Tetrahedron 72 (2016) 347–353

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthetic approach to the functionalized tricyclic core of atropurpuran

Huan Chen, Xiao-Huan Li, Jing Gong, Hao Song *, Xiao-Yu Liu, Yong Qin *

Key Laboratory of Drug Targeting of Ministry of Education, West China School of Pharmacy and State Key Laboratory of Biotherapy, Sichuan University, Chengdu 610041, PR China

ARTICLE INFO

Article history:
Received 16 October 2015
Received in revised form 19 November 2015
Accepted 23 November 2015
Available online 26 November 2015

Keywords:
Atropurpuran
Diterpene
Michael addition
Organocatalyst

ABSTRACT

A strategy for synthesizing the tricyclic fragment **5** of atropurpuran **1** is reported. Rings A and C of atropurpuran were assembled stereoselectively via two intramolecular Michael additions. The advanced tricyclic skeleton **5** shows the correct functionality and stereochemistry for atropurpuran **1**, so the skeleton may serve as a key intermediate in its total synthesis.

1. Introduction

The genus *Aconitum*, an important source of traditional medicines, is widely used in China to treat various diseases, including rheumatic and neurological disorders as well as pain symptoms.[1] Most compounds isolated from *Aconitum* species are structurally classified as C_{18}-, C_{19}- and C_{20}-diterpenoid alkaloids.[2] In 2009, Wang et al. reported the isolation of a novel non-alkaloidal diterpene, atropurpuran **1**, from the roots of *A. hemsleyanum* var. *atropurpureum*.[3]

Atropurpuran **1** features an unprecedented cage-like skeleton containing an unusual tetracyclo[5.3.3.$0^{4,9}$.$0^{4,12}$]-tridecane unit (rings B–E) fused to a highly functionalized cyclohexene fragment (ring A) with two adjacent chiral quaternary centers (Fig. 1). Because of its intriguing structure, atropurpuran has been an attractive target for synthetic chemists around the world. The groups of Kobayashi[4] and Hsung[5] reported elegant approaches, respectively, to the pentacyclic core (fragment A) and to rings B–D (fragment B) of atropurpuran **1**. Work from our group led to the preparation of ring A (fragment C) via an organocatalytic asymmetric intramolecular Michael addition.[6] Despite these advances and continuing efforts, the total synthesis of atropurpuran **1** has not yet been reported. This reflects the difficulty in constructing its rigid pentacyclic structure and in installing its three quaternary stereocenters. Here we describe a substantial advance toward the total synthesis of atropurpuran **1** by constructing the tricyclic framework (fragment D) via intramolecular Michael addition. This fragment may serve as a key intermediate in a future synthetic approach.

2. Results and discussion

We devised a retrosynthetic analysis of atropurpuran **1** (Scheme 1) based on the biosynthetic pathway proposed by Wang and co-workers.[3,7] We envisioned that **1** could be accessed via functional group transformations from the advanced intermediate **2**. The critical ring D of atropurpuran could be forged through an

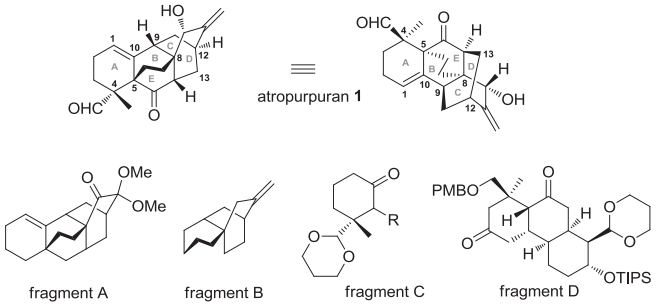
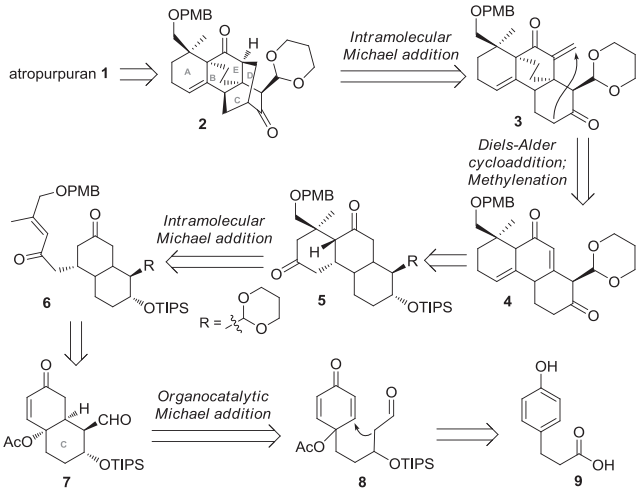


Fig. 1. Structure of atropurpuran **1** and synthesized intermediates.

* Corresponding authors. Tel./fax: +86 28 85503842; e-mail addresses: songhao@scu.edu.cn (H. Song), yongqin@scu.edu.cn (Y. Qin).

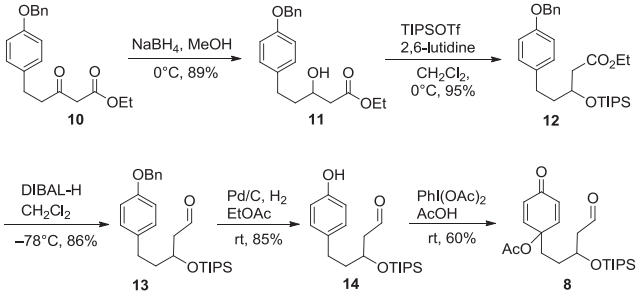
http://dx.doi.org/10.1016/j.tet.2015.11.050
0040-4020/

intramolecular Michael addition of enone **3**, while rings B and E could be constructed via a Diels–Alder cycloaddition and methylenation from compound **4**. Several functional group manipulations of **4** would simplify it to the tricycle **5**. Transformation of the bicyclic intermediate **6** into **5** could be achieved via an intramolecular Michael addition. Compound **6** could be generated from the decalin **7**, containing four contiguous stereogenic centers, which could be derived stereoselectively from aldehyde **8** via an intramolecular organocatalytic Michael addition.[8]



Scheme 1. Retrosynthetic analysis of atropurpuran **1**.

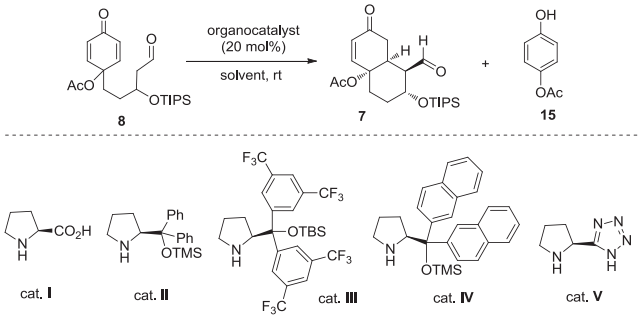
Our synthetic endeavors began with the preparation of cyclohexadienone **8** from the known compound **10** (Scheme 2), which was accessed in three steps from the commercially available acid **9**.[9] Reduction of the ketone carbonyl group in **10** using $NaBH_4$, followed by silyl protection of the resulting alcohol afforded ester **12** in high yield. This ester was then converted into aldehyde **13** in the presence of DIBAL-H. After removal of the benzyl group via hydrogenation, phenol **14** was mixed with $PhI(OAc)_2$/AcOH, generating dearomatization product **8** in 60% yield.[10]



Scheme 2. Synthesis of the Michael addition precursor **8**.

