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7-Siloxy-Substituted Hexahydronaphthalene Derivatives: Samarium Diiodide Promoted Synthesis and Typical Reactions

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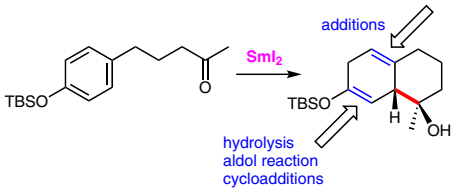
Dedicated to Professor Helmut Vorbrüggen on the occasion of his 90th birthday



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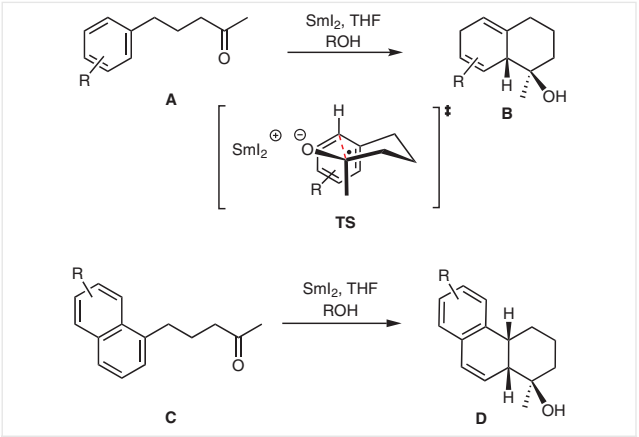
Abstract The samarium diiodide promoted reductive cyclization of a series of γ-aryl ketones with acetoxy, alkoxy, and siloxy groups in *ortho*-, *meta*-, and *para*-positions was investigated. Only precursors with *p*-acetoxy, *p*-*tert*-butoxy, or *p*-siloxy substituents furnished decent yields of the desired 7-oxy-1,2,3,4,6,8a-hexahydronaphthalene derivatives. The products were formed without contamination with the regioisomeric bicyclic products containing conjugated double bonds. Typical reactions exploiting the silyl enol ether moiety of the 7-(*tert*-butyldimethylsiloxy)-1,2,3,4,6,8a-hexahydronaphthalene derivative were performed, allowing stereoselective access to highly substituted hexahydro-, octahydro-, or decahydronaphthalene derivatives.

Key words dearomatization, ketyl, hexahydronaphthalene, radical, samarium diiodide, silyl enol ether



Scheme 1 Samarium diiodide promoted cyclizations of γ-aryl and γ-naphthyl ketones **A** and **C** to bicyclic and tricyclic products **B** and **C**

The dearomatization of arenes or heteroarenes is a fascinating strategy to generate complexity from simple starting materials.[1] Among the reductive methods,[2] samarium diiodide promoted[3] cyclizations of γ-aryl ketones allow efficient and stereoselective access to a variety of polycyclic carbo- and heterocyclic compounds.[4–7] Scheme 1 reveals the overall transformation of simple benzene and naphthalene derivatives **A** and **C**, which provide bicyclic and tricyclic compounds of type **B** and **D**. These reactions require (at least) two equivalents of samarium diiodide and in many cases the addition of strong Lewis bases such as HMPA[8] that strongly increase the reductive power of divalent samarium.[9] The mechanistic details of this transformation have been discussed earlier.[4–7] The stereochemical outcome of the samarium ketyl cyclization is plausibly rationalized by a transition state **TS** (Scheme 1), assuming a chair-like folding of the linker moiety between the carbonyl group and the aryl rings, analogously to the Beckwith–Houk model developed for radical processes.[10]

For simple monosubstituted γ-aryl ketones, we systematically investigated the influence of different substituents on the *ortho*-, *meta*-, or *para*-position on efficacy, stereoselectivity, and position of the two remaining double bonds in the products.[11,12] For most substituents, we obtained clear results, but alkoxy-substituted compounds **E** behaved fairly capriciously (Scheme 2). Standard products of type **F** were obtained in low yield for the *o*-methoxy-substituted precursor, whereas the *m*-methoxy-substituted starting material did not undergo the cyclization at all. The *p*-substituted precursor provided reasonable yields of the cyclization products, but the ratio of the two regioisomers **F** and **G** scattered strongly from experiment to experiment.[13] In addition, in most cases, simple reduction products **H** and re-aromatized cyclization products **I** were isolated in varying quantities.

The 1,2,3,4,6,8a-hexahydronaphthalene derivatives **F** are synthetically valuable intermediates, since they

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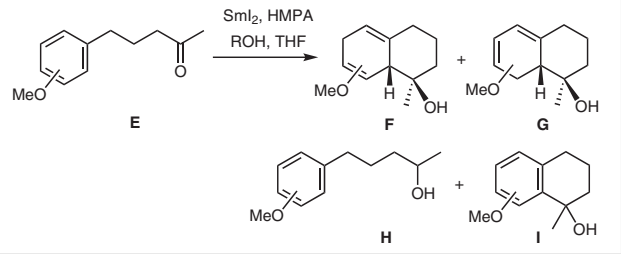
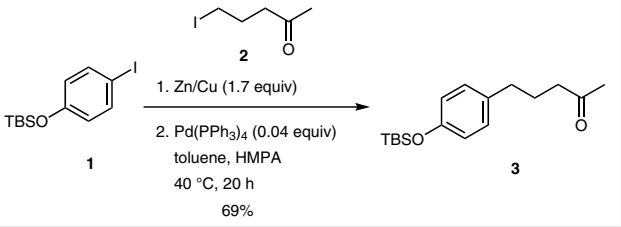


Scheme 2 Samarium diiodide promoted cyclizations of methoxy-substituted γ-aryl ketones **E** and bicyclic products **F**, **G**, and **I**, as well as simple reduction product **H**

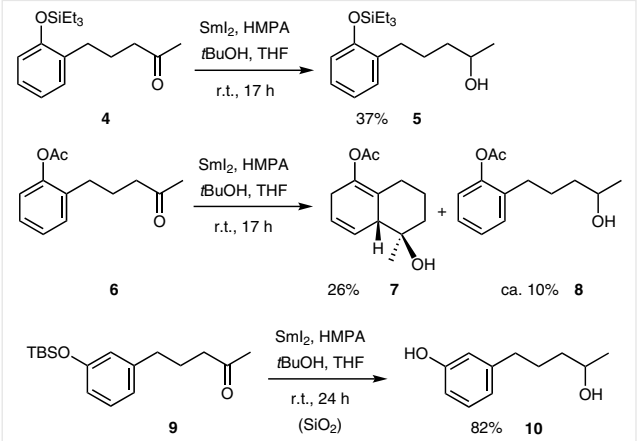
incorporate two olefinic moieties that should allow a variety of subsequent reactions leading to highly substituted compounds in a stereoselective fashion. It was therefore highly desirable to investigate precursors related to **E** that would reliably lead to compounds of type **F**. In this report we discuss cyclization reactions of a series of oxygen-substituted precursor compounds and also describe derivatization of the efficiently obtained 7-(*tert*-butyldimethylsiloxy)-substituted 1,2,3,4,6,8a-hexahydronaphthalene, leading to a quite diverse small library of bicyclic compounds.

The starting materials required for this study were prepared by standard synthetic methods often employing palladium-catalyzed coupling reactions (see Supporting Information). As a typical example, Scheme 3 illustrates the preparation of *tert*-butyldimethylsiloxy-substituted γ-aryl ketone **3**. Following the protocol of Tamaru et al.,[14] the protected *p*-iodophenol (**1**)[15] was coupled under palladium catalysis with the zinc/copper species obtained from γ-iodo ketone **2**,[16] giving the desired compound **3** in good yield.



Scheme 3 Synthesis of γ-aryl ketone **3** by Tamaru coupling of *p*-iodophenol **1** with γ-iodo ketone **2**

For the cyclization reactions we employed the well-established standard reaction conditions[4,11] for this process, which involve the use of an excess of samarium diiodide (2–4 equiv, 0.1 M solution in THF), hexamethylphosphoramide (HMPA) (14–24 equiv) as Lewis base and *tert*-butyl alcohol (2 equiv) as proton source. In most experiments, the reactions were performed at room temperature with aqueous workup after 17 hours. The attempted reductive cyclizations of two *ortho*-substituted precursor compounds **4** and **6** are shown in Scheme 4.

