Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron
Tetrahedron 62 (2006) 10477–10484

Application of the combined C–H activation/Cope rearrangement as a key step in the total syntheses of the assigned structure of (+)-elisabethadione and a (+)-*p*-benzoquinone natural product

Huw M. L. Davies* and Xing Dai

Department of Chemistry, University at Buffalo, The State University of New York, Buffalo, NY 14260-3000, USA

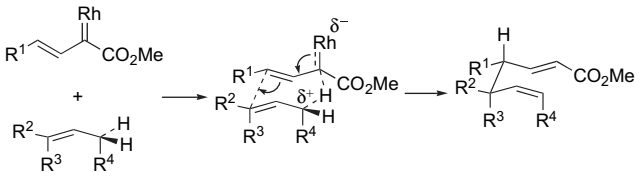
Received 13 January 2006; revised 2 May 2006; accepted 4 May 2006
Available online 7 August 2006

Abstract—The enantioselective total syntheses of the assigned structure of (+)-elisabethadione (**3**) and the (+)-*p*-benzoquinone natural product **4** is described. The stereocontrolled formation of the three key stereocenters in the natural products is achieved in a single step through the combined C–H activation/Cope rearrangement, a C–H functionalization process catalyzed by the dirhodium tetraprolinate, Rh_2(*R*-DOSP)$_4$ (DOSP=(*N*-dodecylbenzenesulfonyl)prolinate).

1. Introduction

Natural product synthesis is the classic proving ground for evaluating new synthetic methods. The successful implementation of a new method in a complex synthesis will require the process to be compatible with a range of functional groups and will demonstrate the viability of the new method compared to the established strategies of organic synthesis. The use of new metal-catalyzed processes in natural product synthesis is especially attractive because it opens up the possibility for the development of unusual organometallic transformations. If chiral catalysts are used, new enantioselective strategies for synthesis could be designed. Thus, the opportunity exists for considering revolutionary retrosynthetic disconnections that would not have been realistic using more conventional chemistry. In this paper, we describe a new C–H functionalization process that has the potential of broad utility for the synthesis of a family of marine diterpenes isolated from gorgonian corals.[1–6]

For the last few years, our group has been exploring the possibility of developing practical methods for enantioselective intermolecular C–H activation by means of metal carbenoid-induced C–H insertion.[7] If sufficient selectivity can be engineered into the chemistry, then the methodology could be extremely attractive because it would avoid many of the functional group manipulations that are often required in a natural product total synthesis. The intermolecular metal carbenoid-induced C–H insertion has been shown to be complimentary to some of the classic strategic reactions in synthesis, such as the aldol reaction,[8] the Mannich reaction,[9] the Michael addition,[10] the Claisen condensation[11] and the Claisen rearrangement.[12] In this paper, we describe the application to natural product total synthesis of a variant of the direct C–H activation, which we have described as the 'combined C–H activation/Cope rearrangement' (Scheme 1).[13] As the name suggests, the process begins as a C–H activation but before this is completed, a Cope rearrangement occurs to form a 1,5-diene.[13b] The reaction is highly diastereoselective (>98% de), which is typical for a Cope rearrangement, and when an appropriate chiral catalyst is used the reaction can also be highly enantioselective (>97% ee).[2g,4c,13]



Scheme 1. General scheme of the combined C–H activation/Cope rearrangement.

In order to demonstrate the synthetic potential of this chemistry, we have explored its application in total synthesis.[2g,4c] Diterpenes isolated from **Pseudopterogorgia elisabethae** were chosen as targets because they have broad range of biological activity and are of intense current interest.[1] This

Keywords: Combined C–H activation/Cope rearrangement; Total synthesis; (+)-Elisabethadione (**3**); Rhodium carbenoid, C–H insertion.
* Corresponding author. Tel.: +1 716 645 6800x2186; fax: +1 716 645 6547; e-mail: hdavies@acsu.buffalo.edu

0040–4020/$ - see front matter © 2006 Published by Elsevier Ltd.
doi:10.1016/j.tet.2006.05.086

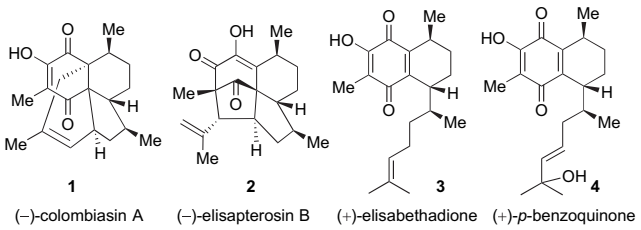
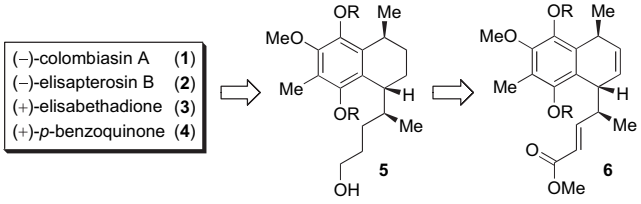


Figure 1. Structures of natural products **1**–**4**.

class of diterpenes exhibits a diverse range of structures, from bicyclic to polycyclic systems as illustrated in the representative examples shown in Figure 1.[2,3,14,15] These targets were considered especially attractive for the application of new methodology because even though a number of total syntheses of these compounds have been reported,[1] controlling the three stereocenters common to this class of diterpenes has been challenging.[2–6] The three stereocenters lack neighboring functional groups and this has been the main cause for the difficulty in developing a direct stereoselective synthesis. Therefore, a C–H activation strategy would be an intriguing approach to solve the stereochemical problem.

The ideal strategy to these synthetic targets not only would efficiently generate the three common stereogenic centers of these natural products, but also would introduce a side chain with appropriate functionality for rapid conversion to the natural products. A generally applicable precursor to the representative targets **1**–**4** would be the alcohol **5** (Scheme 2). This could be easily prepared from the



Scheme 2. Retrosynthetic analysis of natural products **1**–**4**.

