Enantiospecific Syntheses of (+)-Crotepoxide, (+)-Boesenoxide, (+)-*β*-Senepoxide, (+)-Pipoxide Acetate, (−)-*iso*-Crotepoxide, (−)-Senepoxide, and (−)-Tingtanoxide from (−)-Quinic Acid[1]

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A convenient strategy that is ideally suited for the construction of all the naturally occurring cyclohexane diepoxides and cyclohexene epoxides is described. The key intermediate **12**, a 1,3-cyclohexadiene, has been prepared from (−)-quinic acid in 11 steps with 18% overall yield. Singlet oxygen photooxygenation of the 1,3-cyclohexadiene followed by rearrangement of the resultant endoperoxides with either cobalt-*meso*-tetraphenylporphyrin or trimethyl phosphite afforded enantiopure (+)-crotepoxide, (+)-boesenoxide, and (−)-*iso*-crotepoxide or (−)-senepoxide, (+)-*β*-senepoxide, (+)-pipoxide acetate, and (−)-tingtanoxide, respectively.

1. Introduction

Naturally occurring cyclohexane epoxides,[2,3] which belong to a small family of heavily oxygenated cyclohexane derivatives, have attracted considerable attention from the natural product and synthetic chemists due to their unusual structures, biogenesis, and biological activity. (+)-Crotepoxide (**1**)[4] and the recently discovered (+)-boesenoxide (**2**)[5] are members which possess a bisepoxide functionality. (+)-Crotepoxide (**1**) was first discovered by Kupchan *et al.* from the fruits of *Croton macrostachys*[4] and then by Takahashi from *Piper futokadzura*[6] and has been shown to display significant tumor-inhibitory activity against Lewis lung carcinoma in mice (LL) and Walker intramuscular carcinosarcoma in rats (WM).[7]

At roughly the same time, cyclohexene epoxides (+)-pipoxide (**4**) and (−)-senepoxide (**7**) were isolated from *Piper hookeri*[8] and *Uvaria catocarpa*,[9] respectively, and also exhibited interesting biological properties including tumor-inhibitory, antileukemic, and antibiotic activity. The constitution and the absolute configurations of **1**,[10] **4**,[11] and **7**[12] were conclusively established by X-ray crystallography. Recently, two additional oxiranes, (+)-*β*-senepoxide (**3**) and (−)-tingtanoxide (**8**), were discovered.[13] The absolute configurations of crotepoxide (**1**), (+)-boesenoxide (**2**), (+)-*β*-senepoxide (**3**), (+)-pipoxide (**4**), and (+)-pipoxide acetate (**5**) are similar to that of (1*R*,6*S*)-cyclophellitol whereas the absolute configurations of (−)-senepoxide (**7**), (−)-tingtanoxide (**8**), and nonnatural *iso*-crotepoxide (**6**) are related to that of cyclophellitol. (1*R*,6*S*)-Cyclophellitol[14] and cyclophellitol[15] have been demonstrated to be potent *β*-D- and α-D-glucosidase inhibitors, respectively, presumably attributable to the structural resemblance to *β*-D- and α-D-glucose (Figure 1).

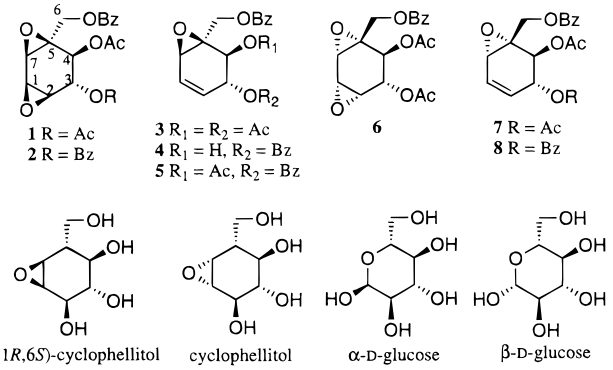

Figure 1. Configurational relationship between cyclohexane/cyclohexene epoxides and monosaccharides.

Most of the earlier syntheses of cyclohexane diepoxides afforded racemic material. Approaches toward (±)-crotepoxide (**1**) were based on transformations from a quinone,[16] a 1,4-cyclohexadiene[17] or a styrene derivative.[18] The first approach was also used to obtain (±)-senepoxide (**7**),[19] and the second approach afforded *iso*-

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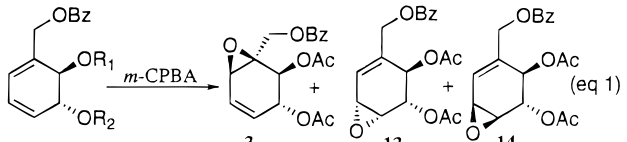
crotepoxide (**6**),[17] (±)-senepoxide (**7**),[20] (±)-*β*-senepoxide (**3**),[20] and (±)-pipoxide (**4**).[11] A Diels−Alder route was employed by Schlessinger to synthesize (±)-senepoxide (**7**) and to provide formal syntheses of (±)-crotepoxide (**1**) and (±)-pipoxide (**4**).[21] Recently, Ogawa et al. published the syntheses of enantiopure crotepoxide (**1**),[22] (+)-*β*-senepoxide (**3**),[23] and (+)-pipoxide (**4**)[23] from (1*S*)-*endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid,[24] a chemically resolved Diels−Alder adduct of furan and acrylic acid.

Our own quest for a general, flexible, and efficient entry to cyclohexane epoxides from (−)-quinic acid (**24**) has already produced cyclophellitol and its diastereomers.[25] In continuation with our investigation into the preparation of potential glycosidase inhibitors,[1,25] we now report facile syntheses of (+)-crotepoxide (**1**), (+)-boesenoxide (**2**), (+)-*β*-senepoxide (**3**), (+)-pipoxide acetate (**5**), (−)-*iso*-crotepoxide (**6**), (−)-senepoxide (**7**), and (−)-tingtanoxide (**8**) and hence further demonstrate the versatility of quinic acid in the fabrication of heavily oxygenated cyclohexanoid natural products. A preliminary account on the construction of **1** and **6** has appeared.[26]

2. Results and Discussion

2.1. Antithetic Analysis and Strategy. All the target molecules share two common stereogenic centers at C-3,4. Compounds **1**, **2**, and **6** are bisepoxides whereas the others are monoepoxides. Crotepoxide (**1**), boesenoxide (**2**), *β*-senepoxide (**3**), and pipoxide acetate (**5**) as a group are distinct from the group comprising *iso*-crotepoxide (**6**), senepoxide (**7**), and tingtanoxide (**8**) by the epoxide stereochemistry, i.e., the former group has *β*-epoxide(s) while the latter has α-epoxide(s). Retrosynthetically, diene **9** with suitable protecting groups was believed to be the key intermediate for the construction of cyclohexane epoxides if we can epoxidize the alkene moiety regio- and stereoselectively.

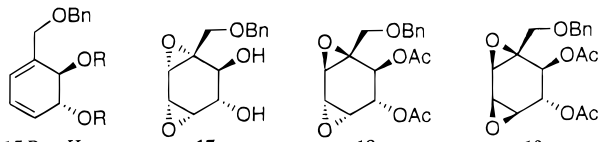
According to literature reports, direct transformation of diene **9** into the target molecules by peracid oxidation posed numerous problems. Ogawa[23] subjected diene **10** to *m*-CPBA and obtained *β*-senepoxide (**3**) together with monoepoxide isomers **13** and **14** in poor yields (eq 1).



9 $R_1 = R_2$ = protecting gp
10 $R_1 = R_2$ = Ac
11 $R_1 = R_2$ = H
12 R_1 =Ac, R_2 = TBDMS

3 (19%) **13** (24%) **14** (14%)

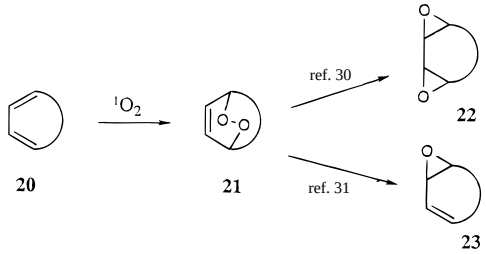
However, the oxirane moiety in senepoxide (**7**) could not be constructed directly via this method. Attempts to prepare crotepoxide (**1**) by direct introduction of the *cis*-1,2:3,4-bisepoxy function to the diene using peracid were also unsuccessful. White[17] found that benzyl diene **15** reacted with *tert*-butyl hydroperoxide in the presence of $VO(acac)_2$ as catalyst to give α-bisepoxide **17** stereospecifically, albeit in 15% yield. Using *m*-CPBA even under the forcing conditions devised by Kishi, a mixture of *trans*-bisepoxide **18** and *β*-*cis*-bisepoxide **19** was obtained from diacetyl diene **16** in a total yield of 55% and in a ratio of 8:1, respectively.[27] Hence, the fabrication of the bisepoxide functionality from **9** using the classical approach does not appear to be efficient and convenient.



