Tetrahedron xxx (xxxx) xxx

Contents lists available at ScienceDirect

Tetrahedron

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

Synthetic studies towards the mannolides: Construction of the bowl-shaped B/C/D ring system

Kunkai Wang, Zhezhe Xu, Xiangchuang Tan, Zhixiang Xie*

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, 222 Tianshui South Road, Lanzhou, 730000, China

ARTICLE INFO

Article history:
Received 26 August 2020
Received in revised form
23 September 2020
Accepted 27 September 2020
Available online xxx

Keywords:
Cephalotane-type diterpenoids
Mannolides
Oxidative dearomatization
Intramolecular Diels-Alder reaction
Aldol reaction

ABSTRACT

The bowl-shaped tricyclo[6.3.1.$0^{4,12}$]dodecane moiety is the core feature of cephalotane-type diterpenoids. As part of our efforts directed towards a total synthesis of mannolide B, the bowl-shaped tricyclo [6.3.1.$0^{4,12}$]dodecane skeleton, a common intermediate of cephalotane-type diterpenoids bearing up to five contiguous stereocenters including two quaternary carbon centers had been constructed. The synthetic strategy was enabled by an efficient application of oxidative dearomatization/intramolecular Diels-Alder reaction to access highly functionalized building block with the tricyclo[5.2.2.$0^{2,6}$]undecane unit from commercially available materials. The key feature was firstly used the cyclic olefins with secondary alcohol as dienophile for the intramolecular inverse electron demand Diels-Alder reaction. Further synthetic studies led to construct ring D by a regioselective Aldol reaction.

1. Introduction

Cephalotaxus, as the sole member of the cephalotaxaceae family, consists of nine species found around the world, of which seven species are widely distributed in China and have been used against leukemia in Chinese traditional medicine [1]. Chemical investigation have resulted in the isolation of the interesting secondary metabolites such as alkaloids and terpenoids with a variety of biological properties, particularly antitumor activity [2]. For instance, the alkaloid homoharringtonine, from *C. fortune*, was approved by the Food and Drug Administration for the treatment of chronic myeloid leukemia in 2012. Be encouraged by this result, studies on terpenoids, particularly cephalotane-type diterpenoids, have drawn a great amount of attention from the phytochemist. Before 2012, only five cephalotane-type diterpenoids had been identified [3]. The first member of the cephalotane-type diterpenoids, harringtonolide (Fig. 1) was isolated and structurally characterized from the seeds of *C. harringtonia* in 1978 by Buta and co-workers [3a]. After 2012, Yue and co-workers have intensified isolation efforts that led to the documentation of 31 additional diterpenes and norditerpenoids [4]. (Fig. 1, selected examples).

Due to the intriguing polycyclic structural features and exciting biological activities, the cephalotane-type diterpenoids as a compelling target, have attracted more and more attention from the synthetic organic community. As the first example of cephalotane-type diterpenoids, a great deal of synthetic strategies has been developed for model studies on harringtonolide [5]. The first total synthesis of hainanolidol was disclosed by Mander and coworkers in 1998 [6]. The critical strategy featured an intramolecular arene cyclopropanation followed by a ring expansion to construct the tropone moiety. In 2013, an intramolecular oxidopyrylium-based [5 + 2]-cycloaddition was developed by Tang and coworkers as a highlight to finish the total synthesis of hainanolidol [7]. The first asymmetric total synthesis of (+)-harringtonolide was achieved by Zhai and coworkers by an intramolecular Diels-Alder reaction and a rhodium-complex-catalyzed intramolecular [3 + 2]-cycloaddition as the key transformation [8]. Recently, Zhao and coworkers described the total synthesis of cephanolides B and C enabled by palladium-catalyzed cascade cyclization and late-stage sp^3 C–H bond oxidation [9].

Mannolides A-C, three new C_{20} cephalotane-type diterpenoids, were isolation by Yue and co-workers from *Cephalotaxus mannii* Hook f. in 2016.[4a] (Fig. 1) Particularly noteworthy, this new C_{20} skeleton could serve as the key biosynthetic intermediate for the coexistent antitumor troponoids (C_{19} cephalotane-type diterpenoids, such as harringtonolide). We became interested in

* Corresponding author.
E-mail address: xiezx@lzu.edu.cn (Z. Xie).

https://doi.org/10.1016/j.tet.2020.131629
0040-4020/

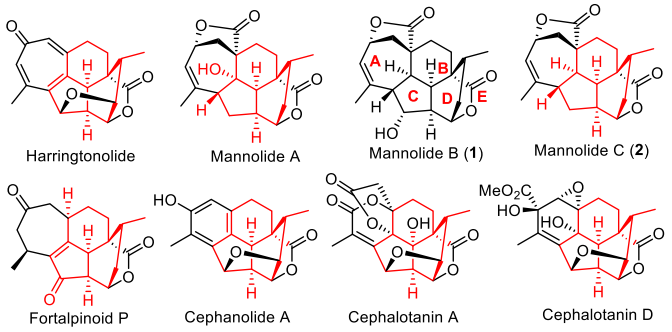


Fig. 1. The structure of select cephalotane-type diterpenoids.

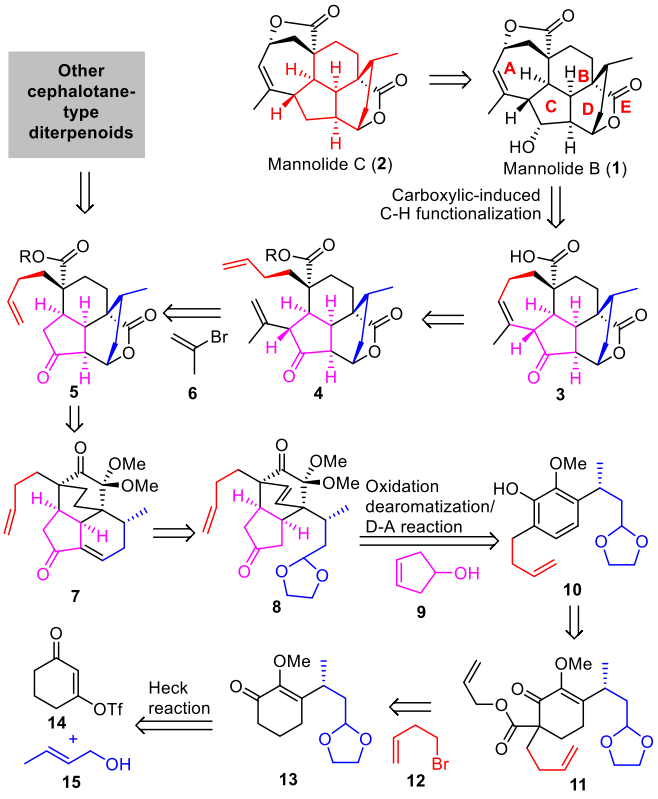
mannolides A-C as a novel C_{20} cephalotane-type diterpenoids possessing polycyclic carbon skeleton, and a more reasonable biosynthetic intermediate for other cephalotane-type diterpenoids from the biogenetic point of view. Here in, we report our progress on the synthetic studies of construction of the bowl-shaped B/C/D ring system of the mannolides A-C.

2. Results and discussion

From the viewpoint of molecular structure, a unique and bowl-shaped tricyclo[6.3.1.$0^{4,12}$]dodecane moiety embodies the common carbon skeleton of cephalotane-type diterpenoids (shown in Fig. 1. red). This cis-fused tricarbocycle is designated as rings B, C, and D, with five to seven contiguous stereocenters including at least one all-carbon quaternary center. Moreover, ring D embeds a bridging δ-lactone unit ring E. The main structural differences of this class of diterpenoids are both in left moiety combined with B/C rings and the oxidation degree of the molecular architecture. Thus if we can construct the bowl-shaped tricyclo[6.3.1.$0^{4,12}$]- dodecane moiety, the cluster syntheses of cephalotane-type diterpenoids will be achieved.