The organocatalytic Michael addition has proven to be a versatile approach for stereocontrolled synthesis of complex molecules with multiple stereocenters.[8] With precursor **8** in hand, we investigated its organocatalytic Michael addition using several proline-type catalysts (Table 1, entries 1–5). Only catalyst **II** afforded the desired addition product **7** as a major stereoisomer, while the other screened catalysts gave low conversion (<5%, cat. **III** and **IV**), required long reaction time (>5 days), or generated complex mixtures (cat. **I** and **V**). Screening various additives, such as phthalimide, picric acid, and *p*-toluenesulfonic acid, failed to improve yield (not shown in Table 1).[11] Screening various solvents showed that CH_2Cl_2 gave the best results (Table 1, entries 2, 6–10), affording the highest stereoselectivity (ee%>99%, dr>19:1) and moderate yield (40%) (entry 2). We speculated that the racemic starting aldehyde **8** might undergo a kinetic resolution during the reaction. Except for generation of the desired product **7**, the other enantiomer of **8** was surprisingly converted to phenol **15** as a main byproduct in most cases. Since its formation involves a reductive C–C bond cleavage, future studies are needed to explain how it forms under these reaction conditions.

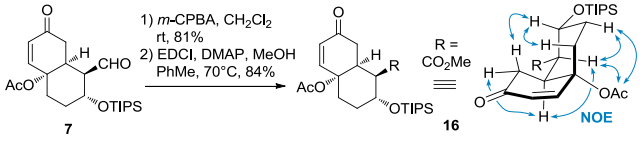
Table 1
The organocatalytic Michael addition reaction of **8**[a]



Entry	Solvent	Catalyst	Time (h)	Yield (%)[b]	ee (%)[c]	dr[c]
1	CH_2Cl_2	cat. **I**	10	20[d]	—[e]	—[e]
2	CH_2Cl_2	cat. **II**	12	40	**>99%**	**>19:1**
3	CH_2Cl_2	cat. **III**	>5 days	<5	—[e]	—[e]
4	CH_2Cl_2	cat. **IV**	>5 days	<5	—[e]	—[e]
5	CH_2Cl_2	cat. **V**	1	—[d]	—[e]	—[e]
6	MeOH	cat. **II**	10	20	94.5	>19:1
7	DME	cat. **II**	10	40	>99%	5:1
8	Et_2O	cat. **II**	72	26	96.6%	7.5:1
9	CH_3CN	cat. **II**	24	35	95.8%	4.7:1
10	DMF	cat. **II**	48	30	85.4%	1.3:1

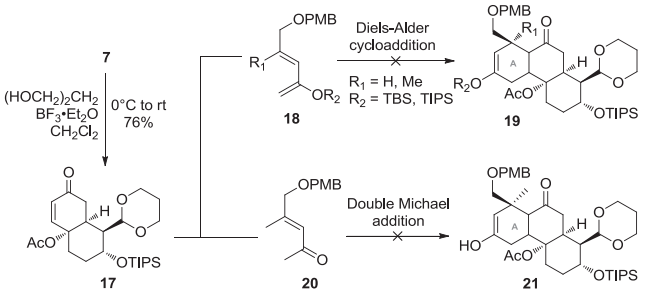
[a] Unless otherwise noted, reactions were performed with 1 equiv of **8** and 20 mol % of catalyst at 25 °C.
[b] Isolated yield.
[c] Determined by chiral HPLC analysis (Chiralpak AD-H).
[d] Complex mixtures.
[e] The ee and dr values were not determined.

The stereochemistry of aldehyde **7** was established by analyzing its methyl ester derivative **16** (Scheme 3). This derivative was obtained efficiently by oxidizing the aldehyde to carboxylic acid, followed by treatment with EDCI/DMAP/MeOH. Extensive NOE experiments (Scheme 3) clearly indicated a *cis*-fused decalin system, as well as *trans* relationships between aldehyde and OTIPS substituents on the newly formed ring.



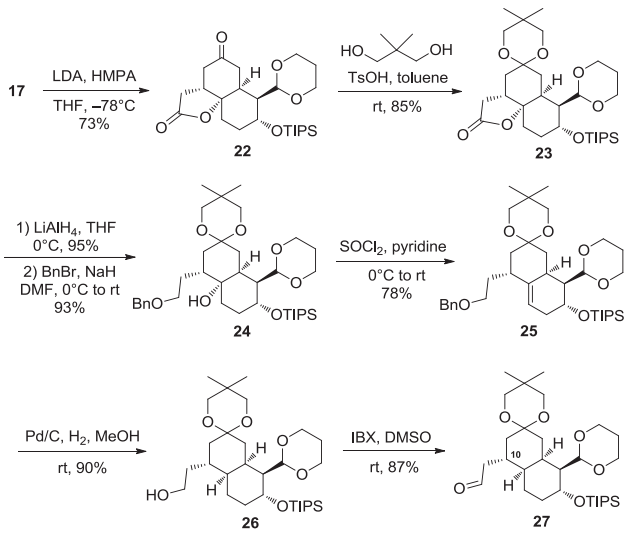
Scheme 3. Structural determination of **7**.

Having successfully assembled ring C of atropurpuran, we continued the synthesis as planned, but encountered several challenges while attempting to forge ring A (Scheme 4). The aldehyde functionality in compound **7** was selectively protected via treatment with 1,3-propanediol and $BF_3{\cdot}Et_2O$ in CH_2Cl_2. Efforts to get enone **17** to undergo Diels–Alder cycloaddition with diene **18** were unsuccessful.[12] Attempts to achieve double Michael addition between **17** and enone **20** also failed,[13] possibly due to steric hindrance of the methyl groups and the protected alcohol.



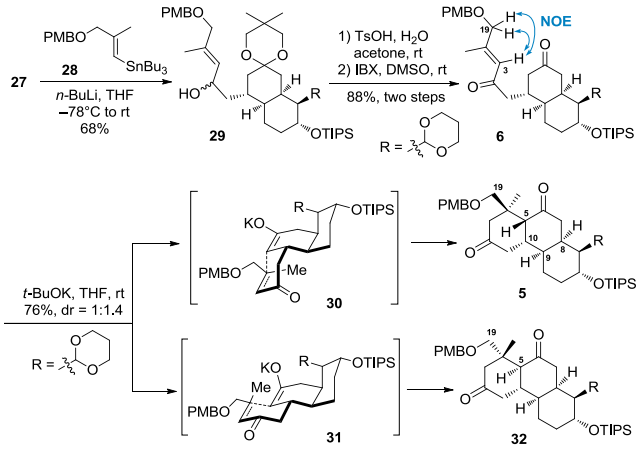
Scheme 4. Attempts to construct ring A.