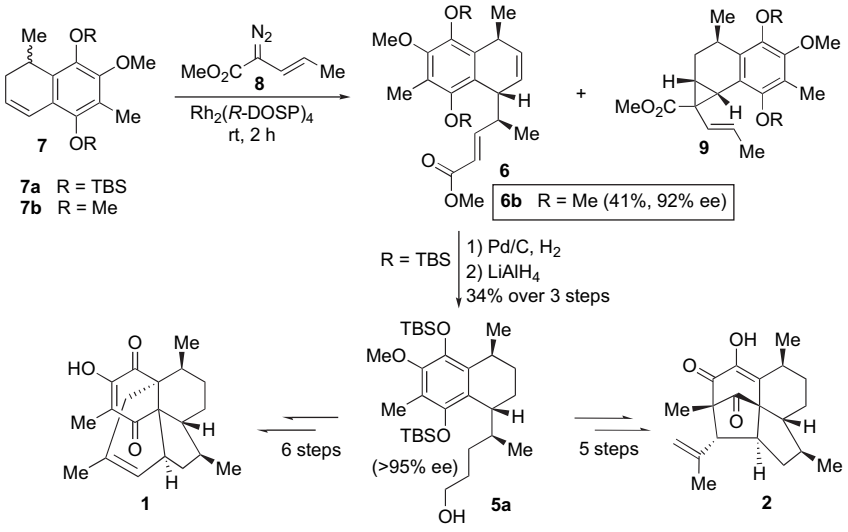
1,5-diene **6**, a product of the combined C–H activation/Cope rearrangement between a dihydronaphthalene and a vinylcarbenoid. We have recently described the application of this strategy to the synthesis of (–)-colombiasin A (**1**) and (–)-elisapterosin B (**2**).[2g] In this paper, we describe the extension of this chemistry to the total synthesis of the assigned structure of (+)-elisabethadione (**3**)[14] and the (+)-*p*-benzoquinone natural product **4**.[15] Both of these compounds display potent anti-inflammatory activity but neither has been previously synthesized.

The initial steps in the synthesis of **3** and **4** follow the same strategy that was used in the synthesis of (–)-colombiasin A (**1**) and (–)-elisapterosin B (**2**).[2g] The crucial step is the combined C–H activation/Cope rearrangement between the dihydronaphthalene **7** and the vinyldiazoacetate **8** (Scheme 3). An exceptional chiral catalyst for this transformation is Rh_2(*R*-DOSP)$_4$. When the reaction is catalyzed by Rh_2(*R*-DOSP)$_4$, one enantiomer of the dihydronaphthalene undergoes a C–H activation/Cope rearrangement to form **6** while the other enantiomer of **7** undergoes cyclopropanation to form **9**. Thus, in this process, the three crucial stereocenters common to these natural products are formed with excellent control of both relative and absolute configuration. The reaction has been equally effective in the reaction with the siloxy derivative **7a** and the methoxy derivative **7b**.[2g] The siloxy derivative **6a** has been effectively converted to (–)-colombiasin A (**1**) and (–)-elisapterosin B (**2**) in a very direct manner (eight and seven steps, respectively).[2g] In this paper, we demonstrate that the methoxy derivative **6b** is ideally functionalized for further manipulation and can be readily utilized for the synthesis of **3** and **4**.

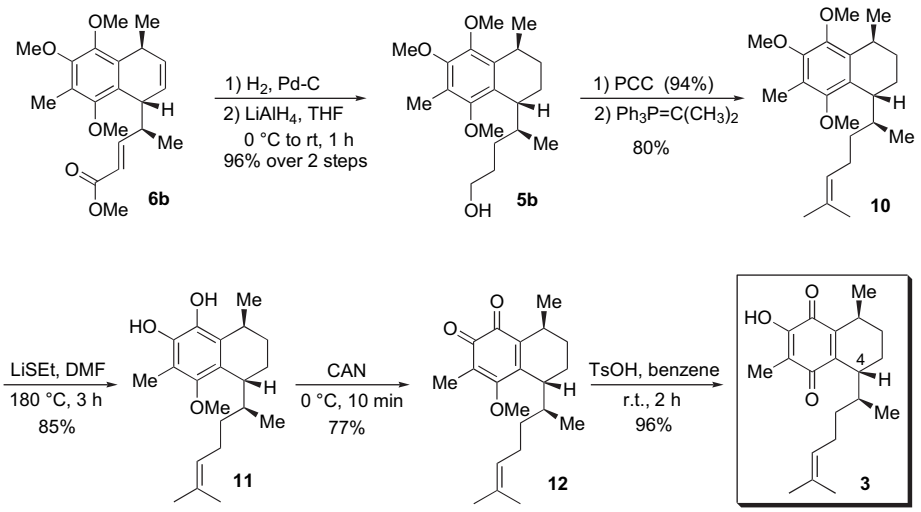
2. Results and discussion

2.1. Total synthesis of the assigned structure of (+)-elisabethadione

(+)-Elisabethadione (**3**) was isolated from the marine organism *P. elisabetha*, collected from the Florida Keys by Kerr



Scheme 3. Key step: combined C–H activation/Cope rearrangement.



Scheme 4. Total synthesis of the assigned structure of (+)-elisabethadione.

and co-workers.[14] Its gross structure was assigned on the basis of detailed NMR analysis, but its stereochemistry was assumed by analogy to other members of this class of biogenetically related natural products.[16] Anti-inflammatory assays indicate that elisabethadione is more potent than the related and commercially used natural products, the pseudopterosins.[17]

Our synthesis of the assigned structure of elisabethadione (**3**) began with the previously described combined C–H activation/Cope rearrangement of the dihydronaphthalene **7b** with the vinyldiazoacetate **8** (Scheme 3).[2g] The Rh_2(*R*-DOSP)$_4$ catalyzed reaction of **7b** and **8** gave a 1:1 mixture of the C–H functionalization product **6b** (41% yield, 92% ee, enantiomeric excess was determined from the alcohol **5b**) and the cyclopropane **9b** (43% yield) as single diastereomers. In this key step, the correct configuration of the three stereocenters in **3** was generated.

The C–H functionalization product **6b** is well suited for further elaboration to **3** (Scheme 4). The 1,5-diene in **6b** was hydrogenated and then the ester group was reduced to the alcohol **5b** in 96% yield over two steps. Oxidation of **5b** with PCC followed by a Wittig reaction on the resultant aldehyde furnished the alkene **10**. Having installed the side chain, the next operation was the oxidation of the aromatic ring to the quinone. Several initial attempts for the demethylation (BBr_3) and the oxidative demethylation [PhI(OAc)$_2$;[18] AgO/HNO_3[19,2b,c]] of **10** failed. Fortunately, heating the compound **10** with lithium ethanethiolate in DMF at 180 °C for 3 h resulted in the formation of the bisphenol **11** in 85% yield (Scheme 4).[20] Oxidation of **11** with cerium ammonium nitrate followed by demethylation and bond reorganization of the resultant red *ortho*-quinone **12** under acidic conditions gave **3**, the assigned structure of elisabethadione, in 96% yield as a yellow oil.