15 R = H
16 R = OAc

17 **18** **19**

Singlet oxygen photooxygenation[28] seems to be the solution to construct the target molecules (Figure 2). Fundamentally, 1,4-cycloaddition of singlet oxygen to a cyclic diene results in the formation of a bicyclic endoperoxide (**20** → **21**).[29] This cycloadduct provides an excellent opportunity to form the *cis*-bisepoxide functionality by metal complex catalyzed rearrangement (**21** → **22**).[30]



20 **21** **22** **23**

Figure 2. Synthetic strategy.

On the other hand, the reduction of endoperoxide by phosphite provides a facile entry to unsaturated monoepoxides (**21** → **23**).[31] The earlier work by White[17] and by Ganem[20] further convinced us that photooxygenation of diene **9** should be an attractive route to cyclohexane diepoxides. The synthetic problem is now reduced to the choice of suitable hydroxy blocking groups (R_1 and R_2) for diene **9**. Analysis of the structure of all the target molecules reveals that R_1 should be an acetyl group in order to shorten the synthetic route. Since diacetate **10** could not be oxidized under the singlet oxygen photooxygenation conditions,[17] R_2 was not recommended to be an acyl group. Finally, we decided to employ diene **12** with R_2 being a silyl group as our key intermediate.

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2.2. Synthesis of Key Intermediate 12. Our previous work has shown that (−)-quinic acid (**24**) could be transformed into the alcohol **25** in seven steps with an overall yield of 47%.[32] Standard benzoylation of **25** in pyridine (pyr) furnished silyl benzoate **26** smoothly in quantitative yield (eq 2). In another approach, through a shorter sequence of functional group manipulation, silyl benzoate **26** could be elaborated from diol **27** which in turn could be derived, in four steps, also from (−)-quinic acid (**24**) according to our previous endeavor.[33]

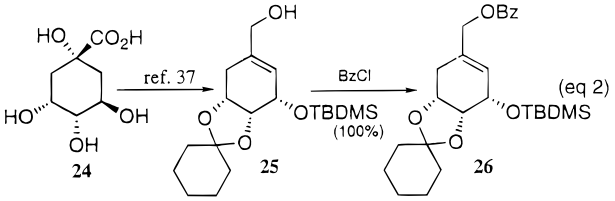
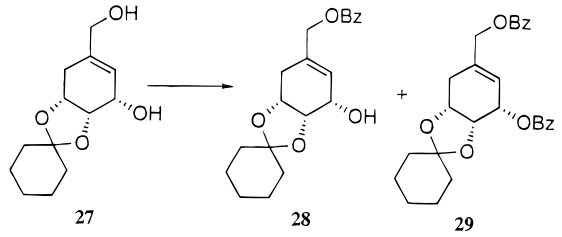


Table 1 summarizes the results of the regioselective benzoylation of the primary hydroxy group in diol **27**. Dibenzoate **29** was identified and isolated as the sole side product. The best result (Table 1, entry 4) of obtaining monobenzoate **28** was by treating diol **27** with 1 equiv of benzoyl chloride and 3 equiv of collidine in dry dichloromethane at −78 °C for 3 h and then at room temperature for another 1 h.

Table 1. Regioselective Benzoylation of 27

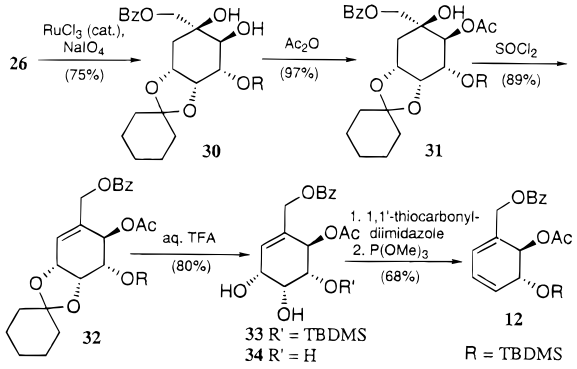


entry	reagents	conditions	isolated yield, %
1	1 equiv of BzCl + 2 equiv of pyr	0 °C	trace **28** 44% **29**
2	1 equiv of BzCl + 2 equiv of Im[34]	10 °C	55% **28** 20% **29**
3	1 equiv of BzCl + 2 equiv of Im	−78 °C → 25 °C	20% **28** 34% **29**
4	1 equiv of BzCl + 3 equiv of collidine[35]	−78 °C → 25 °C	82% **28** 5% **29**

Silylation of the remaining alcohol afforded the desired silyl benzoate **26** in 97% yield. According to this improved procedure, we could shorten the synthetic route by two steps together with an increase of 4% overall yield from quinic acid.

At this stage, we had to transform the silyl benzoate **26** into alkene **12**. The double bond in **26** was subjected to our recently developed ruthenium-catalyzed flash dihydroxylation protocol at the less hindered convex face (β-face) of the bicyclic skeleton to give, exclusively, the desired β-diol **30** in 75% yield (Scheme 1).[36] Alternatively, alkene **26** could be dihydroxylated with a catalytic amount of osmium tetraoxide,[37] leading to **30** as the sole product in the same yield. Selective acetylation of the secondary hydroxy group in **30** gave monoacetate **31**. Through this two-step conversion (**26** → **30** → **31**), the OAc group at C-2 with the correct stereochemistry was established.

Scheme 1



With tertiary alcohol **31** at hand, we set out to prepare alkene **32** via a suitable dehydration protocol. Several literature methods were studied such as phosphorus oxychloride ($POCl_3$)[38] and Martin sulfurane dehydrating agent {$[PhC(CF_3)_2O]_2S(Ph)_2$}.[39] However, these one-pot reactions were found ineffective. The former gave decomposition products while the latter yielded only a trace amount of alkene **32**. Gratifyingly, we discovered that the traditional method of reacting alcohol **31** with thionyl chloride in pyridine[40] at room temperature furnished alkene **32** in good yields. This procedure initially proved inefficient on a large scale (>1 g) (usually the yield decreased from 81% to 50%). We had overcome this problem by slow addition of a solution of alcohol **31** to a mixture of 1.5 equiv of thionyl chloride and 10 equiv of pyridine in dry dichloromethane at 0 °C, followed by stirring the reaction mixture for 12 h at room temperature. The best result obtained by this protocol on a 10 g scale was 86% yield.

Selective hydrolysis of the cyclohexylidene ketal in **32** with 50% aqueous trifluoroacetic acid in dichloromethane afforded vicinal diol **33**. The workup was best conducted after 6 h, and the reaction showed only 95% conversion. Prolonging the reaction time resulted in the isolation of triol **34** as the side product which became the sole product after hydrolysis for 12 h at room temperature. Corey−Winter[41] deoxygenation of the vicinal diol moiety in **33** provided the key intermediate diene **12** that now possessed the functionality required for the bisoxirane formation via a singlet oxygen photooxidation reaction.[29,42]

