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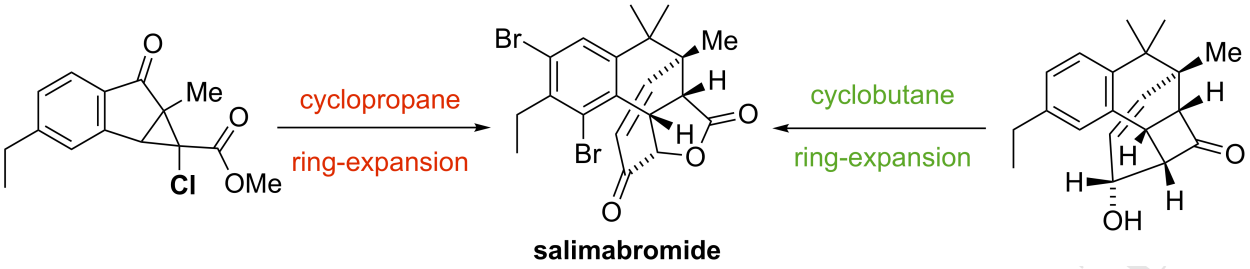

salimabromide

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Ring-Expansion Approaches for the Total Synthesis of Salimabromide

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ABSTRACT

We describe the evolution of a synthetic strategy for the construction of the marine polyketide salimabromide. Combining a bicyclo[3.1.0]hexan-2-one ring-expansion to build up a functionalized naphthalene and an unprecedented rearrangement/cyclization cascade, enabled synthesis of a dearomatized tricyclic subunit of the target compound. Alternatively, an intramolecular ketiminium [2+2]-cycloaddition and subsequent Baeyer–Villiger ring-expansion gave access to the sterically encumbered architecture of salimabromide. Sequential oxidation of the carbon framework finally enabled the total synthesis of this unusual natural product.

1. Introduction

Myxobacteria are a unique class of δ-proteobacteria with an elaborate ability for intercellular communication [1]. In an impressive process of cooperative morphogenesis, these rod-shaped gliding bacteria can aggregate and pile up on starvation conditions, forming so-called fruiting bodies. Within the maturing fruiting body, the cells differentiate into myxospores that are resistant to desiccation. Most myxobacteria also have a fascinating predatory activity on other microorganisms and can lyse a variety of bacteria and fungi to feed on the lysis products [2]. More than 100 natural product scaffolds with a broad range of biological activities were isolated from terrestrial myxobacteria since the last three decades [3]. Only in 1998, the first member of currently ten known marine myxobacterial strains was reported by Iizuka [4]. Difficulties in the cultivation of these bacteria complicate the isolation of natural products and only seven natural product classes have been identified so far (Figure 1) [5]. These include enhygrolide A (**1**) and B (**2**) [6], enhygromic acid (**3**) [7], haliamide (**4**) [8], haliangicins (**5**) [9], salimyxins (**6**) [6] and salimabromide (**7**) [10].

Of those seven classes, the organobromine compound salimabromide (**7**) contains a unique C_{20} framework that does not show any resemblance to other known natural products. Its tetrahydronaphthalene moiety features two contiguous quaternary carbon centers, one of which is asymmetric, and is annealed to a γ-butyrolactone. An enone motif connects the lactone and the saturated half of the tetrahydronaphthalene. The two bromides are located on the aromatic half, resulting in a penta-substituted arene with an uncommon ethyl side chain. First biological

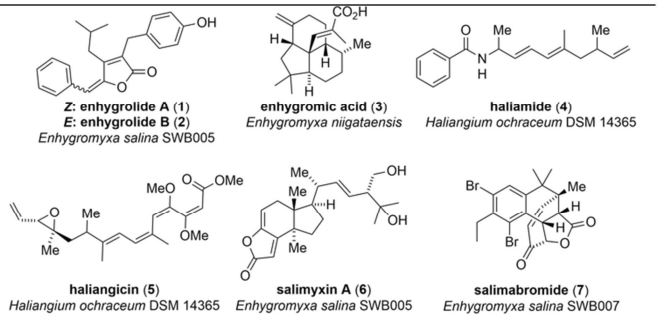
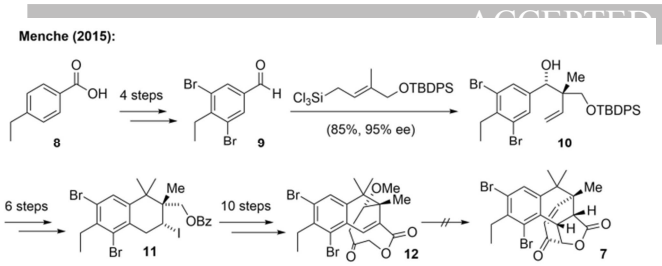


Figure 1 | Natural product classes from marine myxobacteria.

screens were limited as only 0.5 mg of **7** could be isolated [10]. However, they revealed a moderate antibiotic activity against *Arthrobacter cristallopoedes* with a MIC value of 16 µg mL^{-1}.

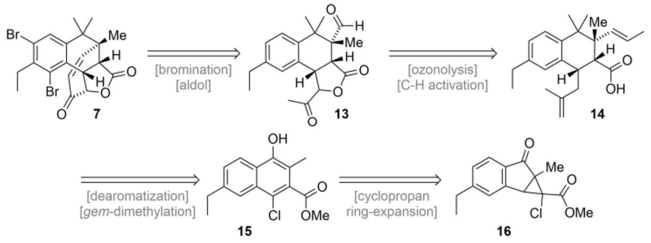
The group of Menche began first synthetic studies shortly after the isolation of **7** in 2013 [11]. In their approach, the crucial quaternary stereocenter was set via an asymmetric Denmark crotylation (95% ee) employing aldehyde **9**. It is interesting to note that **9**, derived from acid **8** in four steps, already contains the sterically demanding bromide substituents. The alcohol **10** was converted to the tetraline **11** within further six steps. For the introduction of the remaining carbon atoms, an additional ten steps were required to give the eight-membered lactone **12**. Unfortunately, the final ring closure of the γ-butyrolactone by an intramolecular Michael-addition as well as the elimination of the neopentylic methoxy group could not be achieved at this stage.



Scheme 1 | Synthetic studies towards salimabromide (**7**) by Menche. TBDPS = *tert*-butyldiphenylsilyl; Bz = benzoyl.

2. Results and discussion

In our retrosynthetic analysis, we envisioned a complementary approach to the one developed by Menche and decided to introduce the bromide substituents of **7** at the very end of the synthesis (Scheme 2). This decision was based on the hypothesis

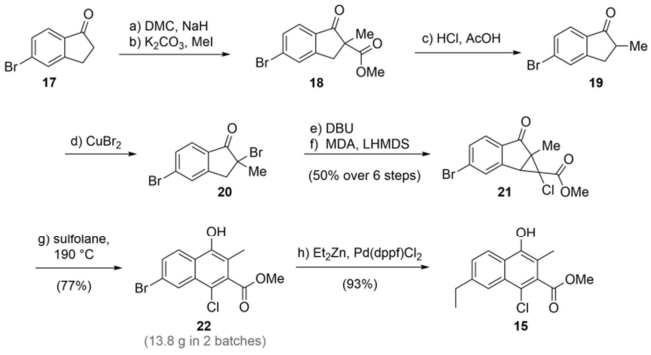


Scheme 2 | Initial retrosynthesis of salimabromide (**7**).

that the biosynthesis involves a late-stage bromination and on steric arguments [10]. The enone of **7** was disconnected via a dynamic kinetic aldol reaction to provide **13** [12]. Further disconnection was accomplished by removal of the lactone and masking of the aldehyde function as an alkene to give **14**. For the construction of **14**, a dearomatization sequence of **15** was planned. Guided by our previously developed ring-expansion methodology, we envisioned to directly trace back **15** to **16** [13–15].

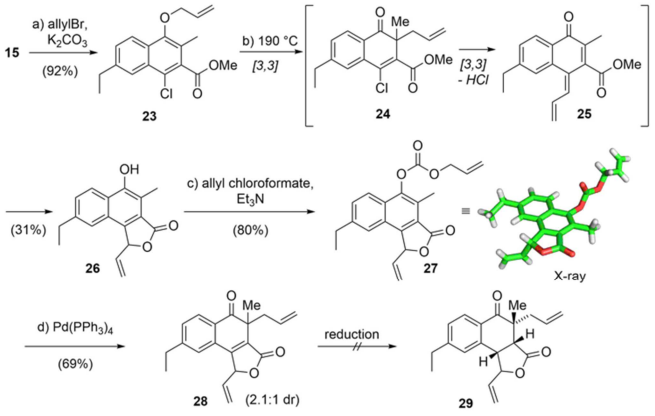
2.1. First Generation Route

We commenced our synthesis with commercially available 5-bromo-1-indanone (**17**) (Scheme 3). From there, cyclopropanated indanone **21** was generated in six steps involving a three-step methylation procedure (**17** to **18** to **19**) [16,17], a bromination



Scheme 3 | Synthesis of naphthol **15** by fragmentation of cyclopropanated indanone **21**. a) DMC, NaH, THF, 0 to 70 °C; b) K_2CO_3, MeI, DMSO, 0 to 23 °C; c) HCl (37%), AcOH, 100 °C; d) $CuBr_2$, EtOAc/$CHCl_3$, 70 °C; e) DBU, benzene, 0 to 23 °C; f) MDA, LHMDS, THF, –78 °C, 50% over 6 steps; g) sulfolane, 190 °C, 77%; h) Et_2Zn, $Pd(dppf)Cl_2$, 1,4-dioxane, 0 to 90 °C, 93%. DMC = dimethylcarbonate, DMSO = dimethylsulfoxide, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, MDA = methyl dichloroacetate, LHMDS = lithium bis(trimethylsilyl)amide, dppf = 1,1'-Bis(diphenylphosphino)ferrocene.

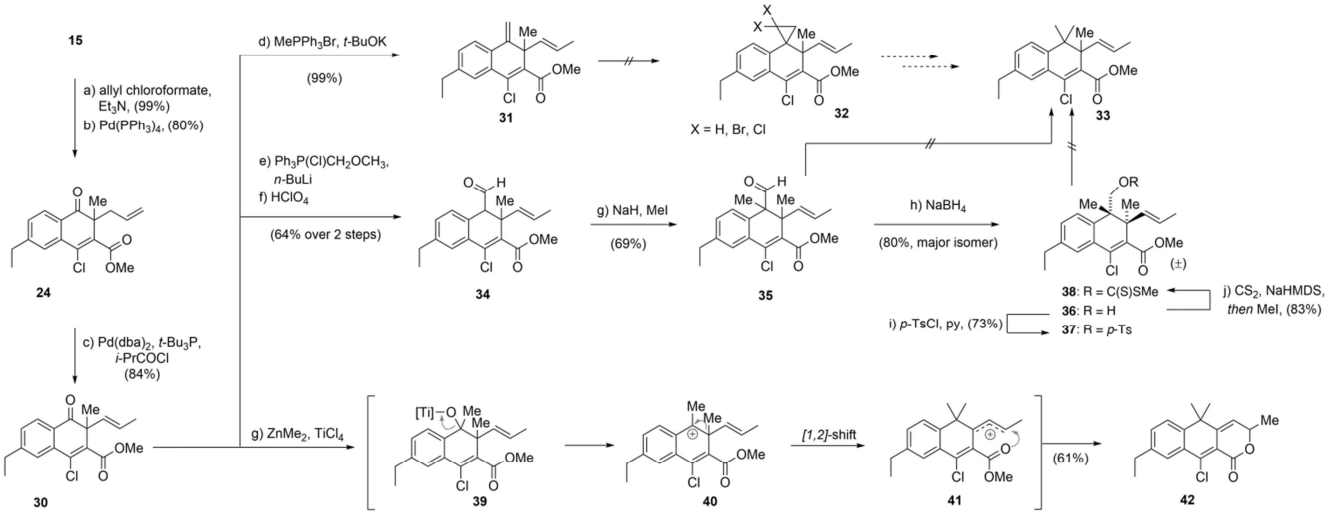
with copper(II) bromide (**19** to **20**) [18,19] followed by elimination and subsequent cyclopropanation with methyl dichloroacetate (MDA, **20** to **21**) [13,20]. The fragmentation was conducted in sulfolane at 190 °C affording naphthol **22** in good yield (77%) on gram-scale [13]. Negishi cross-coupling using freshly prepared diethylzinc introduced the ethyl side chain of **15** in excellent yield [21]. To achieve the dearomatization of the naphthalene we pursued the sequence shown in Scheme 4. First,



Scheme 4 | A tandem Claisen/Cope-rearrangement of phenyl allyl ether **23** and dearomatization of **26**. a) Allyl bromide, K_2CO_3, DMF, 65 °C, 90%; b) sulfolane, 190 °C, 31%; c) allyl chloroformate, Et_3N, THF, 0 °C, 80%; d) $Pd(PPh_3)_4$, toluene/*n*-hexane (9:1), 45 °C, 69%. THF = tetrahydrofuran, DMF = *N*,*N*-dimethylformamide.

15 was allylated under standard conditions (allyl bromide, K_2CO_3, DMF, 65 °C) to give **23** in 92% yield. Heating a solution of **23** in sulfolane at 190 °C induced a tandem Claisen/Cope-rearrangement/cyclization sequence to afford – via the intermediacy of **24** and *p*-quinomethide **25** – the lactone **26** in 31% yield. For the crucial dearomatization, **26** was converted to its allyl carbonate **27** [22]. Exposure to palladium(0) induced the decarboxylative allylation to provide **28** as a mixture of two diastereomers (69%, dr = 2.1:1) [23]. Unfortunately, all attempts to selectively reduce the enone to **29** lead to decomposition, no reaction, isomerization of the vinyl group or reduction of the ketone [24–26].

We therefore decided to go back to **15** and first concentrate on the installation of the *gem*-dimethyl group (Scheme 5). For this purpose, **15** was dearomatized following an analogous procedure as above. In this way, the dearomatized product **24** was obtained in good yields (79% over two steps). Isomerization of the allylic double bond – required for the intended ozonolysis towards **13** – was accomplished by conditions developed by Skrydstrup ($Pd(dba)_2$, *t*-Bu_3P, *i*-PrCOCl, PhMe) in 84% yield [27]. With **31** in hand, we investigated introduction of the *gem*-dimethyl group. First, Wittig olefination proceeded smoothly to give **32** [28]. Unfortunately we were not able to cyclopropanate this alkene by employing the Simmons–Smith protocol (CH_2I_2, $ZnEt_2$) [29], the use of dichlorocarbene or dibromocarbene [30]. In a second approach, a Kluge–Wittig reaction/hydrolysis sequence gave aldehyde **34** which was α-methylated. Noteworthy, rigorous degassing of the solvent (THF) was mandatory to avoid competing oxidation of the enolate and diminished yields of **35**. Attempts to directly reduce this aldehyde by the protocol of Wolff–Kishner [31] or the formation of a thioacetal followed by nickel catalyzed hydrogenation (Mozingo protocol) [32] failed. Therefore, **34** was reduced to the primary alcohol **36**. While it was possible to tosylate this alcohol (**36** to **37**), **33** could not be generated by reduction with lithium aluminum hydride even

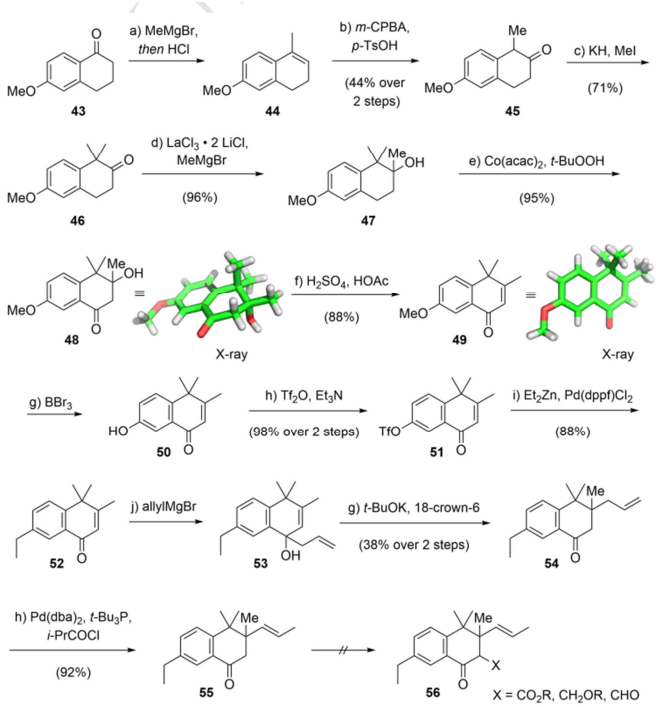


Scheme 5 | Attempts towards the *gem*-dimethylation of dearomatized naphthol **30**. a) Allyl chloroformate, Et_3N, THF, 0 °C, 99%; b) $Pd(PPh_3)_4$, toluene/*n*-hexane (10:1), 45 °C, 80%; c) $Pd(dba)_2$, *t*-Bu_3P, *i*-PrCOCl, toluene, 80 °C, 84%; d) $MePPh_3Br$, *t*-BuOK, THF, 0 to 23 °C, 99%; e) $Ph_3P(Cl)CH_2OCH_3$, *n*-BuLi, THF, 0 to 23 °C, 81%; f) $HClO_4$, Et_2O, 23 °C, 79%; g) NaH, MeI, THF, 0 to 23 °C, 69%; h) $NaBH_4$, MeOH, 0 °C, 80%; i) *p*-TsCl, pyridine, 23 °C, 73%; j) CS_2, NaHMDS, THF, –78 to –65 °C, 83%; g) $TiCl_4$, $ZnMe_2$, CH_2Cl_2, 0 °C, 61%. dba = dibenzylideneacetone, *p*-Ts = *p*-toluenesulfonyl, NaHMDS = sodium bis(trimethylsilyl)amide, py = pyridine.

under elevated temperature (60 °C). Finally, a radical Barton–McCombie deoxygenation of **38** was investigated [33]. However, the intended product was not formed but a complex product mixture was obtained. Direct dimethylation of the ketone using Reetz conditions [34] failed as the strongly Lewis acidic conditions induced a Wagner–Meerwein rearrangement (**39** to **40** to **41**) to give **42** as the sole product [35].

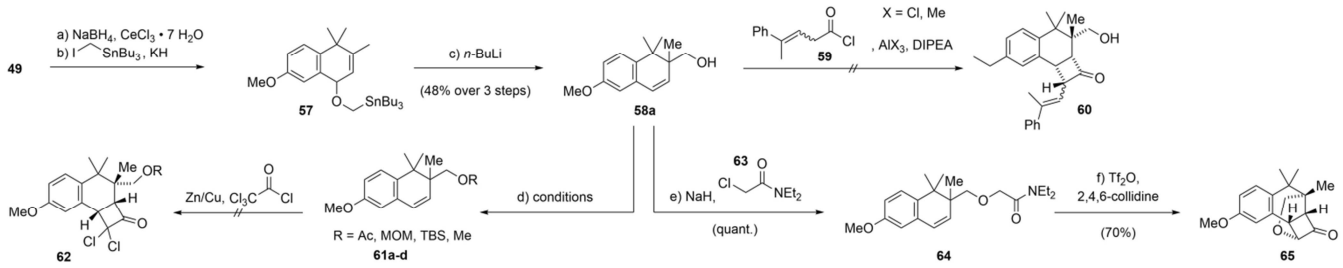
2.2 Second Generation Route

Realizing that introduction of the two quaternary carbon centers is highly problematic at this stage of the synthesis, we abandoned the indanone ring-expansion route and tried to set both centers at an earlier stage. Starting with commercially available methoxytetralone **43**, addition of methylmagnesium bromide and acid-mediated elimination gave known **44** [36]. Epoxidation with concomitant Meinwald-rearrangement afforded ß-tetralone **45** in 44% yield over two steps [37]. Methylation under thermodynamic control using potassium hydride as the base set the *gem*-dimethyl group and afforded tetralone **46** [38]. The vicinal methyl group of **47** was introduced by Grignard addition employing Knochel's conditions ($LaCl_3 \cdot 2$ LiCl, MeMgBr) [39]. Benzylic oxidation with cobalt acetylacetonate [40] gave clean **48** [41] and subsequent acid-mediated elimination afforded enone **49** [42] in good yield [43]. A three-step procedure, involving demethylation, triflation [44] and Negishi cross-coupling [21] with diethylzinc was used to replace the methoxy with an ethyl group yielding **52** (via **50** and **51**, 86% over three steps). Allylation with allylmagnesium bromide (**52** to **53**) followed by an anionic oxy-Cope rearrangement set the quaternary stereocenter of **54** [45,46]. For the isomerization of the allyl group, Skrydrup's conditions again proved to be the method of choice affording **55** in 92% yield [27]. Surprisingly, despite extensive efforts tetralone **55** proved to be reluctant to react at its α-position. We examined several α-acylation and alkylation procedures to introduce the carboxylate for the γ-butyrolactone, however, no carbon-carbon bond formation to give **56** was observed. We reasoned that steric hindrance by the adjacent quaternary stereocenter impedes nucleophilic attack of the enolate.



