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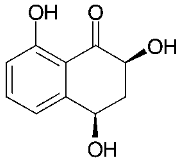
Asymmetric Synthesis of the *cis*- and *trans*-3,4-Dihydro-2,4,8-trihydroxynaphthalen-1(2*H*)-ones

by **Emmanuel Couché**, **Abdellatif Fkyerat**, and **Raffaele Tabacchi***

Institut de Chimie, Université de Neuchâtel, Avenue de Bellevaux 51, Case postale 2, CH-2007 Neuchâtel
(e-mail: Raphael.Tabacchi@unine.ch)

A short and efficient protocol for the asymmetric synthesis of *cis*- and *trans*-3,4-dihydro-2,4,8-trihydroxynaphthalen-1(2*H*)-one (**1** and **2**, resp.) is described, with a phthalide annulation as the key step. Introduction of a OH substituent at position 2 was performed by *Sharpless* dihydroxylation of a silyl enol ether or by means of an *N*-sulfonyloxaziridine. The absolute configuration of each isomer was determined *via Mosher*-ester derivatives. By comparison with previously recorded CD spectra of our natural sample, we established that the natural *trans*- and *cis*-isomers from *Ceratocystis fimbriata* sp. *platani* were the (−)-(2*S*,4*S*)-isomer (−)-**2** and the (+)-(2*S*,4*R*)-isomer (+)-**1**, respectively.

Introduction. – In our investigation of phytotoxic substances produced by *Ceratocystis fimbriata* sp. *platani*, the fungus involved in the canker stain of the plane tree, we have reported the isolation and structural elucidation by spectroscopic methods of (+)-*cis*- and (−)-*trans*-3,4-dihydro-2,4,8-trihydroxynaphthalen-1(2*H*)-ones ((+)-**1** and (−)-**2**) [1].



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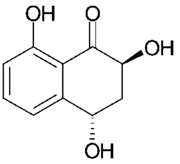

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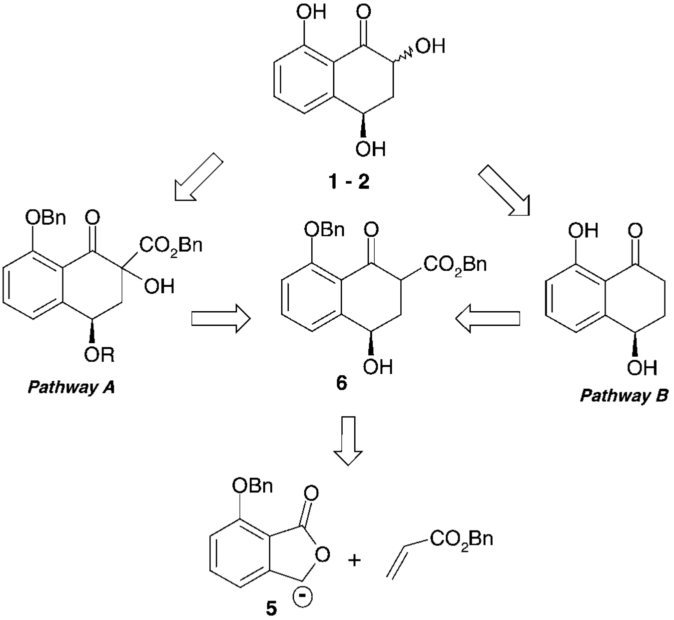
These natural naphthalenones are already known as metabolites involved in the branched pathway of fungal DHN-melanin biosynthesis [2]; a high-molecular-mass black pigment is arranged into a layer structure between the cell wall and the cell membrane of the appressorium. Apart from its protective role against the natural environmental stressors (UV radiations, desiccation, extreme temperatures), the melanization of the appressorium is essential for the pathogenic virulence of the fungus [3]. Relatively little work has been reported on metabolites **1** and **2**. In previous studies, *Fujimoto* and *Satoh* have extracted the (−)-*cis*-isomer from *Penicillium diversum* var. *aureum* [4], realized the synthesis of naphthalenones **1** and **2** in racemic form from juglone, and established the cytotoxic activities of these compounds against *Yoshida* sarcoma cells [5]. The lack of regioselectivity and stereoselectivity of their synthesis and the difficult final separation of the diastereoisomer mixture **1**/**2** performed by reversed-phase HPLC, followed by normal-phase HPLC, encouraged us to propose a new short and efficient protocol for the asymmetric synthesis of these products.

For the stereoselective synthesis of naphthalenones **1** and **2**, we used the key intermediate **6** developed by *Broom* and *Sammes* [6] for the preparation of polysubstituted naphthols, performing a tandem *Michael-Dieckmann* reaction between phthalide anion **5** and a *Michael* acceptor. This method was used numerous times in the synthesis of antitumor antibiotics such as olivomycin A, chrysophanol, or dynemicin A [7]. In 1997, *Bös* and co-workers used this methodology for the synthesis of *O*-methylasparvenone, a serotonin-receptor antagonist [8]. From intermediate **6**, two pathways leading to **1** and **2** can be envisaged (*Scheme 1*), either an α-hydroxylation followed by decarboxylation (*Pathway A*), or decarboxylation followed by oxidation (*Pathway B*). Here, we report the total synthesis of *cis*- and *trans*-2,4,8-trihydroxy-1-tetralone **1** and **2** respectively, by *Pathways A* and *B*.

Scheme 1. *Retrosynthetic Analysis of Naphthalenones* **1** *and* **2**



Results and Discussion. – Although 7-methoxyphthalide could be synthesized in three steps in a one-pot procedure from commercially available 3-methoxybenzyl alcohol [9], the presence of the MeO substituent at the aromatic moiety did not allow us to obtain the final product during the deprotection step. Therefore, we performed the key step with 7-(benzyloxy)phthalide **5**, which was obtained in two steps in good yield from ethyl 2-(acetyloxy)-6-(bromomethyl)benzoate (**3**), the latter being synthesized according to *Hamada* and co-workers [10] (*Scheme 2*). The tandem *Michael-Dieckmann* reaction of the phthalide carbanion with benzyl acrylate afforded the β-keto ester **6** after acidic hydrolysis. A ^{1}H-NMR experiment with β-keto ester **6** in $CDCl_3$ established 26:36:38 for the *cis*-ketonic form/enol form/*trans*-ketonic form. Following *Pathway A* (*Scheme 2*), we then protected the OH group at C(4) of **6**, as tetrahydro-2*H*-pyranyl (THP) ether (→**7b**) prior to the introduction of the OH group by treatment of the corresponding potassium enolate with an oxaziridine [11]. Use of the protecting group THP or ${}^{t}BuMe_2Si$ for OH−C(4) in *Pathway A* was essential to avoid the formation of lactone **12** [12]. However, with a benzyloxy group at the aromatic ring, the protection of OH−C(4) as a (*tert*-butyl)dimethylsilyl ether by treatment with ${}^{t}BuMe_2SiCl$ and 1*H*-imidazole in DMF resulted in a low yield of **7a** (15%). Therefore, we continued the synthesis with the THP-protected **7b**. Treatment of its potassium enolate with *trans*-(±)-3-phenyl-2-(phenylsulfonyl)oxaziridine (**10**) [13] in THF at low temperature afforded a 77:23 *trans*/*cis*-mixture of diastereoisomers *trans*-**8**/**8′** and *cis*-**8**/**8′** (57% overall yield). In contrast, the use of (+)-(camphorylsulfonyl)oxaziridine (**11**) [14], allowed us to obtain the products *trans*-**8**/**8′** with worse diastereoselectivity (de 6%) and a poor 20% yield.

During our work on the introduction of the OH group at C(2) with the oxaziridines **10** and **11**, we studied the different diastereoselectivities produced by these oxidative reagents as a function of the protective groups present in derivatives of **6**. Thus, we obtained exclusively the *cis*-isomer by using oxaziridine **11** and the derivative of **6** with a ${}^{t}BuMe_2SiO$ group at C(4), a COOBn or COOMe group at C(2), and a MeO group at C(8) [12].