Contrary to our expectations, the reported ^{1}H and ^{13}C NMR data for the natural product (+)-elisabethadione, while similar, were different from our synthetic compound **3** (Fig. 2). The NMR, IR, and HRMS data indicated that the synthetic material had the same number of protons, carbons, and molecular weight as the natural material. The specific rotation of the synthetic material (+278, *c* 0.58, $CHCl_3$) was quite different from that of the natural product (+93). On the basis of this data, either the assigned structure of the natural material or our synthetic material is incorrect. Another possibility could be the errors in the reported data for the natural material. Unfortunately, it was not possible to evaluate this possibility because neither an authentic sample nor the original NMR spectra of the natural product were available.[21]

The most convincing method to determine whether the synthetic material had the assigned structure would be X-ray crystallographic analysis. Unfortunately, we were unable to prepare a crystal suitable for X-ray analysis. The NOE

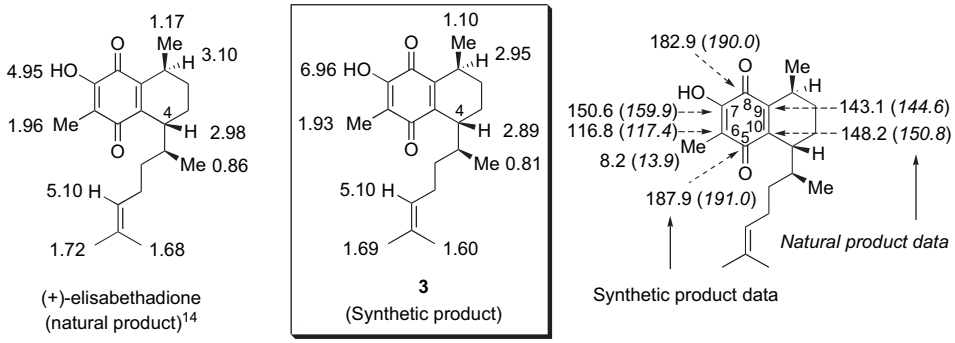
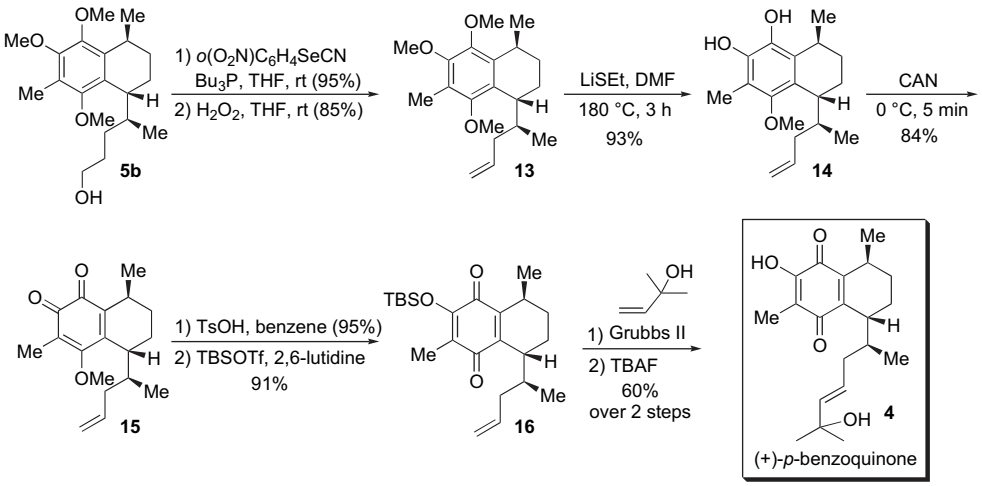


Figure 2. ^{1}H and ^{13}C NMR data of the natural and synthetic (+)-elisabethadione.



Scheme 5. Total synthesis of (+)-*p*-benzoquinone **4**.

studies also proved inconclusive. Therefore, a re-analysis of the synthetic scheme to **3** was made to determine if at any stage, an unexpected diastereomer could conceivably be formed. Five steps in Scheme 4 were identified to have the potential for the introduction of the wrong stereochemistry. The first was the combined C–H activation/Cope rearrangement to form **6b**. This was unlikely to be a problem because the enantio-divergent step to form **6b** has been reliable with a range of substrates.[2g,4c] This included the generation of the siloxy derivative **6a**, which has been successfully converted to (−)-colombiasin A (**1**) and (−)-elisapterosin B (**2**).[2g] The unsaturated ester in **6b** has a potentially epimerizable center at the γ-position, and so isomerization might have occurred under the hydrogenation conditions. The harsh conditions of the demethylation of **10** to **11** (LiSEt, 180 °C) could have caused an isomerization to occur although no obvious pathway is apparent. Finally, the formation of the *ortho*-quinone **12** and its conversion to the *para*-quinone **3** could have caused isomerization because the quinones **12** and **13** do have potentially epimerizable centers. None of these potential epimerization steps, however, is likely because there does not appear to be a driving force for a complete isomerization, especially as the tetrahydronaphthalene is already trans disubstituted.

2.2. Total synthesis of the (+)-*p*-benzoquinone 4

In order to confirm the proposed configuration of the synthetic material as **3**, the total synthesis of a second related natural product, the (+)-*p*-benzoquinone **4**, was conducted using all of the potentially epimerizable steps that has been used in the synthesis of **3**. The general outline of the synthesis is shown in Scheme 5. The synthesis started from the primary alcohol **5b**, the same intermediate used in the synthesis of compound **3**. The terminal alkene **13** was generated by the application of Grieco's selenoxide introduction/elimination procedure.[22] Then performing a similar sequence as used in the synthesis of **3**, **13** was converted to the quinone **16**. Selective demethylation of **13** to form the bisphenol **14**, followed by oxidation with cerium ammonium nitrate gave the *ortho*-quinone **15** in 84% yield. The subsequent isomerization of the *ortho*-quinone **15** gave the *para*-quinone, which was then protected by a TBS group to form **16** in 91% yield. Completion of the synthesis proceeded in a straightforward fashion. Installation of the allylic alcohol by a cross-metathesis reaction catalyzed by the Grubbs' second-generation ruthenium catalyst, using Jacobsen's strategy,[2f] followed by deprotection of the siloxy group afforded the natural product **4** in 60% yield over two steps. The spectral data of synthetic and natural (+)-*p*-benzoquinone **4** were identical (Fig. 3).[15] Furthermore, there was an excellent agreement in the ^{1}H and ^{13}C NMR data for the bicyclic portion of the synthetic material of **3**, the synthetic material of **4**, and the natural material of **4**. Assuming that the natural product **4** is correctly assigned, these results imply that the assigned structure of (+)-elisabethadione is incorrect or the reported spectral data for elisabethadione contain errors.