We then focused on forming ring A via an intramolecular Michael addition, in which the first task was to introduce an aldehyde-terminated side chain at C10. The acetoxyl group in **17** was used as a handle to incorporate the C10 stereogenic center. Intramolecular Michael addition of **17** using LDA/HMPA at −78 °C provided **22** in 73% yield (Scheme 5). The *cis* stereochemical outcome was assigned on the basis of the obtained kinetic product under the reaction conditions, where attacking of the enolate to the enone was supposed to proceed from the less hindered convex face. Protecting the ketone carbonyl group of **22** using neopentyl glycol with TsOH afforded the desired **23**. The lactone ring of **23** was then opened by reduction with $LiAlH_4$, followed by selective mono-protection of the primary alcohol with a benzyl group, finally leading to the intermediate **24**. Treating this compound with $SOCl_2$ in pyridine at 0 °C and eliminating the tertiary alcohol in **24** smoothly furnished alkene **25**. Simultaneous benzyl deprotection and alkene reduction in the presence of H_2 over Pd/C in MeOH gave compound **26** as a single isomer; hydrogenation occurred exclusively from the less hindered convex face. Alcohol oxidation using IBX gave the anticipated aldehyde **27**.



Scheme 5. Establishment of the C10 chiral center.

The final steps of ring A synthesis are shown in Scheme 6. The organolithium species was generated in situ from tributylstannane **28** using *n*-BuLi, and then added to aldehyde **27** to afford **29** in 68% yield.[14] Subsequent deacetalization with TsOH in acetone and IBX oxidation of **29** gave the desired ketone **6** in 88% yield over two steps. The *E*-alkene was confirmed based on NOE correlations observed between H-3 and H_2-19. Ultimately, ring A of atropurpuran was generated in 76% yield via an intramolecular Michael addition of **6** in the presence of *t*-BuOK in THF, leading to a pair of inseparable diastereoisomers (**5** and **32**) in a 1:1.4 ratio. The reaction appears to proceed via two transition states **30** and **31**, which resulted in a *cis* relationship between H-5 and C19 in both products **5** and **32** based on the *E* geometric character in alkene **6**. We considered the stereochemistry at C5, C8, and C10 unimportant at this stage, since it could be eliminated later during assembling rings B and E via Diels–Alder reaction in the planned total synthesis.



Scheme 6. Successful assembly of ring A.

3. Conclusion

In summary, we have synthesized the tricyclic fragment **5** of atropurpuran (**1**) in 18 linear steps from the known keto ester **10**. Our strategy features the first application of an oxidative dearomatization/organocatalytic Michael addition approach to bicyclic compound **7**, thereby establishing three chiral centers in one pot. Ring A of atropurpuran **1** was assembled via another intramolecular Michael addition of diketone **6**. The functionalized tricyclic core **5** may serve as a later-stage intermediate in a future total synthesis of atropurpuran, and such efforts are underway in our laboratory.

4. Experimental section

4.1. General

All commercially available reagents were used without further purification. All solvents were dried and distilled before use; THF and Et_2O were distilled from sodium/benzophenone ketyl; dichloromethane was distilled from calcium hydride; $CHCl_3$ was distilled from P_2O_5. Chromatography was conducted by using 200–300 mesh silica gel. All new compounds gave satisfactory spectroscopic analyses (^1H NMR, ^{13}C NMR, HRMS). NMR spectra were recorded on 400 MHz NMR spectrometer. HRMS spectra were obtained by the FAB method. Chiral HPLC analysis was performed on HP Agilent 1260 apparatus.

4.2. Ethyl 5-(4-(benzyloxy)phenyl)-3-hydroxypentanoate (11)

To a dry round-bottom flask flushed with argon was added the known compound **10** (320 mg, 1.0 mmol) and MeOH (25 mL). The solution was cooled to 0 °C, and was added $NaBH_4$ (36.6 mg, 1.0 mmol) in small portions at 0 °C. The reaction mixture was further stirred for 1 h before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. The MeOH was concentrated in vacuo. Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column

eluting with EtOAc: petroleum ether (1: 5) to give **11** (287 mg, 89%) as pale solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.26 (t, J=7.2 Hz, 3H), 1.68 (m, 1H), 1.80 (m, 1H), 2.46 (d, J=15.6 Hz, 1H), 2.48 (d, J=9.6 Hz, 1H), 2.62 (m, 1H), 2.76 (m, 1H), 3.07 (s, 1H), 3.99 (m, 1H), 4.15 (q, J=7.2 Hz, 2H), 5.03 (s, 2H), 6.89 (d, J=8.8 Hz, 2H), 7.10 (d, J=8.8 Hz, 2H), 7.31–7.43 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.09, 30.76, 38.23, 41.23, 60.65, 67.07, 69.92, 114.69, 127.39, 127.81, 128.48, 129.30, 133.98, 137.08, 156.96, 172.97 ppm; HRMS (M+Na^+) calcd for $C_{20}H_{24}NaO_4$ 351.1572, found 351.1566.

4.3. Ethyl 5-(4-(benzyloxy)phenyl)-3-((triisopropylsilyl)oxy) pe-ntanoate (12)

Under argon, to a 50 mL flask was added **11** (330 mg, 1.0 mmol), dry CH_2Cl_2 (30 mL) and 2,6-lutidine (292 μL, 2.5 mmol). The solution was cooled to 0 °C, and then TIPSOTf (540 μL, 2.0 mmol) was added dropwise, the reaction mixture was further stirred for 1 h before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. Then the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 60) to give **12** (463 mg, 95%) as pale oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (m, 3H), 1.06 (s, 18H), 1.27 (t, J=7.2 Hz, 3H), 1.85 (m, 2H), 2.52 (d, J=2.8 Hz, 1H), 2.55 (d, J=3.6 Hz, 1H), 2.61 (m, 2H), 4.12 (q, J=7.2 Hz, 2H), 4.35 (m, 1H), 5.03 (s, 2H), 6.90 (d, J=8.4 Hz, 2H), 7.10 (d, J=8.4 Hz, 2H), 7.25–7.43 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.48, 17.70, 18.04, 29.97, 39.46, 42.22, 60.26, 69.08, 69.90, 114.69, 127.34, 127.77, 128.45, 129.12, 134.39, 137.13, 156.92, 171.54 ppm; HRMS (M+Na^+) calcd for $C_{29}H_{44}NaO_4Si$ 507.2907, found 507.2901.

4.4. 5-(4-(Benzyloxy)phenyl)-3-((triisopropylsilyl)oxy)penta-nal (13)

Under argon, to a 50 mL flask was added **12** (520 mg, 1.2 mmol) and dry CH_2Cl_2 (30 mL). The solution was cooled to −78 °C, and then DIBAL-H (1M in toluene) (1.76 mL, 1.8 mmol) was added dropwise, the reaction mixture was further stirred for 1 h before it was quenched by addition of MeOH (10 mL) at −78 °C. After stirring at −78 °C for 10 min, added saturated $C_4O_6H_4KNa$ (30 mL). Then the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 50) to give **13** (445 mg, 86%) as colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (m, 3H), 1.05 (s, 18H), 1.89 (m, 2H), 2.62 (m, 4H), 4.37 (m, 1H), 5.04 (s, 2H), 6.91 (d, J=8.8 Hz, 2H), 7.08 (d, J=8.8 Hz, 2H), 7.33–7.43 (m, 5H), 9.86 (t, J=2.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.46, 18.08, 30.30, 39.73, 50.38, 68.03, 69.96, 114.81, 127.39, 127.84, 128.51, 129.13, 133.88, 137.09, 157.03, 202.10 ppm; HRMS (M+Na^+) calcd for $C_{27}H_{40}NaO_3Si$ 463.2644, found 463.2600.