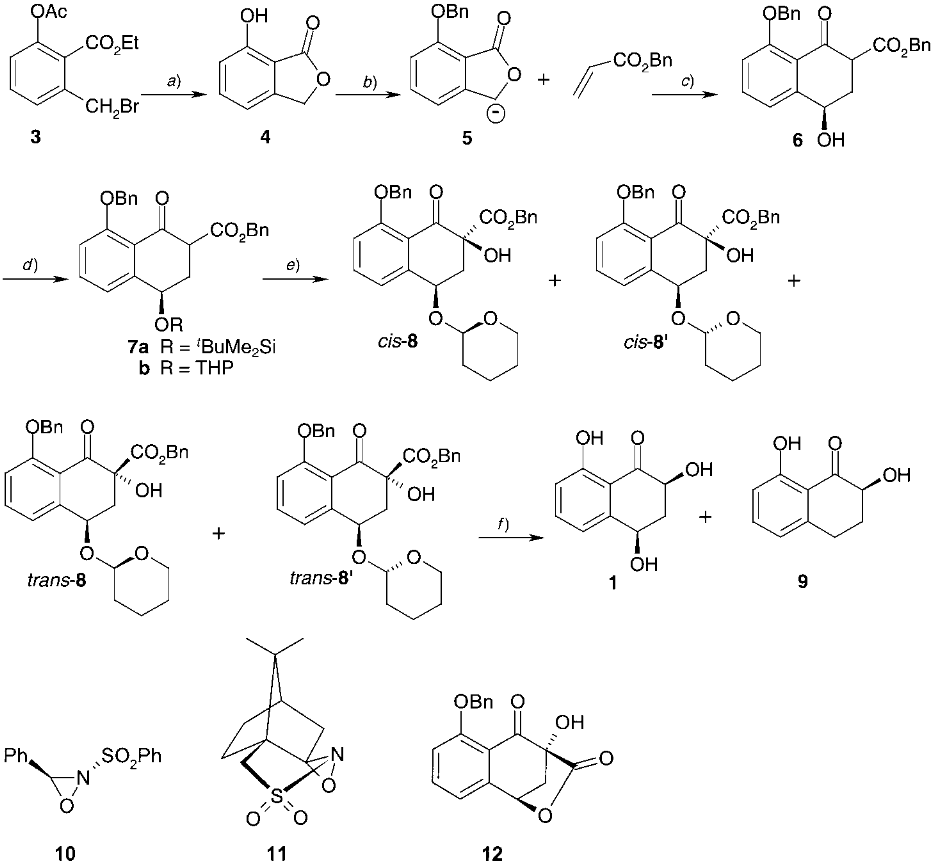
The last step of *Pathway A*, the hydrogenolysis with H_2 over Pd/C in AcOEt, gave exclusively the *cis*-isomer **1** (25%) and a large amount (16%) of by-product **9** starting from *cis*-**8**/**8′**. Hydrogenolysis of *trans*-**8**/**8′** under the same conditions produced epimerization at C(2) resulting in a similar mixture of **1** and **9** (7% yield for each).

The key intermediate of *Pathway B* (*Scheme 3*) was isosclerone (=3,4-dihydro-4,8-dihydroxynaphthalen-1(2*H*)-one; **13**). This product can be obtained by reduction of juglone with $LiAlH_4$ in THF [5]. However, this method provides a 4:1 mixture of the regioisomeric reduction products isosclerone and sclerone (=3,4-dihydro-4,5-dihydroxynaphthalen-1(2*H*)-one). In 1964, *Volkov* and co-workers showed that isosclerone could be obtained exclusively in four steps from juglone [15]. In our case, we obtained directly 8-(benzyloxy)isosclerone by hydrolysis of the tandem *Michael-Dieckmann* reaction mixture containing **6** with distilled water. However, the lack of reproducibility of yield (25–41%), encouraged us to first hydrogenolyze purified **6** over Pd/C in THF. After removal of the catalyst, 1% H_2O was added to the THF solution, and the mixture was heated for 5 h at 50° to provide isosclerone (**13**). Hydrogenolysis in AcOEt as solvent yielded large amounts of the 4-dehydroxylated product **20**.

Silyl enol ether **14** was then obtained from isosclerone (**13**) on treatment with Et_3N, and (*tert*-butyl)dimethylsilyl triflate at room temperature in 1,2-dichloroethane. After purification by column chromatography, **14** was subjected to epoxidation with 3-chloroperbenzoic acid (*m*-CPBA) at −15° [16] to give in 67% yield the *cis*/*trans*-isomers **15**/**16** (56:44). The latter were treated with *Amberlyst 15* in MeOH for 5 days at room temperature, whereupon the target racemic *cis*/*trans*-mixture **1**/**2** (59:41) was isolated in 55% yield.

We also submitted pure silyl enol ether **14** to asymmetric *Sharpless* dihydroxylation [17] at 0° in the presence of $(DHQD)_2PHAL$ (=hydroquinine 1,4-phthalazinediyl ether) or $(DHQ)_2PHAL$ (=hydroquinidine 1,4-phthalazinediyl ether), as chiral ligand and obtained mainly the *trans*-isomer **18** (de 30–56%). After separation of the diastereoisomer mixture **17**/**18**, the enantiomer excess and absolute configuration of

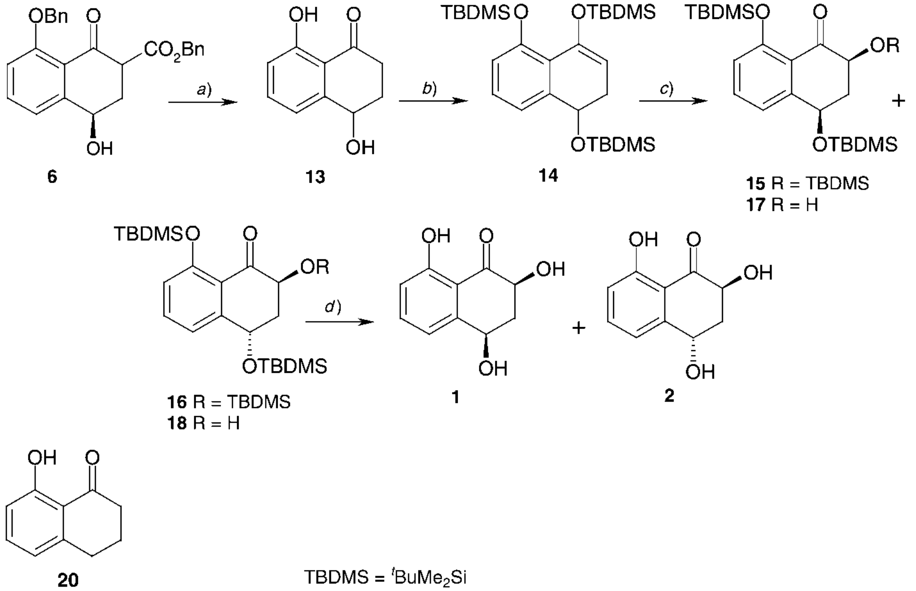
Scheme 2. *Synthesis of* **1** *by* Pathway A (for racemates, only one enantiomer is shown)



a) H_2O/dioxane 1:1, *Δ*, overnight; >90%. *b*) BnBr (2 equiv.), K_2CO_3 (3 equiv.), DMF, r.t., overnight; 65%. *c*) Lithium diisopropylamide (LDA; 2 equiv.), THF. *d*) ^{t}BuMe$_2$SiCl, 1*H*-imidazole, DMF; 15% of **7a**; or 3,4-dihydro-2*H*-pyran (3 equiv.), cat. camphorsulfonic acid (CSA), CH_2Cl_2; 73% of **7b**. *e*) Hexamethyldisilazane potassium salt (KHMDS; 1 equiv.), (+)-(camphorsulfonyl)oxaziridine (**11**) or *trans*-(±)-3-phenyl-2-(phenylsulfonyl)oxaziridine (**10**; 1.5 equiv.), THF, −78 to −10°, 1.5 h; 20–57%. *f*) H_2 (1 atm), 10% Pd/C AcOEt, overnight, r.t.; 7–25% of **1** and 7–16% of **9**

each isomer were determined by formation of their *Mosher* esters with (−)-(*R*)MTPCl ((−)-(*R*)-*α*-methoxy-*α*-(trifluoromethyl)benzeneacetyl chloride). The *Mosher* esters allowed us to establish that the configuration of the main enantiomer was in accordance with the *Sharpless* prediction of the configuration generated upon dihydroxylation of a trisubstituted olefin [17]. Thus, use of (DHQD)$_2$PHAL gave mainly the (2*R*,4*R*)-isomer (−)-**18**, and use of (DHQ)$_2$PHAL afforded mainly the (2*S*,4*S*)-isomer (+)-**18** (*Fig. 1*). In 1994, *Curran* and *Ko* achieved a 74% ee in the dihydroxylation of the olefin precursor for the six-membered *α*-hydroxylactone E-ring of camptothecin [18]. In our case, the presence of the aromatic moiety outside of the attractive area (SW) combined with the presence of the ^{t}BuMe$_2$SiO group at C(4) of the substrate seem to be