Our retrosynthetic analysis toward mannolides B-C (**1**–**2**) was depicted in Scheme 1. We assumed that mannolide C (**2**) could be accessed from mannolide B (**1**) through Barton-McCombie deoxygenation reducing secondary hydroxyl group. The mannolide B could be derived from the acid **3** by utilizing C-H functionalization of carboxylic-induced esterification [10], followed by stereoselective reduction ketone to secondary hydroxyl group. The acid **3** could be achieved via a sequence ring-closing metathesis [11] and hydrolysis of ester of compound **4**, which was prepared by alkylation with **6** from compound **5**. The advanced intermediate **5**, containing the common carbon skeleton of cephalotane-type diterpenoids and ring E, could be as a common intermediate for preparing other cephalotane-type diterpenoids. The key intermediate **5** was envisioned to be synthesized from α, β-unsaturated ketone **7** via sequence oxidative cleavage of diketone, intramolecular oxa-Michael addition to install the ring E and esterification. The ketone **7** should be prepared by sequence selective reduction of disubstituent double bond, hydrolysis of acetal, followed by Aldol reaction to install the α, β-unsaturated ketone. The tricyclo[5.2.2.$0^{2,6}$]undecane unit **8** was traced back to phenol **10** via the oxidative dearomatization, followed by inverse electron demand Diels-Alder reaction [12] with cyclopent-3-en-1-ol (**9**). The phenol **10** was considered to synthesis by alkylation of compound **13** to deliver β-keto ester **11**, followed by decarboxylative aromatization [13]. We reasoned that ketone **13**, containing the first chiral center, could be installed with compound **14** and allylic alcohol **15** through a redox-relay Heck reaction [14].

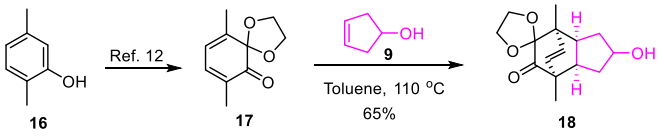
In our strategy, the tricyclo[5.2.2.$0^{2,6}$]undecane moiety,



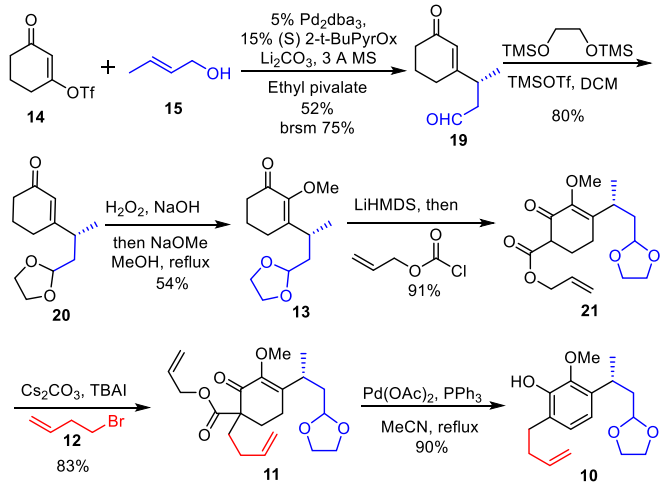
Scheme 1. Retrosynthetic analysis of mannolides B-C.

containing four continuous stereocenters including two quaternary carbon centers, was built up by the inverse electron demand Diels-Alder reaction. Thus, a model study of this reaction was need to verify the performance and the stereochemistry. As shown in Scheme 2, the masked *o*-benzoquinones **17**, prepared from 2,5-dimethylphenol (**16**) in four steps according to the literature [12], was chose to attempt this D-A reaction with dienophile **9**. To our delight, a single product was obtained in reflux toluene with a moderate yield. The relative stereochemistry of the compound **18** was determined by NOE and NOESY as shown in Scheme 2. Although, the relative stereochemistry of **18** is not as expected, it was remedied by selective oxidation cleavage of double bond and reduction of ketone and ketal instead of the original design, reduction of double bond and oxidation cleavage of ketone and ketal.

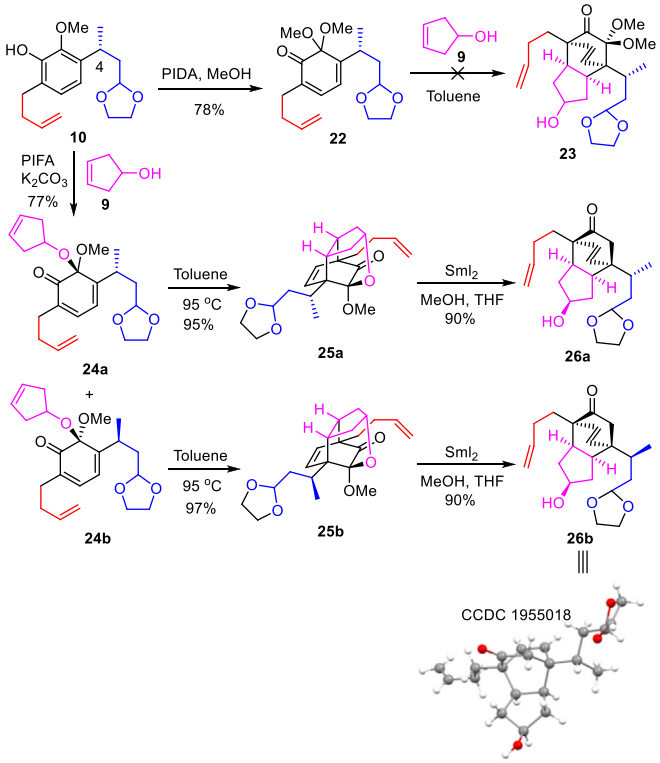
Encouraged by the model study results, our synthesis started to prepare the precursor **10** of Diels-Alder Reaction. As shown in Scheme 3, the known alkenyl triflate **14** [15] was coupled with allylic alcohol **15** through a redox-relay Heck reaction with Sigman's procedure [14] to produce aldehyde **19** in 52% yield. However, presumably for lack of substituents in both α, β-unsaturated ketone **14** (α-substituent) and allylic alcohol **15** (trisubstituted), the enantioselectivity of this reaction was poor no matter what other PyrOx-type ligands [14] and temperature we changed. In order to



Scheme 2. Model study of the inverse electron demand Diels-Alder reaction.



Scheme 3. Prepared the precursor **10** of Diels-Alder reaction.



Scheme 4. Synthetic studies of the Diels-Alder reaction.

verify the subsequent design, we continued to try the following transformation. The compound **19** was selective protection of aldehyde group in the presence of ketone with 1,2-Bis(trimethylsilyloxy) ethane and catalytic TMSOTf (10%) to obtain the glycol acetal **20** [16]. Notable, the glycol acetal **20** need directly purifying by chromatography without any quenching, otherwise it would lead to inverse reaction to recover the starting material **19** completely. Elaboration of **20** to 3-methoxy-α, β-unsaturated ketone **13** proceeded smoothly through two steps transformations, including epoxidation of the α, β-unsaturated ketone and one-pot sodium methoxide epoxide ring-opening [17] with simultaneous hydroxyl group elimination to form the compound **13**.

In the following sequence, we should install butenyl side chain at ketone α-carbon. Treating compound **13** with 4-bromobut-1-ene **12** in various bases and different solvents, we could not get the satisfying results. We envisioned that introducing an active group in **13** could make it to install the butenyl and followed aromatization in conversion feasible. So, allyl carbonate was selected as the active group and the efficient one-step removal of allyloxycarbonyl groups at the aromatization using palladium chemistry. The active group of **13** was introduced by utilizing allyl chloroformate in LiHMDS to deliver β-keto ester **21** [18]. Next, **21** was subjected to alkylation with **12** to produce **11**. After screening a number of bases and additives, we were delighted to find that the best result was carried out with Cs_2CO_3, catalytic tetrabutylammonium iodide and excess **12** in DMF at room temperature, which could produce **11** smoothly in 83% yield. As expected, under the catalysis of $Pd(OAc)_2$ and PPh_3, decarboxylative aromatization proceeded smoothly in a high yield to furnish phenol **10** [13b]. Notice, it was critical to use PPh_3 instead of dppe as ligand in this conversion, due to the coordination of the ethylene glycol protecting group [13a].