Scheme 6| Synthesis of tetralone **55**. a) MeMgBr, THF, 0 °C, *then* HCl, 23 °C; b) *m*-CPBA, CH_2Cl_2/TFE, *p*-TsOH, 0 °C, 44% over 2 steps; c) KH, MeI, THF, 0 to 23 °C, 71%; d) MeMgBr, $LaCl_3 \cdot 2$ LiCl, THF, 0 °C, 96%; e) $Co(acac)_2$, *t*-BuOOH, Me_2CO, 23 °C, 95%; f) H_2SO_4, AcOH, 100 °C, 88%; g) BBr_3, CH_2Cl_2, –78 to 0 °C; h) Tf_2O, Et_3N, CH_2Cl_2, –78 to 23 °C, 98% over two steps; i) Et_2Zn, $Pd(dppf)Cl_2$, 1,4-dioxane, 90 °C, 88%; j) allylMgBr, THF, 0 °C; g) *t*-BuOK, 18-crown-6, THF, 0 to 23 °C, 38% over 2 steps; h) $Pd(dba)_2$, *t*-Bu_3P, *i*-PrCOCl, toluene, 80 °C, 92%. *m*-CPBA = *meta*-chloroperoxybenzoic acid, TFE = 2,2,2-trifluoroethanol, acac = acetylacetonate, Tf = trifluoromethanesulfonate, 18-crown-6 = 1,4,7,10,13,16-hexaoxacyclooctadecane.

As steric hindrance prevented α-functionalization of the ketone, we considered an alternative [2+2]-cycloaddition strategy using the readily available **49** (Scheme 7). Conversion of **49** to **58a** proceeded uneventfully via the intermediacy of **57** and involved a Wittig–Still rearrangement to construct the quaternary

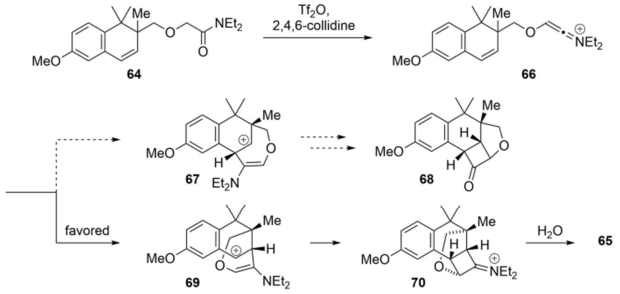


Scheme 7 Investigation of the [2+2]-cycloadditon on **58**. a) $NaBH_4$, $CeCl_3 \cdot 7\ H_2O$, MeOH, 0 °C; b) KH, ICH_2SnBu_3, THF, 0 °C; c) *n*-BuLi, –78 to –45 °C, 48% over 3 steps; d) **61a:** Ac_2O, NEt_3, CH_2Cl_2, 0 °C, 86%; **61b:** DIPEA, MOMCl, CH_2Cl_2, 0 °C, 94%; **61c:** TBSCl, imH, DMF, 0 to 23 °C, 68%; **61d:** NaH, MeI, DMF, 0 to 23 °C, 80%; e) NaH, $ClCH_2CONEt_2$, $(CH_2OMe)_2$, 0 to 23 °C, 97%; e) Tf_2O, 2,4,6-collidine, $(CH_2Cl)_2$, 80 °C, then K_2CO_3, Me_2CO, 70 °C, 70%. DIPEA = *N*,*N*-diisopropylethylamine, DMP = Dess–Martin periodinane, TBS = *tert*-butyldimethylsilyl, MOM = methoxymethyl, Ac = acetyl, imH = imidazole.

stereocenter (48% over three steps) [47,48]. We envisioned the primary alcohol to serve as a handle to control the facial selectivity of the ketene [2+2]-cycloaddition. First, we investigated the use of Lewis acids ($AlMe_3$; $MeAlCl_2$) to control the trajectory of the ketene derived from **59** via coordination to the alkoxide. Unfortunately, no cycloaddition product **60** was observed and only traces of the corresponding ester together with polymeric byproducts were formed. Protection of the primary alcohol (**61a-d** = Ac, MOM, TBS, Me) and cycloaddition with dichloroketene to give **62** was equally unproductive.

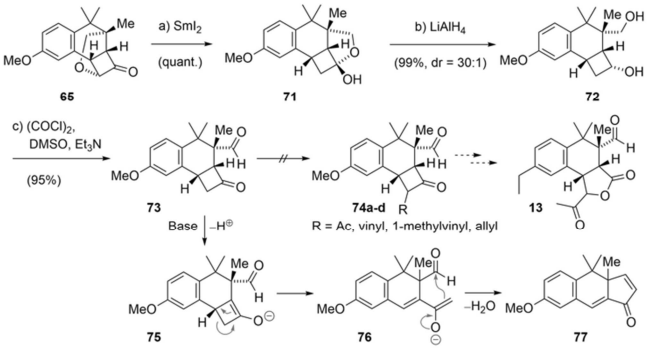
Facing the problems of ketene oligo-and polymerization we resorted to keteniminium salts, which are known to be more electrophilic and reluctant to dimerization [49,50]. Treatment of **58** with 2-chloro-*N*,*N*-diethylacetamide (**63**) gave **64**. We were pleased to see that upon treatment with freshly distilled trifluoromethanesulfonic anhydride and *sym*-collidine at 80 °C, **64** underwent the intramolecular cycloaddition to the iminium salt **70**. The cycloaddition product **65** was formed after hydrolysis in 70% yield and excellent regioselectivity affording exclusively the 6/4- instead of the 5/4-system. The regioselectivity finds its basis in a stepwise mechanism presumably proceeding via the benzylic cation **69** (Scheme 8). This cation should be favored over the secondary cation **67** leading to regioisomer **68**.

With **65** in hand, we cleaved the ether bridge by treatment with



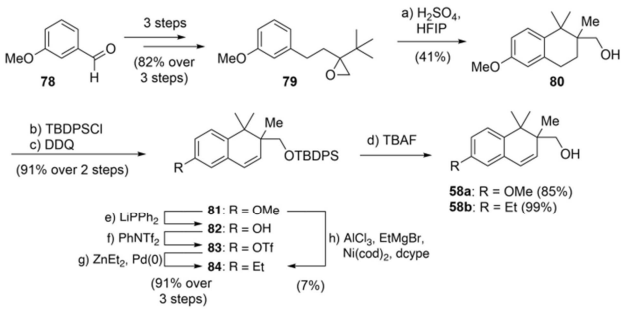
Scheme 8 | Proposed mechanism of the intramolecular [2+2]-cycloaddition of keteniminium ion **64.**

samarium iodide to give lactol **71** (Scheme 9) [51]. Reduction with lithium aluminum hydride afforded diol **72** and oxidation under Swern conditions provided cyclobutanone **73** in 95% yield. All efforts to functionalize the cyclobutanone ring and to convert **73** to **74a-d** failed. Under basic conditions formation of **77** was observed in minor amounts. We believe that **77** is formed via ring-opening of the enolate **75** (stepwise or electrocyclic) and subsequent aldol condensation of **76**.



Scheme 9 | Synthesis of cyclobutanone **71** a) SmI_2, THF/MeOH, 0 °C, quant.; b) $LiAlH_4$, Et_2O, 0 °C, 99%; c) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, –78 to 23 °C, 95%.

At this point, we realized that synthesis of **13**, the key-substrate for the intended kinetic dynamic aldol condensation, might not be possible via the investigated routes. Therefore, we reassessed our strategy once again. Encouraged by the high selectivity of the keteniminium mediated cycloaddition of **64** we decided to investigate an [2+2]-cycloaddition approach using a carbon chain tether (Scheme 10) [52]. For this purpose, we resorted to alcohol **58a**. Since synthesis of **58a** was rather low-yielding so far, we considered other synthetic options to get rapid access to the tetraline core. Inspired by the work of El-Fouty [53] and our desire to rapidly introduce both quaternary carbon centers, we envisioned the synthesis of **80** by a Wagner–Meerwein cyclization sequence of epoxide **79**. [54] When conducting this reaction in 1,1,1,3,3,3-hexafluoroisopropanol (HFIP), 41% of the desired product could be isolated, giving access to large amounts of **80** in four steps involving only two

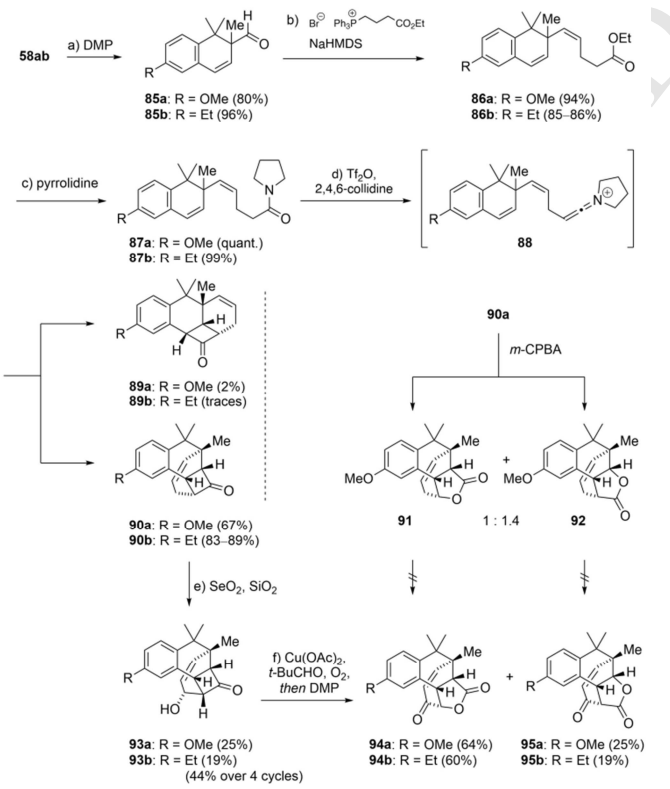


Scheme 10 | Second generation approach to **58ab**. a) H_2SO_4, HFIP, 23 °C, 41%; b) TBDPSCl, imidazole, DMAP, DMF, 23 °C; c) DDQ, 1,4-dioxane, 93 °C, 91% over two steps; d) TBAF, THF, 23 °C, 85–99%; e) $LiPPh_2$, THF, 60 °C; f) $PhNTf_2$, NEt_3, THF, 23 °C, 99% over two steps; g) $ZnEt_2$, $Pd(dppf)Cl_2$, 1,4-dioxane, 70 °C, 92%; h) $AlCl_3$, EtMgBr, $Ni(cod)_2$, dcype, PhMe, *i*-Pr_2O, 100 °C, 7%. HFIP = 1,1,1,3,3,3-hexafluoroisopropanol, DDQ = 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, cod = 1,5-cyclooctadiene, dcype = 1,2-bis(dicyclohexylphosphino)ethane.

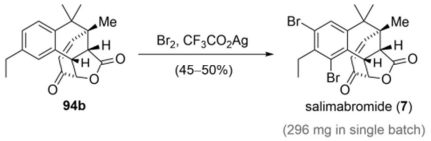
purification steps [54]. For the oxidation to the styrene **81** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), protection of the free alcohol was mandatory as otherwise tetrahydrofuran formation was observed. Deprotection of **81** using tetrabutylammonium fluoride completed the synthesis of **58a**. This sequence shortens the route from nine to seven steps, uses inexpensive reagents and enables large scale synthesis of **58a**. In addition, **81** was used for the installation of the ethyl side chain. A four-step protocol involving demethylation, triflate formation, Negishi cross-coupling using diethylzinc (**82** to **83** to **84**) and cleavage of the silyl protecting group gave **58b**. We also investigated the direct nickel(0)-catalyzed coupling of **81** using the conditions developed by Rueping and Schoenebeck [55]. Under these conditions **84** was only formed in low yields (7%).

With **58a** and **58b** in hand, we continued with the cycloaddition approach. Dess–Martin periodinane (DMP) gave aldehyde **85ab** in 80–96% yield (Scheme 11). A *Z*-selective Wittig olefination [56] afforded ester **86ab** that could be converted into amide **87ab** by heating in neat pyrrolidine [57]. We were pleased to see that **87ab** underwent the envisioned [2+2] cycloaddition in good yields (67% for **90a**, 82–89% for **90b**) and excellent regioselectivity (> 30:1). Only 2% of the undesired [2+2] product **89a** and trace amounts of **89b** were formed. We later found that a very similar approach was investigated by Menche [58,59]. Having successfully built up the full carbon framework of salimabromide (**7**), only Baeyer–Villiger oxidation to expand the cyclobutanone to the γ-butyrolactone and allylic oxidation of the alkene to give the enone were left. Baeyer–Villiger oxidation of the cyclobutanone **90a** promoted by *meta*-chloroperoxybenzoic acid (*m*-CPBA) proceeded smoothly, however, the undesired regioisomer **92** prevailed (**91**:**92** = 1:1.4). As separation of this mixture was impossible at this stage, we directly investigated the allylic oxidation. Efforts to realize the oxidation with rhodium (e.g. bis[rhodium(α,α,α′,α′-tetramethyl-1,3-benzenedipropionic acid)] [60]) or manganese based catalysts (e.g $Mn(OAc)_3$ [61]) in combination with *tert*-butylhydroperoxide were unsuccessful. The use of bromine or selenium dioxide did not lead to any functionalization of the desired position. Next, we tried inversion of the overall sequence and investigated the allylic oxidation first. Exposure of **90a** to a large excess of selenium dioxide (10 equiv) in the presence of fine quartz sand – to prevent selenium dioxide from agglomeration [62] – and terminating the reaction at around 40% conversion to avoid overoxidation, gave **93a** in 25% yield. This alcohol was converted to the lactones **94a** and **94b** by careful treatment with an equimolar amount of *m*-CPBA followed by DMP oxidation of the allylic alcohol. While we were pleased to observe the desired oxidation, we were confronted with an unfavorable regioselectivity (**94a**:**95a** = 1:1.4). Employing conditions previously developed by Bolm ($Cu(OAc)_2$, *t*-BuCHO, O_2) we were able to invert this ratio to favor the desired lactone **94a** (**94a**:**95a** = 2.5:1) [63–65]. Since the overall route using **58b** turned out to be more efficient, we turned our attention to the completion of the synthesis using **90b**. While allylic oxidation of **90b** proceeded with comparable yields, we observed in the Baeyer–Villiger oxidation of **93b** the formation of many sideproducts and a significant drop of selectivity on scales larger than 50 mg. Despite a balanced ratio of the regioisomeric lactones (**94b**:**95b** = 1:1), we found that copper(I) thiophene carboxylate in wet benzene, followed by DMP oxidation in dichloromethane gives reproducible yields of both **94b** and **95b** even on gram scale (see Experimental for details).

Introduction of the remaining bromine substituents was accomplished by treatment of **94b** with bromine and silver trifluoroacetate to give 296 mg of salimabromide (**7**) in a single batch (Scheme 12). The use of silver trifluoroacetate to form highly reactive trifluoroacetyl hypobromite was essential [66,67]. Other bromination reagents (NBS; n-$Bu_4NBr_3/ZnCl_2$; $Br_2/FeBr_3$) only lead to monobromination or decomposition of **94b** [54]. The analytical data for synthetic salimabromide matched those reported in the literature [10].



Scheme 11 | Synthesis of the carbon skeleton of salimabromide (**7**). a) DMP, CH_2Cl_2, 0 to 23 °C; b) NaHMDS, $Ph_3P(Br)(CH_2)_3CO_2Et$, THF, –78 to 23 °C; c) pyrrolidine, 100 °C; d) Tf_2O, 2,4,6-collidine, $(CH_2Cl)_2$, 80 °C, *then* CCl_4, H_2O, reflux; e) SeO_2, SiO_2, 1,4-dioxane, 120–125 °C; f) $Cu(OAc)_2$, *t*-BuCHO, O_2, $(CH_2Cl)_2$, 23 °C, *then* DMP, 0 to 23 °C.



Scheme 12 | Total synthesis of salimabromide. Br_2, CF_3CO_2Ag, TFA, 0 °C, 45–50%.

3. Conclusion

We presented two complementary strategies for the total synthesis of salimabromide. In our initial route we targeted a highly-substituted keto-aldehyde that was thought to be synthesized via ring-expansion of a cyclopropanated indanone and subsequent dearomatization. Although both key-transformations were realized, efforts to introduce the *gem*-dimethyl group as well as the stereocenters connecting the lactone and the tetrahydronaphthalene core failed. In our second approach, we relied on a [2+2]-cycloaddition to construct the carbon skeleton. While intermolecular cycloaddition reactions were unsuccessful, an intramolecular ketiminium [2+2]-cycloaddition showed to be high-yielding and proceeded with excellent regioselectivity. Three regioselective oxidations (allylic, Baeyer–Villiger, late-stage bromination) enabled completion of the total synthesis in 18 steps (longest linear

sequence). The developed route allowed production of 296 mg of salimabromide in a single batch.

Experimental

All reactions were performed in flame-dried glassware fitted with rubber septa under a positive pressure of argon, unless otherwise noted. Air- and moisture-sensitive liquids were transferred *via* syringe or stainless-steel cannula through rubber septa. Solids were added under inert gas counter flow or were dissolved in appropriate solvents. Low temperature-reactions were carried out in a Dewar vessel filled with a cooling agent: acetone/dry ice (−78 °C), water/ice (0 °C). Reaction temperatures above room temperature were conducted in a heated oil bath. The reactions were magnetically stirred and monitored by NMR spectroscopy or analytical thin-layer chromatography (TLC), using aluminum plates precoated with silica gel (0.25 mm, 60-Å pore size, Merck) impregnated with a fluorescent indicator (254 nm). TLC plates were visualized by exposure to ultraviolet light (UV), were stained by submersion in aqueous potassium permanganate solution ($KMnO_4$), ceric ammonium molybdate solution (CAM) or *p*-anisaldehyde solution (Anis), and were developed by heating with a heat gun. Flash-column chromatography was performed as described by Still [68] employing silica gel (60 Å, 40–63 μm, Merck KGaA). The yields refer to chromatographically and spectroscopically (^{1}H and ^{13}C NMR) pure material. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled under nitrogen atmosphere from sodium and benzophenone or sodium/potassium alloy prior to use. Dichloromethane (CH_2Cl_2), Acetonitrile (MeCN), acetone and methanol (MeOH) were purchased from Acros Organics as 'extra dry' reagents and used as received. All other reagents and solvents were purchased from chemical suppliers (Sigma-Aldrich, TCI, Acros Organics, Alfa Aesar, Strem Chemicals, ABCR, Fluorochem) and were used as received. Solvents for extraction, crystallization and flash column chromatography were purchased in technical grade and distilled under reduced pressure prior to use. The molarity of *n*-butyllithium and *tert*-butyllithium solutions was determined by titration against diphenylacetic acid as an indicator (average of three determinations). **NMR spectra** were measured on a Bruker Avance III HD 400 MHz spectrometer equipped with a CryoProbeTM, Bruker Avance Neo 400 MHz spectrometer, Bruker Avance II 600MHz spectrometer, Bruker AXR300, a Varian VXR400 S, Bruker AMX600 or Bruker Avance HD 800. Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual proton in the NMR solvent ($CHCl_3$: δ 7.26, acetone-d_5: δ 2.05, C_6D_5H: δ 7.16). Carbon chemical shifts are expressed in parts per million (δ scale, assigned carbon atom) and are referenced to the carbon resonance of the NMR solvent ($CDCl_3$: δ 77.16, acetone-d_6: δ 29.84, 206.26, C_6D_6: δ 128.06). ^{1}H NMR spectroscopic data are reported as follows: Chemical shift in ppm (multiplicity, coupling constants J (Hz), integration intensity, assigned proton). The multiplicities are abbreviated with s (singlet), br s (broad singlet), d (doublet), t (triplet), q (quartet) and m (multiplet). In case of combined multiplicities, the multiplicity with the larger coupling constant is stated first. Except for multiplets, the chemical shift of all signals, as well for centrosymmetric multiplets, is reported as the center of the resonance range. Additionally to ^{1}H and ^{13}C NMR measurements, 2D NMR techniques such as homonuclear correlation spectroscopy (COSY), total correlation spectroscopy (TOCSY), heteronuclear single quantum coherence (HSQC) and heteronuclear multiple bond coherence (HMBC) were used to assist signal assignment. For further elucidation of 3D structures of the products, nuclear Overhauser enhancement spectroscopy (NOESY) was conducted. Coupling constants J are reported in Hz. All raw fid files were processed and the spectra analyzed using the program MestReNOVA 9.0 from Mestrelab Research S. L. All **mass spectra** were measured by the analytic section of the Department of Chemistry, Ludwig-Maximilians-Universität München and the group of Thomas Müller at the Department of Chemisty, Leopold-Franzens Universität Innsbruck. Mass spectra were recorded on the following spectrometers (ionization mode in brackets): MAT 95 (EI), MAT 90 (ESI) from Thermo Finnigan GmbH and Q Exactive Orbitrap (ESI) from Thermo Fisher Scientific. Mass spectra were recorded in high-resolution. The method used is reported at the relevant section of the experimental section. **IR spectra** were recorded on a PerkinElmer Spectrum BX II FT-IR system. If required, substances were dissolved in CH_2Cl_2 or $CDCl_3$ prior to direct application on the ATR unit. Data are represented as follows: frequency of absorption (cm^{-1}) and intensity of absorption (vs = very strong, s = strong, m = medium, w = weak, br = broad).

