# Supporting Information

## Ring-Expansion of 1-Indanones to 2-Halo-1-naphthols

as an Entry Point to Gilvocarcin Natural Products

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1. General Experimental Details

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. Reactions at low temperatures were carried out in a Dewar vessel filled with a cooling agent: acetone/dry ice (−78 °C), acetonitrile/dry ice (−40 °C) or distilled water/ice (0 °C). Reaction temperatures above 23 °C conducted in a heated oil bath or a metal block. 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 or Macherey-Nagel 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 (KMnO₄) or ceric ammonium molybdate solution (CAM) and were developed by heating with a heat gun.

Flash-Column Chromatography (FCC) was performed as described by Still et al.[1] employing silica gel (60 Å, 40–63 μm, Merck) or magnesium silicate Florisil® (60–100 mesh, Carl Roth). The yields refer to chromatographically and spectroscopically (¹H and ¹³C NMR) pure material.

Solvents and Reagents as pentane (pent), acetonitrile (MeCN), chloroform (CHCl₃), dichloromethane (CH₂Cl₂), diethyl ether (Et₂O), cyclohexane (c-hex), n-hexane (n-hex), ethyl acetate (EtOAc), 1,4-dioxane, N,N-dimethylformamide (DMF), tetrahydrofuran (THF) and toluene (PhMe) were purchased from Acros Organics or Sigma Aldrich as ‘extra dry’ reagents and used as received. Triethylamine (Et₃N, Sigma Aldrich) and N-chlorosuccinimide (NCS, TCI) were used without further purification. Other reagents or solvents were purchased from chemical suppliers (Sigma-Aldrich, TCI, Fisher Scientific or others) and were used as received. Solvents for extraction, crystallization and flash column chromatography as petroleum ether (40–60 °C) were purchased in technical grade and distilled under reduced pressure prior to use. The molarity of n-butyllithium (n-BuLi) and tert-butyllithium (t-BuLi) solutions was determined by titration against diphenyl acetic acid as indicator (average of three determinations).[2]

NMR Spectra were measured on a Bruker Avance Neo 400 MHz spectrometer and a Bruker Avance II 600 MHz spectrometer at Leopold–Franzens–University Innsbruck (LFU Innsbruck). Proton chemical shifts are expressed in parts per million (ppm, δ scale) and are referenced to residual proton in the NMR solvent (CD₂CN: δ = 1.94; CD₂OD: δ = 3.31; CHDCl₂: δ = 5.32; CHCl₃: δ = 7.26). 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 (CD₂CN: δ = 118.26; CD₂OD: δ = 49.00; CD₂Cl₂: δ = 53.84; CDCl₃: δ = 77.16). Fluorine chemical shifts are expressed in parts per million (δ scale) and are referenced to CFCl₃ (Bruker NMR set-up) internal standard. ¹H- and ¹⁹F-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), 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. In addition 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 software MestReNova 12.0.2 from Mestrelab Research.

**Infrared Spectra (IR)** were recorded on a Perkin Elmer Spectrum BX II FT-IR system. If required, substances were dissolved in CH$_2$Cl$_2$ 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).

**High-Resolution Mass Spectra (HRMS)** as ESI-HRMS were recorded on a Thermo Scientific™ Q Exactive™ Orbitrap Mass Spectrometer at LFU Innsbruck. DESI-HRMS as well as LTP-HRMS were recorded on a Thermo Scientific™ LTQ Orbitrap XL™ Hybrid Ion Trap-Orbitrap Mass Spectrometer equipped with a 3-in-1 ambient ionization interface.

**Melting Points (MP)** were measured with an SRS-MPA120 EZ-Melt Melting Point Apparatus in open glass capillaries and are uncorrected.
2. Cyclopropanation–Ring-Expansion (CPRE) of 1-Indanones

2.1 Optimization of the CPRE towards 2-Chloro-1-naphthols

![Chemical structure](image)

| Entry | Reagents | Temperature | Time | Deprotection | Solvent | 13 | 14 |
|-------|----------|-------------|------|--------------|---------|----|----|
| 1     | CCl₃CO₂Et, NaOMe | 0 °C | 4 h | - | pentane-H₂O (0.5 M) | 0% | 0% |
| 2     | CHCl₃, NaOH, BnEt₃NCl | 45 °C | 3 d | - | CH₂Cl₂-H₂O (0.5 M) | 0% | 0% |
| 3     | CHCl₃, KOT-Bu | 0 to 23 °C | 2 h | - | pentane (0.5 M) | 18% | 12% |
| 4     | CHCl₃, KOT-Bu | −78 to 23 °C | 3 h | - | pentane (0.5 M) | 10% | 55% |
| 5     | CHCl₃, KOT-Bu | −78 to 23 °C | 3 h | aq. HCl | pentane (0.5 M) | 0% | 86% |
| 6     | CHCl₃, KOT-Bu | −78 to 23 °C | 2 h | aq. HCl | CH₂Cl₂ (0.5 M) | 0% | 40% |
| 7     | CHCl₃, KOT-Bu | −78 to 23 °C | 2 h | aq. HCl | PhMe (0.5 M) | 0% | 40% |
| 8     | CHCl₃, KOT-Bu | −78 to 23 °C | 2 h | aq. HCl | MeCN (0.5 M) | 0% | 5% |
| 9     | CHCl₃, KOT-Bu | −78 to 23 °C | 2 h | aq. HCl | CHCl₃ (0.5 M) | 0% | 35% |
| 10    | CHCl₃, KOT-Bu | −78 to 23 °C | 2 h | TBAF | pentane (0.2 M) | 0% | 59% |
| 11c   | CHCl₃, KOT-Bu | −78 to 23 °C | 2 h | TBAF | pentane (0.2 M) | 0% | 80% |

a 2.2 equivalents of Cl-source and 2.0 equivalents of base were used.

b "aq. HCl" = 4 M HCl, 40 min, 23 °C. "TBAF" = 1.1 eq TBAF (1 M in THF), 30 min, 23 °C.

c These conditions were preferred over the conditions from Entry 5 for substrate compatibility of a broader scope.
2.2 Optimization of the CPRE towards 2-Bromo-1-naphthols

![Chemical structure diagram]

| Entry | R   | KOt-Bu | CHBr₃ | Solvent  | Temperature | Deprotection                        | 15 | 16 | 17 |
|-------|-----|--------|-------|----------|-------------|-------------------------------------|----|----|----|
| 1     | TMS | 2.0 eq | 2.2 eq| pentane  | ~78 to 23 °C | TBAF-xH₂O, THF, 0.5 h                | 0% | 0% | 33%|
| 2     | TMS | 2.0 eq | 2.2 eq| pentane  | ~78 to 23 °C | TBAF-xH₂O, THF, 0.5 h                | 0% | 0% | 47%|
| 3     | TBS⁵ | 2.0 eq | 2.2 eq| pentane  | ~78 to 23 °C | --                                  | 43%| 36%| 0% |
| 4     | TBS⁵ | 6.0 eq | 5.0 eq| pentane  | ~78 to 23 °C | --                                  | 5% | 76%| 0% |
| 5     | TBS⁵ | 6.0 eq | 5.0 eq| n-hexane | 23 °C       | --                                  | 0% | 79%| 0% |
| 6     | TBS⁵ | 6.0 eq | 5.0 eq| c-hexane | 23 °C     | acq. HCl (2 M), 1 h                  | 0% | 74%| 0% |
| 7     | TBS⁵ | 6.0 eq | 5.0 eq| c-hexane | 23 °C     | TBAF (1 M in THF), 0.5 h              | 0% | 12%| 36%|
| 8     | TBS⁵ | 6.0 eq | 5.0 eq| c-hexane | 23 °C     | KF, MeCN-H₂O, 22 h                   | 0% | 0% | 64%|
| 9     | TBS⁵ | 6.0 eq | 5.0 eq| c-hexane | 23 °C     | KF-Al₂O₃, MeCN-THF, 4.5 h             | 0% | 0% | 0% |
| 10    | TBS⁵ | 6.0 eq | 5.0 eq| c-hexane | 23 °C     | DBU, MeCN-H₂O, 1.5 h                  | 0% | 0% | 67%|
| 11    | TBS⁵ | 6.0 eq | 5.0 eq| c-hexane | 23 °C     | KOAc, DMF-H₂O, 22 h                  | 0% | 0% | 0% |
| 12    | TIPS | 6.0 eq | 5.0 eq| pentane  | 23 °C     | --                                  | 0% | 83%| 0% |
| 13    | TIPS | 6.0 eq | 5.0 eq| pentane  | 23 °C     | TBAF (1 M in THF), 1 h                | 0% | 0% | 60%|
| 14    | TIPS | 4.5 eq | 2.0 eq| pentane  | 23 °C     | --                                  | 0% | 0% | 0% |
| 15    | TIPS | 4.5 eq | 2.0 eq| n-hexane | 23 °C     | KOAc, DMF-H₂O, 1 h                   | 0% | 0% | 0% |
| 16    | TIPS | 4.5 eq | 2.0 eq| n-hexane | ~78 to 23 °C | --                                  | 0% | 88%| 0% |
| 17    | TIPS | 4.5 eq | 2.0 eq| n-hexane | ~78 to 23 °C | KOAc, DMF-H₂O, 1 h                   | 0% | 0% | 85%|
| 18    | TIPS | 2.0 eq | 2.2 eq| pentane  | ~78 to 23 °C | TBAF (1 M in THF), 1 h                | 0% | 0% | 57%|

*Base was added at 23 °C. CHBr₃ was added at the temperature given in the table with subsequent warming to 23 °C.

*Base was added at ~78 °C. CHBr₃ was added at ~78 °C with subsequent warming to 23 °C.

*We want to annotate, that the TBS-protection of 1-indanones is highly sensitive to the used amount of the solvent (benzene) with slightly higher dilutions already leading to significantly lower conversion, even after extended reaction times.

*Repeating this reaction revealed a limited reproducibility of the yield. The best yield is given in the table. For detailed information, see text.

*Repeating this reaction revealed a reliable reproducibility of the yield.
2.3 General Procedures

General Procedure Towards 2-Chloronaphthols (Procedure A)

Triethylamine (158 µL, 1.13 mmol, 1.50 equiv) and trimethylsilyl chloride (145 µL, 1.13 mmol, 1.50 equiv) were added in sequence to a suspension of sodium iodide (11.3 mg, 75.7 µmol, 10 mol%) and indanone (757 µmol, 1 equiv) in acetonitrile (910 µL, 0.83 M) at 0 °C. The resulting suspension was allowed to warm to 23 °C and stirred for 16 hours. After removal of the solvent under reduced pressure, the residue was dissolved in n-hexane (5 mL) and the suspension was filtered through a short plug of Celite®. The filtrate was then concentrated under reduced pressure to afford the crude silyl enol ether. This material was used immediately without further purification.

The crude silyl enol ether was dissolved in pentane (900 µL, 0.84 M), cooled to −78 °C and slowly added to a suspension of potassium tert-butoxide (sublimed grade, 170 mg, 1.51 mmol, 2.00 equiv) in pentane (1.51 mL, 1 M) at −78 °C. The flask of the crude silyl enol ether was rinsed for three times with pentane (3 × 800 µL) and added to the reaction in the same fashion. A solution of chloroform (133 µL, 1.67 mmol, 2.20 equiv) in pentane (1.67 mL, 1 M) was added dropwise to the mixture and the suspension was stirred at −78 °C for 30 minutes before allowing to warm to 23 °C. After stirring for 1.5 hours, water (2 mL) was added to the reaction mixture and the resulting solution was concentrated to 4 mL under reduced pressure. Tetrabutylammonium fluoride trihydrate (358 mg, 1.13 mmol, 1.50 equiv) was added in one portion and the solution was stirred vigorously for 40 minutes. Aqueous hydrochloric acid (1 M, 5 mL) was added and the resulting solution was extracted with ethyl acetate (3 × 10 mL). The organic layer was then washed with water (2 × 10 mL) and a saturated aqueous solution of sodium chloride (10 mL) and the washed solution was dried over magnesium sulfate. Filtration of the dried solution followed by concentration under reduced pressure gave the crude product, which was purified by silica gel chromatography to give the desired 2-chloronaphthols.

General Procedure Towards 2-Bromonaphthols (Procedure B)

Triethylamine (82.0 µL, 588 µmol, 1.40 equiv) and triisopropylsilyl trifluoromethanesulfonate (124 µL, 462 µmol, 1.10 equiv) were sequentially added to a solution of indanone (420 µmol, 1 equiv) in chloroform (5.25 mL, 0.08 M) at 23 °C. The reaction was stirred until full conversion (0.5 to 1.5 h). Reaction progress was visualized by basic Al₂O₃-TLC-monitoring. If remaining starting material was
indicated after two hours of stirring, additional triethylamine (199 µL, 1.43 mmol, 3.40 equiv) and trisopropylsilyl trifluoromethanesulfonate (158 µL, 588 µmol, 1.40 equiv) were added and stirred until full conversion (only needed for substrate 24-Br in our hands). The mixture was diluted with cyclohexane (5 mL), filtered through a short plug of silica and the filtrate was concentrated under reduced pressure at 23 °C. The crude silyl enol ether was used immediately without further purification. The crude silyl enol ether was dissolved in n-hexane (600 µL, 0.7 M), cooled to −78 °C and added to a suspension of potassium tert-butoxide (sublimed grade, 212 mg, 1.89 mmol, 4.50 equiv) in n-hexane (859 µL, 2.2 M) at −78 °C. The flask of the crude silyl enol ether was rinsed with n-hexane (3 × 500 µL) and added to the reaction in the same fashion. After 20 minutes, a solution of freshly distilled bromoform (73.0 µL, 840 µmol, 2.00 equiv) in n-hexane (859 µL, 2.2 M) was added dropwise at −78 °C and stirred at that temperature for one hour. The reaction was then warmed to 23 °C within one hour and stirred for an additional hour. The solvent was removed under reduced pressure to give the crude silylated 2-bromonaphthol, which was dissolved in N,N-dimethylformamide-water (20:1, 1.68 mL, 0.25 M). Potassium acetate (41.0 mg, 420 µmol, 1.00 equiv) was added and the reaction was stirred for one hour at 23 °C. If silica-TLC-monitoring indicated remaining starting material after 1.5 hours, additional potassium acetate (41.0 mg, 420 µmol, 1.00 equiv) was added and the reaction mixture was stirred at 45 °C until full conversion (only needed for substrates 27-Br and 28-Br in our hands). Water (4 mL) was added to the reaction mixture and the resulting solution was extracted with diethyl ether (6 × 4 mL). The combined organic layers were washed with water (8 mL) and a saturated aqueous solution of sodium chloride (8 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated under reduced pressure. Purification by silica gel chromatography gave the desired 2-bromonaphthols.

**General Procedure Towards 2-Bromonaphthols for Substrates 31-Br and 32-Br (Procedure C)**

Procedure C follows the protocol of Procedure B only differing in the deprotection. Instead of dissolving the crude silylated 2-bromonaphthol in N,N-dimethylformamide-water, it was dissolved in tetrahydrofuran (10.5 mL, 0.04 M) and cooled to 0 °C, before tetrabutylammonium fluoride (1 M in tetrahydrofuran, 675 µL, 675 µmol, 1.50 equiv) was added dropwise to the mixture and stirred for one hour at that temperature. Aqueous hydrochloric acid (1 M, 4 mL) was added and the mixture was poured onto a mixture of water and ethyl acetate (1:1, 10 mL). The phases were separated and the aqueous layer was extracted with ethyl acetate (2 × 20 mL). The combined organic layers were washed with water (8 mL) and a saturated aqueous solution of sodium chloride (8 mL). The washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated under reduced pressure. Purification by silica gel chromatography gave the desired 2-bromonaphthols.
2.4 Substrate Scope (2-Chloro-1-naphthols)

2-Chloronaphthalen-1-ol (18-Cl)

\[
\begin{align*}
\text{OH} & \quad \text{Cl} \\
\end{align*}
\]

Isolated: 108 mg (80%)

Data consistent with literature: *Angew. Chem. Int. Ed.*, 2013, 52, 5271–5274.