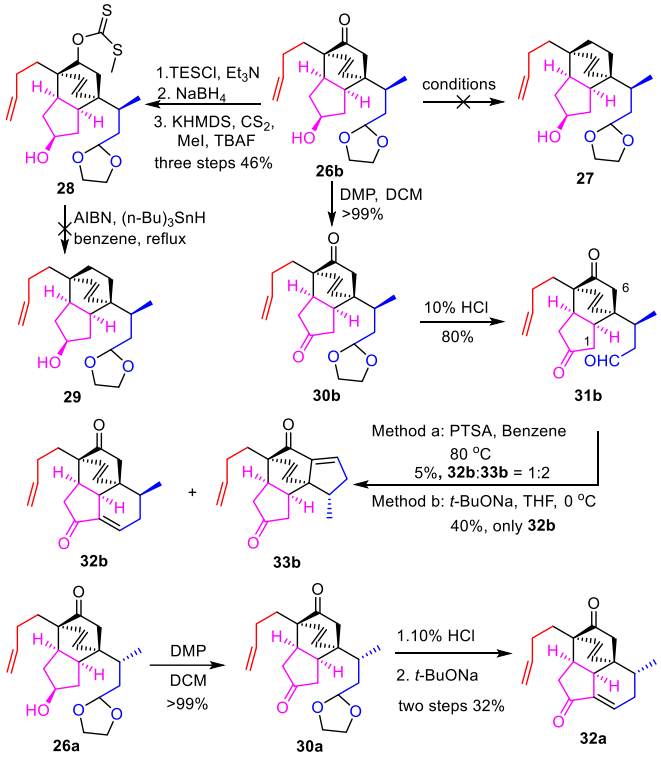
With the desired phenol **10** in hand, we attempted the key oxidative dearomatization/intermolecular Diels-Alder reaction to construct the tricyclo[5.2.2.0^{2,6}]undecane unit, containing four-contiguous stereocenter including two quaternary carbon centers. As shown in Scheme 4, the phenol **10** was oxidized by PIDA in MeOH to obtain *o*-benzoquinones **22** in 78% yield. To our disappointment, we failed to obtain the desired compound **23** by treating diene **22** with dienophile **9**. After extensively attempted (including changed temperature, pressure and Lewis acid), the results were recovery of reactants or decomposed of diene **22**. We speculated that the intramolecular Diels-Alder reaction would have enough activity to make this reaction occur. In addition, the configuration of the side chain C-4-methyl in precursor **10** would be predicated on the ability of exerting diastereofacial control, which alcohol **9** attacked from less steric hindrance, in the oxidative dearomatization step. Thus, we could establish the key four stereocenters including two quaternary carbon centers in tricyclo[5.2.2.0^{2,6}]undecane core of B/C-ring by the C-4-methyl chiral inducing. To our knowledge, although tandem oxidative dearomatization/intramolecular Diels-Alder reaction of primary alcohol had been reported in many total syntheses [19], there was still no single report about secondary alcohol like this reaction. Obviously, primary alcohol had much better activity than secondary in oxidative dearomatization. In the initial attempt, treating a mixture of **10** and excess **9** with oxidant bis(trifluoroacetoxy) iodobenzene (PIFA) at room temperature led to a complex mixture, under Mehta's protocl [19a,c]. After extensive screening the oxidants, solvents and reaction temperatures, the best result was delighted to find (details see SI, Table S1). In the optimal condition, the ethers **24a** and **24b** were obtained in 77% overall yield. Unfortunately, the stereocontrol of C-4 was poor due to single bond free rotation and the ratio of **24a** and **24b** was about 1:1 dr. It was hard to determine which compound had correct configuration for **24a** and **24b**, so we made following conversion to this two diastereomers.

With **24a** and **24b** in hand, we attempted the intramolecular Diels-Alder reaction to construct key intermediates **25a** and **25b** (Scheme 4). Treating **24a** and **24b** in toluene at 95 °C respectively, complicated cage-like compound **25a** and **25b** was obtained in 95% and 97% yield as colorless oil. However, the reaction time was too long and need to shorten. Improving reaction temperature led to another complex compound. Attempting various Lewis acid only led to a complex mixture. In the presence of samarium (II) iodide (0.1M in THF) [20], **25a** and **25b** were converted to compound **26a** and **26b** in a high yield, respectively. Fortunately, the structure of

26b was supported by X-ray diffraction, which allowed to determine **26a** with the correct configuration.

The compound **26b**, with incorrect configuration, was used for attempting the subsequent transformation to screen optimal conditions. Attention was focused on the reduction of the ketone in **26b** (Scheme 5). To our disappointment, it was all failed to reduce the ketone after attempting several reducing systems [21] such as TMSCl-mediated Clemmensen reduction (no reaction) [21a], Wolff-Kishner reduction (decompose) and its Caglioti modification (no reaction) [21b], and Lawesson's reagent (no reaction). Next, we turned our attention to transform ketone to alcoholic derivatives followed by Barton–McCombie deoxygenation or hydride reduction. Barton-McCombie reaction reducing precursor **28** was prepared via three steps: 1) protected the secondary hydroxyl group with TES, 2) reduced ketone to alcohol, 3) transformed the secondary alcohol to thioxoester derivative and deprotected hydroxyl group. No desire product was detected by exposing **28** to tri-*n*-butyltin hydride in refluxing toluene.

After rigorous analysis, the conclusion drawn was that intramolecular Aldol reaction preferred to react at cyclopentanone carbonyl α-position (C-1) rather than cyclohexanone (C-6) because of the steric hindrance. In order to verify this hypothesis, **26b** was oxidized with Dess-Martin periodinane reagent to deliver diketone **30b** in quantity yield (Scheme 5). Inspired by Ito [22a]and Zhai [22b], it was quickly realized that Brönsted-acid could probably be a better choice for deprotection of the cyclic acetal and Aldol reaction in one-pots. However, treatment of **30b** with *p*-toluenesulfonic acid (PTSA) in toluene at room temperature to 80 °C provided a complex mixture. Under carefully screening, 10% HCl in THF at 50 °C caused the deprotection of the cyclic acetal to afford aldehyde **31b** in 80% yield. Moving forward, treating aldehyde **31b** with *p*-toluenesulfonic acid monohydrate (PTSA·H_2O) in benzene at 80 °C for 3 days, (Method a) we obtained the expected product **32b** and **33b** in 5% yield, which was determined by ^{1}H NMR, ^{13}C NMR and HMBC, as



Scheme 5. Synthesis of the bowl-shaped B/C/D ring system.

a 1:2 inseparable isomers. In order to improve the yield and ratio of **32b**, the reaction condition was extensive screening (details see SI, Table S2). The best result was achieved that treating **31b** with *t*-BuONa in THF at 0 °C for the Aldol reaction, the desired compound **32b** was obtained as a single isomer in 40% yield [23]. (Method b) Next, compound **32a** was also synthesized from compound **26a** following the same procedure with 32% yield in three steps.

3. Summary

In conclusion, a synthesis of the BCD-ring system of mannolides B-C via oxidative dearomatization/intramolecular Diels-Alder reaction and regioselective Aldol reaction had been achieved. Furthermore, we developed a novel strategy to synthesize polysubstituted phenol compound from cyclohexen-1-one. The following investigation toward total synthesis of mannolides B-C is currently underway on the basis of present results in the laboratory.

4. Experimental section

4.1. General

Oxygen- and moisture-sensitive reactions were carried out under argon atmosphere. Solvents were purified and dried by standard methods prior to use. All commercially available reagents were used without further purification unless otherwise noted. Column chromatography was performed on silica gel (200–300 mesh). NMR spectra were recorded on Bruker 400 MHz and Oxford 600 MHz spectrometers in the $CDCl_3$. Chemical shifts are reported as δ values relative to internal chloroform (δ 7.26 for ^{1}H NMR and 77.00 for ^{13}C NMR). High resolution mass spectra (HRMS) were obtained on a 4G mass spectrometer by using electrospray ionization (ESI) analyzed by quadrupole time-of-flight (Q-TOF).