*3.1. Methyl 5-bromo-2-methyl-1-oxo-2,3-dihydro-1H-indene-2-carboxylate (**18**)*

To a suspension of sodium hydride (60% dispersion in mineral oil, 19.9 g, 497 mmol, 2.00 equiv) and dimethyl carbonate (39.9 mL, 474 mmol, 2.00 equiv) in tetrahydrofuran (470 mL) in a 3-necked 1-liter round bottom flask fitted with a reflux condenser, dropping funnel and thermometer was added 5-bromo-1-indanone (**17**) (50.0 g, 237 mmol, 1 equiv) in tetrahydrofuran (680 mL) at 0 °C over 45 min. The dark brown reaction mixture was stirred at 0 °C for 30 min, warmed very slowly to 23 °C and carefully heated to 70 °C for 15 h. The solution was cooled to 0 °C and diluted with saturated aqueous ammonium chloride solution (200 mL), aqueous hydrogen chloride solution (2 M; 200 mL) and diethyl ether (300 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 400 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (300 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered through a short pad of Celite® and the filtrate was concentrated. The crude product **S1** was afforded as a dark brown solid and was used without additional purification for the next step. To crude I.71 in dry dimethyl sulfoxide (240 mL) was added potassium carbonate (65.5 g, 474 mmol, 2.00 equiv) portionwise at 0 °C. After dropwise addition of methyl iodide (29.5 mL, 474 mmol, 2.00 equiv) the dark green slurry was stirred at 23 °C for 2 h. The excess methyl iodide was removed by distillation (23 °C, 50 mbar). The reaction mixture was cooled to 0 °C, diluted with saturated aqueous ammonium chloride solution (100 mL), water (100 mL) and ethyl acetate (250 mL). The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 400 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (300 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered through a short pad of Celite® and the filtrate was concentrated. The crude product **18** was afforded as a dark brown solid and was used without additional purification for the next step. An analytical pure sample of **18** was obtained by flash column chromatography on silica gel (9% ethyl acetate in hexanes). **Analytical data for 18: TLC** (20% ethyl acetate in hexanes), R_f = 0.40 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.63 (s, 1H), 7.60 (d, *J* = 7.5 Hz, 1H), 7.51 (d, *J* = 8.6 Hz, 1H), 3.69 (s, 1H), 3.64 (s, 3H), 2.95 (d, *J* = 17.3 Hz, 1H), 1.48 (s, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ: 202.1, 172.0, 154.2, 133.5, 131.6, 130.9, 129.8, 126.1, 56.1, 52.9, 39.6, 21.0. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2953 (*w*), 1742 (*s*), 1710 (*vs*), 1594 (*s*), 1579 (*m*), 1428 (*m*), 1317 (*m*), 1266 (*s*), 1200 (*s*), 1177 (*s*), 1095 (*m*), 1057 (*m*), 964 (*s*), 919 (*m*), 830 (*m*), 769

(*m*), 668 (*m*), 593 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{12}H_{11}O_3{}^{81}Br$ $[M]^+$: 283.9866; found: 283.9875.

*3.2. 5-bromo-2-methyl-2,3-dihydro-1H-inden-1-one (**19**)*

Crude **18** was dissolved in water (82 mL), glacial acetic acid (400 mL) and aqueous hydrogen chloride solution (37%, 125 mL, 924 mmol, 3.90 equiv). The reaction mixture was heated to 100 °C for 16 h. After cooling to 23 °C, the solution was diluted with dichloromethane (300 mL) and water (300 mL) and was carefully neutralized by portionwise addition of sodium bicarbonate (250 g) and aqueous sodium hydroxide solution (10%, 300 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 400 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered through a short pad of Celite® and the filtrate was concentrated. The crude product **19** was afforded as a dark brown solid and was used without additional purification for the next step. An analytical pure sample of **19** was obtained by flash column chromatography on silica gel (2% ethyl acetate in hexanes). **Analytical data for 19: TLC** (20% ethyl acetate in hexanes), R_f = 0.56 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.63 – 7.56 (m, 2H), 7.49 (d, *J* = 8.1 Hz, 1H), 3.37 (dd, *J* = 18.1, 8.8 Hz, 1H), 2.70 (dt, *J* = 12.1, 3.5 Hz, 2H), 1.29 (d, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 208.2, 155.2, 135.3, 131.1, 130.1, 129.9, 125.3, 42.1, 34.7, 16.3. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2964 (*w*), 2930 (*w*), 1707 (*vs*), 1594 (*vs*), 1572 (*m*), 1412 (*m*), 1318 (*m*), 1265 (*m*), 1199 (*m*), 1055 (*m*), 963 (*s*), 882 (*m*) 858 (*m*), 825 (*m*), 764 (*m*), 676 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{10}H_9O^{81}Br$ $[M]^+$: 225.9811; found: 225.9814.

*3.3. 2,5-Dibromo-2-methyl-2,3-dihydro-1H-inden-1-one (**20**)*

To a solution of crude indanone **19** in ethyl acetate (1 L) and chloroform (1 L), was added copper(II) bromide (106 g, 474 mmol, 2.00 equiv). The green suspension was heated to 70 °C and while stirring with a KPG stirrer. After 22 h, the mixture was allowed to cool to 23 °C, filtered through a short pad of Celite® and the filtrate was concentrated. The crude product **20** was used without additional purification for the next step. An analytical pure sample of **20** was obtained by flash column chromatography on silica gel (2% ethyl acetate in hexanes). **Analytical data for 20: TLC** (20% ethyl acetate in hexanes), R_f = 0.57 (UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.72 (d, *J* = 8.2 Hz, 1H), 7.61 (s, 1H), 7.59 (d, *J* = 8.6 Hz, 1H), 3.77 (d, *J* = 18.3 Hz, 1H), 3.47 (d, *J* = 18.3 Hz, 1H), 1.96 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 199.2, 150.7, 132.1, 131.7, 131.4, 129.8, 127.0, 59.2, 46.1, 26.8. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 1723 (*vs*), 1596 (*s*), 1575 (*w*), 1423 (*w*), 1320 (*m*), 1266 (*w*), 1210 (*w*), 1057 (*m*), 973 (*m*), 900 (*w*), 857 (*w*), 831 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{10}H_8O^{79}Br_2$ $[M]^+$: 301.8936; found: 301.8937.

*3.4. Methyl 3-bromo-1-chloro-6a-methyl-6-oxo-1,1a,6,6a-tetrahydrocyclopropa[a]indene-1-carboxylate (**21**)*

To crude indanone **20** in benzene (474 mL) was added 1,8-diazabicyclo[5.4.0]undec-7-ene (106 mL, 711 mmol, 3.00 equiv) at 0 °C. After 5 min, the solution was warmed to 23 °C and was stirred for 45 min. The reaction mixture was diluted with saturated aqueous ammonium chloride solution (100 mL) and diethyl ether (200 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 300 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (200 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered through a short pad of Celite® and the filtrate was concentrated (>200 mbar). The crude indenone **S2** was afforded as a yellow-brown oil and was used immediately without additional purification for the next step. *Note: Indenones undergo facile polymerizations and should therefore be used immediately after preparation. For safety reasons the cyclopropanation was carried out in two parallel batches. The crude material of both batches was subsequently combined and purified together.* To a stirred solution of lithium bis(trimethylsilyl)amide (1 M in tetrahydrofuran, 137 mL, 137 mmol, 1.15 equiv) in tetrahydrofuran (119 mL) in a 3-necked 2 liter round bottom flask fitted with a reflux condenser, dropping funnel and thermometer, was added methyl dichloroacetate (12.9 mL, 125 mmol, 1.05 equiv) over 30 min at −78 °C. After stirring for 105 min, a solution of crude indenone **S2** in tetrahydrofuran (238 mL) was added over 1.5 h and after the addition, the reaction mixture was allowed to warm slowly to 23 °C. After 16 h, the mixture was cooled to 0 °C and diluted with saturated aqueous ammonium chloride solution (200 mL) and ethyl acetate (300 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 300 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (200 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (2 to 3% ethyl acetate in hexanes) to obtain **21** (38.9 g, 50% over 6 steps, inconsequential mixture of diastereomers) as a yellow solid. **Analytical data for 21:** *Note: Traces of the minor diastereomer are visible in the ^{1}H and ^{13}C NMR spectra, but solely the resonances of the major diastereomer are listed below.* **TLC** (20% ethyl acetate in hexanes), R_f = 0.47 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.67 (s, 1H), 7.54 (s, 2H), 3.86 (s, 3H), 3.71 (s, 1H), 1.51 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 197.3, 165.9, 149.4, 134.5, 132.2, 129.9, 129.8, 125.3, 64.9, 53.9, 42.8, 37.3, 9.9. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2954 (*w*), 1717 (*vs*), 1597 (*s*), 1579 (*m*), 1435 (*m*), 1356 (*w*), 1283 (*m*), 1260 (*s*), 1237 (*s*), 1206 (*m*), 1162 (*m*), 1107 (*w*), 1055 (*m*), 988 (*w*), 952 (*m*), 938 (*m*), 889 (*m*), 836 (*m*), 788 (*w*), 777 (*w*), 738 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{13}H_{10}O_3{}^{79}Br^{35}Cl$ $[M]^+$: 327.9496; found: 327.9505.

*3.5. Methyl 7-bromo-1-chloro-4-hydroxy-3-methyl-2-naphthoate (**22**)*

Note: The reaction was carried out in two parallel batches. The crude material of both batches was subsequently combined and purified together. A solution of **21** (8.90 g, 27.0 mmol, 1 equiv) in sulfolane (54 mL) was heated to 190 °C for 5.5 h and then cooled to 23 °C. The reaction mixture was diluted with diethyl ether (200 mL) and water (200 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 × 300 mL). The combined organic layers were washed successively with saturated aqueous sodium chloride solution (200 mL) and water (3 × 300 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (14% ethyl acetate in hexanes) to provide **22** (13.8 g, 77%) as a brown solid. **Analytical data for 22: TLC** (20% ethyl acetate in hexanes), R_f = 0.18 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.18 (s, 1H), 7.94 (d, *J* = 8.9 Hz, 1H), 7.57 (d, *J* = 8.9 Hz, 1H), 5.65 (s, 1H), 4.02 (s, 3H), 2.25 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 168.5, 148.4, 133.5, 130.6, 130.5, 126.8, 124.2, 123.8, 122.2, 118.9, 115.0, 53.2, 13.3. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3330 (*w*), 2951 (*w*), 1695 (*vs*), 1619 (*w*), 1583 (*m*), 1558 (*w*), 1439 (*s*), 1378 (*m*), 1361 (*m*), 1275 (*vs*), 1247 (*vs*), 1177 (*m*), 1111 (*m*), 1074 (*m*), 1053 (*m*), 962 (*m*), 927 (*s*), 874 (*m*), 863 (*m*), 823 (*vs*), 761 (*m*), 741 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{13}H_{10}O_3{}^{79}Br^{35}Cl$ $[M]^+$: 327.9496; found: 327.9492.

*3.6. Methyl 1-chloro-7-ethyl-4-hydroxy-3-methyl-2-naphthoate (**15**)*

Note: The reaction setup has to be flame-dried very carefully, since otherwise the yield decreases significantly. To [1,1'-Bis(diphenylphosphino)ferrocene]palladium(II) dichloride (400 mg, 0.546 mmol, 0.0180 equiv) was added a solution of **22** (10.0 g, 30.3 mmol, 1 equiv) in 1,4-dioxane (25 mL). The red suspension was cooled to 0 °C and a freshly prepared solution of diethylzinc (1 M in toluene, 60.1 mL, 60.7 mmol, 2.00 equiv) was added very carefully over 30 min. After the addition, the dark red mixture was allowed to warm to 23 °C over 30 min and the beige suspension was then heated carefully to 90 °C. After 3 h, it was cooled to 0 °C and methanol (20 mL) was added dropwise. Water (100 mL) and aqueous hydrochloric acid solution (2 M, 100 mL) were added, the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 200 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (200 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered through a short pad of Celite® and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (9% ethyl acetate in hexanes) to obtain **15** (7.82 g, 93%) as a red-brown oil. **Analytical data for 15: TLC** (20% ethyl acetate in hexanes), R_f = 0.31 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 8.6 Hz, 1H), 7.97 (q, *J* = 0.9 Hz, 1H), 7.45 (dd, *J* = 8.7, 1.7 Hz, 1H), 5.37 (s, 1H), 4.03 (s, 3H), 2.86 (q, *J* = 7.6 Hz, 2H), 2.32 (s, 3H), 1.63 (s, 1H), 1.36 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 168.6, 148.2, 143.7, 132.7, 130.0, 128.3, 123.9, 122.7, 121.6, 119.6, 113.1, 52.9, 29.3, 15.6, 13.1. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3475 (*w*), 2362 (*m*), 1715 (*s*), 1438 (*m*), 1387 (*m*), 1293 (*m*), 1239 (*vs*), 1053 (*m*), 668 (*m*) cm^{-1}.**HRMS** (EI) calcd for $C_{15}H_{15}O_3{}^{35}Cl$ $[M]^+$: 278.0704; found: 278.0699.

*3.7. Methyl 4-(allyloxy)-1-chloro-7-ethyl-3-methyl-2-naphthoate (**23**)*

To a solution of **15** (100 mg, 0.359 mmol, 1 equiv) in dimethylformamide (1.2 mL) were successively added potassium carbonate (74.4 mg, 0.538 mmol, 1.50 equiv) and allyl bromide (34.2 µL, 47.7 mmol, 1.10 equiv) and the reaction mixture was heated to 65 °C. After 1.5 h, water (10 mL) and diethyl ether (15 mL) were added, the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 15 mL). The combined organic layers were washed with aqueous hydrochloric acid solution (2 M, 30 mL) and saturated aqueous sodium chloride solution (30 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated under reduced pressure. The residue was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to yield **23** (103 mg, 90%) as a colorless oil. **Analytical data for 23: TLC** (20% ethyl acetate in hexanes), R_f = 0.58 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.02 (s, 1H), 8.01 (d, *J* = 6.6 Hz, 1H), 7.45 (dd, *J* = 8.6, 0.9 Hz, 1H), 6.18 (ddt, *J* = 17.1, 11.6, 5.9 Hz, 1H), 5.50 (d, *J* = 17.2 Hz, 1H), 5.33 (d, *J* = 10.4 Hz, 1H), 4.45 (d, *J* = 6.6 Hz, 2H), 4.01 (s, 3H), 2.85 (q, *J* = 7.3 Hz, 2H), 2.37 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 168.2, 152.1, 143.6, 133.6, 133.3, 130.4, 129.0, 127.9, 123.4, 123.0 (2C), 122.6, 118.0, 75.2, 52.8, 29.3, 15.6, 13.5. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2965 (*w*), 1736 (*vs*), 1598 (*w*), 1436 (*m*), 1385 (*m*), 1330 (*m*), 1315 (*m*), 1280 (*m*), 1231 (*s*), 1214 (*m*), 1170 (*m*), 1113 (*m*), 1051 (*s*), 991 (*m*), 972 (*m*), 937 (*m*), 877 (*m*), 833 (*m*), 757 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{18}H_{19}O_3{}^{35}Cl$ $[M]^+$: 318.1017; found: 318.1020.

*3.8. 8-Ethyl-5-hydroxy-4-methyl-1-vinylnaphtho[1,2-c]furan-3(1H)-one (**26**)*

A solution of **23** (1.56 g, 4.90 mmol, 1 equiv) in sulfolane (10 mL) was heated to 190 °C. After 2 h, water (100 mL) and diethyl ether (100 mL) were added, the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 100 mL). The combined organic layers were washed successively with water (5 × 100 mL) and saturated aqueous sodium chloride solution (100 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (10% ethyl acetate in hexanes) to afford **26** (407.7 mg, 31%) as a yellow solid. **Analytical data for 26: TLC** (20% ethyl acetate in hexanes), R_f = 0.23 (UV, CAM, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.22 (d, *J* = 8.7 Hz, 1H), 7.64 (d, *J* = 1.0 Hz, 1H), 7.53 (dd, *J* = 8.7, 1.7 Hz, 1H), 6.04 (d, *J* = 7.8 Hz, 1H), 5.92 (ddd, *J* = 17.0, 9.9, 7.7 Hz, 1H), 5.75 (d, *J* = 16.8 Hz, 1H), 5.52 (d, *J* = 10.3 Hz, 1H), 5.50 (s, 1H), 2.83 (q, *J* = 7.5 Hz, 2H), 2.70 (s, 3H), 1.32 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.4, 150.8, 143.4, 140.0, 134.7, 129.8, 126.6, 125.8, 123.1, 122.0, 121.7, 121.2, 112.4, 80.7, 29.1, 15.4, 9.2. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3418 (*w*), 2966 (*w*), 1733 (*vs*), 1582 (*w*), 1469 (*w*), 1395 (*w*), 1371 (*w*), 1299 (*w*), 1262 (*w*), 1198 (*w*), 1013 (*m*), 977 (*m*), 939 (*w*), 834 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{17}H_{16}O_3$ $[M]^+$: 268.1094; found: 268.1074.

*3.9. Allyl (8-ethyl-4-methyl-3-oxo-1-vinyl-1,3-dihydronaphtho[1,2-c]furan-5-yl) carbonate (**27**)*

To a solution of **26** (500 mg, 1.86 mmol, 1 equiv) in tetrahydrofuran (9.3 mL) was added triethylamine (0.363 mL, 2.61 mmol, 1.40 equiv). After 10 min, the reaction mixture was cooled to 0 °C and allyl chloroformate (0.238 mL, 2.24 mmol, 1.20 equiv) was added. After 15 min, water (100 mL) was added, the layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (70 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (9% ethyl acetate in hexanes) to afford **27** (528 mg, 80%) as a light-yellow solid. **Analytical data for 27: TLC** (20% ethyl acetate in hexanes), R_f = 0.35 (UV, CAM, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.90 (d, *J* = 8.7 Hz, 1H), 7.71 (d, *J* = 0.8 Hz, 1H), 7.57 (dd, *J* = 8.7, 1.6 Hz, 1H), 6.10 (d, *J* = 7.7 Hz, 1H), 6.10 – 5.88 (m, 2H), 5.80 (d, *J* = 16.7 Hz, 1H), 5.56 (d, *J* = 9.9 Hz, 1H), 5.48 (dq, *J* = 17.2, 1.4 Hz, 1H), 5.39 (dq, *J* = 10.4, 1.1 Hz, 1H), 4.81 (dt, *J* = 5.8, 1.3 Hz, 2H), 2.83 (q, *J* = 7.6 Hz, 2H), 2.66 (s, 3H), 1.31 (d, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 170.4, 153.0, 146.1, 145.7, 143.8, 134.0, 131.3, 131.0, 128.5, 126.7, 124.4, 122.3, 122.3, 122.1, 121.8, 120.1, 80.7, 69.8, 29.1, 15.4, 10.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2921 (*w*), 1746 (*vs*), 1610 (*w*), 1411 (*w*), 1356 (*w*), 1304 (*w*), 1232 (*s*), 1196 (*m*), 1147 (*m*), 1027 (*m*), 1013 (*m*), 972 (*m*), 938 (*m*), 924 (*m*), 886 (*m*), 840 (*m*), 778 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{21}H_{20}O_5$ $[M]^+$: 352.1305; found: 352.1309.

*3.10. 4-Allyl-8-ethyl-4-methyl-1-vinyl-1,4-dihydronaphtho[1,2-c]furan-3,5-dione (**28**)*

Tetrakis(triphenylphosphine)palladium(0) (32.8 mg, 0.0284 mmol, 0.100 equiv) was added to a Schlenk flask and the flask was purged with argon. Carbonate **27** (100 mg, 0.284 mmol, 1 equiv) was added and the flask was purged with argon. The reactants were dissolved in degassed toluene (7.5 mL) and degassed *n*-hexanes (0.75 mL) and stirred at 45 °C for 45 min. The reaction mixture was filtered through a plug of silica gel and rinsed thoroughly with diethyl ether (100 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to

obtain **28** (60 mg, 69%, mixture of diastereomers) as a yellow oil. *Note: A small sample of the diastereomeric mixture was used to separate the diastereomers by flash column chromatography on silica gel (5% ethyl acetate in hexanes).* **Analytical data for the major isomer 28: TLC** (20% ethyl acetate in hexanes), R_f = 0.29 (UV, $KMnO_4$). **^{1}H NMR** (800 MHz, $CDCl_3$) δ: 8.11 (d, *J* = 8.0 Hz, 1H), 7.43 (dd, *J* = 8.0, 1.7 Hz, 1H), 7.28 – 7.26 (m, 1H), 5.89 (ddd, *J* = 17.0, 10.0, 7.9 Hz, 1H), 5.77 (d, *J* = 8.4 Hz, 1H), 5.76 (d, *J* = 17.0 Hz, 1H), 5.57 (d, *J* = 10.0 Hz, 1H), 5.33 (dddd, *J* = 16.8, 10.1, 8.2, 6.6 Hz, 1H), 4.97 (dq, *J* = 16.9, 1.3 Hz, 1H), 4.80 (dd, *J* = 10.1, 1.9 Hz, 1H), 2.96 (dd, *J* = 13.5, 8.2 Hz, 1H), 2.81 (dd, *J* = 13.5, 6.5 Hz, 1H), 2.74 (qd, *J* = 7.5, 2.9 Hz, 2H), 1.53 (s, 3H), 1.28 (d, *J* = 7.6 Hz, 3H). **^{13}C NMR** (201 MHz, $CDCl_3$) δ: 200.8, 170.0, 153.0, 151.7, 133.5, 132.8, 132.4, 131.4, 130.7, 128.9, 128.3, 124.4, 122.5, 118.7, 80.5, 48.6, 42.6, 29.2, 23.1, 15.0. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2920 (*m*), 2363 (*w*), 1756 (*vs*), 1679 (*m*), 1600 (*m*), 1456 (*w*), 1378 (*w*), 1239 (*m*), 1015 (*m*), 853 (*w*), 797 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{20}H_{20}O_3$ $[M]^+$: 308.1407; found: 308.1410.