2,7-Dichloronaphthalen-1-ol (19-Cl)

\[
\begin{align*}
\text{Cl} & \quad \text{OH} & \quad \text{Cl} \\
\end{align*}
\]

Isolated: Yellow oil, 121 mg (75%)

**TLC** (20% diethyl ether in pentane): \( R_f = 0.70 \) (UV, KMnO₄).

\(^1\text{H NMR}\) (400 MHz, chloroform-\( d \)) \( \delta \) 8.20 (d, \( J = 2.1 \) Hz, 1H), 7.70 (d, \( J = 8.7 \) Hz, 1H), 7.43 (dd, \( J = 8.8, 2.1 \) Hz, 1H), 7.38 – 7.32 (m, 2H), 6.00 (s, 1H).

\(^{13}\text{C NMR}\) (101 MHz, chloroform-\( d \)) \( \delta \) 146.5, 132.3, 131.5, 129.3, 127.7, 126.3, 125.1, 121.4, 120.8, 114.8.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_{\max} \): 3513 (m, br), 1586 (w), 1265 (s), 1090 (vs), 899 (m) cm\(^{-1}\).

**HRMS** (ESI) calc. for C\(_{10}\)H\(_7\)OCl \([\text{M-H}]^-\) : 210.9723 found: 210.9724.

5-Bromo-2-chloronaphthalen-1-ol (20-Cl)

\[
\begin{align*}
\text{Br} & \quad \text{Cl} & \quad \text{OH} \\
\end{align*}
\]

Isolated: Orange solid, 160 mg (82%)

**TLC** (20% diethyl ether in pentane): \( R_f = 0.75 \) (UV, KMnO₄).

**mp**: 86–90 °C.

\(^1\text{H NMR}\) (400 MHz, chloroform-\( d \)) \( \delta \) 8.19 (d, \( J = 8.5 \) Hz, 1H), 7.76 (dd, \( J = 11.6, 8.3 \) Hz, 2H), 7.44 (d, \( J = 9.2 \) Hz, 1H), 7.32 (t, \( J = 7.9 \) Hz, 1H), 6.04 (s, 1H).

\(^{13}\text{C NMR}\) (101 MHz, chloroform-\( d \)) \( \delta \) 147.1, 131.8, 130.9, 127.2, 126.5, 125.6, 122.6, 122.1, 120.3, 114.7.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_{\max} \): 3509 (w), 1619 (m), 1395 (w), 1237 (s), 1192 (vs), 870 (w) cm\(^{-1}\).

**HRMS** (ESI) calc. for C\(_{10}\)H\(_8\)BrClO \([\text{M-H}]^-\) : 254.9218 found: 254.9220.
2-Chloro-6-fluoronaphthalen-1-ol (21-Cl)

Isolated: Colorless solid, 116 mg (78%)

TLC (20% diethyl ether in pentane): \( R_f = 0.80 \) (UV, KMnO\(_4\)).

mp: 82–85 °C.

\(^1\)H NMR (400 MHz, chloroform-\(d\)) \( \delta \) 8.10 (dd, \( J = 9.2, 5.6 \) Hz, 1H), 7.29 – 7.23 (m, 2H), 7.20 – 7.13 (m, 2H), 5.92 (s, 1H).

\(^{13}\)C NMR (101 MHz, chloroform-\(d\)) \( \delta \) 161.3 (d, \( J = 247 \) Hz), 147.3 (d, \( J = 1.3 \) Hz), 134.3 (d, \( J = 9.4 \) Hz), 127.2, 124.9 (d, \( J = 9.2 \) Hz), 121.4, 120.2 (d, \( J = 5.1 \) Hz), 116.3 (d, \( J = 25.3 \) Hz), 112.9 (d, \( J = 2.8 \) Hz), 110.9 (d, \( J = 20.9 \) Hz).

IR (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3521 (w), 1632 (m), 1511 (vs), 1257 (s), 955 (m), 867 (w) cm\(^{-1}\).

HRMS (ESI) calc. for C\(_{10}\)H\(_5\)ClFO [M-H]: 195.0018 found: 195.0018.

5-Iodo-2-chloronaphthalen-1-ol (22-Cl)

Isolated: Colorless solid, 178 mg (77%)

TLC (20% diethyl ether in pentane): \( R_f = 0.80 \) (UV, KMnO\(_4\)).

mp: 79–80 °C.

\(^1\)H NMR (400 MHz, chloroform-\(d\)) \( \delta \) 8.24 (dt, \( J = 8.4, 1.0 \) Hz, 1H), 8.08 (dd, \( J = 7.3, 1.2 \) Hz, 1H), 7.62 (dd, \( J = 9.1, 0.9 \) Hz, 1H), 7.43 (d, \( J = 9.1 \) Hz, 1H), 7.18 (dd, \( J = 8.4, 7.3 \) Hz, 1H), 6.02 (s, 1H).

\(^{13}\)C NMR (101 MHz, chloroform-\(d\)) \( \delta \) 146.9, 138.4, 134.1, 127.3, 127.0, 125.3, 124.8, 123.1, 114.6, 98.9.

IR (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3430 (w), 1455 (s), 1245 (vs), 1189 (m), 1147 (s), 1070 (m) cm\(^{-1}\).

HRMS (ESI) calc. for C\(_{10}\)H\(_5\)OICl [M-H]: 302.9079 found: 302.9080.

2-Chloro-7-(trifluoromethyl)naphthalen-1-ol (23-Cl)

Isolated: Colorless solid, 103 mg (55%)

TLC (20% diethyl ether in pentane): \( R_f = 0.69 \) (UV, KMnO\(_4\)).

mp: 98–99 °C.

\(^1\)H NMR (400 MHz, chloroform-\(d\)) \( \delta \) 8.54 (s, 1H), 7.88 (d, \( J = 8.6 \) Hz, 1H), 7.68 – 7.66 (dd, \( J = 8.7, 1.0 \) Hz, 1H), 7.50 (d, \( J = 8.8 \) Hz, 1H), 7.43 (d, \( J = 8.8 \) Hz, 1H), 6.11 (s, 1H).
13C NMR (101 MHz, chloroform-d) δ 174.9, 134.3, 128.8, 128.3, 128.0 (q, J = 32.5 Hz), 124.3 (q, J = 272 Hz), 123.4, 122.4 (q, J = 3.1 Hz), 120.8, 120.4 (q, J = 4.6 Hz), 114.9.

IR (Diamond-ATR, neat) ʋ max: 3399 (w), 1458 (m), 1301 (m), 1243 (m), 1078 (w), 909 (w) cm⁻¹.

HRMS (ESI) calc. for C₁₁H₅ClF₃O [M-H]⁻: 244.9987 found: 244.9987.

8-Bromo-2-chloro-5-fluoronaphthalen-1-ol (24-Cl)

\[
\begin{array}{c}
\text{Br} \\
\text{OH} \\
\text{F} \\
\text{Cl}
\end{array}
\]

Isolated: Yellow solid, 157 mg (75%)

TLC (20% diethyl ether in pentane): Rᵣ = 0.80 (UV, KMnO₄).

mp: 92–94 °C.

1H NMR (400 MHz, chloroform-d) δ 7.69 – 7.64 (m, 2H), 7.55 – 7.51 (m, 2H), 6.99 (t, J = 8.9 Hz, 1H).

13C NMR (101 MHz, chloroform-d) δ 158.4 (d, J = 253 Hz), 147.7 (d, J = 3.5 Hz), 132.6 (d, J = 8.5 Hz), 128.5 (d, J = 1.9 Hz), 125.8 (d, J = 17.6 Hz), 122.8 (d, J = 4.1 Hz), 118.9, 114.0 (d, J = 8.2 Hz), 110.8 (d, J = 21.7 Hz), 110.1 (d, J = 4.4 Hz).

IR (Diamond-ATR, neat) ʋ max: 3460 (m), 3089 (w), 1445 (s), 1416 (m), 1140 (m), 920 (w) cm⁻¹.

HRMS (ESI) calc. for C₁₀H₅BrClFO [M-H]⁻: 272.9124 found: 272.9124.

2-Chloro-6-(methoxymethoxy)naphthalen-1-ol (25-Cl)

\[
\begin{array}{c}
\text{O} \\
\text{O} \\
\text{Cl} \\
\text{OH}
\end{array}
\]

Isolated: Brown solid, 119 mg (66%)

TLC (20% diethyl ether in pentane): Rᵣ = 0.79 (UV, KMnO₄).

mp: 261 °C (decomposition).

1H NMR (400 MHz, chloroform-d) δ 8.14 (d, J = 9.1 Hz, 1H), 7.33 (d, J = 3.3 Hz, 1H), 7.31 (d, J = 10.1 Hz, 1H), 7.27 – 7.21 (m, 2H), 6.01 (s, 1H), 5.30 (s, 2H), 3.53 (s, 3H).

13C NMR (101 MHz, chloroform-d) δ 155.8, 147.2, 134.7, 126.7, 123.9, 120.4, 120.1, 119.0, 112.0, 109.9, 94.5, 56.3.

IR (Diamond-ATR, neat) ʋ max: 3550 (w), 3060 (m), 1472 (m), 1320 (vs), 1068 (m), 855 (w) cm⁻¹.

HRMS (ESI) calc. for C₁₂H₁₀ClO₃ [M-H]⁻: 237.0324 found: 237.0323.
5-(Benzyloxy)-2-chloronaphthalen-1-ol (26-Cl)

\[
\begin{align*}
\text{Isolated: Yellowish gum, 153 mg (71\%)} \\
\text{TLC (20\% diethyl ether in pentane): } R_f = 0.50 \text{ (UV, KMnO}_4\text{).} \\
^{1}H \text{ NMR (400 MHz, chloroform-}d\text{) } \delta 7.87 \text{ (dd, } J = 9.0, 0.89 \text{ Hz, 1H), 7.80 (dt, } J = 8.4, 0.9 \text{ Hz, 1H), 7.52} \\
\text{– 7.51 (m, 2H), 7.44 – 7.40 (m, 3H), 7.37 – 7.34 (m, 2H), 6.93 (dd, } J = 7.7, 0.9 \text{ Hz, 1H), 5.97 (s, 1H),} \\
\text{5.24 (s, 2H).} \\
^{13}C \text{ NMR (101 MHz, chloroform-}d\text{) } \delta 154.5, 146.9, 137.0, 128.8, 128.2, 127.5, 126.4, 125.7, 125.2, \\
115.6, 114.7, 114.6, 106.3, 70.4. \text{ (Note: One } ^{13}\text{C-signal is missing due to overlap.)} \\
\text{IR (Diamond-ATR, neat) } \tilde{\nu}_\text{max}: 3550 \text{ (w), 1512 (vs), 1457 (s), 1110 (m), 1008 (w)} \text{ cm}^{-1}. \\
\text{HRMS (EI) calc. for } C_{17}H_{13}ClO_2 [M]^+: 284.0599 \text{ found: 284.0599.}
\end{align*}
\]

2-Chloro-6,7-dimethoxynaphthalen-1-ol (27-Cl)

\[
\begin{align*}
\text{Isolated: Grey solid, 150 mg (83\%)} \\
\text{TLC (50\% dichloromethane in cyclohexane): } R_f = 0.23 \text{ (UV, CAM).} \\
\text{mp: 99–103 °C.} \\
^{1}H \text{ NMR (400 MHz, chloroform-}d\text{) } \delta 7.45 \text{ (s, 1H), 7.20 (d, } J = 8.7 \text{ Hz, 1H), 7.17 (d, } J = 8.8 \text{ Hz,} \\
1\text{H), 7.01 (s, 1H), 6.05 (s, 1H), 4.00 (s, 3H), 3.96 (s, 3H).} \\
^{13}C \text{ NMR (101 MHz, chloroform-}d\text{) } \delta 150.0, 149.6, 146.0, 129.2, 124.2, 119.8, 119.4, 112.4, \\
106.3, 101.0, 56.0, 55.9. \\
\text{IR (Diamond-ATR, neat) } \tilde{\nu}_\text{max}: 3525 \text{ (w), 3071 (w), 1427 (vs), 1219 (m), 1163 (s), 869 (s)} \text{ cm}^{-1}. \\
\text{HRMS (ESI) calc. for } C_{12}H_{10}ClO_3 [M-H]^+: 237.0324 \text{ found: 237.0322.} \text{ (Note: Higher yields were obtained following the general procedure B using chloroform instead of bromoform.)}
\end{align*}
\]

2-Chloro-6-methoxynaphthalen-1-ol (28-Cl)

\[
\begin{align*}
\text{Isolated: Colorless solid, 128 mg (81\%)} \\
\text{TLC (20\% diethyl ether in pentane): } R_f = 0.58 \text{ (UV, KMnO}_4\text{).} \\
\text{mp: 72–74 °C.}
\end{align*}
\]
\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 7.97 (d, \(J = 9.2\) Hz, 1H), 7.16 (d, \(J = 8.8\) Hz, 1H), 7.08 (d, \(J = 8.9\) Hz, 1H), 7.02 (dd, \(J = 9.2, 2.5\) Hz, 1H), 6.89 (d, \(J = 2.4\) Hz, 1H), 5.86 (s, 1H), 3.75 (s, 3H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 158.3, 147.3, 134.8, 126.6, 123.8, 119.8, 119.7, 118.7, 111.6, 105.8, 55.4.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 8.13 (d, \(J = 8.9\) Hz, 1H), 7.31 (d, \(J = 8.8\) Hz, 1H), 7.23 (d, \(J = 8.9\) Hz, 1H), 7.16 – 7.10 (m, 2H), 5.97 (s, 1H), 1.05 (s, 9H), 0.27 (s, 6H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 154.4, 147.3, 134.9, 126.5, 123.9, 122.2, 120.2, 119.8, 115.0, 111.7, 25.8, 18.4, –4.2.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 8.33 (d, \(J = 7.6\) Hz, 2H), 8.16 (d, \(J = 8.5\) Hz, 1H), 7.70 (t, \(J = 7.4\) Hz, 1H), 7.57 (q, \(J = 8.0\) Hz, 3H), 7.46 (d, \(J = 9.1\) Hz, 1H), 7.40 (d, \(J = 7.5\) Hz, 1H), 7.37 (d, \(J = 9.1\) Hz, 1H), 6.09 (s, 1H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 165.2, 147.4, 146.8, 134.1, 130.5, 129.3, 128.9, 127.0, 126.7, 126.1, 125.9, 120.5, 119.4, 114.6, 114.6.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 7.97 (d, \(J = 9.2\) Hz, 1H), 7.16 (d, \(J = 8.8\) Hz, 1H), 7.08 (d, \(J = 8.9\) Hz, 1H), 7.02 (dd, \(J = 9.2, 2.5\) Hz, 1H), 6.89 (d, \(J = 2.4\) Hz, 1H), 5.86 (s, 1H), 3.75 (s, 3H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 158.3, 147.3, 134.8, 126.6, 123.8, 119.8, 119.7, 118.7, 111.6, 105.8, 55.4.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 8.13 (d, \(J = 8.9\) Hz, 1H), 7.31 (d, \(J = 8.8\) Hz, 1H), 7.23 (d, \(J = 8.9\) Hz, 1H), 7.16 – 7.10 (m, 2H), 5.97 (s, 1H), 1.05 (s, 9H), 0.27 (s, 6H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 154.4, 147.3, 134.9, 126.5, 123.9, 122.2, 120.2, 119.8, 115.0, 111.7, 25.8, 18.4, –4.2.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 8.33 (d, \(J = 7.6\) Hz, 2H), 8.16 (d, \(J = 8.5\) Hz, 1H), 7.70 (t, \(J = 7.4\) Hz, 1H), 7.57 (q, \(J = 8.0\) Hz, 3H), 7.46 (d, \(J = 9.1\) Hz, 1H), 7.40 (d, \(J = 7.5\) Hz, 1H), 7.37 (d, \(J = 9.1\) Hz, 1H), 6.09 (s, 1H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 165.2, 147.4, 146.8, 134.1, 130.5, 129.3, 128.9, 127.0, 126.7, 126.1, 125.9, 120.5, 119.4, 114.6, 114.6.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 7.97 (d, \(J = 9.2\) Hz, 1H), 7.16 (d, \(J = 8.8\) Hz, 1H), 7.08 (d, \(J = 8.9\) Hz, 1H), 7.02 (dd, \(J = 9.2, 2.5\) Hz, 1H), 6.89 (d, \(J = 2.4\) Hz, 1H), 5.86 (s, 1H), 3.75 (s, 3H).

\[^{13}C\text{ NMR}\] (101 MHz, chloroform-\(d\)) \(\delta\) 158.3, 147.3, 134.8, 126.6, 123.8, 119.8, 119.7, 118.7, 111.6, 105.8, 55.4.

\[^{1}H\text{ NMR}\] (400 MHz, chloroform-\(d\)) \(\delta\) 8.13 (d, \(J = 8.9\) Hz, 1H), 7.31 (d, \(J = 8.8\) Hz, 1H), 7.23 (d, \(J = 8.9\) Hz, 1H), 7.16 – 7.10 (m, 2H), 5.97 (s, 1H), 1.05 (s, 9H), 0.27 (s, 6H).