Scheme 3. *Synthesis of* **1** *and* **2** *by* Pathway B (for racemates, only one enantiomer is shown)



a) 1. H_2 (1 atm), 10% Pd/C, THF, overnight, then removal of Pd/C; 2. additionof 1% H_2O, 50°, 5 h; 41%. *b*) ^{t}BuMe$_2$SiOTf (3 equiv.), Et_3N (4.5 equiv.), 1,2-dichloroethane; 90%. *c*) *m*-CPBA, CH_2Cl_2, 15°; 67% (de 12%); or K_2CO_3 (3 equiv.), 2% OSO_4, 5% (DHQD)$_2$PHAL or (DHQ)$_2$PHAL, $K_3[Fe(CN)_6]$, (3 equiv.), methanesulfonamide (1 equiv.), ^{t}BuOH/H_2O 1 : 1, 0°, overnight; 33–39%. *d*) *Amberlyst 15*, MeOH, r.t., 5–6 days.

responsible for the low ee (12–30%). However, much to our surprise, the isomer (+)-**17** obtained with (DHQ)$_2$PHAL exhibited an ee of 94%. These differences of ee could be attributed to the instability of the *Mosher* esters in $CDCl_3$ in the presence of pyridine. However, the nondestructive circular-dichroism measurements confirmed the above observations. The optical rotations at 546 nm of compounds **17** and in MeOH **18** are given in *Table 1* and their CD spectra in *Fig. 2*.

The products **17** and **18** were deprotected in MeOH with *Amberlyst 15* during 5 days, providing the final compounds **1** and **2**, respectively. The rotations of **1** and **2** (see *Table 2*) indicate that an inversion of sign occurred between the protected form and the final product, in the case of the *trans*-isomers **2**, *e.g.*, (+)-**18** was transformed to (–)-**2**

Table 1. *Asymmetric Dihydroxylation of Silyl Enol Ether* **14**

Equiv. OsO_4	Ligand	Equiv. ligand	Products	de [%]	ee [%]	Yield [%]	$[\alpha]_{546}^{20}$ [a])
0.02	AD-mix α	0.05	(+)-**17**	30	> 94	33	+ 38.6 ± 0.7 (c = 0.40)
			(+)-**18**		30		*ca.* 0 (c = 0.67)
0.02	AD-mix β	0.05	(–)-**17**	56	22	39	– 15.7 ± 1.0 (c = 0.30)
			(–)-**18**		12		– 0.5 ± 0.3 (c = 1.02)

[a]) In MeOH; c in g/100 ml.

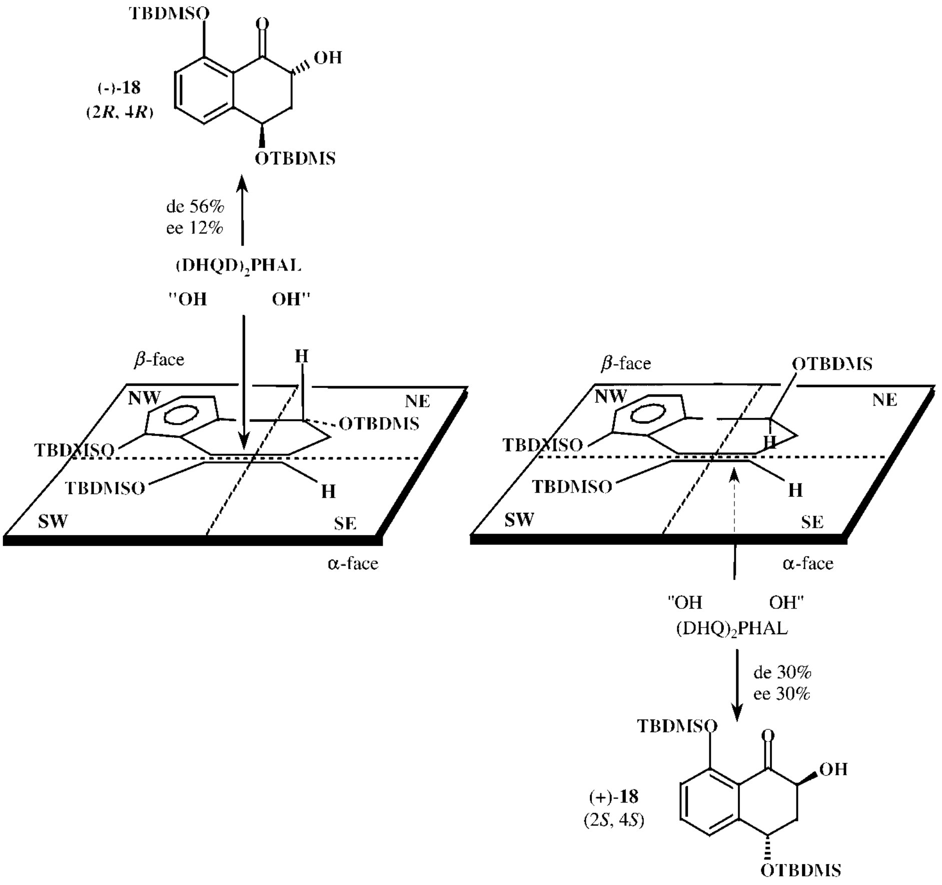


Fig. 1. *Asymmetric dihydroxylation of silyl enol ether* **14**

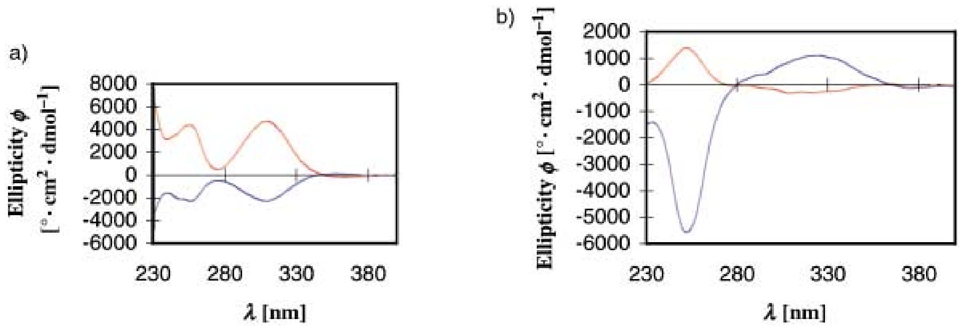


Fig. 2. *CD Spectra* a) *of (+)*-**17** (red) *and* (−)-**17** (blue) *and* b) *of (+)*-**18** (blue) *and (−)*-**18** (red)

([α] determined under the same conditions). However, this sign inversion could be caused by epimerization of *trans* compound **18** to *cis*-isomer **1**, which has a higher [α] than the *trans*-isomer **2**. Thus, if the *trans*-isomer has a specific rotation $[\alpha] = +1$, the presence of a few percent of the epimer with higher [α] can reverse the sign of the sample. The CD spectra of isomers **1** and **2** are similar to those of derivatives **17** and **18**, respectively (see *Fig. 2*). Finally, comparison with previously recorded CD spectra of our natural sample established that our natural *trans*- and *cis*-isomers were the (−)-(2*S*,4*S*)-isomer (−)-**2** and the (+)-(2*S*,4*R*)-isomer (+)-**1**.