*3.11. Methyl 4-(((allyloxy)carbonyl)oxy)-1-chloro-7-ethyl-3-methyl-2-naphthoate (**S3**)*

To a solution of **15** (4.00 g, 14.4 mmol, 1 equiv) in tetrahydrofuran (72 mL) was added triethylamine (2.79 mL, 20.1 mmol, 1.40 equiv), the mixture was cooled to 0 °C and allyl chloroformate (1.83 mL, 17.2 mmol, 1.20 equiv) was added. After 10 min, saturated aqueous ammonium chloride solution (100 mL) was added, the layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with saturated aqueous hydrogen chloride solution (100 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The product **S3** (5.15 g, 99%) was obtained as an orange oil and used without further purification. **Analytical data for S3: TLC** (20% ethyl acetate in hexanes), R_f = 0.43 (UV, $KMnO_4$). **^{1}H NMR** (599 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 1.8 Hz, 1H), 7.79 (d, *J* = 8.5 Hz, 1H), 7.49 (dd, *J* = 8.7, 1.7 Hz, 1H), 6.24 – 5.78 (m, 1H), 5.46 (dq, *J* = 16.9, 1.5 Hz, 1H), 5.37 (dq, *J* = 10.6, 1.3 Hz, 1H), 4.88 – 4.59 (m, 2H), 4.01 (s, 3H), 2.85 (q, *J* = 7.6 Hz, 2H), 2.29 (s, 3H), 1.33 (t, *J* = 7.5 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 167.6, 152.9, 144.1, 143.8, 132.8, 131.1, 130.2, 129.9, 126.5, 126.2, 123.3, 123.1, 121.3, 120.0, 69.8, 52.9, 29.3, 15.6, 13.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2361 (*m*), 1764 (*m*), 1736 (*m*), 1437 (*w*), 1232 (*vs*), 940 (*w*), 668 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{19}H_{20}O_5{}^{35}Cl$ $[M]^+$: 362.0916; found: 362.0917.

*3.12. methyl 3-allyl-1-chloro-7-ethyl-3-methyl-4-oxo-3,4-dihydronaphthalene-2-carboxylate (**24**)*

Tetrakis(triphenylphosphine)palladium(0) (669 mg, 0.579 mmol, 7.00 mol%) was added to a Schlenk flask and the flask was purged with argon. **S3** (3.00 g, 8.27 mmol, 1 equiv) was added and the flask was purged with argon. Degassed toluene (219 mL) and degassed *n*-hexane (22 mL) were added and the solution was stirred at 45 °C for 15 h. The reaction mixture was filtered through a plug of silica gel and the plug was thoroughly rinsed with diethyl ether (200 mL). The filtrate was concentrated and the residue was purified by flash column chromatography on silica gel (2% ethyl acetate and 1% acetic acid in hexanes) to obtain **24** (2.1 g, 80%) as a light-yellow oil. **Analytical data for 24: TLC** (20% ethyl acetate in hexanes), R_f = 0.44 (UV, $KMnO_4$) **^{1}H NMR** (599 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 7.8 Hz, 1H), 7.67 (d, *J* = 1.6 Hz, 1H), 7.34 (dd, *J* = 8.2, 1.7 Hz, 1H), 5.74 – 5.32 (m, 1H), 4.99 (dt, *J* = 17.0, 1.6 Hz, 1H), 4.93 – 4.77 (m, 1H), 3.91 (s, 3H), 2.76 (p, *J* = 7.6 Hz, 3H), 2.52 (dd, *J* = 13.7, 6.5 Hz, 1H), 1.41 (s, 3H), 1.30 (t, *J* = 7.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 198.4, 166.4, 151.9, 137.9, 134.4, 132.2, 129.7, 127.7, 127.6, 127.5, 125.4, 118.8, 52.5, 52.3, 44.2, 29.3, 23.7, 15.0. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2970 (*w*), 1729 (*vs*), 1679 (*m*), 1598 (*m*), 1453 (*w*), 1434 (*m*), 1284 (*m*), 1248 (*m*), 1231 (*m*), 1195 (*m*), 1044 (*w*), 994 (*w*), 924 (*w*), 848 (*w*) 701 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{18}H_{19}O_3{}^{35}Cl$ $[M]^+$: 318.1017; found: 318.1016.

*3.13. Methyl (E)-1-chloro-7-ethyl-3-methyl-4-oxo-3-(prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**30**)*

To bis(dibenzylidenacetone)palladium(0) (113 mg, 0.0196 mmol, 10.0 mol%) was added a solution of **24** (625 mg, 1.96 mmol, 1 equiv) in degassed toluene (5.3 mL), tri-*t*-butylphosphine (1 M in toluene, 0.196 mL, 0.196 mmol, 10.0 mol%) and then isobutyryl chloride (0.078 M in degassed toluene, 2.51 mL, 0.196 mmol, 10.0 mol%). The reaction mixture was heated to 80 °C for 41 h, diluted with ethyl acetate (50 mL) and then concentrated. The residue was purified by flash column chromatography on silica gel (2% ethyl acetate and 1% acetic acid in hexanes) to afford **30** (523 mg, 84%) as a yellow oil. **Analytical data for 30:** *Note: The product* **30** *could not be separated from traces of remaining starting material* **24** *since both were co-polar during column chromatography.* **TLC** (20% ethyl acetate in hexanes), R_f = 0.56 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 7.9 Hz, 1H), 7.65 (d, *J* = 1.6 Hz, 1H), 7.33 (dd, *J* = 7.9, 1.6 Hz, 1H), 5.67 (dq, *J* = 15.6, 6.5 Hz, 1H), 5.43 (dq, *J* = 15.4, 1.6 Hz, 1H), 3.85 (s, 3H), 2.76 (q, *J* = 7.6 Hz, 2H), 1.65 (dd, *J* = 6.5, 1.6 Hz, 3H), 1.52 (s, 3H), 1.29 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 197.0, 166.4, 151.9, 137.8, 134.3, 129.8, 129.7, 128.4, 128.2, 127.3, 127.3, 125.6, 54.2, 52.4, 29.4, 21.5, 18.2, 15.2. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2967 (*w*), 1729 (*vs*), 1683 (*s*), 1598 (*s*), 1447 (*m*), 1433 (*m*), 1373 (*w*), 1270 (*vs*), 1230 (*s*), 1198 (*s*), 1121 (*m*), 1061 (*m*), 1043 (*s*), 983 (*m*), 958 (*s*), 846 (*m*), 806 (*m*), 698 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{18}H_{19}O_3{}^{35}Cl$ $[M]^+$: 318.1017; found: 318.1014.

*3.14. Methyl (E)-1-chloro-7-ethyl-3-methyl-4-methylene-3-(prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**31**)*

To a solution of methyltriphenylphosphonium bromide (1.03 g, 2.89 mmol, 2.00 equiv) in tetrahydrofuran (14 mL) was added potassium *tert*-butoxide (324 mg, 2.89 mmol, 2.00 equiv). After 1.5 h, the reaction mixture was cooled to 0 °C, a solution of **30** (460 mg, 1.44 mmol, 1 equiv) in tetrahydrofuran (9 mL) was added and the reaction mixture was allowed to warm to 23 °C. After 4 h, water (70 mL) was added, the layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 70 mL). The combined organic extracts were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes) to yield **31** (455 mg, 99%) as a yellow oil. **Analytical data for 31: TLC** (20% ethyl acetate in hexanes), R_f = 0.56 (UV, CAM, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.48 (d, *J* = 1.7 Hz, 1H), 7.45 (d, *J* = 7.8 Hz, 1H), 7.16 (dd, *J* = 7.9, 1.8 Hz, 1H), 5.67 – 5.56 (m, 2H), 5.44 (s, 1H), 5.18 (s, 1H), 3.80 (s, 3H), 2.68 (q, *J* = 7.6 Hz, 2H), 1.77 – 1.66 (m, 3H), 1.42 (s, 3H), 1.26 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 167.5, 148.3, 144.8, 136.8, 133.3, 132.2, 129.4, 128.8, 128.3, 125.8, 125.3, 124.7, 112.7, 52.1, 47.3, 28.9, 23.7, 18.2, 15.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2966 (*w*), 1755 (*vs*), 1602 (*w*), 1485 (*w*), 1432 (*m*), 1264 (*s*), 1235 (*s*), 1193 (*m*), 1154 (*m*), 1091 (*w*), 1043 (*m*), 962 (*m*), 898 (*m*), 836 (*m*), 737 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{19}H_{21}O_2{}^{35}Cl$ $[M]^+$: 316.1225; found: 316.1222.

*3.15. Methyl-1-chloro-7-ethyl-4-(methoxymethylene)-3-methyl-3-((E)-prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**S4**).*

To a suspension of (methoxymethyl)triphenylphosphonium chloride (1.19 g, 3.48 mmol, 3.70 equiv) in tetrahydrofuran (4.7 mL) was added *n*-butyllithium (2.36 M in hexanes, 1.24 mL, 2.92 mmol, 3.10 equiv) over 5 min at 0 °C. After the addition was completed, the reaction mixture was warmed to 23 °C, stirred at this temperature for 20 min and then cooled to 0 °C. A solution of **30** (300 mg, 0.941 mmol, 1 equiv) in tetrahydrofuran (4.7 mL) was added and the reaction mixture was warmed to 23 °C. After 2 h, saturated aqueous ammonium chloride solution (15 mL) was added and the layers were separated. The aqueous phase was extracted with ethyl acetate (3 × 20 mL) and the combined organic extracts were washed with saturated aqueous sodium chloride solution (15 mL). The washed organic solution was dried over sodium sulfate and the dried solution was filtered and concentrated. The residue was purified by flash column chromatography on silica gel (2% ethyl acetate in hexanes) to afford **S4** (265 mg, 81%, inconsequential 1:1 mixture of diastereomers) as a light-yellow oil. **Analytical data for S4:** *Note: Singals marked with an asterisk belong to the same diastereomer.* **TLC** (20% ethyl acetate in hexanes), R_f = 0.47 (UV, CAM). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.81 (d, *J* = 8.0 Hz, 1H)*, 7.48 (d, *J* = 1.9 Hz, 1H)*, 7.46 (d, *J* = 1.9 Hz, 1H), 7.20 (d, *J* = 7.9 Hz, 1H), 7.15 (dd, *J* = 8.0, 1.9 Hz, 1H)*, 7.07 (dd, *J* = 8.0, 1.9 Hz, 1H), 6.43 (s, 1H), 6.14 (s, 1H)*, 5.73 – 5.63 (m, 1H), 5.62 – 5.57 (m, 1H+1H*), 5.46 (dq, *J* = 15.4, 6.4 Hz, 1H), 3.80 (s, 3H), 3.78 (s, 3H)*, 3.70 (s, 3H)*, 3.66 (s, 3H), 2.64 (qd, *J* = 7.6, 5.4 Hz, 2H+2H*), 1.75 – 1.67 (m, 3H)*, 1.64 (dd, *J* = 6.4, 1.6 Hz, 3H), 1.54 (s, 3H), 1.38 (s, 3H)*, 1.24 (td, *J* = 7.6, 3.6 Hz, 3H+3H*). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 167.6, 167.5*, 146.8, 145.9*, 142.8, 142.7*, 136.6, 136.6*, 134.6, 133.3*, 131.8, 129.3*, 129.1, 128.9*, 128.7*, 128.7*, 128.5, 128.5*, 128.0, 125.9*, 124.9, 124.7*, 123.4, 123.0, 116.6, 116.4*, 60.8*, 60.7, 52.0, 52.0*, 45.6, 45.3*, 28.9, 28.7*, 24.0*, 23.0, 18.2*, 18.0, 15.6*, 15.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2965 (*m*), 1748 (*vs*), 1641 (*s*), 1432 (*m*), 1260 (*s*), 1239 (*s*), 1145 (*m*), 1103 (*m*), 1043 (*m*), 977 (*m*), 833 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{20}H_{23}O_3{}^{35}Cl$ $[M]^+$: 346.1330; found: 346.1330.

*3.16. Methyl (E)-1-chloro-7-ethyl-4-formyl-3-methyl-3-(prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**34**)*

To **S4** (265 mg, 0.764 mmol, 1 equiv) in diethyl ether (13 mL) was added perchloric acid (70% in water, 0.395 mL, 4.56 mmol, 6.00 equiv) and the reaction mixture was vigorously stirred for 19 h. The mixturw was diluted with diethyl ether (15 mL) and water (15 mL), and then sodium bicarbonate (400 mg) was carefully added. The layers were separated and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic extracts were washed with saturated sodium chloride solution (15 mL), dried over sodium sulfate and the dried solution was filtered and concentrated. The residue was purified by flash column chromatography on Davisil© (2% ethyl acetate in hexanes) to yield **34** (202 mg, 79%, inconsequential mixture of diastereomers) as a colorless oil. **Analytical data for 34:** *Note: The singals, which could be assigned to the major diastereomer, are marked with an asterisk.* **TLC** (20% ethyl acetate in hexanes), R_f = 0.47 (UV, CAM, $KMnO_4$). **^{1}H NMR** (599 MHz, C_6D_6) δ: 9.62 (d, *J* = 4.5 Hz, 1H), 9.54 (d, *J* = 4.5 Hz, 1H)*, 7.63 (d, *J* = 11.9 Hz, 1H+1H*), 6.88 – 6.63 (m, 2H+2H*), 5.77 – 5.59 (m, 1H), 5.51 (dqd, *J* = 15.3, 6.5, 2.4 Hz, 1H+1H*), 5.33 (dd, *J* = 15.6, 2.1 Hz, 1H*), 3.44 (app d, *J* = 4.06 Hz, 3H+3H*), 3.23 (d, *J* = 4.7 Hz, 1H)*, 3.18 (d, *J* = 4.9 Hz, 1H), 2.31 (dq, *J* = 19.5, 7.5 Hz, 2H+2H*), 1.41 (dd, *J* = 6.7, 1.6 Hz, 3H), 1.29 – 1.25 (m, 9H*), 0.99 (t, *J* = 7.7 Hz, 3H), 0.96 (t, *J* = 7.7 Hz, 3H)*. **^{13}C NMR** (151 MHz, C_6D_6) δ: 198.0, 197.6*, 166.7*, 145.2, 145.1*, 136.5, 135.1*, 133.3, 131.4, 131.1, 130.6, 130.1, 129.8, 129.3, 129.2, 128.6, 128.5, 125.9, 125.5, 63.0, 62.3*, 51.7*, 51.6, 43.8, 42.8*, 28.9, 28.8*, 23.0, 21.6*, 18.1, 17.9*, 15.5, 15.4*. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2967 (*w*), 1724 (*vs*), 1603 (*w*), 1434 (*w*), 1266 (*s*), 1203 (*w*), 1046 (*w*), 964 (*w*), 834 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{19}H_{21}O_3{}^{35}Cl$ $[M]^+$: 332.1174; found: 332.1155.

*3.17. methyl (E)-1-chloro-7-ethyl-4-formyl-3,4-dimethyl-3-(prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**35**)*

To sodium hydride (60% dispersion in mineral oil, 32.9 mg, 0.823 mmol, 2.00 equiv) was added a degassed solution of **34** (137 mg, 0.412 mmol, 1 equiv) and methyl iodide (0.256 mL, 4.12 mmol, 10.0 equiv) in tetrahydrofuran (5.9 mL) at 0 °C. The solution was allowed to warm to 23 °C and after 5.5 h, saturated aqueous ammonium chloride solution (10 mL) was added. The layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (toluene) to obtain **35** (98 mg, 69%) as a light-yellow oil. **Analytical data for 35: TLC** (20% ethyl acetate in hexanes), R_f = 0.45 (UV, CAM, $KMnO_4$). **^{1}H NMR** (800 MHz, C_6D_6) δ: 9.82 (s, 1H), 7.68 (d, *J* = 1.9 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 6.83 (dd, *J* = 7.9, 1.9 Hz, 1H), 5.50 – 5.30 (m, 2H), 3.43 (s, 3H), 2.33 (q, *J* = 7.6 Hz, 2H), 1.35 (s, 3H), 1.34 – 1.30 (m, 3H), 1.24 (s, 3H), 1.00 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (201 MHz, C_6D_6) δ: 199.8, 166.7, 144.5, 141.5, 136.1, 133.2, 131.1, 130.3, 129.9, 127.3, 127.1, 125.9, 56.2, 51.6, 46.2, 28.7, 18.1, 18.0, 15.4, 14.0. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2969 (*w*), 2362 (*w*), 1731 (*vs*), 1605 (*w*), 1434 (*w*), 1373 (*w*), 1268 (*m*), 1154 (*w*), 1102 (*w*), 1042 (*w*), 968 (*w*), 890 (*w*), 816 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{20}H_{23}O_3{}^{35}Cl$ $[M]^+$: 346.1330; found: 346.1341.

*3.18. methyl (E)-1-chloro-7-ethyl-4-(hydroxymethyl)-3,4-dimethyl-3-(prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**36**)*

To a solution of **35** (15.0 mg, 0.0432 mmol, 1 equiv) in methanol (0.4 mL) was added sodium borohydride (2.45 mg, 0.0649 mmol, 1.50 equiv) at 0 °C. After 25 min, saturated aqueous ammonium chloride solution (10 mL) was added. The layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (11% ethyl acetate in hexanes) to obtain **I.143** (12 mg, 80%, major isomer) as a colorless oil. **Analytical data for 36:** *Note: Signals in the ^{13}C NMR which could only be assigned by cross-coupling in the HMBC are marked with an asterisk. The relative stereochemistry was assigned by NOE correlations of* **36**: **TLC** (20% ethyl acetate in hexanes), R_f = 0.21 (UV, CAM, ANIS, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.53 (d, *J* = 1.7 Hz, 1H), 7.23 (d, *J* = 7.9 Hz, 1H), 7.18 (dd, *J* = 7.9, 1.9 Hz, 1H), 5.50 (dt, *J* = 18.0, 6.4 Hz, 1H), 5.34 (d, *J* = 15.6 Hz, 1H), 3.90 (dd, *J* = 10.9, 3.9 Hz, 1H), 3.82 (s, 3H), 3.51 (t, *J* = 9.8 Hz, 1H), 2.67 (q, *J* = 7.6 Hz, 2H), 1.60 (dd, *J* = 6.3, 1.5 Hz, 3H), 1.30 (s, 3H), 1.26 (t, *J* = 7.6 Hz, 3H), 1.21 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 167.6, 143.3, 135.9, 131.0, 129.9, 129.2, 127.9*, 127.4*, 126.0, 125.4, 66.0, 52.2, 46.5, 45.8, 29.9, 28.6, 18.3, 16.4*, 16.4, 15.5. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3430 (*w*), 2964 (*m*), 1731 (*vs*), 1629 (*w*), 1607 (*w*), 1433 (*m*), 1375 (*w*), 1268 (*vs*), 1196 (*w*), 1151 (*m*), 1040 (*s*), 968 (*m*), 890 (*w*), 833 (*w*), 723 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{20}H_{25}O_3{}^{35}Cl$ $[M]^+$: 348.1487; found: 348.1492.

*3.19. methyl (E)-1-chloro-7-ethyl-3,4-dimethyl-3-(prop-1-en-1-yl)-4-((tosyloxy)methyl)-3,4-dihydronaphthalene-2-carboxylate (**37**)*

To **36** (14.0 mg, 0.0401 mmol, 1 equiv) and *p*-toluene-sulfonyl chloride (23.0 mg, 0.120 mmol, 3.00 equiv) was added pyridine (0.3 mL). After stirring for 48 h, the reaction mixture was diluted with saturated aqueous ammonium chloride solution (15 mL), the layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (14% ethyl acetate in hexanes) to afford **37** (14.8 mg, 73%) as a colorless oil. **Analytical data for 37:** *Note: Due to severe signal broadening in the NMR spectra some signals are missing or possess inaccurate integrals. Signals in the ^{13}C NMR which could only be assigned by cross-coupling in the HMBC are marked with an asterisk.* **TLC** (20% ethyl acetate in hexanes), R_f = 0.31 (UV, ANIS, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.29 (s, 1H), 7.21 – 7.10 (m, 4H), 5.44 (dq, *J* = 15.4, 6.4 Hz, 1H), 5.20 (s, 1H), 4.08 (s, 2H), 3.77 (s, 3H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.41 (s, 3H), 1.55 (d, *J* = 4.9 Hz, 3H), 1.27 (t, *J* = 7.6 Hz, 6H), 1.16 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 167.2, 144.5, 143.3, 135.1*, 132.2, 129.8, 129.3, 129.1, 128.1, 127.8, 125.0, 72.6, 52.1, 46.6*, 44.1, 29.9*, 28.6, 21.8, 18.2, 16.7, 15.5. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2965 (*w*), 1729 (*s*), 1628 (*w*), 1451 (*w*), 1434 (*w*), 1361 (*m*), 1269 (*m*), 1189 (*s*), 1176 (*vs*), 1097 (*m*), 1041 (*m*), 979 (*s*), 912 (*m*), 830 (*s*), 813 (*s*), 731 (*m*), 666 (*s*) cm^{-1}. **HRMS** (EI) calcd for $C_{27}H_{31}O_5{}^{35}ClS$ $[M]^+$: 502.1575; found: 502.1574.