Note: Higher yields were obtained following the general procedure B using chloroform instead of bromoform.

6-((Tert-butyldimethylsilyl)oxy)-2-chloronaphthalen-1-ol (29-Cl)

6-Chloro-5-hydroxynaphthalen-1-yl benzoate (30-Cl)
6-Chloro-5-hydroxynaphthalen-2-yl pivalate (31-Cl)

Isolated: Colorless solid, 133 mg (63%)

TLC (20% diethyl ether in pentane): $R_t = 0.82$ (UV, KMnO$_4$).

mp: 141–143 °C (decomposition).

$^1$H NMR (400 MHz, chloroform-$d$) $\delta$ 8.20 (d, $J = 9.1$ Hz, 1H), 7.46 (d, $J = 2.0$ Hz, 1H), 7.35 (d, $J = 8.8$ Hz, 1H), 7.29 (d, $J = 8.9$ Hz, 1H), 7.22 (dd, $J = 9.1, 2.1$ Hz, 1H), 6.05 (s, 1H), 1.41 (s, 9H).

$^{13}$C NMR (101 MHz, chloroform-$d$) $\delta$ 177.4, 149.6, 147.3, 133.9, 126.9, 124.0, 122.5, 121.4, 120.6, 118.4, 113.5, 39.3, 27.3.

IR (Diamond-ATR, neat) $\tilde{\nu}_{\text{max}}$: 3426 (w), 2956 (m), 1730 (vs), 1389 (s), 1067 (s), 869 (m) cm$^{-1}$.

HRMS (ESI) calc. for C$_{15}$H$_{14}$ClO$_3$ [M-H]: 277.0637 found: 277.0639.

2-Chloro-4-phenylnaphthalen-1-ol (32-Cl)

Isolated: Colorless solid, 158 mg (82%)

TLC (20% diethyl ether in pentane): $R_t = 0.67$ (UV, KMnO$_4$).

mp: 123–125 °C.

$^1$H NMR (400 MHz, chloroform-$d$) $\delta$ 8.32 (d, $J = 8.3$ Hz, 1H), 7.85 (d, $J = 8.5$ Hz, 1H), 7.55 (t, $J = 7.5$ Hz, 1H), 7.52 – 7.41 (m, 6H), 7.36 (s, 1H), 6.04 (s, 1H).

$^{13}$C NMR (101 MHz, chloroform-$d$) $\delta$ 146.6, 139.6, 133.9, 131.5, 130.3, 128.5, 127.5, 126.9, 126.7, 126.2, 124.7, 122.5, 113.2. (Note: One $^{13}$C-signal is missing due to overlap.)

IR (Diamond-ATR, neat) $\tilde{\nu}_{\text{max}}$: 3513 (w), 3057 (w), 1587 (m), 1389 (s), 1067 (s), 869 (m) cm$^{-1}$.

HRMS (ESI) calc. for C$_{16}$H$_{14}$ClO$_3$ [M-H]: 253.0426 found: 253.0427.

2-Chloro-3-methylnaphthalen-1-ol (33-Cl)

Isolated: Colorless solid, 110 mg (75%)

TLC (20% diethyl ether in pentane): $R_t = 0.90$ (UV, KMnO$_4$).

mp: 68–70 °C.
H NMR (400 MHz, chloroform-d) δ 8.32 – 8.07 (m, 1H), 7.77 – 7.64 (m, 1H), 7.53 – 7.37 (m, 2H), 7.29 (s, 1H), 6.08 (s, 1H), 2.52 (s, 3H).

C NMR (101 MHz, chloroform-d) δ 147.1, 133.4, 132.6, 126.9, 126.8, 125.2, 122.9, 122.1, 120.6, 115.6, 20.8.

IR (Diamond-ATR, neat) ʋmax: 3517 (w), 3056 (m), 1590 (vs), 1230 (m), 1224 (s), 1033 (w) cm⁻¹.

HRMS (ESI) calc. for C11H8ClO [M–H]⁻: 191.0269 found: 191.0269.

2.5 Substrate Scope (2-Bromo-1-naphthols)

((2-Bromonaphthalen-1-yl)oxy)(tert-butyl)dimethylsilane (16-TBS)

Isolated: Colorless oil, 60.9 mg (43%), see Table 2

TLC (pentane): Rf = 0.64 (UV, CAM).

H NMR (400 MHz, chloroform-d) δ 8.08 (dt, J = 6.8, 3.3 Hz, 1H), 7.78 (dq, J = 6.0, 3.4 Hz, 1H), 7.55 (d, J = 8.8 Hz, 1H), 7.47 (dt, J = 6.4, 3.4 Hz, 2H), 7.36 (d, J = 8.7 Hz, 1H), 1.14 (s, 9H), 0.30 (s, 6H).

C NMR (101 MHz, chloroform-d) δ 148.9, 134.1, 130.6, 129.0, 127.9, 126.4, 125.7, 123.2, 122.7, 110.1, 26.4, 19.1, –2.5.

IR (Diamond-ATR, neat) ʋmax: 2939 (w), 1639 (vs), 1602 (m), 1431 (s), 972 (s), 858 (m) cm⁻¹.

HRMS (ESI) calc. for C16H22BrOSi [M+H]⁺: 337.0618 found: 337.0599.

2-Bromonaphthalen-1-ol (18-Br)

Isolated: 79.6 mg (85%)

Data consistent with literature: J. Org. Chem., 2018, 83, 8036–8053.

2-Bromo-7-chloronaphthalen-1-ol (19-Br)

Isolated: Off-white solid, 88.9 mg (82%)

TLC (25% dichloromethane in cyclohexane): Rf = 0.50 (UV, CAM).

mp: 78–81 °C.

H NMR (400 MHz, chloroform-d) δ 8.22 (dd, J = 2.1, 0.8 Hz, 1H), 7.71 (d, J = 8.8 Hz, 1H), 7.48 (d, J = 8.8 Hz, 1H), 7.45 (dd, J = 8.8, 2.2 Hz, 1H), 7.29 (d, J = 8.8 Hz, 1H), 5.97 (s, 1H).
\[ ^{13}\text{C NMR} \: (101 \text{ MHz, chloroform-}d) \: \delta \: 147.6, 132.3, 132.1, 129.3, 128.8, 127.9, 125.1, 121.7, 121.2, 105.2. \]

\( \text{IR (Diamond-ATR, neat) } \tilde{\nu}_{\text{max}}: 3466 \text{ (m), } 1589 \text{ (w), } 1566 \text{ (m), } 1265 \text{ (vs), } 808 \text{ (w) \ cm}^{-1}. \)

\( \text{HRMS (ESI) calc. for } \text{C}_{10}\text{H}_{5}\text{BrClO } [\text{M-H}]: 254.9218 \text{ found: 254.9214}. \)

2,5-Dibromophthalen-1-ol (20-Br)

\[
\begin{array}{c}
\text{OH} \\
\text{Br} \\
\text{Br}
\end{array}
\]

Isolated: 110 mg (87%)

Data consistent with literature: *Tetrahedron Lett.*, 2005, 46, 4187–4191.

2-Bromo-6-fluoronaphthalen-1-ol (21-Br)

\[
\begin{array}{c}
\text{OH} \\
\text{Br} \\
\text{F}
\end{array}
\]

Isolated: 90.1 mg (89%)

Data consistent with literature: *Org. Biomol. Chem.*, 2004, 2, 3018–3025.

2-Bromo-5-iodonaphthalen-1-ol (22-Br)

\[
\begin{array}{c}
\text{OH} \\
\text{Br}
\end{array}
\]

Isolated: Beige solid, 106 mg (72%)

\( \text{TLC (25\% ethyl acetate in cyclohexane): } R_t = 0.55 \text{ (UV, CAM)}. \)

\( \text{mp: 61–63 ^\circ C}. \)

\[ ^1\text{H NMR} \: (400 \text{ MHz, chloroform-}d) \: \delta \: 8.25 \text{ (dt, } J = 8.3, 0.9 \text{ Hz, } 1\text{H}), 8.09 \text{ (dd, } J = 7.3, 1.1 \text{ Hz, } 1\text{H}), 7.57 \text{ (dd, } J = 9.1, 0.7 \text{ Hz, } 1\text{H}), 7.54 \text{ (d, } J = 9.2 \text{ Hz, } 1\text{H}), 7.17 \text{ (dd, } J = 8.4, 7.3 \text{ Hz, } 1\text{H}), 5.99 \text{ (s, } 1\text{H}). \)

\[ ^{13}\text{C NMR} \: (101 \text{ MHz, chloroform-}d) \: \delta \: 148.1, 138.6, 134.7, 129.9, 127.1, 125.8, 124.8, 123.4, 105.1, 98.9. \]

\( \text{IR (Diamond-ATR, neat) } \tilde{\nu}_{\text{max}}: 3332 \text{ (w), } 1447 \text{ (s), } 1409 \text{ (m), } 1241 \text{ (vs), } 1074 \text{ (s), } 999 \text{ (m) \ cm}^{-1}. \)

\( \text{HRMS (ESI) calc. for } \text{C}_{10}\text{H}_{5}\text{BrIO } [\text{M-H}]: 346.8574 \text{ found: 346.8570}. \)

2-Bromo-7-(trifluoromethyl)naphthalen-1-ol (23-Br)

\[
\begin{array}{c}
\text{F}_3\text{C} \\
\text{Br}
\end{array}
\]

Isolated: White solid, 75.8 mg (62%)
TLC (cyclohexane): \( R_f = 0.27 \) (UV, CAM).

mp: 83 °C.

\(^1\)H NMR (400 MHz, chloroform-\(d_2\)) \( \delta \) 8.58 – 8.54 (m, 1H), 7.88 (d, \( J = 8.4 \) Hz, 1H), 7.67 (dd, \( J = 8.6, 1.9 \) Hz, 1H), 7.61 (d, \( J = 8.8 \) Hz, 1H), 7.37 (d, \( J = 8.8 \) Hz, 1H), 6.08 (s, 1H).

\(^13\)C NMR (101 MHz, Chloroform-\(d_2\)) \( \delta \) 149.1, 135.0 (d, \( J = 0.8 \) Hz), 130.9, 128.8, 128.1 (q, \( J = 32.5 \) Hz), 124.4 (q, \( J = 272 \) Hz), 123.4, 122.6 (q, \( J = 3.1 \) Hz), 121.2, 120.7 (q, \( J = 4.6 \) Hz), 105.4.

\(^19\)F NMR (376 MHz, chloroform-\(d_2\), \( CFCl_3 \) as internal standard) \( \delta \) –62.3 (s).

IR (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3359 (w), 3298 (m), 1397 (s), 1129 (vs), 1103 (m), 909 (w) cm\(^{-1}\).

HRMS (ESI) calc. for \([M-H]^–\): 288.9481 found: 288.9480.

2,8-Bibromo-5-fluoronaphthalen-1-ol (24-Br)

Isolated: Colorless crystals, 90.0 mg (67%)

TLC (13% ethyl acetate in cyclohexane): \( R_f = 0.56 \) (UV, CAM).

mp: 72 °C.

\(^1\)H NMR (400 MHz, chloroform-\(d_2\)) \( \delta \) 7.68 – 7.61 (m, 3H), 7.57 (dd, \( J = 9.0, 0.8 \) Hz, 1H), 6.98 (dd, \( J = 9.4, 8.3 \) Hz, 1H).

\(^13\)C NMR (101 MHz, chloroform-\(d_2\)) \( \delta \) 158.5 (d, \( J = 253 \) Hz), 148.6 (d, \( J = 3.5 \) Hz), 132.4 (d, \( J = 8.5 \) Hz), 131.2 (d, \( J = 1.8 \) Hz), 126.2 (d, \( J = 17.5 \) Hz), 122.7 (d, \( J = 4.2 \) Hz), 114.2 (d, \( J = 8.1 \) Hz), 110.9 (d, \( J = 21.7 \) Hz), 110.0 (d, \( J = 4.4 \) Hz), 109.2 (d, \( J = 0.7 \) Hz).

\(^19\)F NMR (376 MHz, chloroform-\(d_2\), \( CFCl_3 \) as internal standard) \( \delta \) –119.9 (dd, \( J = 9.4, 5.3 \) Hz).

IR (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3391 (w), 3069 (w), 1554 (vs), 1425 (s), 1120 (m), 880 (w) cm\(^{-1}\).

HRMS (ESI) calc. for \( C_{10}H_{4}Br_{2}FO \) [M-H]: 316.8618 found: 316.8622.

2-Bromo-6-(methoxymethoxy)naphthalen-1-ol (25-Br)

Isolated: Brownish oil, 53.5 mg (45%)

TLC (14% ethyl acetate in cyclohexane): \( R_f = 0.44 \) (UV, CAM).

\(^1\)H NMR (400 MHz, chloroform-\(d_2\)) \( \delta \) 8.16 (dt, \( J = 9.2, 0.7 \) Hz, 1H), 7.42 (d, \( J = 8.8 \) Hz, 1H), 7.33 (d, \( J = 2.4 \) Hz, 1H), 7.25 – 7.19 (m, 2H), 5.95 (s, 1H), 5.29 (s, 2H), 3.53 (s, 3H).

\(^13\)C NMR (101 MHz, chloroform-\(d_2\)) \( \delta \) 156.0, 148.4, 135.2, 129.1, 124.2, 120.7, 120.4, 119.0, 109.9, 102.2, 94.6, 56.3.

IR (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3552 (w), 3160, (w) 1618 (s), 1335 (m), 1230 (s), 775 (w) cm\(^{-1}\).
HRMS (ESI) calc. for C_{12}H_{10}BrO_{3} [M-H]⁻: 280.9819 found: 280.9822.

5-(Benzylxy)-2-bromonaphthalen-1-ol (26-Br)

Isolated: White solid, 96.7 mg (70%)

TLC (20% diethyl ether in pentane): \( R_f = 0.50 \) (UV, KMnO₄).

mp: 89 °C.

^{1}H NMR (400 MHz, chloroform-d) \( \delta \) 7.87 (dd, \( J = 9.0, 0.89 \) Hz, 1H), 7.80 (dt, \( J = 8.4, 0.9 \) Hz, 1H), 7.52 – 7.51 (m, 2H), 7.44 – 7.40 (m, 3H), 7.37 – 7.34 (m, 2H), 6.93 (dd, \( J = 7.7, 0.9 \) Hz, 1H), 5.97 (s, 1H), 5.24 (s, 2H).