2.3. Syntheses of (+)-Crotepoxide (1), (+)-Boesenoxide (2), and (−)-*iso*-Crotepoxide (6). The photoen-

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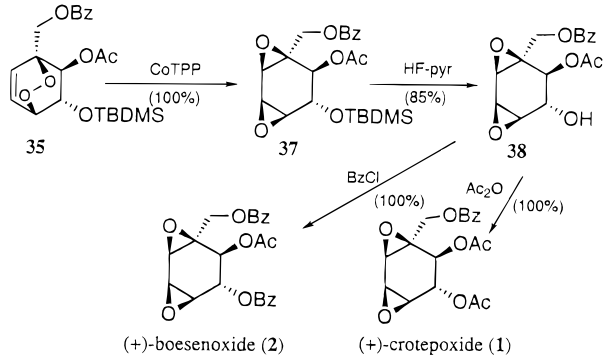
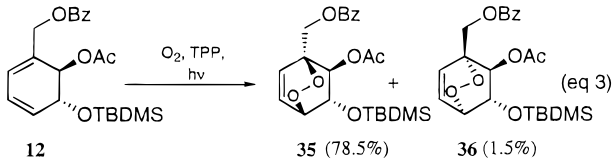
Scheme 2



doperoxidation reaction[42] was set up as follows: diene **12** was mixed with a catalytic amount (substrate:catalyst, ca. 1000:1) of the sensitizer tetraphenylporphyrin (TPP) in carbon tetrachloride (singlet oxygen has a long lifetime in CCl_4)[43] at 0 °C. Oxygen gas was bubbled into the solution. After 3 min, the reaction mixture was illuminated with a projection lamp (450 W) for 5 h. A mixture of endoperoxides **35** and **36** in a respective ratio of 54:1 was obtained, readily separable by flash chromatography (eq 3). On the basis of the spectral data, we



were unable to assign the stereochemistry of the compounds at this stage. The exact stereochemistry was determined by converting the endoperoxides into the target molecules. As expected, the photooxidation of **12** proceeded selectively at the less hindered β-face, giving the β-endoperoxide **35** as the preponderant product. The high diastereoselectivity (**35**:**36** = 54:1) indicated that it was highly efficient to use the *tert*-butyldimethyl silyl ether as the stereodirecting group in the endoperoxidation. Subjection of the endoperoxide **35** to the cobalt-*meso*-tetraphenylporphyrin (CoTPP) catalyzed rearrangement reaction[44] at 0 °C gave smoothly the bisepoxide **37** in essentially quantitative yield.

With the bisepoxide in hand, we should obtain the target molecules simply by desilylation and esterification (Scheme 2). Exposure of bisepoxide **37** to pyridinium hydrogen fluoride[45] resulted in the cleavage of the silyl ether, providing alcohol **38** in 85% yield. Finally, acetylation of the free alcohol in **38** yielded crotepoxide (**1**), mp 146−148 °C (Et_2O−hexane) (lit.[4] mp 150−151 °C); $[\alpha]^{26}_D$ = +71.9 (*c* = 0.6, $CHCl_3$) {lit.[4] $[\alpha]^{25}_D$ = +74 (*c* = 1.7, $CHCl_3$)}. On the other hand, benzoylation of **38** furnished, for the first time, optically active boesenoxide (**2**), mp 169−170 °C (Et_2O-hexane) (lit.[5] mp 171−172 °C); $[\alpha]^{20}_D$ = +34.9 (*c* = 0.1, $CHCl_3$) {lit.[5] $[\alpha]^{20}_D$ = +35.0 (*c* = 0.1, $CHCl_3$)}. The first enantiospecific synthesis of optically active *iso*-crotepoxide (**6**) could be realized along

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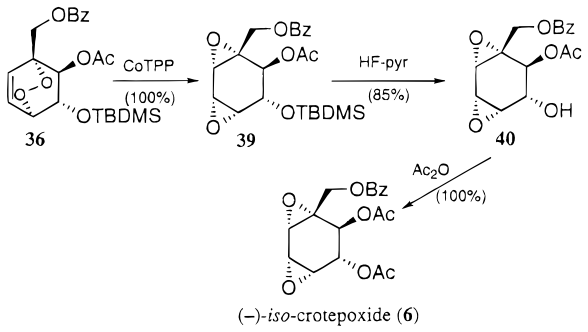
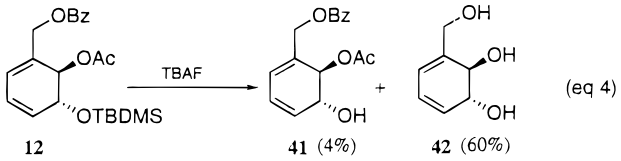
Scheme 3

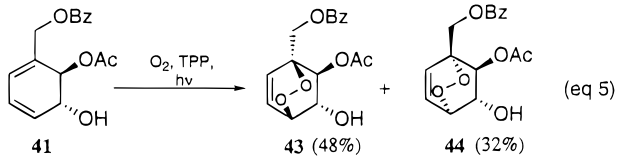


a similar line as shown in Scheme 3. The α-endoperoxide **36** underwent CoTPP catalyzed rearrangement without incidence to the α-bisepoxide **39** in quantitative yield. Desilylation of **39** gave alcohol **40** that was acetylated to yield *iso*-crotepoxide (**6**) as an oil: $[\alpha]^{27}_D$ = −35.8 (*c* = 0.7, $CHCl_3$). The ^{1}H NMR spectral data were in close agreement with the reported values[17] of racemic **6**.

As expected, the high stereoselectivity of photooxygenation of diene **12** does not provide an efficient route to cyclohexane epoxides having an α-epoxide moiety. To remedy this situation, we needed to find an alternative avenue, and diene **41** should be a suitable intermediate for the photooxidation. Initial attempts to desilylate the diene **12** with TBAF in THF or HF−pyridine in acetonitrile resulted in 4% of monoalcohol **41** and 60% of the undesired triol **42** with the former protocol (eq 4). The

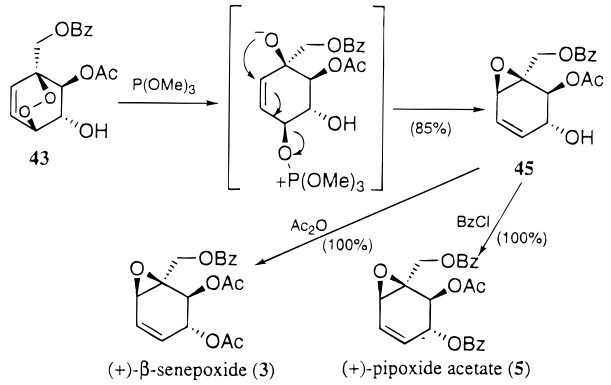


latter procedure led to the recovery of most of the starting material together with only a trace amount of the desired alcohol **41**. The best result of desilylation of **12** was achieved with 48% aqueous HF in acetonitrile, providing the alcohol **41** exclusively in 80% yield. Acetylation of alcohol **41** led to the benzoyl diacetate diene **10**. Surprisingly, photooxygenation of **10** could not be effected. In another report,[17] it was found that benzyl ether diacetate **16** was also unreactive toward singlet oxygen. Presumably, the presence of two electron-withdrawing groups (acetate) diminished the nucleophilicity of the diene toward photoendoperoxidation. Photooxygenation of diene−alcohol **41** was successful and gave a mixture of β-endoperoxide **43** and α-endoperoxide **44** in a ratio of 3:2 (eq 5). It is noteworthy that in the absence of the

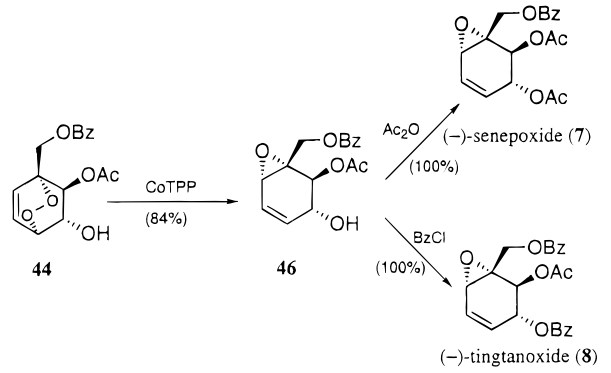


bulky silyl group at C-2 production of the α-endoperoxide becomes significant. The mixture of endoperoxides could be separated by flash chromatography. On treatment with a catalytic amount of CoTPP, β-endoperoxide **43** rearranged smoothly to the corresponding bisepoxide **38**, which was identical to the product of desilylation of bisepoxide **37**. This bisepoxide **38** was also converted into

Scheme 4



Scheme 5



crotepoxide (**1**) and bosenoxide (**2**). In a similar manner, treatment of α-endoperoxide **44** with CoTPP followed by acetylation of the resulting α-bisoxirane furnished *iso*-crotepoxide (**6**) (Scheme 3).

2.4. Syntheses of the (+)-*β*-Senepoxide (3), (+)-Pipoxide Acetate (5), (−)-Tingtanoxide (8), and (−)-Senepoxide (7). With the *β*-endoperoxide **43** in hand, we conducted reductive rearrangement[29b] using trimethyl phosphite in benzene to give cyclohexene epoxide **45** exclusively in 85% yield (Scheme 4). It is noteworthy that this reaction is highly regio- and stereoselective, and none of the regio- or stereoisomer was isolated.