4.2. Experimental procedures and data of synthetic intermediates

4.2.1. 2′-hydroxy-4′,7′-dimethyl-2′,3′,3a′,4′,7′,7a′-hexahydro-1′H-spiro[[1,3]dioxolane-2,8′-[4,7]ethanoinden]-9′-one(*18*)

The solution of the compound **17** (41.7 mg, 0.23 mmol, 1.0 equiv.) and **9** (77.7 mg, 0.92 mmol, 4.0 equiv.) in 0.2 mL toluene was stirred at 110 °C for 24 h. The solvent was concentrated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to afford the product compound **18** (29.3 mg, 65%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.04 (dd, J = 8.3, 0.8 Hz, 1H), 5.73 (dd, J = 8.3, 1.3 Hz, 1H), 4.41–4.23 (m, 3H), 4.09–3.94 (m, 2H), 2.85 (dd, J = 18.2, 10.5 Hz, 1H), 2.52 (dd, J = 18.0, 9.5 Hz, 1H), 1.84 (dd, J = 12.0, 7.6 Hz, 2H), 1.56 (s, 1H), 1.39–1.21 (m, 3H), 1.15 (s, 3H), 1.11 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 209.04, 139.07, 131.84, 102.63, 73.44, 66.53, 66.36, 51.80, 45.36, 44.92, 43.27, 38.36, 38.33, 15.28, 14.66.

4.2.2. 3-(3-Oxocyclohex-1-en-1-yl)butanal (*19*)

A solution of 1,3-Cyclohexanedione (11.2 g, 100 mmol, 1.00 equiv.) and pyridine (15.70 g, 16.0 mL, 200 mmol, 2.00 equiv.) in dichloromethane (500 mL) was cooled to −78 °C. Trifluoromethanesulfonic anhydride (20.0 mL, 120 mmol, 1.20 equiv.) was added slowly and the reaction mixture was stirred at −78 °C for 10 min. The reaction mixture was warmed up to 0 °C and after consumption of the diketone (monitored by TLC). HCl (1 M, 200 mL) was added. The reaction mixture was extracted with dichloromethane (3 × 250 mL), the organic layer was washed with saturated $NaHCO_3$ (100 mL), brine, dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 8:1) to yield compound **14** (21.47 g, 88 mmol, 88%)

as yellowish oil. Data is consistent with that reported in the literature. To a dry 500 mL Schlenk flask equipped with a stir bar was added Pd_2dba_3 (3.15 g, 3.44 mmol, 0.05 equiv.), ligand (S) 2-t-BuPyrOx (2.80 g, 10.31 mmol, 0.15 equiv.), 3 Å MS (13.74 g, 200 mg/mmol), and ethyl pivalate (345 mL). To this flask, a three-way adapter fitted with a balloon of Ar was added, and the flask was evacuated via house vacuum and refilled with Ar three times while stirring. The resulting mixture was stirred for 15 min. To this, the corresponding alkenyl alcohol **15** (7.0 ml, 82.44 mmol, 1.2 equiv.), alkenyl triflate **14** (16.76 g, 68.7 mmol, 1.0 equiv.) and Li_2CO_3 (7.61 g, 103.05 mmol, 1.5 equiv.) were added. The resulting mixture was stirred for another 48 h at room temperature. The solvent was concentrated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 2:1) to afford the product compound **19** (5.93 g, 52%, brsm 75%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.73 (t, J = 1.5 Hz, 1H), 5.87 (s, 1H), 2.88 (m, 1H), 2.66 (ddd, J = 17.2, 6.5, 1.4 Hz, 1H), 2.52 (ddd, J = 17.2, 7.5, 1.6 Hz, 1H), 2.42−2.29 (m, 4H), 2.06−1.93 (m, 2H), 1.16 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 200.25, 199.71, 168.32, 124.80, 48.41, 37.44, 35.32, 28.01, 22.77, 19.00. HRMS (ESIMS) calcd for $C_{10}H_{15}O_2^+$ $[M + H]^+$ 167.1067, found 167.1071.

4.2.3. 3-(1-(1,3-dioxolan-2-yl)propan-2-yl)cyclohex-2-en-1-one (**20**)

A solution of the compound **19** (5.93 g, 35.7 mmol, 1.0 equiv.) and 1,2-bis-trimethylsilyloxyethane (8.84 g, 42.8 mmol, 1.2 equiv.) in dichloromethane (140 mL) was cooled to −78 °C and treated with TMSOTf (0.65 mL, 3.57 mmol, 0.1 equiv.). The mixture was stirred for 3 h at −78 °C. The reaction was then directly purified by chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to afford the product compound **20** (6.01 g, 80%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (s, 1H), 4.75 (t, J = 4.8 Hz, 1H), 3.90−3.85 (m, 2H), 3.79−3.75 (m, 2H), 2.54−2.49 (m, 1H), 2.33−2.24 (m, 4H), 1.99−1.88 (m, 2H), 1.86−1.79 (m, 1H), 1.70−1.63 (m, 1H), 1.09 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 199.97, 169.99, 124.91, 102.81, 64.70, 64.69, 38.39, 37.51, 37.34, 26.76, 22.76, 19.25. HRMS (ESIMS) calcd for $C_{12}H_{19}O_3^+$ $[M + H]^+$ 211.1329, found 211.1332.

4.2.4. 3-(1-(1,3-dioxolan-2-yl)propan-2-yl)-2-methoxycyclohex-2-en-1-one (**13**)

To a cooled (0 °C) and stirred solution of the compound **20** (6.01 g, 28.57 mmol, 1.0 equiv.) in 140 mL methanol was added (14.5 mL, 142.90 mmol, 5.0 equiv.) of 30% hydrogen peroxide and 10% sodium hydroxide (12.5 mL, 31.43 mmol, 1.1 equiv.) during 30 min. The mixture was stirred for 4 h at 0 °C, then the reaction was quenched with saturated NH_4Cl solution, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried with anhydrous $NaSO_4$, filtered and the solvents were evaporated under reduced pressure to leave the residue that was taken directly to the next step as crude. To a solution of above residue in 570 mL methanol was added 1M (in methanol) sodium methoxide (42.9 mL, 42.86 mmol, 1.5 equiv.) and the mixture was refluexed for 36 h, the solution was evaporated under reduced pressure, saturated NH_4Cl solution was added, and the mixture was extracted with ethyl acetate. The solvent was concentrated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to afford the product compound **13** (3.70 g, 54%) as yellowish oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.71 (t, J = 4.8 Hz, 1H), 3.90−3.84 (m, 2H), 3.78−3.73 (m, 2H), 3.58 (s, 3H), 3.34−3.25 (m, 1H), 2.39−2.35 (m, 2H), 2.30−2.26 (m, 2H), 1.90−1.83 (m, 2H), 1.80−1.73 (m, 1H), 1.70−1.64 (m, 1H), 1.03 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.08, 152.56, 148.10, 103.16, 64.65, 64.63, 59.87, 38.59, 37.98, 29.32, 24.37, 22.29, 18.95. HRMS (ESIMS) calcd for $C_{13}H_{21}O_4^+$ $[M + H]^+$ 241.1434, found 241.1439.

4.2.5. Allyl 4-(1-(1,3-dioxolan-2-yl)propan-2-yl)-3-methoxy-2-oxocyclohex-3-ene-1-carboxylate (**21**)

A solution of 1.06 M Lithium bis(trimethylsilyl)amide (43.70 mL, 46.31 mmol, 3.00 equiv.) in THF (78 mL) was cooled to −78 °C. The compound **13** (3.7048 g, 15.43 mmol, 1.0 equiv.) was added slowly. The reaction mixture was stirred at −78 °C for 2 h. Then, allyl carbonochloridate (3.28 mL, 30.88 mmol, 2.0 equiv.) was added quickly in one portion at −78 °C. The reaction was quenched by saturated NH_4Cl and extracted with ethyl acetate. The combined organic layers were washed with brine, dried with anhydrous $NaSO_4$. The solvent was concentrated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to afford the product compound **21** (4.52 g, 91%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.94−5.85 (m, 1H), 5.32 (dd, J = 17.2, 1.3 Hz, 1H), 5.22 (d, J = 10.4 Hz, 1H), 4.76−4.73 (m, 1H), 4.70−4.58 (m, 2H), 3.93−3.86 (m, 2H), 3.82−3.75 (m, 2H), 3.63 (s, 3H), 3.43−3.39 (m, 1H), 3.35−3.30 (m, 1H), 2.49−2.24 (m, 3H), 2.19−2.11 (m, 1H), 1.85−1.69 (m, 2H), 1.07 (dd, J = 6.8, 5.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 189.69, 189.62, 169.56, 169.51, 152.72, 152.51, 147.53, 147.45, 131.67, 118.50, 103.21, 103.11, 65.70, 64.81, 64.76, 64.73, 59.87, 59.84, 53.94, 53.82, 38.05, 37.94, 29.52, 25.40, 25.32, 22.71, 22.58, 19.10, 19.01. HRMS (ESIMS) calcd for $C_{17}H_{25}O_6^+$ $[M + H]^+$ 325.1646, found 325.1649.