4.5. 5-(4-Hydroxyphenyl)-3-((triisopropylsilyl)oxy)pentanal (14)

13 (520 mg, 1.2 mmol), EtOAc (15 mL) and palladium on carbon (10% Pd/C, wet, 52 mg) was added under a balloon of hydrogen for 24 h. The mixture was then filtrated through Celite. The filtrate was concentrated in vacuo and purified by silica gel column chromatography eluting with EtOAc: petroleum ether (1: 5) to afford **14** (352 mg, 85%) as colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (m, 3H), 1.05 (s, 18H), 1.89 (m, 2H), 2.62 (m, 4H), 4.37 (m, 1H), 4.94 (s, 1H), 6.74 (d, J=8.4 Hz, 2H), 7.03 (d, J=8.4 Hz, 2H), 9.87 (t, J=2.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.44, 18.05, 30.30, 39.74, 50.32, 68.07, 115.28, 129.24, 133.39, 153.89, 203.12 ppm; HRMS (M+Na^+) calcd for $C_{20}H_{34}NaO_3Si$ 337.2175, found 337.2143.

4.6. 4-Oxo-1-(5-oxo-3-((triisopropylsilyl)oxy)pentyl)cyclo-hexa-2,5-dien-1-yl acetate (8)

(Diacetoxyiodo)benzene (377 mg, 1.2 mmol) was added to a solution of phenol **14** (410 mg, 1.2 mmol) in AcOH (15 mL) at 25 °C and the resulting solution stirred for 20 min. The reaction was added saturated $NaHCO_3$ until the pH=7. Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 3) to give **8** (287 mg, 60%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.04 (s, 21H), 1.59 (m, 2H), 1.89 (td, J=12.0, 7.6 Hz 2H), 2.06 (s, 3H), 2.61 (dd, J=6.0, 2.0 Hz, 2H), 4.36 (m, 1H), 6.27 (d, J=10.0 Hz, 2H), 6.79 (d, J=10.4 Hz, 2H), 9.81 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.33, 17.63, 18.00, 21.14, 30.99, 34.08, 50.37, 67.21, 76.37, 115.21, 129.04, 148.06, 169.35, 185.07, 201.14 ppm; HRMS (M+Na^+) calcd for $C_{22}H_{36}NaO_5Si$ 431.2230, found 431.21954.

4.7. (1*R*,2*R*,4a*R*,8a*S*)-1-Formyl-7-oxo-2-((triisopropylsilyl) oxy)-1,2,3,4,4a,7,8,8a-octahydronaphthalen-4a-yl acetate (7) and 4-hydroxyphenyl acetate (15)

Catalyst II (12.7 mg, 0.04 mmol) was added a solution of **8** (80 mg, 0.2 mmol) in CH_2Cl_2 (15 mL) at 0 °C. The resulting mixture was stirred at 0 °C for 12 h before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. Then the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 5) to give **7** (11.8 mg, 40%) and **15** (10.4 mg, 35%) as colourless oil.

7: $[\alpha]_D^{20}$=+ 93 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.06 (s, 21H), 1.75 (m, 2H), 2.00 (m, 2H), 2.13 (s, 3H), 2.37 (dd, J=17.6, 13.2 Hz, 1H), 2.69 (m, 2H), 3.42 (m, 1H), 4.40 (m, 1H), 5.92 (d, J=10.4 Hz, 1H), 7.11 (d, J=10.4 Hz, 1H), 9.92 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.31, 18.01, 21.72, 29.56, 30.05, 36.68, 38.23, 55.29, 66.18, 78.36, 127.39, 152.58, 169.79, 195.76, 203.21 ppm; HRMS (M+Na^+) calcd for $C_{22}H_{36}NaO_5Si$ 431.2230, found 431.2224. HPLC: DAICEL AD-H Chiralpak, 97:3 Hexane/isopropanol, flow 1.0 mL/min; retention time: major enantiomer 8.52 min, minor enantiomer 10.04 min.

15: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.28 (s, 3H), 5.09 (s, 1H), 6.77 (d, J=8.8 Hz, 2H), 6.92 (d, J=8.8 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.07, 115.96, 122.44, 144.09, 153.28, 170.18 ppm; HRMS (M+Na^+) calcd for $C_8H_8O_3$ 152.0473, found 152.0477.

4.8. (1*R*,2*R*,4a*R*,8a*S*)-Methyl 4a-acetoxy-7-oxo-2-((triiso-propyl-silyl)oxy)-1,2,3,4,4a,7,8,8a-octahydronaphthalene-1-carboxy-late (16)

To a 50 mL flask was added **7** (100 mg, 0.24 mmol) and CH_2Cl_2 (30 mL). The mixture was added $NaHCO_3$ (41.2 mg, 0.49 mmol) and *m*-CPBA (84.6 mg, 0.49 mmol). The solution was further stirred for 4 h at 25 °C before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. Then the aqueous layer was extracted with CH_2Cl_2 (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 2) to give **S1** (84.2 mg, 81%) as brown oil.[15] $[\alpha]_D^{20}$=+ 50 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.00 (s, 21H), 1.64 (m, 2H), 1.91 (m, 1H),

2.11 (s, 3H), 2.21 (d, *J*=11.2 Hz, 1H), 2.41 (dd, *J*=18.0, 14.0 Hz, 1H), 2.55 (dd, *J*=9.0, 5.2 Hz, 1H), 2.80 (dd, *J*=10.2, 4.4 Hz, 1H), 3.28 (dt, *J*=8.0, 5.6 Hz, 1H), 4.24 (m, 1H), 5.88 (d, *J*=10.0 Hz, 1H), 7.03 (d, *J*=10.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.50, 18.03, 21.71, 29.35, 29.49, 29.57, 37.19, 39.23, 50.07, 66.54, 78.55, 127.20, 152.59, 169.88, 176.40, 196.32 ppm; HRMS (M+Na$^+$) calcd for $C_{22}H_{35}NaO_6Si$ 423.2206, found 423.2208. To a 50 mL flask was added **S1** (150 mg, 0.35 mmol) and PhMe (30 mL). The mixture was added EDCI (203 mg, 1.06 mmol), DMAP (8.6 mg, 0.07 mmol) and MeOH (143 μL, 3.5 mmol) at 25 °C. The mixture was further stirred for 4 h at 70 °C before it was quenched by addition of saturated NH_4Cl (10 mL). Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 10) to give **16** (130 mg, 84%) as colourless solid. $[\alpha]_D^{20}$=+ 46 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.05 (s, 21H), 1.74 (m, 2H), 1.95 (m, 2H), 2.15 (s, 3H), 2.26 (m, 1H), 2.82–2.86 (dd, *J*=4.8, 0.4 Hz, 2H), 3.27 (m, 1H), 3.66 (s, 3H), 4.29 (m, 1H), 5.91 (d, *J*=10.4 Hz, 1H) 7.05 (d, *J*=10.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.55, 18.08, 21.80, 29.47, 29.64, 37.54, 39.37, 50.35, 51.64, 66.68, 78.69, 127.35, 152.61, 169.95, 172.17, 196.46 ppm; HRMS (M+Na$^+$) calcd for $C_{23}H_{38}NaO_6Si$ 438.2438, found 438.2441.

