A simple entry into enantiopure hydrindanes, hydroisoquinolones and diquinanes from 3,10-dioxygenated dicyclopentadienes: Application to the synthesis of (+)-coronafacic acid and a formal synthesis of (+)-coriolin

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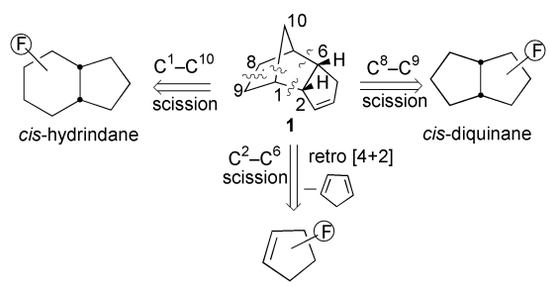
A ready access to enantiopure 3,10-dioxygenated tricyclo[5.2.1.$0^{2,6}$]decane derivatives is reported. An efficient enzymatic kinetic resolution is employed through transesterification in the presence of lipase PS immobilized on Celite. Absolute configuration of the tricyclo[5.2.1.$0^{2,6}$]decan-10-one derivatives has been secured through correlation with (1*R*,2*S*)-1-aminoindan-2-ol. The promising utility of these enantiopure tricyclo[5.2.1.$0^{2,6}$]decane derivatives in synthesis has been demonstrated through the preparation of several optically pure *cis*-hydrindanes **15–18**, employing the Haller–Bauer reaction as the key step for unbridging the trinorbornyl system. The *cis*-hydrindane (−)-**16** has been further elaborated to the natural product (+)-coronafacic acid (+)-**24**. In an interesting sequence, *cis*-hydrindanone (+)-**18** has been transformed into *cis*-hydroisoquinolones (+)-**30** and (+)-**33** *via* photorearrangement of the derived oxaziridines **29** and **32**, respectively. The hydroisoquinolones (+)-**30** and (+)-**33** can serve as useful enantiopure building blocks for the synthesis of complex indole alkaloids. Oxidative cleavage of the trinorbornene double bond in the tricyclo[5.2.1.$0^{2,6}$]decan-10-one derivative (−)-**37** and functional-group adjustments leads to the optically pure diquinane (+)-**38**, an advanced intermediate in the total synthesis of (+)-coriolin (+)-**34**.

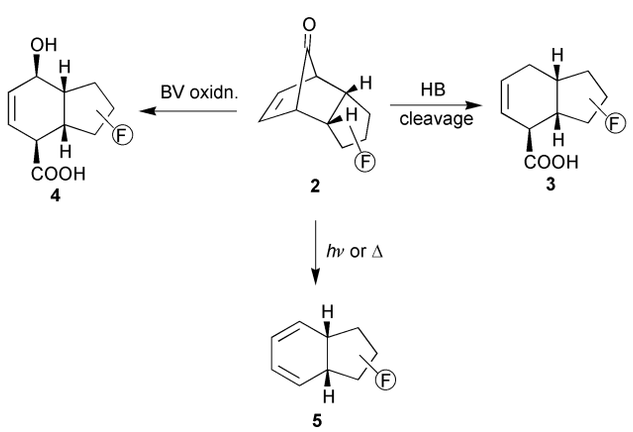
Introduction

Carbocylic-ring construction is an intrinsic component of natural-product synthesis. A range of methodologies based on annulations, cycloadditions (inter- and intramolecular) and cyclizations among others have been developed in this context. Another strategy that has considerable potential to access various carbocyclic frameworks is through restructuring/modification of abundantly and readily available (in some cases commercially available) carbocyclic building blocks. An example of this approach is the utilization of cheap, commercially available *endo*-tricyclo[5.2.1.$0^{2,6}$]deca-3,8-diene (**1**, dicyclopentadiene), a waste product from downstream processing in petroleum refineries and formally a [4 + 2]-dimer of cyclopenta-1,3-diene.[1]

The C_{10}-*endo*-tricylic diene **1** has been extensively explored as a versatile building block in the synthesis of cyclopentanoids and related natural products by many researchers, most notably by the groups of Ogasawara[1a] and Zwanenburg.[1b] The main strategic consideration in the use of **1** has been the installation of the requisite functionalization pattern on the *endo*-disposed five-membered ring in a stereocontrolled manner, taking advantage of its accessibility only from the open *exo*-face, and its retrieval through a retro-Diels–Alder reaction (Scheme 1).[1] However, a limiting aspect of this approach is that half the carbon content and two carbocyclic rings of **1** are inevitably lost during the retro-Diels–Alder reaction-based liberation of the requisite five-membered ring. On the other hand, **1** can also be recognized as a repository of six–five (hydrindane) and five–five (diquinane) fused carbocyclic rings through scission of C1–C10 and C8–C9 bonds, respectively (Scheme 1). The six–five fused ring system can be extracted only when additional functionalization is present on the C10 bridge carbon as in **2** where one can remove the bridge (*e.g.*, C1–C10 cleavage) through several options such as base-mediated Haller–Bauer



Scheme 1



Scheme 2

(H–B) cleavage (**2** ⟶ **3**),[2] Baeyer–Villiger (B–V) oxidation (**2** ⟶ **4**)[3] or thermal or photodecarbonylation (**2** ⟶ **5**)[4] (Scheme 2). Following this strategy, it is possible to extract the *cis*-hydrindane framework with secured stereochemistry at

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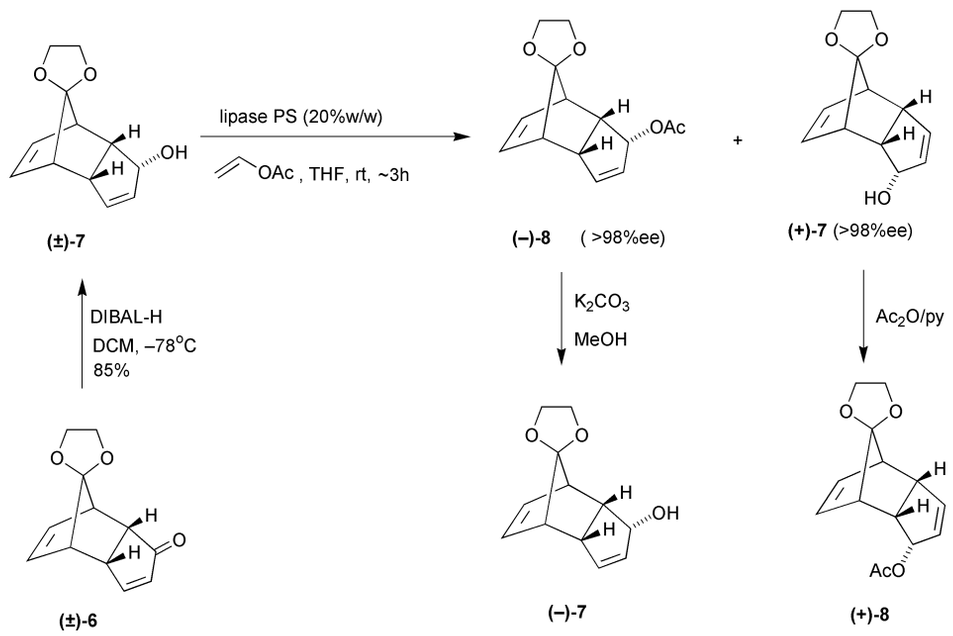


Scheme 3

many centers from the tricyclo[5.2.1.0^{2,6}]decan-8-en-10-one system **2**, fully retaining its carbon content.