4.2.6. Allyl 4-(-1-(1,3-dioxolan-2-yl)propan-2-yl)-1-(but-3-en-1-yl)-3-methoxy-2-oxocyclohex-3-ene-1-carboxylate (**11**)

To a clean dry 100 ml flask with a magnetic stirring bar was loaded compound **21** (3.54 g, 10.99 mmol, 1.0 equiv.), Cs_2CO_3 (4.29 g, 13.19 mmol, 1.2 equiv.), tetrabutylammonium iodide (405.6 mg, 1.10 mmol, 0.1 equiv.) and DMF 55 mL. To the above solution was added 4-bromobut-1-ene (4.46 mL, 43.96 mmol, 4.0 equiv.). The reaction was stirred at room temperature for 12 h. The reaction mixture diluted with ethyl acetate, washed with water and brine, dried with anhydrous $NaSO_4$. The solvent was concentrated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to afford the product compound **11** (3.43 g, 83%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89−5.73 (m, 2H), 5.30−5.25 (m, 1H), 5.20 (d, J = 10.4 Hz, 1H), 5.01 (dd, J = 17.1, 1.3 Hz, 1H), 4.93 (d, J = 10.2 Hz, 1H), 4.72 (dt, J = 14.1, 4.8 Hz, 1H), 4.65−4.52 (m, 2H), 3.94−3.85 (m, 2H), 3.80−3.74 (m, 2H), 3.59 (d, J = 1.3 Hz, 3H), 3.31−3.22 (m, 1H), 2.51−2.21 (m, 3H), 2.14−1.60 (m, 8H), 1.05 (dd, J = 7.0, 4.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.86, 191.60, 171.20, 171.03, 150.44, 150.09, 147.50, 147.30, 137.90, 137.86, 131.56, 131.51, 118.77, 118.70,114.84, 114.82, 103.30, 103.22, 65.67, 64.78, 64.75, 64.71, 59.40, 59.23, 56.95, 56.74, 38.07, 37.92, 33.10, 32.53, 29.85, 29.52, 29.47, 28.87, 28.76, 21.46, 21.32, 19.14, 19.06. HRMS (ESIMS) calcd for $C_{21}H_{31}O_6^+$ $[M + H]^+$ 379.2115, found 379.2120.

4.2.7. 3-(1-(1,3-dioxolan-2-yl)propan-2-yl)-6-(but-3-en-1-yl)-2-methoxyphenol (**10**)

In a dry argon-purged flask were placed $Pd(OAc)_2$ (204.8 mg, 0.91 mmol, 0.1 equiv.) and PPh_3 (119.6 mg, 0.46 mmol, 0.05 equiv.) in dry acetonitrile (180 mL). The mixture was stirred at room temperature for 30 min. The compound **11** (3.43 g, 9.12 mmol, 1.0 equiv) in dry acetonitrile (10 ml) was added and the reaction was refluxed for 1 h. The resulting mixture was then concentrated in *vacuo* and chromatographed on silica gel (petroleum ether/ethyl acetate = 8:1) to give the compound **10** (2.40 g, 90%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.87 (d, J = 8.0 Hz, 1H), 6.68 (d, J = 8.0 Hz, 1H), 5.95−5.85 (m, 1H), 5.69 (s, 1H), 5.06 (dd, J = 17.1,

1.5 Hz, 1H), 4.97 (d, J = 10.2 Hz, 1H), 4.71 (dd, J = 6.2, 4.0 Hz, 1H), 3.98–3.90 (m, 2H), 3.84–3.76 (m, 5H), 3.37–3.28 (m, 1H), 2.71–2.68 (m, 2H), 2.40–2.34 (dd, J = 15.1, 7.2 Hz, 2H), 2.04–1.97 (m, 1H), 1.89–1.82 (m, 1H), 1.26 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.72, 144.32, 138.57, 137.01, 126.11, 125.60, 117.26, 114.54, 103.36, 64.79, 64.65, 61.75, 41.55, 33.73, 29.30, 27.94, 22.78. HRMS (ESIMS) calcd for $C_{17}H_{24}O_4Na^+$ $[M + Na]^+$ 315.1567, found 315.1575.

4.2.8. 5-(1-(1,3-dioxolan-2-yl)propan-2-yl)-2-(but-3-en-1-yl)-6,6-dimethoxycyclohexa-2,4-dien-1-one (**22**)

In a dry argon-purged flask was placed compound **10** (8.2 mg, 0.028 mmol, 1.0 equiv.) in dry MeOH (0.7 mL). The mixture was stirred at 0 °C for 5 min. PIDA (11.8 mg, 0.036 mmol, 1.3 equiv.) was added. Then the reaction was warmed up to rt. The reaction mixture was extracted with ethyl acetate, the organic layer was washed with brine, dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 8:1) to yield compound **22** (7.1 mg, 78%) as yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (d, J = 6.5 Hz, 1H), 6.16 (d, J = 6.5 Hz, 1H), 5.78 (ddt, J = 16.8, 10.2, 6.6 Hz, 1H), 4.98 (t, J = 13.7 Hz, 2H), 4.89 (t, J = 5.0 Hz, 1H), 4.02–3.91 (m, 2H), 3.88–3.76 (m, 2H), 3.20 (d, J = 2.5 Hz, 6H), 2.92–2.77 (m, 1H), 2.36 (t, J = 7.5 Hz, 2H), 2.21 (dd, J = 14.1, 7.1 Hz, 2H), 1.96 (dt, J = 13.7, 5.2 Hz, 1H), 1.73 (ddd, J = 13.9, 8.8, 5.1 Hz, 1H), 1.21 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.07, 155.13, 137.70, 136.69, 134.98, 121.71, 115.21, 103.56, 95.15, 64.79, 64.56, 50.86, 50.80, 40.96, 32.54, 29.18, 27.91, 21.54.

4.2.9. 5-(1-(1,3-dioxolan-2-yl)propan-2-yl)-2-(but-3-en-1-yl)-6-(cyclopent-3-en-1-yloxy)-6-methoxycyclohexa-2,4-dien-1-one (**24a**) and its isomer **24b**

In a dry argon-purged flask was placed K_2CO_3 (973.4 mg, 7.05 mmol, 1.2 equiv.), cyclopent-3-en-1-ol **9** (5.0 mL, 58.69 mmol, 10 equiv.) and compound **10** (1.72 g, 5.87 mmol, 1.0 equiv.) in dry THF (1.2 mL). The mixture was stirred at −78 °C for 5 min [Bis(-trifluoroacetoxy)iodo]benzene (3.43 g, 9.12 mmol, 1.0 equiv.) in dry THF (10 ml) was dropwise added. Then the reaction was warmed up to 0 °C in 8 h. The reaction mixture was extracted with ethyl acetate, the organic layer was washed with saturated $NaHCO_3$, brine, dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 32:1) to yield compound **24a** (773.4 mg, 35%) and **24b** (925.7 mg, 42%) as yellow oil.