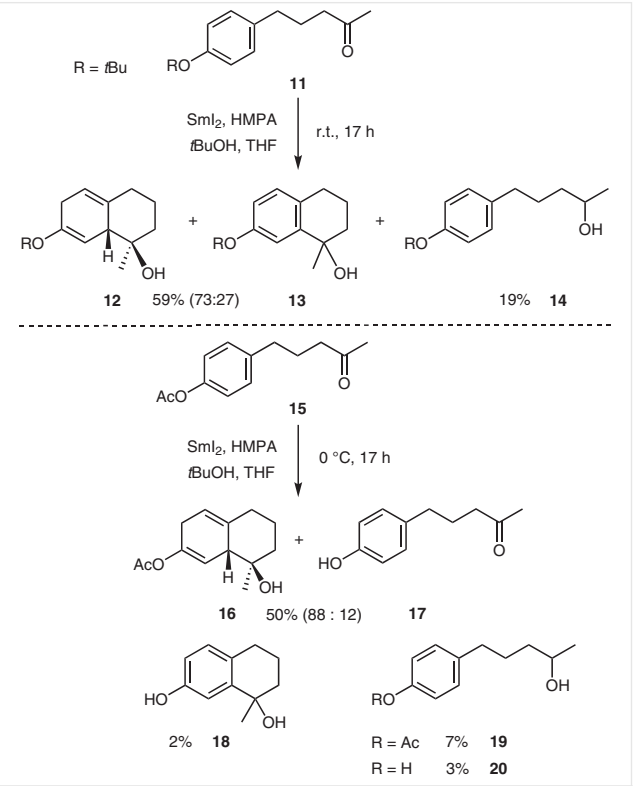


Scheme 4 Attempted reductive cyclizations of *ortho*- and *meta*-substituted precursors **4**, **6**, and **9** (cyclization products such as **7** are formed as racemic mixtures, the drawn formulas in this report describe the relative configuration of products)

Whereas the *o*-triethylsiloxy-substituted compound **4** did not give the expected cyclization product, but only low yields of the simple reduction product **5**, the *o*-acetoxy-substituted precursor **6** afforded the desired bicyclic product **7** in 26% yield and the secondary alcohol **8** (together with low quantities of unknown impurities) in 10% yield (Scheme 4). These results confirm that *ortho*-donor-substituted γ-aryl ketones are poor substrates for samarium diiodide promoted cyclizations,[11] but 5-acetoxy-substituted 1,2,3,4,6,8a-hexahydronaphthalenes such as **7** are available at least in low yields. No attempts to optimize this reaction were undertaken. The *m*-(*tert*-butyldimethylsiloxy)-substituted γ-aryl ketone **9** underwent reduction to the secondary alcohol **10** (under complete desilylation of the phenol moiety during chromatographic purification) and no cyclization was observed (Scheme 4), which may be explained by the unfavorable electronic effect of donor substituents in this position.[11]

Our preliminary experiments[11] indicated that *para*-substituted precursor compounds should afford higher cyclization yields. The *p*-*tert*-butoxy-substituted γ-aryl ketone **11** provided a 73:27 mixture of 7-*tert*-butoxy-1,2,3,4,6,8a-hexahydronaphthalene **12** and its oxidation product **13** in 59% yield (Scheme 5). The secondary alcohol **14** was also isolated in 19% yield. Compound **13** was very likely formed from **12** by oxidation during workup and/or chromatography. By improving these stages of the experiment, it should be possible to achieve higher amounts of **12**, but no attempts were made to avoid this undesired oxidation. The *p*-acetoxy precursor **15** furnished the expected bicyclic product **16**, isolated in a mixture with deacetylated starting material **17** (88:12, 50% yield) (Scheme 5). In other fractions we found small amounts of compounds **18**–**20** (2–7%). While these two experiments look promising, we did not

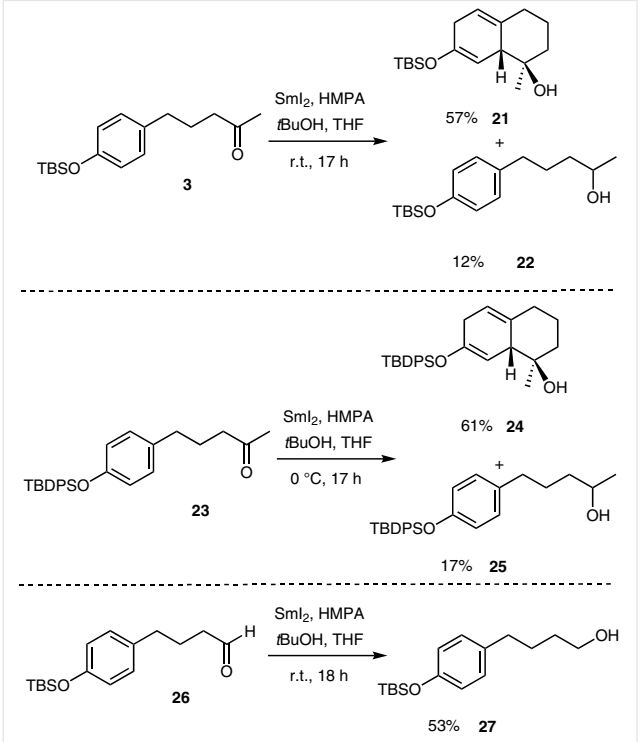
pursue an optimization by modifying the reaction conditions since the precursors with *p*-siloxy substituents turned out to be clearly superior (see below).



Scheme 5 Reductive cyclizations of *para*-substituted precursors **11** and **15** leading to bicyclic products **12** and **16** as major products

The reactions of three *p*-siloxy-substituted precursor compounds **3**, **23**, and **26** are depicted in Scheme 6. The *p*-(*tert*-butyldimethylsiloxy)-substituted γ-aryl ketone **3** was smoothly converted into the desired 1,2,3,4,6,8a-hexahydronaphthalene **21**, cleanly obtained in 57% yield. The only side product we identified was the secondary alcohol **22** (12%). A very similarly efficient cyclization was observed with precursor **23** bearing the even more bulky *p*-(*tert*-butyldiphenylsiloxy) substituent. Now the cyclization product **24** was obtained in 61% yield and the reduction product **25** in 17% yield. Inspired by these good results, we also subjected γ-aryl aldehyde **26** to the cyclization conditions, but only the primary alcohol **27** was isolated as a result of the simple reduction of the aldehyde function by samarium diiodide. This confirms our earlier findings that γ-aryl aldehydes are generally unsuitable starting materials for the dearomatizing cyclization process.[4,11]

In summary, we observed that the two siloxy-substituted precursor ketones **3** and **23** delivered the highest conversions in favor of cyclization and the best yields of the desired 7-oxy-1,2,3,4,6,8a-hexahydronaphthalene derivatives

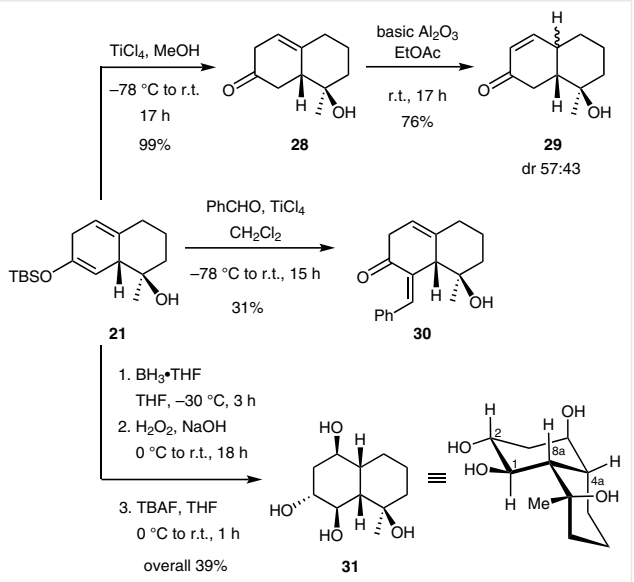


Scheme 6 Reductive cyclizations of *p*-siloxy-substituted precursors **3**, **23**, and **26** leading to bicyclic products **21** and **24** and reduction products **22**, **25**, and **27**

(Scheme 6). Due to the better atom economy, (*tert*-butyldimethylsiloxy) compound **3** is the precursor of choice. We therefore studied a few typical subsequent reactions of its cyclization product **21**. This diastereomerically pure compound is interestingly functionalized, since it contains a silyl enol ether unit, a second (less activated) trisubstituted double bond and a tertiary alcohol group.