Table 2. *Rotatory Power of Final Product* **1** *and* **2**

Substrat	Products	Yield [%]	de [%]	$[\alpha]^{20}_{546}$ [a])	
(−)-**17**	(−)-**1**	80	100	-4.9 ± 3.7	($c = 0.082$)
(−)-**18**	(+)-**2**	46	52	$+3.4 \pm 1.3$	($c = 0.090$)
(+)-**17**	(+)-**1**	92	100	$+6.2 \pm 1.3$	($c = 0.240$)
(+)-**18**	(−)-**2**	51	64	-11.4 ± 0.5	($c = 0.630$)

[a]) In MeOH, *c* in g/100 ml.

Conclusions. – An asymmetric synthesis of *cis*- and *trans*-2,4,8-trihydroxynaphthalen-1(2*H*)-ones **1** and **2** was achieved, in which *Sharpless* dihydroxylation of the silyl enol ether **14** and a tandem *Michael-Dieckmann* reaction producing **6** were the most efficient steps. Although the natural anthracycline antibiotics comprising the structure **1** or **2** do not exist, they could be used as building blocks for the synthesis of artificial anthracyclines of clinical use for the treatment of various human solid tumors and leukemias.

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Experimental Part

General. Benzyl acrylate was prepared from acryloyl chloride and benzyl alcohol with Et_3N in CH_2Cl_2 and purified by distillation over hydroquinone monomethyl ether. CC = column chromatography. M.p.: *Büchi 510* melting-point apparatus; corrected. Optical rotations: *Perkin-Elmer 241* polarimeter. Circular dichroism: *Jasco 710*; [ϕ] (λ). IR Spectra: *Perkin-Elmer FT-IR 1720*; in cm^{-1}. NMR Spectra: *Bruker AMX-400*; δ in ppm rel. to $SiMe_4$, *J* in Hz. ESI-MS: *Finnigan LCQ*; in *m/z* (rel. %). Microanalyses were performed in the Mikroelementaranalytisches Laboratorium, ETH-Zürich.

*7-Hydroxyisobenzofuran-1-(3*H*)-one* (= *7-Hydroxyphthalide*; **4**). To a stirred (stirring bar) soln. of ethyl 2-(acetyloxy)-6-(bromomethyl)benzoate (25 g, 0.113 mol) [9] in CCl_4 (500 ml), *N*-bromosuccinimide (28 g, 0.124 mol) and benzoyl peroxide (2.6 g, 0.011 mol) were added in small portions. The mixture was heated under reflux for 4 h, then cooled to r.t., and evaporated to give *ethyl 2-(acetyloxy)-6-(bromomethyl)benzoate* (**3**) as a pale yellow oil. The latter was suspended crude without further purification in H_2O/dioxane 1:1 (200 ml) and then heated under reflux overnight. The solvent was evaporated and the resulting beige solid recrystallized from petroleum ether (70–90°): 13.7 g (81%) of **4**. White crystals. M.p. 135–136°. ^{1}H-NMR (200 MHz, $CDCl_3$): 5.35 (*s*, 2 H−C(3)); 6.98 (*t*, *J* = 8, H−C(4), H−C(6)); 7.59 (*t*, *J* = 8, H−C(5)).

*7-(Benzyloxy)isobenzofuran-1(3*H*)-one* (= *7-(Benzyloxy)phthalide*; **5**). To **4** (6 g, 0.04 mol) and K_2CO_3 (16.6 g, 0.12 mol) in dry DMF under Ar (100 ml), benzyl bromide (9.5 ml, 0.08 mol) was added dropwise at r.t. The mixture was stirred at r.t. until consumption of the starting material (TLC monitoring) and then poured an ice (100 g). The pale yellow solid obtained was dissolved in AcOEt, the aq. layer extracted with AcOEt, the combined org. phase washed with brine (100 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by CC (silica gel, AcOEt/hexane 2 : 8): 6.2 g (65%) of **5**. Recrystallization from AcOEt/hexane gave white crystals. M.p. 109°. IR (KBr): 1764*s*, 1746*m*, 1616*m*, 1604*m*, 1498*s*, 1489*s*, 1454*s*. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.25 (*s*, 2 H–C(3)); 5.35 (*s*, 2 H–C(8)); 6.93 (*d*, *J* = 8.3, H–C(6)); 7.01 (*dd*, *J* = 0.6, 7.5, H–C(4)); 7.32 (*m*, 1 H); 7.39 (*m*, 2 H); 7.53 (*m*, 3 H). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): 69.07 (C(3)); 70.80 (C(8)); 112.93 (C(6)); 114.35; 114.39 (C(4)); 127.13; 128.37; 129.10; 136.44; 136.53; 149.82; 158.12 (C(7)); 169.23 (C(1)). ESI-MS (pos.): 263 ([*M* + Na]$^+$), 258 ([*M* + H_2O]$^+$); MS-MS of 258: 241 ([*M* + H]$^+$). Anal. calc. for $C_{15}H_{12}O_3$ (240.26): C 74.99, H 5.03; found: C 74.92, H 4.96.

Benzyl 8-(Benzyloxy)-1,2,3,4-tetrahydro-4-hydroxy-1-oxonaphthalene-2-carboxylate (**6**). To a soln. of **5** (2 g, $8.33 \cdot 10^{-3}$ mol) in freshly distilled THF (375 ml) at – 40° under Ar, 2M lithium diisopropylamide (8.33 ml, $1.67 \cdot 10^{-2}$ mol) was added dropwise by syringe (→ light-orange soln.). After 5 min, a soln. of benzyl acrylate (1.735 g, $1.07 \cdot 10^{-2}$ mol) in dry THF (35 ml) was slowly added by syringe while maintaining the temp. at – 40° (→ cloudy and bleached mixture). Then the mixture was allowed to warm to – 10° within 1.5 h and quenched by addition of 1M HCl (100 ml) followed by dist. H_2O (100 ml). The aq. layer was extracted with AcOEt (3 × 150 ml), the combined org. extract washed with brine (100 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by CC (silica gel, AcOEt/hexane 1 : 1): 1.13 g (41%) of **6**. Pale yellow oil. R_f (AcOEt/hexane 1 : 1; UV) 0.39. IR (KBr): 3426*s*, 1739*s*, 1680*m*, 1600*s*, 1271*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): *cis:* 2.44 – 2.71 (*m*, 2 H–C(3)); 3.73 (*dd*, *J* = 5.5, 9.4, H–C(2)); 4.90 – 5.48 (*m*, 5 H); 6.79 – 7.66 (*m*, 13 H); enol: 2.80 (*m*, 2 H–C(3)); 4.73 (*t*, *J* = 6.6, H–C(4)); 4.90 – 5.48 (*m*, 5 H); 6.79 – 7.66 (*m*, 13 H); 13.03 (*s*, OH); *trans:* 2.30 – 2.71 (*m*, H–C(3)); 4.15 (*dd*, *J* = 5.1, 10.5, H–C(2)); 4.90 – 5.48 (*m*, 5 H); 6.79 – 7.66 (*m*, 13 H). ESI-MS (pos.): 425 ([*M* + Na]$^+$).