4.9. (1*R*,2*R*,4a*R*,8a*S*)-1-(1,3-Dioxan-2-yl)-7-oxo-2((triisopropylsilyl)oxy)-1,2,3,4,4a,7,8,8a-octahydronaphthalen-4a-yl acetate (17)

Under argon, to a 25 mL flask was added **7** (230 mg, 0.56 mmol), 1,3-propanediol (86 mg, 1.12 mmol) and dry CH_2Cl_2 (15 mL). The solution was cooled to 0 °C and then added $BF_3\cdot Et_2O$ (15 μL, 0.11 mmol), then warm to 25 °C for 8 h before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. Then the aqueous layer was extracted with CH_2Cl_2 (3×10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 8) to give **17** (200 mg, 76%) as colourless oil. $[\alpha]_D^{20}$=+ 148 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.07 (s, 21H), 1.28 (m, 2H), 1.68 (m, 2H), 1.88 (m, 1H), 2.05 (m, 1H), 2.10 (s, 3H), 2.24 (m, 1H), 2.36 (dd, *J*=18.4, 13.6 Hz, 1H), 3.19 (dd, *J*=18.4, 5.2 Hz, 1H), 3.35 (dt, *J*=13.6 Hz, 1H), 3.60 (td, *J*=11.2 Hz, 1H), 3.71 (td, *J*=11.6, 2.4 Hz, 1H), 4.08 (m, 3H), 4.95 (d, *J*=3.6 Hz, 1H), 5.91 (d, *J*=10.4 Hz, 1H), 7.11 (d, *J*=10.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.43, 17.95, 21.53, 25.73, 29.40, 30.32, 36.99, 38.53, 45.76, 66.33, 66.86, 79.51, 102.40, 126.86, 153.23, 169.69, 198.52 ppm; HRMS (M+Na$^+$) calcd for $C_{25}H_{42}NaO_5Si$ 489.2609, found 489.2642.

4.10. (3a*S*,6a*S*,7*R*,8*R*,10a*R*)-7-(1,3-Dioxan-2-yl)-8-((triisopropyl-silyl)oxy)octahydro-2*H*-naphtho[8a,1-*b*]furan-2,5(3*H*)-dione (22)

Under argon, to a 50 mL flask was added **17** (450 mg, 0.96 mmol) and dry THF (25 mL). The solution was cooled to −78 °C, and then LDA (1M in THF, 3.84 mL, 3.84 mmol) was added dropwise, the reaction mixture was further stirred for 30 min before it was quenched by addition of saturated NH_4Cl (20 mL). Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 3) to give **22** (328 mg, 73%) as yellow oil. $[\alpha]_D^{20}$=+ 117 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (m, 3H), 1.06 (s, 18H), 1.33 (m, 2H), 2.01 (m, 2H), 2.16 (dd, *J*=4.4 Hz, 1H), 2.23 (m, 1H), 2.23 (d, *J*=6.4 Hz, 1H), 2.42 (m, 1H), 2.47 (d, *J*=5.4 Hz, 1H), 2.56 (m, 1H), 2.78 (dt, *J*=14.4 Hz, 2H), 2.87 (d, *J*=8.8 Hz, 1H), 3.17 (dd, *J*=4.8 Hz, 2H), 3.62 (td, *J*=11.2 Hz, 1H), 3.74 (td, *J*=11.2 Hz, 1H), 4.04 (m, 2H), 4.09 (m, 1H), 4.99 (d, *J*=3.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.89, 18.18, 25.95, 31.48, 32.15, 35.00, 37.09, 38.83, 39.72, 41.95, 45.97, 66.54, 67.04, 84.95, 100.33, 174.55, 209.89 ppm; HRMS (M+Na+) calcd for $C_{25}H_{42}NaO_5Si$ 489.2651, found 489.2642.

4.11. (3a′*S*,6a′*S*,7′*R*,8′*R*,10a′*R*)-7′-(1,3-Dioxan-2-yl)-5,5-dimethyl-8′-((triisopropylsilyl)oxy)octahydrospiro[[1,3]dioxane-2,5′-naphtho[8a,1-*b*]furan]-2′(3′*H*)-one (23)

To a 50 mL flask was added **22** (320 mg, 0.68 mmol), 2,2-dimethyl-1,3-propanediol (107 mg, 1.0 mmol), trimethoxymethane (15 μL, 0.13 mmol), Ts-OH (23.6 mg, 0.13 mmol) and toluene (20 mL). The reaction mixture was further stirred at 25 °C for 1 h before it was quenched by addition of saturated $NaHCO_3$ (20 mL). Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 8) to give **23** (320 mg, 85%) as pale white oil. $[\alpha]_D^{20}$=− 18.33 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (s, 3H), 1.05 (s, 21H), 1.14 (s, 3H), 1.21 (m, 2H), 1.40 (d, *J*=13.2 Hz, 1H), 1.66 (dd, *J*=14.4, 6.4 Hz, 2H), 1.80 (m, 1H), 1.88 (m, 1H), 2.01 (m, 3H), 2.16 (m, 1H), 2.32 (m, 1H), 2.42 (m, 2H), 3.19 (dd, *J*=16.8, 12.4 Hz, 1H), 3.38 (m, 2H), 3.59–3.80 (m, 4H), 4.01 (td, *J*=10.8, 4.4 Hz, 1H), 4.10 (td, *J*=12.4, 5.6 Hz, 2H), 4.98 (d, *J*=4.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.89, 18.02, 22.35, 23.16, 26.54, 27.04, 29.72, 29.98, 32.41, 33.86, 34.07, 34.46, 40.57, 45.42, 66.50, 66.86, 66.94, 69.37, 70.28, 85.45, 98.00, 101.04, 176.28 ppm; HRMS (M+Na$^+$) calcd for $C_{30}H_{52}NaO_5Si$ 575.3327, found 575.3374.

4.12. (4′*R*,4a′*R*,7′*R*,8′*R*,8a′*S*)-4′-(2-(Benzyloxy)ethyl)-8′-(1,3-dioxan-2-yl)-5,5-dimethyl-7′-((triisopropylsilyl)oxy)octahydro-1′H-spiro[[1,3]dioxane-2,2′-naphthalen]-4a′-ol (24)