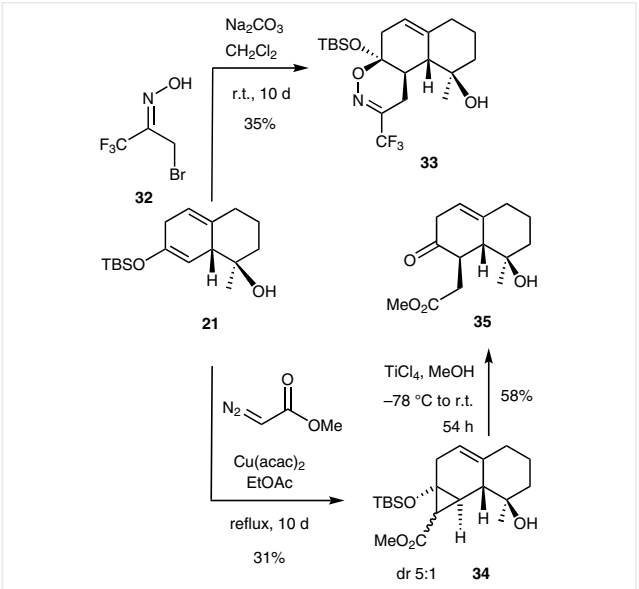
We first cleaved the silyl enol ether moiety by employing catalytic amounts of hydrogen chloride generated in situ from $TiCl_4$ in methanol providing the expected ketone **28** in almost quantitative yield (Scheme 7). This compound is also available in 83% yield by saponification of the acetoxy-substituted compound **16**. The unconjugated double bond was shifted under basic conditions to give the α,β-unsaturated ketone **29** with a newly formed stereogenic center at the bridgehead, resulting in a 57:43 mixture of the two diastereomers. A Mukaiyama aldol condensation[17] reaction using benzaldehyde and the Lewis acid titanium tetrachloride shows the potential of the electron-rich double bond of **21** to react with strong electrophiles. The enone **30** was isolated in 31% yield (Scheme 7). The most intriguing transformation of **21** concerns its exhaustive hydroboration. Reaction with an excess of borane–THF complex, followed by standard oxidative workup provided the silylated precursor of tetrol **31** (47% yield). Desilylation with tetra-*n*-butylammonium fluoride gave compound **31** in 39% overall

yield (Scheme 7). Both double bonds apparently undergo the hydroboration in an entirely stereoselective fashion, although the moderate mass balance does not exclude formation of other isomers. Compound **31** is a solid, but suitable crystals for an X-ray analysis could not be obtained. The tentative configurational assignment is compatible with the coupling constants observed in the ^{1}H NMR spectrum and the conformation of the *cis*-decalin system as depicted in Scheme 7. Bridgehead proton 8a-H shows coupling constants of 4.2 Hz to 4a-H and 11.1 Hz to 1-H, which in turn couples with 2-H (8.8 Hz); the signal for 2-H appears as a ddd with coupling constants of 5.1, 8.8, and 13.7 Hz, indicating the 2-OH and 1-OH are in equatorial positions. The assumed configuration is the result of two subsequent borane additions to the more sterically available convex face of **21**. Compounds such as **21** can be regarded as *cis*-fused polycyclitols and bicyclic sugar analogs. They may also be of interest as building blocks for supramolecular chemistry.[18]



Scheme 7 Typical reactions of compound **21** leading to ketone **28**, enone **29**, aldol condensation product **30**, and tetrol **31**

Silyl enol ethers are often suitable substrates in cycloaddition reactions with electron-deficient species and we therefore employed **21** in a hetero-Diels–Alder reaction with an in situ generated fluorinated α-nitrosoalkene (Scheme 8). Treatment of α-bromo oxime **32** with base generated 3,3,3-trifluoro-2-nitrosopropene,[19] which slowly added to the electron-rich double bond of **21**. This transformation required a large excess of the nitrosoalkene precursor (10 equiv), since additions to silyl enol ethers with substituents in the γ-position to the siloxy group are known to be less efficient;[20] the moderate yield of 35% for compound **33** was therefore not unexpected. The copper-catalyzed cyclopropanation of **21** was also not high yielding, but, with this reaction leading to siloxycyclopropane **34** in 31% yield, we could demonstrate that donor–acceptor cyclopropanes[21] of this type are also available from 7-siloxy-1,2,3,4,6,8a-hexahydronaphthalene derivatives. Of the four diastereomers possible, only those two are formed that derive from an attack of the copper carbenoid to the sterically more accessible convex face *cis* to the bridgehead hydrogen.[22] As a consequence, by acid-promoted ring-opening[23] of the siloxycyclopropanes **34**, only the resulting bicyclic γ-keto ester **35** was isolated as a single diastereomer (58% yield).



Scheme 8 Cycloadditions of compound **21** leading to 1,2-oxazine derivative **33** and donor–acceptor cyclopropane **34**

The transformations depicted in Schemes 7 and 8 were not optimized, since the focus of this study was the efficient generation of bicyclic precursor compounds such as **21**. Nevertheless, the results demonstrate that 7-siloxy-substituted 1,2,3,4,6,8a-hexahydronaphthalenes are excellent starting materials for many subsequent reactions leading to interestingly functionalized products of synthetic value. Compounds such as **28**–**30** or **33**–**35** offer various possibilities for further functionalization.

In this study we reinvestigated the samarium diiodide promoted cyclizations of γ-aryl ketones with oxygen substituents in different positions of the aryl group. The results confirm earlier findings that only *para*-substituted precursor compounds provide the expected dearomatized cyclization products in good yields and reasonable chemoselectivity. Although *p*-*tert*-butoxy- and *p*-acetoxy-substituted precursors **11** and **15** gave the expected 1,2,3,4,6,8a-hexahydronaphthalene derivatives **12** and **16** in moderate yields, these transformations are not practical, since the side products could not be removed easily. Good results were obtained with *p*-(*tert*-butyldimethylsiloxy)- and *p*-(*tert*-butyldiphenylsiloxy)-substituted aryl ketones **3** and **23** that afforded the desired dearomatized compounds **21**

and **24** in ca. 60% yield after chromatographic purification. Probably due to the low polarity, size, and stability of the siloxy groups, small amounts of side products could be easily separated from the major components **21** and **24**. No isomeric products were identified with differing position of the double bonds. The silyl enol ether moiety of **21** was employed in a screening of typical subsequent reactions. These transformations demonstrate that 7-siloxy-substituted 1,2,3,4,6,8a-hexahydronaphthalenes are good precursor compounds for the synthesis of functionalized bicyclic compounds in a stereoselective fashion.

NMR spectra were recorded on either Bruker (AC 250, AC 500, AVANCE III) or JOEL (ECX 400, Eclipse 500) instruments at 300 K. ^{13}C NMR spectra are proton-decoupled. For detailed peak assignments, 2D spectra were obtained (COSY, HMQC, HMBC, and NOESY). For ^{1}H NMR spectroscopy, the singlets of chloroform (δ = 7.26) or benzene (δ = 7.28) were used as internal standards; for ^{13}C NMR spectroscopy, either the triplet of $CDCl_3$ (δ = 77.0) or the doublet of C_6D_6 (δ = 128.5) was used. IR spectra were recorded on a JASCO FT/IR-4100 type A instrument with a TGS detector. Mass spectra were recorded on an Agilent 6210 ESI-TOF or a Finnigan MAT 711 (EI, 80 eV, 8 kV) instrument. Elemental analyses were performed on a Perkin-Elmer CHN-Analyzer 2400, Vario EL, or Vario ELIII instrument. Melting points were measured on a Reichert apparatus Thermovar and are uncorrected.

Preparative column chromatography was performed on silica gel (230–400 mesh, Merck or Fluka) or on neutral alumina (100–250 mesh, Fluka, activity grade I; deactivation to obtain activity grade III by addition of 6% H_2O). HPLC separations were performed on a Nucleosil 50-5 column with a Rheodyne injection system. The compounds were detected with a Knauer variable UV detector and Knauer refractometer.

Solvents: anhydrous THF, CH_2Cl_2, Et_2O, and MeCN were prepared by using a Braun Solvent Purification System 800. HMPA and Et_3N were distilled before use (CaH_2) and stored over activated 4 Å molecular sieves or KOH. MeOH, *t*BuOH, dimethylacetamide (DMA), and DMF were purchased in p.A. quality and stored under argon with activated 4 Å molecular sieves. Hexane (mixture of isomers) was distilled from CaH_2. EtOAc was distilled from K_2CO_3 and $CaCl_2$.

Reactions were generally performed under argon in flame-dried flasks. Solvents and reagents were added by syringes (polypropylene or Hamilton microliter syringes) through a septum or a three-way valve under positive argon pressure. Solids were added as a solution or as powder or chunks under positive argon pressure.

For syntheses of starting materials, descriptions of unsuccessful cyclization reactions, and copies of NMR spectra of selected compounds, see the Supporting Information.