*3.20. methyl (E)-1-chloro-7-ethyl-3,4-dimethyl-4-((((methylthio)carbonothioyl)oxy)methyl)-3-(prop-1-en-1-yl)-3,4-dihydronaphthalene-2-carboxylate (**38**)*

To a solution of **36** (12.0 mg, 0.0344 mmol, 1 equiv) in tetrahydrofuran (0.26 mL) was added sodium bis(trimethylsilyl)amide (1 M in tetrahydrofuran, 0.172 mL, 0.172 mmol, 5.00 equiv) at −78 °C. After 30 min, carbon disulfide (0.0415 mL, 0.688 mmol, 20.0 equiv) was added and the reaction was allowed to warm to −65 °C. After 30 min, methyl iodide (0.0428 mL, 0.688 mmol, 20.0 equiv) was added and the reaction mixture was stirred for 75 min. Saturated aqueous ammonium chloride solution (15 mL) was added, the layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 20 mL). The combined organic extracts were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to obtain **38** (12.6 mg, 83%) as a colorless oil. **Analytical data for 38:** *Note: Due to severe signal broadening in the NMR spectra some signals are missing or possess inaccurate integrals. Signals in the ^{13}C NMR which could only be assigned by cross-coupling in the HMBC are marked with an asterisk.* **TLC** (20% ethyl acetate in hexanes), R_f = 0.50 (UV, ANIS, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.58 – 7.44 (m, 1H), 7.18 (d, *J* = 1.2 Hz, 2H), 5.64 – 5.37 (m, 2H), 4.75 (s, 2H), 3.81 (s, 3H), 2.67 (q, *J* = 7.8 Hz, 2H), 2.45 (s, 3H), 1.65 (d, *J* = 6.1 Hz, 3H), 1.36 (s, 3H), 1.31 – 1.18 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 215.5, 167.4, 143.4, 137.3*, 135.8*, 130.2, 129.7, 129.5, 128.2, 125.3, 77.0*, 52.1, 47.2*, 44.7, 28.6, 18.9, 18.4, 17.2, 15.5, 10.6*. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2964 (*w*), 1730 (*vs*), 1607 (*w*), 1488 (*w*), 1449 (*w*), 1432 (*m*), 1375 (*w*), 1268 (*s*), 1253 (*s*), 1209 (*s*), 1153 (*m*), 1067 (*vs*), 1041 (*m*), 967 (*m*), 911 (*w*), 832 (*w*), 731 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{22}H_{27}O_3{}^{35}ClS_2$ $[M]^+$: 438.1085; found: 438.1077.

*3.21. 10-Chloro-8-ethyl-3,5,5-trimethyl-3,5,9,9a-tetrahydro-1H-benzo[g]isochromen-1-one (**42**)*

To titanium(IV) chloride (1 M in dichloromethane, 0.941 mL, 0.941 mmol, 6.00 equiv) in a Schlenk tube, which was wrapped in aluminum foil, was added dimethylzinc (15wt% in toluene, 0.784 mL, 0.941 mmol, 6.00 equiv) over 5 min at 0 °C. After 25 min, a solution of **30** (50.0 mg, 0.157 mmol, 1 equiv) in dichloromethane (1.6 mL) was added over 5 min. The reaction mixture was stirred for 8 h at 0 °C before saturated aqueous ammonium chloride solution (10 mL) was added. The layers were separated and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was purified by flash column chromatography on silica gel (2% ethyl acetate and 1% acetic acid in hexanes) to yield **42** (29 mg, 61%) as a light-yellow oil. **Analytical data for 42: TLC** (20% ethyl acetate in hexanes), R_f = 0.23 (UV, CAM, $KMnO_4$). **^{1}H NMR** (599 MHz, $CDCl_3$) δ: 7.85 (d, *J* = 1.9 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.24 (dd, *J* = 8.0, 1.9 Hz, 1H), 5.94 (d, *J* = 2.9 Hz, 1H), 5.03 (qd, *J* = 6.8, 3.2 Hz, 1H), 2.69 (q, *J* = 7.7 Hz, 2H), 1.48 (s, 3H), 1.47 (d, *J* = 7.0 Hz, 3H), 1.43 (s, 3H), 1.26 (t, *J* = 7.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 163.6, 143.1, 143.0, 142.6, 136.8, 130.7, 130.2, 127.6, 123.8, 123.3, 117.9, 74.5, 38.3, 28.9, 28.6, 27.2, 22.1, 15.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2967 (*m*), 1729 (vs), 1556 (*m*), 1463 (*m*), 1379 (*m*), 1379 (*m*), 1286 (*m*), 1210 (*m*), 1159 (*m*), 895 (*w*), 835 (*w*), 835 (*w*), 786 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{18}H_{19}O_2{}^{35}Cl$ $[M]^+$: 302.7975; found: 302.1071.

*3.22. 7-methoxy-4-methyl-1,2-dihydronaphthalene (**44**)*

To 6-methoxy-3,4-dihydronaphthalen-1(2H)-one (**43**) (10.0 g, 56.7 mmol, 1 equiv) in tetrahydrofuran (100 mL) was added methylmagnesium bromide solution (3 M in diethyl ether, 28.4 mL, 85.1 mmol, 1.50 equiv) at 0 °C. The ice bath was removed after the addition and the reaction mixture was stirred for 17 h. The mixture was cooled to 0 °C and aqueous hydrochloric acid solution (2 M, 200 mL) was added until pH=2. The reaction was stirred for 5 h, diluted with water (100 mL) and the layers were separated. The aqueous phase was extracted with diethyl ether (3 × 200 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution (200 mL), the washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The residue was used without further purification. An analytical pure sample of **44** was obtained by flash column chromatography on silica gel (2% ethyl acetate in hexanes). **Analytical data for 44: TLC** (20% ethyl acetate in hexanes), R_f = 0.63 ($KMnO_4$, ANIS). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.16 (d, *J* = 8.2 Hz, 1H), 6.88 – 6.62 (m, 2H), 5.73 (ddd, *J* = 6.0, 3.8, 1.6 Hz, 1H), 3.81 (s, 3H), 2.75 (t, *J* = 8.0 Hz, 2H), 2.29 – 2.16 (m, 2H), 2.03 (q, *J* = 1.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 158.5, 138.3, 131.9, 129.2, 124.0, 123.0, 113.7, 110.9, 55.4, 29.0, 23.3, 19.5. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2932 (*w*), 1605 (*m*), 1496 (*s*), 1427 (*m*), 1302 (*m*), 1249 (*vs*), 1141 (*s*), 1032 (*s*), 867 (*m*), 819 (*s*), 674 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{12}H_{14}O$ $[M]^+$: 174.1039; found: 174.1041.

*3.23. 6-methoxy-1-methyl-3,4-dihydronaphthalen-2(1H)-one (**45**)*

To a solution of crude **44** in dichloromethane (283 mL) and 2,2,2-trifluoroethanol (71 mL) were added 3-chloro-peroxybenzoic acid (75% in water, 16.3 g, 70.9 mmol, 1.25 equiv) and *p*-toluenesulfonic acid monohydrate (13.5 g, 70.9 mmol, 1.25 equiv) subsequently at 0 °C. After stirring for 20 min, saturated aqueous sodium bicarbonate solution (200 mL) and dichloromethane (200 mL) were added, the layers were separated and the aqueous layer was extracted with

dichloromethane (3 × 200 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (6% ethyl acetate in hexanes) to obtain **45** (4.76 g, 44% over 2 steps) as a yellow oil. **Analytical data for 45: TLC** (20% ethyl acetate in hexanes), R_f = 0.45 ($KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.11 (d, *J* = 8.3 Hz, 1H), 6.83 – 6.76 (m, 2H), 3.81 (s, 3H), 3.47 (qd, *J* = 6.9, 0.9 Hz, 1H), 3.15 – 2.91 (m, 2H), 2.62 (dt, *J* = 17.5, 5.9 Hz, 1H), 2.48 (ddd, *J* = 17.5, 9.0, 6.1 Hz, 1H), 1.45 (d, *J* = 7.0 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 212.5, 158.5, 138.1, 130.1, 127.3, 113.3, 112.3, 55.4, 46.8, 37.3, 28.4, 14.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2937 (*w*), 1713 (*vs*), 1610 (*m*), 1579 (*w*), 1497 (*s*), 1454 (*m*), 1261 (*s*), 1160 (*m*), 1037 (*m*), 864 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{12}H_{14}O_2$ $[M]^+$: 190.0988; found: 190.0994.

*3.24. 6-methoxy-1,1-dimethyl-3,4-dihydronaphthalen-2(1H)-one (**46**)*

To a suspension of freshly washed potassium hydride (4.55 g, 114 mmol, 1.20 equiv) in degassed tetrahydrofuran (40 mL) was added a degassed solution of **45** (18.0 g, 94.6 mmol, 1 equiv) in tetrahydrofuran (500 mL) over 25 min at 0 °C. After 20 min, the ice bath was removed and the reaction mixture was stirred at 23 °C. After 1 h, the mixture was cooled to 0 °C, methyl iodide (11.8 mL, 189 mmol, 2.00 equiv) was added and the ice bath was removed after the addition. After 25 min at 23 °C, the mixture was again cooled to 0 °C, saturated aqueous ammonium chloride solution (200 mL) and ethyl acetate (100 mL) were added, the layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 200 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (6% ethyl acetate in hexanes) to afford **46** (13.6 g, 71%) as a yellow oil. **Analytical data for 46: TLC** (20% ethyl acetate in hexanes), R_f = 0.39 ($KMnO_4$, ANIS, UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.29 (s, 1H), 6.84 (ddd, *J* = 8.7, 2.8, 0.7 Hz, 1H), 6.73 (d, *J* = 2.6 Hz, 1H), 3.83 (s, 3H), 3.09 (t, *J* = 6.9 Hz, 2H), 2.79 – 2.63 (m, 2H), 1.44 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 215.0, 158.1, 136.6, 135.8, 127.4, 113.3, 112.9, 55.4, 47.4, 37.3, 28.9, 27.2 (2C). **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2968 (*w*), 1709 (*vs*), 1609 (*m*), 1500 (*s*), 1464 (*m*), 1307 (*m*), 1265 (*s*), 1228 (*m*), 1138 (*m*), 1035 (*s*), 814 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{13}H_{16}O_2$ $[M]^+$: 204.1145; found: 204.1133.

*3.25. 6-methoxy-1,1,2-trimethyl-1,2,3,4-tetrahydronaphthalen-2-ol (**47**)*

To a solution of **46** (2.74 g, 13.4 mmol, 1 equiv) in tetrahydrofuran (13 mL) was added lanthanum(III) chloride bis(lithium chloride) complex solution (0.3 M in tetrahydrofuran, 44.7 mL, 13.4 mmol, 1 equiv). After 1 h, the solution was cooled to 0 °C and methylmagnesium bromide solution (3 M in diethyl ether, 6.71 mL, 20.1 mmol, 1.50 equiv) was added dropwise over 20 min (syringe pump). After 20 min, saturated aqueous ammonium chloride solution (50 mL) and diethyl ether (50 mL) were added, the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (20 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (14% ethyl acetate in hexanes) to obtain **47** (2.83 g, 96%) as a colorless oil. **Analytical data for 47: TLC** (20% ethyl acetate in hexanes), R_f = 0.23 (ANIS). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.27 (d, *J* = 8.7 Hz, 1H), 6.75 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.60 (d, *J* = 2.7 Hz, 1H), 3.78 (s, 3H), 2.98 (dt, *J* = 17.6, 7.1 Hz, 1H), 2.81 (dt, *J* = 17.5, 6.8 Hz, 1H), 2.04 – 1.79 (m, 2H), 1.32 (s, 3H), 1.27 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 157.4, 137.4, 135.5, 128.1, 113.0, 112.8, 73.7, 55.3, 41.5, 32.8, 27.1, 27.0, 25.4, 24.3. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3470 (*w*), 2969 (*m*), 1608 (*m*), 1499 (*vs*), 1464 (*m*), 1373 (*w*), 1315 (*m*), 1237 (*s*), 1084 (*m*), 1037 (*s*), 911 (*m*), 818 (*s*) cm^{-1}. **HRMS** (EI) calcd for $C_{14}H_{20}O_2$ $[M]^+$: 220.1458; found: 220.1452.

*3.26. 3-hydroxy-7-methoxy-3,4,4-trimethyl-3,4-dihydronaphthalen-1(2H)-one (**48**)*

To a solution of **47** (843 mg, 3.83 mmol, 1 equiv) in dry acetone (7.7 mL) was added cobalt(II) acetylacetonate (197 mg, 0.765 mmol, 0.200 equiv). To the resulting purple suspension was added dropwise *tert*-butyl hydroperoxide (5.5 M in decane, 2.78 mL, 15.3 mmol, 4.00 equiv). After 2 d, saturated aqueous ammonium chloride solution (20 mL) and ethyl acetate (20 mL) were added. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (20 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (25% ethyl acetate in hexanes) to afford **48** (854 mg, 95%) as a green oil. **TLC** (20% ethyl acetate in hexanes), Rf = 0.056 (ANIS, UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.50 (d, *J* = 3.0 Hz, 1H), 7.41 (d, *J* = 8.7 Hz, 1H), 7.14 (dd, *J* = 8.7, 3.0 Hz, 1H), 3.84 (s, 3H), 2.89 (s, 2H), 1.44 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 196.8, 158.2, 143.5, 131.8, 127.8, 122.6, 109.1, 75.7, 55.7, 55.6, 50.0, 42.5, 24.7, 24.6. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3483 (*m*), 2975 (*m*), 1677 (*vs*), 1608 (*s*), 1493 (*s*), 1418 (*m*), 1325 (*s*), 1291 (*vs*), 1262 (*s*), 1087 (*m*), 1032 (*s*), 883 (*w*), 830 (*w*), 705 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{14}H_{18}O_3$ $[M]^+$: 234.1250; found: 234.1249.

*3.27. 7-methoxy-3,4,4-trimethylnaphthalen-1(4H)-one (**49**)*

A mixture of **48** (270 mg, 1.15 mmol, 1 equiv) in acetic acid (11.5 mL) and sulfuric acid (97%, 30 µL) was heated to 100 °C for 10 min. After cooling to 23 °C, the reaction mixture was diluted with water (30 mL) and dichloromethane (50 mL). Sodium bicarbonate was slowly added until pH=7. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (25% ethyl acetate in hexanes) to obtain **49** (220 mg, 88%) as a yellow solid. **Analytical data for 49: TLC** (60% ethyl acetate in hexanes), R_f = 0.50 ($KMnO_4$, UV). **^{1}H NMR** (800 MHz, $CDCl_3$) δ: 7.63 (d, *J* = 3.0 Hz, 1H), 7.50 (d, *J* = 8.8 Hz, 1H), 7.16 (dd, *J* = 8.7, 3.0 Hz, 1H), 6.32 (q, *J* = 1.3 Hz, 1H), 3.88 (s, 3H), 2.14 (d, *J* = 1.3 Hz, 3H), 1.48 (s, 6H). **^{13}C NMR** (201 MHz, $CDCl_3$) δ: 184.5, 165.9, 158.2, 144.1, 131.7, 127.9, 126.6, 121.4, 107.6, 55.7, 40.3, 28.7 (2C), 20.3. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2975 (*w*), 1657 (*vs*), 1608 (*m*), 1497 (*s*), 1425 (*s*), 1296 (*s*), 1230 (*w*), 1032 (*w*), 870 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{14}H_{16}O_2$ $[M]^+$: 216.1145; found: 216.1145.

*3.28. 5,5,6-trimethyl-8-oxo-5,8-dihydronaphthalen-2-yl trifluoromethanesulfonate (**51**)*

To a solution of **49** (200 mg, 0.925 mmol, 1 equiv) in dichloromethane (4.6 mL) was added dropwise boron tribromide (1 M, in dichloromethane, 4.62 mL, 4.62 mmol, 5 equiv) at

−78 °C. The reaction mixture was allowed to warm to 0 °C over 2 h and methanol (3 mL) was added dropwise. Water (40 mL) was added, the layers were separated and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product **50** was used in the next step without further purification. To a solution of crude **50** in dichloromethane (4.6 mL) was added triethylamine at −78 °C and the mixture was stirred for 5 min before trifluoromethanesulfonic anhydride (0.230 mL, 1.39 mmol, 1.50 equiv) was added over 10 min. The reaction was allowed to warm to 23 °C over 3 h and saturated aqueous sodium bicarbonate solution (15 mL) and dichloromethane (20 mL) were added. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (14% ethyl acetate in hexanes) to afford **51** (302 mg, 98% over 2 steps) as a yellow solid. **Analytical data for 41: TLC** (33% ethyl acetate in hexanes), R_f = 0.26 ($KMnO_4$, UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 8.05 (d, *J* = 2.9 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.47 (dd, *J* = 8.8, 2.9 Hz, 1H), 6.36 (t, *J* = 1.3 Hz, 1H), 2.17 (d, *J* = 1.3 Hz, 3H), 1.53 (s, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 182.5, 166.2, 151.1, 148.4, 132.8, 129.2, 126.4, 125.3, 118.9 (q, *J* = 320.3 Hz) 118.8, 40.7, 28.7 (2C), 20.5. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2980 (*w*), 1660 (*s*), 1579 (*w*), 1486 (*w*), 1421 (*s*), 1314 (*m*), 1290 (*m*), 1204 (*vs*), 1137 (*vs*), 1109 (*m*), 918 (*vs*), 875 (*m*), 841 (*s*), 811 (*s*), 767 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{14}H_{13}O_4F_3S$ $[M]^+$: 334.0481; found: 334.0490.

*3.29. 7-ethyl-3,4,4-trimethylnaphthalen-1(4H)-one (**52**)*

Note: The reaction setup has to be flame-dried very carefully, since the yield otherwise decreases significantly. To [1,1'-bis(diphenylphosphino)ferrocene]palladium(II) dichloride (41.1 mg, 0.0562 mmol, 0.0180 equiv) was added a solution of **51** (1.04 g, 3.12 mmol, 1 equiv) in 1,4-dioxane (2.6 mL). The red suspension was cooled to 0 °C and diethylzinc solution (15wt% in toluene, 4.27 mL, 6.25 mmol, 2.00 equiv) was added dropwise. After stirring for 10 min, the yellow solution was heated to 90 °C for 70 min, cooled to 0 °C and treated with methanol (5 mL). Water (15 mL) was added, the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with aqueous hydrogen chloride solution (2 M, 20 mL) and saturated aqueous sodium chloride solution (20 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (17% ethyl acetate in hexanes) to obtain **52** (590 mg, 88%) as a yellow oil. **TLC** (20% ethyl acetate in hexanes), R_f = 0.35 ($KMnO_4$, UV). **^{1}H NMR** (599 MHz, $CDCl_3$) δ: 8.01 (d, *J* = 2.1 Hz, 1H), 7.50 (d, *J* = 8.2 Hz, 1H), 7.42 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.32 (d, *J* = 1.5 Hz, 1H), 2.71 (q, *J* = 7.6 Hz, 2H), 2.13 (d, *J* = 1.1 Hz, 3H), 1.49 (s, 6H), 1.27 (t, *J* = 7.7 Hz, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 184.9, 165.6, 148.8, 142.6, 132.5, 130.4, 126.8, 126.5, 125.2, 40.4, 28.7, 28.5, 20.3, 15.5. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2971 (*m*), 2873 (*w*), 1657 (*vs*), 1610 (*m*), 1462 (*w*), 1427 (*m*), 1307 (*m*), 1270 (*w*), 1117 (*w*), 1011 (*w*), 876 (*m*), 837 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{15}H_{18}O_2$ $[M]^+$: 214.1352; found: 214.1351.

*3.30. 3-allyl-7-ethyl-3,4,4-trimethyl-3,4-dihydronaphthalen-1(2H)-one (**54**)*

To a solution of **52** (590 mg, 2.75 mmol, 1 equiv) in tetrahydrofuran (5.5 mL) was added dropwise allylmagnesium bromide solution (1 M in diethyl ether, 4.13 mL, 4.13 mmol, 1.50 equiv) at 0 °C. After 1 h, the mixture was cooled to 0 °C and saturated aqueous sodium bicarbonate solution (10 mL) and dichloromethane (10 mL) were added. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 15 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product **53** was used without further purification. A mixture of 18-crown-6 (1.45 g, 5.50 mmol, 2.00 equiv) and potassium *tert*-butoxide (617 mg, 5.50 mmol, 2.00 equiv) in tetrahydrofuran (46 mL) was stirred at 0 °C for 1 h. A solution of crude **53** in tetrahydrofuran (10 mL) was added over 10 min and after complete addition, the reaction mixture was allowed to warm to 23 °C. After 2 h, saturated aqueous sodium bicarbonate solution (40 mL) and dichloromethane (40 mL) were added. The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 40 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (2% ethyl acetate in hexanes) to obtain **54** (270 mg, 38% over 2 steps) as a yellow oil. **Analytical data for 54: TLC** (20% ethyl acetate in hexanes), R_f = 0.59 ($KMnO_4$, UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.84 (s, 1H), 7.38 (s, 2H), 5.78 (ddt, *J* = 15.0, 10.1, 7.5 Hz, 1H), 5.08 (dd, *J* = 10.1, 2.0 Hz, 1H), 4.98 (d, *J* = 17.0 Hz, 1H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.60 (s, 2H), 2.17 – 2.13 (m, 2H), 1.35 (s, 3H), 1.34 (s, 3H), 1.25 (t, *J* = 7.6 Hz, 3H), 0.99 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 198.4, 149.9, 142.1, 134.5, 134.2, 131.3, 126.4, 125.7, 118.6, 46.1, 41.2, 40.9, 40.4, 28.3, 20.9, 15.4. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2969 (*s*), 1683 (*vs*), 1639 (*w*), 1611 (*m*), 1456 (*m*), 1376 (*m*), 1296 (*m*), 1263 (*m*), 1093 (*m*), 999 (*m*), 913 (*m*), 835 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{18}H_{24}O$ $[M]^+$: 256.1822; found: 256.1820.