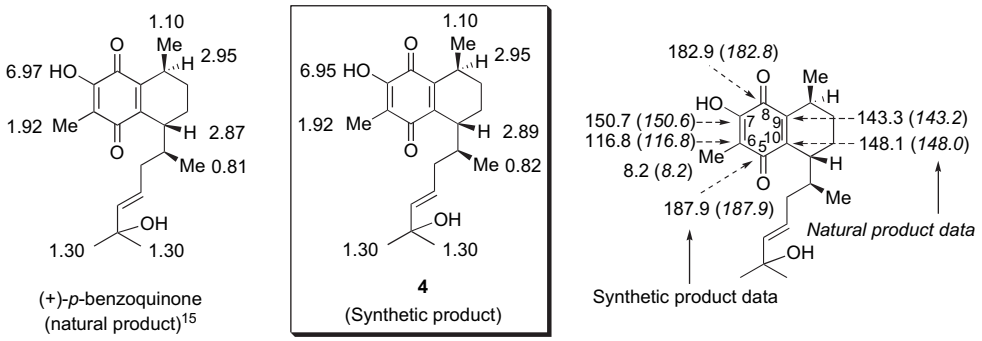


Figure 3. ^{1}H and ^{13}C NMR data of the natural and synthetic (+)-*p*-benzoquinone.

3. Conclusion

In summary, we have developed the first total syntheses of the assigned structure of (+)-elisabethadione (**3**) and the (+)-*p*-benzoquinone natural product **4**. The synthesis featured a Rh_2(*R*-DOSP)$_4$ catalyzed combined C–H activation/Cope rearrangement for the formation of the three key stereocenters in a single step.

4. Experimental

4.1. General

All reactions were carried out under an atmosphere of argon in an oven-dried glassware with magnetic stirring. Low temperature (−78 °C) was maintained using dry ice/acetone. Hexanes, THF, DCM, CH_3CN, and Et_2O were purified by passage through a bed of activated alumina. Purification of reaction products was carried out by flash chromatography using silica gel 60 (230–400 mesh). ^{1}H NMR spectra were measured at 300, 400, or 500 MHz spectrometers and are reported in parts per million using TMS as an internal standard (TMS at 0.00 ppm). Data were reported as (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, br=broad; coupling constant(s) in hertz; integration). ^{13}C NMR spectra were recorded at 75 or 125 MHz spectrometer and reported in parts per million using solvent as an internal standard ($CDCl_3$ at 77.0 ppm).

4.1.1. (*S*,2*E*)-Methyl 4-((1*S*,4*R*)-1,4-dihydro-5,7,8-trimethoxy-1,6-dimethylnaphthalen-4-yl)pent-2-enoate (6b). A solution of methyl vinyldiazoacetate **8** (3.40 g, 24.2 mmol, 3.0 equiv) in dry degassed 2,2-dimethylbutane (20 mL) was added by syringe pump over a 1 h period at room temperature to a solution of dihydronaphthalene **7b** (2.00 g, 8.1 mmol) and Rh_2(*R*-DOSP)$_4$ (306 mg, 0.16 mmol, 0.02 equiv) in dry degassed 2,2-dimethylbutane (30 mL). Once the addition had finished the brown solution was stirred at room temperature for an additional 30 min. The solvent was removed under vacuum to give a brown gum. Purification by column chromatography on silica gel (eluting with 7–10% ether/pentane) gave the *title compound* **6b** (1.19 g, 41%) along with cyclopropane **9b** (1.27 g, 43%). R_f 0.36 (7:1 pentane/ether); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.20 (dd, J=16.0, 6.0 Hz, 1H), 5.85 (dd, J=16.0, 2.0 Hz, 1H), 5.84 (m, 1H), 5.49 (ddd, J=10.0, 4.0, 2.0 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 3.76 (s, 3H), 3.72 (s, 3H), 3.71 (m, 1H), 3.45 (m, 1H), 3.12 (m, 1H), 2.19 (s, 3H), 1.27 (d, J=7.0 Hz, 3H), 0.55 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.5, 154.3, 152.2, 150.4, 147.4, 133.0, 132.9, 124.9, 123.3, 121.2, 119.7, 60.7, 60.3, 60.0, 51.4, 40.6, 39.3, 30.4, 23.9, 12.0, 9.3; IR (neat) 2953, 1723, 1651, 1462, 1318, 1079, 1015 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{21}H_{28}O_5Na$, required: 383.1829; found: 383.1837.

4.1.2. (*S*)-4-((1*S*,4*R*)-1,2,3,4-Tetrahydro-5,7,8-trimethoxy-1,6-dimethylnaphthalen-4-yl)pentan-1-ol (5b). To a solution of ester **6b** (944 mg, 2.62 mmol) in ethanol (50 mL) was added 5% palladium on carbon (ca. 50 mg). The suspension was placed on a Parr Hydrogenator at 45 psi for 3 h. The reaction mixture was filtered through a pad of Celite™ on silica gel. The filtrate was concentrated in vacuo to give a clear gum, which was used without further purification for the next step. The crude product was dissolved in dry tetrahydrofuran (60 mL) and cooled to 0 °C. Lithium aluminum hydride (5.24 mL, 1.0 M in THF, 5.24 mmol, 2.0 equiv) was added and the mixture was stirred at room temperature for 1 h. Water (20 mL) was added drop-wise followed by ether (40 mL). The organic layer was separated, and the aqueous layer was extracted with ether (20×4 mL). The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluent 20–33% ether/pentane) to give the *title compound* as a clear gum (847 mg, 94% over two steps, 92% ee). The enantiomeric excess of **5b** was determined by HPLC (Daicel Chiralcel OD-H, hexanes/*i*-PrOH=99:1, flow rate=0.7 mL/min) t_R=21.3 min (major), t_R=23.3 min (minor). $[\alpha]_D^{25}$ 6.4 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 3H), 3.80 (s, 3H), 3.64 (s, 3H), 3.61 (m, 2H), 3.16 (m, 1H), 2.85 (m, 1H), 2.17 (s, 3H), 1.92–2.03 (m, 2H), 1.75–1.79 (m, 2H), 1.66 (m, 1H), 1.58 (m, 1H), 1.45 (m, 1H), 1.35 (m, 2H), 1.14 (d, J=7.0 Hz, 3H), 0.75 (d, J=7.0 Hz, 3H), OH signal was not observed; ^{13}C NMR (125 MHz, $CDCl_3$) δ 152.7, 149.5, 147.1, 134.8, 128.6, 122.2, 63.3, 60.5, 60.2, 59.9, 37.4, 35.4, 31.2, 30.6, 27.0, 26.4, 23.2, 18.5, 18.1, 9.4; IR (neat) 2932, 1403, 1071, 731 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{20}H_{32}O_4Na$ [M]$^+$, required: 359.2193; found: 359.2197.