*Benzyl 8-(Benzyloxy)-4-{[(*tert*-butyl)dimethylsilyl]oxy}-1,2,3,4-tetrahydro-1-oxonaphthalene-2-carboxylate* (**7a**). To a mixture of **6** (640 mg, $1.59 \cdot 10^{-3}$ mol) and 1*H*-imidazole (216 mg, $3.18 \cdot 10^{-3}$ mol) in dry DMF (20 ml) at r.t. under Ar, ^{t}BuMe$_2$SiCl (478 mg, $3.18 \cdot 10^{-3}$ mol) was added with a spatula. The mixture was stirred at r.t. overnight and poured into ice/2M HCl (15 ml). The aq. layer was extracted with Et_2O (3 × 20 ml), the combined org. extract washed with brine (2 × 20 ml) dried ($MgSO_4$), mixed with silica gel, and evaporated, and the resulting powder purified by CC (silica gel, AcOEt/hexane 1 : 4): 120 mg (15%) **7a**. Pale yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): *cis:* 2.54 (*m*, 2 H–C(3)); 3.73 (*dd*, *J* = 6.1, 6.9, H–C(2)); 4.95 (*dd*, *J* = 6.9, 7.5, H–C(4)); 5.17 – 5.37 (*m*, 4 H); 6.96 – 7.59 (*m*, 13 H); enol: 0.16 (*s*, 3 H); 0.19 (*s*, 3 H); 1.00 (*s*, 9 H); 2.53 (*dd*, *J* = 11.9, 14.7, H–C(3)); 2.84 (*dd*, *J* = 5.5, 14.7, H–C(3)); 4.80 (*dd*, *J* = 5.5, 11.9, H–C(4)); 5.17 – 5.37 (*m*, 4 H); 6.96 – 7.59 (*m*, 13 H); 12.98 (*s*, OH); *trans:* 2.41 (*dt*, *J* = 6.2, 13.5, H–C(3)); 2.56 (*ddd*, *J* = 3.1, 4.2, 13.5, H–C(3)); 4.10 (*dd*, *J* = 5.6, 9.0, H–C(2)); 5.01 (*dd*, *J* = 3.1, 6.2, H–C(4)); 5.17 – 5.37 (*m*, 4 *J* = 6.96 – 7.59 (*m*, 13 H); *cis*/*trans:* 0.05 (*s*, 3 H); 0.22 (*s*, 6 H); 0.24 (*s*, 3 H); 0.91 (*s*, 9 H); 1.02 (*s*, 9 H). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): *cis:* 36.30 (C(3)); 55.11 (C(2)); 68.64 (C(4)); enol: – 4.44; – 4.12; 18.70; 26.32, 30.73 (C(3)); 67.71 (C(4)); 95.13 (C(2)); 167.12 (C(1)); *trans:* 35.23 (C(3)); 52.13 (C(2)); 69.71 (C(4)); *cis*/*trans:* 191.29 (C(1)); 191.75 (C(1)); *cis*/enol/*trans:* – 4.38; – 4.22; – 4.17; – 3.77; 18.48; 18.62; 26.16; 26.28; 66.40; 66.75; 67.35; 67.42; 70.98; 71.63; 113.44; 114.12; 114.23; 117.94; 118.40; 118.51; 120.07; 120.60; 120.86; 126.21 – 137.38 (*m*); 146.02 (C(4a)); 147.68 (C(4a)); 149.49 (C(4a)); 157.63 (C(8)); 159.45 (C(8)); 159.48 (C(8)); 170.11 (C(9)); 171.01 (C(9)); 172.93 (C(9)).

*Benzyl 8-(Benzyloxy)-1,2,3,4-tetrahydro-1-oxo-4-[(tetrahydro-2*H*-pyran-2-yl)oxy]naphthalene-2-carboxylate* (**7b**). To a mixture of **6** (371 mg, $9.23 \cdot 10^{-4}$ mol) and CSA (15 mg) in dry CH_2Cl_2 (30 ml) at r.t. under Ar, 3,4-dihydro-2*H*-pyran (250 µl, $2.77 \cdot 10^{-3}$ mol) was added by syringe. The mixture was stirred at r.t. for 2.5 h and quenched by addition of dist. H_2O (20 ml). The aq. layer was extracted with AcOEt (2 × 20 ml), the combined org. extract washed with brine (2 × 20 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by CC (silica gel, AcOEt/hexane 3 : 7): 327 mg (73%) of **7b**. Colorless oil. R_f (AcOEt/hexane 3 : 7; UV) 0.30. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 1.46 – 1.90 (*m*, 36 H); 2.43 – 2.76 (*m*, 10 H); 2.78 (*m*, 2 H); 3.52 (*m*, 6 H); 3.86 (*m*, 6 H); 4.52 (*t*, *J* = 3.3, 2 H); 4.72 (*m*, 2 H); 4.96 (*t*, *J* = 2.5, 2 H); 5.20 – 5.35 (*m*, 24 H); 6.95 – 7.14 (*m*, 6 H); 7.29 – 7.54 (*m*, 18 H); 12.96 (*s*, OH); 12.98 (*s*, OH). ESI-MS (pos.): 510 ([*M* + H + Na]$^+$), 509 ([*M* + Na]$^+$); MS-MS of 509: 401 ([*M* + Na – THP]$^+$); MS-MS of 401: 310 ([*M* + Na – THP – Bn]$^+$).

*Benzyl (*2RS,4SR*)-8-(Benzyloxy)-1,2,3,4-tetrahydro-2-hydroxy-1-oxo-4-{[(*2SR*)-tetrahydro-2*H*-pyran-2-yl]oxy}naphthalene-2-carboxylate* (*cis*-**8**), *Benzyl (*2RS,4SR*)-8-(Benzyloxy)-1,2,3,4-tetrahydro-2-hydroxy-1-oxo-4-{[(*2RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}naphthalene-2-carboxylate* (*cis*-**8′**), *Benzyl (*2RS,4RS*)-8-(Benzyloxy)-1,2,3,4-tetrahydro-2-hydroxy-1-oxo-4-{[(*2RS*)-tetrahydro-2*H*-pyran-2-yl]oxy}naphthalene-2-carboxylate* (*trans*-**8**), *and Benzyl (*2RS,4RS*)-8-(Benzyloxy)-1,2,3,4-tetrahydro-2-hydroxy-1-oxo-4-{[(*2SR*)-tetrahydro-2*H*-pyran-2-yl]oxy}naphthalene-2-carboxylate* (*trans*-**8′**). To a soln. of **7b** (296 mg, $6.09 \cdot 10^{-4}$ mol) in dry THF (15 ml) under Ar at – 78°, 0.5M KHMDS in toluene (1.18 ml, $6.09 \cdot 10^{-4}$ mol) was added by syringe. A soln. of *trans*-(±)-3-phenyl-2-(phenylsulfonyl)oxaziridine (**10**; 239 mg, $9.14 \cdot 10^{-4}$ mol) in dry THF (5 ml) was added dropwise, and the temp. of the mixture was allowed to rise to − 10° within 1.5 h. The mixture was quenched at − 10° by addition of sat. aq. Na_2SO_4 soln. (10 ml), the aq. layer extracted with AcOEt (3 × 15 ml), the combined org. extract washed with brine (2 × 20 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by CC (silica gel, AcOEt/hexane 3 : 7): 41 mg (13%) of *cis*-**8**/*cis*-**8′** 1 : 1 as colorless oil and 134 mg (44%) of *trans*-**8**/*trans*-**8′** 1 : 1 as colorless oil.

The procedure was repeated with **7b** (163 mg, $3.54 \cdot 10^{-4}$ mol) in dry THF (25 ml), 0.5M KHMDS in toluene (708 µl, $3.54 \cdot 10^{-4}$ mol), and (+)-(camphorsulfonyl)oxaziridine (**11**; 115 mg, $5.31 \cdot 10^{-4}$ mol) in dry THF (5 ml). Purification by CC (silica gel, AcOEt/hexane 3 : 7) gave 14.1 mg (9%) of *cis*-**8**/*cis*-**8′** 1 : 1 as colorless oil and 17.2 mg (11%) of *trans*-**8**/*trans*-**8′** 2 : 1 as colorless oil.

Data of cis-**8**/cis-**8′**: R_f (AcOEt/hexane 3 : 7; UV) 0.23. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): *cis*-**8**: 1.55 – 1.91 (*m*, 6 H); 2.43 (*dd*, *J* = 8.3, 13.6, H−C(3)); 3.21 (*dd*, *J* = 5.0, 13.6, H−C(3)); 3.55 (*m*, H−C(6′)); 3.93 (*m*, H−C(6′)); 5.06 – 5.30 (*m*, 5 H); 6.94 – 7.58 (*m*, 13 H); *cis*-**8′**: 1.55 – 1.91 (*m*, 6 H); 2.23 (*dd*, *J* = 9.4, 13.1, H−C(3)); 3.14 (*dd*, *J* = 5.1, 13.1, H−C(3)); 3.55 (*m*, H−C(6′)); 3.93 (*m*, H−C(6′)); 5.06 – 5.30 (*m*, 5 H); 6.94 – 7.58 (*m*, 13 H); *cis*-**8**/*cis*-**8′**: 4.74 (*m*, H−C(2′)); 4.88 (*m*, H−C(2′)). ESI-MS (pos.): 525 ($[M + Na]^+$).

