δ_B = 5.58 (2'-H^B), δ = 137.64 (C-9'a) ↔ δ = 7.33 (8'-H), δ = 142.05 (C-9') ↔ δ = 4.01 (9'-OMe), δ = 142.05 (C-9') ↔ δ = 7.63 (7'-H), δ = 145.76 (C-3'a) ↔ δ_A = 5.52 (2'-H^A) and δ_B = 5.58 (2'-H^B), δ = 145.76 (C-3'a) ↔ δ = 7.02 (4'-H), δ = 147.38 (C-6') ↔ δ = 3.95 (6'-OMe), δ = 147.38 (C-6') ↔ δ = 5.84 (5-H), δ = 147.38 (C-6') ↔ δ = 6.98 (4'-H), δ = 147.38 (C-6') ↔ δ = 7.63 (7'-H), δ = 175.25 (C-2) ↔ δ_A = 2.74 (3-H^A) and δ_B = 2.94 (3-H^B). **Melting point:** 133°C. **Optical rotation (38):** $[\alpha]_D^{20}$ = –4.2 (*c* = 0.793, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{17}H_{16}O_7$ $[M+Na]^+$ = 355.07882; found 355.07901 (+0.52 ppm). **IR (film):** *v* = 3455, 3060, 2945, 2845, 1775, 1625, 1585, 1510, 1485, 1445, 1405, 1385, 1345, 1275, 1205, 1160, 1105, 1070, 1015, 990, 925, 895, 875, 815, 800, 785, 735, 690 cm^{-1}. **Enantiomeric excess (38): >99.9% *ee*.** The *ee* was determined by chiral HPLC (OD 3, heptane:EtOH = 50:50, λ = 237 nm, flow: 1.0 mL/min, t_R(**38**) 4.41 min, t_R(*ent*-**38**) not detected). To develop a separation method fo chiral HPLC a mixture of both enantiomers was measured (OD-3 heptane:EtOH = 50:50, λ = 237 nm, flow: 1.0 mL/min, t_R(**38**) = 4.41 mi t_R(*ent*-**38**) = 5.36 min). The optical antipode *ent*-**38** was synthesize analogously by using the $(DHQD)_2PHAL$-ligand in the Sharples asymmetric dihydroxylation procedure. **Optical rotation (*ent*-38):** $[\alpha]_D$ = +2.9 (*c* = 0.777, $CHCl_3$). **Enantiomeric excess (*ent*-38): 99.8% *ee*** The *ee* was determined by chiral HPLC (OD-3, heptane:EtOH = 50:5(λ = 237 nm, flow: 1.0 mL/min, t_R(**38**) = 4.44 min, t_R(*ent*-**38**) = 5.34 min).

(7b*S*,10a*S*,12*R*)-4,7-Dimethoxy-12-methyl-7b,10,10a,12-tetrahydro-9*H*-furo[2'',3'':5',6']pyrano[3',4':2,3]naphtho[1,8-*de*][1,3]dioxin-9-one (39)



Procedure 1: (4*S*,5*S*)-5-(6,9-Dimethoxynaphtho[1,8-*de*][1,3 dioxin-5 yl]-4-hydroxydihydrofuran-2(3*H*)-one (**38**, 102.8 mg, 0.309 mmol) wa dissolved in CH_2Cl_2 (3 mL). The suspension was cooled to 0°C an acetaldehyde (129 µL, 102 mg, 2.32 mmol, 7.5 equiv.) was added. A this temperature BF·OEt_2 (392 µL, 439 mg, 3.09 mmol, 10.0 equiv.) wa added dropwise. Afterwards the ice-bath was removed, the solutio was allowed to warm up to room temperature and stirred for 30 mi The reaction was quenched by the addition of aq. saturated NaHC solution (5 mL) and the stirred vigorously