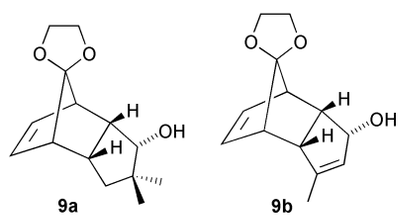
We and others have recently shown that readily and abundantly available *endo*-tricyclo[5.2.1.0^{2,6}]dec-8-en-10-one derivatives, *e.g.* **2**, are important building blocks for the synthesis of natural products based on the *cis*-hydrindane skeleton.[5–12] However, these studies have utilized only the racemic derivatives of **2**. Since the tricyclo[5.2.1.0^{2,6}]decane system possesses intrinsic chirality, there is the prospect of accessing the *cis*-hydrindanes and related systems derived from it in optically active form. Keeping this objective in mind, enzymatic[13] transesterification or hydrolysis was chosen as the preferred approach, among other options, in view of the fact that simple tricyclo[5.2.1.0^{2,6}]decane derivatives, without C10-oxygen functionality, have been shown to be eminently amenable to such resolution.[1] We report here the first enzymatic resolution of the 10-oxygenated *endo*-dicyclopentadiene system and demonstrate its utility in the synthesis of a range of useful enantiomerically pure compounds (EPCs).[14]

Results and discussion

Enzymatic kinetic resolution

After several attempts, it was found that fairly clear-cut kinetic acylation in *endo*-allylic alcohol (±)-**7**, readily available from enone (±)-**6**[15] on reduction with diisobutylaluminium hydride (DIBAL-H), could be effected with vinyl acetate in organic medium and lipase PS on Celite (Amano) to furnish the acetate (−)-**8** (> 98% ee, 44% yield) and alcohol (+)-**7** (> 98% ee, 46% yield). Enantiomeric purities were determined using NMR with chiral shift reagent, and confirmed through comparison (see Experimental section) with literature values.[16] The enantiomeric excess (ee) of alcohol (+)-**7** and acetate (−)-**8** was further cross-checked by converting them into their acetate (+)-**8** and alcohol (−)-**7**, respectively (Scheme 3). To our knowledge, there is only one literature report of enantiopure 5,10-dioxotricyclo[5.2.1.0^{2,6}]decane derivatives, obtained through classical resolution methods, to which absolute configuration was assigned following chiro-optical probes.[16]

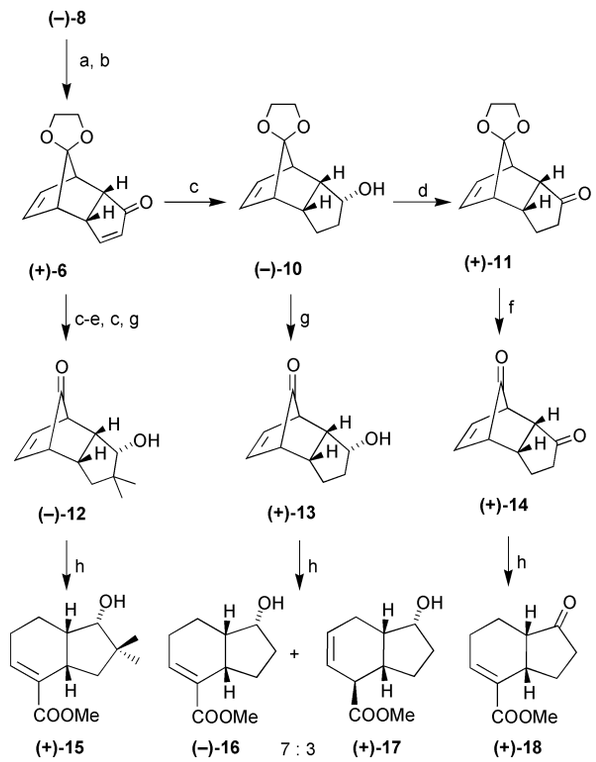
Interestingly, (±)-**7** was the only 10-oxygenated tricyclo[5.2.1.0^{2,6}]decane derivative that was readily resolved by the enzyme used by us. Several other tricyclic alcohol derivatives, such as **9a**, **9b**, (−)-**10** and (+)-**13**[5] with different functionalization in the pendant five-membered ring, were either not accepted by the enzyme or gave poor ees. However, optically



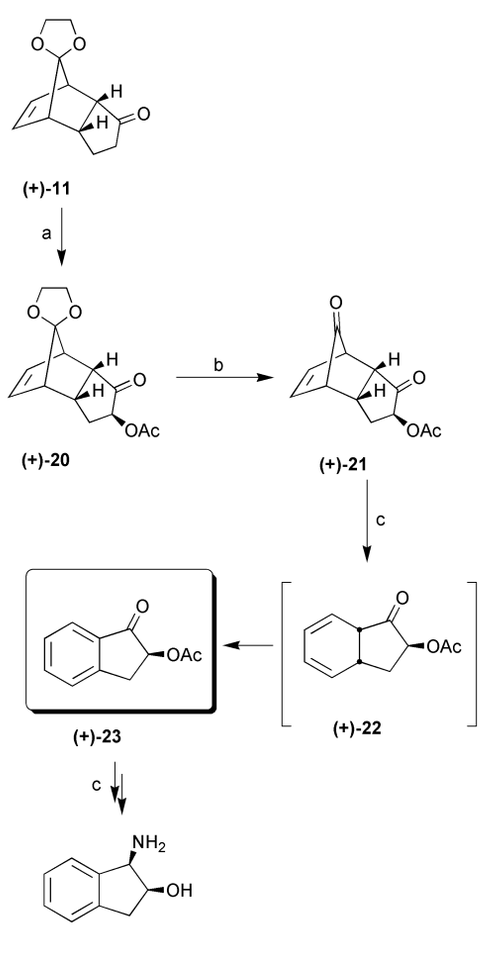
pure allylic acetate (−)-**8** and/or allylic alcohol (+)-**7** obtained here were considered adequate for further studies.

Synthesis of enantiomerically pure *cis*-hydrindanes

We have previously shown that *cis*-hydrindanes can be obtained from tricyclo[5.2.1.0^{2,6}]decan-10-one derivatives by employing the Haller–Bauer cleavage (**2** ⟶ **3**, Scheme 2) as the key step.[2,5] The availability of (−)-**8** and (+)-**7** now provided the opportunity to access a range of *cis*-hydrindanes in optically pure form. For this purpose, allylic acetate (−)-**8** was elaborated into 10-oxotricyclodecane derivatives (−)-**12**, (+)-**13** and (+)-**14** *via* the intermediacy of ketals (+)-**6**, (−)-**10** and (+)-**11**, respectively, by employing routine functional-group transformations (Scheme 4). The tricyclic ketones (−)-**12**, (+)-**13** and (+)-**14** were subjected to base-mediated Haller–Bauer cleavage to furnish hydrindanes (+)-**15**, (−)-**16** and (+)-**17**, and (+)-**18**, respectively, in preparatively useful yields. A notable feature of the base mediated C–C bond cleavage in the tricyclic ketones **12**–**14** was the high level of regioselectivity. The preferential cleavage of the C1–C10 bond could possibly arise from the remote directing effect of the bystander C3 electron-withdrawing substituent (homoconjugative involvement of the carbonyl or hydroxy group).[17] Also, during the Haller–Bauer cleavage under basic conditions, the double bond in the six-membered ring invariably migrates and conjugates with the carboxylic acid moiety, unless the reaction is done under very carefully controlled conditions.[6] These nonracemic chiral hydrindanes **15–18** are obvious attractive building blocks for natural products, particularly sesquiterpenes. While the availability of the chiral hydrindanes was a satisfying outcome, it was essential at this stage to unambiguously establish the absolute configuration of these compounds. Although chiro-optical methods have been previously employed[16] to derive the configuration of tricyclo[5.2.1.0^{2,6}]decan-10-one derivatives, we carried out several correlations through synthesis to secure earlier assignments.



Scheme 4 *Reagents and conditions*: (a) K_2CO_3, MeOH, 100%; (b) TPAP, NMMO, DCM–acetonitrile (9 : 1) 90%; (c) $NaBH_4$, EtOH, 100%; (d) PCC, DCM, 72%; (e) KOBu^t, MeI, ^{t}BuOH, 90%; (f) 60% H_2SO_4, DCM, 92%; (g) Amberlyst-15, acetone 90%; (h) 30–50% aq. NaOH, benzene, reflux; then CH_2N_2, diethyl ether, 65–70%.