^{13}C NMR (101 MHz, chloroform-d) \( \delta \) 154.5, 148.0, 137.0, 128.8, 128.2, 127.7, 127.5, 126.5, 126.2, 125.7, 116.0, 114.9, 106.4, 105.3, 70.4.

IR (Diamond-ATR, neat) \( \tilde{\nu} \max \): 3546 (w), 3399 (w), 1701 (s), 1461 (vs), 1343 (m), 948 (m) cm⁻¹.

HRMS (ESI) calc. for C_{17}H_{12}BrO₂ [M-H]⁻: 327.0026 found: 327.0028.

2-Bromo-6,7-dimethoxynaphthalen-1-ol (27-Br)

Isolated: 52.3 mg (44%)

Data consistent with literature: Tetrahedron, 1998, 54, 9875–9894.

2-Bromo-6-methoxynaphthalen-1-ol (28-Br)

Isolated: 49.9 mg (47%)

Data consistent with literature: Tetrahedron Lett., 2005, 46, 4187–4191.

2-Bromo-6-((tert-butyldimethylsilyl)oxy)naphthalen-1-ol (29-Br)

Isolated: White solid, 34.1 mg (23%)

TLC (13% dichloromethane in cyclohexane): \( R_f = 0.38 \) (UV, KMnO₄).

mp: 58 °C.
\[ \text{H NMR (400 MHz, chloroform-}d\text{)} \delta 8.12 (d, J = 9.0 \text{ Hz, 1H}), 7.40 (d, J = 8.8 \text{ Hz, 1H}), 7.16 (d, J = 8.9 \text{ Hz, 1H}), 7.12 (d, J = 2.3 \text{ Hz, 1H}), 7.09 (dd, J = 9.0, 2.4 \text{ Hz, 1H}), 5.90 (s, 1H), 1.02 (s, 9H), 0.25 (s, 6H). \]

\[ \text{IR (Diamond-ATR, neat) } \bar{\nu}_{\text{max}}: 3499 (w), 2945 (m), 1702 (s), 1588 (vs), 1420 (s), 970 (s), 845 (m) \text{ cm}^{-1}. \]

\[ \text{HRMS (ESI) calc. for C}_{16}\text{H}_{20}\text{BrO}_{2} [\text{M-H}^-]: 351.0421 \text{ found: 351.0424.} \]

**Note:** \( \text{S1-Br} \) was obtained in 23% along with 30% of unprotected 6-hydroxynaphthol \( \text{S1-Br} \) (see next) following protocol B.

**2-Bromonaphthalene-1,6-diol (S1-Br)**

\[
\begin{align*}
\text{Isolated: White solid, 30.1 mg (30\%)}
\end{align*}
\]

\[ \text{mp: } 90^\circ \text{C.} \]

\[ \text{H NMR (400 MHz, chloroform-}d\text{)} \delta 8.14 (d, J = 8.9 \text{ Hz, 1H}), 7.41 (d, J = 8.8 \text{ Hz, 1H}), 7.14 - 7.06 (m, 2H), 5.93 (s, 1H), 5.19 (s, 1H). \]

\[ \text{IR (Diamond-ATR, neat) } \bar{\nu}_{\text{max}}: 3451 (w), 1624 (s), 1587 (vs), 1385 (m), 1230 (s), 972 (s) \text{ cm}^{-1}. \]

\[ \text{HRMS (ESI) calc. for C}_{10}\text{H}_{6}\text{BrO}_{2} [\text{M-H}^-]: 236.9557 \text{ found: 236.9561.} \]

**Note:** \( \text{S2-Br} \) was obtained in 59% following protocol B omitting the deprotection step.

\((6\text{-bromo-5-((triisopropylsilyl)oxy)naphthalen-2-yl)oxy})(\text{tert-butyl})\text{dimethylsilane (S2-Br)}\)

\[
\begin{align*}
\text{Isolated: Yellow oil, 126 mg (59\%)}
\end{align*}
\]

\[ \text{TLC (13% dichloromethane in cyclohexane): } R_l = 0.63 \text{ (UV, CAM).} \]

\[ \text{H NMR (400 MHz, chloroform-}d\text{)} \delta 7.99 (d, J = 9.1 \text{ Hz, 1H}), 7.46 (d, J = 8.8 \text{ Hz, 1H}), 7.18 (d, J = 8.8 \text{ Hz, 1H}), 7.12 (d, J = 2.4 \text{ Hz, 1H}), 7.07 (dd, J = 9.0, 2.4 \text{ Hz, 1H}), 1.53 (h, J = 7.4 \text{ Hz, 3H}), 1.14 (d, J = 7.5 \text{ Hz, 18H}), 1.02 (s, 9H), 0.25 (s, 6H). \]

\[ \text{IR (Diamond-ATR, neat) } \bar{\nu}_{\text{max}}: 3318 (w), 2850 (m), 1601 (s), 1331 (s), 841 (w) \text{ cm}^{-1}. \]

\[ \text{HRMS (ESI) calc. for } \text{C}_{25}\text{H}_{42}\text{BrO}_{2}\text{Si}_{2} [\text{M+H}]^+: 509.1901 \text{ found: 509.1903.} \]

**Note:** \( \text{S2-Br} \) was obtained in 59% following protocol B omitting the deprotection step.
6-Bromo-5-hydroxynaphthalen-2-yl pivalate (31-Br)

![Structural formula]

Isolated: Colorless solid, 14.9 mg (11%)

**TLC** (50% dichloromethane in cyclohexane): $R_f = 0.51$ (UV, CAM).

**mp:** 122–124 °C.

1H NMR (400 MHz, chloroform-d) $\delta$ 8.01 (d, $J = 9.1$ Hz, 1H), 7.25 – 7.22 (m, 1H), 7.05 – 6.96 (m, 3H), 5.77 (s, 1H), 1.18 (s, 9H).

13C NMR (101 MHz, chloroform-d) $\delta$ 177.3, 149.8, 148.5, 134.5, 129.4, 124.2, 122.4, 121.4, 121.1, 118.4, 103.8, 39.3, 27.3.

IR (Diamond-ATR, neat) $\tilde{\nu}_{\max}$: 3420 (w), 1831 (s), 1670 (vs), 1393 (s), 1212 (m), 1067 (s), 889 (s) cm$^{-1}$.

HRMS (ESI) calc. for C$_{15}$H$_{14}$BrO$_3$ [M-H]$^-$: 321.0132 found: 321.0133.

Note: S3-Br was obtained in 91% following protocol B omitting the deprotection step.

((2-Bromo-4-phenylnaphthalen-1-yl)oxy)triisopropylsilane (S3-Br)

![Structural formula]

Isolated: Colorless oil, 174 mg (91%)

**TLC** (12% dichloromethane in cyclohexane): $R_f = 0.79$ (UV, CAM).

1H NMR (400 MHz, chloroform-d) $\delta$ 8.21 (d, $J = 8.4$ Hz, 1H), 7.84 (d, $J = 8.2$ Hz, 1H), 7.57 – 7.39 (m, 8H), 1.60 (h, $J = 7.5$ Hz, 3H), 1.20 (d, $J = 7.6$ Hz, 18H).

13C NMR (101 MHz, chloroform-d) $\delta$ 149.5, 139.6, 134.9, 132.1, 131.2, 130.3, 129.2, 128.4, 127.5, 126.5, 126.4, 125.9, 123.1, 109.0, 18.3, 14.6.

IR (Diamond-ATR, neat) $\tilde{\nu}_{\max}$: 3518 (w), 2957 (m), 1587 (vs), 1456 (s), 1340 (vs), 850 (w) cm$^{-1}$.

HRMS (ESI) calc. for C$_{25}$H$_{32}$BrOSi [M+H]$^+$: 455.1400 found: 455.1407.

Note: S3-Br was obtained in 91% following protocol B omitting the deprotection step.

2-Bromo-4-phenynaphthalen-1-ol (32-Br)

![Structural formula]

Isolated: yellow-brown solid in oily film (crude mixture)

**TLC** (12% dichloromethane in cyclohexane): $R_f = 0.45$ (UV, CAM).

**mp:** 118 °C.
$^1$H NMR (400 MHz, chloroform-$d$) $\delta$ 8.33 (d, $J = 8.2$ Hz, 1H), 7.83 (d, $J = 8.5$ Hz, 1H), 7.59 – 7.38 (m, 8H), 6.01 (s, 1H).

$^{13}$C NMR (101 MHz, chloroform-$d$) $\delta$ 147.8, 139.5, 134.3, 132.1, 130.3, 128.5, 127.5, 127.0, 126.2, 126.2, 124.7, 122.7, 103.7.

IR (Diamond-ATR, neat) $\tilde{\nu}$ max: 3522 (w), 3157 (w), 1534 (s), 1457 (vs), 1113 (m), 797 (m) cm$^{-1}$.

HRMS (ESI) calc. for C$_{16}$H$_{10}$BrO [M-H]$^-$: 296.9921 found: 296.9924.

Note: 32-Br turned out to be highly sensitive to oxygen and silica, thus only partial purification was possible.

2-Bromo-3-methylnaphthalen-1-ol (33-Br)

![Chemical structure of 2-Bromo-3-methylnaphthalen-1-ol]

Isolated: Orange crystals, 57.7 mg (58%)

TLC (25% dichloromethane in cyclohexane): $R_f = 0.50$ (UV, CAM).

mp: 60–63 °C.

$^1$H NMR (400 MHz, chloroform-$d$) $\delta$ 8.19 (d, $J = 7.9$ Hz, 1H), 7.70 (d, $J = 7.5$ Hz, 1H), 7.54 – 7.40 (m, 2H), 7.31 (t, $J = 1.1$ Hz, 1H), 6.09 (s, 1H), 2.54 (d, $J = 1.0$ Hz, 3H).

$^{13}$C NMR (101 MHz, chloroform-$d$) $\delta$ 148.3, 134.7, 133.2, 127.1, 126.9, 125.3, 122.7, 122.4, 120.6, 108.4, 23.7.

IR (Diamond-ATR, neat) $\tilde{\nu}$ max: 3243 (w), 3021 (m), 1691 (s), 1321 (vs), 1124 (m), 903 (s) cm$^{-1}$.

HRMS (ESI) calc. for C$_{11}$H$_{8}$BrO [M-H]$^-$: 234.9764 found: 234.9759.
3. Synthesis of Defucogilvocarcin M

3.1 Synthesis of linear precursor 40

5-(Benzyloxy)-2-bromonaphthalen-1-ol (26-Br)

Triethylamine (833 µL, 6.01 mmol, 1.40 equiv) and triisopropylsilyl trifluoromethanesulfonate (1.27 mL, 4.72 mmol, 1.10 equiv) were added in sequence to a solution of indanone 34 (1.02 g, 4.29 mmol, 1 equiv) in chloroform (53.6 mL, 0.08 M) at 23 °C. The reaction was stirred for two hours. The mixture was diluted with 30 mL of cyclohexane, filtered through a short plug of silica and the filtrate was evaporated under reduced pressure at 23 °C to afford the crude silyl enol ether. This material was used immediately without further purification.

The crude intermediate 15-TIPS was dissolved in n-hexane (6.13 mL, 0.7 M), cooled to −78 °C and slowly added to a suspension of potassium tert-butoxide (sublimed grade, 2.17 g, 19.3 mmol, 4.50 equiv) in n-hexane (8.78 mL, 2.2 M) at −78 °C. The flask of the crude intermediate was rinsed for three times (3 × 5.11 mL) and added to the reaction in the same fashion. After 20 minutes, a solution of freshly distilled bromoform (751 µL, 8.58 mmol, 2.00 equiv) in n-hexane (3.90 mL, 2.2 M) was added dropwise to the mixture and stirred for one hour at −78 °C. The reaction was warmed to 23 °C within one hour and stirred for an additional hour at that temperature. The solvent was removed under reduced pressure to give the crude silylated 2-bromonaphthol, which was dissolved in N,N-dimethylformamide-water (20:1, 17.2 mL, 0.25 M). Potassium acetate (548 mg, 5.58 mmol, 1.30 equiv) was added and the reaction was stirred for two hours at 23 °C. Water (40 mL) was added to the reaction mixture and the resulting solution was extracted with diethyl ether (6 × 40 mL). The combined organic layers were washed with water (80 mL) and a saturated aqueous solution of sodium chloride (80 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure. Purification by silica gel chromatography (30% grading to 70% dichloromethane in cyclohexane) gave bromonaphthol 35 (987 mg, 3.00 mmol, 70%) as a beige solid.

For analytical data: see 26-Br.
5-(Benzyloxy)-2-bromonaphthalene-1,4-dione (36)

5-(Benzyloxy)-2-bromonaphthalen-1-ol 35 (4.00 g, 12.2 mmol, 1 equiv) was dissolved in acetonitrile (203 mL, 0.061 M) upon gentle heating. Then the solution was cooled to 0 °C and a suspension of (diacetoxyiodo)benzene (8.61 g, 26.7 mmol, 2.20 equiv) in water (100 mL, 0.27 M) was slowly added to the mixture. The cooling bath was removed and the reaction was stirred for 20 minutes at 23 °C before a saturated aqueous solution of sodium hydrogen carbonate (150 mL) was added. The mixture was extracted with dichloromethane (3 × 300 mL) and the combined organic layers were washed with a saturated aqueous solution of sodium chloride (150 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure. Purification by silica gel chromatography (30% grading to 80% dichloromethane in cyclohexane) gave the desired benzoquinone 36 (2.54 g, 7.41 mmol, 61%) as yellow needles.

Data consistent with literature: *J. Chem. Soc., Perkin Trans. 1, 2001*, 1612–1623.

We observed one significant difference:

Data from Literature: \(^1H\) NMR (400 MHz, chloroform-\(d\)) \(\delta 7.73 \ (dd, \ J = 8.5, 1.1 \ Hz, 1H)\).

Our obtained data: \(^1H\) NMR (400 MHz, chloroform-\(d\)) \(\delta 7.84 \ (dd, \ J = 7.7, 1.0 \ Hz, 1H)\).

5-(Benzyloxy)-2-bromonaphthalene-1,4-diol (37)

A solution of sodium dithionite (11.5 g, 65.9 mmol, 5.22 equiv) in water (165 mL, 0.4 M) was slowly added to a solution of 5-(benzyloxy)-2-bromonaphthalene-1,4-dione 36 (4.33 g, 12.6 mmol, 1 equiv) in ethyl acetate (126 mL, 0.1 M) within ten minutes via a dropping funnel and then vigorously stirred for one hour at 23 °C. The solution was diluted with water (100 mL) and extracted with ethyl acetate (3 × 100 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (100 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product. Purification was performed by silica gel chromatography (20% grading to 50% dichloromethane in cyclohexane) to afford air-sensitive dihydroquinone 37 (3.97 g, 11.5 mmol, 91%) as a brown solid.

\textbf{TLC} (50% dichloromethane in cyclohexane): \(R_f = 0.41 \) (CAM).

\textbf{mp}: 132–134 °C.
\(^1\)H NMR (400 MHz, chloroform-\(d\)) \(\delta\) 9.02 (s, 1H), 7.83 (dd, \(J = 8.6, 1.0\) Hz, 1H), 7.51 – 7.39 (m, 5H), 7.36 (dd, \(J = 8.6, 7.7\) Hz, 1H), 6.94 (dd, \(J = 7.8, 1.0\) Hz, 1H), 6.91 (s, 1H), 5.51 (s, 1H), 5.27 (s, 2H).

\(^{13}\)C NMR (101 MHz, chloroform-\(d\)) \(\delta\) 155.3, 148.3, 141.1, 135.1, 129.3, 129.1, 128.2, 126.4, 126.3, 116.7, 115.3, 112.1, 106.7, 105.3, 72.0.