for 1 min. The organic phas was separated and the aq. phase was extracted with CH_2Cl_2 (2×8 mL The combined organic extracts were dried over Na_2SO_4 and the solver was removed in vacuo. The oily residue was purified by flas chromatography [d = 1.5 cm, h = 12 cm, F = 8 mL; CH/EE 2:1 (F1-13 1:1 (14-36)] to obtain the product [F10-33, R_f (2:1) = 0.2, 86.3 mg, 78% *ds* = 100:0] as a colorless solid.– **Procedure 2**: (4*S*,5*S*)-5-(6,9 dimethoxynaphtho[1,8-*de*][1,3 dioxin-5-yl]-4-hydroxydihydrofuran-2(3*H* one (**62**, 12.7 mg, 0.038 mmol) was dissolved in CH_2Cl_2 (1 mL). Th suspension was cooled to 0°C and acetaldehyde dimethyl aceta (30.4 µL, 25.8 mg, 0.287 mmol, 7.5 equiv.) was added. At thi temperature BF·OEt_2 (48.4 µL, 54.2 mg, 0.382 mmol, 10.0 equiv.) wa added dropwise. Afterwards the ice-bath was removed, the solution was allowed to warm up to room temperature and stirred for 30 min. The reaction was quenched by the addition of aq. saturated $NaHCO_3$ solution (1 mL) and the stirred vigorously for 1 min. The organic phase was separated and the aq. phase was extracted with CH_2Cl_2 (2×5 mL). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed in vacuo. The residue was purified by flash chromatography (d = 1.5 cm, h = 10 cm, F = 8 mL; CH/EE 2:1) to obtain the product [F10-20, R_f (2:1) = 0.2, 10.7 mg, 78%, *ds* = 100:0) as a colorless solid.– **^{1}H NMR** (400.13 MHz, $CDCl_3$): δ = 1.72 (d, 3H, $J_{12\text{-}CH_3,12}$ = 6.3 Hz, 12-CH_3), AB signal (δ_A = 2.76, δ_B = 2.90, J_{AB} = 17.1 Hz, A signal shows no further splitting, B signal further splitted by $J_{B,10a}$ =

4.5 Hz, 10-H^A and 10-H^B), 4.03 (s, 3H, 4-OMe), 4.10 (s, 3H, 7-OMe), 4.36 (dd, 1H, $J_{10a,B}$ = 4.2 Hz, $J_{10a,7b}$ = 2.4 Hz, 10a-H), 4.96 (q, 1H, $J_{12,12\text{-}CH_3}$ = 6.3 Hz, 12-H), 5.56 (d, 1H, $J_{7b,10a}$ = 2.3 Hz, 7b-H), AB signal (δ_A = 5.55, δ_B = 5.58, J_{AB} = 4.9 Hz, A and B signal show no further splitting, 2-H^A and 2-H^B), 7.33 (d, 1H, $J_{5,6}$ = 9.2 Hz, 5-H), 7.71 (d, 1H, $J_{6,5}$ = 9.2 Hz, 6-H). A **NOESY** spectrum (400.13 MHz, $CDCl_3$) allowed additional assignments of ^{1}H resonances by the occurrence of crosspeaks [δ(^{1}H) ↔ δ(^{1}H)]: δ = 4.03 (4-OMe) ↔ δ = 7.33 (5-H), δ = 4.10 (7-OMe) ↔ δ = 7.71 (6-H), δ = 4.96 (12-H) ↔ δ = 4.36 (10a-H this cross-peak proves that 12-H and 10a-H are oriented *cis* relative to one another). **^{13}C NMR** (100.61 MHz, $CDCl_3$): δ = 21.15 (12-*C*H$_3$), 38.38 (C-10), 57.30 (4-O*C*H$_3$), 64.58 (7-O*C*H$_3$), 69.86 (C-12), 72.01 (C-10a), 73.04 (C-7b), 90.89 (C-2), 115.83 (C-5), 116.66 (C-6), 117.29 and 117.37 (C-7a and C-12c), 119.87 (C-12a), 122.54 (C-6a), 137.27 (C-3a), 140.76 (C-12b), 142.53 (C-4), 152.73 (C-7), 175.57 (C-9). 