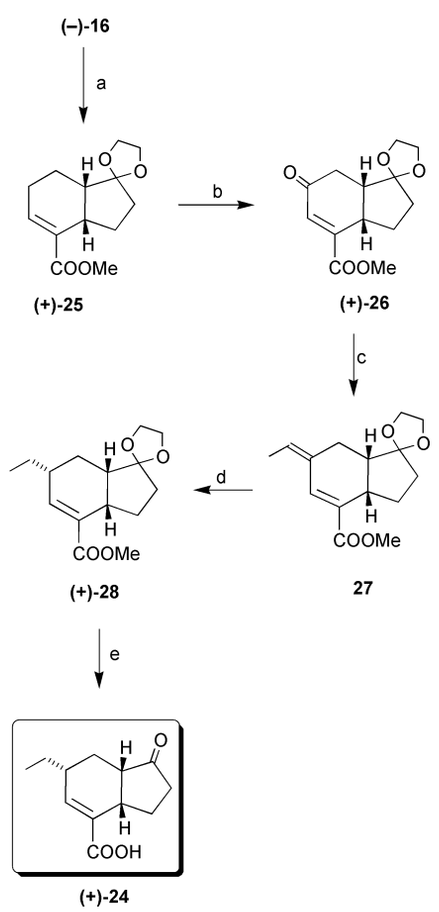
Scheme 5 *Reagents and conditions*: (a) $Pb(OAc)_4$, benzene, reflux, 80%; (b) 50% H_2SO_4, DCM, 85%; (c) ≈160 °C, neat, 55%.

Synthesis of (1*R*, 2*S*)-1-aminoindan-2-ol

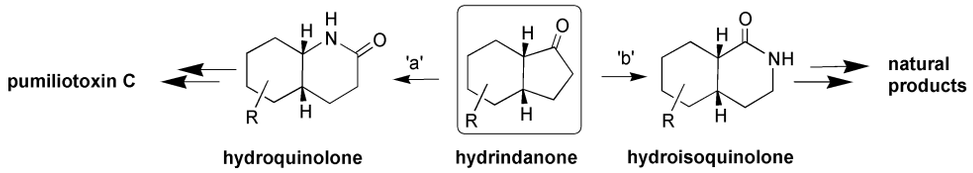
Enantiomerically pure aminoindanol **19** [18] is currently receiving considerable attention, as it is the key component in the HIV-protease inhibitor Indinavir [19a] and in several chiral auxiliaries [19b] and catalysts [19c] for asymmetric cycloadditions and reductions. Considering this, we sought to prepare **19** from enantiomerically pure tricyclic ketone (+)-**11**. Reaction of (+)-**11** with lead tetraacetate gave acetoxy ketone (+)-**20** as a single isomer in regio- and stereoselective manner. The acetoxy ketone (+)-**20** on acetal deprotection furnished dione (+)-**21**. Thermally induced extrusion of CO from (+)-**21** and aromatization of intermediate diene **22** led to (2*S*)-acetoxyindan-1-one (+)-**23**, which has been previously converted into *cis*-1-aminoindan-2-ol (+)-**19** by several other groups (Scheme 5).[20] This correlation and comparison with literature values (see Experimental section) established the absolute configuration of our building blocks (−)-**8** and (+)-**7** derived from enzymatic resolution.

Synthesis of (+)-coronafacic acid

Coronafacic acid (+)-**24** is a hydrindane-based phytotoxin, isolated from the culture broth of *Pseudomonas coronafacience*, whose absolute stereochemistry is well established.[21] It has been a popular synthetic target for over two decades.[5,22] Herein, we describe a synthesis of (+)-coronafacic acid (+)-**24** from (−)-**16**. Hydrindane (−)-**16** obtained from tricyclic keto alcohol (+)-**13** *via* base-mediated Haller–Bauer cleavage was elaborated to (+)-coronafacic acid (+)-**24**, $[\alpha]_D$ $+105 \times 10^{-1}$ deg cm^2 g^{-1} (lit.,[21] $[\alpha]_D$ +109), through the intermediacy of (+)-**25**, (+)-**26**, **27** and (+)-**28** as outlined (Scheme 6). A pleasing feature of our approach is the chemo- and stereoselective catalytic reduction of the ethylidene group in **27** from the convex face.



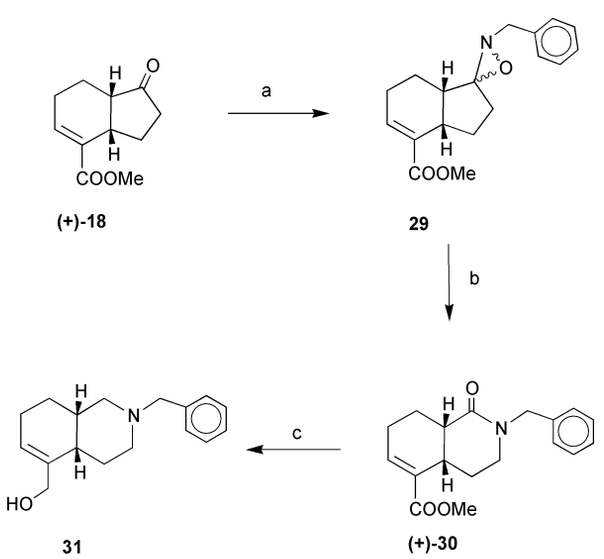
Scheme 6 *Reagents and conditions*: (a) i, TPAP, NMMO, DCM–acetonitrile (9 : 1), 90%; ii, $(CH_2OH)_2$, PTSA, benzene, reflux, 8 h, 95%; (b) PDC, *t*-BuOOH, Celite, benzene, 0.5 h, 61%; (c) $EtPPh_3Br$, *n*-BuLi, benzene, 15 min, 57%; (d), Pd/C, H_2EtOAc, 10 min, 86%; (e) 25% aq. HCl, reflux, 4 h, 70%.



Scheme 7

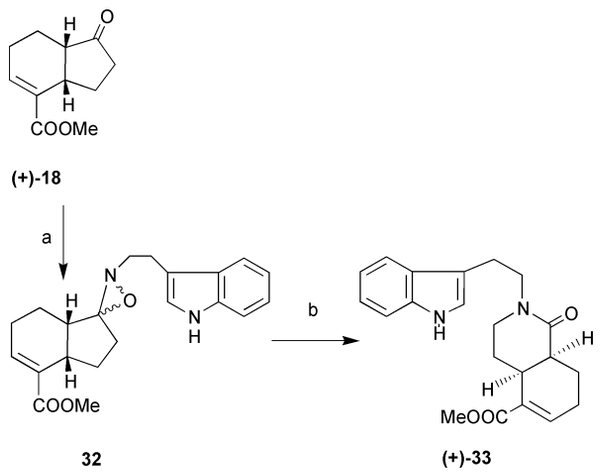
Synthesis of enantiopure hydroisoquinolones

We have recently demonstrated the conversion of *cis*-hydrindanones derived from tricyclo[5.2.1.$0^{2,6}$]decan-10-one derivatives into *cis*-hydroquinolones *via* classical Beckmann rearrangement *en route* to the syntheses of (±)-pumiliotoxin C[6] and (±)-perhydrogephyrotoxin,[23] path 'a' (Scheme 7). At this stage, we wished to amplify the utility of these enantiopure *cis*-hydrindanones for accessing *cis*-hydroisoquinolones as well, path 'b' (Scheme 7), as this ring system is prevalent as a part structure in many natural products. It has been noted by Lattes *et al*.[24] that irradiation of oxaziridines derived from their corresponding ketones gave lactams with opposite regiochemistry (see 'b' in Scheme 7) compared with the classical Beckmann rearrangement. The explanation given was that the carbon substituent 'anti' to the lone pair on the oxaziridine nitrogen migrated preferentially to a formally electron-deficient nitrogen.[24] To explore this possibility, *cis*-hydrindanone ester (+)-**18** was condensed with benzylamine to furnish an imine which on chemoselective epoxidation of the imine double bond gave oxaziridine derivative **29**. Irradiation of oxaziridine **29** led to a clean rearrangement and hydroisoquinolone ester (+)-**30** was obtained in moderate yield. The amide carbonyl in (+)-**30** was reduced with AlH_3 to give **31** in which the ester moiety was also reduced to the allylic alcohol (Scheme 8). Hydroisoquinolone **31** is a useful building block for the synthesis of yohimbinoid alkaloids.[25]



Scheme 8 *Reagents and conditions*: (a) i, benzylamine, toluene, reflux; ii, MCPBA, toluene, DCM, −78 °C, 50%; (b) *hv*, acetonitrile, ≈ 60%; (c) AlH_3, THF, −78 °C, 1 h, 55%.