IR (Diamond-ATR, neat) \(\tilde{\nu}_{\text{max}}\): 3203 (w), 3117 (m), 1720 (s), 1523 (s), 1222 (vs), 921 (m) cm\(^{-1}\).

HRMS (ESI) calc. for C\(_{17}\)H\(_{12}\)BrO\(_3\) [M-H]: 342.9975 found: 342.9976.

8-(Benzyloxy)-3-bromo-4-((2-iodo-3-methoxy-5-methylbenzyl)oxy)naphthalen-1-ol (39-I)

5-(Benzyloxy)-2-bromonaphthalene-1,4-diol 37 (349 mg, 1.01 mmol, 1.15 equiv) was dissolved in degassed \(N,N\)-dimethylformamide (760 \(\mu\)L, 1.33 M) and cooled to 0 °C. Potassium carbonate (140 mg, 1.01 mmol, 1.15 equiv) was added and the mixture was stirred for five minutes at 0 °C. A solution of 1-(bromomethyl)-2-iodo-3-methoxy-5-methylbenzene 38-I (300 mg, 0.880 mmol, 1 equiv) in degassed \(N,N\)-dimethylformamide (700 \(\mu\)L, 1.26 M) was added dropwise to the reaction and rinsed with additional \(N,N\)-dimethylformamide (700 \(\mu\)L, 1.26 M). The mixture was heated to 50 °C and stirred for one hour. The mixture was allowed to cool to 23 °C and diluted with a solution of lithium chloride (4 M, 10 mL) and then extracted with ethyl acetate (3 × 50). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (50 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product. Purification was performed by silica gel chromatography (33 % dichloromethane in cyclohexane) to afford quinone 39-I (366 mg, 605 \(\mu\)mol, 69%) as an orange foam, accompanied by recovered benzyl bromide 38-I (54.0 mg, 158 \(\mu\)mol, 18%).

TLC (50% dichloromethane in cyclohexane): \(R_I = 0.54\) (CAM).

\(^1\)H NMR (400 MHz, chloroform-d) \(\delta\) 9.29 (s, 1H), 7.75 (dd, \(J = 8.5, 0.9\) Hz, 1H), 7.51 – 7.40 (m, 5H), 7.40 – 7.38 (m, 1H), 7.35 (dd, \(J = 8.6, 7.7\) Hz, 1H), 7.03 (s, 1H), 6.93 (dd, \(J = 7.8, 0.9\) Hz, 1H), 6.67 (s, 1H), 5.28 (s, 2H), 5.04 (s, 2H), 3.91 (s, 3H), 2.43 (s, 3H).

\(^{13}\)C NMR (101 MHz, chloroform-d) \(\delta\) 157.8, 155.8, 151.6, 144.2, 141.2, 139.9, 135.0, 131.4, 129.3, 129.2, 128.2, 127.1, 122.1, 116.5, 115.3, 114.8, 113.9, 111.4, 106.4, 85.0, 79.3, 72.0, 56.7, 21.7.

IR (Diamond-ATR, neat) \(\tilde{\nu}_{\text{max}}\): 3498 (m), 3390 (w), 3104 (w), 1780 (m), 1495 (s), 1394 (vs), 1123 (s), 909 (m) cm\(^{-1}\).
5-(Benzylxy)-2-bromo-1-((2-iodo-3-methoxy-5-methylbenzyl)oxy)-4-methoxynaphthalene (40-I)

Sodium bi(trimethylsilyl)amide (1 M in tetrahydrofuran, 1.55 mL, 1.59 mmol, 1.05 equiv) was added to a solution of naphthol 39-I (919 mg, 1.52 mmol, 1 equiv) in tetrahydrofuran (2.17 mL, 0.7 M) at –78 °C followed by dimethyl sulfate (160 µL, 1.69 mmol, 1.11 equiv). The reaction was allowed to warm to 23 °C and stirred for three hours at that temperature. A saturated aqueous solution of sodium hydrogen carbonate (10 mL) was added, and the solution was extracted with ethyl acetate (4 × 20 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (15 mL) and the washed solution was dried over sodium sulfate. The dried solution was evaporated under reduced pressure to give the crude product. Purification was performed by silica gel chromatography (20% grading to 70% dichloromethane in cyclohexane) to afford quinone 40-I (864 mg, 1.40 mmol, 92%) as a white solid.

**TLC** (30% dichloromethane in cyclohexane): \( R_f = 0.54 \) (CAM).

**mp:** 94–96 °C.

\(^1\)H NMR (400 MHz, chloroform-\(d\)) \( \delta \) 7.75 (dd, \( J = 8.5, 1.0 \) Hz, 1H), 7.59 (d, \( J = 7.4 \) Hz, 2H), 7.45 – 7.37 (m, 4H), 7.34 (t, \( J = 7.3 \) Hz, 1H), 6.98 (dd, \( J = 7.8, 1.0 \) Hz, 1H), 6.97 (s, 1H), 6.68 (d, \( J = 1.9 \) Hz, 1H), 5.21 (s, 2H), 5.07 (s, 2H), 3.95 (s, 3H), 3.92 (s, 3H), 2.44 (s, 3H).

\(^{13}\)C NMR (101 MHz, chloroform-\(d\)) \( \delta \) 157.8, 156.7, 154.5, 145.3, 141.3, 139.9, 137.5, 132.2, 128.6, 127.8, 127.1, 122.0, 118.2, 115.4, 113.3, 111.4, 109.8, 109.4, 84.9, 79.2, 71.6, 56.8, 56.7, 21.7.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 2193 (w), 1790 (m), 1623 (w), 1473 (s), 1374 (vs), 1223 (s), 909 (m), 712 (w) cm\(^{-1}\).

**HRMS** (ESI) calc. for \( \text{C}_{26}\text{H}_{21}\text{BrIO}_4 [\text{M}+\text{H}]^+ \): 618.9975 found: 618.9970.
(2-Bromo-3-methoxy-5-methylphenyl)methanol (S5)

To a solution of benzyl alcohol S4[3] (1.14 g, 7.49 mmol, 1 equiv) in toluene (74.9 mL, 0.1 M) n-butyllithium (2.40 M in n-hexane, 6.71 mL, 16.1 mmol, 2.15 equiv) was added dropwise over ten minutes at −40 °C. After stirring for four hours at 23 °C, the reaction was cooled to −40 °C before tetrahydrofuran (15 mL, 0.5 M) was added. To this mixture a solution of 1,2-dibromo-1,1,2,2-tetrachloroethane (4.15 g, 12.7 mmol, 1.70 equiv) in tetrahydrofuran (2 mL, 6.35 M) was added dropwise and stirred for 15 hours at 23 °C. A saturated solution of ammonium chloride (120 mL) was added and the mixture was extracted with diethyl ether (3 × 200 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (100 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered, and the filtrate was evaporated under reduced pressure. Purification by silica gel chromatography (20% diethyl ether in pentane) gave the title compound S5 (945 mg, 4.09 mmol, 55%) as a white solid.

TLC (50% diethyl ether in pentane): Rf = 0.38 (UV, CAM)

mp: 99–101 °C.

1H NMR (400 MHz, CDCl3) δ 6.92 (d, J = 2.0 Hz, 1H), 6.68 (d, J = 2.1 Hz, 1H), 4.73 (d, J = 6.5 Hz, 2H), 3.89 (s, 3H), 2.34 (s, 3H), 2.05 – 1.96 (m, 1H).

13C NMR (101 MHz, CDCl3) δ 155.7, 140.9, 138.5, 121.7, 112.1, 108.5, 65.3, 56.4, 21.5.

IR (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3255 (s), 2899 (w), 1603 (m), 1302 (vs), 1031 (m), 842 (w) cm$^{-1}$.

HRMS (ESI) calc. for C$_9$H$_{11}$NaBrO$_2$ [M+Na]$^+$: 252.9835 found: 252.9833.

2-Bromo-1-(bromomethyl)-3-methoxy-5-methylbenzene (38-Br)

Alcohol S5 (0.786 g, 3.40 mmol, 1 equiv) and tetrabromomethane (2.26 g, 6.802 mmol, 2.00 equiv) were dissolved in dichloromethane (34.0 mL, 0.1 M) and cooled to 0 °C. Triphenylphosphine (1.78 g, 6.80 mmol, 2.00 equiv) was added and the reaction was stirred for 45 min while slowly warming to 23 °C. The solvent was removed under reduced pressure and the crude product was purified by silica gel chromatography (5% diethyl ether in pentane) to give benzyl bromide 38-Br (792 mg, 2.69 mmol, 79%) as a white solid.

NOTE: Addition of triphenylphosphine prior to tetrabromomethane led to significant dimerization of S5 forming the corresponding dibenzylether (not shown).
TLC (66% diethyl ether in pentane) \( R_f = 0.76 \) (UV, CAM).

mp: 81–82 °C.

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 6.90 (d, \( J = 2.0 \) Hz, 1H), 6.66 (d, \( J = 2.1 \) Hz, 1H), 4.60 (s, 2H), 3.89 (s, 3H), 2.32 (s, 3H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 156.1, 141.3, 139.0, 122.1, 112.5, 108.9, 65.8, 56.8, 21.9.

IR (Diamond-ATR, neat) \( \tilde{\nu}_{\max} \): 1565 (w), 1349 (s), 1261 (w), 1004 (s), 957 (m), 714 (w) cm\(^{-1}\).

HRMS (ESI) calc. for C\(_9\)H\(_{11}\)Br\(_2\)O [M+H]\(^+\): 292.9171 found: 292.9178.

8-(Benzylxy)-3-bromo-4-((2-bromo-3-methoxy-5-methylbenzyl)oxy)naphthalen-1-ol (39-Br)

5-(Benzylxy)-2-bromonaphthalene-1,4-diol 37 (194 mg, 561 \( \mu \)mol, 1.1 equiv) was dissolved in degassed \( \text{N,N-dimethylformamide} \) (350 \( \mu \)L, 1.60 M) and cooled to 0 °C. Potassium carbonate (81 mg, 587 \( \mu \)mol, 1.15 equiv) was added and the mixture was stirred for five minutes at 0 °C. A solution of 1-(bromomethyl)-2-bromo-3-methoxy-5-methylbenzene 38-Br (150 mg, 510 \( \mu \)mol, 1 equiv) in degassed \( \text{N,N-dimethylformamide} \) (350 \( \mu \)L, 1.46 M) was added dropwise to the reaction and rinsed with additional \( \text{N,N-dimethylformamide} \) (300 \( \mu \)L, 1.70 M). The mixture was heated to 50 °C and stirred for one hour. The mixture was allowed to cool to 23 °C and diluted with a solution of lithium chloride (4 M, 5 mL) and then extracted with ethyl acetate (3 \( \times \) 30). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (40 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product. Purification was performed by silica gel chromatography (33 % dichloromethane in cyclohexane) to afford quinone 39-Br (223 mg, 400 \( \mu \)mol, 78%) as a yellow foam, accompanied by recovered benzyl bromide 38-Br (21.0 mg, 71.4 \( \mu \)mol, 14%).

TLC (33 % dichloromethane in cyclohexane) \( R_f = 0.17 \) (UV, CAM).

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 9.29 (s, 1H), 7.75 (dd, \( J = 8.6, 0.9 \) Hz, 1H), 7.51 – 7.40 (m, 5H), 7.39 – 7.32 (m, 2H), 7.02 (s, 1H), 6.93 (dd, \( J = 7.8, 0.9 \) Hz, 1H), 6.74 (d, \( J = 1.9 \) Hz, 1H), 5.28 (s, 2H), 5.09 (s, 2H), 3.92 (s, 3H), 2.42 (s, 3H).

\(^13\)C NMR (101 MHz, CDCl\(_3\)) \( \delta \) 155.7, 155.7, 151.6, 144.1, 138.6, 137.9, 135.0, 131.3, 129.2, 129.1, 128.1, 127.1, 121.9, 116.4, 115.2, 114.7, 113.8, 112.3, 108.2, 106.3, 74.7, 72.0, 56.5, 21.8.
**5-(Benzyloxy)-2-bromo-1-((2-bromo-3-methoxy-5-methylbenzyl)oxy)-4-methoxynaphthalene (40-Br)**

Sodium bi(trimethylsilyl)amide (1 M in tetrahydrofuran, 200 µL, 200 µmol, 1.05 equiv) was added to a solution of naphthol 39-Br (106 mg, 190 µmol, 1 equiv) in tetrahydrofuran (571 µL, 0.40 M) at −78 °C followed by dimethyl sulfate (20 µL, 211 µmol, 1.11 equiv). The reaction was allowed to warm to 23 °C and stirred for three hours at that temperature. (*Note: After one hour, 1.50 mL tetrahydrofuran were added to prevent gel-formation.*) A saturated aqueous solution of sodium hydrogen carbonate (10 mL) was added and the solution was extracted with ethyl acetate (4 × 15 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (15 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product. Purification was performed by silica gel chromatography (50% grading to 70% dichloromethane in cyclohexane) to afford quinone 40-Br (93 mg, 163 µmol, 86%) as a white solid.

**TLC** (50 % dichloromethane in cyclohexane) *R*$_f$ = 0.44 (UV, CAM).

**mp:** 84–86 °C.

$^1$H NMR (300 MHz, CDCl$_3$) δ 7.77 (dd, *J* = 8.4, 1.0 Hz, 1H), 7.64 – 7.55 (m, 2H), 7.48 – 7.31 (m, 5H), 6.99 (d, *J* = 8.0 Hz, 2H), 6.76 (d, *J* = 1.9 Hz, 1H), 5.21 (s, 2H), 5.14 (s, 2H), 3.95 (s, 3H), 3.93 (s, 3H), 2.43 (s, 3H).

$^{13}$C NMR (101 MHz, chloroform-δ) δ 156.7, 155.7, 154.4, 145.4, 138.6, 138.1, 137.5, 132.2, 128.6, 127.8, 127.8, 127.1, 121.9, 118.2, 115.3, 113.3, 112.3, 109.8, 109.4, 108.2, 74.6, 71.6, 56.8, 56.6, 21.8.

**IR** (Diamond-ATR, neat) *ν*$_{max}$: 2223 (m), 1797 (m), 1601 (m), 1470 (vs), 1424 (s), 1221 (s), 937 (m), 710 (w) cm$^{-1}$.