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 = 21.15 (12-C*H*$_3$) ↔ δ = 1.72 (12-C*H*$_3$), δ = 38.38 (C-10) ↔ δ_A = 2.76 (10-H^A) and δ_B = 2.90 (10-H^B), δ = 57.30 (4-O*C*H$_3$) ↔ δ = 4.03 (4-OMe), δ = 64.58 (7-O*C*H$_3$) ↔ δ = 4.10 (7-OMe), δ = 69.86 (C-12) ↔ δ = 4.96 (12-H), δ = 72.01 (C-10a) ↔ δ = 4.36 (10a-H), δ = 73.04 (C-7b) ↔ δ = 5.56 (7b-H), δ = 90.89 (C-2) ↔ δ_A = 5.55 (2-H^A) and δ_B = 5.58 (2-H^B), δ = 115.83 (C-5) ↔ δ = 7.33 (5-H), δ = 116.66 (C-6) ↔ δ = 7.71 (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 ^{1}H resonances [δ(^{13}C) ↔ δ(^{1}H); in grey: cross-peaks linked via 2 or 4 covalent bonds] [δ = 117.29 and δ = 117.37 (C-7a and C-12c)] ↔ [δ = 4.96 (12-H), δ = 5.56 (7b-H) and δ = 7.71 (6-H)], δ = 119.87 (C-12a) ↔ δ = 1.72 (12-CH$_3$), δ = 119.87 (C-12a) ↔ δ = 4.96 (12-H), δ = 119.87 (C-12a) ↔ δ = 5.56 (7b-H), δ = 122.54 (C-6a) ↔ δ = 7.33 (5-H), δ = 137.27 (C-3a) ↔ [δ_A = 5.55 (2-H^A) and δ_B = 5.58 (2-H^B)], δ = 137.27 (C-3a) ↔ δ = 7.33 (5-H), δ = 137.27 (C-3a) ↔ δ = 7.71 (6-H), δ = 140.76 (C-12b) ↔ δ = 4.96 (12-H), δ = 140.76 (C-12b) ↔ [δ_A = 5.55 (2-H^A) and δ_B = 5.58 (2-H^B)], δ = 142.53 (C-4) ↔ δ = 4.03 (4-OMe), δ = 142.53 (C-4) ↔ δ = 7.33 (5-H), δ = 142.53 (C-4) ↔ δ = 7.71 (6-H), δ = 152.73 (C-7) ↔ δ = 4.10 (7-OMe), δ = 152.73 (C-7) ↔ δ = 5.56 (7b-H), δ = 152.73 (C-7) ↔ δ = 7.71 (6-H), δ = 175.57 (C-9) ↔ [δ_A = 2.74 (10-H^A) and δ_B = 2.94 (10-H^B)], δ = 175.57 (C-9) ↔ δ = 4.36 (10a-H). **Melting point:** 189°C. **Optical rotation:** $[\alpha]^D_{20}$ = –144.3 (*c* = 1.0, $CHCl_3$). **HRMS** (pos. ESI): Calcd. for $C_{19}H_{18}O_7$ $[M+Na]^+$ = 381.09447; found 381.09479 (+0.82 ppm). **IR (film):** *v* = 2965, 2935, 2830, 1775, 1635, 1615, 1505, 1445, 1405, 1390, 1370, 1355, 1310, 1290, 1280, 1210, 1170, 1140, 1115, 1085, 1065, 1035, 980, 965, 910, 895, 780 cm^{-1}.

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Keywords: aryne Diels-Alder reaction • asymmetric Sharpless dihydroxylation • naphthoquinonopyrano-γ-lactones • natural product synthesis • oxa-Pictet Spengler cyclizations • protective groups