5-[4-(*tert*-Butyldimethylsiloxy)phenyl]pentan-2-one (3)

Analogous to the literature procedure,[15] the Zn/Cu couple (1.57 g, 24.2 mmol) and **2**[16] (3.15 g, 14.9 mmol) were suspended in toluene (25 mL) and HMPA (6.89 mL, 7.35 g, 41.0 mmol) was added. The mixture was stirred for 1 h at 40 °C. To this suspension was added a solution of **1**[14] (4.73 g, 14.2 mmol) and $Pd(PPh_3)_4$ (0.65 g, 0.57 mmol) in toluene (10 mL). The mixture was stirred for 20 h at 40 °C and then cooled to r.t.; then Et_2O (25 mL) was added and the mixture was washed with 1 N aq HCl (50 mL) and sat. aq $NaHCO_3$ (50 mL). The organic phase was dried ($MgSO_4$) and concentrated in vacuo. After column chromatography (silica gel, hexanes/EtOAc 18:1), ketone **3** was isolated.

Yield: 2.84 g (69%); colorless oil.

IR (film, ATR): 3025–2860 (=C-H, C-H), 1715 (C=O), 1510 (C=C), 1250 (Si-Me) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.18 (s, 6 H, $SiMe_2$), 0.97 (s, 9 H, CMe_3), 1.86 (quin, *J* = 7.4 Hz, 2 H, 4-H), 2.11 (s, 3 H, 1-H), 2.41 (t, *J* = 7.4 Hz, 2 H, 3-H), 2.54 (t, *J* = 7.4 Hz, 2 H, 5-H), 6.75, 7.01 (2 d, *J* = 8.4 Hz, 2 H each, Ar).

^{13}C NMR (126 MHz, $CDCl_3$): δ = –4.5 (q, $SiMe_2$), 18.2 (s, CMe_3), 25.4 (t, C-4), 25.7 (q, CMe_3), 29.9 (q, C-1), 34.2 (t, C-5), 42.8 (t, C-3), 119.9, 129.3, 134.2, 153.7 (2 d, 2 s, Ar), 208.0 (s, C-2).

Anal. Calcd for $C_{17}H_{28}O_2Si$ (292.5): C, 69.81; H, 9.65. Found: C, 69.38; H, 9.66.

Preparation of a 0.1 M SmI_2 Stock Solution

THF (320 mL) was placed in a flame-dried and argon-filled flask attached with a three-way valve. Argon was bubbled through the solvent for 40 min. Samarium (5.54 g, 36.8 mmol) and iodine (8.13 g, 32.0 mmol) were subsequently added. The suspension was stirred at r.t. until the color turned to dark blue (2–18 h). The flask was then wrapped in aluminum foil to exclude light and stored at r.t. The concentration was determined by titration of the SmI_2 solution against a 0.1 M iodine solution in THF.

SmI_2-Promoted Cyclizations; General Procedure (GP)

HMPA (14–24 equiv) was added to a previously prepared 0.1 M stock solution of SmI_2 in THF (2–4 equiv) under argon and the solution was stirred for 20 min. The solution turned from dark blue to dark violet. In a second flask, the substrate (1 equiv) and *t*BuOH (2 equiv) were dissolved in THF (10 mL/mmol cyclization precursor) under argon. Argon was bubbled through the solution for 20 min. The substrate solution was then transferred by syringe to the SmI_2 solution at r.t. if not mentioned otherwise. The mixture was stirred until the color changed from violet to grey. Sat. aq $NaHCO_3$ solution or sat. aq Na-K-tartrate solution (20 mL) was added and the mixture was extracted with Et_2O (3 × 30 mL). The combined organic layers were washed with H_2O and brine (2 × 30 mL each) and dried ($MgSO_4$) and the solvents were removed under reduced pressure to give the crude product still containing small amounts of HMPA. Flash chromatography on silica gel or on alumina (activity grade III) yielded the products.

Cyclization of Aryl Ketone 6

According to the GP, **6** (100 mg, 0.45 mmol), SmI_2 (11.4 mL, 1.14 mmol), HMPA (1.19 mL, 1.22 g, 6.81 mmol), and *t*BuOH (0.09 mL, 67 mg, 0.91 mmol) furnished after 17 h and workup with Na-K-tartrate solution the crude product. After column chromatography (silica gel, hexanes/EtOAc 7:3) cyclization product **7** was isolated (26 mg, 26%). In a second fraction, a mixture of **7** and **8** containing small amounts of an unidentified olefin was isolated (14 mg).

(1*R**,8a*R**)-5-Acetoxy-1-methyl-1,2,3,4,6,8a-hexahydro-1-naphthol (7)

Yield: 26 mg (26%); colorless oil.

IR (film, ATR): 3400 (O-H), 3010–2860 (=C-H, C-H), 1750 (C=O), 1600 (C=C) cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.10 (s, 3 H, 1-Me), 1.34 (tq, *J* = 4.0, 13.4 Hz, 1 H, 3-H), 1.52–1.60 (m, 2 H, 2-H^1, 4-H^1), 1.62–1.72 (m, 2 H, 3-H^2, OH), 1.79 (dddd, *J* = 1.6, 2.8, 4.0, 12.4 Hz, 1 H, 2-H^2), 2.14 (s, 3 H, COMe), 2.47 (m_c, 1 H, 4-H^2), 2.71–2.76 (m, 2 H, 6-H), 2.83 (m_c, 1 H, 8a-H), 5.76 (dtd, *J* = 1.4, 3.3, 10.2 Hz, 1 H, 7-H), 5.83 (tdd, *J* = 2.0, 3.1, 10.2 Hz, 1 H, 8-H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.7 (q, CO*Me*), 21.7 (q, 1-Me), 22.9 (t, C-3), 25.7 (t, C-4), 28.3 (t, C-6), 41.5 (t, C-2), 50.4 (d, C-8a), 74.7 (s, C-1), 122.8 (s, C-4a), 124.1, 124.2 (2 d, C-7, C-8), 138.9 (s, C-5), 169.1 (s, CO).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{18}O_3Na$: 245.1154; found: 245.1122.

2-(4-Hydroxypentyl)phenyl Acetate (8)

^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (d, *J* = 6.2 Hz, 3 H, 5-H), 2.17 (s, 3 H, COMe), 3.93 (sext, *J* = 6.2 Hz, 1 H, 4-H), 6.75–6.89, 7.03–7.13 (2 m, 2 H each, Ar).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 20.5 (q, CO*Me*), 23.9 (q, C-5), 68.7 (d, C-4), 115.6, 120.5, 127.2, 130.2 (4 d, Ar), 153.9 (s, CO).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{18}O_3Na$: 245.1154; found: 245.1142.

Cyclization of Aryl Ketone 11

According to the GP, **11** (200 mg, 0.85 mmol), SmI_2 (25.6 mL, 2.56 mmol), HMPA (2.69 mL, 2.75 g, 15.4 mmol), and *t*BuOH (0.16 mL, 127 mg, 1.71 mmol) furnished after 17 h and workup with $NaHCO_3$ solution the crude product. After column chromatography (alumina, hexanes/EtOAc 4:1), **12** and **13** were isolated as a mixture (73:27); yield: 120 mg (59%). In a second fraction, **14** was isolated as colorless oil; yield: 38 mg (19%).

(1*R**,8a*R**)-7-*tert*-Butoxy-1-methyl-1,2,3,4,6,8a-hexahydro-1-naphthol (12)

^{1}H NMR (700 MHz, $CDCl_3$): δ = 1.07 (s, 3 H, Me), 1.42 (s, 9 H, CMe_3), 1.63 (dt, *J* = 4.1, 12.9 Hz, 1 H, 2-H^1), 2.26 (m_c, 1 H, 4-H^1), 5.31 (td, *J* = 1.8, 3.6 Hz, 1 H, 8-H), 5.42 (tt, *J* = 1.5, 3.5 Hz, 1 H, 5-H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 22.4 (q, 1-Me), 30.1 (q, C*Me*$_3$), 106.0 (d, C-8), 119.3 (d, C-5).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{24}O_2Na$: 259.1663; found: 259.1655.

7-*tert*-Butoxy-1-methyl-1,2,3,4-tetrahydro-1-naphthol (13)

^{1}H NMR (700 MHz, $CDCl_3$): δ = 6.80 (dd, *J* = 2.5, 8.2 Hz, 1 H, Ar), 6.99 (d, *J* = 8.2 Hz, 1 H, Ar), 7.27 (d, *J* = 2.5 Hz, 1 H, Ar).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 30.3 (q, C*Me*$_3$), 33.1 (q, 1-Me), 123.8, 124.4, 130.4 (3 d, Ar).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{22}O_2Na$: 257.1512; found: 257.1510.