4.1.3. (*S*)-4-((1*S*,4*R*)-1,2,3,4-Tetrahydro-5,7,8-trimethoxy-1,6-dimethylnaphthalen-4-yl)pentanal. To a solution of **5b** (210 mg, 0.62 mmol) in dry DCM (20 mL), pyridinium chlorochromate (202 mg, 0.94 mmol, 1.5 equiv) was added in one portion at 0 °C. The reaction mixture was stirred at room temperature for 1.5 h and then diluted with ether (100 mL). The crude reaction mixture was filtered through a plug of Celite on silica gel. The filtrate was concentrated in vacuo to give a yellow oil. Purification by column chromatography on silica gel (eluting with 13% ether/pentane) gave the *title compound* as a clear gum (194 mg, 94%). ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.74 (br s, 1H), 3.85 (s, 3H), 3.80 (s, 3H), 3.64 (s, 3H), 3.16 (m, 1H), 2.83 (m, 1H), 2.32–2.50 (m, 2H), 2.17 (s, 3H), 1.90–2.01 (m, 2H), 1.78 (m, 2H), 1.56–1.69 (m, 2H), 1.48 (m, 1H), 1.40 (d, J=7.0 Hz, 3H), 0.78 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 203.3, 152.9, 149.7, 147.1, 134.7, 127.9, 122.3, 60.5, 60.1, 59.9, 42.4, 37.5, 35.6, 27.4, 27.0, 26.4, 23.2, 18.8, 18.1, 9.4; IR (neat) 2933, 1724 (C=O), 1457, 1403, 1072 cm^{-1}; HRMS *m*/*z* (EI) calcd for $C_{20}H_{30}O_4Na$ [M]$^+$, required: 357.2036, found: 357.2033.

4.1.4. (1*R*,4*S*)-1,2,3,4-Tetrahydro-5,6,8-trimethoxy-4,7-dimethyl-1-((*S*)-6-methylhept-5-en-2-yl)naphthalene (10). *n*-BuLi (*n*-hexane solution, 0.54 mL, 0.87 mmol, 2.90 equiv) was added drop-wise to a solution of isopropyltriphenylphosphonium iodide (389 mg, 0.90 mmol, 3.0 equiv) in dry THF (15 mL) at 0 °C under argon. The mixture was stirred for 1 h at the same temperature. A solution of aldehyde **17** (100 mg, 0.29 mmol) in dry THF (20 mL) was charged into the solution at 0 °C, and the resulting solution was stirred for an additional 30 min at the same temperature. The reaction was allowed to warm to room temperature for 30 min, and then refluxed under argon for

another 2 h. After cooling down, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ether. The organic layer was washed with brine and dried over Na_2SO_4, and concentrated in vacuo. Purification by column chromatography on silica gel (eluting with 2% ether/pentane) gave the *title compound* (86 mg, 80%). $[\alpha]_D^{25}$ 6.4 (*c* 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.13 (t, *J*=7.0 Hz, 1H), 3.85 (s, 3H), 3.81 (s, 3H), 3.65 (s, 3H), 3.15 (m, 1H), 2.88 (m, 1H), 2.18 (s, 3H), 1.91–2.07 (m, 4H), 1.79 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.45 (m, 1H), 1.22–1.38 (m, 2H), 1.14 (d, *J*=7.5 Hz, 3H), 0.72 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.0, 149.5, 147.0, 134.9, 130.8, 128.7, 125.3, 122.2, 60.5, 60.1, 59.9, 37.5, 35.74, 35.71, 27.0, 26.7, 26.4, 25.7, 23.2, 18.6, 18.3, 17.6, 9.5; IR (neat) 2930, 1458, 1404, 1074, 1030 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{23}H_{36}O_3Na$ $[M]^+$, required: 383.2557, found: 383.2562.

4.1.5. (5*R*,8*S*)-5,6,7,8-Tetrahydro-4-methoxy-3,8-dimethyl-5-((*S*)-6-methylhept-5-en-2-yl)naphthalene-1,2-diol (11). To a solution of ethanethiol (2.07 g, 33.31 mmol) in dry hexanes (15 mL) at 0 °C under argon was added *n*-butyllithium (5.20 mL, 8.33 mmol, 1.6 M in hexanes). The mixture was stirred at room temperature for 30 min. Then the mixture was concentrated in vacuo to give a white powder. The white powder and **10** (100 mg, 0.23 mmol) were dissolved in dry DMF (15 mL) at room temperature and the mixture was heated to reflux (180 °C oil bath) for 3 h. The reaction mixture was allowed to cool down to room temperature, acidified with 5% hydrochloric acid, and extracted with Et_2O (2×50 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with 13% ether/pentane) gave the *title compound* (76 mg, 85%) as a yellow oil. $[\alpha]_D^{25}$ 13.0 (*c* 0.94, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.13 (t, *J*=7.0 Hz, 1H), 4.92 (s, 1H), 4.78 (s, 1H), 3.63 (s, 3H), 3.05 (m, 1H), 2.86 (m, 1H), 2.18 (s, 3H), 2.00 (m, 4H), 1.80 (m, 2H), 1.69 (s, 3H), 1.60 (s, 3H), 1.50 (m, 1H), 1.30 (m, 2H), 1.18 (d, *J*=7.0 Hz, 3H), 0.74 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.7, 140.1, 136.9, 130.8, 127.3, 125.3, 124.7, 114.9, 60.5, 37.6, 35.7, 35.5, 26.7, 26.5 (2C), 25.7, 21.6, 18.8, 18.2, 17.6, 9.2; IR (neat) 3419, 2957, 2927, 1450, 1292, 1093, 1008 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{21}H_{32}O_3$ $[M]^+$, required: 332.2346; found: 332.2346.

4.1.6. (5*R*,8*S*)-5,6,7,8-Tetrahydro-4-methoxy-3,8-dimethyl-5-((*S*)-6-methylhept-5-en-2-yl)naphthalene-1,2-dione (12). To a solution of diol **11** (76 mg, 0.228 mmol) in CH_3CN (8 mL), a solution of cerium ammonium nitrate (376 mg, 0.686 mmol, 3.0 equiv) in distilled water (8 mL) was added by syringe at 0 °C. The resulting red solution was stirred at 0 °C for 10 min. The reaction mixture was quenched with water (10 mL) and extracted with Et_2O (2×40 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with 20% ether/pentane) gave the *title compound* (58 mg, 77%) as an orange red oil. $[\alpha]_D^{25}$ 271.0 (*c* 0.0317, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 5.11 (br t, *J*=7.0 Hz, 1H), 3.92 (s, 3H), 2.89 (m, 1H), 2.65 (m, 1H), 2.06–1.98 (m, 2H), 1.98 (s, 3H), 1.93–1.88 (m, 1H), 1.86–1.73 (m, 2H), 1.70 (s, 3H), 1.67 (m, 1H), 1.62 (s, 3H), 1.44–1.34 (m, 3H), 1.08 (d, *J*=7.0 Hz, 3H), 0.85 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.1, 179.4, 167.7, 150.6, 140.2, 131.5, 124.3, 119.6, 61.2, 37.1, 36.4, 35.6, 26.2, 26.1, 25.8, 25.7, 21.3, 18.5, 17.7, 17.5, 9.7; IR (neat) 2924, 1732, 1673, 1657, 1454, 1376, 1234 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{21}H_{30}O_3Na$ $[M]^+$, required: 353.2078, found: 353.2097.