24a: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (d, J = 6.5 Hz, 1H), 6.12 (d, J = 6.5 Hz, 1H), 5.85–5.74 (m, 1H), 5.62–5.59 (m, 1H), 5.57–5.54 (m, 1H), 5.03–4.96 (m, 3H), 4.87 (t, J = 5.1 Hz, 1H), 3.96–3.88 (m, 2H), 3.82–3.77 (m, 2H), 3.08 (s, 3H), 2.91–2.83 (m, 1H), 2.63–2.57 (m, 1H), 2.54–2.42 (m, 2H), 2.40–2.29 (m, 2H), 2.26–2.13 (m, 2H), 2.05–1.96 (m, 2H), 1.68–1.61 (m, 1H), 1.19 (d, J = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.32, 155.76, 137.76, 136.74, 134.78, 128.59, 128.04, 121.08, 115.20, 103.56, 95.09, 71.80, 64.76, 64.46, 51.75, 42.04, 41.14, 40.81, 32.52, 29.69, 28.07, 21.03. HRMS (ESIMS) calcd for $C_{22}H_{30}O_5Na^+$ $[M + Na]^+$ 397.1985, found 397.1992.

24b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (d, J = 6.5 Hz, 1H), 6.10 (d, J = 6.5 Hz, 1H), 5.85–5.75 (m, 1H), 5.63–5.56 (m, 2H), 5.05–4.85 (m, 4H), 3.99–3.93 (m, 2H), 3.86–3.80 (m, 2H), 3.11 (s, 3H), 2.92–2.83 (m, 1H), 2.63–2.47 (m, 2H), 2.43–2.31 (m, 3H), 2.26–2.16 (m, 2H), 2.10–2.05 (m, 1H), 1.95–1.89 (m, 1H), 1.78–1.71 (m, 1H), 1.20 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.24, 155.65, 137.78, 136.67, 134.83, 128.53, 128.10, 120.98, 115.19, 103.52, 95.50, 72.09, 64.80, 64.60, 51.56, 41.24, 40.73, 40.60, 32.50, 29.34, 28.07, 22.26. HRMS (ESIMS) calcd for $C_{22}H_{30}O_5Na^+$ $[M + Na]^+$ 397.1985, found 397.1992.

4.2.10. 4a-(1-(1,3-dioxolan-2-yl)propan-2-yl)-7-(but-3-en-1-yl)-8a-methoxy-3,4,4a,8a-tetrahydro-2H-4,7,2 (epiethane[1,1,2]triyl) chromen-8(7H)-one (**25a**) and its isomer **25b**

The solution of the compound **24a** (390 mg, 1.04 mmol) in 20 mL toluene was stirred at 95 °C for 14 days. The solvent was concentrated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to afford the product compound **25a** (372 mg, 95%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 (s, 1H), 5.90–5.80 (m, 2H), 5.04 (dd, J = 17.1, 1.5 Hz, 1H), 4.97–4.91 (m, 2H), 4.37 (s, 1H), 3.98–3.89 (m, 2H), 3.85–3.79 (m, 2H), 3.63 (s, 3H), 2.45 (t, J = 9.0 Hz, 1H), 2.45 (t, J = 9.0 Hz, 1H), 2.27–1.79 (m, 8H), 1.56–1.49 (m, 1H), 1.45–1.32 (m, 3H), 1.10 (t, J = 5.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.34, 138.41, 138.41, 130.03, 114.56, 104.61, 94.83, 75.58, 64.71, 64.42, 53.72, 52.17, 49.25, 43.06, 37.56, 37.01, 36.59, 32.50, 28.61, 28.19, 17.27. HRMS (ESIMS) calcd for $C_{22}H_{30}O_5Na^+$ $[M + Na]^+$ 397.1985, found 397.1985.

In the same procedure, **24b** (452 mg, 1.20 mmol) was transformed to **25b** (438.6 mg) with 97% as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.29 (d, J = 8.5 Hz, 1H), 5.93–5.82 (m, 2H), 5.09–5.05 (m, 1H), 5.00–4.95 (m, 2H),4.37 (s, 1H), 4.00–3.90 (m, 2H), 3.87–3.82 (m, 2H), 3.68 (s, 3H), 2.49–2.45 (m, 2H), 2.26–2.22 (m, 1H), 2.19–2.12 (m, 3H), 2.04 (d, J = 12.0 Hz, 1H), 1.98–1.81 (m, 2H), 1.58–1.51 (m, 1H), 1.45–1.31 (m, 3H), 1.06 (d, J = 6.5 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 207.21, 138.51, 138.51, 130.72, 114.64, 105.50, 94.70, 75.40, 64.73, 64.33, 53.77, 52.29, 49.99, 43.80, 39.55, 36.96, 36.67, 32.69, 28.68, 28.25, 17.65. HRMS (ESIMS) calcd for $C_{22}H_{30}O_5Na^+$ $[M + Na]^+$ 397.1985, found 397.1984.

4.2.11. (3a,4,7a)-4-(1-(1,3-dioxolan-2-yl)propan-2-yl)-7-(but-3-en-1-yl)-2-hydroxy-2,3,3a,4,7,7a-hexahydro-1H-4,7-ethanoinden-8-one (**26a**)

The compound **25a** (360 mg, 0.96 mmol, 1.0 equiv.) was dissolved in the methanol. The reaction mixture was degassed 3 times. 0.1M (in THF) SmI_2 (57.6 mL, 5.76 mmol, 6.0 equiv.) was injected into the reaction at room temperature. After the solution was stirred for 1 h, it was exposed to air until dark color disappeared. Brine was added, the reaction mixture was extracted with ethyl acetate, the organic layer was dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure. The residue was purified by column chromatography (silica gel, petroleum ether/ethyl acetate = 2:1) to yield compound **26a** (331.4 mg, 90%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.38 (d, J = 8.5 Hz, 1H), 6.03 (d, J = 8.5 Hz, 1H), 5.90–5.80 (m, 1H), 5.04 (dd, J = 17.1, 1.5 Hz, 1H), 4.97–4.91 (m, 2H), 4.21–4.12 (m, 1H), 4.0–3.93 (m, 2H), 3.88–3.81 (m, 2H), 2.33–1.84 (m, 9H), 1.84–1.72 (m, 3H), 1.58–1.45 (m, 2H), 1.26–1.18 (m, 2H), 1.02 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.06, 138.95, 138.77, 132.07, 114.41, 103.82, 73.83, 64.90, 64.65, 56.23, 46.11, 43.42, 40.63, 39.94, 37.36, 35.83, 35.43, 31.27, 28.58, 28.31, 15.64. HRMS (ESIMS) calcd for $C_{21}H_{31}O_4^+$ $[M + H]^+$ 347.2217, found 347.2224.

4.2.12. (3a,4,7a)-4-(1-(1,3-dioxolan-2-yl)propan-2-yl)-7-(but-3-en-1-yl)-2-hydroxy-2,3,3a,4,7,7a-hexahydro-1H-4,7-ethanoinden-8-one (**26b**)

As prepared for **26a**, the **25b** (430.6 mg, 1.15 mmol) was transformed to **26b** (358.3 mg) with 90% as a white solid; mp 99–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.37 (d, J = 8.5 Hz, 1H), 6.01 (d, J = 8.4 Hz, 1H), 5.90–5.80 (m, 1H), 5.03 (d, J = 17.1 Hz, 1H), 4.96–4.90 (m, 2H), 4.21–4.13 (m, 1H), 3.98–3.92 (m, 2H), 3.87–3.81 (m, 2H), 2.29–1.92 (m, 9H), 1.82–1.68 (m, 3H), 1.59–1.45 (m, 2H), 1.32–1.23 (m, 1H), 1.03 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 213.05, 139.21, 138.76, 131.92, 114.41, 103.81, 73.83, 64.89, 64.62, 56.29, 45.96, 43.26, 40.56, 40.15, 37.27, 36.69, 35.50, 31.58, 28.56, 28.29, 15.35. HRMS (ESIMS) calcd for $C_{21}H_{31}O_4^+$ $[M + H]^+$

347.2217, found 347.2226.