Having established all the requisite stereocenters, we then acetylated the alcohol in cyclohexene epoxide **45** to give (+)-*β*-senepoxide (**3**); mp 69−71 °C (Et_2O−hexane) (lit.[13] mp 72−73 °C); $[\alpha]^{20}_D = +62.9$ ($c = 0.1$, $CHCl_3$) {lit.[13] $[\alpha]^{25}_D = +62.0$ ($c = 0.6$, $CHCl_3$)}. On the other hand, benzoylation of the alcohol in **45** gave (+)-pipoxide acetate (**5**): mp 172−173 °C (Et_2O−hexane) (lit.[13] mp 171−172 °C); $[\alpha]^{20}_D = +8.9$ ($c = 1.0$, $CHCl_3$) {lit.[13] $[\alpha]^{28}_D = +9.0$ ($c = 4.4$, $CHCl_3$)}.

The α-endoperoxide **44** was treated with trimethyl phosphite in a similar manner, furnishing cyclohexene epoxide **46** in 85% yield. Standard acetylation of **46** afforded target molecule (−)-senepoxide (**7**): mp 85−86 °C (Et_2O−hexane) (lit.[9] mp 85 °C); $[\alpha]^{20}_D = -194.6$ ($c = 0.2$, $CHCl_3$) {lit.[9] $[\alpha]^{25}_D = -197.0$ ($c = 1.2$, $CHCl_3$)}. Benzoylation of **46** provided (−)-tingtanoxide (**8**): mp 69−71 °C (Et_2O−hexane) (lit.[13] mp 72−73 °C); $[\alpha]^{20}_D = -303$ ($c = 0.1$, $CHCl_3$) {lit.[13] $[\alpha]^{28}_D = -306$ ($c = 6.3$, $CHCl_3$)} respectively (Scheme 5).

3. Conclusions

In conclusion, (+)-crotepoxide (**1**) and (+)-boesenoxide (**2**) were synthesized from (−)-quinic acid (**24**) via photoendoperoxidation of diene **12** in 15 steps with 9% overall yields. On the other hand, (−)-*iso*-crotepoxide (**6**) was prepared from (−)-quinic acid (**24**) via photooxygenation of diene **41** in 15 steps with 3% overall yield. (+)-Pipoxide acetate (**5**) and (+)-*β*-senepoxide (**3**) were constructed from (−)-quinic acid (**24**) via rearrangement of *β*-endoperoxide **43** in 15 steps with 6% overall yield in each case. On the other hand, (−)-senepoxide (**7**) and (−)-tingtanoxide (**8**) were fabricated from (−)-quinic acid (**24**) via rearrangement of α-endoperoxide **44** in 15 steps with 3% overall yield. Enantiospecific syntheses of (+)-boesenoxide (**2**), (−)-*iso*-crotepoxide (**6**), (−)-senepoxide (**7**), and (−)-tingtanoxide (**8**) are reported for the first time.

4. Experimental Section

Melting points are reported in degrees Celsius and are uncorrected. Optical rotations were measured at 589 nm. IR spectra were recorded on a FT-IR spectrometer as thin films on NaCl disks. Unless stated to the contrary, NMR spectra were measured in solutions of $CDCl_3$ at 250 MHz (^1H) or at 62.9 MHz (^{13}C). Spin−spin coupling constants (*J*) were measured directly from the spectra. Carbon and hydrogen elemental analyses were carried out at either the Shanghai Institute of Organic Chemistry, The Chinese Academy of Sciences, China, or the MEDAC Ltd., Department of Chemistry, Brunel University, Uxbridge, U.K. All reactions were monitored by analytical TLC on aluminum precoated with silica gel $60F_{254}$ (E. Merck), and compounds were visualized with a spray of either 5% w/v dodecamolybdophosphoric acid in ethanol or 5% v/v concentrated sulfuric acid in ethanol and subsequent heating. All columns were packed wet using E. Merck silica gel 60 (230−400 mesh) as the stationary phase and eluted using flash39 chromatographic technique. Pyridine was distilled over barium oxide and stored in the presence of potassium hydroxide pellets. THF was distilled from sodium benzophenone ketyl under a nitrogen atmosphere. CH_2Cl_2 was distilled over phosphorus pentoxide and stored in the presence of 4 Å molecular sieves. Other reagents were purchased from commercial suppliers and were used without purification.

(+)-Crotepoxide (1). To a solution of the alcohol **38** (320 mg, 1.0 mmol), TEA (312 μL, 2.0 mmol), and a catalytic amount of DMAP in dry CH_2Cl_2 (50 mL) was added acetic anhydride (104 μL, 1.1 mmol) at room temperature. The solution was stirred at room temperature for 12 h and poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 2:1) provided (+)-crotepoxide (**1**) (362 mg, 100%) as a white solid: mp 146−148 °C (lit.[4] mp 150−151 °C); $R_f = 0.50$ (Et_2O−hexane, 4:1); $[\alpha]^{26}_D$ +71.9 ($c = 0.6$, $CHCl_3$) (lit.[4] $[\alpha]^{25}_D$ +74 ($c = 1.7$, $CHCl_3$); IR (thin film) 1725, 1750 cm^{-1}; ^1H NMR δ 2.03 (3H, s), 2.13 (3H, s), 3.11 (1H, dd, $J = 1.6$, 3.9 Hz), 3.46 (1H, dd, $J = 2.7$, 3.9 Hz), 3.67 (1H, d, $J = 2.7$ Hz), 4.24 (1H, d, $J = 12.1$ Hz), 4.58 (1H, d, $J = 12.1$ Hz), 4.99 (1H, dd, $J = 1.6$, 9.0 Hz), 5.71 (1H, d, $J = 9.0$ Hz), 7.47 (2H, t, $J = 7.1$ Hz), 7.57 (1H, t, $J = 7.6$ Hz), 8.02 (2H, d, $J = 7.0$ Hz); ^{13}C NMR δ 20.6, 48.0, 52.6, 53.8, 59.4, 62.5, 69.5, 70.4, 128.6, 129.2, 129.8, 133.5, 165.8, 169.7, 170.0.

(+)-Boesenoxide (2). To a solution of the alcohol **38** (160 mg, 0.5 mmol), TEA (156 μL, 1.0 mmol), and a catalytic amount of DMAP in dry CH_2Cl_2 (20 mL) was added benzoyl chloride (70 μL, 0.6 mmol) at room temperature. The solution was stirred at room temperature for 12 h and poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (EtOAc−hexane, 1:2) provided (+)-boseneoxide (**2**) (362 mg, 100%) as a white solid: mp 169−170 °C (lit.[5] mp 171−172 °C); $R_f = 0.62$ (EtOAc−hexane, 1:1); $[\alpha]^{20}_D$ +34.9 ($c = 0.1$, $CHCl_3$)

(lit.[5] $[\alpha]^{20}_D$ +35.0 (c = 0.1, $CHCl_3$); IR (thin film) 1725, 1745 cm^{-1}; ^1H NMR δ 2.07 (3H, s), 3.20 (1H, dd, J = 1.6, 3.9 Hz), 3.48 (1H, dd, J = 2.7, 3.9 Hz), 3.72 (1H, d, J = 2.7 Hz), 4.28 (1H, d, J = 12.0 Hz), 4.62 (1H, d, J = 12.0 Hz), 5.17 (1H, dd, J = 1.6, 9.5 Hz), 5.95 (1H, d, J = 9.5 Hz), 7.43 (4H, m), 7.59 (2H, m), 8.04 (4H, m); ^{13}C NMR δ 21.3, 48.9, 53.7, 54.6, 60.5, 63.1, 70.1, 71.9, 129.3, 129.8, 130.5, 134.2, 166.2, 166.5, 170.7.