4.1.7. Elisabethadione (3). To a solution of *ortho*-quinone **12** (20 mg, 0.06 mmol) in benzene (5 mL) at room temperature under argon was added 4-methylbenzenesulfonic acid monohydrate (23.0 mg, 0.12 mmol, 2.0 equiv). The mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with ether (50 mL), washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with 2–7% ether/pentane) gave the *title compound* (18 mg, 96%) as a yellow oil. $[\alpha]_D^{25}$ 278.0 (*c* 0.58, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 6.97 (s, OH, 1H), 5.10 (br t, *J*=7.0 Hz, 1H), 2.95 (m, 1H), 2.89 (m, 1H), 2.10–1.94 (m, 2H), 1.93 (s, 3H), 1.88–1.74 (m, 3H), 1.69 (s, 3H), 1.63 (m, 1H), 1.60 (s, 3H), 1.49–1.43 (m, 1H), 1.35–1.21 (m, 2H), 1.10 (d, *J*=7.0 Hz, 3H), 0.81 (d, *J*=7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 187.9, 182.9, 150.6, 148.2, 143.1, 131.3, 124.5, 116.8, 36.9, 36.0, 35.7, 26.3, 26.1, 26.0, 25.7, 20.8, 18.1, 17.7, 17.6, 8.2; IR (neat) 3675, 2970, 2920, 1738, 1714, 1406, 1242, 1067 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{20}H_{28}O_3$ $[M]^+$, required: 316.2033; found: 316.2026. ^1H NMR (500 MHz, benzene) δ 6.73 (s, OH, 1H), 5.25 (m, 1H), 2.93 (m, 1H), 2.83 (m, 1H), 2.20–1.95 (m, 3H), 1.92 (s, 3H), 1.68 (s, 3H), 1.57 (s, 3H), 1.55 (m, 2H), 1.42–1.26 (m, 3H), 1.51 (m, 1H), 0.97 (d, *J*=7.0 Hz, 3H), 0.71 (d, *J*=7.0 Hz, 3H).

4.1.8. (1*R*,4*S*)-1,2,3,4-Tetrahydro-5,6,8-trimethoxy-4,7-dimethyl-1-((*S*)-pent-4-en-2-yl)naphthalene (13).[22] To a stirring solution of **5b** (95 mg, 0.28 mmol) and *o*-nitrophenyl selenocyanate (192 mg, 0.85 mmol) in dry THF (7 mL) under argon at room temperature was added tri-*n*-butylphosphine (212 μL, 0.85 mmol). After stirring for 3 h, the reaction mixture was quenched with ethanol (4 mL) and concentrated. The crude product was used directly for the next step. ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J*=8.0 Hz, 1H), 7.52 (m, 2H), 7.30 (m, 1H), 3.84 (s, 3H), 3.80 (s, 3H), 3.62 (s, 3H), 3.16 (m, 1H), 2.98–2.83 (m, 3H), 2.17 (s, 3H), 2.10–1.65 (m, 6H), 1.54–1.40 (m, 3H), 1.14 (d, *J*=6.8 Hz, 3H), 0.76 (d, *J*=6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.8, 149.6, 147.1, 146.9, 134.8, 134.1, 133.4, 129.2, 128.2, 126.4, 125.1, 122.2, 60.5, 60.2, 59.9, 37.3, 35.8, 35.5, 27.0, 26.6, 26.5 (2C), 23.2, 18.7, 18.4, 9.4; IR (neat) 2931, 1513, 1330, 1071, 729 cm^{-1}; HRMS *m/z* (EI) calculated for $C_{26}H_{35}NO_5Se$ $[M]^+$, required: 521.1675; found: 521.1675.

To a solution of the above crude product in THF (7 mL) was slowly added 30% aqueous hydrogen peroxide (0.35 mL) at 0 °C. Stirring was continued for 1 day at room temperature. Water was added and extracted with ether (twice). The combined organic extracts were washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel (eluting with 2–5% ether/pentane) to give **13** (80 mg, 90% yield) as colorless oil. ^1H NMR (500 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.02–4.95

(m, 2H), 3.85 (s, 3H), 3.80 (s, 3H), 3.63 (s, 3H), 3.16 (m, 1H), 2.86 (m, 1H), 2.17 (s, 3H), 2.10–1.92 (m, 4H), 1.80–1.75 (m, 2H), 1.49–1.45 (m, 1H), 1.14 (d, J=7.0 Hz, 3H), 0.76 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.0, 149.5, 147.0, 138.9, 134.8, 128.5, 122.2, 114.9, 60.5, 60.1, 59.9, 40.0, 37.8, 35.2, 27.0, 26.5, 23.2, 18.6, 18.1, 9.4; IR (neat) 2956, 1458, 1404, 1072 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{20}H_{30}O_3$ $[M]^+$, required: 318.2189; found: 318.2200.

4.1.9. (5*R*,8*S*)-5,6,7,8-Tetrahydro-4-methoxy-3,8-dimethyl-5-((*S*)-pent-4-en-2-yl)naphthalene-1,2-diol (14). To a solution of alcohol ethanethiol (0.47 g, 7.54 mmol) in dry hexanes (10 mL) at 0 °C under argon was added *n*-butyllithium (2.36 mL, 3.77 mmol, 1.6 M in hexanes). The mixture was stirred at room temperature for 30 min. Then the mixture was concentrated in vacuo to give white powder. The white powder and **13** (60 mg, 0.18 mmol) were dissolved in dry DMF (10 mL) at room temperature and the mixture was heated to reflux (180 °C oil bath) for 3 h. The red-brown reaction mixture was allowed to cool down to room temperature, acidified with 5% hydrochloric acid, and extracted with Et_2O (2×50 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with 7–13% ether/pentane) gave the *title compound* (50 mg, 93%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.02–4.95 (m, 2H), 3.61 (s, 3H), 3.07 (m, 1H), 2.84 (m, 1H), 2.17 (s, 3H), 2.08–1.90 (m, 4H), 1.85–1.72 (m, 2H), 1.51–1.46 (m, 1H), 1.18 (d, J=7.0 Hz, 3H), 0.77 (d, J=7.0 Hz, 3H), OH signals were not observed; ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 140.2, 139.0, 137.1, 127.3, 124.6, 115.0, 114.9, 60.5, 39.9, 37.8, 35.0, 26.7, 26.2, 21.6, 18.7, 18.0, 9.2; IR (neat) 3437, 2932, 1451, 1294, 1097, 1006, 907 cm^{-1}; HRMS *m/z* (ESI) calcd for $C_{18}H_{26}O_3$ $[M+1]^+$, required: 291.1955, found: 291.1949.