**HRMS** (ESI) calc. for C$_{27}$H$_{22}$Br$_2$O$_4$ [M+H]$: 571.0114$ found: 571.0116.
3.2 Intramolecular Biaryl Coupling

1-(Benzyloxy)-10,12-dimethoxy-8-methyl-6H-dibenzo[\(c,h\)]chromene (41a)

Tert-butyllithium (1.48 M in pentane, 630 µL, 930 µmol, 4.00 equiv) was added dropwise to a solution of ether 40-I (144 mg, 232.5 µmol, 1 equiv) in tetrahydrofuran (2.33 mL, 0.1 M) at –78 °C and stirred for one hour at that temperature. A freshly prepared solution of CuCN·2LiCl (41.0 mg, 232.5 µmol, 1 equiv) in tetrahydrofuran (233 µL, 1 M) was added dropwise to the reaction and stirred for two hours while warming to –40 °C. A solution of 1,3-dinitrobenzene (156 mg, 930 µmol, 4.00 equiv) in tetrahydrofuran (930 µL, 1 M) was added and the reaction was stirred for 1.5 hours while warming to 10 °C. The reaction was stopped by the addition of methanolic hydrochloric acid (5 mL) and stirred for 30 minutes, before a saturated aqueous solution of ammonium chloride (5 mL) was added. The mixture was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (20 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product. The remaining crude mixture was purified by two consecutive applications of silica gel chromatography (A: 10% dichloromethane in cyclohexane; B: 3% diethyl ether in pentane) to afford dibenzochromene 41a (36.4 mg, 88.4 µmol, 38%) as a white solid.

\[ \text{TLC (57\% dichloromethane in cyclohexane): } R_t = 0.37 \text{ (UV, CAM).} \]

\[ \text{mp: } 167–169 \, ^\circ \text{C}. \]

\[ ^1H \text{ NMR (400 MHz, chloroform-}d) \delta 8.00 \text{ (s, 1H), 7.91} \text{ (dd, } J = 8.5, 1.1 \text{ Hz, 1H), 7.66 – 7.59} \text{ (m, 2H), 7.44 – 7.40} \text{ (m, 2H), 7.35} \text{ (dd, } J = 8.3, 7.8 \text{ Hz, 1H), 7.35 – 7.31} \text{ (m, 1H), 6.95} \text{ (dd, } J = 7.8, 1.1 \text{ Hz, 1H), 6.79} \text{ (s, 1H), 6.69} \text{ (s, 1H), 5.22} \text{ (s, 2H), 5.09} \text{ (s, 2H), 3.96} \text{ (s, 3H), 3.95} \text{ (s, 3H), 2.40} \text{ (s, 3H).} \]

\[ ^13C \text{ NMR (101 MHz, chloroform-}d) \delta 156.4, 155.8, 150.8, 144.8, 139.0, 137.9, 134.6, 128.5, 128.3, 127.6, 127.2, 126.0, 118.3, 118.2, 117.7, 116.7, 115.6, 112.9, 109.7, 107.8, 71.8, 69.5, 57.5, 56.0, 21.7. \]

\[ \text{IR (Diamond-ATR, neat) } \tilde{\nu}_{\text{max}}: 2104 \text{ (w), 1590} \text{ (m), 1377} \text{ (m), 1346} \text{ (s), 1286} \text{ (s), 1133} \text{ (vs), 1051} \text{ (s), 843} \text{ (m), 756} \text{ (w) cm}^{-1}. \]

\[ \text{HRMS (ESI) calc. for } C_{27}H_{23}O_4 [M+H]^+: 413.1747 \text{ found: 413.1746.} \]
10,12-Dimethoxy-8-methyl-6H-dibenzo[c,h]chromen-1-ol (41b)

Tert-butyllithium (1 M in pentane, 9.70 mL, 14.7 mmol, 11.0 equiv) was added dropwise to a solution of ether 40-I (825 mg, 1.33 mmol, 1 equiv) in tetrahydrofuran (13.3 mL, 0.1 M) at −78 °C and stirred for 30 minutes. A freshly prepared solution of CuCN-2LiBr (351 mg, 1.33 mmol, 1.00 equiv) in tetrahydrofuran (3.51 mL, 0.38 M) was added dropwise to the reaction and stirred for two hours while warming to −40 °C. A solution of 1,3-dinitrobenzene (896 mg, 5.33 mmol, 4.00 equiv) in tetrahydrofuran (8.96 mL, 0.59 M) was added and the reaction was warmed to 23 °C over a period of 30 minutes and stirred for two hours at that temperature. The reaction was stopped by the addition of methanolic hydrochloric acid (15 mL) and stirred for 30 minutes, before a saturated aqueous solution of ammonium chloride (15 mL) was added. The mixture was extracted with diethyl ether (3 × 60 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (50 mL) and the washed solution was dried over sodium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product. Residual dinitrobenzene was largely removed by sublimation at 0.1 mbar and 40 °C for 20 hours. The remaining crude mixture was purified by two consecutive applications of silica gel chromatography (A: 25% dichloromethane in cyclohexane; B: 5% diethyl ether in pentane) to afford dibenzochromene 41b (155 mg, 0.480 mmol, 36%) as a yellow solid.

**TLC** (50% dichloromethane in cyclohexane): \( R_f = 0.26 \) (CAM).

**mp:** 174 °C.

**\(^1\)H NMR** (400 MHz, chloroform-\(d\)) \( \delta \) 9.44 (s, 1H), 7.91 (s, 1H), 7.73 (dd, \( J = 8.4, 1.1 \) Hz, 1H), 7.35 (dd, \( J = 8.4, 7.6 \) Hz, 1H), 6.88 (dd, \( J = 7.7, 1.1 \) Hz, 1H), 6.79 (s, 1H), 6.69 (dt, \( J = 1.7, 0.8 \) Hz, 1H), 5.08 (s, 2H), 4.09 (s, 3H), 3.95 (s, 3H), 2.40 (s, 3H).

**\(^{13}\)C NMR** (101 MHz, chloroform-\(d\)) \( \delta \) 156.2, 154.4, 149.9, 145.4, 139.1, 134.4, 127.8, 127.4, 118.4, 116.8, 116.5, 114.8, 113.4, 112.8, 111.1, 104.3, 69.4, 56.4, 56.0, 21.7.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3553 (m), 3092 (m), 2004 (m), 1741 (w), 1652 (w), 1223 (s), 1103 (vs), 1030 (m), 972 (s) cm\(^{-1}\).

**HRMS** (ESI) calc. for C\(_{20}\)H\(_{17}\)O\(_4\) [M-H]\(^-\): 321.1132 found: 321.1137.
Optimization Studies for the anticipated Stille–Kelly coupling

All solids (dihalogen 40, palladium catalyst and additives) were placed into a 20-mL-pressure tube in a glove box. All liquids (solvent and stannane) were added outside of the glove box via canula under an argon counterflow. The pressure tube was sealed with a Teflon® screw-cap and then put into a pre-heated oil bath under light exclusion. After the given reaction time, the oil bath was removed to allow the reaction to cool to 23 °C.

For reactions using DMF or NMP as solvent (Entries 7, 20, 28 and 29): The mixture was diluted with a solution of lithium chloride (4 M, 5 mL) and then extracted with ethyl acetate (3 × 10). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (10 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure to give the crude product.

For reactions using 1,4-dioxane, acetonitrile (MeCN), toluene (PhMe) or tetrahydrofuran (THF) (Entries 1–6, 8–19, 21–27 and 30–41): The suspension was filtered through a short plug of Celite® and the solvent was removed. The crude residue was taken up with CDCl₃ for a ¹H NMR measurement. For Entries 1, 19, 39, 40 and 41: Then, the crude product was purified via flash column chromatography on silica gel (50% dichloromethane in cyclohexane) to afford product 41a as a white solid.
Table 1: Screening conditions for the Stille–Kelly coupling

| Entry | X          | R (eq.) | Pd-cat. (eq.) | Additive (eq.) | Solvent | Temp. | Time | 41a (%) | Result |
|-------|------------|---------|---------------|----------------|---------|-------|------|---------|---------|
| 1     | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 13 h | 31%     | 1.7     |
| 2     | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 13 h | n.i.    | 1       |
| 3     | i-Pr       | Me [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 13 h | n.i.    | complex mixture |
| 4     | Br         | Me [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 13 h | n.i.    | complex mixture |
| 5     | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 13 h | 0.5     | 3       |
| 6     | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | CuI (0.4)| 1,4-dioxane | 130 °C | 12 h | n.i.    | 0       |
| 7     | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | DMF     | 130 °C | 12 h | n.i.    | 0       |
| 8     | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | PhMe    | 130 °C | 12 h | 1      | 0       |
| 9     | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 130 °C | 12 h | 0.6     | 1       |
| 10    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 130 °C | 12 h | 2       | 1.3     |
| 11    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | LiCl (3.2)| 1,4-dioxane | 140 °C | 16 h | 0.3     | 0.3     |
| 12    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | CsF (2.2)| 1,4-dioxane | 140 °C | 16 h | 0.1     | 2       |
| 13    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | MeCN    | 140 °C | 16 h | n.i.    | 1       |
| 14    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 16 h | 0.3     | 0.8     |
| 15    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | CuI (1.5)| 1,4-dioxane | 140 °C | 16 h | 0.2     | 1       |
| 16    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | MeCN    | 140 °C | 16 h | 1.1     | 1       |
| 17    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 16 h | 0.9     | 1.3     |
| 18    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | AsPh₃ (1.0)| 1,4-dioxane | 140 °C | 16 h | n.i.    | 1       |
| 19    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | 1,4-dioxane | 140 °C | 16 h | 44%     | 0       |
| 20    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | DMF    | 140 °C | 16 h | n.i.    | complex mixture |
| 21    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | LiCl (3.2)| 1,4-dioxane | 140 °C | 16 h | n.i.    | 1       |
| 22    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | CsF (2.2)| 1,4-dioxane | 140 °C | 16 h | n.i.    | 1       |
| 23    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | CuI (1.5)| 1,4-dioxane | 140 °C | 16 h | n.i.    | 1       |
| 24    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | MeCN    | 140 °C | 16 h | n.i.    | complex mixture |
| 25    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | NbBu₄ (1.4)| PhMe    | 140 °C | 16 h | n.i.    | 1       |
| 26    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | MeCN    | 140 °C | 16 h | n.i.    | 1       |
| 27    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | NMP    | 140 °C | 16 h | n.i.    | 0       |
| 28    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | CuI (1.5)| NMP    | 140 °C | 16 h | n.i.    | 0       |
| 29    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | THF    | 140 °C | 16 h | n.i.    | 0       |
| 30    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | PhMe   | 80 °C  | 16 h | n.i.    | 1       |
| 31    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | PhMe   | 100 °C | 16 h | n.i.    | 1       |
| 32    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | MeCN   | 120 °C | 16 h | n.i.    | 0       |
| 33    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | THF    | 120 °C | 16 h | n.i.    | 0       |
| 34    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | PhMe   | 120 °C | 16 h | n.i.    | 0       |
| 35    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.1            | -       | THF    | 120 °C | 16 h | n.i.    | 10      |
| 36    | Br         | Me [1.1] | Pd(dpdpf)Cl₂ | 0.17           | -       | MeCN   | 140 °C | 13 h | 0.1     | 1       |
| 37    | i-Pr       | Me [1.1] | Pd(dpdpf)Cl₂ | 0.17           | -       | THF    | 140 °C | 13 h | n.i.    | 1       |
| 38    | Br         | Me [1.1] | Pd(dpdpf)Cl₂ | 0.17           | -       | MeCN   | 140 °C | 13 h | 0.4     | 1.8     |
| 39    | i-Pr       | Me [1.1] | Pd(dpdpf)Cl₂ | 0.17           | -       | MeCN   | 140 °C | 13 h | 2       | 1.3     |
| 40    | Br         | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.4            | -       | MeCN   | 140 °C | 14 h | 74%     | mainly 41a + partial decomposition |
| 41    | i-Pr       | Bu [1.1] | Pd(dpdpf)Cl₂ | 0.4            | -       | MeCN   | 140 °C | 14 h | 74%     | mainly 41a + partial decomposition |

*Unless otherwise indicated, all reactions were performed on a 23.6 µmol scale, ° isolated yield (n.i. = no isolation was performed), / crude ¹H-NMR: ratios of integrals of the main-signals (bold numbers highlight the most prominent signals), ² unidentified side-product, /0.4 equiv. of AsPh₃ (0.04 M), ° Scale: 87.4 µmol, / Scale: 175 µmol, (SP = side-product).
1-(benzyl oxy)-10,12-dimethoxy-8-methyl-6H-dibenzo[\textit{c},\textit{h}]chromene (41a)

Dibromide 40-Br (100 mg, 175 µmol, 1 equiv) and tetrakis(triphenylphosphine)palladium(0) (80.8 mg, 69.9 µmol, 0.40 equiv) were placed in a 20-mL-pressure tube inside a glovebox before bis(tributyltin) (94 µL, 187 µmol, 1.07 equiv) and degassed acetonitrile (8.74 mL, 0.02 M) were added to the pressure tube via syringe under argon counterflow outside of the glove box. The pressure tube was sealed, covered with aluminum foil and heated to 140 °C for twelve hours under constant stirring. After cooling to 23 °C the solvent of the reaction mixture was removed under reduced pressure and the crude product was purified by flash column chromatography on silica gel (50 % cyclohexane in dichloromethane) to yield tetracycle 41a (45 mg, 63 %) as a white solid.

For analytical data of compound 41a: see above.

3.3 Mild benzylic Oxidation of a quinone-based Chromene using DDQ and THP

1-Isopropoxy-10,12-dimethoxy-8-methyl-6H-dibenzo[\textit{c},\textit{h}]chromene (41c)

Sodium hydride (60% dispersion in mineral oil, 5.04 mg, 129 µmol, 1.30 equiv) was added to a solution of naphtol 41b (32.0 mg, 99.3 µmol, 1 equiv) in N,N-dimethylformamide (764 µL, 0.13 M) at 0 °C. After 30 minutes, 2-iodopropane (20 µL, 200 µmol, 2.00 equiv) was added in one portion to the mixture and then stirred for seven hours at 70 °C. The reaction was allowed to cool to 23 °C before water (2 mL) was added and then extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (10 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was evaporated under reduced pressure. Purification by silica gel chromatography (5% ethyl acetate in cyclohexane) gave the title compound 41c (30.0 mg, 82.4 µmol, 83%) as a white solid.

TLC (10% ethyl acetate in cyclohexane): $R_f = 0.34$ (UV, CAM, KMnO$_4$).
mp: 179 °C.

$^1$H NMR (400 MHz, chloroform-$d$) $\delta$ 7.96 (s, 1H), 7.91 (dd, $J$ = 8.4, 1.1 Hz, 1H), 7.34 (t, $J$ = 8.0 Hz, 1H), 6.95 (dd, $J$ = 7.6, 1.2 Hz, 1H), 6.78 (s, 1H), 6.68 (s, 1H), 5.08 (s, 2H), 4.56 (hept, $J$ = 5.8 Hz, 1H), 3.96 (s, 3H), 3.94 (s, 3H), 2.39 (s, 3H), 1.41 (d, $J$ = 6.0 Hz, 6H).

$^{13}$C NMR (101 MHz, chloroform-$d$) $\delta$ 156.4, 154.5, 150.6, 145.1, 138.9, 134.5, 128.5, 119.8, 118.3, 117.4, 116.8, 115.9, 114.1, 112.8, 108.6, 73.2, 69.5, 57.9, 56.0, 22.2, 21.7.

IR (Diamond-ATR, neat) $\tilde{\nu}_{\text{max}}$: 3031 (m), 2970 (m), 1534 (m), 1302 (m), 1274 (m), 1249 (w) cm$^{-1}$.

HRMS (ESI) calc. for C$_{23}$H$_{25}$O$_4$ [M+H]$^+$: 365.1747 found: 365.1742.

1-Isopropoxy-10,12-dimethoxy-8-methyl-6H-dibenzo[c,h]chromen-6-one (42)

Tert-butyl hydroperoxide (5.5 M in nonane, 15.0 µL, 82.4 µmol, 2.00 equiv) followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (14.0 mg, 61.8 µmol, 1.50 equiv) were added to a solution of tetracycle 41c (15 mg, 41.2 µmol, 1 equiv) in 1,4-dioxane (458 µL, 0.09 M) at 23 °C and stirred for two hours at that temperature. The solvent was removed under reduced pressure and the crude solid was re-dissolved in dichloromethane (458 µL, 0.09 M). 1,8-Diazabicyclo(5.4.0)undec-7-ene (30.7 µL, 206 µmol, 5.00 equiv) was added and the mixture was stirred for one hour at 23 °C. The solvent was removed and the crude mixture was directly subjected to silica gel chromatography (10% cyclohexane in dichloromethane) to afford isopropylated defucogilvocarcin M 42 (13.2 mg, 35.0 µmol, 85%) as a yellowish solid.

Data consistent with literature: J. Org. Chem., 2009, 74, 4080–4093.