(+)-*β*-Senepoxide (3). Following the same procedure as for acetylation of **38**, cyclohexene oxide **45** (30 mg, 0.1 mmol) gave a quantitative yield of (+)-*β*-senepoxide (**3**) as a white solid, after fractionation by flash chromatography (Et_2O−hexane, 2:1): mp 69−71 °C (lit.[13] mp 72−73 °C); R_f = 0.54 (EtOAc−hexane, 1:1); $[\alpha]^{20}_D$ +62.9 (c = 0.1, $CHCl_3$) (lit.[13] $[\alpha]^{25}_D$ +62 (c = 0.55, $CHCl_3$); IR (thin film), 1747 cm^{-1}; ^1H NMR δ 2.05 (3H, s), 2.14 (3H, s), 3.58 (1H, dd, J = 1.9, 4.1 Hz), 4.37 (1H, d, J = 12.1 Hz), 4.63 (1H, d, J = 12.0 Hz), 5.56 (1H, dt, J = 2.0, 8.3 Hz), 5.68 (1H, d, J = 8.4 Hz), 5.77 (1H, dt, J = 2.0, 9.9 Hz), 6.07 (1H, dt, J = 2.0, 10.1 Hz),7.46 (2H, t, J = 6.4 Hz), 7.57 (1H, t, J = 7.1 Hz), 8.03 (2H, d, J = 7.1 Hz); ^{13}C NMR δ 20.7, 20.9, 54.5, 58.3, 62.2, 71.3, 124.1, 128.5, 129.3, 129.8, 133.4, 165.8, 170.2.

Pipoxide Acetate (5). Following the same procedure as for benzoylation of **38**, cyclohexene oxide **45** (30 mg, 0.1 mmol) gave a quantitative yield of pipoxide acetate (**5**) as a colorless oil, after fractionation by flash chromatography (Et_2O−hexane, 1:1): R_f = 0.58 (Et_2O−hexane, 1:1); $[\alpha]^{20}_D$ +8.9 (c = 1.3, $CHCl_3$) (lit.[13] $[\alpha]^{28}_D$ +9.0 (c = 4.4, $CHCl_3$); IR (thin film), 1732 cm^{-1}; ^1H NMR δ 2.11 (3H, s), 3.63 (1H, dd, J = 1.9, 3.8 Hz), 4.42 (1H, d, J = 12.1 Hz), 4.68 (1H, d, J = 12.0 Hz), 5.89 (1H, ddd, J = 1.7, 4.2, 6.9 Hz), 5.92 (1H, m), 6.09 (1H, ddd, J = 2.6, 3.8, 9.9 Hz), 7.46 (4H, m), 7.57 (2H, m), 8.04 (4H, m); ^{13}C NMR δ 20.6, 54.5, 58.4, 62.3, 71.2, 72.2, 124.3, 128.5, 129.5, 129.6, 129.8, 133.3, 133.6, 165.8, 170.1.

(−)-*iso*-Crotepoxide (6). Following the same procedure as for the acetylation of **38**, the alcohol **40** (21 mg, 0.07 mmol) gave a quantitative yield of (−)-*iso*-crotepoxide (**6**) as a colorless oil, after fractionation by flash chromatography (Et_2O−hexane, 4:1): R_f = 0.45 (EtOAc−hexane, 1:1); $[\alpha]^{27}_D$ −35.8 (c = 0.7, $CHCl_3$); IR (thin film), 1720 cm^{-1}; ^1H NMR δ 2.00 (3H, s), 2.11 (3H, s), 3.42 (1H, d, J = 4.0 Hz), 3.50 (1H, d, J = 2.7 Hz), 3.57 (1H, dd, J = 2.7, 4.0 Hz), 4.39 (2H, ABq, J = 12.3 Hz), 5.36 (2H, s), 7.47 (2H, t, J = 6.4 Hz), 7.60 (1H, t, J = 7.1 Hz), 8.02 (2H, d, J = 7.1 Hz); ^{13}C NMR δ 20.4, 20.7, 47.9, 53.1, 53.2, 56.9, 63.1, 68.7, 70.9, 76.0, 128.6, 129.3, 129.7, 133.5, 165.8, 169.4, 170.4; HRMS calcd for $C_{18}H_{19}O_8$ 363.1080 (HM^+), found 363.1072 (HM^+).

(−)-Senepoxide (7). Following the same procedure as for the preparation of **1**, cyclohexene oxide **46** (30 mg, 0.1 mmol) gave a quantitative yield of (−)-senepoxide (**7**) as a white solid, after fractionation by flash chromatography (Et_2O−hexane, 2:1): mp 85−86 °C (lit.[9] mp, 85 °C); R_f = 0.55 (EtOAc−hexane, 1:1); $[\alpha]^{20}_D$ −194.6 (c = 0.2, $CHCl_3$) (lit.[9] $[\alpha]^{25}_D$ −197 (c = 1.2, $CHCl_3$); IR (thin film), 1732 cm^{-1}; ^1H NMR δ 2.07 (3H, s), 2.10 (3H, s), 3.47 (1H, d, J = 3.3 Hz), 4.25 (1H, d, J = 12.5 Hz), 4.85 (1H, d, J = 12.5 Hz), 5.19 (1H, dd, J = 2.0, 5.6 Hz), 5.59 (1H, d, J = 1.3 Hz),6.09 (1H, dd, J = 4.9, 9.3 Hz), 6.39 (1H, dd, J = 3.9, 10.0 Hz), 7.47 (2H, t, J = 6.4 Hz), 7.58 (1H, t, J = 7.1 Hz), 8.06 (2H, d, J = 7.1 Hz); ^{13}C NMR δ 20.6, 20.9, 49.7, 61.6, 64.0, 67.3, 67.6, 128.5, 128.9, 129.0, 129.6, 129.8, 133.3, 166.0, 170.0.

(−)-Tingtanoxide (8). Following the same procedure as for benzoylation of **38**, cyclohexene oxide **46** (30 mg, 0.1 mmol) gave a quantitative yield of (−)-tingtanoxide (**8**) as a colorless oil, after fractionation by flash chromatography (Et_2O−hexane, 1:1): mp 69−71 °C (Et_2O−hexane) (lit.[13] mp 72−73 °C); R_f = 0.69 (EtOAc−hexane, 1:1); $[\alpha]^{20}_D$ −303 (c = 1.0, $CHCl_3$) (lit.[13] $[\alpha]^{28}_D$ −306 (c = 6.3, $CHCl_3$); IR (thin film), 1732 cm^{-1}; ^1H NMR δ 2.09 (3H, s), 3.53 (1H, d, J = 3.7 Hz), 4.33 (1H, d, J = 12.5 Hz), 4.86 (1H, d, J = 12.5 Hz), 5.46 (1H, dd, J = 2.5, 5.5 Hz), 5.74 (1H, d, J = 0.8 Hz), 6.19 (1H, dd, J = 4.8, 9.2 Hz), 6.43 (1H, dd, J = 4.0, 9.9 Hz), 7.46 (4H, m), 7.57 (2H, m), 8.04 (4H, m); ^{13}C NMR δ 20.7, 50.1, 61.6, 64.5, 67.2, 67.6, 124.6, 128.5, 129.1, 129.2, 129.8, 133.3, 133.5, 165.9, 170.0.

(3*R*,4*R*)-4-*O*-Acetyl-5-(benzoyloxymethyl)-3-*O*-(*tert*-butyldimethylsilyl)cyclohexa-1,5-diene-3,4-diol (12). To a solution of the diol **33** (109 mg, 0.25 mmol) in toluene (25 mL) was added 1,1′-thiocarbonyldiimidazole (66.7 mg, 0.37 mmol) in three equal portions within 3 h. The mixture was heated under reflux for 24 h and filtered through a thin layer pad of silica gel. Removal of the solvent from the filtrate under reduced pressure gave a yellow oil. Without further purification, the oil was dissolved in trimethyl phosphite (25 mL) and the solution was heated under reflux for 24 h. Solvent removal under reduced pressure followed by flash chromatography (Et_2O−hexane, 1:10) provided the diene **12** (68.5 mg, 68%) as a colorless oil: R_f = 0.43 (Et_2O−hexane, 1:6); $[\alpha]^{22}_D$ −2.5 (c = 28.9, $CHCl_3$); IR (thin film) 1724 cm^{-1}; ^1H NMR δ 0.07 (6H, s) 0.87 (9H, s), 2.02 (3H, s), 4.48 (1H, ddd, J = 1.3, 3.5, 8.0 Hz), 4.85 (2H, s), 5.80 (1H, dd, J = 1.0, 8.0 Hz), 5.86 (1H, m), 5.98 (1H, ddd, J = 1.4, 5.3, 9.7 Hz), 6.17 (1H, dt, J = 1.1, 5.3 Hz), 7.44 (2H, t, J = 6.4 Hz), 7.54 (1H, t, J = 7.5 Hz), 8.04 (2H, d, J = 8.3 Hz); MS m/z (relative intensity) 402 (M^+, 1). Anal. Calcd for $C_{22}H_{30}O_5Si$: C, 65.64; H, 7.51. Found: C, 66.04; H, 7.68.