Under argon, to a 50 mL flask was added **23** (350 mg, 0.63 mmol) and dry THF (20 mL). The solution was cooled to 0 °C, and was added LAH (29 mg, 0.76 mmol) in small portions at 0 °C. The reaction mixture was further stirred for 1 h before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. The mixture was then filtrated through Celite. The filtrate was concentrated in vacuo and purified by silica gel column chromatography eluting with EtOAc: petroleum ether (1: 2) to afford **S2** (335 mg, 95%) as pale white oil.[15] $[\alpha]_D^{20}$=+ 44.28 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (s, 3H), 1.06 (s, 21H), 1.08 (s, 3H), 1.24 (m, 2H), 1.35 (d, *J*=13.2 Hz, 2H), 1.69 (m, 1H), 1.73–1.83 (m, 4H), 1.93–2.10 (m, 4H), 2.19 (m, 2H), 2.45 (s, 1H), 3.21 (dt, *J*=14.8 Hz, 1H), 3.35 (t, *J*=8.8 Hz, 2H), 3.63–3.70 (m, 5H), 3.77 (td, *J*=10.8, 4.0 Hz, 1H), 4.07 (dd, *J*=9.6, 5.2 Hz, 2H), 4.15 (dd, *J*=6.8, 5.6 Hz, 1H), 4.98 (d, *J*=3.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.87, 18.09, 22.45, 22.99, 26.52, 29.20, 29.55, 29.72, 31.44, 31.54, 31.64, 34.55, 35.89, 42.78, 45.10, 62.25, 66.45, 66.98, 67.19, 69.29, 70.14, 71.88, 98.34, 101.58 ppm; HRMS (M+Na$^+$) calcd for $C_{30}H_{56}NaO_5Si$ 579.3642, found 579.3687. Under argon, to a 50 mL flask was added **S2** (340 mg, 0.61 mmol) and dry DMF (25 mL). The solution was cooled to 0 °C, and was added NaH (17.6 mg, 0.73 mmol) in small portions at 0 °C. The reaction mixture was further added BnBr (145 μL, 1.2 mmol) after stirring for 10 min. The reaction mixture was further stirred for 1 h at 25 °C before it was quenched by addition of saturated NH_4Cl (10 mL) at 0 °C. Then the aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 10) to give **24** (367 mg, 93%) as pale white oil. $[\alpha]_D^{20}$=+ 41 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (s, 3H), 1.05 (s, 3H), 1.06 (s, 21H), 1.24 (m, 2H), 1.33 (d, *J*=13.2 Hz, 2H), 1.61 (m, 2H), 1.64 (d, *J*=5.6 Hz, 1H), 1.75–1.82 (m, 3H), 1.85–2.11 (m, 4H), 2.27 (m, 2H), 2.52 (s, 1H), 3.16 (d, *J*=14.4 Hz,

1H), 3.33 (t, *J*=9.6 Hz, 2H), 3.43 (td, *J*=9.2, 4.0 Hz, 1H), 3.57 (q, *J*=5.2 Hz, 1H), 3.64 (t, *J*=12.4 Hz, 2H), 4.05 (m, 2H), 4.15 (d, *J*=9.6 Hz, 1H), 4.47 (s, 2H), 4.99 (d, *J*=3.6 Hz, 1H), 7.26–7.40 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.97, 18.19, 22.58, 23.14, 26.63, 29.34, 29.80, 31.70, 32.05, 34.91, 36.52, 42.69, 45.18, 66.53, 67.04, 67.37, 69.30, 70.26, 70.52, 71.60, 72.79, 98.40, 101.71, 127.45, 127.62, 128.27, 138.25 ppm; HRMS (M+Na^+) calcd for $C_{37}H_{62}NaO_5Si$ 669.4110, found 669.4157.

4.13. (((4′*R*,7′*R*,8′*R*,8a′*S*)-4′-(2-(Benzyloxy)ethyl)-8′-(1,3-dioxan-2-yl)-5,5-dimethyl-3′,4′,6′,7′,8′,8a′-hexahydro-1′*H* spiro[[1,3] dioxane-2,2′-naphthalen]-7′-yl)oxy)triisopropylsilane (25)

Under argon, to a 50 mL flask was added **24** (360 mg, 0.55 mmol) and dry pyridine (20 mL). The solution was cooled to 0 °C, and was added SO_2Cl (80.7 μL, 1.11 mmol) at 0 °C. Then the reaction mixture was further stirred for 2 h at 25 °C before it was quenched by addition of saturated $NaHCO_3$ (10 mL) at 0 °C. Then the aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 15) to give **25** (273 mg, 78%) as yellow oil. $[\alpha]_D^{20}$=+ 113 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (s, 3H), 1.03 (s, 3H), 1.06 (s, 21H), 1.14 (m, 1H), 1.33 (d, *J*=13.2 Hz, 1H), 1.63 (dd, *J*=13.6, 6.4 Hz, 1H), 1.71 (m, 1H), 1.98 (m, 4H), 2.33 (dt, *J*=16.4, 4.4 Hz, 1H), 2.51 (m, 1H), 2.73 (d, *J*=13.6 Hz, 1H), 3.04 (d, *J*=12.4 Hz, 1H), 3.34 (m, 4H), 3.62 (m, 3H), 3.76 (t, *J*=10.8 Hz, 1H), 4.12 (m, 4H), 4.55 (q, *J*=12.0 Hz, 2H), 4.87 (d, *J*=4.4 Hz, 1H), 5.17 (s, 1H), 7.24–7.33 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.73, 18.14, 22.68, 23.03, 26.31, 29.14, 29.88, 33.06, 35.12, 35.38, 38.67, 39.26, 47.46, 65.78, 66.43, 67.06, 68.81, 69.60, 70.20, 72.80, 98.89, 101.73, 117.39, 127.33, 127.71, 128.21, 138.72, 140.93 ppm; HRMS (M+Na^+) calcd for $C_{37}H_{60}NaO_5Si$ 651.4057, found 651.4061.

4.14. 2-((4′*R*,4a′*S*,7′*R*,8′*R*,8a′*R*)-8′-(1,3-Dioxan-2-yl)-5,5-dimethyl -7′-((triisopropylsilyl)oxy)octahydro-1′*H*-spiro[[1,3] dioxane-2,2′-naphthalen]-4′-yl)ethanol (26)

25 (290 mg, 0.46 mmol), MeOH (20 mL), and palladium on carbon (10 wt% Pd/C, wet, 29 mg) was added under a balloon of hydrogen for 24 h. The mixture was then filtrated through Celite. The filtrate was concentrated in vacuo and purified by silica gel column chromatography eluting with EtOAc: petroleum ether (1: 5) to afford **26** (225 mg, 90%) as colourless oil. $[\alpha]_D^{20}$=+ 55 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (s, 3H), 1.05 (s, 21H), 1.09 (s, 3H), 1.18 (d, *J*=13.2 Hz, 1H), 1.26 (t, *J*=7.2 Hz, 1H), 1.29 (d, *J*=13.2 Hz, 1H), 1.52 (dd, *J*=14.0, 5.2 Hz, 1H), 1.55 (m, 3H), 1.68 (m, 2H), 1.77 (m, 3H), 2.03 (m, 1H), 2.10 (m, 1H), 2.20 (d, *J*=14.0, 5.2 Hz, 1H), 2.34 (d, *J*=13.6 Hz, 1H), 2.93 (s, 1H), 3.35 (d, *J*=11.6 Hz, 2H), 3.53 (d, *J*=11.6 Hz, 1H), 3.63–3.81 (m, 5H), 4.06 (m, 2H), 4.36 (s, 1H), 4.55 (d, *J*=5.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.23, 18.10, 22.10, 22.50, 22.92, 25.79, 27.65, 29.63, 29.92, 30.00, 32.94, 36.54, 38.24, 39.33, 49.58, 62.32, 66.38, 66.84, 67.05, 69.38, 69.78, 99.23, 101.74 ppm; HRMS (M+Na^+) calcd for $C_{30}H_{56}NaO_5Si$ 563.3731, found 563.3738.