4.1.10. (5*R*,8*S*)-5,6,7,8-Tetrahydro-4-methoxy-3,8-dimethyl-5-((*S*)-6-methylhept-5-en-2-yl)naphthalene-1,2-dione (15). A solution of diol **14** (50 mg, 0.17 mmol) in CH_3CN (5 mL) was cooled to 0 °C. A solution of cerium ammonium nitrate (254 mg, 0.46 mmol, 2.7 equiv) in distilled water (4 mL) was added by syringe. The reaction mixture was stirred at 0 °C for 5 min. The red reaction mixture was quenched with water (10 mL) and extracted with Et_2O (2×40 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting 13% ether/pentane) gave the *title compound* (41 mg, 84%) as an orange red oil. ^{1}H NMR (500 MHz, benzene-d_6) δ 5.68 (m, 1H), 5.02–4.98 (m, 2H), 3.03 (s, 3H), 2.91 (m, 1H), 2.41 (m, 1H), 2.02–1.81 (m, 3H), 1.69 (s, 3H), 1.57–1.48 (m, 1H), 1.44–1.33 (m, 2H), 1.12 (m, 1H), 1.08 (d, J=7.0 Hz, 3H), 0.65 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, benzene-d_6) δ 180.9, 179.5, 166.4, 149.2, 140.5, 138.0, 121.0, 116.0, 60.2, 40.2, 36.8, 36.4, 26.6, 26.1, 21.4, 18.4, 17.4, 9.5; IR (neat) 2959, 1657, 1643, 1578, 1322, 1232, 983 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{18}H_{24}O_3Na$ $[M]^+$, required: 311.1618; found: 311.1614.

4.1.11. (5*S*,8*R*)-5,6,7,8-Tetrahydro-3-hydroxy-2,5-dimethyl-8-((*S*)-pent-4-en-2-yl)naphthalene-1,4-dione. To a solution of *ortho*-quinone **15** (41 mg, 0.14 mmol) in benzene (8 mL) at room temperature under argon was added 4-methylbenzenesulfonic acid monohydrate (54 mg, 0.28 mmol, 2.0 equiv). The mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with ether (50 mL), washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with 2–5% ether/pentane) gave the *title compound* (37 mg, 95%) as yellow oil. $[\alpha]_D^{25}$ 312 (*c* 0.64, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.94 (s, OH, 1H), 5.80 (m, 1H), 5.04–4.98 (m, 2H), 2.95 (m, 1H), 2.89 (m, 1H), 2.09–1.89 (m, 3H), 1.93 (s, 3H), 1.88–1.74 (m, 2H), 1.65–1.57 (m, 1H), 1.51–1.45 (m, 1H), 1.10 (d, J=7.0 Hz, 3H), 0.83 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.9, 182.9, 150.6, 148.1, 143.3, 137.8, 116.9, 115.9, 40.3, 37.0, 35.2, 26.2, 26.0, 20.8, 18.0, 17.6, 8.2; IR (neat) 3383, 2961, 1636, 1340, 1235, 912 cm^{-1}; HRMS *m/z* (EI) calcd for $C_{17}H_{22}O_3$ $[M]^+$, required: 274.1563; found: 274.1564.

4.1.12. Dione (16). To a solution of the above *para*-quinone (22 mg, 0.076 mmol) in DCM (3 mL) at 0 °C under argon were added 2,6-lutidine (25 mg, 0.229 mmol, 3.0 equiv) and TBSOTf (24 mg, 0.092 mmol, 1.2 equiv) successively. The mixture was stirred at 0 °C for 30 min. The reaction mixture was quenched with saturated $NaHCO_3$ (4 mL) and extracted with Et_2O (2×30 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with pure pentane to 1% ether/pentane) gave the *title compound* (26 mg, 91%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.80 (m, 1H), 5.04–4.97 (m, 2H), 2.94 (m, 1H), 2.84 (m, 1H), 2.09–1.90 (m, 3H), 1.93 (s, 3H), 1.87–1.79 (m, 1H), 1.77–1.71 (m, 1H), 1.63–1.58 (m, 1H), 1.48–1.43 (m, 1H), 1.05 (d, J=7.0 Hz, 3H), 0.97 (s, 9H), 0.82 (d, J=7.0 Hz, 3H), 0.30 (s, 3H), 0.23 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 188.8, 183.2, 152.3, 145.5, 144.7, 138.0, 124.4, 115.8, 40.3, 36.7, 34.9, 26.2, 26.1, 25.8 (3C), 20.9, 19.0, 18.0, 17.5, 9.0, −3.9, −4.0; IR (neat) 2956, 1658, 1234, 1165, 836 cm^{-1}; HRMS *m/z* (ESI) calcd for $C_{23}H_{36}O_3Si$ $[M+1]^+$, required: 389.2506; found: 389.2506.

4.1.13. (+)-*p*-Benzoquinone (4). To a solution of terminal olefin **16** (15 mg, 0.038 mmol) in DCM (2 mL) were added 2-methyl-3-buten-2-ol (20 μL, 0.193 mmol, 5.00 equiv) and Grubbs' second-generation catalyst (3.3 mg, 0.0038 mmol, 0.10 equiv). The red reaction mixture was refluxed for 12 h then directly filtered through a pipette column, eluting with 13% ether/pentane to give a yellow oil.

To a solution of the above crude product in THF (4 mL) at 0 °C under argon was added TBAF (38 μL, 0.038 mmol, 1.0 M solution in THF, 1.0 equiv). The yellow solution turned out to purple immediately. After 1 min, the reaction mixture was quenched with saturated H_2O (4 mL) and extracted with Et_2O (2×30 mL). The combined extracts were washed with water and brine, dried over Na_2SO_4, and concentrated. Purification by column chromatography on silica gel (eluting with 13–25% ether/pentane) gave the *title compound* **4** (7.7 mg, 60% over two steps) as a yellow oil. $[\alpha]_D^{25}$ 270 (*c* 0.40, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.95 (s, OH, 1H), 5.62 (m, 2H), 2.95 (br q, J=7.0 Hz, 1H), 2.89 (br t, J=4.5 Hz, 1H), 2.04–1.91 (m, 2H), 1.92 (s, 3H), 1.91–1.79

(m, 2H), 1.78–1.73 (m, 1H), 1.65–1.57 (m, 1H), 1.50–1.45 (m, 1H), 1.30 (s, 6H), 1.10 (d, J=7.0 Hz, 3H), 0.82 (d, J=7.0 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 187.9, 182.9, 150.7, 148.1, 143.3, 139.6, 126.2, 116.8, 70.6, 38.5, 37.4, 35.3, 29.8, 29.7, 26.2, 26.0, 20.8, 18.2, 17.6, 8.2; HRMS m/z (EI) calcd for $C_{20}H_{28}O_4$ $[M]^+$, required: 332.1982; found: 332.1982.