(1*R*,2*R*,3*S*)-5-(Benzoyloxymethyl)-3-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-cyclohexylidenee-4-cyclohexen-1,2,3-triol (26). A solution of allylic alcohol **28** (344 mg, 1.0 mmol), imidazole (136 mg, 2.0 mmol), *tert*-butyldimethylsilyl chloride (181 mg, 1.2 mmol), and a catalytic amount of DMAP in dry CH_2Cl_2 (50 mL) was stirred at room temperature for 12 h. The mixture was poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 1:10) provided the title compound **26** (445 mg, 97%) as a colorless oil: R_f = 0.57 (Et_2O−hexane, 1:4); $[\alpha]^{26}_D$ +13.7 (c = 1.7, $CHCl_3$); IR (thin film) 1722 cm^{-1}; ^1H NMR δ 0.13 (6H, s), 0.93 (9H, s), 1.36−1.60 (10H, m), 2.02 (1H, d, J = 16.0 Hz), 2.44 (1H, d, J = 16.0 Hz), 4.20 (1H, s), 4.41 (1H, m), 4.51 (1H, m), 4.76 (2H, s), 5.89 (1H, br s), 7.42 (2H, t, J = 7.6 Hz), 7.54 (1H, t, J = 6.9 Hz), 8.06 (2H, d, J = 7.4 Hz); ^{13}C NMR δ 4.5 (×2), 18.3, 23.6, 23.9, 25.3, 25.8, 25.9, 29.9, 33.9, 35.7, 67.1, 69.3, 72.5, 77.2, 109.1, 128.2, 129.5, 129.6, 129.9, 130.2, 131.7, 132.7, 166.1; MS m/z (relative intensity) 458 (M^+, 4.3). Anal. Calcd for $C_{26}H_{38}O_5Si$: C, 68.09; H, 8.35. Found: C, 67.85; H, 8.27.

(1*R*,2*R*,3*S*)-5-(Benzoyloxymethyl)-1,2-*O*-cyclohexylidene-4-cyclohexene-1,2,3-triol (28). To a solution of the diol **27** (240 mg, 1.0 mmol) and collidine (263 μL, 2.0 mmol) in dry CH_2Cl_2 (50 mL) at −78 °C was added a solution of benzoyl chloride (115 μL, 1.0 mmol) in 10 mL of CH_2Cl_2 dropwise over 5 min. The reaction mixture was allowed to warm to room temperature and stirred for 2 h. The resulting mixture was then poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 2:1) provided the benzoate **28** (282 mg, 82%) as a white solid: R_f = 0.62 (Et_2O−hexane, 4:1); $[\alpha]^{26}_D$ +13.7 (c = 1.7, $CHCl_3$); IR (thin film) 1721, 3489 cm^{-1}; ^1H NMR δ 1.36−1.60 (10H, m), 2.04 (1H, d, J = 15.8 Hz), 2.24 (1H, d, J = 14.9 Hz), 2.47 (1H, d, J = 16.0 Hz), 3.88 (1H, s), 4.49 (2H, br s), 4.76 (2H, t, J = 13.7 Hz), 5.91 (br s, 1H), 7.42 (2H, t, J = 7.6 Hz), 7.54 (1H, t, J = 6.9 Hz), 8.06 (2H, d, J = 7.4 Hz); MS (FAB) m/z (relative intensity) 344 (M^+, 3). Anal. Calcd for $C_{20}H_{24}O_5$: C, 69.75; H, 7.02. Found: C, 69.76, H, 6.87.

(1*R*,2*R*,3*S*,4*S*,5*S*)-5-(Benzoyloxymethyl)-3-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-cyclohexylidenecyclohexane-1,2,3,4,5-pentol (30). To a vigorously stirred solution of the alkene **26** (459 mg, 1.0 mmol) in EtOAc−CH_3CN (6 mL−6 mL) at 0 °C (ice−water bath) was added a solution of $RuCl_3 \cdot 3H_2O$ (19 mg, 0.07 mmol) and $NaIO_4$ (320 mg, 1.5 mmol) in distilled water (2 mL). The biphasic mixture was stirred vigorously for 3 min and quenched with saturated aqueous $Na_2S_2O_3$ (10 mL). The aqueous phase was separated and extracted with EtOAc (3 × 15 mL). The combined organic extracts were dried ($MgSO_4$) and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 1:2) afforded the diol **30** (370 mg, 75%) as a white solid: mp 116−117 °C; R_f = 0.31

(Et_2O−hexane, 1:2); $[\alpha]^{26}_D$ −22.2 (c = 1.6, $CHCl_3$); IR (thin film) 1724, 3473 cm^{-1}; ^1H NMR δ 0.15 (3H, s), 0.16 (3H, s), 0.94 (9H, s), 1.38−1.75 (10H, m), 1.83 (1H, ddd, J = 1.85, 8.45, 14.2 Hz), 2.13 (1H, dd, J = 6.2, 14.2 Hz), 2.60 (1H, d, J = 1.8), 2.62 (1H, d, J = 2.25 Hz), 3.91 (1H, dd, J = 2.25, 9.45 Hz), 4.07 (1H, dd, J = 3.75, 9.45 Hz), 4.25 (1H, d, J = 11.2 Hz), 4.27−4.40 (m, 3H, m), 7.44 (2H, t, J = 7.75 Hz), 7.57 (1H, t, J = 6.0 Hz), 8.05 (2H, d, J = 5.1 Hz); ^{13}C NMR δ −4.3, −4.4, 18.2, 23.7, 24.1, 25.1, 25.9, 35.0, 35.5, 38.2, 68.8, 70.5, 71.2, 72.0, 73.3, 76.3, 109.9, 128.4, 129.7, 130.0, 133.1, 166.5; MS m/z (relative intensity) 493 (M^+, 2). Anal. Calcd for $C_{26}H_{40}O_7Si$: C, 63.38; H, 8.18. Found: C, 63.38; H, 8.21.

(1*R*,2*R*,3*R*,4*S*,5*S*)-4-*O*-Acetyl-5-(benzoyloxymethyl)-3-*O*-(*tert*-butyl-dimethylsilyl)-1,2-*O*-cyclohexylidenecyclohexane-1,2,3,4,5-pentol (31). To a solution of the diol **30** (493 mg, 1.0 mmol), pyridine (172 μL, 2.0 mmol), and a catalytic amount of DMAP in dry CH_2Cl_2 (50 mL) was added acetic anhydride (104 μL, 1.1 mmol) at room temperature. The solution was stirred at room temperature for 12 h and poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 1:2) provided monoacetate **31** (519 mg, 97%) as a colorless oil: R_f = 0.31 (Et_2O−hexane, 1:1); $[\alpha]^{26}_D$ −19.1 (c = 1.0, $CHCl_3$); IR (thin film) 1725, 1750, 3448 cm^{-1}; ^1H NMR δ 0.13 (3H, s), 0.17 (3H, s), 0.86 (9H, s), 1.38−1.75 (10H, m), 2.05 (3H, s), 2.21−2.32 (2H, m), 2.62 (1H, br s), 4.05 (1H, d, J = 11.5 Hz), 4.26−4.42 (4H, m), 5.39 (1H, d, J = 9.13 Hz), 7.44 (2H, t, J = 7.75 Hz), 7.57 (1H, t, J = 6.0 Hz), 8.05 (2H, d, J = 5.1 Hz); MS m/z (relative intensity) 535 (M^+, 3). Anal. Calcd for $C_{28}H_{42}O_8Si$: C, 62.89; H, 7.92. Found: C, 63.13; H, 8.23.