To further probe the efficacy of our hydroisoquinolone synthesis, hydrindanone ester (+)-**18** was condensed with tryptamine. The resulting imine on epoxidation with *m*-chloroperbenzoic acid (MCPBA) gave oxaziridine derivative **32**. Irradiation of **32** furnished the *cis*-hydroisoquinolone (+)-**33** in reasonable yield (Scheme 9). The structural features of lactam (+)-**33** closely relate to the advanced intermediates for the synthesis of pentacyclic alkaloids reserpine and yohimbine.



Scheme 9 *Reagents and conditions*: (a) i, tryptamine, molecular sieves, diethyl ether, reflux; ii, MCPBA, −78 °C, 66%; (b) *hv*, acetonitrile, ≈ 60%.

A formal synthesis of (+)-coriolin *via* Schuda's intermediate

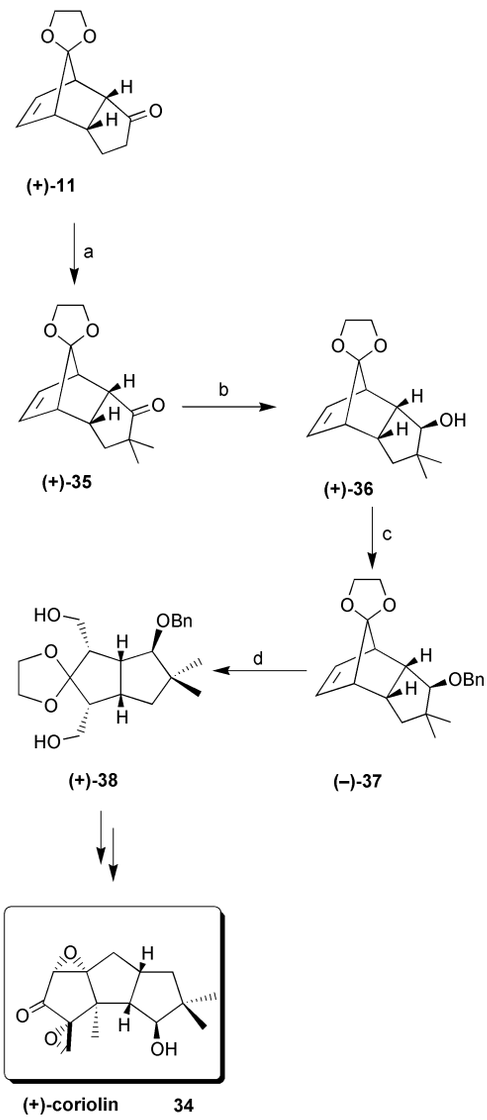
The ready availability of enantiopure tricyclo[5.2.1.$0^{2,6}$]decane derivatives also prompted us to explore the synthesis of somewhat unrelated but interesting structures. Earlier studies by Schuda *et al*. have shown that a diquinane moiety can be extracted from the tricyclo[5.2.1.$0^{2,6}$]dec-8-en-10-one frame through cleavage of the trinorbornene double bond. The diquinane moiety so obtained has been transformed to the highly oxygenated triquinane natural product (+)-coriolin **34**.[26,27] The availability of the enantiopure tricyclodecane system suggested possible access to optically pure diquinanes. Tricyclic ketone (+)-**11** was *gem*-dimethylated to furnish (+)-**35**. On reduction with Li/NH_3 the tricyclic ketone (+)-**35** yielded the thermodynamically stable *exo*-alcohol (+)-**36** and the hydroxylic functionality was protected as the benzyl ether to give (−)-**37**. The double bond in (−)-**37** was cleaved using the sequence of OsO_4-mediated catalytic dihydroxylation, periodate cleavage and $NaBH_4$ reduction to furnish diquinane (+)-**38** in moderate yield (Scheme 10). The spectral data for (+)-**38** were found to be identical (see Experimental section) with those of the Schuda intermediate[27] of coriolin. Since diquinane **38** has been previously elaborated to the triquinane natural product *rac*-coriolin, our preparation of (+)-**38** can be regarded as a formal synthesis of (+)-coriolin **34**.[26]

In summary, we have developed a straightforward protocol, of preparative value, for the enzymatic kinetic resolution of tricyclic allylic alcohol (±)-**7**, employing transesterification in the presence of lipase PS enzyme. The absolute configurations of (+)-**7** and (−)-**8** have been established through correlation with (+)-1-aminoindan-2-ol (+)-**19.** Allylic acetate (−)-**8** has been elaborated to optically pure *cis*-hydrindanes, *cis*-hydroisoquinolones, *cis*-diquinane ring system (coriolin intermediate) and (+)-coronafacic acid **24**.

Experimental

General

Mps are uncorrected. IR spectra were recorded on JASCO FT-IR 5300 or Perkin-Elmer 1310 spectrometers, for solid samples as KBr wafers and liquid samples as thin films between NaCl



Scheme 10 *Reagents and conditions*: (a) MeI, KOBu^t, *t*-BuOH, 91%; (b) Li, NH_3, THF, 15 min, 70%; (c) KH, BnBr, *n*-Bu_4NI, THF, 1 h, 90%; (d) i, OsO_4, NMMO, acetone–water–*t*-BuOH; ii, $NaIO_4$, aq. THF; iii, $NaBH_4$, MeOH, 50% (for 3 steps).

plates. ^{1}H NMR spectra were recorded at 200 MHz and ^{13}C NMR spectra were recorded at 50 MHz on a Bruker AC 200 spectrometer for solutions in $CDCl_3$. *J*-Values are in Hz. Column chromatography was performed using Acmes silica gel (100–200 mesh). Elemental analyses were performed on a Perkin-Elmer 240C-CHN analyzer. Optical rotations were measured on a JASCO DIP 370 digital polarimeter at 25 °C, with $[a]_D$ values given in units of 10^{-1} deg cm^2 g^{-1}. The enzyme (lipase PS immobilized on Celite) used for the present study was obtained from Amano Pharmaceuticals Co. Ltd., Japan. All reactions were monitored employing TLC using an appropriate solvent system for development. Yields reported here are of materials judged homogeneous by TLC and NMR spectroscopy. All solvent extracts were washed with brine and dried over anhydrous Na_2SO_4.

Spiro([1,3]dioxolane-2,10′-tricyclo[5.2.1.0^{2,6}]deca-4′,8′-diene)-3′-ol (±)-7

To a solution of enone (±)-**6**[15] (7 g, 34.3 mmol) in dry dichloromethane (DCM) (20 ml) at −78 °C was added DIBAL-H (35 ml, 35 mmol; 1 M in hexane) under N_2 and the reaction mixture was stirred for 15 min. The reaction was quenched with saturated aq. NH_4Cl, diluted with DCM, and the organic layer was separated. The aqueous layer was further extracted with DCM and the combined organic extracts were washed with water and dried. The residue obtained after the removal of the solvent was passed through a silica gel pad to afford the allylic alcohol (±)-**7** (≈7 g). Recrystallization from diethyl ether furnished pure (±)-**7** (6.1 g, 85%), mp 133–135 °C (lit.,[16] 135–136 °C); ν_{max} (KBr)/cm^{-1} 3447 (OH); δ_H (200 MHz) 6.27 (m, 1H, olefinic), 5.93–5.88 (m, 1H, olefinic), 5.68 (m, 1H, olefinic), 5.56 (m, 1H, olefinic), 4.80 (t, 1H, *J* 5, C*H*OH), 3.97–3.78 (m, 4H, ketal), 3.46 (br s, 1H), 3.14 (dt, 1H, *J* 8, 3.5), 2.78 (m, 2H), 1.36 (d, 1H, *J* 8); δ_C (50 MHz) 136.4, 133.6, 132.0, 131.9, 127.8, 76.9, 64.9, 64.2, 51.2, 50.9, 48.8, 44.4.