*3.31. (E)-7-ethyl-3,4,4-trimethyl-3-(prop-1-en-1-yl)-3,4-dihydronaphthalen-1(2H)-one (**55**)*

To bis(dibenzylidenacetone)palladium(0) (66.1 mg, 0.115 mmol, 10.0 mol%) was added subsequently a solution of **54** (295 mg, 1.15 mmol, 1 equiv) in degassed toluene (3.3 mL), tri-*t*-butylphosphine (1 M in toluene, 0.115 mL, 0.115 mmol, 10.0 mol%) and isobutyryl chloride (0.078 M in degassed toluene, 1.47 mL, 0.115 mmol, 10.0 mol%). The reaction mixture was heated to 80 °C for 2 d, diluted afterwards with ethyl acetate (30 mL) and concentrated. The residue was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes) to afford **55** (272 mg, 92%) as a yellow oil. **Analytical data for 55: TLC** (20% ethyl acetate in hexanes), R_f = 0.58 ($KMnO_4$, UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.86 (d, *J* = 1.9 Hz, 1H), 7.40 – 7.33 (m, 2H), 5.61 (d, *J* = 15.7 Hz, 1H), 5.47 (dq, *J* = 15.6, 6.2 Hz, 1H), 2.83 (d, *J* = 17.3 Hz, 1H), 2.66 (q, *J* = 7.6 Hz, 2H), 2.53 (d, *J* = 17.4 Hz, 1H), 1.67 (d, *J* = 6.2 Hz, 3H), 1.33 (s, 3H), 1.28 (s, 3H), 1.24 (t, *J* = 7.6 Hz, 3H), 1.06 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 198.6, 149.7, 142.0, 135.9, 134.1, 130.9, 126.4, 125.8, 124.5, 48.1, 43.5, 40.6, 28.3, 26.8, 24.5, 21.7, 18.5, 15.4. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2968 (*m*), 2936 (*w*), 1683 (*vs*), 1611 (*w*), 1491 (*w*), 1452 (*w*), 1376 (*w*), 1290 (*w*), 1264 (*w*), 1096 (*w*), 975 (*w*), 834 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{18}H_{24}O$ $[M]^+$: 256.1822; found: 256.1821.

*3.32. (6-methoxy-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methanol (**58a**)*

To a solution of **48** (870 mg, 4.02 mmol, 1 equiv) in methanol (34 mL) were added cerium(III) chloride heptahydrate (1.65 g, 4.42 mmol, 1.10 equiv) and sodium borohydride (228 mg, 6.03 mmol, 1.50 equiv) respectively at 0 °C. After 1 h, the mixture was diluted with pH7 buffer solution (20 mL) and dichloromethane (20 mL). The layers were separated and the

aqueous layer was extracted with dichloromethane (3 × 20 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was used immediately without further purification. *Note: The product is very sensitive toward acidic conditions. Therefore, it was used immediately in the next step.* To washed potassium hydride (242 mg, 6.03 mmol, 1.50 equiv) was added a solution of the crude alcohol in tetrahydrofuran (60 mL) at 0 °C. After 10 min, a solution of tributyl(iodomethyl)stannane (1.91 g, 4.42 mmol, 1.10 equiv) in tetrahydrofuran (15 mL) was added. After 105 min, the mixture was diluted with pH7 buffer solution (30 mL) and dichloromethane (30 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product **57** was used immediately without further purification. To a solution of crude **57** in tetrahydrofuran (80 mL) was added *n*-butyllithium (2.51 M in hexanes, 2.08 mL, 5.23 mmol, 1.30 equiv) dropwise over 5 min at −78 °C. The reaction was allowed to warm to −45 °C over 2 h and was diluted with saturated aqueous ammonium chloride solution (30 mL) and water (20 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 40 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (17% ethyl acetate in hexanes) to obtain **58a** (450 mg, 48% over three steps) as a yellow oil. **Analytical data for 58a: TLC** (25% ethyl acetate in hexanes), R_f = 0.26 ($KMnO_4$, CAM, UV). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.18 (d, *J* = 8.5 Hz, 1H), 6.73 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.59 (d, *J* = 2.8 Hz, 1H), 6.46 (d, *J* = 9.6 Hz, 1H), 5.68 (d, *J* = 9.6 Hz, 1H), 3.79 (s, 3H), 3.62 (d, *J* = 10.8 Hz, 1H), 3.39 (d, *J* = 10.8 Hz, 1H), 1.29 (s, 4H), 1.13 (s, 3H), 1.09 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 157.9, 137.3, 135.5, 133.3, 127.3, 125.2, 112.9, 112.2, 67.8, 55.3, 43.0, 38.6, 25.8, 21.6, 17.7. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3409 (*m*), 2969 (*m*), 2877 (*w*), 1746 (*w*), 1602 (*m*), 1490 (*m*), 1309 (*m*), 1259 (*vs*), 1154 (*w*), 1035 (*vs*), 777 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{15}H_{20}O_2$ $[M]^+$: 232.1458; found: 232.1458.

*3.33. 6-Methoxy-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methyl acetate (**61a**)*

To a solution of **58a** (10.0 mg, 0.0430 mmol, 1 equiv) in dichloromethane (0.43 mL) were added triethylamine (17.9 µL, 0.129 mmol, 3.00 equiv), acetic anhydride (10.5 µl, 0.112 mmol, 2.60 equiv) and 4-dimethylaminopyridine (0.526 mg, 0.00430 mmol, 0.100 equiv) at 0 °C. After 30 min, the reaction mixture was diluted with saturated aqueous sodium bicarbonate solution (10 mL), the layers were separated and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to afford **61a** (10.2 mg, 86%) as a colorless oil. **Analytical data for 61a: TLC** (20% ethyl acetate in hexanes), R_f = 0.31 (UV, CAM).**^{1}H NMR** (599 MHz, $CDCl_3$) δ: 7.18 (d, *J* = 8.3 Hz, 1H), 6.72 (dd, *J* = 8.3, 2.8 Hz, 1H), 6.58 (d, *J* = 2.7 Hz, 1H), 6.39 (d, *J* = 9.7 Hz, 1H), 5.67 (d, *J* = 9.5 Hz, 1H), 4.01 (q, *J* = 10.7 Hz, 2H), 3.78 (s, 3H), 1.94 (s, 3H), 1.27 (s, 3H), 1.18 (s, 3H), 1.07 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 171.4, 158.0, 136.8, 135.1, 133.2, 126.7, 125.2, 112.8, 112.2, 68.6, 55.4, 41.4, 39.0, 24.7, 22.5, 21.0, 17.8. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2971 (*m*), 1738 (*s*), 1603 (*m*), 1491 (*m*), 1375 (*m*), 1260 (*s*), 1237 (*vs*), 1154 (*m*), 1034 (*s*), 856 (*s*), 777 (*s*) cm^{-1}.**HRMS** (EI) calcd for $C_{17}H_{22}O_3$ $[M]^+$: 274.1563; found: 274.1564.

*3.34. 6-Methoxy-2-((methoxymethoxy)methyl)-1,1,2-trimethyl-1,2-dihydronaphthalene (**61b**)*

To a solution of **58a** (20.0 mg, 0.0861 mmol, 1 equiv) in dichloromethane (0.43 mL) were added *N*,*N*-diisopropylethylamine (59.6 µL, 0.344 mmol, 4.00 equiv), 4-dimethylaminopyridine (1.05 mg, 0.008641 mmol, 0.100 equiv) and chloromethyl methyl ether (22.9 µL, 0.301 mmol, 3.50 equiv) respectively at 0 °C. The reaction mixture was allowed to warm to 23 °C and after 4 h, saturated aqueous ammonium chloride solution (10 mL) was added. The layers were separated, the aqueous layer was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with saturated aqueous sodium chloride solution (10 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to provide **61b** (22.3 mg, 94%) as a colorless oil. **Analytical data for 61b: TLC** (20% ethyl acetate in hexanes), R_f = 0.43 (UV, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.18 (dd, *J* = 8.4, 0.6 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.58 (d, *J* = 2.8 Hz, 1H), 6.37 (d, *J* = 9.6 Hz, 1H), 5.77 (d, *J* = 9.6 Hz, 1H), 4.59 – 4.52 (m, 2H), 3.79 (s, 3H), 3.45 (s, 2H), 3.32 (s, 3H), 1.22 (s, 3H), 1.19 (s, 3H), 1.10 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 158.0, 137.0, 136.6, 133.5, 125.7, 125.2, 112.5, 112.1, 97.0, 72.3, 55.3, 55.3, 42.0, 39.1, 24.3, 22.9, 17.9. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2968 (*w*), 2931 (*w*), 1602 (*w*), 1464 (*w*), 1309 (*w*), 1260 (*m*), 1149 (*m*), 1105 (*m*), 1037 (*vs*), 916 (*w*), 854 (*w*), 776 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{17}H_{24}O_3$ $[M]^+$: 276.1720; found: 276.1715.

*3.35. tert-Butyl((6-methoxy-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methoxy)dimethyl-silane (**61c**)*

To a solution of **58a** (20.0 mg, 0.0861 mmol, 1 equiv) in dimethylformamide (0.21 mL) were added imidazole (11.7 mg, 0.172 mmol, 2.00 equiv) and *tert*-butyldimethylsilyl chloride (19.5 mg, 0.129 mmol, 1.50 equiv) at 0 °C and the reaction was allowed to warm to 23 °C. After 20 h, saturated aqueous ammonium chloride solution (10 mL) was added and the layers were separated. The aqueous layer was extracted with diethyl ether (3 × 10 mL) and the combined organic layers were washed with saturated aqueous sodium chloride solution (10 mL). The washed solution was dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to obtain **61c** (20.2 mg, 68%) as a colorless oil. **Analytical data for 61c: TLC** (20% ethyl acetate in hexanes), R_f = 0.68 (UV, CAM). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.17 (dd, *J* = 8.4, 0.6 Hz, 1H), 6.71 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.56 (d, *J* = 2.8 Hz, 1H), 6.33 (d, *J* = 9.6 Hz, 1H), 5.71 (d, *J* = 9.6 Hz, 1H), 3.79 (s, 3H), 3.51 (s, 2H), 1.21 (d, *J* = 3.6 Hz, 6H), 1.02 (s, 3H), 0.86 (s, 9H), -0.03 (d, *J* = 2.4 Hz, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 157.8, 137.5, 137.1, 133.7, 125.6, 125.1, 112.4, 111.9, 67.0, 55.3, 43.1, 39.0, 26.0, 24.5, 23.2, 18.4, 17.6, -5.4, -5.4. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2955 (*m*), 2928 (*m*), 2855 (*w*), 1602 (*w*), 1463 (*m*), 1360 (*w*), 1309 (*w*), 1259 (*s*), 1072 (*s*), 1038 (*s*), 1005 (*m*), 849 (*vs*), 835 (*vs*), 773 (*vs*), 668 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{21}H_{34}O_2Si$ $[M]^+$: 346.2323; found: 346.2322.

*3.36. 6-Methoxy-2-(methoxymethyl)-1,1,2-trimethyl-1,2-dihydronaphthalene (**61d**)*

To a solution of **58a** (20.0 mg, 0.0861 mmol, 1 equiv) in dimethylformamide (0.43 mL) was added sodium hydride (60% dispersion in mineral oil, 6.89 mg, 0.172 mmol, 2.00 equiv) at 0 °C. After 15 min, methyl iodide (9.65 mL, 0.155 mmol,

1.80 equiv) was added and the mixture was allowed to warm to 23 °C over 2.5 h. Saturated aqueous ammonium chloride solution (10 mL) was added and the layers were separated. The aqueous layer was extracted with ethyl acetate (3 × 10 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (5% ethyl acetate in hexanes) to provide **61d** (17 mg, 80%) as a colorless oil. **Analytical data for 61d: TLC** (20% ethyl acetate in hexanes), R_f = 0.61 (UV, CAM). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.18 (d, *J* = 8.4 Hz, 1H), 6.72 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.59 (d, *J* = 2.7 Hz, 1H), 6.37 (d, *J* = 9.6 Hz, 1H), 5.75 (d, *J* = 9.6 Hz, 1H), 3.79 (s, 3H), 3.33 – 3.22 (m, 5H), 1.22 (s, 3H), 1.18 (s, 3H), 1.09 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 157.9, 137.0, 136.9, 133.5, 125.5, 125.2, 112.5, 112.0, 77.4, 59.5, 55.3, 42.2, 39.1, 24.4, 22.8, 17.8. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2970 (*m*), 2932 (*m*), 1886 (*m*), 1602 (*m*), 1572 (*m*), 1489 (*m*), 1464 (*m*), 1361 (*w*), 1309 (*m*), 1282 (*m*), 1261 (*vs*), 1194 (*m*), 1154 (*m*), 1105 (*vs*), 1089 (*s*), 1037 (*s*), 982 (*w*), 871 (*w*), 777 (*m*) cm^{-1}.**HRMS** (EI) calcd for $C_{16}H_{22}O_2$ $[M]^+$: 246.1620; found: 246.1614.

*3.37. N,N-diethyl-2-((6-methoxy-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methoxy)acetamide (**64**)*

To a solution of **58a** (100 mg, 0.430 mmol, 1 equiv) in 1,2-dimethoxyethane (2.2 mL) was added sodium hydride (60% dispersion in mineral oil, 51.6 mg, 1.29 mmol, 3.00 equiv) at 0 °C and after 20 min 2-chloro-*N*,*N*-diethylacetamide (88.7 µL, 0.646 mmol, 1.50 equiv). The reaction was allowed to warm slowly to 23 °C over 17 h and diluted with saturated aqueous ammonium chloride solution (10 mL) and water (5 mL). The layers were separated, the aqueous layer was extracted with ethyl acetate (3 × 15 mL) and the combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (33% ethyl acetate in hexanes) to afford **64** (144 mg, 97%) as a colorless oil. **Analytical data for 64: TLC** (33% ethyl acetate in hexanes), R_f = 0.17 (UV, CAM). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.16 (d, *J* = 8.4 Hz, 1H), 6.70 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.56 (d, *J* = 2.7 Hz, 1H), 6.34 (d, *J* = 9.6 Hz, 1H), 5.78 (d, *J* = 9.7 Hz, 1H), 4.04 (q, *J* = 13.2 Hz, 2H), 3.78 (s, 3H), 3.47 – 3.25 (m, 6H), 1.26 – 1.04 (m, 15H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 168.5, 157.9, 136.9, 136.7, 133.4, 125.6, 125.2, 112.4, 112.0, 76.0, 71.3, 55.3, 42.3, 41.1, 39.8, 39.0, 24.3, 22.8, 17.9, 14.4, 12.9. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2971 (*m*), 2935 (*m*), 2874 (*w*), 1645 (*vs*), 1603 (*m*), 1572 (*w*), 1464 (*m*), 1431 (*m*), 1381 (*w*), 1362 (*w*), 1309 (*m*), 1261 (*vs*), 1222 (*m*), 1153 (*m*), 1102 (*m*), 1088 (*m*), 1036 (*m*), 947 (*w*), 871 (*w*), 791 (*w*), 779 (*w*), 734 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{21}H_{31}O_3N$ $[M]^+$: 345.2298; found: 345.2295.

*3.38. 7-methoxy-3,4,4-trimethyl-2a,3,4,8b-tetrahydro-1,3-(epoxymethano)cyclobuta[a]naphthalen-2(1H)-one (**65**)*

To a solution of **64** (60.0 mg, 0.174 mmol, 1 equiv) in 1,2-dichloroethane (6 mL) were added 2,4,6-collidine (11.7 µL, 0.868 mmol, 5.00 equiv) and trifluoromethanesulfonic anhydride (1 M in dichloromethane, 0.868 mL, 0.868 mmol, 5.00 equiv) and the reaction mixture was heated to 80 °C. After 75 min, potassium carbonate (120 mg, 0.868 mmol, 5.00 equiv), acetone (6 mL) and water (6 mL) were added and the mixture was heated to 70 °C. After 2 h, aqueous hydrochloric acid solution (2 M, 20 mL) was added and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (20 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (14% ethyl acetate in hexanes) to yield **65** (33 mg, 70%) as a yellow oil. **Analytical data for 65: TLC** (25% ethyl acetate in hexanes), R_f = 0.41 (CAM, ANIS, $KMnO_4$). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.36 (d, *J* = 8.7 Hz, 1H), 6.83 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.69 (d, *J* = 2.8 Hz, 1H), 4.66 (dd, *J* = 6.7, 4.3 Hz, 1H), 4.05 (dt, *J* = 12.1, 0.9 Hz, 1H), 3.80 (s, 3H), 3.50 (d, *J* = 12.1 Hz, 1H), 3.41 (tt, *J* = 6.1, 0.7 Hz, 1H), 3.27 (dd, *J* = 6.0, 4.3 Hz, 1H), 1.41 (s, 3H), 1.08 (s, 3H), 1.06 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 204.8, 158.0, 139.1, 130.3, 126.3, 113.7, 113.6, 93.0, 71.9, 64.2, 55.3, 45.9, 38.1, 35.8, 30.9, 21.5, 20.8. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2975 (*m*), 2865 (*w*), 1780 (*vs*), 1610 (*m*), 1501 (*m*), 1465 (*m*), 1316 (*w*), 1260 (*m*), 1249 (*m*), 1153 (*w*), 1053 (*m*), 1037 (*m*), 908 (*m*), 818 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{17}H_{20}O_3$ $[M]^+$: 272.1407; found: 272.1406.

*3.39. 7-methoxy-3a,4,4-trimethyl-3,3a,4,8b-tetrahydro-1H-benzo[f]cyclobuta[cd]isobenzofuran-1a(1a1H)-ol (**71**)*

To a degassed solution of **65** (12.0 mg, 0.0441 mmol, 1 equiv) in tetrahydrofuran (1.2 mL) and methanol (0.6 mL) was added dropwise a solution of samarium(II) iodide (0.1 M in tetrahydrofuran, 3.52 mL, 0.352 mmol, 8.00 equiv) at 0 °C. After 1 h, water (10 mL) and aqueous hydrochloric acid solution (2 M, 10 mL) were added and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (33% ethyl acetate in hexanes) to afford **71** (12 mg, quant.) as a colorless oil. **Analytical data for 71: TLC** (33% ethyl acetate in hexanes), R_f = 0.26 (CAM). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.24 (d, *J* = 8.8 Hz, 1H), 6.73 (dd, *J* = 8.7, 2.8 Hz, 1H), 6.58 (d, *J* = 2.7 Hz, 1H), 3.78 (s, 3H), 3.68 (d, *J* = 8.9 Hz, 1H), 3.51 (d, *J* = 8.9 Hz, 1H), 3.34 (td, *J* = 10.4, 5.0 Hz, 1H), 3.05 (ddd, *J* = 12.9, 11.2, 1.7 Hz, 1H), 2.75 – 2.66 (m, 2H), 2.23 (dd, *J* = 13.0, 5.1 Hz, 1H), 1.28 (s, 6H), 1.06 (s, 3H). **^{13}C NMR** (101 MHz, CDCl3) δ: 157.8, 139.4, 136.8, 126.1, 112.8, 112.3, 106.4, 76.7, 55.3, 53.6, 46.6, 44.2, 37.9, 29.5, 23.6, 22.2, 21.9. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3391 (*w*), 2971 (*m*), 1608 (*m*), 1575 (*w*), 1502 (*m*), 1424 (*w*), 1364 (*w*), 1284 (*s*), 1254 (s), 1216 (*w*), 1158 (*m*), 1125 (*w*), 1037 (*vs*), 867 (*m*), 815 (*m*), 728 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{17}H_{22}O_3$ $[M]^+$: 274.1563; found: 274.1572.

*3.40. 3-(hydroxymethyl)-7-methoxy-3,4,4-trimethyl-1,2,2a,3,4,8b-hexahydrocyclobuta[a]naphthalen-2-ol (**72**)*

To a solution of **71** (12.0 mg, 0.0437 mmol, 1 equiv) in diethyl ether (3 mL) was added lithium aluminum hydride (16.6 mg, 0.437 mmol, 10.0 equiv) at 0 °C and the reaction mixture was allowed to slowly warm to 23 °C. After 4 h, the reaction mixture was diluted with saturated aqueous ammonium chloride solution (15 mL), the layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (10 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (33% ethyl acetate in hexanes) to yield **72** (12 mg, 99%, d.r. = 30:1) as a colorless oil. **Analytical data for 72: TLC** (50% ethyl acetate in hexanes), R_f = 0.20 (CAM). **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.09 (d, *J* = 8.5 Hz, 1H), 6.66 (dd, *J* = 8.6, 2.8 Hz, 1H), 6.59 (d, *J* = 2.7 Hz, 1H), 4.52 (dt, *J* = 9.7, 8.1 Hz, 1H), 3.77 (s, 3H), 3.55 – 3.44 (m, 2H), 3.35 (s, 2H), 3.12 (q, *J* = 8.9 Hz, 1H), 3.03 (dt, *J* = 12.0, 6.0 Hz, 1H), 2.90 (dtd, *J* = 11.3, 8.0, 3.3 Hz, 1H), 2.00 (q, *J* = 10.1 Hz, 1H), 1.31 (s, 3H), 1.18 (s, 3H), 1.02 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 158.2, 140.7, 137.0, 124.9, 112.3, 111.1, 65.5, 65.1,

55.3, 49.8, 42.9, 41.1, 40.1, 27.9, 27.3, 21.5, 18.7. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3217 (*m*), 2970 (*m*), 2934 (*m*), 1606 (*m*), 1576 (*w*), 1495 (*m*), 1465 (*m*), 1365 (*w*), 1310 (*m*), 1247 (*s*), 1198 (*m*), 1112 (*m*), 1031 (*vs*), 849 (*m*), 808 (*m*), 735 (*s*), 703 (*m*) cm^{-1}. **HRMS** (EI) calcd for $C_{17}H_{24}O_3$ $[M]^+$: 276.1720; found: 276.1726.