*4.2.13. (3a,4,7a)-4-(-1-(1,3-dioxolan-2-yl)propan-2-yl)-7-(but-3-en-1-yl)-1,3,3a,4,7,7a-hexahydro-2H-4,7-ethanoindene-2,8-dione (**30b**)*

To a solution of the compound **26b** (358.3 mg, 1.03 mmol, 1.0 equiv.) in dichloromethane (20 mL) was cooled to 0 °C and treated with DMP (873.7 mg, 2.06 mmol, 2.0 equiv.). The mixture was stirred for 8 h at room temperature. The reaction was then directly purified by chromatography on silica gel (petroleum ether/ethyl acetate = 3:1) to afford the product compound **30b** (354.5 mg, >99%) as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.43 (d, J = 8.5 Hz, 1H), 6.09 (d, J = 8.5 Hz, 1H), 5.87–5.77 (m, 1H), 5.02 (dd, J = 17.1, 1.3 Hz, 1H), 4.89 (dd, J = 5.8, 3.7 Hz, 1H), 3.95–3.88 (m, 2H), 3.84–3.77 (m, 2H), 2.62–2.52 (m, 2H), 2.37–2.23 (m, 3H), 2.23–2.09 (m, 2H), 2.05–2.196 (m, 1H), 1.90 (d, J = 18.9 Hz, 1H), 1.85–1.76 (m, 2H), 1.69–1.45 (m, 4H), 1.02 (d, J = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 216.47, 211.21, 138.30, 138.30, 131.58, 114.64, 103.49, 64.86, 64.58, 56.48, 46.28, 40.62, 39.93, 39.30, 38.92, 38.15, 36.57, 31.03, 28.50, 28.44, 15.43. HRMS (ESIMS) calcd for $C_{21}H_{29}O_4^+$ $[M + H]^+$ 345.2060, found 345.2069.

*4.2.14. 3-((3aS,4S,7S,7aR)-7-(but-3-en-1-yl)-2,8-dioxo-1,2,3,3a, 7, 7a-hexahydro-4H-4,7-ethanoinden-4-yl) butanal (**31b**)*

To a stirred solution of the compound **30b** (33.5 mg, 0.10 mmol, 1.0 equiv.) in 1.8 mL THF was added 0.68 mL10% HCl. The mixture was stirred for 2 h at 50 °C, then the reaction was quenched with saturated $NaHCO_3$ solution, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried with anhydrous $NaSO_4$, filtered and the solvents were evaporated under reduced pressure to leave the aldehyde **31b** (24 mg, 80%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (d, J = 1.6 Hz, 1H), 6.44 (d, J = 8.6 Hz, 1H), 6.17 (d, J = 8.5 Hz, 1H), 5.85 (dd, J = 17.0, 10.3 Hz, 1H), 5.11–4.94 (m, 2H), 2.72–2.48 (m, 3H), 2.48–2.28 (m, 4H), 2.28–2.10 (m, 2H), 2.10–2.01 (m, 1H), 1.99 (m, 1H), 1.94–1.76 (m, 2H), 1.65 (m, 1H), 1.54 (m, 1H), 1.03 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 215.97, 210.47, 200.80, 138.23, 137.51, 132.36, 114.88, 56.61, 46.86, 45.79, 40.68, 39.96, 39.39, 39.05, 38.12, 29.37, 28.55, 28.52, 15.59.

*4.2.15. (2a,2a^1,3,5a,6)-3-(but-3-en-1-yl)-6-methyl-2a,2a^1,6,7-tetrahydro-3H-3,5a-ethanoacenaphthylene-1,10(2H)-dione (**32b**); 4-(but-3-en-1-yl)-8-methyl-1,3a,4,7,8,8b-hexahydro-2H-4,8a-etheno-as-indacene-2,5(3H)-dione (**33b**)*

Method a: In a dry argon-purged flask, the solution of the aldehyde **31b** (16 mg, 0.053 mmol) in 0.53 mL benzene was added PTSA (3.0 mg, 0.016 mmol, 0.3 equiv.) at 80 °C for 3 days. The mixture was extracted with ethyl acetate. the organic layer was dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to afford the product compound **32b:33b** = 1:2 inseparable isomer (0.8 mg, 5%).

32b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.61–6.59 (m, 2H), 6.14 (d, J = 8.4 Hz, 1H), 5.92–5.82 (m, 1H), 5.10–5.05 (m, 1H), 4.99 (d, J = 9.8 Hz, 1H), 2.74–2.58 (m, 3H), 2.46 (dd, J = 19.5, 10.1 Hz, 1H), 2.24–2.16 (m, 2H), 2.12–2.02 (m, 1H), 1.94–1.80 (m, 5H), 1.59–1.51 (m, 1H), 1.07 (d, J = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.75, 205.30, 140.28, 138.50, 138.48, 133.89, 131.34, 114.74, 56.69, 46.19, 42.76, 39.58, 38.32, 35.44, 33.86, 32.91, 28.71, 28.35, 16.10. HRMS (ESIMS) calcd for $C_{19}H_{23}O_2^+$ $[M + H]^+$ 283.1693, found 283.1700.

33b: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.76 (d, J = 8.4 Hz, 1H), 6.56 (s, 1H), 6.09 (d, J = 8.4 Hz, 1H), 5.94–5.79 (m, 1H), 5.03 (dd, J = 34.4, 13.6 Hz, 2H), 2.88 (m, 1H), 2.76–1.71 (m, 12H), 1.23 (d, J = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 216.55, 197.45, 139.92, 138.55, 137.70, 135.16, 131.76, 114.70, 58.69, 57.88, 43.41, 42.59, 41.40, 39.96, 39.73, 34.51, 28.83, 28.42, 18.65.

*4.2.16. (2a,2a^1,3,5a,6)-3-(but-3-en-1-yl)-6-methyl-2a,2a^1,6,7-tetrahydro-3H-3,5a-ethanoacenaphthylene-1,10(2H)-dione (**32b**)*

Method b: In a dry argon-purged flask, the solution of the above aldehyde **31b** (24 mg, 0.08 mmol) in 1.9 mL THF was added sodium tert-butoxide (11.2 mg, 0.12 mmol, 1.2 equiv) at 0 °C. After 5 min, saturated NH_4Cl solution was added, and the mixture was extracted with ethyl acetate. the organic layer was dried over Na_2SO_4, filtered and the solvents were evaporated under reduced pressure, and the resulting residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to afford the product compound **32b** (10.9 mg, 40%) as a colorless oil.

*4.2.17. (3a,4,7a)-4-(-1-(1,3-dioxolan-2-yl)propan-2-yl)-7-(but-3-en-1-yl)-1,3,3a,4,7,7a-hexahydro-2H-4,7-ethanoindene-2,8-dione (**30a**)*

In the same procedure, **26a** (280.0 mg, 0.81 mmol, 1.0 equiv) was transformed to **30a** (278.2 mg) with 99% as colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.47 (d, J = 8.5 Hz, 1H), 6.13 (d, J = 8.5 Hz, 1H), 5.90–5.85 (m, 1H), 5.05 (dd, J = 17.1, 1.6 Hz, 1H), 4.97 (dd, J = 10.2, 1.4 Hz, 1H), 4.92 (dd, J = 6.2, 3.3 Hz, 1H), 3.99–3.92 (m, 2H), 3.88–3.81 (m, 2H), 2.70–2.54 (m, 2H), 2.45–2.29 (m, 2H), 2.24–2.12 (m, 3H), 2.08–1.99 (m, 1H), 1.93 (d, J = 19.0 Hz, 1H), 1.90–1.70 (m, 4H), 1.63–1.48 (m, 2H), 1.05 (d, J = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 216.59, 211.59, 138.36, 138.31, 131.87, 114.74, 103.46, 64.96, 64.72, 56.52, 46.51, 41.11, 40.05, 39.22, 39.04, 38.41, 35.80, 30.87, 28.58, 28.54, 15.83. HRMS (ESIMS) calcd for $C_{21}H_{29}O_4^+$ $[M + H]^+$ 345.2060, found 345.2065.