Defucogilvocarcin M (45)

Tert-butyl hydroperoxide (5.5 M in nonane, 56.4 µL, 310 µmol, 2.00 equiv) followed by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (44.0 mg, 194 µmol, 1.25 equiv) were added to a solution of tetracycle 41b (50.0 mg, 155 µmol, 1 equiv) in 1,4-dioxane (1.72 mL, 0.09 M) at 23 °C and stirred for two hours at that temperature. The solvent was removed under reduced pressure and the crude solid was re-dissolved in dichloromethane (3.10 mL, 0.09 M). 1,8-Diazabicyclo(5.4.0)undec-7-ene (69.5 µL, 465 µmol, 3.00 equiv) was added and the mixture was stirred for one hour at 23 °C. The solvent was
removed under reduced pressure and the crude mixture was directly subjected to silica gel chromatography (60% diethyl ether in cyclohexane) to afford defucogilvocarcin M 45 (41.7 mg, 124.1 µmol, 80%) as a white solid.

**TLC** (25% diethyl ether in pentane): $R_f = 0.17$ (UV, KMnO₄).

**HRMS** (ESI) calc. for $C_{20}H_{17}O_5$ [M+H]+: 337.1071 found: 337.1066.

Comparison with the reported spectral Data of Defucogilvocarcin M in CDCl₃:

![Defucogilvocarcin M (45)](image)

| Atom Number | This work (400 MHz, 101 MHz) | Suzuki’s work¹ (-)² |
|-------------|-----------------------------|---------------------|
|             | $^1$H                        | $^1$C               | $^1$H                        | $^1$C               |
| 1           | 8.04 (dd, $J = 8.4, 1.1$ Hz, 1H) | 113.5              | 8.05 (dd, $J = 7.6, 0.7$ Hz, 1H) | 113.4              |
| 2           | 7.48 (t, $J = 8.1$ Hz, 1H)    | 128.5              | 7.48 (dd, $J = 7.6, 7.6$ Hz, 1H) | 128.4              |
| 3           | 6.99 (dd, $J = 7.7, 1.1$ Hz, 1H) | 112.5              | 6.99 (dd, $J = 7.6, 0.7$ Hz, 1H) | 112.4              |
| 4           | 154.3                        |                    | 154.2                        |                    |
| 5           | 113.1                        |                    | 112.9                        |                    |
| 6           | 151.9                        |                    | 151.8                        |                    |
| 7           | 8.23 (s, 1H)                 | 101.8              | 8.23 (s, 1H)                 | 101.8              |
| 8           | 114.7                        |                    | 114.6                        |                    |
| 9           | 141.3                        |                    | 141.3                        |                    |
| 10          | 126.3                        |                    | 126.2                        |                    |
| 11          | 9.33 (s, 1H)                 | 9.34 (s, 1H)       | 9.34 (s, 1H)                 | 123.0              |
| 12          | 4.07 (s, 3H)                 | 56.3               | 4.12 (s, 3H)                 | 56.2               |
| 13          | 161.4                        |                    | 161.2                        |                    |
| 14          | 123.1                        |                    | 123.0                        |                    |
| 15          | 7.88 (dd, $J = 1.7, 0.9$ Hz, 1H) | 122.8              | 7.89 (s, 1H)                 | 122.8              |
| 16          | 140.0                        |                    | 139.9                        |                    |
| 17          | 7.06 (d, $J = 1.7$ Hz, 1H)   | 118.1              | 7.07 (s, 1H)                 | 118.1              |
| 18          | 157.0                        |                    | 157.0                        |                    |
| 19          | 121.8                        |                    | 121.8                        |                    |
| 20          | 2.47 (s, 3H)                 | 21.8               | 2.48 (s, 3H)                 | 21.6               |
| 21          | 4.03 (s, 3H)                 | 56.1               | 4.07 (s, 3H)                 | 56.0               |

¹ Takemura, K. Imura, T. Matsumoto, K. Suzuki. Concise Three-Component Synthesis of Defucogilvocarcin M. Org. Lett., 2004, 6, 2503–2505.

² Frequency was not mentioned by the authors.
**1-(Benzyloxy)-10,12-dimethoxy-8-methyl-6H-dibenz[o,h]chromen-6-one (44)**

Cyclic ether 41a (1.02 g, 2.46 mmol, 1 equiv) was dissolved in 1,4-dioxane (27.4 mL, 0.09 M). 2,3-dichloro-5,6-dicyano-p-benzoquinone (839 mg, 3.70 mmol, 1.5 equiv) was added to the solution, followed by tert-butyl hydroperoxide (5.5 M in nonane, 896 µL, 2.93 mmol, 2.00 equiv) and stirred for two hours at 23 °C. The solvent was removed under reduced pressure and the residual crude solid was dissolved in dichloromethane (49.3, 0.05 M). 1,8-Diazabicyclo(5.4.0)undec-7-ene (1.47 mL, 9.84 mmol, 4.00 equiv) was added and the mixture was stirred for one hour at 23 °C. The solvent was removed and the crude mixture was directly subjected to silica gel chromatography (10% grading to 1% cyclohexane in dichloromethane) to afford aglycone 44 (807 mg, 1.89 mmol, 77%) as a white solid.

**TLC** (25% ethyl acetate in cyclohexane): $R_f = 0.27$ (UV, CAM).

**mp:** 221 °C.

**$^1$H NMR** (400 MHz, chloroform-d) δ 8.36 (s, 1H), 8.22 (dd, $J = 8.5, 1.0$ Hz, 1H), 7.92 (s, 1H), 7.64 – 7.59 (m, 2H), 7.50 (t, $J = 8.1$ Hz, 1H), 7.43 (dd, $J = 8.5, 7.8$ Hz, 2H), 7.38 – 7.32 (m, 1H), 7.11 (s, 1H), 7.04 (dd, $J = 7.8, 1.0$ Hz, 1H), 5.22 (s, 2H), 4.06 (s, 3H), 3.99 (s, 3H), 2.48 (s, 3H).

**$^{13}$C NMR** (101 MHz, CDCl$_3$) δ 161.6, 157.3, 155.8, 153.0, 140.6, 139.9, 137.6, 128.5, 127.7, 127.2, 127.1, 126.9, 123.3, 122.9, 122.1, 118.2, 118.1, 115.4, 113.9, 110.3, 104.4, 71.6, 56.6, 56.3, 21.8.

**IR** (Diamond-ATR, neat) $\tilde{\nu}_{\text{max}}$: 1716 (m), 1592 (s), 1398 (m), 1336 (s), 1297 (vs), 1122 (w), 1062 (m), 852 (m), 746 (w) cm$^{-1}$.

**HRMS** (ESI) calc. for C$_{27}$H$_{23}$O$_5$ [M+H]$^+$: 427.1540 found: 427.1547.
4. Meta-functionalization of 2-Bromo-5-iodo-1-naphthol

Treatment of 2-bromo-5-iodonaphthol \(22-\text{Br}\) with N-chlorosuccinimide (NCS) in acetonitrile affords quantitative conversion to bench-stable enone \(47\). The succinimide could be removed by filtration of \(47\) through a short plug of silica with only little decomposition (less than 10%), while aqueous basic work-up results in partial decomposition accompanied with significant enolization. Interestingly, in a first attempt the use of Nagata’s reagent led to nucleophilic attack of mainly the ethyl group (40%) and only minor amounts of the cyanide (25%), while in any other attempt to reproduce this result the cyanide \(\text{S8-CN}\) was isolated as main product (Entry 1). Similarly, \(\text{AlEt}_3\) underwent conjugate addition in 85% overall (Entry 2), while a one-pot transformation starting from naphthol \(22-\text{Br}\) showed almost quantitative overall yield (Entry 5). The use of \(\text{SnCl}_4\) allowed for the application of Mukaiyama-Aldol conditions (Entry 3) as well as for the installation of nonactivated anisole (Entry 4). It is noteworthy, that both products have been isolated as a mixture of 2-chloro- and 2-bromonaphthols, indicating a \(\text{SnCl}_4\)-induced halogen shuffle. For all entries, naphthol \(22\) was isolated as minor side-product (between 3 and 15%). Since several of the known stable phenols and naphthols in their keto-form are decorated with halogens (especially in the ortho-position)\(^4\) we conclude that the bromine and the iodine might contribute to the stability of the dienone-form \(47\) by their electronegativity. However, similar dearomatization reactions are known for less-substituted systems (compare reference 24a).

\[
\text{Entry} \quad \text{Nucleophile} \quad \text{Conditions} \quad R \quad \text{S8} \quad \text{rac-S9}
\]

| Entry | Nucleophile | Conditions | R | S8 | rac-S9 |
|-------|-------------|------------|---|----|-------|
| 1     | \(\text{Et}_2\text{AlCN}\) | PhMe, \(–78\) to \(23\) °C, 2.5 h | \(\text{O-CN}\) | 58\%\(^a\) | –\(^b\) |
| 2     | \(\text{Et}_3\text{Al}\) | PhMe, \(–78\) °C, 5 min | \(\text{C}\) | 60\% | 25\% |
| 3     | \(\text{OTMS \text{S10}}\) | \(\text{SnCl}_4, \text{CH}_2\text{Cl}_2, –78\) to \(23\) °C, 8 h | \(\text{O}\) | 36\%\(^c\) | – |
| 4     | \(\text{PhOMe}\) | \(\text{SnCl}_4, \text{CH}_2\text{Cl}_2, 23\) °C, 2 h | \(\text{C}\) | 38\%\(^d\) | – |
| 5\(^e\) | \(\text{Et}_3\text{Al}\) | \(\text{NCS, MeCN, 23}\) °C, 3 h then \(\text{AlEt}_3, \text{PhMe, –78}\) °C, 5 min \(\text{O}\) | 41\% | 56\% |

\(^a\)along with 8\% of \(R = \text{Et}\). \(^b\)according to the crude \(^1\text{H-NMR}\) the cyano-tetralone is mainly formed, which decomposes to \(\text{S8-CN}\) during purification over silica. \(^c\):1-mix of 2-Br/2-Cl-naphthol. \(^d\):1-mix of 2-Br/2-Cl-naphthol. \(^e\)in one-pot from \(22-\text{Br}\).
2-Bromo-4-chloro-5-iodonaphthalen-1(4H)-one (47)

N-Chlorosuccinimide (66.0 mg, 495 µmol, 1.10 equiv) was added to a solution of naphthol 22-Br (157 mg, 450 µmol, 1 equiv) in acetonitrile (3.00 mL, 0.15 M) in three portions over 30 minutes at 23 °C. After three hours, the mixture was diluted with a mixture of cyclohexane and ethyl acetate (1:1) and quickly filtered over a short plug of silica to obtain the desired product 47 in approximately 95% purity (171 mg, 446 µmol, 99%).

**TLC** (14% ethyl acetate in cyclohexane): \( R_f = 0.38 \) (UV, CAM, KMnO₄).

**mp**: 75 °C (decomposition).

**¹H NMR** (400 MHz, chloroform-d) \( \delta \) 8.22 (dd, \( J = 7.8, 1.3 \) Hz, 1H), 8.16 (dd, \( J = 7.8, 1.3 \) Hz, 1H), 7.62 (d, \( J = 5.3 \) Hz, 1H), 7.30 – 7.22 (m, 1H), 5.67 (d, \( J = 5.3 \) Hz, 1H).

**¹³C NMR** (101 MHz, chloroform-d) \( \delta \) 177.2, 145.1, 144.0, 141.2, 131.9, 131.2, 128.8, 126.4, 100.5, 56.9.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_{\text{max}} \): 3093 (w), 2949 (m), 1732 (m), 1613 (m), 1423 (w), 871 (s), 793 (m), 742 (m) cm⁻¹.

**HRMS** (ESI) calc. for C₁₀H₄BrClIO [M-H]⁻: 380.8184 found: 380.8188.

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2-Bromo-3-ethyl-5-iodonaphthalen-1-ol (S8-Et)

3-Bromo-4-hydroxy-8-iodo-2-naphthonitrile (S8-CN)

Diethylaluminium cyanide (Nagata’s reagent) (1 M in PhMe, 138 µL, 138 µmol, 1.20 equiv) was added dropwise to a solution of enone 47 (44.0 mg, 115 µmol, 1 equiv) in toluene (1.15 mL, 0.1 M) at –78 °C. After two hours of stirring at that temperature, the residual solid dry-ice was removed from the external acetone bath to initiate slow warming to 23 °C within 50 minutes. After stirring for ten minutes at 23 °C, the red solution was diluted with water (3 mL) and extracted with diethyl ether (3 × 5 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (5 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered and the filtrate was concentrated under reduced pressure to give a crude mixture containing 9% of S8-Et and 63% of presumably S9-CN as indicated by internal-standard-¹H-NMR. Purification by silica gel chromatography (11% ethyl acetate in cyclohexane + 2% acetic acid) afforded compound S8-Et.
(3.50 mg, 9.20 µmol, 8%) as a white solid and compound **S8-CN** (24.9 mg, 66.7 µmol, 58%) as a yellow solid.

**Compound S8-Et**

**TLC** (14% diethyl acetate in cyclohexane): \( R_f = 0.59 \) (UV, CAM, KMnO₄).

**mp**: 69 °C.

**¹H NMR** (400 MHz, chloroform-\( d \)) \( \delta \) 8.25 (d, \( J = 8.4 \) Hz, 1H), 8.11 (dd, \( J = 7.4, 1.1 \) Hz, 1H), 7.57 (s, 1H), 7.15 (dd, \( J = 8.4, 7.3 \) Hz, 1H), 6.19 (s, 1H), 2.95 (q, \( J = 7.5 \) Hz, 2H), 1.38 (t, \( J = 7.5 \) Hz, 3H).

**¹³C NMR** (101 MHz, chloroform-\( d \)) \( \delta \) 148.3, 142.0, 138.7, 134.0, 126.3, 123.8, 123.5, 123.4, 108.9, 98.5, 30.3, 14.4.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_\text{max} \): 3304 (w), 1521 (s), 1434 (vs), 1209 (s), 1144 (s), 798 (w) cm\(^{-1}\).

**HRMS** (ESI) calc. for C₁₂H₉BrIO \([M-H]^-\): 374.8887 found: 374.8891.

**Compound S8-CN**

**TLC** (14% diethyl acetate in cyclohexane): \( R_f = 0.17 \) (UV, CAM, KMnO₄).

**mp**: 70–72 °C.

**¹H NMR** (400 MHz, dichloromethane-\( d_2 \)) \( \delta \) 8.63 (dd, \( J = 7.4, 1.3 \) Hz, 1H), 8.50 (dd, \( J = 8.4, 1.3 \) Hz, 1H), 7.37 (dd, \( J = 8.4, 7.4 \) Hz, 1H), 7.22 (s, 1H).

**¹³C NMR** (101 MHz, dichloromethane-\( d_2 \)) \( \delta \) 154.3, 147.5, 130.7, 130.7, 130.0, 126.1, 125.2, 117.5, 114.9, 110.8, 89.8.

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_\text{max} \): 3527 (w), 2248 (s), 1599 (s), 1203 (s), 1123 (vs), 982 (w) cm\(^{-1}\).

**HRMS** (ESI) calc. for C₁₁H₄BrINO \([M-H]^-\): 371.8526 found: 371.8529.

2-Bromo-3-ethyl-5-iodonaphthalen-1-ol (S8-Et)

2-Bromo-4-chloro-3-ethyl-5-iodo-3,4-dihydronaphthalen-1(2H)-one (S9-Et)

Triethylaluminium (25 wt% in PhMe, 23.0 µL, 51.3 µmol, 1.20 equiv) was added dropwise to a solution of enone 47 (16.4 mg, 42.8 µmol, 1 equiv) in toluene (428 µL, 0.1 M) at −78 °C. After 15 minutes of stirring at that temperature, the red solution was diluted with water (2 mL) and extracted with diethyl ether (3 × 3 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (4 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered, and the filtrate was evaporated under reduced pressure. Purification by silica gel chromatography (3% ethyl acetate in cyclohexane) afforded compound **S8-Et** (9.70 mg, 25.7 µmol, 60%) as a while solid and compound **S9-Et** (4.40 mg, 10.7 µmol, 25%) as a reddish solid.
For analytical data of compound **S8-Et**: see above.