Data of trans-**8**/trans-**8′**: R_f (AcOEt/hexane 3 : 7; UV) 0.16. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): *trans*-**8**: 1.55 – 1.88 (*m*, 6 H); 2.66 (*dd*, *J* = 4.4, 13.4, H−C(3)); 2.93 (*dd*, *J* = 7.7, 13.4, H−C(3)); 3.60 (*m*, H−C(6′)); 3.97 (*m*, H−C(6′)); 4.84 (*t*, *J* = 2.9, H−C(2′)); 5.07 – 5.25 (*m*, 5 H); 6.98 – 7.58 (*m*, 13 H); *trans*-**8′**: 1.55 – 1.88 (*m*, 6 H); 2.43 (*dd*, *J* = 4.1, 13.7, H−C(3)); 2.90 (*dd*, *J* = 6.2, 13.7, H−C(3)); 3.60 (*m*, H−C(6′)); 3.97 (*m*, H−C(6′)); 4.91 (*t*, *J* = 2.1, H−C(2′)); 5.07 – 5.25 (*m*, 5 H); 6.98 – 7.58 (*m*, 13 H). ESI-MS (pos.): 525 ($[M + Na]^+$).

*Benzyl (2*RS*,4*SR*)-8-(Benzyloxy)-1,2,3,4-tetrahydro-2,4-dihydroxy-1-oxonaphthalene-2-carboxylate.* Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 2.31 (*dd*, *J* = 7.6, 13.6, H−C(3)); 3.08 (*dd*, *J* = 5.2, 13.6, H−C(3)); 5.06 – 5.30 (*m*, 5 H); 6.94 – 7.58 (*m*, 13 H).

*(1*RS*,9*RS*)-6-(Benzyloxy)-9-hydroxy-11-oxatricyclo [7.2.1.0^{2,7}]dodeca-2,4,6-triene-8,10-dione* (**12**). Colorless oil. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 2.82 (*d*, *J* = 11.4, H−C(3)); 3.22 (*dd*, *J* = 5.5, 11.4, H−C(3)); 5.02 – 5.24 (*m*, 2 H); 5.57 (*d*, *J* = 5.5, H−C(4)); 7.10 – 7.58 (*m*, 8 H).

cis-*3,4-Dihydro-2,4,8-trihydroxynaphthalen-1(2*H*)-one* (**1**) *and 3,4-dihydro-2,8-dihydroxynaphthalen-1-(2*H*)-one* (**9**). To a soln. of *trans*-**8**/*trans*-**8′** (130 mg, $2.59 \cdot 10^{-4}$ mol) in AcOEt (10 ml), 10% Pd/C (15 mg) was added. The mixture was stirred overnight under H_2 (1 atm). After filtration over *Celite*, the org. layer was washed with 1M HCl the aq. layer extracted with AcOEt (3 × 15 ml), the combined org. extract washed with brine (2 × 20 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by CC (silica gel, AcOEt/hexane 1 : 4 and 1 : 1): 3.3 mg (7%) of **9** as colorless oil and 3.7 mg (7%) of **1** as pale yellow oil that turned red on contact with air.

The same procedure was repeated with *cis*-**8**/*cis*-**8′** (40 mg, $7.96 \cdot 10^{-5}$ mol) in AcOEt (5 ml). CC (silica gel, AcOEt/hexane 1 : 4 and 1 : 1) gave 2.3 mg (16%) of **9** and 3.8 mg (25%) of **1**.

Data of **1**: R_f (AcOEt/hexane 1 : 1; UV) 0.09. ^{1}H-NMR (400 MHz, CD_3OD; COSY): 2.04 (*dt*, *J* = 11.6, 13.3, H−C(3)); 2.66 (*dt*, *J* = 4.6, 11.6, H−C(3)); 4.44 (*dd*, *J* = 4.6, 13.3, H−C(2)); 4.95 (*dd*, *J* = 4.6, 11.6, H−C(4)); 6.88 (*d*, *J* = 8.2, H−C(7)); 7.23 (*dd*, *J* = 1.0, 7.8, H−C(5)); 7.57 (*dd*, *J* = 7.8, 8.2, H−C(6)). ^{13}C-NMR (100 MHz, CD_3OD; HETCOR): 41.88 (C(3)); 66.26 (C(4)); 71.17 (C(2)); 113.97 (C(8a)); 116.22 (C(7)); 116.73 (C(5)); 136.99 (C(6)); 149.31 (C(4a)); 162.62 (C(8)); 204.98 (C(1)). APCI-MS (pos.): 195 ($[M + H]^+$).

Data of **9**: R_f (AcOEt/hexane 1 : 1; UV) 0.40. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 1.59 (*s*, OH); 2.06 (*m*, H−C(3)); 2.52 (*m*, H−C(3)); 3.06 (*m*, 2 H−C(4)); 4.40 (*dd*, *J* = 5.4, 13.2, H−C(2)); 6.76 (*dd*, *J* = 0.9, 7.5, H−C(7)); 6.85 (*d*, *J* = 8.4, H−C(5)); 7.44 (*t*, *J* = 8.0, H−C(6)); 11.60 (*s*, OH). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): 28.06 (C(4)); 31.55 (C(3)); 73.60 (C(2)); 115.50 (C(8a)); 115.95 (C(7)); 119.71 (C(5)); 137.58 (C(6)); 145.66 (C(4a)); 163.06 (C(8)); 204.73 (C(1)). ESI-MS (neg.): 177 ($[M − H]^-$).

*3,4-Dihydro-4,8-dihydroxynaphthalen-1-(2*H*)-one* (= *Isosclerone*; **13**). To a soln. of **6** (1.1 g, $2.74 \cdot 10^{-3}$ mol) in dry THF (120 ml) 10% Pd/C (75 mg) was added. The mixture was stirred overnight under H_2 (1 atm). After filtration over *Celite*, dist. H_2O (1 ml) was added and the mixture stirred at 50° for 5 h. The solvent was evaporated and the crude product purified by CC (silica gel, AcOEt/hexane 1 : 1): 194 mg (40%) of **13**. Pale yellow crystals, which were recrystallized from hexane. White crystals. M.p. 98 – 99°. R_f (AcOEt/hexane 1 : 1; UV) 0.26. IR (KBr): 3264*m*, 1637*s*, 1616*s*, 1454*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 1.82 (*s*, OH); 2.19 (*m*, H−C(3)); 2.34 (*m*, H−C(3)); 2.64 (*ddd*, *J* = 4.8, 8.3, 17.9, H−C(2)); 3.00 (*ddd*, *J* = 4.7, 8.3, 17.9, H−C(2)); 4.91 (*dd*, *J* = 3.7, 7.4, H−C(4)); 6.92 (*d*, *J* = 8.4, H−C(7)); 7.01 (*dd*, *J* = 0.8, 7.5, H−C(5)); 7.49 (*dd*, *J* = 7.5, 8.4, H−C(6)); 12.41 (*s*, OH). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): 31.48 (C(3)); 34.52 (C(2)); 67.64 (C(4)); 115.22 (C(8a)); 117.36 (C(7)); 117.70 (C(5)); 136.95 (C(6)); 145.86 (C(4a)); 162.66 (C(8)); 204.26 (C(1)). EI-

MS: 178 (17, $M^{+\bullet}$), 160 (6.5, $[M-H_2O]^{+\bullet}$), 132 (25), 121 (100), 77 (25), 65 (44.5). DCI-MS (NH_3): 179 ($[M+H]^+$).

*3,4-Dihydro-8-hydroxynaphthalen-1(2*H*)-one* (**20**). If the transformation **6** → **13** was performed in AcOEt or MeOH as solvent, also **20** was formed. White solid. R_f (AcOEt/hexane 1:1; UV) 0.55. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 2.09 (*quint.*, *J* = 6.1, 2 H−C(3)); 2.67 (*t*, *J* = 6.1, 2 H−C(4)); 2.91 (*t*, *J* = 6.1, 2 H−C(2)); 6.70 (*dd*, *J* = 0.9, 8.4, H−C(5)); 6.78 (*dd*, *J* = 0.9, 7.5, H−C(7)); 7.33 (*dd*, *J* = 7.5, 8.4, H−C(6)); 12.43 (*s*, OH). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): 22.87 (C(3)); 29.75 (C(2)); 38.92 (C(3)); 115.49 (C(7)); 117.03 (C(8a)); 118.82 (C(5)); 136.28 (C(6)); 145.51 (C(4a)); 162.87 (C(8)); 205.21 (C(1)). DCI-MS (NH_3): 163 ($[M+H]^+$).