Enzymatic kinetic resolution of allylic alcohol (±)-7

A mixture of (±)-**7** (4 g, 19.4 mmol) and vinyl acetate (6 ml, 60 mmol) in tetrahydrofuran (THF) (20 ml) was stirred with the enzyme lipase PS on Celite (≈800 mg, 20% w/w) supplied by Amano, at rt for 3–4 h. The reaction mixture was filtered through a Celite pad. The combined filtrate and washings (DCM) were evaporated under reduced pressure. The residue obtained was chromatographed on a silica gel column to furnish allylic acetate (−)-**8** (2.12 g, 44%) and alcohol (+)-**7** (1.88 g, 46%). The alcohol (+)-**7** (1′*S*,2′*S*,3′*S*,6′*R*,7′*R*)-spiro([1,3]dioxolane-2,10′-tricyclo[5.2.1.0^{2,6}]deca-4′,8′-dien)-3′-ol was recrystallized from diethyl ether, mp 134 °C (lit.,[16] 135–136 °C); $[a]_D^{25}$ +139.7 (*c* 1, $CHCl_3$, ee > 98%) [lit.,[16] +142.2 (*c* 0.45, $CHCl_3$)].

(1′*R*,2′*R*,3′*R*,6′*S*,7′*S*)-Spiro([1,3]dioxolane-2,10′-tricyclo-[5.2.1.0^{2,6}]deca-4′,8′-dien)-3′-yl acetate (−)-**8**: $[a]_D^{25}$ −55.7 (*c* 1.4, $CHCl_3$, ee > 98%); ν_{max} (neat)/cm^{-1} 1734 (C=O); δ_H (200 MHz) 6.13–6.08 (m, 1H, olefinic), 5.88–5.83 (m, 1H, olefinic), 5.68–5.54 (m, 3H), 3.93–3.80 (m, 4H, ketal), 3.46 (m, 1H), 3.35–3.22 (m, 1H), 2.76–2.71 (m, 1H), 2.59 (m, 1H), 2.05 (s, 3H); δ_C (50 MHz) 170.7, 135.7, 132.5, 132.2, 130.4, 127.2, 79.2, 64.9, 64.3, 50.7, 50.1, 49.0, 42.5, 21.1.

Hydrolysis of acetate (−)-8

To a solution of acetate (−)-**8** (2 g, 8 mmol) in aq. methanol (10 ml) was added K_2CO_3 (1 g) and the mixture was stirred at rt for 2 h. The reaction mixture was diluted with water and extracted with diethyl ether. Evaporation off of solvent furnished the alcohol (−)-**7** (1.7 g, quantitative) and this recrystallized from hexane–ethyl acetate, mp 134–135 °C; $[a]_D^{25}$ +137.8 (*c* 1.7, $CHCl_3$).

Acetylation of (+)-7

To an ice-cold solution of alcohol (+)-**7** (100 mg, 0.53 mmol) in dry pyridine (1 ml) was added Ac_2O (0.2 ml) and the mixture was stirred for 2 h. The reaction was quenched with crushed ice and extracted with diethyl ether. The extract was washed successively with cold dil. HCl, water and brine. Evaporation off of the solvent furnished the alcohol (+)-**8** (110 mg, 95%), $[a]_D^{25}$ +53.7 (*c* 0.8, $CHCl_3$). The spectral properties (^{1}H and ^{13}C NMR) of (−)-**8** and (+)-**7** were identical with those of the racemic compounds.

(1′*R*,2′*R*,6′*S*,7′*S*)-Spiro([1,3]dioxolane-2,10′-tricyclo[5.2.1.0^{2,6}]-deca-4′,8′-dien)-3′-one (+)-6

To a mixture of allylic alcohol (−)-**7** (1.05 g, 5 mmol), *N*-methylmorpholine *N*-oxide (NMMO) (1.8 g, 10 mmol) and powdered molecular sieves (4 Å) in 10 ml of acetonitrile–DCM (1 : 9) was added a catalytic amount of tetrapropylammonium perruthenate (TPAP) (≈50 mg) and the mixture was stirred for 1 h under N_2. The resulting black solution was diluted with DCM and filtered through a silica gel pad. Evaporation off of the solvent furnished enone (+)-**6** (900 mg, 90%), which was recrystallized from hexane–diethyl ether, mp 93 °C (lit.,[15] 93–94 °C); $[a]_D^{25}$ +120.4 (*c* 0.45, $CHCl_3$) [lit.,[16] +117.6 (*c* 0.4, $CHCl_3$)]; ν_{max} (KBr)/cm^{-1} 1697 (C=O); δ_H (200 MHz) 7.36 (dd,

1H, *J* 6, 3), 6.11 (m, 1H), 6.01 (m, 1H), 5.90 (m, 1H), 4.05–3.80 (m, 4H, ketal), 3.59 (m, 1H), 3.04 (br s, 1H), 2.96 (t, 1H, *J* 5), 2.83 (m, 1H).

(1*R*′,2′*R*,6′*S*,7′*S*)-Spiro([1,3]dioxolane-2,10′-tricyclo-[5.2.1.0^{2,6}]dec-8′-en)-3′-one (+)-11

To an ice-cold solution of enone (+)-**6** (760 mg, 3.72 mmol) in absolute ethanol (8 ml) was added sodium borohydride (155 mg, 4 mmol). After stirring of the mixture for 1 h at rt, ethanol was removed under reduced pressure. The residue was diluted with water and extracted with ethyl acetate, the combined extracts were washed and evaporation off of solvent furnished alcohol (−)-**10** (762 mg, quantitative). A slurry of pyridinium chlorochromate (PCC) (600 mg, 3 mmol) and Celite (≈2 g) in DCM (15 ml) was placed in a 100 ml three-necked round-bottomed flask equipped with an addition funnel. To this, was added the alcohol (−)-**10** (420 mg, 2 mmol), obtained above, as a solution in DCM (10 ml) dropwise over a period of 30 min, and the reaction mixture was stirred for 7 h at rt. The reaction mixture was diluted with diethyl ether (50 ml) and passed through a silica gel pad. The ethereal eluate was washed with water and dried. Removal of solvent furnished a yellow oil (+)-**11** (280 mg, 72%), $[a]_D^{25}$ +160.7 (*c* 0.7, $CHCl_3$); ν_{max} (neat)/ cm^{-1} 1725 (C=O); δ_H (200 MHz) 6.26–6.20 (m, 2H, olefinic), 3.88 (br s, 4H, ketal), 3.40–2.75 (m, 4H), 2.40–175 (m, 4H).[15]

(1*R*,2*R*,3*S*,6*S*,7*S*)-3-Hydroxy-4,4-dimethyltricyclo[5.2.1.0^{2,6}]-dec-8-en-10-one (−)-12

A solution of potassium *tert*-butoxide (200 mg, 1.8 mmol) in *tert*-butyl alcohol (5 ml) was cooled (ice-bath) and a solution of ketone (+)-**11** (120 mg, 0.6 mmol) in *tert*-butyl alcohol (5 ml) was added rapidly, followed by the addition of MeI (0.15 ml, 340 mg, 2.39 mmol). The reaction mixture was allowed to warm up and was refluxed for 5 h before being poured into 10 ml of water and extracted with diethyl ether. The combined extracts were washed, dried and concentrated to furnish a light yellow oil (125 mg, 90%). To an ice-cold solution of the above dimethylated ketone (125 g, 0.52 mmol) in methanol (5 ml) was added sodium borohydride (25 mg, 0.65 mmol). After stirring of the mixture for 3 h at rt, methanol was removed under reduced pressure. The residue was diluted with water and extracted with ethyl acetate and the combined extracts were washed and dried. The crude alcohol (125 mg) obtained after the removal of diethyl ether was dissolved in acetone (5 ml), Amberlyst-15 resin was added, and the heterogeneous mixture was stirred at rt for 12 h. Filtration to remove the resin and concentration furnished the keto alcohol (−)-**12** (93 mg, 90%), $[a]_D^{25}$ −4.7 (*c* 0.3, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3450 (OH), 1740 (C=O); δ_H (200 MHz) 6.67–6.63 (m, 1H, olefinic), 6.33–6.29 (m, 1H, olefinic), 3.78–3.73 (m, 1H, C*H*OH), 3.11–2.87 (m, 4H), 1.58–1.48 (m, 1H), 1.05–0.99 (m, 1H) 0.96 (s, 3H, CH_3), 0.95 (s, 3H, CH_3); δ_C (50 MHz) 202.1, 134.5, 127.4, 81.5, 50.1, 49.8, 45.9, 44.9, 41.2, 38.7, 26.5, 22.0. The spectral properties (^{1}H and ^{13}C NMR) of (−)-**12** were identical with those of the racemic compound.[5]