5-(4-*tert*-Butoxyphenyl)pentan-2-ol (14)

IR (film, ATR): 3370 (O-H), 3025–2855 (=C-H, C-H), 1610 (C=C), 1160 (C-O) cm^{-1}.

^{1}H NMR (700 MHz, $CDCl_3$): δ = 1.18 (d, *J* = 6.2 Hz, 3 H, 1-H), 1.32 (s, 9 H, CMe_3), 1.43–1.53 (m, 3 H, 3-H, OH), 1.59–1.76 (m, 2 H, 4-H), 2.58 (m_c, 2 H, 5-H), 3.80 (sext, *J* = 6.2 Hz, 1 H, 2-H), 6.88, 7.05 (2 d, *J* = 8.5 Hz, 2 H each, Ar).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 23.5 (q, C-1), 27.6 (t, C-3), 28.8 (q, C*Me*$_3$), 35.2 (t, C-5), 38.8 (t, C-3), 68.0 (d, C-2), 78.1 (s, C*Me*$_3$), 124.1, 128.6 (2 d, Ar), 137.2, 153.2 (2 s, Ar).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{15}H_{24}O_2Na$: 259.1663; found: 259.1645.

Cyclization of Aryl Ketone 15

According to the GP, **15** (229 mg, 1.04 mmol), SmI_2 (31.2 mL, 3.12 mmol), HMPA (3.28 mL, 3.35 g, 18.7 mmol), and *t*BuOH (154 mg, 2.08 mmol) furnished after 17 h at 0 °C and workup with $NaHCO_3$ solution the crude product. After column chromatography (alumina, hexanes/EtOAc 3:1) three fractions were obtained. Fraction 1: **19**: yield: 15 mg (7%); fraction 2: mixture of **16** and **17** (88:12): yield: 115 mg (50%; calculated yields 44% and 6%); fraction 3: mixture of **20** and **18** (60:40): yield: 10 mg (3% and 2%).

(1*R**,8a*R**)-7-Acetoxy-1-methyl-1,2,3,4,6,8a-hexahydro-1-naphthol (16)

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.07 (s, 3 H, Me), 1.33 (tq, *J* = 4.1, 13.3 Hz, 1 H, 3-H^1), 1.54 (br s, 1 H, OH), 1.58 (dt, *J* = 4.1, 13.3 Hz, 1 H, 2-H^1), 1.65–1.74 (m, 1 H, 3-H^2), 1.77–1.84 (m, 1 H, 2-H^2), 1.85–1.98 (m, 1 H, 4-H^1), 2.11 (s, 3 H, COMe), 2.19 (tdt, *J* ≈ 1.7, 4.1, 13.3 Hz, 1 H, 4-H^2), 2.70–2.77 (m, 2 H, 6-H), 2.85 (dt, *J* = 3.5, 7.7 Hz, 1 H, 8a-H), 5.37 (tt, *J* = 1.7, 3.4 Hz, 1 H, 5-H), 5.54 (td, *J* = 1.5, 3.5 Hz, 1 H, 8-H); the ^{1}H NMR data agree with those of the literature.[11b]

Phenol 17

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.86 (quin, *J* = 7.4 Hz, 2 H, 4-H), 2.12 (s, 3 H, 1-H), 2.43 (t, *J* = 7.4 Hz, 2 H, 3-H), 2.54 (t, *J* = 7.4 Hz, 2 H, 5-H), 5.75 (br s, 1 H, OH), 6.77, 7.01 (2 d, *J* = 8.6 Hz, 2 H each, Ar).

Diol 18

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.53 (s, 3 H, Me), 5.17 (br s, 1 H, OH), 6.68 (dd, *J* = 2.70, 8.3 Hz, 1 H, Ar), 6.94 (d, *J* = 8.3 Hz, 1 H, Ar), 7.07 (d, *J* = 2.7 Hz, 1 H, Ar).

Pentan-2-ol 19

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.20 (d, *J* = 6.3 Hz, 3 H, 5-H), 1.47–1.66 (m, 4 H, 2-H, 3-H), 2.03 (s, 3 H, COMe), 2.54 (t, *J* = 7.4 Hz, 2 H, 1-H), 4.91 (sext, *J* = 6.3 Hz, 1 H, 4-H), 4.98 (br s, 1 H, OH), 6.75, 7.03 (2 d, *J* = 8.6 Hz, 2 H each, Ar).

Pentan-2-ol 20

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.18 (d, *J* = 6.2 Hz, 3 H, 5-H), 2.55 (t, *J* = 7.5 Hz, 2 H, 1-H), 3.82 (sext, *J* = 6.2 Hz, 1 H, 4-H), 5.51 (br s, 1 H, OH), 6.74, 7.03 (2 d, *J* = 8.6 Hz, 2 H each, Ar).

Cyclization of Aryl Ketone 3

According to the GP, **3** (400 mg, 1.37 mmol), SmI_2 (54.7 mL, 5.47 mmol), HMPA (5.71 mL, 5.88 g, 32.8 mmol), and *t*BuOH (0.26 mL, 203 mg, 2.74 mmol) furnished after 17 h and workup with $NaHCO_3$ solution the crude product. After column chromatography (alumina, hexanes/EtOAc 9:1), **21** was isolated as a colorless solid (231 mg, 57%). In other fractions, precursor **3** (19 mg, 5%) and **22** (50 mg, 12%) were isolated.

(1*R**,8a*R**)-7-(*tert*-Butyldimethylsiloxy)-1-methyl-1,2,3,4,6,8a-hexahydro-1-naphthol (21)

Mp 46–48 °C.

IR (ATR): 3325 (O-H), 3030–2820 (=C-H, C-H), 1700 (C=C), 1660 (C=C), 1200 (C-O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.16 (s, 6 H, $SiMe_2$), 0.93 (s, 9 H, CMe_3), 1.04 (s, 3 H, 1-Me), 1.34 (tq, *J* = 4.1, 13.4 Hz, 1 H, 3-H^1), 1.38 (br s, 1 H, OH), 1.58 (dt, *J* = 4.1, 13.1 Hz, 1 H, 2-H^1), 1.67–1.75 (m, 1 H, 3-H^2), 1.78–1.84 (m, 1 H, 2-H^2), 1.90–1.99 (m, 1 H, 4-H^1), 2.19 (tdd, *J* = 2.2, 4.1, 13.4 Hz, 1 H, 4-H^2), 2.59–2.64 (m, 2 H, 6-H), 2.78 (m_c, 1 H, 8a-H), 5.02 (td, *J* = 1.8, 3.6 Hz, 1 H, 8-H), 5.37 (tt, *J* = 1.6, 3.4 Hz, 1 H, 5-H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = –4.3 (q, $SiMe_2$), 18.0 (s, *C*Me_3), 21.9 (q, 1-Me), 24.2 (t, C-3), 25.7 (q, C*Me*$_3$), 30.8 (t, C-6), 34.3 (t, C-4), 41.7 (t, C-2), 50.7 (d, C-8a), 74.9 (s, C-1), 101.3 (d, C-8), 117.7 (d, C-5), 136.0 (s, C-4a), 149.7 (s, C-7).

Anal. Calcd for $C_{17}H_{30}O_2Si$ (294.5): C, 69.33; H, 10.27. Found: C, 68.72; H, 10.34.

5-[4-(*tert*-Butyldimethylsiloxy)phenyl]pentan-2-ol (22)

IR (film, ATR): 3355 (O-H), 3060–2855 (=C-H, C-H), 1620 (C=C) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.19 (s, 6 H, $SiMe_2$), 0.99 (s, 9 H, CMe_3), 1.18 (d, *J* = 6.2 Hz, 3 H, 1-H), 1.40–1.52 (m, 2 H, 3-H), 1.58–1.74 (m, 3 H, 4-H, OH), 2.56 (t, J = 7.6 Hz, 2 H, 5-H), 3.80 (sext, J = 6.2 Hz, 1 H, 2-H), 6.55, 7.03 (2 d, *J* = 8.4 Hz, 2 H each, Ar).

^{13}C NMR (176 MHz, $CDCl_3$): δ = –4.5 (q, $SiMe_2$), 18.1 (s, *C*Me_3), 23.4 (q, C-1), 25.7 (q, CMe_3), 27.7 (t, C-4), 35.0 (t, C-5), 38.8 (t, C-3), 67.9 (d, C-2), 119.7, 129.1 (2 d, Ar), 135.0, 153.5 (2 s, Ar).