*1,4,5-Tris{[(*tert*-butyl)dimethylsilyl]oxy}-1,2-dihydronaphthalene* (**14**). To a soln. of **13** (190 mg, $1.07 \cdot 10^{-3}$ mol) in 1,2-dichloroethane (20 ml) under Ar, Et_3N (670 µl, $4.82 \cdot 10^{-3}$ mol; freshly distilled over KOH) was added by syringe at r.t. Then ^{t}BuMe$_2$SiOTf (740 µl, 3.21 10^{-3} mol) was added dropwise by syringe, and the mixture was stirred for 25 min. Then silica gel (2 g) was directly added to the soln., and the mixture was purified by CC (silica gel, AcOEt/hexane 2:98): 500.5 mg (90%) of **14**. Colorless oil. R_f (AcOEt/hexane 2:98; UV) 0.63. IR (film): 1635*m*, 1472*s*, 1256*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 0.07–0.16 (*m*, 18 H); 0.93 (*s*, 9 H); 0.96 (*s*, 9 H); 0.99 (*s*, 9 H); 2.23 (*m*, 2 H−C(2)); 4.63 (*dd*, *J* = 6.3, 11.0, H−C(1)); 5.16 (*dd*, *J* = 4.0, 6.6, H−C(3)); 6.74 (*d*, *J* = 8.0, H−C(6)); 7.05 (*dt*, *J* = 1.1, 7.5, H−C(8)); 7.13 (*t*, *J* = 7.7, H−C(7)). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): −4.46; −4.31; −4.10; −4.00; −3.82; −3.37; 26.36; 26.45; 26.49; 32.56 (C(2)); 70.71 (C(1)); 104.91 (C(3)); 117.60 (C(6)); 121.70 (C(8)); 124.83 (C(4a)); 128.32 (C(7)); 143.45 (C(8a)); 149.19 (C(5)); 152.19 (C(4)). ESI-MS (pos.): 538 ($[M+H_2O]^+$).

cis*-2,4,8-Tris{[(*tert*-butyl)dimethylsilyl]oxy}-3,4-dihydronaphthalen-1(2*H*)-one* (**15**) *and* trans*-2,4,8-Tris{[(*tert*-butyl)dimethylsilyl]oxy}-3,4-dihydronaphthalen-1(2*H*)-one* (**16**). To a soln. of **14** (95 mg, $1.82 \cdot 10^{-4}$ mol) in 1,2-dichloroethane (10 ml) under Ar at −15° (ice/acetone bath), 70% *m*-CPBA (45 mg, $1.82 \cdot 10^{-4}$ mol) in 1,2-dichloroethane (2 ml) was added dropwise by syringe. The mixture was stirred at r.t. for 1.5 h. After evaporation, the crude product was purified by CC (silica gel, AcOEt/hexane 2:98). 66 mg (67%) of **15**/**16** 56:44. Colorless oil. R_f (AcOEt/hexane 2:98; UV) 0.35. IR (film): 2930*m*, 2858*s*, 1708*s*, 1594*m*, 1463*s*, 1255*s*, 927*s*, 835*s*, 779*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): **15**: 2.19 (*dt*, *J* = 11.7, 13.1, H−C(3)); 2.52 (*dt*, *J* = 4.8, 13.1, H−C(3)); 4.25 (*dd*, *J* = 4.8, 13.1, H−C(2)); 4.96 (*dd*, *J* = 4.9, 11.2, H−C(4)); 6.83 (*m*, H−C(7)); 7.19 (*dt*, *J* = 1.0, 7.8, H−C(5)); 7.39 (*t*, *J* = 8.0, H−C(6)); **16**: 2.31 (*m*, 2 H−C(3)); 4.65 (*dd*, *J* = 4.6, 8.6, H−C(2)); 5.10 (*dd*, *J* = 3.9, 5.8, H−C(4)); 6.83 (*m*, H−C(7)); 6.99 (*d*, *J* = 7.6, H−C(5)); 7.39 (*t*, *J* = 8.0, H−C(6)); **15**/**16**: 0.07–0.16 (*m*, 18 H); 0.93 (*s*, 9 H); 0.96 (*s*, 9 H); 0.99 (*s*, 9 H). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): **15**: 43.92 (C(3)); 68.69 (C(4)); 74.22 (C(2)); 119.33 (C(5)); **16**: 42.04 (C(3)); 68.13 (C(4)); 72.64 (C(2)); 120.87 (C(5)); **15**/**16**: −4.96 to −3.71 (*m*); 18.48; 18.59; 18.84; 18.91; 18.94; 19.09; 26.19; 26.28; 26.30; 26.34; 121.33 (C(7)); 121.70 (C(7)); 122.32 (C(8a)); 122.57 (C(8a)); 133.96 (C(6)); 134.02 (C(6)); 147.09 (C(4a)); 148.84 (C(4a)); 156.52 (C(8)); 156.68 (C(8)); 195.35 (C(1)); 195.61 (C(1)). ESI-MS (pos.): 559 ($[M+Na]^+$). Anal. calc. for $C_{28}H_{52}O_4Si_3$ (536.98): C 62.63, H 9.76; found: C 62.60, H 9.82.

trans*-3,4-Dihydro-2,4,8-trihydroxynaphthalen-1(2*H*)-one* (**2**). To a soln. of **15**/**16** (de 12%; 66 mg, $1.23 \cdot 10^{-4}$ mol) in MeOH (10 ml), *Amberlyst 15* was added. The mixture was stirred for 5–6 days and then filtered. After evaporation, the crude product was purified by CC (silica gel, AcOEt/hexane 1:1): 13.5 mg (55%) of **1**/**2** 59:41 (de 18%) as pale yellow oil.

Data of **2**: Pale yellow solid. R_f (AcOEt/hexane 1:1; UV) 0.09. ^{1}H-NMR (400 MHz, CD_3OD; COSY): 2.27 (*ddd*, *J* = 3.2, 11.7, 13.2, H−C(3)); 2.51 (*ddd*, *J* = 3.9, 5.1, 13.2, H−C(3)); 4.81 (*dd*, *J* = 5.0, 11.7, H−C(2)); 4.99 (*t*, *J* = 3.4, H−C(4)); 6.92 (*dd*, *J* = 1.1, 8.4, H−C(7)); 6.98 (*dq*, *J* = 0.6, 7.5, H−C(5)); 7.56 (*dd*, *J* = 7.5, 8.4, H−C(6)). ^{13}C-NMR (100 MHz, CD_3OD; HETCOR): 39.18 (C(3)); 66.59 (C(4)); 68.33 (C(2)); 114.25 (C(8a)); 117.41 (C(7)); 120.06 (C(5)); 137.34 (C(6)); 145.21 (C(4a)); 162.65 (C(8)); 205.12 (C(1)).

The same protocol was applied to (+)- and (−)-**17** or (+)- and (−)-**18**. From pure (+)-**18** (111 mg; $[\alpha]^{20}_{546} = +4.1 \pm 0.3$), 31.5 mg (51%) of **1**/(−)-**2** was obtained: de 64% for (−)-**2**, $[\alpha]^{20}_{546} = -11.4 \pm 0.5$ (*c* = 0.630, MeOH).

From pure (+)-**17** (28 mg; $[\alpha]^{20}_{546} = +32.1 \pm 0.5$), 12 mg (92%) of (+)-**1** was obtained: de 100% for (+)-**1**, $[\alpha]^{20}_{546} = +6.2 \pm 1.3$ (*c* = 0.240, MeOH).

From pure (−)-**18** (40 mg; $[\alpha]^{20}_{546} = -0.5 \pm 0.2$), 11.7 mg (64%) of **1**/(+)-**2** was obtained: de 52% for (+)-**2**, $[\alpha]^{20}_{546} = +3.4 \pm 1.3$ (*c* = 0.090, MeOH).

From pure (−)-**17** (11 mg; $[\alpha]^{20}_{546} = -10.3 \pm 0.9$), 4.1 mg (80%) of (−)-**1** was obtained: de 100% for (−)-**1**, $[\alpha]^{20}_{546} = -4.9 \pm 1.3$ (*c* = 0.082, MeOH).