(1*R*,2*R*,3*R*,6*S*,7*S*)-3-Hydroxytricyclo[5.2.1.0^{2,6}]dec-8-en-10-one (+)-13

A mixture of alcohol (−)-**10** (1.5 g, 7.2 mmol), acetone (10 ml) and a catalytic amount of Amberlyst-15 resin was stirred at rt for 8 h. Filtration to remove the resin and concentration of the filtrate furnished the keto alcohol (+)-**13** (1.05 g, 90%) as a colourless solid, which was recrystallized, mp 118 °C; $[a]_D^{25}$ +16.5° (*c* 0.2, $CHCl_3$); ν_{max} (KBr)/cm^{-1} 3408 (OH), 1771 (C=O); δ_H (200 MHz) 6.66–6.38 (m, 2H, olefinic), 4.48 (q, 1H, *J* 6.2, C*H*OH), 3.08 (m, 2H, allylic), 2.85–2.65 (m, 2H), 1.86–1.40 (series of m, 4H); δ_C (50 MHz) 207.0, 133.6, 128.8, 75.6, 51.3, 49.8, 46.2, 40.9, 37.0, 26.2.[5,28]

(1*R*,2*R*,6*R*,7*S*)-Tricyclo[5.2.1.0^{2,6}]dec-8-ene-3,10-dione (+)-14

To a cold solution of ketal (+)-**11** (1 g, 4.8 mmol) in DCM (10 ml) was added 60% H_2SO_4 (4 ml) and the mixture was stirred at rt for 1.5 h, diluted with water, and extracted with DCM. The organic layer was washed with water and dried. The crude material obtained after removal of the solvent was charged on a silica gel column and eluted with 25% ethyl acetate–hexane to furnish the enedione (+)-**14** (720 mg, 92%), $[a]_D^{25}$ +333.3 (*c* 0.75, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1774 (norbornyl C=O), 1732 (C=O); δ_H (200 MHz) 6.50–6.42 (m, 2H, olefinic), 3.32–2.93 (m, 4H), 2.29–1.60 (m, 4H); δ_C (50 MHz) 218.5, 200.3, 132.4, 131.1, 51.6, 49.0, 47.5, 39.5, 34.8, 23.1. The spectral data (^{1}H and ^{13}C NMR) were compared with those of the racemic compound[5] and found to be identical.

Methyl (1*S*,6*S*,7*S*)-7-hydroxy-8,8-dimethylbicyclo[4.3.0]non-2-ene-2-carboxylate (+)-15

To a solution of keto alcohol (−)-**12** (80 mg, 0.42 mmol) in benzene (20 ml) was added 10 ml of 40% aq. NaOH, and the contents were refluxed for 36 h. The aqueous layer was separated, washed with diethyl ether, and acidified with cold dil. HCl. On extraction with ethyl acetate the crude acid was obtained, which was dissolved in diethyl ether (5 ml) and an excess of ethereal diazomethane was added (ice-bath). Excess of diazomethane was destroyed (acetic acid) and the residue obtained after the removal of the solvent was chromatographed on a silica gel column. Elution with 20% ethyl acetate–hexane gave α,β-*unsaturated ester* (+)-**15** (62 mg, 66%), $[a]_D^{25}$ +5.2 (*c* 0.8, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1700 (C=O); δ_H (200 MHz) 7.02–6.92 (m, 1H, olefinic), 4.01–3.92 (m, 1H, C*H*OH), 3.82 (s, 3H, $COOCH_3$), 3.10–2.82 (m, 1H), 2.70–1.92 (m, 4H), 1.90–1.30 (m, 4H), 1.14 (s, 3H, CH_3), 1.12 (s, 3H, CH_3); δ_C (50 MHz) 162.0, 139.8, 133.4, 83.2, 51.4, 46.0, 42.0, 40.9, 33.8, 30.1, 25.2, 25.1, 18.4 (Calc. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.52; H, 8.90%).

Methyl (1*S*,6*S*,7*R*)-7-hydroxybicyclo[4.3.0]non-2-ene-2-carboxylate (−)-16 and methyl (1*S*,2*S*,6*S*,7*R*)-7-hydroxybicyclo-[4.3.0]non-3-ene-2-carboxylate (+)-17

To a solution of keto alcohol (+)-**13** (1 g, 7.2 mmol) in benzene (100 ml) was added 50% aq. NaOH (50 ml), and the contents were refluxed for 3 h. The aqueous layer was separated, washed with diethyl ether, and acidified with cold dil. HCl. On extraction with ethyl acetate and evaporation a mixture of crude acids was obtained. This was dissolved in diethyl ether (10 ml) and an excess of ethereal diazomethane was added (ice-bath). Excess of diazomethane was destroyed (acetic acid) and the residue obtained after the removal of solvent was chromatographed on a silica gel column. Elution with 20% ethyl acetate–hexane gave α,β-*unsaturated ester* (−)-**16** (600 mg) and β,γ-*unsaturated ester* (+)-**17** (240 mg) in 7 : 3 ratio and 70% overall yield. For (−)-**16**: $[a]_D^{25}$ −3.6 (*c* 0.5, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3424 (OH), 1713 (C=O); δ_H (200 MHz) 7.01 (br s, 1H, olefinic), 4.40 (q, 1H, *J* 6.6, C*H*OH), 3.71 (s, 3H, $COOCH_3$), 2.85 (m, 1H), 2.50–1.15 (series of m, 9H); δ_C (50 MHz) 167.8, 139.4, 133.4, 75.0, 51.4, 41.7, 35.6, 35.1, 28.4, 25.3, 17.3 (Calc. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.2. Found: C, 67.38; H, 8.25%).

For (+)-**17**: $[a]_D^{25}$ +113.2 (*c* 1.45, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3499 (OH), 1732 (C=O); δ_H (200 MHz) 6.17–6.02 (m, 1H, olefinic), 5.80–5.65 (m, 1H, olefinic), 4.23 (m, 1H, C*H*OH), 3.68 (s, 3H, $COOCH_3$), 2.56–1.67 (series of m, 9H); δ_C (50 MHz) 176.5, 130.2, 124.5, 74.8, 51.5, 45.8, 44.9, 37.1, 33.2, 28.6, 28.0 (Calc. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.2. Found: C, 67.45; H, 8.28%).

Methyl (1*S*,6*S*)-7-oxobicyclo[4.3.0]non-2-ene-2-carboxylate (+)-18

To a solution of the dione (+)-**14** (500 mg, 3.1 mmol) in benzene (100 ml) was added 50 ml of 30% aq. NaOH and the

contents were refluxed for 3 h. The aqueous layer was separated, washed with diethyl ether, and acidified with cold dil. HCl. On extraction with ethyl acetate and washing, the crude α,β-unsaturated acid was obtained. This material was dissolved in diethyl ether (10 ml) and an excess of ethereal diazomethane was added (ice-bath). Excess of diazomethane was destroyed (acetic acid) and the residue obtained after the removal of the solvent was charged on a silica gel column. Elution with 5% ethyl acetate–hexane gave the α,β-*unsaturated ester* (+)-**18** (340 mg, 68%), $[a]_D^{25}$ +157.8 (*c* 0.3, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1730 (C=O), 1710 (ester C=O); δ_H (200 MHz) 7.05–7.01 (m, 1H, olefinic), 3.37 (s, 3H, $COOCH_3$), 3.20–3.10 (m, 1H, allylic bridge), 2.50–1.62 (series of m, 9H); δ_C (50 MHz) 220.5, 167.8, 140.5, 131.5, 51.4, 46.4, 36.9, 35.6, 27.2, 23.7, 19.3 (Calc. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 68.10; H, 7.25%).