*3.41. 7-methoxy-3,4,4-trimethyl-2-oxo-1,2,2a,3,4,8b-hexahydrocyclobuta[a]naphthalene-3-carbaldehyde (**73**)*

To a solution of oxalyl chloride (2 M in dichloromethane, 151 µL, 0.302 mmol, 2.20 equiv) in dichloromethane (1.5 mL) was added dimethyl sulfoxide (47.9 µL, 0.674 mmol, 4.90 equiv) at −78 °C. After stirring for 3 min, a solution of **72** (38.0 mg, 0.137 mmol, 1 equiv) dichloromethane (1 mL) was added and after further 25 min triethylamine (191 µL, 1.37 mmol, 10.0 equiv) was added. The reaction mixture was stirred for 10 min at −78 °C and was then directly warmed to 23 °C. After 10 min, saturated aqueous sodium bicarbonate solution (10 mL) was added, the layers were separated and the aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were dried over sodium sulfate, the dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes, triethylamine pretreated silica gel) to obtain **73** (35.5 mg, 95%) as a colorless oil. *Note: Signals in the ^{13}C NMR which could only be assigned by cross-coupling in the HMBC are marked with an asterisk.* **Analytical data for 73: TLC** (20% ethyl acetate in hexanes), R_f = 0.18 (ANIS). **^{1}H NMR** (400 MHz, C_6D_6) δ: 9.12 (br s, 1H), 6.89 (d, *J* = 8.5 Hz, 1H), 6.68 – 6.59 (m, 2H), 3.31 (s, 3H), 3.24 (br s, 1H), 3.08 (ddd, *J* = 17.2, 9.6, 3.8 Hz, 1H), 2.95 (tdt, *J* = 9.6, 6.0, 1.1 Hz, 1H), 2.83 (ddd, *J* = 10.3, 3.7, 2.8 Hz, 1H), 1.05 (s, 3H), 1.01 (s, 3H), 0.73 (s, 3H). **^{13}C NMR** (101 MHz, C_6D_6) δ: 206.7, 202.2, 159.2, 140.3, 135.5, 125.4, 113.4, 112.3, 63.9, 55.9, 54.7, 53.1, 39.7, 26.3, 25.9, 21.7*, 16.3. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2973 (*w*), 2933 (*w*), 2728 (*w*), 1774 (*vs*), 1718 (*s*), 1607 (*m*), 1574 (*w*), 1494 (*m*), 1465 (*m*), 1388 (*m*), 1298 (*m*), 1249 (*s*), 1155 (*m*), 1087 (*m*), 1034 (*s*), 854 (*w*), 820 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{17}H_{20}O_3$ $[M]^+$: 272.1407; found: 272.1409.

*3.42. 7-methoxy-3a,4,4-trimethyl-3a,4-dihydro-1H-cyclopenta[b]naphthalen-1-one (**77**)*

To a solution of **73** (5.00 mg, 0.0184 mmol, 1 equiv) in tetrahydrofuran (0.2 mL) was added lithium bis(trimethylsilyl)amide (1 M in tetrahydrofuran, 22.0 µL, 0.0220 mmol, 1.20 equiv) at −78 °C. After 1 h, freshly distilled trimethylsilyl chloride (over CaH_2, 3.52 µL, 0.0275 mmol, 1.50 equiv) was added and the mixture was allowed to warm to 23 °C. After 3 h, dichloromethane (5 mL) was added, the reaction mixture was filtered through a small plug of Celite® and the filtrate was concentrated. The residue was used without further purification. To acetone (2.03 µL, 0.0276 mmol, 1.50 equiv) in dichloromethane (0.1 mL) was added titanium(IV) chloride (3.04 µL, 0.0276 mmol, 1.50 equiv) followed by the addition of a solution of crude product in dichloromethane (0.3 mL) at −78 °C. The reaction mixture was allowed to warm to 23 °C over 17 h. pH7 Buffer solution (10 mL) and diethyl ether (10 mL) were added, the layers were separated and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (10 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated. The crude product was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes) to provide trace amounts of **77** as colorless oil. **Analytical data for 77: TLC** (20% ethyl acetate in hexanes), R_f = 0.26 (UV, CAM, $KMnO_4$). **^{1}H NMR** (400 MHz, C_6D_6) δ: 7.20 (s, 1H), 6.99 (d, *J* = 8.5 Hz, 1H), 6.86 (dd, *J* = 6.0, 1.1 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.8 Hz, 1H), 6.63 (d, *J* = 2.8 Hz, 1H), 6.24 (d, *J* = 6.0 Hz, 1H), 3.27 (s, 3H), 1.08 (s, 3H), 0.76 (s, 3H), 0.69 (s, 3H). **^{13}C NMR** (101 MHz, C_6D_6) δ: 194.6, 162.4, 158.9, 143.1, 139.3, 136.4, 133.0, 126.1, 124.4, 115.9, 115.0, 54.9, 49.9, 39.6, 26.3, 20.4, 20.3. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2966 (*w*), 2929 (*w*), 1689 (*vs*), 1645 (*vs*), 1605 (*m*), 1566 (*m*), 1482 (*w*), 1465 (*w*), 1372 (*w*), 1322 (*w*), 1249 (*m*), 1229 (*vs*), 1205 (*w*), 1146 (*w*), 1082 (*w*), 1057 (*w*), 1036 (*m*), 853 (*w*), 816 (*s*), 709 (*w*) cm^{-1}. **HRMS** (EI) calcd for $C_{17}H_{18}O_3$ $[M]^+$: 254.1301; found: 254.1301.

*3.43. 6-methoxy-1,1,2-trimethyl-1,2-dihydronaphthalene-2-carbaldehyde (**85a**)*

To a solution of alcohol **58a** (1.17 g, 5.04 mmol, 1 equiv) in dry dichloromethane (50 mL) was added potassium carbonate (1.39 g, 10.1 mmol, 2.00 equiv) and Dess–Martin periodinane (4.27 g, 10.1 mmol, 2.00 equiv) at 0 °C. The suspension was stirred at 0 °C for 30 min and at 23 °C for 1.5 h. Excess Dess–Martin periodinane was quenched by addition of saturated aqueous sodium bicarbonate solution (35 mL) and saturated aqueous sodium thiosulfate solution (20 mL). The organic layer was separated and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over sodium sulfate and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (1% ethyl acetate in cyclohexane initially, grading to 5% ethyl acetate in cyclohexane) afforded aldehyde **85a** (0.92 g, 80%) as a colorless oil. **Analytical data for 85a: TLC** (10% ethyl acetate in cyclohexane) R_f = 0.37 (UV) **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 9.35 (s, 1H), 7.20 (d, *J* = 8.5 Hz, 1H), 6.77 (dd, *J* = 8.5, 2.7 Hz, 1H), 6.65 – 6.61 (m, 2H), 5.49 (d, *J* = 9.5 Hz, 1H), 3.80 (s, 3H), 1.28 (s, 3H), 1.20 (s, 3H), 1.17 (s, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 202.8, 158.4, 135.4, 133.1, 130.6, 129.9, 125.6, 113.6, 112.8, 55.4, 54.8, 38.7, 25.3, 22.5, 14.3. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 3032 (*w*), 2971 (*w*), 2871 (*w*), 2833 (*w*), 2715 (*w*), 1715 (*s*), 1634 (*w*), 1601 (*m*), 1570 (*m*), 1495 (*m*), 1463 (*m*), 1427 (*m*), 1386 (*w*), 1363 (*w*), 1308 (*m*), 1283 (*m*), 1259 (*s*), 1223 (*m*), 1192 (*w*), 1175 (*m*), 1153 (*m*), 1093 (*m*), 1034 (*s*), 961 (*w*), 933 (*w*), 908 (*m*), 871 (*m*), 856 (*m*), 818 (*m*), 791 (*w*), 773 (*s*), 754 (*w*), 731 (*s*), 712 (*m*), 683 (*w*), 621 (*w*), 582 (*w*), 553 (*w*), 527 (*m*), 498 (*w*), 431 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{15}H_{18}NaO_2$ $[M+Na]^+$: 253.1199; found: 253.1185.

*3.44. ethyl (Z)-5-(6-methoxy-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)pent-4-enoate (**86a**)*

To a stirred suspension of [3-(ethoxycarbonyl)propyl]triphenylphosphonium bromide (2.85 g, 6.23 mmol, 1.60 equiv) in tetrahydrofuran (25 mL) was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 7.1 mL, 7.1 mmol, 1.8 equiv) at 0 °C. The orange mixture was stirred for 30 min at 0 °C and was then cooled to −78 °C. A solution of aldehyde **85a** (0.90 g, 3.90 mmol, 1 equiv) in tetrahydrofuran (4.2 mL) was added slowly. After 15 min, the reaction was allowed to warm to 23 °C and stirred at 23 °C for 4 h. Excess amide was quenched by addition of saturated aqueous ammonium chloride solution (21 mL). The mixture was extracted with diethyl ether (3 × 50 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (70 mL) and the washed solution was dried over sodium sulfate. The solution was filtered and the filtrate was concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) to afford the title compound **86a** (1.20 g, 94%) as a colorless oil. **Analytical data for 86a: TLC** (10% ethyl acetate in cyclohexane) R_f = 0.45 (UV) **^{1}H NMR** (400 MHz, $CDCl_3$) δ:

7.18 (d, *J* = 8.5 Hz, 1H), 6.72 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.58 (d, *J* = 2.7 Hz, 1H), 6.31 (d, *J* = 9.6 Hz, 1H), 5.99 (d, *J* = 9.6 Hz, 1H), 5.46 (d, *J* = 12.0 Hz, 1H), 5.36 (dt, *J* = 12.0, 7.2 Hz, 1H), 4.14 (q, *J* = 7.1 Hz, 2H), 3.78 (s, 3H), 2.73 – 2.62 (m, 1H), 2.50 (tdd, *J* = 14.7, 7.2, 1.3 Hz, 1H), 2.37 (t, *J* = 7.5 Hz, 2H), 1.28 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 1.16 (s, 3H), 1.09 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 173.1, 157.9, 139.0, 136.5, 135.7, 133.2, 129.7, 125.2, 124.6, 112.3, 112.0, 60.4, 55.2, 45.1, 40.9, 34.7, 26.1, 24.9, 22.5, 21.6, 14.3. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 2972 (*m*), 2937 (*w*), 2873 (*w*), 2833 (*w*), 1732 (*s*), 1636 (*w*), 1602 (*m*), 1571 (*w*), 1489 (*m*), 1464 (*m*), 1427 (*w*), 1371 (*m*), 1308 (*m*), 1281 (*m*), 1259 (*s*), 1214 (*m*), 1171 (*k*), 1151 (*s*), 1089 (*m*), 1062 (*w*), 1035 (*s*), 910 (*m*), 871 (*m*), 856 (*m*), 818 (*m*), 778 (*m*), 730 (*s*), 648 (*w*), 631 (*w*), 597 (*w*), 554 (*w*), 473 (*w*), 433 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{21}H_{28}NaO_3$ $[M+Na]^+$: 351.1931, found: 351.1926.

*3.45. (Z)-5-(6-methoxy-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)-1-(pyrrolidin-1-yl)pent-4-en-1-one (**87a**)*

The ester **86a** (1.20 g, 3.65 mmol, 1 equiv) was dissolved in dry and colorless pyrrolidine (4.5 mL, 55 mmol, 15 equiv) in a pressure tube under argon. The tube was sealed and heated at 100 °C. The reaction mixture was stirred for 65 h and was then cooled to 23 °C. Excess pyrrolidine was removed under reduced pressure. Purification by flash column chromatography on silica gel (50% ethyl acetate in cyclohexane) afforded the title compound **87a** (1.38 g, quant.) as a pale-yellow oil. **Analytical data for 87a: TLC** (50% ethyl acetate in cyclohexane) R_f = 0.27 (CAM) **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.17 (d, *J* = 8.4 Hz, 1H), 6.71 (dd, *J* = 8.4, 2.8 Hz, 1H), 6.57 (d, *J* = 2.7 Hz, 1H), 6.29 (d, *J* = 9.6 Hz, 1H), 6.00 (d, *J* = 9.6 Hz, 1H), 5.46 – 5.36 (m, 2H), 3.78 (s, 3H), 3.47 (t, *J* = 6.8 Hz, 2H), 3.40 (t, *J* = 6.8 Hz, 2H), 2.73 – 2.62 (m, 1H), 2.59 – 2.47 (m, 1H), 2.31 (t, *J* = 7.7 Hz, 2H), 1.99 – 1.89 (m, 2H), 1.89 – 1.80 (m, 2H), 1.27 (s, 3H), 1.16 (s, 3H), 1.08 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 171.1, 157.9, 139.4, 136.8, 135.4, 133.5, 130.7, 125.3, 124.6, 112.4, 112.0, 55.3, 46.8, 45.8, 45.2, 41.0, 35.3, 26.3, 26.2, 25.1, 24.6, 22.6, 21.7. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 2969 (*m*), 2872 (*w*), 2833 (*w*), 1641 (*s*), 1602 (*m*), 1571 (*w*), 1489 (*m*), 1433 (*s*), 1380 (*w*), 1359 (*w*), 1340 (*w*), 1309 (*w*), 1282 (*w*), 1260 (*s*), 1225 (*w*), 1192 (*w*), 1171 (*w*), 1152 (*w*), 1089 (*w*), 1035 (*m*), 870 (*w*), 857 (*w*), 818 (*w*), 780 (*w*), 727 (*w*), 632 (*w*), 549 (*w*), 421 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{23}H_{31}NNaO_2$ $[M+Na]^+$: 376.2247, found: 376.2240

*3.46. 7-methoxy-3,4,4-trimethyl-2a,3,4,8b-tetrahydro-3,1-prop[1]enocyclobuta[a]naphthalen-2(1H)-one (**90a**)*

To a vigorously stirred solution of freshly distilled trifluoromethanesulfonic anhydride (0.77 mL, 4.55 mmol, 1.20 equiv) in dry 1,2-dichloroethane (47 mL) at 80 °C was added dropwise a solution of amide **87a** (1.34 g, 3.79 mmol, 1 equiv) and 2,4,6-collidine (0.60 mL, 4.55 mmol, 1.20 equiv) in 1,2-dichloroethane (47 mL) via a dropping funnel over a period of 2 h. The initial yellowish reaction mixture turned red-brownish, stirring was continued at 80 °C for 24 h and was cooled to 23 °C. The dark red-brownish reaction mixture was concentrated under reduced pressure. To the crude iminium salt was added tetrachloromethane (20 mL) and water (20 mL) and the dark brown mixture was heated at reflux at 80 °C for 5 h under an atmosphere of argon. The organic layer was separated and the aqueous phase was extracted with dichloromethane (3 × 15 mL). The combined organic layers were dried over sodium sulfate, filtered and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane) afforded cyclobutanone **90a** (0.72 g, 67%) as a pale yellow solid and cyclobutanone **89a** (0.02 g, 2%) as a colorless oil. **Analytical Data for 90a: TLC** (10% ethyl acetate in cyclohexane) R_f = 0.21 (UV, CAM) **^{1}H NMR** (400 MHz, Acetone-d_6) δ: 7.20 (d, *J* = 8.4 Hz, 1H), 6.75 – 6.67 (m, 2H), 5.37 (ddt, *J* = 12.5, 2.7, 1.8 Hz, 1H), 5.11 (dddd, *J* = 12.5, 5.1, 2.6, 1.1 Hz, 1H), 3.75 (s, 3H), 3.72 (d, *J* = 8.2 Hz, 1H), 3.67 – 3.60 (m, 1H), 3.48 (ddd, *J* = 8.3, 6.6, 1.9 Hz, 1H), 2.21 (dtd, *J* = 18.5, 5.1, 1.6 Hz, 1H), 1.98 (dq, *J* = 18.5, 2.8 Hz, 1H), 1.37 (s, 3H), 1.24 (s, 3H), 1.10 (s, 3H). **^{13}C NMR** (101 MHz, Acetone-d_6) δ: 209.2, 158.2, 139.7, 136.7, 134.5, 126.6, 126.5, 114.8, 112.9, 64.9, 61.7, 55.3, 41.5, 41.1, 30.6, 28.3, 27.6, 21.9, 21.9. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 2969 (*w*), 2909 (*w*), 2834 (*w*), 1776 (*s*), 1608 (*w*), 1576 (*w*), 1497 (*w*), 1464 (*w*), 1424 (*w*), 1387 (*w*), 1370 (*w*), 1324 (*w*), 1304 (*w*), 1281 (*w*), 1255 (*m*), 1246 (*m*), 1220 (*w*), 1160 (*w*), 1112 (*w*), 1090 (*w*), 1062 (*w*), 1037 (*w*), 975 (*w*), 929 (*w*), 857 (*w*), 822 (*w*), 760 (*w*), 701 (*w*), 688 (*w*), 601 (*w*), 570 (*w*), 483 (*w*), 410 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{19}H_{22}NaO_2$ $[M+Na]^+$: 305.1512, found: 305.1472. **Analytical Data for 89a: TLC** (10% ethyl acetate in cyclohexane) R_f = 0.27 (UV, CAM) **^{1}H NMR** (600 MHz, $CDCl_3$) δ: 7.10 (d, *J* = 8.6 Hz, 1H), 6.84 (dd, *J* = 2.8, 1.2 Hz, 1H), 6.63 (ddd, *J* = 8.6, 2.8, 1.0 Hz, 1H), 5.46 (ddd, *J* = 10.4, 6.7, 1.9 Hz, 1H), 5.42 (ddd, *J* = 10.2, 2.9, 1.5 Hz, 1H), 4.28 (dt, *J* = 9.8, 2.0 Hz, 1H), 3.71 (s, 3H), 3.62 (dddd, *J* = 9.9, 7.0, 3.2, 1.7 Hz, 1H), 3.04 (td, *J* = 9.8, 1.5 Hz, 1H), 2.28 (ddd, *J* = 16.9, 6.7, 1.8 Hz, 1H), 2.06 (dddd, *J* = 17.0, 7.0, 2.9, 2.0 Hz, 1H), 1.34 (s, 3H), 1.11 (s, 3H), 1.02 (s, 3H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ: 212.6, 157.8, 137.5, 134.9, 130.9, 126.2, 125.1, 112.4, 112.0, 58.9, 55.7, 55.3, 39.9, 38.7, 34.6, 25.5, 22.1, 21.9, 20.4. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$ 3034 (*w*), 2969 (*m*), 2838 (*w*), 1775 (*s*), 1606 (*m*), 1575 (*w*), 1496 (*m*), 1464 (*w*), 1400 (*w*), 1383 (*w*), 1369 (*w*), 1320 (*w*), 1302 (*m*), 1257 (*m*), 1229 (*m*), 1178 (*w*), 1158 (*w*), 1141 (*w*), 1117 (*w*), 1091 (*w*), 1037 (*m*), 1016 (*w*), 956 (*w*), 927 (*w*), 868 (*w*), 850 (*w*), 815 (*w*), 757 (*w*), 731 (*w*), 698 (*m*), 589 (*w*), 560 (*w*), 526 (*w*), 507 (*w*), 479 (*w*), 442 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{19}H_{22}NaO_2$ $[M+Na]^+$: 305.1512, found: 305.1465.