*Data of (+)-***2**: CD (MeOH, *c* = $9.00 \cdot 10^{-4}$ g · cm^{-3}, 1 = 1 mm): 489 (257), 0 (281), −71 (309), 0 (329). $[\alpha]^{20}_{546} = +3.4 \pm 1.3$ (*c* = 0.090, MeOH).

*Data of (–)-***2**: CD (MeOH, $c = 4.00 \cdot 10^{-4}$ g · cm^{-3}, $l = 1$ mm): –2989 (258), 0 (284), 272 (301), 0 (320). $[\alpha]_{546}^{20} = -8.9 \pm 1.9$ ($c = 0.040$, MeOH).

*Data of (+)-***1**: CD (MeOH, $c = 9.20 \cdot 10^{-5}$ g · cm^{-3}, $l = 5$ mm): 754 (230), 233 (241), 795 (262), 152 (280), 520 (304), 0 (326), –285 (341), 0 (365). $[\alpha]_{546}^{20} = +2.2 \pm 3.3$ ($c = 0.092$, MeOH).

*Data of (–)-***1**: CD (MeOH, $c = 8.21 \cdot 10^{-4}$ g · cm^{-3}, l = 1 mm): –346 (231), –159 (240), –526 (262), 102 (282), –224 (307), 0 (329), 112 (341), 0 (365). $[\alpha]_{546}^{20} = -4.9 \pm 1.3$ ($c = 0.082$, MeOH).

cis-*4,8-Bis{[(*tert-*butyl)dimethylsilyl]oxy}-3,4-dihydro-2-hydroxynaphthalen-1(*2H*)one* (**17**) *and* trans-*4,8-Bis{[(*tert-*butyl)dimethylsilyl]oxy}-3,4-dihydro-2-hydroxynaphthalen-1(*2H*)-one* (**18**). A mixture of K_2CO_3 (175 mg, $1.27 \cdot 10^{-3}$ mol), 2.5% OsO_4 soln. (86 µl, $8.4 \cdot 10^{-6}$ mol) in ^{t}BuOH, and $(DHQD)_2(PHAL)$ (16 mg, $2.1 \cdot 10^{-5}$ mol) in dist. H_2O (2.1 ml) was stirred at r.t. for 10 min. Then $K_3Fe(CN)_6$ (418 mg, $1.27 \cdot 10^{-3}$ mol) was added. When all salts were dissolved, ^{t}BuOH (500 µl) and methanesulfonamide (40 mg, $4.23 \cdot 10^{-4}$ mol) were added. The flask was cooled to 0°, and **14** (220 mg, $4.23 \cdot 10^{-4}$ mol) diluted in ^{t}BuOH (1.5 ml) was added. The mixture was stirred overnight at 0° and quenched with Na_2SO_3 (300 mg). After 45 min stirring r.t., dist. H_2O (3 ml) was added. The aq. layer was extracted with AcOEt (3 × 15 ml), the combined org. extract washed with brine (20 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by CC (silica gel, AcOEt/hexane 2:98 and 5:95): 15 mg (9%) of (–)-**17** as white solid and 53.9 mg (30%) of (–)-**18** as colorless oil.

Replacing the chiral ligand by $(DHQ)_2$PHAL (16 mg, $2.1 \cdot 10^{-5}$ mol) in exactly the same protocol gave 20.1 mg (11%) of (+)-**17** as white solid and 37.7 mg (21%) of (+)-**18** as colorless oil.

*Data of (+)-***17**: R_f (AcOEt/hexane 5:95; UV) 0.22. $[\alpha]_{546}^{20} = +38.6 \pm 0.7$ ($c = 0.402$, MeOH). IR (film): 3434*m*, 2930*s*, 2858*s*, 1690*s*, 1592*m*, 1465*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 0.29 (*s*, 3 H); 0.31 (*s*, 3 H); 0.33 (*s*, 3 H); 0.34 (*s*, 3 H); 1.08 (*s*, 9 H); 1.12 (*s*, 9 H); 2.04 (*dt*, $J = 11.1$, 13.2, H–C(3)); 2.72 (*dt*, $J = 5.0$, 11.7, H–C(3)); 4.37 (*dd*, $J = 5.0$, 13.2, H–C(2)); 5.21 (*dd*, $J = 5.0$, 10.9, H–C(4)); 6.97 (*d*, $J = 8.1$, H–C(7)); 7.31 (*dd*, $J = 1.0$, 7.8, H–C(5)); 7.57 (*t*, $J = 8.0$, H–C(6)). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): –4.41; –3.88; –3.81; –3.72; 19.24; 19.65; 26.63; 26.67; 44.28 (C(3)); 69.34 (C(4)); 73.17 (C(2)); 121.02 (C(5)); 122.21 (C(8a)); 122.75 (C(7)); 135.61 (C(6)); 150.92 (C(4a)); 157.65 (C(8)); 198.72 (C(1)). ESI-MS (pos.): 445 ($[M + Na]^+$). CD (MeOH, $c = 2.01 \cdot 10^{-4}$ g · cm^{-3}, $l = 5$ mm): 6936 (230), 3150 (240), 4380 (255), 499 (275), 4744 (309), 0 (349), –195 (364).

*Data of (+)-***18**: Colorless oil. R_f (AcOEt/hexane 5:95; UV) 0.17. $[\alpha]_{546}^{20} = -0.5 \pm 0.3$ ($c = 1.018$, MeOH). IR (film): 3471*m*, 2955*s*, 1688*s*, 1594*s*, 1464*s*. ^{1}H-NMR (400 MHz, $CDCl_3$; COSY): 0.12 (*s*, 3 H); 0.22 (*s*, 3 H); 0.24 (*s*, 3 H); 0.29 (*s*, 3 H); 0.89 (*s*, 9 H); 1.06 (*s*, 9 H); 2.14 (*dt*, $J = 3.1$, 12.6, H–C(3)); 2.56 (*ddd*, $J = 3.2$, 5.3, 12.6, H–C(3)); 4.84 (*dd*, $J = 4.8$, 13.1, H–C(2)); 4.99 (*t*, $J = 3.1$, H–C(4)); 6.87 (*dd*, $J = 1.0$, 8.2, H–C(7)); 6.90 (*dd*, $J = 1.0$, 8.0, H–C(5)); 7.42 (*t*, $J = 8.0$, H–C(6)). ^{13}C-NMR (100 MHz, $CDCl_3$; HETCOR): –4.51; –4.47; –4.31; –4.27; 17.99; 18.40; 25.68; 25.72; 40.21 (C(3)); 68.29 (C(4)); 69.15 (C(2)); 120.98 (C(8a)); 121.32 (C(5)); 122.09 (C(7)); 134.72 (C(6)); 146.10 (C(4a)); 156.24 (C(8)); 198.23 (C(1)). ESI-MS (pos.): 445 ($[M + Na]^+$). CD (MeOH, $c = 1.35 \cdot 10^{-4}$ g · cm^{-3}, $l = 5$ mm): –5573 (252), 0 (280), 110 (325), 0 (365).

*Data of (–)-***17**: $[\alpha]_{546}^{20} = -15.7 \pm 1.0$ ($c = 0.300$, MeOH). CD (MeOH, $c = 2.40 \cdot 10^{-4}$ g · cm^{-3}, $l = 5$ mm): –3624 (230), –1594 (240), –2275 (256), –486 (275), –2299 (309), 0 (346), 115 (358).

*Data of (–)-***18**: $[\alpha]_{546}^{20} =$ *ca.* 0 ($c = 0.674$, MeOH). CD (MeOH, $c = 2.04 \cdot 10^{-4}$ g · cm^{-3}, $l = 5$ mm): 1400 (252), $[\phi]_{274} = 0$ (274), –305 (322), 0 (362).

Determination of Enantiomer Excesses. In a NMR tube (dried for 24 h at 130°), optically active **17** or **18** (10 mg ($2.37 \cdot 10^{-5}$ mol) was dissolved in dry $CDCl_3$ (1.5 ml). With a 100-µl graduated capillary dry pyridine (50 µl, $4.59 \cdot 10^{-4}$ mol) and (–)-(*R*)-MTPCl (20 µl, $1.068 \cdot 10^{-4}$ mol) were added. The mixture was left at r.t. overnight, and then the ^{1}H-NMR was measured.

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