**Compound S9-Et**

**TLC** (20% dichloromethane in pentane): $R_f = 0.24$ (UV, CAM, KMnO$_4$).

**mp:** 69 °C.

**$^1$H NMR** (400 MHz, chloroform-$d$) δ 8.14 (dd, $J = 7.9$, 1.3 Hz, 1H), 8.10 (dd, $J = 7.8$, 1.4 Hz, 1H), 7.18 (t, $J = 7.8$ Hz, 1H), 5.88 (d, $J = 4.3$ Hz, 1H), 5.51 (d, $J = 3.0$ Hz, 1H), 2.95 – 2.82 (m, 1H), 2.12 – 1.94 (m, 1H), 1.07 – 0.95 (m, 4H).

**$^{13}$C NMR** (151 MHz, chloroform-$d$) δ 188.2, 146.2, 141.1, 131.3, 131.2, 128.7, 101.5, 64.8, 55.2, 52.6, 21.5, 12.2.

**IR** (Diamond-ATR, neat) $\tilde{\nu}_{\text{max}}$: 3012 (w), 1732 (s), 1637 (m), 1584 (s), 1429 (s), 1192 (m), 1038 (vs), 721 (w) $^{-1}$.

**HRMS** (ESI) calc. for C$_{12}$H$_{12}$BrClIO $[\text{M+H}]^+$: 412.8799 found: 412.8797.

**2-Bromo-3-ethyl-5-iodonaphthalen-1-ol (S8-Et)**

**2-Bromo-4-chloro-3-ethyl-5-iodo-3,4-dihydronaphthalen-1(2H)-one (S9-Et)**

$N$-Chlorosuccinimide (8.40 mg, 63.0 µmol, 1.10 equiv) was added to a solution of naphthol **22-Br** (20.0 mg, 57.3 µmol, 1 equiv) in acetonitrile (600 µL, 0.10 M) in two portions over 15 minutes at 23 °C. After three hours, the solvent was removed under reduced pressure. The obtained crude solid was re-dissolved in toluene (800 µL, 0.07 M) and cooled to $-78$ °C before triethylaluminium (25 wt% in PhMe, 31.4 µL, 68.8 µmol, 1.20 equiv) was added dropwise. After ten minutes of stirring at that temperature, the solution was diluted with water (2 mL) and extracted with diethyl ether (3×3 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (4 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered, and the filtrate was concentrated under reduced pressure. Purification by silica gel chromatography (3% ethyl acetate in cyclohexane) to afford compound **S8-Et** (8.90 mg, 23.5 µmol, 41%) as a while solid and compound **S9-Et** (13.7 mg, 33.2 µmol, 58%) as a reddish solid.

For analytical data: see above.
1-(3-Bromo-4-hydroxy-8-iodonaphthalen-2-yl)propan-2-one (S8-ac-Br)
1-(3-Chloro-4-hydroxy-8-iodonaphthalen-2-yl)propan-2-one (S8-ac-Cl)

Tin(IV)-chloride (1 M in dichloromethane, 42.2 µL, 42.2 µmol, 1.10 equiv) was added dropwise to a solution of enone 47 (14.7 mg, 38.3 µmol, 1 equiv) and silyl enol ether S10 (85% purity, 8.00 µL, 42.2 µmol, 1.10 equiv) in dichloromethane (500 µL, 0.08 M) at −78 °C. The reaction was stirred for two hours while slowly warming to 23 °C. Additional silyl enol ether S10 (85% purity, 50.0 µL, 264 µmol, 6.88 equiv) was added dropwise and the reaction was stirred at 23 °C for 30 minutes. After addition of water (4 mL), the crude mixture was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with a saturated aqueous solution of sodium chloride (5 mL) and the washed solution was dried over magnesium sulfate. The dried solution was filtered. The filtrate was evaporated under reduced pressure and purified by silica gel chromatography (15% dichloromethane in cyclohexane) to give the title compounds S8-ac-Br and S8-ac-Cl (5.40 mg, 13.3 mmol, 37%) as an inseparable mixture in a ratio of 2:1.

Mixture (2:1) of S8-ac-Br and S8-ac-Cl

TLC (80% dichloromethane in cyclohexane): Rf = 0.32 (UV, CAM, KMnO4).

1H NMR (400 MHz, chloroform-d) δ 8.25 (dt, J = 8.4, 1.0 Hz, 1H), 8.22 (dt, J = 8.4, 1.0 Hz, 0.5H), 8.10 (dd, J = 7.4, 1.2 Hz, 1H), 8.09 (dd, J = 7.4, 1.1 Hz, 0.5H), 7.56 (s, 1H), 7.55 (s, 0.5H), 7.19 – 7.15 (m, 1.5H), 6.13 (s, 1H), 6.12 (s, 0.5H), 4.05 (s, 2H), 4.03 (s, 1H), 2.28 (s, 4.5H).

13C NMR (101 MHz, chloroform-d) δ 204.7, 204.7, 148.8, 147.6, 139.1, 138.9, 134.0, 133.4, 132.2, 127.0, 127.0, 126.8, 126.7, 124.1, 123.9, 123.5, 123.3, 115.9, 108.6, 98.5, 98.5, 51.8, 49.4, 29.9, 29.8.

IR (Diamond-ATR, neat) v_max: 3432 (w), 1761 (s), 1620 (s), 1229 (s), 1093 (s), 938 (m), 798 (w) cm⁻¹.

HRMS (ESI) calc. for C13H6BrIO2 [M−H]⁻ : 402.8836 found: 402.8831.

HRMS (ESI) calc. for C13H6ClO2 [M−H]⁻ : 358.9341 found: 358.9337.
2-Bromo-5-iodo-3-(4-methoxyphenyl)naphthalen-1-ol (S8-an-Br)
2-Chloro-5-iodo-3-(4-methoxyphenyl)naphthalen-1-ol (S8-an-Cl)

Tin(IV)-chloride (1 M in dichloromethane, 242 µL, 242 µmol, 1.20 equiv) was added dropwise to a solution of ketone 47 (42.0 mg, 110 µmol, 1 equiv) and anisole (239 µL, 2.19 mmol, 20.0 equiv) in dichloromethane (1.38 mL, 0.08 M) at –30 °C. The reaction was slowly warmed to 23 °C within 1.5 hours and then stirred for further 30 minutes at that temperature. The solvent was removed under reduced pressure to give an orange-brown solid. The sensitive crude product was dissolved in a mixture of cyclohexane and ethyl acetate (19:1) and immediately subjected to flash-column-chromatography on silica gel under a nitrogen-stream to give an inseparable mixture of compounds S8-an-Br and S8-an-Cl (19.0 mg, 41.8 µmol, 38%) in a ratio of 4:1.

Mixture (4:1) of S8-an-Br and S8-an-Cl

**TLC** (14% ethyl acetate in cyclohexane): \( R_f = 0.45 \) (UV, CAM, KMnO₄).

\[ ^1H \text{ NMR} \quad (400 \text{ MHz, chloroform-}d) \delta 8.40 \text{ (dd, } J = 8.4, 1.3 \text{ Hz, } 1.25 \text{H}), \delta 8.31 – 8.21 \text{ (m, } 0.5 \text{H}), 8.25 \text{ (dd, } J = 7.3, 1.3 \text{ Hz, } 1 \text{H}), 8.11 \text{ (td, } J = 7.3, 1.2 \text{ Hz, } 0.5 \text{H}), 7.50 \text{ (s, } 1.25 \text{H}), 7.21 – 7.16 \text{ (m, } 2.5 \text{H}), 7.12 \text{ (dd, } J = 8.4, 7.3 \text{ Hz, } 1.25 \text{H}), 7.00 – 6.94 \text{ (m, } 2.5 \text{H}), 5.98 \text{ (s, } 1.25 \text{H}), 3.89 \text{ (s, } 0.75 \text{H}), 3.89 \text{ (s, } 3 \text{H}). \]

\[ ^{13}C \text{ NMR} \quad (101 \text{ MHz, chloroform-}d) \delta 159.7, 147.8, 143.2, 135.2, 133.0, 132.7, 132.7, 131.7, 126.8, 126.4, 123.6, 113.5, 103.7, 92.4, 55.5. \]

**IR** (Diamond-ATR, neat) \( \tilde{\nu}_\text{max} \): 3131 (w), 1689 (m), 1513 (vs), 1074 (s), 999 (m), 783 (w) cm\(^{-1}\).

**HRMS** (ESI) calc. for C₁₇H₁₁BrIO₂ [M-H]: 452.8993 found: 452.8995.

**HRMS** (ESI) calc. for C₁₇H₁₁ClO₂ [M-H]: 408.9498 found: 408.9492.

\(^1\text{Only the set of signals for the 2-bromo-naphthol S8-an-Br is given due to the low intensity of the 2-chloro-naphtho-signals.} \)
5. NMR-Spectra

18-Cl
$^1$H-NMR, 400 MHz
CDCl$_3$

$^{13}$C-NMR, 101 MHz
CDCl$_3$
19-Cl

$^1$H-NMR, 400 MHz
CDCl$_3$

19-Cl

$^{13}$C-NMR, 101 MHz
CDCl$_3$
20-Cl

$^1$H-NMR, 400 MHz
CDCl$_3$

20-Cl

$^{13}$C-NMR, 101 MHz
CDCl$_3$
21-Cl
$^1$H-NMR, 400 MHz
CDCl$_3$

21-Cl
$^{13}$C-NMR, 101 MHz
CDCl$_3$
22-CI
$^1$H-NMR, 400 MHz
CDCl$_3$

22-CI
$^{13}$C-NMR, 101 MHz
CDCl$_3$
23-Cl
$^1$H-NMR, 400 MHz
CDCl$_3$

23-Cl
$^{13}$C-NMR, 101 MHz
CDCl$_3$
24-Cl

$^1$H-NMR, 400 MHz
CDCl$_3$

24-Cl

$^{13}$C-NMR, 101 MHz
CDCl$_3$
25-Cl

$^1$H-NMR, 400 MHz
CDCl$_3$

25-Cl

$^{13}$C-NMR, 101 MHz
CDCl$_3$
26-Cl
$^1$H-NMR, 400 MHz
CDCl$_3$

26-Cl
$^{13}$C-NMR, 101 MHz
CDCl$_3$
$^{1}H$-NMR, 400 MHz
CDCl$_3$

$^{13}C$-NMR, 101 MHz
CDCl$_3$
28-Cl

$^1$H-NMR, 400 MHz
CDCl$_3$

28-Cl

$^{13}$C-NMR, 101 MHz
CDCl$_3$
29-CI

$^1$H-NMR, 400 MHz  
CDCl$_3$

29-CI

$^{13}$C-NMR, 101 MHz  
CDCl$_3$
32-Cl

$^1$H-NMR, 400 MHz

CDCl$_3$

---

32-Cl

$^{13}$C-NMR, 101 MHz

CDCl$_3$
33-Cl
$^1$H-NMR, 400 MHz
CDCl$_3$

33-Cl
$^{13}$C-NMR, 101 MHz
CDCl$_3$
16-TBS
$^1$H-NMR, 400 MHz
CDCl$_3$

16-TBS
$^{13}$C-NMR, 101 MHz
CDCl$_3$
20-Br

$^1$H-NMR, 400 MHz
CDC$_3$

20-Br

$^{13}$C-NMR, 101 MHz
CDC$_3$

60
21-Br
$^{19}$F-NMR, 376 MHz
CDCl$_3$

22-Br
$^1$H-NMR, 400 MHz
CDCl$_3$
22-Br
$^{13}$C-NMR, 101 MHz
CDCl$_3$

23-Br
$^1$H-NMR, 400 MHz
CDCl$_3$
23-Br

$^{13}$C-NMR, 101 MHz
CDCl$_3$

23-Br

$^{19}$F-NMR, 376 MHz
CDCl$_3$
24-Br
$^{19}$F-NMR, 376 MHz
CDCl$_3$

25-Br
$^1$H-NMR, 400 MHz
CDCl$_3$
25-Br
\[^{13}\text{C-NMR, 101 MHz}\]
CDCl₃

26-Br
\[^{1}H\text{-NMR, 400 MHz}\]
CDCl₃
26-Br
$^{13}\text{C-NMR, 101 MHz}$
$\text{CDCl}_3$

29-Br
$^1\text{H-NMR, 400 MHz}$
$\text{CDCl}_3$
29-Br
$^{13}\text{C-NMR}, 101 \text{ MHz}$
$\text{CDCl}_3$

S1-Br
$^1\text{H-NMR}, 400 \text{ MHz}$
$\text{CDCl}_3$
S1-Br
$^{13}$C-NMR, 101 MHz
CDCl$_3$

S2-Br
$^1$H-NMR, 400 MHz
CDCl$_3$
**S2-Br**

$^{13}$C-NMR, 101 MHz

CDCl$_3$

---

**31-Br**

$^1$H-NMR, 400 MHz

CDCl$_3$
$^{13}$C-NMR, 101 MHz
CDCl$_3$

$^1$H-NMR, 400 MHz
CDCl$_3$
\begin{align*}
\text{S3-Br} \quad \text{\textsuperscript{13}C-NMR, 101 MHz} \\
\text{CDCl}_3
\end{align*}

\begin{align*}
\text{32-Br} \quad \text{\textsuperscript{1}H-NMR, 400 MHz} \\
\text{CDCl}_3
\end{align*}
32-Br
$^{13}$C-NMR, 101 MHz
CDCl$_3$

33-Br
$^1$H-NMR, 400 MHz
CDCl$_3$
33-Br
$^{13}$C-NMR, 101 MHz
CDCl$_3$

36
$^1$H-NMR, 400 MHz
CDCl$_3$
36
$^{13}$C-NMR, 101 MHz
CDCl$_3$

37
$^1$H-NMR, 400 MHz
CDCl$_3$
$^{13}$C-NMR, 101 MHz
CDCl$_3$

$^1$H-NMR, 400 MHz
CDCl$_3$
38-Br
$^{13}$C-NMR, 101 MHz
CDCl$_3$

39-Br
$^1$H-NMR, 400 MHz
CDCl$_3$
39-Br
$^{13}\text{C-NMR}$, 101 MHz
$\text{CDCl}_3$

40-Br
$^1\text{H-NMR}$, 400 MHz
$\text{CDCl}_3$
40-Br

$^{13}$C-NMR, 101 MHz
CDCl$_3$

41a

$^1$H-NMR, 400 MHz
CDCl$_3$
$^{13}$C-NMR, 101 MHz

CDCl$_3$

$^1$H-NMR, 400 MHz

CDCl$_3$
$^{13}$C-NMR, 101 MHz
CDCl$_3$

$^1$H-NMR, 400 MHz
CDCl$_3$
41c

$^{13}$C-NMR, 101 MHz
CDCl$_3$

Defucogilvocarin M (45)

$^1$H-NMR, 400 MHz
CDCl$_3$
44
$^{13}$C-NMR, 101 MHz
CDCl$_3$

47
$^1$H-NMR, 400 MHz
CDCl$_3$
$^{13}$C-NMR, 101 MHz

CDCl$_3$

$^1$H-NMR, 400 MHz

CDCl$_3$
S8-Et
$^{13}$C-NMR, 101 MHz
CDCl$_3$

S8-CN
$^1$H-NMR, 400 MHz
CD$_2$Cl$_2$
S8-CN
$^{13}$C-NMR, 101 MHz
CD$_2$Cl$_2$

S9-Et
$^1$H-NMR, 400 MHz
CDCl$_3$
\[ \text{S8-Et} \]

\[ ^{13}\text{C-NMR, 101 MHz} \]

\[ \text{CDCl}_3 \]

\[ \text{S8-ac-Br} \quad (2 : 1) \quad \text{S8-ac-Cl} \]

\[ ^1\text{H-NMR, 400 MHz} \]

\[ \text{CDCl}_3 \]
$^{13}$C-NMR, 101 MHz
CDCl$_3$

$^1$H-NMR, 400 MHz
CDCl$_3$
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