(1*R*,2*R*,3*S*,4*R*)-4-*O*-Acetyl-5-(benzoyloxymethyl)-3-*O*-(*tert*-butyldimethylsilyl)-1,2-*O*-cyclohexylidene-5-cyclohexene-1,2,3,4-tetraol (32). To a solution of thionyl chloride (0.89 mL, 12.0 mmol) in dry CH_2Cl_2 (600 mL) at 0 °C was added dropwise a solution of tertiary alcohol **31** (5.35 g, 10.0 mmol) in dry CH_2Cl_2 (200 mL) and pyridine (2.58 mL, 30.0 mmol) for 2.5 h at 0 °C. The resultant mixture was stirred for 12 h at room temperature and poured into a solution of saturated aqueous NH_4Cl (100 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 100 mL), and the combined organic extracts were washed with brine (100 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 1:4) provided the alkene **32** (4.60 g, 89%) as a colorless oil: R_f = 0.66 (Et_2O−hexane, 1:2); $[\alpha]^{26}_D$ +45.5 (c = 1.0, $CHCl_3$); IR (thin film) 1721 cm^{-1}; ^1H NMR δ 0.13 (3H, s), 0.17 (3H, s), 0.89 (9H, s), 1.38−1.75 (10H, m), 2.07 (3H, s), 3.97 (1H, dd, J = 2.3, 8.3 Hz), 4.39 (1H, m), 4.62 (1H, m), 4.76 (2H, br s), 5.81 (1H, m), 5.92 (1H, d, J = 8.3 Hz), 7.44 (2H, t, J = 7.75 Hz), 7.53 (1H, t, J = 6.0 Hz), 8.04 (2H, d, J = 5.1 Hz); MS m/z (relative intensity) 517 (M^+, 2). Anal. Calcd for $C_{28}H_{40}O_7Si$: C, 65.09; H, 7.80. Found: C, 64.70; H, 8.04.

(1*R*,2*R*,3*S*,4*R*)-4-*O*-Acetyl-5-(benzoyloxymethyl)-3-*O*-(*tert*-butyl-dimethylsilyl)-5-cyclohexene-1,2,3,4-tetrol (33). To a solution of compound **32** (517 mg, 1.0 mmol) in CH_2Cl_2 (25 mL) was added 2 mL of 50% aqueous TFA. The mixture was stirred vigorously at room temperature for 6 h and poured into an aqueous solution of $NaHCO_3$ (10 mL, 5% w/v). The aqueous phase was extract with CH_2Cl_2 (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 2:1) provided the title compound **33** (331 mg, 80%) as a white solid with 95% conversion: mp 79−80 °C (Et_2O−hexane); R_f = 0.43 (Et_2O−hexane, 3:1); $[\alpha]^{26}_D$ −66.7 (c = 1.5, $CHCl_3$); IR (thin film) 3450, 1724 cm^{-1}; ^1H NMR δ 0.16 (6H, s), 0.87 (9H, s), 2.01 (3H, s), 2.68 (1H, d, J = 11.6 Hz), 2.91 (1H, d, J = 9.2 Hz), 3.87 (1H, ddd, J = 2.2, 4.7, 9.2 Hz), 4.08 (1H, t, J = 2.5 Hz), 4.15 (1H, m), 4.81 (2H, s), 5.45 (1H, d, J = 3.4 Hz), 6.34 (1H, d, J = 4.8 Hz), 7.42 (2H, t, J = 6.5 Hz), 7.58 (1H, t, J = 5.9 Hz), 8.06 (2H, d, J = 7.0 Hz); MS m/z (relative intensity) 437 (M^+, 1). Anal. Calcd for $C_{22}H_{32}O_7Si$: C, 60.53; H, 7.39. Found: C, 60.32; H, 7.30.

Silylated β-Endoperoxide 35 and Silylated α-Endoperoxide 36. Oxygen was bubbled through a solution of the diene **12** (402 mg, 1.0 mmol) in CCl_4 (70 mL) at 0 °C containing a catalytic amount (0.1 mol %) of 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine (0.6 mg, 1 × 10^{-3} mmol). After 5 min, the reaction mixture was irradiated with 450 W projection lamp for 7 h and poured into a thin layer pad of silica gel. Removal of the solvents under reduced pressure followed by flash chromatography (Et_2O−hexane, 1:5) gave 339.8 mg of β-endoperoxide **35** and 6.3 mg of α-endoperoxide **36** as colorless oils (80%). The ratio of **35** to **36** (ca. 54:1) was determined by the isolated yields. Pure compounds were obtained by flash chromatography. The less polar **35** was obtained as a colorless oil: R_f = 0.45 (Et_2O−hexane, 1:3); ^1H NMR δ 0.07 (6H, s), 0.86 (9H, s), 2.17 (3H, s), 4.14 (1H, dd, J = 1.4, 2.0 Hz), 4.41 (1H, d, J = 12.0 Hz), 4.52 (1H, d, J = 12.0 Hz), 4.56 (1H, m), 4.84 (1H, d, J = 1.5 Hz), 6.71 (2H, m), 7.45 (2H, m), 7.55 (1H, t, J = 7.3 Hz), 8.04 (2H, d, J = 7.3 Hz). The more polar **36** was obtained as a colorless oil: R_f = 0.27 (Et_2O−hexane, 1:3); ^1H NMR δ 0.07 (6H, s), 0.86 (9H, s), 2.17 (3H, s), 3.69 (1H, s), 4.47 (1H, d, J = 12.9 Hz), 4.59 (2H, m), 5.20 (1H, s), 6.46 (1H, d, J = 8.3 Hz), 6.79 (1H, dd, J = 6.3, 8.2 Hz), 7.45 (2H, t, J = 7.4 Hz), 7.56 (1H, t, J = 7.2 Hz), 8.04 (2H, d, J = 7.1 Hz).

Silylated β-Bisepoxide 37. A solution of the β-endoperoxide **35** (109 mg, 0.25 mmol) in $CHCl_3$ (10 mL) was added 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine cobalt(II) (0.7 mg, 1 × 10^{-3} mmol) at 0 °C. The reaction was stirred for 3 h and poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 1:3) provided the bisepoxide **37** (109 mg, 100%) as a white solid: mp 68−71 °C; R_f = 0.50 (Et_2O−hexane, 1:1); $[\alpha]^{22}_D$ +38.7 (c = 3.4, $CHCl_3$); IR (thin film) 1725 cm^{-1}; ^1H NMR δ 0.07 (3H, s), 0.08 (3H, s), 0.85 (9H, s), 2.17 (3H, s), 3.07 (1H, dd, J = 0.9, 4.0 Hz), 3.40 (1H, dd, J = 2.7, 4.0 Hz), 3.61 (1H, d, J = 2.5 Hz), 3.90 (1H, dd, J = 1.4, 9.1 Hz), 4.23 (1H, d, J = 12.1 Hz), 4.51 (1H, d, J = 12.1 Hz), 5.58 (1H, d, J = 9.2 Hz), 7.46 (2H, t, J = 7.3 Hz), 7.58 (1H, t, J = 7.2 Hz), 8.02 (2H, d, J = 7.1 Hz); HRMS calcd for $C_{22}H_{30}O_7SiNa$ 457.1653 (NaM^+), found 457.1692 (NaM^+).

β-Bisepoxide 38. (a) From 37. To a solution of the silylated bisepoxide **37** (44 mg, 0.1 mmol) in THF (10 mL) was added 3 drops of pyridinium fluoride (pH = 5). The reaction was stirred vigorously for 12 h and quenched with saturated NH_4Cl (5 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 5 mL), and the combined organic extracts were washed with brine (5 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (Et_2O−hexane, 1:1) provided the title compound **38** (27 mg, 84%) as a white solid: mp 134−136 °C; R_f = 0.27 (EtOAc−hexane, 1:1); $[\alpha]^{25}_D$ +75.8 (c = 0.3, $CHCl_3$); IR (thin film) 3300, 1722 cm^{-1}; ^1H NMR δ 2.17 (3H, s), 2.63 (1H, d, J = 5.5 Hz), 3.03 (1H, m), 3.18 (1H, dd, J = 1.3, 2.7 Hz), 3.43 (1H, dd, J = 2.7, 3.8 Hz), 3.63 (1H, dd, J = 2.7 Hz), 3.97 (1H, ddd, J = 1.3, 5.5, 6.8 Hz), 4.23 (1H, d, J = 12.1 Hz), 4.60 (1H, d, J = 12.1 Hz), 5.47 (1H, d, J = 8.8 Hz), 7.46 (2H, t, J = 7.3 Hz), 7.57 (1H, t, J = 7.2 Hz), 8.02 (2H, d, J = 7.1 Hz); HRMS calcd for $C_{16}H_{16}O_7Na$ 343.0784 (NaM^+), found 343.0787 (NaM^+).