4.15. 2-((4′*R*,4a′*S*,7′*R*,8′*R*,8a′*R*)-8′-(1,3-Dioxan-2-yl)-5,5-dimethyl-7′-((triisopropylsilyl)oxy)octahydro-1′*H*-spiro[[1,3] dioxane-2,2′-naphthalen]-4′-yl)acetaldehyde (27)

To a 50 mL flask was added **26** (330 mg, 0.61 mmol) and DMSO (25 mL). The mixture was added IBX (684 mg, 2.44 mmol). Then the reaction mixture was further stirred for 8 h at 25 °C before it was quenched by addition of saturated Na_2SO_3. Then the aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 12) to give **27** (286 mg, 87%) as pale white oil. $[\alpha]_D^{20}$=+ 15.5 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (s, 3H), 0.96 (s, 3H), 1.05 (s, 21H), 1.30 (m, 3H), 1.61 (m, 5H), 1.82 (m, 1H), 2.04 (m, 2H), 2.17 (m, 2H), 2.43 (m, 1H), 2.54 (dd, 1H, *J*=17.6, 5.6 Hz), 2.68 (dd, *J*=17.6, 8.0 Hz, 1H), 3.33 (d, *J*=11.6 Hz, 1H), 3.41 (q, *J*=5.2 Hz, 2H), 3.58 (d, *J*=11.2 Hz, 1H), 3.68 (m, 2H), 4.06 (t, *J*=6.4 Hz, 2H), 4.37 (s, 1H), 4.53 (d, *J*=5.6 Hz, 1H), 9.83 (s, 1H) ppm; HRMS (M+Na^+) calcd for $C_{30}H_{54}NaO_5Si$ 561.3587, found 561.3538.

4.16. (*E*)-1-((4′*R*,4a′*S*,7′*R*,8′*R*,8a′*R*)-8′-(1,3-Dioxan-2-yl)-5,5-dimethyl-7′-((triisopropylsilyl)oxy)octahydro-1′*H*-spiro[[1,3] dioxane-2,2′-naphthalen]-4′-yl)-5-((4-methoxybenzyl)oxy)-4-methylpent-3-en-2-ol (29)

Under argon, to a 50 mL flask was added **27** (723.3 mg, 1.5 mmol) and dry THF (20 mL). The solution was cooled to −78 °C, and was added *n*-BuLi (2.5 M in hexane, 0.6 mL, 1.5 mmol) at −78 °C. The solution was stirred for 10 min at −78 °C, then **27** (161 mg, 0.3 mmol) in dry THF (10 mL) was added. The reaction mixture was further stirred for 2 h at −78 °C before it was quenched by addition of saturated NH_4Cl (10 mL). Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 3) to give **29** (a mixture 1: 1) (148.5 mg, 68%) as colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76 (m, 3H), 0.87 (m, 6H), 1.03 (m, 3H), 1.04 (m, 21H), 1.20–1.32 (m, 4H), 1.67 (s, 3H), 1.96–2.14 (m, 4H), 2.27 (d, *J*=14.0 Hz, 1H), 2.35 (d, *J*=13.6 Hz, 1H), 3.22–3.41 (m, 3H), 3.44–3.54 (m, 1H), 3.63–3.74 (m, 4H), 3.81 (s, 3H), 3.89 (s, 2H), 4.07 (m, 2H), 4.37 (m, 2H), 4.55 (d, *J*=4.8 Hz, 1H), 4.62 (s, 1H), 5.50 (m, 1H), 7.24 (m, 2H), 7.33 (m, 2H) ppm; HRMS (M+Na^+) calcd for $C_{42}H_{70}NaO_9Si$ 753.4738, found 753.4752.

4.17. (4*S*,4a*S*,7*R*,8*R*,8a*R*)-8-(1,3-Dioxan-2-yl)-4-((*E*)-5-((4-meth-oxybenzyl)oxy)-4-methyl-2-oxopent-3-en-1-yl)-7 ((trii-sopropyl-silyl)oxy)octahydronaphthalen-2(1*H*)-one (6)

To a 50 mL flask was added **29** (263 mg, 0.3 mmol), acetone/H_2O=20/1 (21 mL). The mixture was added Ts-OH (62 mg, 0.36 mmol). Then the reaction mixture was further stirred for 1 h at 25 °C before it was added H_2O (10 mL). The acetone was concentrated in vacuo. Then the aqueous layer was extracted with EtOAc (3×10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was dissolved in DMSO (25 mL). The mixture was added IBX (300 mg, 1.07 mmol). Then the reaction mixture was further stirred for 3 h at 25 °C before it was quenched by addition of saturated Na_2SO_3. Then the aqueous layer was extracted with EtOAc (3×25 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 5) to give **6** (202 mg, 88% for two steps) as pale white oil. $[\alpha]_D^{20}$=+ 26.85 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (m, 2H), 1.03 (s, 21H), 1.30 (d, *J*=12.8 Hz, 2H), 1.59 (m, 2H), 1.83 (m, 1H), 2.04 (s, 3H), 2.08–2.34 (m, 5H), 2.51 (d, *J*=16.0 Hz, 1H), 2.59 (td, *J*=18.4, 5.6 Hz, 2H), 2.75 (m, 1H), 3.64 (m, 2H), 3.81 (s, 3H), 3.93 (s, 2H), 4.09 (td, *J*=13.0, 4.4 Hz, 2H), 4.33 (s, 1H), 4.46 (s, 2H), 4.60 (d, *J*=5.6 Hz, 1H), 6.29 (s, 1H), 6.88 (d, *J*=8.4 Hz, 2H), 7.26 (d, *J*=6.8 Hz, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.15, 16.41, 18.10, 22.76, 25.68, 27.79, 29.28, 32.89, 36.20, 38.44, 42.21, 45.78, 47.34, 48.96, 55.20, 66.10, 66.78, 67.08, 72.22, 73.73, 101.68, 113.79, 122.22, 125.24, 128.18, 129.26, 129.77, 153.28, 199.73, 212.87 ppm; HRMS (M+Na^+) calcd for $C_{37}H_{58}NaO_7Si$ 665.3798, found 665.3844.

4.18. (1*R*,4a*S*,4b*R*,7*R*,8*R*,8a*R*,10a*R*)-8-(1,3-Dioxan-2-yl)-1-(((4-methoxybenzyl)oxy)methyl)-1-methyl-7-((triisopropylsilyl) oxy) decahydrophenanthrene-3,10(2*H*,4b*H*)-dione (5) and (1*S*,4a*S*, 4b*R*,7*R*,8*R*,8a*R*,10a*S*)-8-(1,3-dioxan-2-yl)-1-(((4-methoxybenz-yl)oxy)methyl)-1-methyl-7 ((triisopropylsilyl) oxy)decahydro-phenanthrene-3,10(2*H*,4b*H*)-dione (32)

Under argon, to a 10 mL flask was added **6** (20 mg, 0.03 mmol) and dry THF (3 mL). The mixture was added *t*-BuOK (1 M in THF). The solution was further stirred for 2 h at 25 °C before it was quenched by addition of saturated NH_4Cl (10 mL). Then the aqueous layer was extracted with EtOAc (3×20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. The crude product was subjected to a silica gel column eluting with EtOAc: petroleum ether (1: 4) to give **5** and **32** as an inseparable mixture (15 mg, 1:1.4, 76%) as colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$, all signals for both diastereomers are listed) δ 0.88 (m, 1H), 1.04 (s, 21H), 1.25 (s, 3H), 1.30 (m, 3H), 1.67 (m, 1H), 1.84 (s, 1H), 2.04 (m, 1H), 2.17–2.37 (m, 5H), 2.56 (m, 3H), 2.76 (m, 1H), 3.42/3.48 (d, *J*=12.0 Hz, 1H), 3.56 (s, 1H), 3.58 (d, *J*=11.6 Hz, 1H), 3.64 (m, 2H), 3.81 (s, 3H), 4.06 (td, *J*=13.6, 3.6 Hz, 2H), 4.34 (s, 1H), 4.48 (s, 2H), 4.58 (d, *J*=5.2 Hz, 1H), 6.87 (d, *J*=8.4 Hz, 2H), 7.24 (d, *J*=8.8 Hz, 2H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, all signals for both diastereomers are listed) δ 12.14, 13.78, 13.96, 18.13, 22.62, 22.68, 22.78, 25.69, 29.20, 29.69, 32.97, 35.70, 35.96, 38.24, 38.28, 38.81, 38.87, 45.79, 47.21, 47.25, 48.89, 55.25, 61.31, 61.58, 62.37, 66.04, 66.83, 67.12, 71.79, 72.12, 76.78, 101.64, 113.78, 129.41, 129.44, 129.65, 159.27, 204.72, 205.10, 212.46 ppm; HRMS ($M+Na^+$) calcd for $C_{37}H_{58}KO_7Si$ 681.3589, found 681.3593.