(1′*R*,2′*R*,4′*S*,6′*S*,7′*S*)-3′-Oxospiro([1,3]dioxolane-2,10′-tricyclo[5.2.1.0^{2,6}]dec-8′-en)-4′-yl acetate (+)-20

To a solution of the ketone (+)-**11** (100 mg, 0.48 mmol) in dry benzene (5 ml), was added $Pb(OAc)_4$ (320 mg, 0.72 mmol) and the mixture was refluxed under N_2 for 6 h. The reaction mixture was cooled, quenched with ethylene glycol, diluted with water, and extracted with ethyl acetate. The organic layer was washed and dried. The crude residue obtained after the removal of the solvent was charged on a silica gel column and eluted with 10% ethyl acetate–hexane to furnish *compound* (+)-**20** (100 mg, 80%), $[a]_D^{25}$ +139.5 (*c* 0.9, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1742 (C=O); δ_H (200 MHz) 6.50–6.46 (m, 1H, olefinic), 6.26–6.20 (m, 1H, olefinic), 4.64 (t, 1H, *J* 11, C*H*OAc), 3.98–3.70 (m, 4H, OCH_2-CH_2O), 3.15 (m, 2H, allylic), 2.96 (m, 1H), 2.81 (m, 1H), 2.17–2.04 (m, 1H), 2.05 (s, 3H, $OCOCH_3$), 1.90 (m, 1H); δ_C (50 MHz) 213.5, 169.7, 134.8, 134.3, 126.6, 76.6, 65.1, 64.6, 50.9, 50.7, 49.7, 35.4, 29.4, 20.5 (Calc. for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.90; H, 6.22%).

(1*R*,2*R*,4*S*,6,7*S*)-3,10-Dioxotricyclo[5.2.1.0^{2,6}]dec-8-en-4-yl acetate (+)-21

To an ice-cold solution of ketal (+)-**20** (90 mg, 0.34 mmol) in DCM (5 ml) was added 50% H_2SO_4 (1 ml) and the reaction mixture was stirred for 15 min at the same temp. The reaction mixture was diluted with DCM (5 ml), washed, dried, and concentrated to furnish *dione* (+)-**21** (65 mg, 85%), $[a]_D^{25}$ +156.1 (*c* 1.2, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1780 (norbornyl C=O), 1743 (C=O); δ_H (200 MHz) 6.77–6.74 (m, 1H, olefinic), 6.59–6.56 (m, 1H, olefinic), 4.56 (t, 1H, *J* 11.4, C*H*OAc), 3.35–3.05 (m, 4H), 2.30–1.95 (m, 2H), 2.08 (s, 3H, $OCOCH_3$); δ_C (50 MHz) 211.2, 198.6, 169.9, 133.3, 132.6, 76.4, 51.3, 50.3, 46.1, 32.7, 30.5, 20.5 (Calc. for $C_{12}H_{12}O_4$: C, 65.45; H, 5.49. Found: C, 65.60; H, 5.51%).

(2*S*)-1-Oxodihydroinden-2-yl acetate (+)-23

Dione (+)-**21** (48 mg, 0.21 mmol) was heated at 160 °C (± 5 °C) for 20 min. The residue obtained was loaded on a silica gel column and eluted with 5% ethyl acetate–hexane to furnish acetoxyindanone (+)-**23** (22 mg, 55%), mp 80 °C (lit.,[20] 80.5–81.5 °C); $[a]_D^{25}$ +17.5 (*c* 0.57, MeOH) [lit.,[20] +19 (*c* 1.0, MeOH)]; ν_{max} (neat)/cm^{-1} 1728 (C=O); δ_H (200 MHz) 7.80 (d, 1H, *J* 7.5), 7.65–7.61 (m, 1H), 7.47–7.42 (m, 2H), 5.43 (dd, 1H, *J* 8, 5, C*H*OAc), 3.67 (dd, 1H, *J* 17, 8, benzylic), 3.05 (dd, 1H, *J* 17, 5, benzylic), 2.19 (s, 3H, $OCOCH_3$); δ_C (50 MHz) 200.5, 170.4, 150.4, 135.8, 134.5, 128.1, 126.6, 124.5, 74.0, 33.4, 20.7.

Methyl (1*S*,6*S*)-spiro(bicyclo[4.3.0]non-2-ene-7,2′-[1,3]-dioxolane)-2-carboxylate (+)-25

A mixture of alcohol (−)-**16** (210 mg, 1 mmol), NMMO (320 mg, 2 mmol) and powdered molecular sieves (4 Å) in 5 ml of acetonitrile–DCM (1 : 9) was stirred at rt for 10 min, under nitrogen. A catalytic amount of TPAP (≈10 mg) was added and stirring was continued for another 1 h. The resultant black solution was diluted with DCM and filtered through a small silica gel pad. Evaporation off of the solvent and passage of the residue through a silica gel column furnished (+)-**18** (190 mg) in 90% yield. A mixture of (+)-**18** (160 mg, 0.83 mmol), ethylene glycol (0.1 ml) and cat. toluene-*p*-sulfonic acid (PTSA) in dry benzene (10 ml) was refluxed for 8 h. The reaction mixture was cooled, diluted with water, and extracted with diethyl ether. The combined organic layer was washed with saturated aq. $NaHCO_3$ and dried. The residue obtained on removal of the solvent was passed through a silica gel column using 20% ethyl acetate–hexane as eluent to give the *ketal* (+)-**25** (175 mg, 95%), $[a]_D^{25}$ +5.3 (*c* 1.7, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1730 (C=O); δ_H (200 MHz) 6.98–6.93 (m, 1H, olefinic), 3.91–3.85 (m, 4H, OCH_2-CH_2O), 3.71 (s, 3H, $COOCH_3$), 3.30–3.26 (m, 1H), 3.05–3.01 (m, 1H), 2.40–1.20 (m, 8H); δ_C (50 MHz) 167.6, 139.1, 133.2, 118.7, 64.7, 63.7, 51.3, 43.6, 35.8, 33.1, 28.0, 25.0, 19.5 (Calc. for $C_{13}H_{18}O_4$: C, 65.53; H, 7.61. Found: C, 65.50; H, 7.64%).

Methyl (1*S*,6*S*)-4-oxospiro(bicyclo[4.3.0]non-2-ene-7,2′-[1,3]-dioxolane)-2-carboxylate (+)-26

To an ice-cold solution of the ketal (+)-**25** (125 mg, 0.52 mmol) in benzene (5 ml) were added Celite (200 mg), pyridinium dichromate (PDC) (375 mg, 1.05 mmol) and 70% *tert*-butyl hydroperoxide (0.1 ml). The reaction mixture was stirred at rt for 0.5 h and then filtered through a small Celite pad. The crude product obtained after evaporation off of the solvent was charged on a silica gel column and eluted with 30% ethyl acetate–hexane to furnish *enone* (+)-**26** (78 mg, 61%), $[a]_D^{25}$ +9 (*c* 1.7, $CHCl_3$); ν_{max} (neat)/cm^{-1} 1720 (C=O), 1690 (C=O); δ_H (200 MHz) 6.70 (s, 1H, olefinic), 3.90–3.84 (m, 4H, OCH_2-CH_2O), 3.82 (s, 3H, $COOCH_3$), 3.30–3.26 (m, 1H), 2.62–2.58 (m, 1H), 2.44–1.54 (m, 6H); δ_C (50 MHz) 198.2, 166.7, 149.1, 131.7, 117.3, 65.0, 64.7, 52.2, 43.9, 35.4, 35.1, 33.8, 27.8 (Calc. for $C_{13}H_{16}O_5$: C, 61.89; H, 6.39. Found: C, 61.79; H, 6.35%).

Methyl (1*S*,4*R*,6*S*)-4-ethylspiro(bicyclo[4.3.0]non-2-ene-7,2′-[1,3]dioxolane)-2-carboxylate (+)-28

To a suspension of ethyltriphenylphosphonium bromide (75 mg, 0.21 mmol) in dry benzene (2 ml) was added *n*-butyllithium in hexane (0.2 ml, 0.3 mmol) at rt, under N_2. To the red–orange ylide solution was added immediately a solution of enone (+)-**26** (30 mg, 0.15 mmol) in dry benzene (3 ml) and the mixture was stirred at room temperature for 15 min, quenched with water, and extracted with ethyl acetate. The combined extracts were washed and dried. The residue obtained after evaporation off of the solvent was filtered through a silica gel column by elution with 20% ethyl acetate–hexane to furnish the Wittig product **27** (16 mg, 57%). A solution of the diene **27** (16 mg, 0.06 mmol) in dry ethyl acetate (2 ml) was stirred at rt over 10% Pd/C catalyst under hydrogen. After 10 min, the catalyst was filtered off and the mixture was evaporated to furnish the α,β-*unsaturated ester* (+)-**28** (13 mg, 86%), $[a]_D^{25}$ +59.4 (*c* 0.4, $CHCl_3$); δ_H (200 MHz) 6.84 (m, 1H, olefinic), 3.91 (m, 4H, ketal), 3.73 (s, 3H, $COOCH_3$), 2.96 (m, 1H), 2.30–180 (m, 6H), 1.60–1.25 (m, 4H), 0.98 (t, 3H, *J* 7.3, Me); δ_C (50 MHz) 167.8, 143.4, 133.1, 118.8, 64.9, 63.8, 51.5, 44.9, 37.9, 36.5, 33.1, 28.3, 28.1, 26.5, 11.3 (Calc. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.55; H, 8.28%).