*3.47. 11-hydroxy-7-methoxy-3,4,4-trimethyl-2a,3,4,8b-tetrahydro-3,1-prop[1]enocyclobuta[a]naphthalen-2(1H)-one (**93a**)*

To finely grinded selenium dioxide (2.13 g, 19.2 mmol, 10.0 equiv) and oven-dried (100 °C) fine white quartz sand (2.19 g, 19.0 equiv, particle size >230mesh) in a flame-dried pressure tube (15 mL) equipped with a magnetic stirring bar was added cyclobutanone **90a** (541 mg, 1.92 mmol, 1 equiv). After sparging with argon for 10 min, dry 1,4-dioxane (9.6 mL) was added. The tube was sealed and the vigorously stirred reaction mixture was heated at 125 °C (700 rpm) for 7 h. The reaction mixture was cooled to 23 °C and filtered through a pad of Celite®. The Celite® plug was washed with ethyl acetate (200 mL) and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (1% ethyl acetate in cyclohexane initially, grading to 10% ethyl acetate in cyclohexane, grading to 25% ethyl acetate in cyclohexane, grading to 50% ethyl acetate in cyclohexane) afforded slightly impure **93a** (165 mg) as an orange foam. Cyclobutanone **90a** (294 mg, 54%) was recovered. Purification of the impure product **93a** by flash column chromatography (10% ethyl acetate in dichloromethane) afforded the allylic alcohol **93a** (142 mg, 25%) as a colorless sticky foam. **Analytical Data for 93a: TLC** (25% ethyl acetate in cyclohexane) R_f = 0.30 (UV, CAM) **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.19 (d, *J* = 8.7 Hz, 1H), 6.75 (ddd, *J* = 8.7, 2.8, 0.7 Hz, 1H), 6.66 (dd, *J* = 2.8, 0.9 Hz, 1H), 5.42 (dt, *J* = 12.6, 1.8 Hz, 1H), 5.34 (ddd, *J* = 12.7, 2.5, 1.9 Hz, 1H), 4.04 – 3.97 (m, 1H), 3.83 (dddd, *J* = 8.6, 6.4, 4.3, 1.9 Hz, 1H), 3.78 (s, 3H), 3.73 (t, *J* = 8.5 Hz, 1H), 3.48 (ddd, *J* = 8.3, 6.6, 1.7 Hz, 1H), 1.98 (d, *J* = 9.4 Hz, 1H), 1.39 (s, 3H), 1.28 (s, 3H), 1.09 (s, 3H). **^{13}C NMR**

(101 MHz, $CDCl_3$) δ: 208.5, 157.5, 138.6, 135.8, 132.3, 130.0, 126.2, 113.9, 112.8, 68.1, 67.5, 64.7, 55.3, 42.5, 40.5, 28.4, 27.7, 22.0, 21.9. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 3420 (*w br*), 2971 (*w*), 2909 (*w*), 2836 (*w*), 2251 (*w*), 1771 (*s*), 1607 (*m*), 1575 (*w*), 1496 (*m*), 1477 (*w*), 1464 (*w*), 1425 (*w*), 1388 (*w*), 1371 (*w*), 1325 (*w*), 1309 (*w*), 1244 (*m*), 1174 (*m*), 1163 (*m*), 1128 (*w*), 1107 (*w*), 1090 (*w*), 1057 (*w*), 1032 (*s*), 974 (*w*), 908 (*m*), 879 (*m*), 852 (*w*), 816 (*m*), 775 (*m*), 726 (*s*), 701 (*m*), 688 (*m*), 647 (*m*), 588 (*m*), 552 (*w*), 529 (*w*), 492 (*w*), 453 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{19}H_{22}NaO_3$ $[M+Na]^+$: 321.1461, found: 321.1416.

*3.48. 8-methoxy-4,5,5-trimethyl-3a,4,5,9b-tetrahydro-4,1-prop[1]enonaphtho[1,2-c]furan-3,12(1H)-dione (**94a**)*

To a solution of allylic alcohol **93a** (50.0 mg, 0.168 mmol, 1 equiv) in 1,2-dichloroethane (4.4 mL) was added pivalaldehyde (0.09 mL, 0.8 mmol, 5 equiv) and copper(II) acetate monohydrate (33.5 mg, 0.168 mmol, 1.00 equiv). The flask was capped with a septum and sparged with oxygen gas from a balloon for 2 min. The solution was stirred under oxygen at 23 °C until monitoring by thin layer chromatography indicated full conversion of the starting material (1.5 h). Sodium bicarbonate (70.4 mg, 0.838 mmol, 5.00 equiv) and Dess–Martin periodinane (142 mg, 0.335 mmol, 2.00 equiv) were added and the reaction was stirred at 23 °C. After 1 h, an additional portion of Dess-Martin periodinane (142 mg, 0.335 mmol, 2.00 equiv) was added and the reaction was stirred at 23 °C for 1 h. Excess Dess–Martin periodinane was quenched by addition of saturated aqueous sodium bicarbonate solution (9 mL) and saturated aqueous sodium thiosulfate solution (4.5 mL). The mixture was extracted with dichloromethane (3 × 25 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (10% ethyl acetate in cyclohexane initially, grading to 25% ethyl acetate in cyclohexane) afforded a mixture of lactones **94a** and **95a**. Separation by slow flash column chromatography on silica gel (5% ethyl acetate in cyclohexane initially, grading to 10% ethyl acetate in cyclohexane) afforded lactone **94a** (34 mg, 64%) and lactone **95a** (13 mg, 25%) as both colorless crystalline solids. **Analytical Data for 94a: TLC** (25% ethyl acetate in cyclohexane) R_f = 0.27 (UV, CAM) **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.21 (d, *J* = 8.8 Hz, 1H), 6.78 (ddd, *J* = 8.9, 2.8, 0.6 Hz, 1H), 6.61 (dd, *J* = 2.8, 0.8 Hz, 1H), 6.10 (dd, *J* = 13.1, 1.5 Hz, 1H), 5.63 (dd, *J* = 13.1, 1.9 Hz, 1H), 5.03 (dd, *J* = 8.6, 2.0 Hz, 1H), 4.05 (t, *J* = 8.7 Hz, 1H), 3.75 (s, 3H), 3.15 (dd, *J* = 8.7, 1.5 Hz, 1H), 1.58 (s, 3H), 1.42 (s, 3H), 1.21 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 195.8, 176.9, 158.2, 148.2, 135.7, 128.4, 127.6, 126.2, 114.9, 113.0, 84.6, 55.4, 45.7, 43.7, 42.3, 39.6, 28.6, 22.2, 21.4. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 2978 (*w*), 2838 (*w*), 1776 (*s*), 1680 (*s*), 1612 (*m*), 1579 (*w*), 1503 (*m*), 1479 (*w*), 1466 (*m*), 1427 (*w*), 1392 (*w*), 1377 (*w*), 1368 (*w*), 1331 (*w*), 1314 (*m*), 1284 (*m*), 1258 (*s*), 1242 (*s*), 1206 (*m*), 1180 (*m*), 1155 (*s*), 1109 (*m*), 1090 (*w*), 1065 (*w*), 1028 (*s*), 992 (*w*), 958 (*w*), 923 (*w*), 905 (*w*), 877 (*w*), 825 (*s*), 753 (*m*), 722 (*w*), 704 (*w*), 692 (*w*), 666 (*w*), 602 (*w*), 563 (*w*), 547 (*w*), 498 (*w*), 457 (*w*), 432 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{19}H_{20}NaO_4$ $[M+Na]^+$: 335.1254, found: 335.1194. **Analytical Data for 95a: TLC** (25% ethyl acetate in cyclohexane) R_f = 0.20 (UV) **^{1}H NMR** (400 MHz, $CDCl_3$) δ: 7.18 (d, *J* = 8.8 Hz, 1H), 6.78 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.59 (dd, *J* = 2.8, 0.8 Hz, 1H), 6.04 (dd, *J* = 13.2, 1.8 Hz, 1H), 5.70 (dd, *J* = 13.2, 1.7 Hz, 1H), 5.10 (dd, *J* = 8.2, 1.8 Hz, 1H), 4.18 (t, *J* = 8.5 Hz, 1H), 3.90 (dd, *J* = 8.8, 1.7 Hz, 1H), 3.75 (s, 3H), 1.49 (s, 3H), 1.43 (s, 3H), 1.25 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ: 192.2, 171.6, 158.3, 148.0, 135.6, 130.8, 127.9, 127.3, 114.9, 113.6, 81.5, 60.1, 55.4, 49.2, 43.2, 40.6, 28.6, 23.2, 19.0. **IR** (ATR, $CDCl_3$) $\tilde{\nu}_{max}$: 2977 (*w*), 2927 (*w*), 1774 (*s*), 1673 (*m*), 1612 (*m*), 1578 (*w*), 1502 (*m*), 1465 (*w*), 1426 (*w*), 1392 (*w*), 1374 (*w*), 1358 (*w*), 1341 (*w*), 1316 (*w*), 1260 (*m*), 1243 (*m*), 1204 (*w*), 1159 (*m*), 1091 (*w*), 1065 (*w*), 1019 (*m*), 958 (*w*), 925 (*w*), 865 (*w*), 844 (*w*), 813 (*w*), 783 (*w*), 753 (*w*), 705 (*w*), 656 (*w*), 607 (*w*), 546 (*w*), 514 (*w*), 497 (*w*), 447 (*w*) cm^{-1}. **HRMS** (ESI) calcd for $C_{19}H_{20}NaO_4$ $[M+Na]^+$: 335.1254, found: 335.1199.

*3.49. tert-butyl((6-ethyl-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methoxy)diphenylsilane (**84**)*

To aluminum chloride (133 mg, 1.00 mmol, 3.00 equiv) in an oven dried Schlenk flask was added dry toluene (1.0 mL) and ethyl magnesium bromide solution (3 M in diethylether, 1.00 mL, 3.00 mmol, 12.0 equiv). The suspension was irradiated in an ultrasonic bath for 15 min. To a second Schlenk flask equipped with a magnetic stirring bar was added bis(1,5-cyclooctadiene)nickel(0) (5.8 mg, 21 µmol, 25 mol%) and 1,2-bis(dicyclohexylphosphino)ethane (8.9 mg, 21 µmol, 25 mol%) and protected dehydrotetraline **81** (45.0 mg, 95.6 µmol, 1 equiv) in a glovebox. Toluene (0.5 mL) and diisopropyl ether (0.5 mL) were added. The suspension of aluminum chloride and ethyl magnesium bromide (0.50 mL, 0.50 mmol $AlEt_3$, 5.2 equiv) was transferred to this solution. The resulting bright yellow suspension was heated to 100 °C for 19 h and then cooled to 23 °C. Excess ethyl metal species were quenched by slow addition of saturated aqueous potassium sodium tartrate solution (5 mL) and the biphasic mixture was stirred for 2 h at 23 °C. The aqueous phase was separated and extracted with ethyl acetate (3 × 5 mL). The combined organic phases were washed with saturated aqueous sodium chloride solution (5 mL) and dried over sodium sulfate. The dried solution was filtered and concentrated. The crude product was purified by flash column chromatography on silica gel (20% ethyl acetate in hexanes) to provide ethyl tetraline **84** (3.1 mg, 7%) as a colorless oil. **Analytical Data for 84:** The physical data were identical in all respects to those previously reported [54].

*3.50. tert-butyl((6-ethyl-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methoxy)diphenylsilane (**84**)*

To a solution of triflate **83** (15.0 g, 25.5 mmol, 1 equiv) in dry dioxane (130 mL) was added [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) (250 mg, 0.34 mmol, 1.3 mol%). The orange suspension was cooled to 0 °C causing partial crystallization of the solvent. Diethylzinc (1 M in hexanes, 38.2 mL, 38.2 mmol, 1.50 equiv) was added and the ice bath was removed. When all dioxane was melted again, a yellow clear solution was formed. The reaction mixture was heated at 70 °C for 1 h and was then cooled to 0 °C. Excess diethylzinc of the brownish solution was quenched by addition of methanol (20 mL), water (100 mL) and saturated aqueous ammonium chloride solution (100 mL). The mixture was extracted with ethyl acetate (3 × 150 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (100 mL) and the washed solution was dried over sodium sulfate. The filtrate was concentrated under reduced pressure, passed through a plug of silica (5% ethyl acetate in cyclohexane) and used without further purification in the next step. **Analytical Data for 84:** The physical data were identical in all respects to those previously reported [54].

*3.51. (6-ethyl-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)methanol (**58b**)*

To a stirred solution of protected alcohol **84** (ca. 25.5 mmol, 1 equiv) in tetrahydrofuran (130 mL) was added a solution of tetrabutylammonium fluoride (1 M in THF, 35 mL, 35 mmol, 1.4 equiv) at 0 °C. The ice bath was removed after 15 min and the

reaction was stirred at 23 °C for 18 h. Excess fluoride was quenched by addition of water (50 mL). The reaction was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (50 mL) and the washed solution was dried over sodium sulfate. The filtrate was concentrated under reduced pressure. Purification by flash column chromatography (1% ethyl acetate in cyclohexane initially, grading to 5% ethyl acetate in cyclohexane) afforded the title compound **58b** (5.9 g, 99%) as a colorless viscous oil. **Analytical Data for 58b:** The physical data were identical in all respects to those previously reported [54].

*3.52. 6-ethyl-1,1,2-trimethyl-1,2-dihydronaphthalene-2-carbaldehyde (**85b**)*

To a solution of oxalyl chloride (4.4 mL, 50 mmol, 2.0 equiv) in dichloromethane (250 mL) was added a solution of dimethyl sulfoxide (4.4 mL, 63 mmol, 2.5 equiv) in dichloromethane dropwise at –78 °C. The mixture was stirred for 30 min before a solution of alcohol **58b** (5.8 g, 25 mmol, 1 equiv) in dichloromethane (25 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 1 h before triethylamine (17 mL, 0.13 mol, 5.0 equiv) was added. The reaction was stirred for 30 min at –78 °C and 4 h at 23 °C. Excess base was quenched by the addition of saturated aqueous ammonium chloride solution (100 mL). The biphasic mixture was extracted with diethyl ether (3 × 200 mL). The combined organic layers were washed with concentrated aqueous sodium chloride solution (200 mL) and dried over sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. Purification by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) afforded aldehyde **85b** as colorless oil (5.7 g, 99%). **Analytical Data for 85b:** The physical data were identical in all respects to those previously reported [54].

*3.53. ethyl (Z)-5-(6-ethyl-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)pent-4-enoate (**86b**)*

To a stirred suspension of [3-(ethoxycarbonyl)propyl]triphenylphosphonium bromide (17 g, 38 mmol, 1.50 equiv) in tetrahydrofuran (150 mL) was added sodium bis(trimethylsilyl)amide (1.0 M in THF, 12.6 mL, 12.6 mmol, 1.70 equiv) at 0 °C. The yellow-orange mixture was stirred for 30 min at 0 °C and was then cooled to −78 °C. A solution of aldehyde **85b** (5.7 g, 25 mmol, 1 equiv) in tetrahydrofuran (20 mL) was added slowly. After 15 min, the reaction was allowed to warm to 23 °C and stirred at 23 °C for 5 h. Excess amide was quenched by addition of saturated aqueous ammonium chloride solution (100 mL). The mixture was extracted with diethyl ether (3 × 300 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (200 mL) and the washed solution was dried over sodium sulfate. The filtrate was concentrated under reduced pressure and the crude product was purified by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) to afford the title compound **86b** (7.0 g, 86%) as a colorless oil. **Analytical Data for 86b:** The physical data were identical in all respects to those previously reported [54].

*3.54. (Z)-5-(6-ethyl-1,1,2-trimethyl-1,2-dihydronaphthalen-2-yl)-1-(pyrrolidin-1-yl)pent-4-en-1-one (**87b**)*

The ester **86b** (7.0 g, 21 mmol, 1 equiv) was dissolved in dry and colorless pyrrolidine (26 mL, 0.32 mol, 15 equiv) in a pressure tube under argon. The tube was sealed and heated at 100 °C. The reaction mixture was stirred for 60 h and then allowed to cool to 23 °C. Excess pyrrolidine was removed under reduced pressure. Purification by flash column chromatography on silica gel (50% ethyl acetate in cyclohexane) afforded the title compound **87b** (7.5 g, 99%) as a pale-yellow oil. **Analytical Data for 87b:** The physical data were identical in all respects to those previously reported [54].

*3.55. 7-ethyl-3,4,4-trimethyl-2a,3,4,8b-tetrahydro-3,1-prop[1]enocyclobuta[a]- naphthalen-2(1H)-one (**90b**)*

To a vigorously stirred solution of freshly distilled trifluoromethanesulfonic anhydride (4.50 mL, 26.8 mmol, 1.30 equiv) in dry 1,2-dichloroethane (270 mL) at 80 °C was added dropwise a solution of amide **87b** (7.25 g, 20.6 mmol, 1 equiv) and 2,4,6-collidine (3.54 mL, 26.8 mmol, 1.30 equiv) in 1,2-dichloroethane (270 mL) via a dropping funnel over a period of 3.5 h. The initial yellowish reaction mixture turned red-brownish, stirring was continued at 80 °C for 20 h and then the reaction mixture was concentrated under reduced pressure. To the crude iminium salt was added tetrachloromethane (100 mL) and water (100 mL) and the dark brown mixture was heated at reflux at 80 °C for 5 h under an atmosphere of argon. The organic layer was separated and the aqueous phase was extracted with dichloromethane (3 × 50 mL). The combined organic layers were dried over sodium sulfate and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane grading to 10% ethyl acetate in cyclohexane) afforded cyclobutanone **90b** (4.8 g, 83%) as a pale yellowish oil that solidified upon storage. **Analytical Data for 90b:** The physical data were identical in all respects to those previously reported [54].

*3.56. 7-ethyl-11-hydroxy-3,4,4-trimethyl-2a,3,4,8b-tetrahydro-3,1- prop[1]enocyclobuta[a]naphthalen-2(1H)-one (**93b**)*

To finely grinded selenium dioxide (21 g, 0.19 mol, 10 equiv) and oven-dried (100 °C) fine white quartz sand (21 g, 0.35 mol, 19 eq, particle size >230 mesh) in a flame-dried pressure tube equipped with a magnetic stirring bar was added cyclobutanone **90b** (5.2 g, 19 mmol, 1 equiv). After sparging with nitrogen for 5 min, dry 1,4-dioxane (93 mL) was added. The tube was sealed and the vigorously stirred reaction mixture was heated at 120 °C for 6 h. The reaction mixture was cooled to 23 °C and filtered through a pad of Celite®. The Celite® was washed with ethyl acetate (200 mL) and the filtrate was concentrated under reduced pressure. Purification by flash column chromatography (1% ethyl acetate in cyclohexane initially, grading to 10% ethyl acetate in cyclohexane, grading to 25% ethyl acetate in cyclohexane, grading to 50% ethyl acetate in cyclohexane) afforded slightly impure **93b** (1.21 g) as an orange oil. Cyclobutanone **90b** (3.38 g, 65%) was recovered and used in the next cycle following the same procedure. After four cycles, the product fractions were combined and collectively purified by flash column chromatography on silica gel (dichloromethane grading to 10% ethyl acetate in dichloromethane) to afford the allylic alcohol **93b** (2.42 g, 44%) as a slightly yellow wax. **Analytical Data for 93b:** The physical data were identical in all respects to those previously reported [54].

*3.57. 8-ethyl-4,5,5-trimethyl-3a,4,5,9b-tetrahydro-4,1-prop[1]enonaphtho[1,2- c]furan-3,12(1H)-dione (**94b**)*

A flask charged with allylic alcohol **93b** (1.27 g, 4.29 mmol, 1 equiv) and copper(I) thiophene-2-carboxylate (82 mg, 0.43 mmol, 0.10 equiv) was sparged with oxygen for 5 min. Water saturated benzene (11 mL) was added and the suspension was stirred till the allylic alcohol was solved completely. Pivaldehyde (3.26 mL, 30.0 mmol, 7 equiv) was added in seven portions (1 equivalent/hour). The green-blueish reaction mixture was stirred after complete addition at 23 °C for 18 h. Another

portion of copper(I) thiophene-2-carboxylate (82 mg, 0.43 mmol, 0.10 equiv) was added and the mixture was stirred for 5 h. Excess peroxy-species were quenched by the addition of saturated aqueous sodium thiosulfate solution (5 mL) and saturated aqueous sodium bicarbonate solution (25 mL). The biphasic mixture was extracted with dichloromethane (4 × 30 mL). The combined organic layers were dried over sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. The crude product was solved in dichloromethane (40 mL). Sodium bicarbonate (1.08 g, 12.9 mmol, 3.00 equiv) and Dess–Martin periodinane (3.64 g, 8.58 mmol, 2.00 equiv) were added at 0 °C. The reaction was stirred for 15 min at 0 °C and 1.5 h at 23 °C. Excess periodinane was quenched by the addition of saturated aqueous sodium thiosulfate solution (10 mL) and saturated aqueous sodium bicarbonate solution (50 mL). The biphasic mixture was extracted with dichloromethane (4 × 30 mL). The combined organic layers were dried over sodium sulfate and filtered. The filtrate was concentrated under reduced pressure. Purification by flash column chromatography on silica gel (5% ethyl acetate in cyclohexane) afforded lactone **94b** (445 mg, 33%) and regioisomeric lactone **95b** (433 mg, 32%) as both colorless crystalline solids. **Analytical Data for 94b and 95b:** The physical data were identical in all respects to those previously reported [54].

3.58. Salimabromide (7)

A flask charged with lactone **94b** (438 mg, 1.41 mmol, 1 equiv) and silver trifluoroacetate (935 mg, 4.23 mmol, 3.00 equiv) was sparged with nitrogen. Trifluoroacetic acid (10 mL) was added and the mixture was stirred at 0 °C until a clear solution was formed. Bromine (0.22 mL, 4.2 mmol, 3.0 equiv) was added dropwise under rigorous stirring. The white-orange suspension was stirred for 10 min at 0 °C. Excess bromine and trifluoroacetic acid were quenched by the addition of saturated aqueous sodium thiosulfate solution (10 mL) and saturated aqueous sodium bicarbonate solution (250 mL). The suspension was extracted with dichloromethane (4 × 50 mL). The combined organic extracts were dried over sodium sulfate. The dried solution was filtered and concentrated under reduced pressure. Purification by flash column chromatography on silica gel afforded salimabromide (**7**) (296 mg, 45%) and monobrominated product (7-bromo) (115 mg, 21%) as both colorless crystalline solids. The physical data were identical in all respects to those previously reported [10,54].

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Author contributions

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Supplementary data

Supplementary data related to this article can be found at "XY".

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