Anal. Calcd for $C_{17}H_{30}O_2Si$ (294.5): C, 69.33; H, 10.27. Found: C, 69.96; H, 9.73.

Cyclization of Aryl Ketone 23

According to the GP, **23** (540 mg, 1.30 mmol), SmI_2 (38.9 mL, 3.90 mmol), HMPA (4.08 mL, 4.18 g, 23.3 mmol), and *t*BuOH (192 mg, 2.59 mmol) furnished after 17 h and workup with $NaHCO_3$ solution the crude product. After column chromatography (alumina, hexanes/EtOAc 9:1), **24** was isolated. In a second fraction, **25** was isolated.

(1*R,8a*R**)-7-(*tert*-Butyldiphenylsiloxy)-1-methyl-1,2,3,4,6,8a-hexahydro-1-naphthol (24)**

Yield: 330 mg (61%); colorless oil.

IR (film, ATR): 3380 (O-H), 3070–2855 (=C-H, C-H), 1660 (C=C), 1610 (C=C), 1110 (C-O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.63 (s, 3 H, Me), 1.06 (s, 9 H, CMe_3), 1.24 (tq, *J* = 4.3, 13.0 Hz, 1 H, 3-H^1), 1.45 (dt, *J* ≈ 4.1, 13.0 Hz, 1 H, 2-H^1), 1.57 (br s, 1H, OH), 1.60–1.67 (m, 2 H, 2-H^2, 3-H^2), 1.81–1.90, 2.10–2.15 (2 m, 1 H each, 4-H), 2.55–2.63 (m, 1 H, 8a-H), 2.69–2.75 (m, 2 H, 6-H), 4.66 (d, J = 3.6 Hz, 1 H, 8-H), 5.28–5.35 (tt, J ≈ 1.6, 3.3 Hz, 1H, 5-H), 7.35–7.46, 7.71–7.77 (2 m, 6 H, 4 H, Ph).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 19.1 (s, CMe_3), 21.3 (q, Me), 24.0 (t, C-3), 26.5 (q, C*Me*$_3$), 30.9 (t, C-6), 34.1 (t, C-4), 40.4 (t, C-2), 50.5 (d, C-8a), 74.6 (s, C-1), 101.2 (d, C-8), 117.2 (d, C-5), 127.6, 129.8 (2 d, Ph), 133.4 (s, Ph), 135.5 (d, Ph), 136.0 (s, C-4a), 149.5 (s, C-7).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{27}H_{34}O_2NaSi$: 441.2258; found: 441.2218.

5-[4-(*tert*-Butyldiphenylsiloxy)phenyl]pentan-2-ol (25)

Yield: 90 mg (17%).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.10 (s, 9 H, CMe_3), 1.16 (d, *J* = 6.2 Hz, 3 H, 1-H), 1.33 (br s, 1 H, OH), 1.36–1.51, 1.59–1.70 (2 m, 2 H each, 3-H, 4-H), 2.50 (t, *J* = 7.6 Hz, 2 H, 5-H), 3.78 (sext, *J* = 6.2 Hz, 1 H, 2-H), 6.69, (2 d, *J* = 8.5 Hz, 2 H each, Ar), 7.34–7.40, 7.40–7.46, 7.71–7.75 (3 m, 4 H, 2 H, 4 H, Ph).

(8*R,8a*R**)-8-Hydroxy-8-methyl-3,5,6,7,8,8a-hexahydronaphthalen-2(1*H*)-one (28)**

$TiCl_4$ (1 drop) was added to a solution of silyl enol ether **21** (71 mg, 0.24 mmol) in MeOH (16 mL) at –78 °C. The solution was stirred at this temperature for 2 h. Due to incomplete conversion, additional $TiCl_4$ (1 drop) was added and the solution was stirred overnight and the mixture was allowed to reach r.t. H_2O (10 mL) and brine (10 mL) were added and the mixture was extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. After column chromatography (silica gel, hexanes/EtOAc 4:1), ketone **28** was isolated.

Yield: 43 mg (99%); colorless oil.

IR (film, ATR): 3400 (O-H), 3040 (=C-H), 2965–2865 (C-H), 1700 (C=O) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$,): δ = 0.97 (s, 3 H, Me), 1.38 (tq, *J* = 4.4, 13.2 Hz, 1 H, 6-H^1), 1.54 (dt, *J* = 4.4, 13.2, Hz, 1 H, 7-H^1), 1.67–1.78 (m, 2-H, 6-H^2, 7-H^2), 1.91–2.02 (m, 1 H, 5-H^1), 2.22 (tdd, *J* = 2.1, 4.4, 13.1 Hz, 1 H, 5-H^2), 2.48 (ddd, *J* = 1.1, 8.9, 15.1 Hz, 2 H, 1-H^1, OH)*, 2.60 (d, *J* ≈ 8.9 Hz, 1 H, 8a-H), 2.67–2.77 (m, 2 H, 3-H^1, 1-H^2), 2.86–2.94 (m, 1 H, 3-H^2), 5.41 (m, 1 H, 4-H); * broad signal for OH.

^{13}C NMR (126 MHz, $CDCl_3$): δ = 20.8 (q, Me), 24.5 (t, C-6), 34.6 (t, C-5), 38.1 (t, C-1) 39.3 (t, C-3), 42.2 (t, C-7), 51.2 (d, C-8a), 74.5 (s, C-8), 117.2 (d, C-4), 138.4 (s, C-4a), 210.5 (s, C-2).

HRMS (EI, 80 eV, 40 °C): *m*/*z* [M]$^+$ calcd for $C_{12}H_{16}O_2$: 180.1150; found: 180.1151.

(8*R,8a*R**)-8-Hydroxy-8-methyl-4a,5,6,7,8,8a-hexahydronaphthalen-2(1*H*)-one (29)**

Ketone **28** (9 mg, 0.05 mmol) was dissolved in EtOAc (0.5 mL), and then basic alumina (100 mg) was added. The suspension was stirred at r.t. overnight and then filtered through Celite. The filtrate was concentrated under reduced pressure and enone **29** was isolated as a mixture of *cis* and *trans* isomers.

Yield: 7 mg (76%); *cis*/*trans* 57:43.

IR (film, ATR): 3355 (O-H), 3055–2845 (=C-H, C-H), 1675 (C=O) cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ (major isomer) = 1.20 (s, 3 H, 8-Me), 1.44–1.82 (m, 7 H, OH, 5-H, 6-H, 7-H), 2.11 (m_c, 1 H, 8a-H), 2.32 (dd, *J* = 14.3 Hz, 16.7 Hz, 1 H, 1-H^1), 2.37 (dd, *J* = 5.0, 16.7 Hz, 1 H, 1-H^2), 2.73–2.82 (m, 1 H, 4a-H), 5.96 (d, *J* = 10.7 Hz, 1 H, 3-H), 7.02 (dd, *J* = 5.9, 10.7 Hz, 1 H, 4-H).

^{13}C NMR (176 MHz, $CDCl_3$): δ (major isomer) = 28.9 (q, Me), 33.5 (d, C-4a), 36.5 (t, C-1), 44.2 (d, C-8a), 128.3 (d, C-3), 155.4 (d, C-4), 199.4 (s, C-2).

^1H NMR (700 MHz, $CDCl_3$): δ (minor isomer) = 1.23 (s, 3 H, 8-Me), 1.44–1.82 (m, 7 H, OH, 5-H, 6-H, 7-H), 2.17 (dd, *J* = 14.5, 16.5 Hz, 1 H, 1-H^1), 2.25 (m_c, 1 H, 8a-H), 2.49 (dd, *J* = 1.0, 16.5 Hz, 1 H, 1-H^2), 2.59 (m_c, 1 H, 4a-H), 5.90 (dd, *J* = 1.0, 10.1 Hz, 1 H, 3-H), 6.78 (d, *J* = 10.1 Hz, 1 H, 4-H).

^{13}C NMR (176 MHz, $CDCl_3$): δ (minor isomer) = 28.8 (q, Me), 38.2 (t, C-1), 49.9 (d, C-8a), 126.4 (d, C-3), 157.1 (d, C-4), 198.2 (s, C-2).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_{16}O_2Na$: 203.1048; found: 203.1030.