*4.2.18. (2a,2a^1,3,5a,6)-3-(but-3-en-1-yl)-6-methyl-2a,2a^1,6,7-tetrahydro-3H-3,5a-ethanoacenaphthylene-1,10(2H)-dione (**32a**)*

In the same procedure, **30a** (30.5 mg, 0.09 mmol, 1.0 equiv) was transformed to **32a** (10.2 mg) as a white solid with 32% yield in two steps. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.65 (d, J = 8.4 Hz, 1H), 6.57 (dd, J = 7.4, 3.1 Hz, 1H), 6.13 (d, J = 8.4 Hz, 1H), 5.93–5.83 (m, 1H), 5.08 (dd, J = 17.2, 1.3 Hz, 1H), 5.00 (d, J = 10.1 Hz, 1H), 2.83–2.80 (m, 1H), 2.66–2.45 (m, 3H), 2.18–1.99 (m, 5H), 1.89–1.79 (m, 2H), 1.73 (dd, J = 18.3, 1.5 Hz, 1H), 1.61–1.54 (m, 1H), 1.13 (d, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 211.63, 205.33, 139.64, 138.46, 138.16, 132.82, 131.44, 114.77, 56.61, 42.84, 41.62, 39.52, 38.45, 37.31, 32.48, 30.53, 28.66, 28.13, 17.96. HRMS (ESIMS) calcd for $C_{19}H_{23}O_2^+$ $[M + H]^+$ 283.1693, found 283.1701.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

We gratefully acknowledge financial support from the NNSFC (Grants 21672088, 21772079 and 21971096) and the Natural Science Foundation of Gansu Province (18JR4RA003).

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2020.131629.

References

[1] W.J. Zheng, L.G. Fu, In Zhongguo Zhiwu Zhi, vol. 7, Science Press, Beijing, 1978,

pp. 423–432.
[2] H. Abdelkafi, B. Nay, Nat. Prod. Rep. 29 (2012) 845–869.
[3] (a) J.G. Buta, J.L. Flippen, W.R. Lusby, J. Org. Chem. 43 (1978) 1002–1003;
(b) N.J. Sun, Z. Xue, X.T. Liang, L. Huang, Acta Pharm. Sin. 14 (1979) 39–43;
(c) J. Du, M.H. Chiu, R.L. Nie, J. Nat. Prod. 62 (1999) 1664–1665;
(d) K.D. Yoon, D.G. Jeong, Y.H. Hwang, J.M. Ryu, J. Kim, J. Nat. Prod. 70 (2007) 2029–2032.
[4] (a) G. Ni, H. Zhang, Y.-Y. Fan, H.C. Liu, J. Ding, J.M. Yue, Org. Lett. 18 (2016) 1880–1883;
(b) J.B. Xu, Y.Y. Fan, L.S. Gan, Y.B. Zhou, J. Li, J.M. Yue, Chem. Eur J. 22 (2016) 14648–14654;
(c) J.X. Zhao, Y.Y. Fan, J.B. Xu, L.S. Gan, C.H. Xu, J. Ding, J.M. Yue, J. Nat. Prod. 80 (2017) 356–362;
(d) Y.Y. Fan, J.B. Xu, H.C. Liu, L.S. Gan, J. Ding, J.M. Yue, J. Nat. Prod. 80 (2017) 3159–3166;
(e) Z.P. Ge, H.C. Liu, G.C. Wang, Q.F. Liu, C.H. Xu, J. Ding, Y.Y. Fan, J.M. Yue, J. Nat. Prod. 82 (2019) 1565–1575.
[5] (a) D.H. Rogers, J.C. Morris, F.S. Roden, B. Frey, G.R. King, F.W. Russkamp, R.A. Bell, L.N. Mander, Pure Appl. Chem. 68 (1996) 515–522;
(b) H.B. Zhang, D.C. Appels, D.C.R. Hockless, L.N. Mander, Tetrahedron Lett. 39 (1998) 6577–6580;
(c) D.H. Rogers, B. Frey, F.S. Roden, F.W. Russkamp, A.C. Willis, L.N. Mander, Aust. J. Chem. 52 (1999) 1093–1108;
(d) B. Frey, A.P. Wells, F. Roden, T.D. Au, D.C. Hockless, A.C. Willis, L.N. Mander, Aust. J. Chem. 53 (2000) 819–830;
(e) L.N. Mander, T.P. O'Sullivan, Synlett (2003) 1367–1369;
(f) T.P. O'Sullivan, H.B. Zhang, L.N. Mander, Org. Biomol. Chem. 5 (2007) 2627–2635;
(g) Z.Q. Ma, B. Cheng, H.B. Zhai, Asian J. Org. Chem. 3 (2014) 1097–1101.
[6] B. Frey, A.P. Wells, D.H. Rogers, L.N. Mander, J. Am. Chem. Soc. 120 (1998) 1914–1915.
[7] M. Zhang, N. Liu, W.P. Tang, J. Am. Chem. Soc. 135 (2013) 12434–12438.
[8] H.J. Zhang, L. Hu, Z.Q. Ma, R.N. Li, Z. Zhang, C. Tao, B. Cheng, Y. Li, H.F. Wang, H.B. Zhai, Angew. Chem. Int. Ed. 55 (2016) 11638–11641.
[9] L. Xu, C. Wang, Z.W. Gao, Y.M. Zhao, J. Am. Chem. Soc. 140 (2018) 5653–5658.
[10] (a) N. Basickes, A. Sen, Polyhedron 14 (1995) 197–202;
(b) M.A. Bigi, S.A. Reed, M.C. White, J. Am. Chem. Soc. 134 (2012) 9721–9726.
[11] (a) K. Nakashima, K. Inoue, M. Sono, M. Tori, J. Org. Chem. 67 (2002) 6034–6040;
(b) B. Nosse, R.B. Chhor, W.B. Jeong, C. Bohm, O. Reiser, Org. Lett. 5 (2003) 941–944.
[12] M. Iwatsu, D. Urabe, M. Inoue, Heterocycles 82 (2010) 491–504.
[13] (a) J. Tsuji, Pure Appl. Chem. 58 (1986) 869–878;
(b) T. Takahashi, K. Shimizu, T. Doi, J. Tsuji, J. Am. Chem. Soc. 110 (1988) 2674–2676.
[14] C. Zhang, B. Tutkowski, R.J. DeLuca, L.A. Joyce, O. Wiest, M.S. Sigman, Chem. Sci. 8 (2017) 2277–2282.
[15] M.H. Kunzmann, N.C. Bach, B. Bauer, S.A. Sieber, Chem. Sci. 5 (2014) 1158–1167.
[16] A. Pollex, A. Millet, J. Muller, M. Hiersemann, L. Abraham, J. Org. Chem. 70 (2005) 5579–5591.
[17] T.Z. Wang, N.H. Vo, L.A. Paquette, J. Am. Chem. Soc. 115 (1993) 1676–1683.
[18] B.M. Trost, R.N. Bream, J. Xu, Angew. Chem. Int. Ed. 45 (2006) 3109–3112.
[19] (For selective examples:) (a) G. Mehta, P. Maity, Tetrahedron Lett. 48 (2007) 8865–8868;
(b) J.G.M. Morton, C. Draghici, L.D. Kwon, J.T. Njardarson, Org. Lett. 11 (2009) 4492–4495;
(c) G. Mehta, P. Maity, Tetrahedron Lett. 52 (2011) 1749–1752;
(d) S.S. Duan, D. Long, C.G. Zhao, G.Y. Zhao, Z.Y. Yuan, X.G. Xie, J.G. Fang, X.G. She, Org. Chem. Front. 3 (2016) 1137–1143.
[20] W.J. Juo, T.H. Lee, W.C. Liu, S. Ko, S.K. Chittimalla, C.P. Rao, C.C. Liao, J. Org. Chem. 72 (2007) 7992–8004.
[21] (a) S. Xu, T. Toyama, J. Nakamura, H. Arimoto, Tetrahedron Lett. 51 (2010) 4534–4537;
(b) J.L. Giner, J. Feng, Org. Biomol. Chem. 15 (2017) 2823–2830.
[22] (a) T. Kobayashi, K. Tokumoto, Y. Tsuchitani, H. Abe, H. Ito, Tetrahedron 71 (2015) 5918–5924;
(b) X.M. Chen, H.J. Zhang, X.K. Yang, H.Q. Lv, X.R. Shao, C. Tao, H.F. Wang, B. Cheng, Y. Li, J.J. Guo, J. Zhang, H.B. Zhai, Angew. Chem. Int. Ed. 57 (2018) 947–951.
[23] (a) H. Watanabe, M. Takano, M. Nakada, J. Synth. Org. Chem. Jpn 66 (2008) 1116–1125;
(b) M. Krebs, M. Kalinowski, W. Frey, B. Claasen, A. Baro, R. Schobert, S. Laschat, Tetrahedron 69 (2013) 7373–7380.