(b) From 43. Following the same procedure as for α-endoperoxide rearrangement of **37**, β-endoperoxide **43** (32 mg, 0.1 mmol) gave a quantitative yield of β-bisepoxide **38** as a white solid, after flash chromatography (Et_2O−hexane, 4:1).

Silylated α-Bisepoxide 39. Following the same procedure as for 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine cobalt(II) mediated rearrangement of **35**, the α-endoperoxide **36** (11 mg, 0.03 mmol) gave α-bisepoxide **39** (11 mg, 100%) as a colorless oil, after fractionation by flash chromatography (Et_2O−hexane, 1:2): R_f = 0.32 (Et_2O−hexane, 1:1); $[\alpha]^{22}_D$ −48.1 (c = 0.8, $CHCl_3$); IR (thin film) 1726 cm^{-1}; ^1H NMR δ 0.07 (3H, s), 0.09 (3H, s), 0.87 (9H, s), 2.17 (3H, s), 3.25 (1H, d, J = 4.0 Hz), 3.40 (1H, d, J = 2.7 Hz), 3.48 (1H, dd, J = 2.8, 4.0 Hz), 4.22 (2H, m), 4.46 (1H, d, J = 12.3 Hz), 5.18 (1H, d, J = 9.8 Hz),

7.47 (2H, t, J = 7.3 Hz), 7.60 (1H, t, J = 7.2 Hz), 8.01 (2H, d, J = 7.1 Hz); HRMS calcd for $C_{22}H_{30}O_7SiNa$ 457.1653 (NaM^+), found 457.1606 (NaM^+).

α-Bisepoxide 40. Following the same procedure as for the α-endoperoxide rearrangement of **37**, α-endoperoxide **44** (21 mg, 0.07 mmol) gave a quantitative yield of α-bisepoxide **40** as a white solid, after flash chromatography (Et_2O−hexane, 4:1): mp 131−133 °C; R_f = 0.50 (EtOAc−hexane, 4:1); $[\alpha]^{22}_D$ −47.7 (c = 0.9, $CHCl_3$); IR (thin film) 3430, 1722 cm^{-1}; ^1H NMR δ 2.08 (3H, s), 2.65 (1H, d, J = 12.3 Hz), 3.32 (1H, dd, J = 3.8, 4.9 Hz), 3.59 (1H, dd, J = 2.7, 3.7 Hz), 3.64 (1H, d, J = 2.8 Hz), 4.11 (1H, dt, J = 4.7, 11.0 Hz), 4.26 (1H, d, J = 12.6 Hz), 4.61 (1H, d, J = 12.7 Hz), 5.37 (1H, d, J = 4.5 Hz),7.43 (2H, t, J = 7.4 Hz), 7.58 (1H, t, J = 7.2 Hz), 8.03 (2H, d, J = 7.1 Hz); HRMS calcd for $C_{16}H_{16}O_7Na$ 343.0784 (NaM^+), found 343.0797 (NaM^+).

(3*R*,4*R*)-4-*O*-Acetyl-5-(benzoyloxymethyl)cyclohexa-1,5-diene-3,4-diol (41). A solution of diene **12** (100 mg, 0.25 mmol) in CH_3CN (10 mL) was added a drop of 48% aqueous HF. The solution was stirred vigorously at room temperature for 6 h and poured into a pad of silica gel. Removal of the solvents under reduced pressure followed by flash chromatography (Et_2O−hexane, 2:1) afforded the alcohol **41** (64 mg, 80%) as a colorless oil: R_f = 0.31 (Et_2O−hexane, 2:1); $[\alpha]^{24}_D$ −150 (c = 0.3, $CHCl_3$); {lit.[2] $[\alpha]^{24}_D$ −150 (c = 1.2, $CHCl_3$)}; IR (thin film) 3417, 1728 cm^{-1}; ^1H NMR δ 2.06 (3H, s), 2.35 (1H, br s), 4.48 (1H, m), 4.90 (2H, dd, J = 13.4, 17.4, Hz), 5.73 (1H, dd, J = 7.1 Hz), 6.03 (2H, ddd, J = 3.7, 9.5, 12.5 Hz), 6.22 (1H, m), 7.44 (2H, t, J = 6.4 Hz), 7.54 (1H, t, J = 7.5 Hz), 8.04 (2H, d, J = 8.3 Hz).

***β*-Endoperoxide 43 and α-Endoperoxide 44.** Following the same procedure as for the endoperoxidation of **12**, diene **41** (8.2 mg, 0.02 mmol) gave a mixture of β- and α-endoperoxides as colorless oils, after fractionation by flash chromatography (Et_2O−hexane, 1:1): The less polar β-endoperoxide **43** was obtained (4.0 mg, 48%) as a colorless oil: R_f = 0.40 (EtOAc−hexane, 1:1); ^1H NMR δ 2.21 (3H, s), 3.30 (1H, d, J = 2.4 Hz), 4.08 (1H, s), 4.21 (1H, d, J = 1.4 Hz), 4.55 (1H, d, J = 12.2 Hz), 4.64 (1H, d, J = 12.2 Hz), 4.77 (1H, t, J = 4.5 Hz), 6.77 (2H, m), 7.47 (2H, m), 7.60 (1H, t, J = 7.3 Hz), 8.03 (2H, d, J = 7.3 Hz). The more polar α-endoperoxide **44** was obtained (2.6 mg, 32%) as a colorless oil: R_f = 0.33 (EtOAc−hexane, 1:1); ^1H NMR δ 2.06 (3H, s), 3.34 (1H, br s), 3.60 (1H, br s), 4.57 (1H, d, J = 12.6 Hz), 4.66 (1H, d, J = 12.8 Hz), 4.81 (2H, m), 6.43 (1H, d, J = 8.4 Hz), 6.81 (1H, dd, J = 6.5, 8.3 Hz),7.45 (2H, t, J = 7.4 Hz), 7.56 (1H, t, J = 7.2 Hz), 8.04 (2H, d, J = 7.1 Hz).

Cyclohexene Epoxide 45. A solution of the α-endoperoxide **43** (32 mg, 0.1 mmol) in benzene (10 mL) was added 5 drops of trimethyl phosphite. The reaction was reflux for 12 h and poured into saturated aqueous NH_4Cl (10 mL). The aqueous phase was extracted with CH_2Cl_2 (3 × 10 mL), and the combined organic extracts were washed with brine (10 mL), dried ($MgSO_4$), and filtered. Concentration of the filtrate followed by flash chromatography (EtOAc−hexane, 1:2) provided the oxirane **45** (26 mg, 85%) as a white solid: mp 88−89 °C; R_f = 0.34 (EtOAc−hexane, 1:1); $[\alpha]^{20}_D$ +57.7 (c = 0.4, $CHCl_3$); IR (thin film) 3441, 1725 cm^{-1}; ^1H NMR δ 2.22 (3H, s), 3.55 (1H, t, J = 3.3 Hz), 4.36 (1H, d, J = 12.0 Hz), 4.42 (1H, s), 5.36 (1H, d, J = 12.0 Hz), 5.97 (2H, m), 7.46 (2H, t, J = 6.4 Hz), 7.60 (1H, t, J = 7.1 Hz), 8.03 (2H, d, J = 7.1 Hz); HRMS calcd for $C_{16}H_{16}O_6$ 305.1025 (MH^+), found 305.1027 (MH^+).

Cyclohexene Epoxide 46. Following the same procedure as for reductive rearrangement of **45**, α-endoperoxide **44** (32 mg, 0.1 mmol) gave 84% of **46** as a colorless oil, after fractionation by flash chromatography (Et_2O−hexane, 2:1): R_f = 0.40 (EtOAc−hexane, 1:1); $[\alpha]^{20}_D$ −104.4 (c = 0.9, $CHCl_3$); IR (thin film) 3520, 1738 cm^{-1}; ^1H NMR δ 2.06 (3H, s), 2.18 (1H, s br), 3.58 (1H, d, J = 4.0 Hz), 4.06 (1H, dd, J = 3.8, 6.0 Hz), 4.25 (1H, d, J = 12.6 Hz), 4.85 (1H, d, J = 12.6 Hz), 5.62 (1H, d, J = 2.0 Hz), 6.32 (2H, m), 7.47 (2H, t, J = 6.4 Hz), 7.59 (1H, t, J = 7.1 Hz), 8.06 (2H, d, J = 7.1 Hz); HRMS calcd for $C_{16}H_{16}O_6$ 305.1025 (MH^+), found 305.1033 (MH^+).

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