(8*R,8a*S**,*Z*)-1-Benzylidene-8-hydroxy-8-methyl-3,5,6,7,8,8a-hexahydronaphthalen-2(1*H*)-one (30)**

A 1 M solution of $TiCl_4$ in CH_2Cl_2 (0.37 mL, 0.37 mmol) was diluted with CH_2Cl_2 (2.7 mL). At –78 °C a solution of **21** (100 mg, 0.34 mmol) in CH_2Cl_2 (1.2 mL) was added. After addition of benzaldehyde (37 µL, 39 mg, 0.37 mmol) at this temperature, the solution was stirred overnight and the temperature was allowed to reach r.t. H_2O (10 mL) was added and the mixture was extracted with Et_2O (3 × 30 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated under reduced pressure. After column chromatography (silica gel, hexanes/EtOAc 3:1), a mixture of enone **30** and substrate **21** (9:1, 33 mg) was isolated as colorless oil.

Calculated yields: enone **30**: 30 mg (31%); **21**: 3 mg (3%).

IR (film, ATR): 3375 (O-H), 3020–2855 (=C-H, C-H), 1690 (C=O), 1635, 1590 (C=C) cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 1.04 (s, 3 H, Me), 1.41 (tq, *J* = 4.3, 13.4 Hz, 1 H, 6-H^1), 1.65 (dt, *J* = 4.0, 13.4 Hz, 1 H, 7-H^1), 1.73 (br s, 1 H, OH), 1.81–1.83 (m, 1 H, 7-H^2), 1.84–1.89 (m, 1 H, 6-H^2), 2.18 (dt, *J* = 5.1, 13.0 Hz, 1 H, 5-H^1), 2.36 (m_c, 1 H, 5-H^2), 2.69–2.71 (m, 2 H, 3-H^1, 8a-H), 3.02 (m_c, 1 H, 3-H^2), 6.75 (m_c, 1 H, 4-H), 7.27 (s, 1 H, PhC*H*), 7.30–7.32 (m, 1 H, Ar), 7.37–7.39, 7.42–7.43 (2 m, 2 H each, Ar).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 21.0 (q, Me), 25.0 (t, C-6), 35.6 (t, C-5), 37.7(t, C-3), 42.1 (t, C-7), 50.2 (d, C-8a), 75.3 (s, C-8), 119.1 (d, C-4), 128.2, 128.4, 129.8 (3 d, Ph), 129.9 (d, PhC), 130.9 (s, C-1), 135.6 (s, Ar), 143.8 (s, C-4a), 199.9 (s, C-2).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{20}O_2Na$: 291.1361; found: 291.1359.

(1*R,3*R**,4*R**,4a*S**,5*R**,8a*R**)-3-(*tert*-Butyldimethylsiloxy)-5-methyldecahydronaphthalene-1,4,5-triol**

Compound **21** (102 mg, 0.31 mmol) was dissolved in THF (9 mL) and cooled to –30 °C. A 1 M solution of BH_3·THF in THF (1.40 mL, 1.40 mmol) was added and the mixture was stirred for 3 h while being allowed to warm to r.t. It was then cooled to 0 °C and subsequently 2 M aq NaOH (2 mL) and H_2O_2 (30 weight% in H_2O; 0.7 mL, 6.85 mmol) were added dropwise and stirring was continued for 18 h. Sat. aq $Na_2S_2O_3$ (1.4 mL) was added and the mixture was extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. After column chromatography (silica gel, hexanes/EtOAc 9:1 to 4:1 to 0:1), the product was isolated.

Yield: 54 mg (47%); colorless oil.

IR (film, ATR): 3380 (O-H), 2930–2850 (C-H), 1470 (C-C) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 0.09 (s, 6 H, $SiMe_2$), 0.89 (s, 9 H, CMe_3), 1.10–1.80*, 1.89–1.96, 2.05–2.60 (3 m, 13 H, 1-H, 4-H, CH, CH_2, OH), 1.44* (s, 3 H, 5-Me), 3.56 (dd, *J* = 8.5, 11.1 Hz, 1 H, 4-H), 3.81 (m_c, 1 H, 1-H), 3.86 (ddd, *J* = 3.4, 4.9, 8.5 Hz, 1 H, 3-H); * overlapping signals.

^{13}C NMR (100 MHz, $CDCl_3$): δ = –4.7, –4.0 (2 q, $SiMe_2$), 17.9, 25.8 (s, q, CMe_3), 21.4, 25.5 (2 t, CH_2), 32.3 (q, 5-Me), 34.7, 35.7 (t, CH_2), 40.5, 45.8 (2 d, C-4a, C-8a), 71.5, 73.1, 74.2 (3 d, C-1, C-3, C-4), 72.6 (s, C-5).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{34}O_4NaSi$: 353.2119; found: 353.2135.

(1*R,2*R**,4*R**,4a*R**,8*R**,8a*S**)-8-Methyldecahydronaphthalene-1,2,4,8-tetrol (31)**

At 0 °C, 1 M TBAF in THF (207 µL) was added to a solution of the product obtained above (54 mg, 0.16 mmol) in THF (4 mL). The mixture was stirred for 1 h at r.t.; then MeOH (0.1 mL) was added, all volatiles were removed in a stream of argon, and the crude material was subjected to column chromatography (silica gel, CH_2Cl_2/MeOH 4:1).

Yield: 29 mg (82%); colorless solid; mp 79–81 °C.

IR (ATR): 3450–3250 (O-H), 2965–2830 (=C-H, C-H) cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 1.17–1.33 (m, 2 H, 5-H), 1.34 (s, 3 H, 8-Me), 1.47–1.58 (m, 2 H, 6-H^1, 7-H^1), 1.59–1.69 (m, 2 H, 3-H^1, 7-H^2), 1.77 (tq, *J* = 4.3, 12.9 Hz, 1 H, 6-H^2), 1.88 (dd, *J* = 4.2, 11.1 Hz, 1 H, 8a-H), 1.93 (m_c, 1 H, 3-H^2), 2.36 (m_c, 1 H, 4a-H), 3.50 (dd, *J* = 8.8, 11.1 Hz, 1 H, 1-H), 3.70 (ddd, *J* = 5.1, 8.8, 13.7 Hz, 1 H, 2-H), 3.75 (m_c, 1 H, 4-H).

^{13}C NMR (126 MHz, $CDCl_3$): δ = 22.6 (t, C-5), 26.9 (t, C-6), 32.5 (q, 8-Me), 35.9 (t, C-7), 36.3 (t, C-3), 41.4 (d, C-4a), 47.7 (d, C-8a), 72.2 (d, C-4), 73.1 (s, C-8), 73.5 (d, C-2), 74.4 (d, C-1).

Anal. Calcd for $C_{11}H_{20}O_4$ (216.3): C, 61.09; H, 9.32. Found: C, 61.08; H, 9.31.

(4a*R,10*R**,10a*R**,10b*R**)-4a-(*tert*-Butyldimethylsiloxy)-10-methyl-2-(trifluoromethyl)-4a,5,7,8,9,10,10a,10b-octahydro-1*H*-naphtho[1,2-*e*][1,2]oxazin-10-ol (33)**

Compound **21** (50 mg, 0.17 mmol), α-bromo oxime **32** (35 mg, 0.17 mmol), and Na_2CO_3 (360 mg, 3.4 mmol) were suspended in CH_2Cl_2 (30 mL) and the mixture was stirred at r.t. for 4 d. Additional **32** (in total: 350 mg, 1.70 mmol) was added in six portions over a period of 6 d. The mixture was filtered through a pad of Celite and concentrated in vacuo. After column chromatography (silica gel, hexanes/EtOAc 9:1), **33** was isolated.

Yield: 25 mg (35%); colorless solid; mp 54–56 °C.

IR (ATR): 3450 (O-H), 3080–2860 (=C-H, C-H), 1635 (C=N), 1500 (C=C), 1190, 1140 (CF_3) cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 0.08, 0.19 (2 s, 3 H each, $SiMe_2$), 0.85 (s, 9 H, CMe_3), 1.16 (s, 3 H, 10-Me), 1.23 (br s, 1 H, OH), 1.34 (tq, *J* = 4.1, 13.4 Hz, 1 H, 8-H^1), 1.57 (dt, *J* = 4.1, 13.0 Hz, 1 H, 9-H^1), 1.63–1.68 (m, 1 H, 8-H^2), 1.72–1.76 (m, 1 H, 9-H^2), 1.83–1.87 (m, 1H, 10a-H), 1.89–1.96 (m, 1 H, 7-H^1), 2.18 (tdd, *J* = 2.2, 4.1, 14.0 Hz, 1 H, 7-H^2), 2.27–2.33 (m, 2 H, 5-H^1, 10b-H), 2.52 (dd, *J* = 17.2, 6.3 Hz, 1 H, 5-H^2), 2.71 (ddd, *J* = 1.0, 6.8, 18.6 Hz, 1 H, 1-H^1), 3.07 (d, *J* = 18.6 Hz, 1 H, 1-H^2), 5.28–5.32 (m, 1 H, 6-H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = –4.1, –2.7 (2 q, $SiMe_2$), 17.8 (s, CMe_3), 21.7 (q, 10-Me), 22.4 (t, C-1), 23.3 (t, C-8), 25.6 (q, CMe_3), 28.1 (d, C-10), 32.6 (d, C-10b), 34.4 (t, C-7), 36.4 (t, C-5), 43.9 (t, C-9), 51.4 (d, C-10a), 116.8 (d, C-6), 120.7 (q, J_{CF} = 274.4 Hz, CF_3), 122.1 (s, C-4a), 136.8 (s, C-6a), 147.5 (q, J_{CF} = 33.7 Hz, C-2).