Acknowledgements

This work was supported by grants from the National Natural Science Foundation of China (21321061, 21132006 and 21572140).

Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2015.11.050.

References and notes

1. Benn, M. H.; Jacyno, J. M. In *Alkaloids: Chemical and Biological Perspective*; Pelletier, S. W., Ed.; John Wiley and Sons: New York, NY, 1983; Vol. 1, pp 153–210.
2. For reviews, see: (a) Wang, F. P.; Liang, X. T. In *The Alkaloids: Chemistry and Biology*; Cordell, G. A., Ed.; Elsevier: New York, NY, 2002; Vol. 59, pp 1–280; (b) Wang, F. P.; Chen, Q. H.; Liang, X. T. In *The Alkaloids: Chemistry and Biology*; Cordell, G. A., Ed.; Elsevier: New York, NY, 2009; Vol. 67, pp 1–78; (c) Wang, F. P.; Chen, Q. H. In *The Alkaloids: Chemistry and Biology*; Cordell, G. A., Ed.; Elsevier: New York, NY, 2010; Vol. 69, pp 1–577.
3. Tang, P.; Chen, Q. H.; Wang, F. P. *Tetrahedron Lett.* **2009**, *50*, 460.
4. Suzuki, T.; Sasaki, A.; Egashira, N.; Kobayashi, S. *Angew. Chem., Int. Ed.* **2011**, *50*, 9177.
5. Hayashi, R.; Ma, Z. X.; Hsung, R. P. *Org. Lett.* **2012**, *14*, 252.
6. Chen, H.; Zhang, D.; Xue, F.; Qin, Y. *Tetrahedron* **2013**, *69*, 3141.
7. For a new biosynthetic proposal, see: Weber, M.; Owens, K.; Sarpong, R. *Tetrahedron Lett.* **2015**, *56*, 3600.
8. For a related review, see: (a) Maertens, G.; Ménard, M.-A.; Canesi, S. *Synthesis* **2014**, *46*, 1573 For selected examples, see: (b) Hayashi, Y.; Gotoh, H.; Tamura, T.; Yamagushi, H.; Masui, R.; Shoji, M. *J. Am. Chem. Soc.* **2005**, *127*, 16028; (c) Vo, N. T.; Pace, R. D. M.; O'Hara, F.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 404; (d) Calter, M. A.; Wang, J. *Org. Lett.* **2009**, *11*, 2205; (e) Bournaud, C.; Marchal, E.; Quintard, A.; Sulzer-Mossé, S.; Alexakis, A. *Tetrahedron: Asymmetry* **2010**, *21*, 1666; (f) Gu, Q.; You, S.-L. *Org. Lett.* **2011**, *13*, 5192; (g) Corbett, M. T.; Xu, Q.; Johnson, J. S. *Org. Lett.* **2014**, *16*, 2362; (h) Tissot, M.; Phipps, R. J.; Lucas, C.; Leon, R. M.; Pace, R. D. M.; Ngouansavanh, T.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 13498; (i) Yamagata, A. D. G.; Datta, S.; Jackson, K. E.; Stegbauer, L.; Paton, R. S.; Dixon, D. J. *Angew. Chem., Int. Ed.* **2015**, *54*, 4899; (j) Zou, L.-H.; Philipps, A. R.; Raabe, G.; Enders, D. *Chem.—Eur. J.* **2015**, *21*, 1004.
9. Peuchmaur, M.; Saïdani, N.; Botté, C.; Maréchal, E.; Vial, H.; Wong, Y.-S. *J. Med. Chem.* **2008**, *51*, 4870.
10. For selected reviews on dearomatization reactions, see: (a) Zhuo, C.-X.; Zhang, W.; You, S.-L. *Angew. Chem., Int. Ed.* **2012**, *51*, 12662; (b) Ding, Q.; Ye, Y.; Fan, R. *Synthesis* **2013**, *45*, 1 For recent examples, see: (c) Wu, Q.-F.; Liu, W.-B.; Zhuo, C.-X.; Rong, Z.-Q.; Ye, K.-Y.; You, S.-L. *Angew. Chem., Int. Ed.* **2011**, *50*, 4455; (d) Yin, Q.; Wang, S.-G.; Liang, X.-W.; Gao, D.-W.; Zheng, J.; You, S.-L. *Chem. Sci.* **2015**, *6*, 4179; (e) Huang, S.; Kötzner, L.; De, C. K.; List, B. *J. Am. Chem. Soc.* **2015**, *137*, 3446.
11. For details, see Supporting Information.
12. For selected reviews, see: (a) Corey, E. J. *Angew. Chem., Int. Ed.* **2002**, *41*, 1650; (b) Nicolaou, K. C.; Snyder, S. A.; Montagnon, T.; Vassilikogiannakis, G. *Angew. Chem., Int. Ed.* **2002**, *41*, 1668; (c) Juhl, M.; Tanner, D. *Chem. Soc. Rev.* **2009**, *38*, 2983; (d) Funel, J. A.; Abele, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 3822; (e) Wan, C. Y.; Deng, J.; Liu, H.; Bian, M.; Li, A. *Sci. China Chem.* **2014**, *57*, 926; (f) Mackay, E. G.; Sherburn, M. S. *Synthesis* **2015**, *47*, 1.
13. For related examples, see: (a) Jung, M. E.; Ho, D. G. *Org. Lett.* **2007**, *9*, 375; (b) Kanoh, N.; Sakanishi, K.; Iimori, E.; Nishimura, K.; Iwabuchi, Y. *Org. Lett.* **2011**, *13*, 2864; (c) Amat, M.; Arioli, F.; Pérez, M.; Molins, E.; Bosch, J. *Org. Lett.* **2013**, *15*, 2470; (d) Jin, J.; Qiu, F. G. *Adv. Synth. Catal.* **2014**, *356*, 340.
14. (a) Angoh, A. G.; Clive, D. L. J. *J. Chem. Soc., Chem. Commun.* **1984**, *8*, 534; (b) Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1986**, *108*, 5655; (c) Yajima, A.; Qin, Y.; Zhou, X.; Kawanishi, N.; Xiao, X.; Wang, J.; Zhang, D.; Wu, Y.; Nukada, T.; Yabuta, G.; Qi, J.-H.; Asano, T.; Sakagami, Y. *Nat. Chem. Biol.* **2008**, *4*, 235.
15. The structures of **S1** and **S2**, see Supporting Information.