Acknowledgements

This work was supported by the National Science Foundation (CHE-0350536). We thank Professor Steven Diver for valuable discussion about the metathesis reaction conditions and Professor Russell Kerr for helpful discussions about the natural product **3**.

Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2006.05.086.

References and notes

1. For a general review on the isolation, synthesis, and biosynthesis of these natural products, see: Heckrodt, T. J.; Mulzer, J. *Top. Curr. Chem.* **2005**, *244*, 1–42.
2. For Colombiasin A, see: (a) isolation: Rodriguez, A. D.; Ramirez, C. *Org. Lett.* **2000**, *2*, 507–510; for total synthesis: (b) Nicolaou, K. C.; Vassilikogiannakis, G.; Magerlein, W.; Kranich, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 2482–2486; (c) Nicolaou, K. C.; Vassilikogiannakis, G.; Magerlein, W.; Kranich, R. *Chem.—Eur. J.* **2001**, *7*, 5359–5371; (d) Kim, A. I.; Rychnovsky, S. D. *Angew. Chem., Int. Ed.* **2003**, *42*, 1267–1270; (e) Harrowven, D. C.; Pascoe, D. D.; Demurtas, D.; Bourne, H. O. *Angew. Chem., Int. Ed.* **2005**, *44*, 1221–1222; (f) Boezio, A. A.; Jarvo, E. R.; Lawrence, B. M.; Jacobsen, E. N. *Angew. Chem., Int. Ed.* **2005**, *44*, 6046–6050; (g) Davies, H. M. L.; Dai, X.; Long, M. L. *J. Am. Chem. Soc.* **2006**, *128*, 2485–2490.
3. For Elisapterosin B, see: (a) isolation: Rodriguez, A. D.; Ramirez, C.; Rodriguez, I. I.; Barnes, C. L. *J. Org. Chem.* **2000**, *65*, 1390–1398; for total synthesis: (b) Waizumi, N.; Stankovic, A. R.; Rawal, V. H. *J. Am. Chem. Soc.* **2003**, *125*, 13022–13023; Refs. 2d–g.
4. For Erogorgiaene, see: (a) isolation: Rodriguez, A. D.; Ramirez, C. *J. Nat. Prod.* **2001**, *64*, 100–102; for total synthesis: (b) Cesati, R. R.; Armas, J. D.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2004**, *126*, 96–101; (c) Davies, H. M. L.; Walji, A. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 1733–1735; for formal synthesis: (d) Harmata, M.; Hong, X. *Tetrahedron Lett.* **2005**, *46*, 3847–3849.
5. For total synthesis of Elisabethin A, see: (a) Heckrodt, T. J.; Mulzer, J. *J. Am. Chem. Soc.* **2003**, *125*, 4680–4681; for review: (b) Zanoni, G.; Franzini, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 4837–4841.
6. For Pseudopteroxazole, see: (a) Johnson, T. W.; Corey, E. J. *J. Am. Chem. Soc.* **2001**, *123*, 4475–4479; (b) Davidson, J. P.; Corey, E. J. *J. Am. Chem. Soc.* **2003**, *125*, 13486–13489; (c) Harmata, M.; Hong, X.; Barnes, C. L. *Org. Lett.* **2004**, *6*, 2201–2203; (d) Harmata, M.; Hong, X. *Org. Lett.* **2005**, *7*, 3581–3583.
7. For recent reviews: (a) Davies, H. M. L.; Beckwith, R. E. J. *Chem. Rev.* **2003**, *103*, 2861–2903; (b) Davies, H. M. L.; Oystein, L. *Synthesis* **2004**, *16*, 2595–2608.
8. (a) Davies, H. M. L.; Beckwith, R. E. J.; Antoulinakis, E. G.; Jin, Q. *J. Org. Chem.* **2003**, *68*, 6126–6132; (b) Davies, H. M. L.; Antoulinakis, E. G. *Org. Lett.* **2000**, *2*, 4153–4156.
9. (a) Davies, H. M. L.; Hansen, T.; Hopper, D. W.; Panaro, S. A. *J. Am. Chem. Soc.* **1999**, *121*, 6509–6510; (b) Davies, H. M.; Venkataramani, C. *Org. Lett.* **2001**, *3*, 1773–1775; (c) Davies, H. M. L.; Venkataramani, C. *Angew. Chem., Int. Ed.* **2002**, *41*, 2197–2199; (d) Davies, H. M. L.; Jin, Q. *Org. Lett.* **2004**, *6*, 1769–1772.
10. Davies, H. M. L.; Ren, P. *J. Am. Chem. Soc.* **2001**, *123*, 2070–2071.
11. Davies, H. M. L.; Yang, J.; Nikolai, J. *J. Organomet. Chem.* **2005**, *690*, 6111–6124.
12. (a) Davies, H. M. L.; Gregg, T. M. *Tetrahedron Lett.* **2002**, *43*, 4951–4953; (b) Davies, H. M. L.; Walji, A. M.; Townsend, R. J. *Tetrahedron Lett.* **2002**, *43*, 4981–4983; (c) Davies, H. M.; Ren, P.; Jin, Q. *Org. Lett.* **2001**, *3*, 3587–3590.
13. (a) Davies, H. M. L.; Jin, Q. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5472–5475; (b) Davies, H. M. L.; Jin, Q. *J. Am. Chem. Soc.* **2004**, *126*, 10862–10863.
14. For isolation: Ata, A.; Kerr, R. G.; Moya, C. E.; Jacobs, R. S. *Tetrahedron* **2003**, *59*, 4215–4222.
15. For isolation: Rodriguez, A. D.; Shi, Y.-P. *Tetrahedron* **2000**, *56*, 9015–9023.
16. Ata, A.; Kerr, R. G. *Tetrahedron Lett.* **2000**, *41*, 5821–5825.
17. (a) Look, S. A.; Fenical, W.; Matsumoto, G. K.; Clardy, J. *J. Org. Chem.* **1986**, *51*, 5140–5145; (b) Look, S. A.; Fenical, W.; Jacobs, R. S.; Clardy, J. *Proc. Natl. Acad. Sci. U.S.A.* **1986**, *83*, 6238–6240; (c) Roussis, V.; Wu, Z.; Fenical, W. *J. Org. Chem.* **1990**, *55*, 4916–4922.
18. Tohma, H.; Morioka, H.; Harayama, Y.; Hashizume, M.; Kita, Y. *Tetrahedron Lett.* **2001**, *42*, 6899–6902.
19. Snyder, C. D.; Rapoport, H. *J. Am. Chem. Soc.* **1972**, *94*, 227–231.
20. Dehmel, F.; Schmalz, H.-G. *Org. Lett.* **2001**, *3*, 3579–3582.
21. Private communications with Professor Russell G. Kerr and Dr. Athar Ata.
22. Grieco, P. A.; Gilman, S.; Nishizawa, M. *J. Org. Chem.* **1976**, *41*, 1485–1486.