HRMS (ESI-TOF): *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{32}F_3NO_3NaSi$: 442.2001; found: 442.2009.

Methyl (1a*R,7*R**,7a*R**,7b*S**)-1a-(*tert*-Butyldimethylsiloxy)-7-hydroxy-7-methyl-1a,2,4,5,6,7,7a,7b-octahydro-1*H*-cyclopropa[*a*]-naphthalene-1-carboxylate (34)**

$Cu(acac)_2$ (8.9 mg) was added to a solution of **21** (100 mg, 0.34 mmol) in EtOAc (24 mL). The mixture was heated to reflux and a solution of methyl diazoacetate (170 mg) in EtOAc (6 mL) was slowly added over a period of 4.5 h. After 72 h and 79 h, both $Cu(acac)_2$ (8.9 mg, 0.1 equiv at a time, in total 27 mg, 0.09 mmol) and a solution of methyl diazoacetate (170 mg, 5 equiv at a time, in total 510 mg, 5.10 mmol) in EtOAc (6 mL) were added. After 92 h of stirring at reflux, the suspension was filtered and the filtrate was concentrated in vacuo. After column chromatography (silica gel, hexanes/EtOAc 9:2), **34** was isolated as a mixture of *trans*/*cis*-isomers (*trans*/*cis* refers to the positions of the OTBS and the CO_2Me groups).

Yield: 39 mg (31%); *trans*/*cis* 5:1.

IR (film, ATR): 3430 (O-H), 2950–2860 (=C-H, C-H), 1730 (C=O), 1630 (C=C), 1170 (C-O), 1110 (C-O) cm^{-1}.

^1H NMR (700 MHz, C_6D_6): δ (*trans*-**34**; major isomer) = 0.16*, 0.20 (2 s, 3 H each, $SiMe_2$), 0.90 (s, 9 H, CMe_3), 1.10 (s, 3 H, Me), 1.13 (tq, *J* = 4.2, 13.4 Hz, 1 H, 5-H^1), 1.35 (dt, *J* = 4.5, 13.4 Hz, 1 H, 6-H^1), 1.46 (m_c, 1 H, 5-H^2), 1.60 (m_c, 1 H, 6-H^2), 1.72* (m_c, 1 H, 4-H^1), 1.94 (m_c, 1 H, 4-H^2), 1.95 (d, *J* = 11.0 Hz, 1 H, 1-H), 2.07 (d, *J* = 11.0 Hz, 1 H, 7b-H), 2.45 (m_c, 1 H, 2-H^1), 2.58* (m_c, 1 H, 7a-H), 2.89 (m_c, 1 H, 2-H^2), 3.31 (s, 3 H, OMe), 5.02 (m_c, 1 H, 3-H); * overlapping signals of both diastereomers.

^{13}C NMR (176 MHz, C_6D_6): δ (*trans*-**34**; major isomer) = –3.7, –3.0 (2 q, $SiMe_2$), 17.8 (s, CMe_3), 20.9 (q, Me), 24.6 (d, C-7b), 25.6 (t, C-5), 25.8 (q, CMe_3), 29.4 (d, C-1), 31.3 (t, C-2), 35.4 (t, C-4), 42.7 (t, C-6), 48.1 (d, C-7a), 50.9 (q, OMe), 58.3 (s, C-1a), 74.5 (s, C-7), 116.9 (d, C-3), 136.5 (s, C-3a), 168.9 s, CO).

^1H NMR (700 MHz, C_6D_6): δ (*cis*-**34**; minor isomer) = 0.16*, 0.26 (2 s, 3 H each, SiMe), 1.00 (s, 9 H, CMe_3, 1.05 (s, 3 H, Me), 1.26 (m_c, 1 H, 6-H^1), 1.56–1.58 (m, 1 H, 6-H^2), 1.70–1.74* (m, 2 H, 4-H^1, 1-H), 1.94 (m_c, 1 H, 4-H^2), 2.00 (m_c, 1 H, 7a-H), 2.36 (m_c, 1 H, 2-H^1), 2.54–2.56* (m, 1 H, 2-H^2), 2.73 (d, *J* = 6.0 Hz, 1H, 7b-H), 3.46 (s, 3 H, OMe), 4.88 (m_c, 1 H, 3-H); * overlapping signals of both diastereomers.

^{13}C NMR (176 MHz, C_6D_6): δ (*cis*-**34**; minor isomer) = –3.4, –2.6 (2 q, $SiMe_2$), 18.2 (s, CMe_3), 21.1 (q, Me), 26.1 (t, C-5), 27.1 (d, C-7b), 30.0 (d, C-1), 33.5 (t, C-2), 35.2 (t, C-4), 51.3 (q, OMe), 51.6 (d, C-7a), 63.6 (s, C-1a), 74.5 (s, C-7), 116.5 (d, C-3), 135.6 (s, C-3a), 171.5 (s, CO); the signal of CMe_3 could not be identified.

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{34}O_4NaSi$: 389.2119; found: 389.2123.

Methyl (1*R,8*R**,8a*R**)-2′-(8-Hydroxy-8-methyl-2-oxo-1,2,3,5,6,7,8,8a-octahydronaphthalen-1-yl)acetate (35)**

$TiCl_4$ (2 drops) was added to a solution of compound **34** (19 mg, 0.052 mmol, *cis*/*trans* mixture) in MeOH (5 mL) at –78 °C and the solution was stirred at this temperature for 3 h. Due to incomplete conversion, additional $TiCl_4$ (2 drops) was added and the solution was stirred for 54 h, allowing the mixture to reach r.t. H_2O (10 mL) and brine (10 mL) were added and the mixture was extracted with Et_2O (3 × 20 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. After column chromatography (silica gel, hexanes/EtOAc 3:1), **35** was isolated.

Yield: 8 mg (58%); colorless oil.

IR (film, ATR): 3375 (O-H), 3020–2870 (=C-H, C-H), 1720, 1685 (C=O), 1495 (C=C) cm^{-1}.

^1H NMR (700 MHz, $CDCl_3$): δ = 1.12 (s, 3 H, 8-Me), 1.38 (tq, *J* = 4.2, 13.4 Hz, 1 H, 6-H^1), 1.52–1.59 (m, 1 H, 7-H^1), 1.73–1.79 (m, 1 H, 6-H^2), 1.81–1.85 (m, 1 H, 7-H^2), 1.87 (br s, 1 H, OH), 1.93–2.03 (m, 1 H, 5-H^1), 2.27 (tdd, *J* = 1.9, 4.2, 13.3 Hz, 1 H, 5-H^2), 2.38–2.41 (m, 1 H, 8a-H), 2.70, 2.74 (AB-part of ABX-system, J_{AB} = 16.3 Hz, J_{AX} = 6.7 Hz, J_{BX} = 7.1 Hz, 1 H each, 2′-H), 2.84–2.94 (m, 2 H, 3-H), 3.20 (X-part of ABX-system, J_{AX} = 6.7 Hz, J_{BX} = 7.1 Hz, additional couplings, *J* = 0.7, 3.8 Hz, 1 H, 1-H), 3.69 (s, 3 H, OMe), 5.43–5.50 (m, 1 H, 4-H).

^{13}C NMR (176 MHz, $CDCl_3$): δ = 20.7 (q, Me), 24.3 (t, C-6), 34.0 (d, C-8a), 34.8 (t, C-5), 36.3 (t, C-2′), 37.9 (t, C-3), 42.8 (t, C-7), 43.7 (d, C-1), 51.7 (q, OMe), 74.9 (s, C-8), 116.9 (d, C-4), 137.5 (s, C-4a), 174.2 (s, C-1′), 209.9 (s, C-2).

HRMS (ESI-TOF): *m*/*z* $[M + Na]^+$ calcd for $C_{14}H_{20}O_4Na$: 275.1254; found: 275.1256.

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Supporting Information

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