(+)-Coronafacic acid (+)-24

A solution of the ketal ester (+)-**28** (12 mg, 0.025 mmol) in 25% aq. hydrochloric acid (2 ml) was refluxed for 4 h. The reaction mixture was cooled, diluted with water (2 ml), and extracted with ethyl acetate. The organic extract was washed with water and dried. Solvent was evaporated off and the residue was filtered through a silica gel column by elution with 50% ethyl acetate–hexane to furnish the acid (+)-**24** (8 mg, 70%), $[a]_D^{25}$ +105 (*c* 0.1, MeOH), [lit.,[21] +109 (*c* 0.5, MeOH)];

δ_H (200 MHz) 7.07 (br s, 1H, olefinic), 3.08 (m, 1H), 2.70–2.10 (m, 5H), 2.01–1.05 (m, 5H), 0.99 (t, 3H, *J* 7.3, Me); δ_C (50 MHz) 220.0, 171.4, 146.8, 130.9, 46.7, 38.2, 38.0, 36.1, 28.2, 27.8, 25.8, 11.2. The spectral data of synthetic (+)-**24** were compared with those of the natural product[21] and found to be identical.

Methyl (4a*S*,8a*S*)-2-benzyl-1-oxo-1,2,3,4,4a,7,8,8a-octahydroisoquinoline-5-carboxylate (+)-30

To a solution of the ketone (+)-**18** (250 mg, 1.29 mmol) in dry toluene (10 ml) was added an excess of benzylamine (0.5 ml) and the mixture was refluxed for 10 h with the removal of water using a Dean–Stark apparatus. After usual work-up, the crude reaction product was dissolved in DCM and *m*-chloroperbenzoic acid (MCPBA) (450 mg, 1.30 mmol; 50%) was added at −78 °C. After being stirred for 2 h at the same temperature, the reaction mixture was diluted with diethyl ether and washed successively with saturated aq. $NaHCO_3$ and water. The residue obtained after evaporation of the mixture was charged on a silica gel column. Elution with 10% ethyl acetate–hexane furnished the oxaziridine **29** (150 mg, 50% based on the recovery of starting material), ν_{max} (neat)/cm^{-1} 1713 (ester C=O); δ_H (200 MHz) 7.37–7.27 (m, 5H, ArH), 6.99 (t, 1H, *J* 3.5, olefinic), 3.85 (s, 2H, benzylic), 3.72 (s, 3H, $COOCH_3$), 3.15 (q, 1H, *J* 4.5), 2.45–1.30 (series of m, 9H); δ_C (50 MHz) 167.3, 140.2, 136.4, 131.9, 128.6 (4C), 127.6, 94.2, 60.8, 51.5, 43.2, 36.3, 29.3, 25.9, 24.5, 19.2.

The oxaziridine **29** (150 mg, 0.5 mmol) as a solution in dry acetonitrile (10 ml), degassed by flushing N_2 for 10 min, was irradiated with a 125 W Hg lamp in a quartz tube under a stream of N_2 for 6 h. After removal of the solvent, the residue was filtered through a small silica gel column to give the *isoquinolinone* (+)-**30** (90 mg, 60%), $[\alpha]_D^{25}$ +41.7 (*c* 0.46, $CHCl_3$); ν_{max} (neat)/ cm^{-1} 1710 (ester C=O), 1638 (lactam C=O); δ_H (200 MHz) 7.35–7.20 (m, 5H, ArH), 7.11 (t, 1H, *J* 4, olefinic), 4.73 (1/2 ABq, 1H, *J* 14.5, benzylic), 4.48 (1/2 ABq, 1H, *J* 14.5, benzylic), 3.73 (s, 3H, $COOCH_3$) 3.32 (ddd, 1H, *J* 16.5, 9, 4), 3.16 (dd, 1H, *J* 5.5, 3), 2.92 (m, 1H), 2.68–2.52 (m, 1H), 2.36–1.55 (series of m, 6H); δ_C (50 MHz) 172.2, 167.0, 141.1, 137.1, 131.4, 128.6 (2C), 127.9 (2C), 127.4, 51.6, 50.2, 46.6, 40.9, 32.6, 25.7 (2C), 22.6 (Calc. for $C_{18}H_{21}NO_3$: C, 72.22; H, 7.07; N, 4.68. Found: C, 72.40; H, 6.95; N, 4.60%).

(4a*S*,8a*S*)-2-Benzyl-1,2,3,4,4a,7,8,8a-octahydroisoquinolin-5-ylmethanol 31

A solution of lactam (+)-**30** (60 mg, 0.2 mmol) in THF (3 ml) was introduced into a solution of AlH_3 (≈0.5 mmol, generated from $LiAlH_4$ and $AlCl_3$ in THF) at −78 °C. After stirring of the mixture for 1 h at the same temperature, the reaction was quenched with brine and diluted with diethyl ether. The organic layer was washed and dried. After evaporation of the mixture, the residue was charged on a silica gel column and eluted with 30% ethyl acetate–hexane to furnish the isoquinoline **31** (28 mg, 55%), ν_{max} (neat)/cm^{-1} 3348 (OH); δ_H (200 MHz) 7.34–7.26 (m, 5H, ArH), 5.61 (br s, 1H), 4.05 (ABq, 2H, *J* 6.6, C*H*$_2$OH), 3.54 (1/2 ABq, 1H, *J* 15, benzylic), 3.42 (1/2 ABq, 1H, *J* 15, benzylic), 2.78–2.70 (m, 2H), 2.35–1.40 (series of m, 10H); δ_C (50 MHz) 140.9, 128.9 (2C), 128.1 (3C), 126.9, 123.9, 65.6, 63.3, 58.6, 54.0, 34.8, 34.3, 28.2, 25.3, 23.2.

Methyl (4a*S*,8a*S*)-2-[2-(1*H*-indol-3-yl)ethyl]-1-oxo-1,2,3,4,4a,7,8,8a-octahydroisoquinoline-5-carboxylate (+)-33

A mixture of ketone (+)-**18** (200 mg, 1.03 mmol) and tryptamine (330 mg, 2.06 mml) in dry diethyl ether (10 ml) was refluxed for 24 h in the presence of powdered molecular sieves (4 Å). The reaction mixture was cooled to −78 °C and MCPBA (350 mg, 1 mmol; 50%) in DCM (5 ml) was added. After being stirred for 0.5 h at the same temperature, the reaction mixture was diluted with diethyl ether and washed with saturated aq. $NaHCO_3$. After removal of the solvent, the residue was charged on a silica gel column and eluted with 10% ethyl acetate–hexane to furnish the oxaziridine **32** (180 mg, 66% yield based on the recovery of starting material), ν_{max} (neat)/cm^{-1} 3410 (NH), 1709 (ester C=O); δ_H (200 MHz) 8.13 (br s, 1H, NH), 7.62 (d, 1H, *J* 7.5), 7.36 (d, 1H, *J* 8), 7.25–7.03 (m, 3H, ArH), 6.72 (s, 1H, olefinic), 3.76 (s, 3H, $COOCH_3$), 3.22–2.85 (m, 6H), 2.45–1.30 (series of m, 8H).

The oxaziridine **32** (150 mg, 0.42 mmol) as a solution in dry acetonitrile (10 ml), degassed by flushing N_2 for 10 min, was irradiated with a 450 W Hg lamp in a quartz tube under a blanket of N_2 for 6 h. After removal of the solvent, the residue was filtered through a small silica gel column to give the *isoquinolinone* (+)-**33** (92 mg, 61%), $[\alpha]_D^{25}$ +35.1 (*c* 1, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3270 (NH), 1709 (ester C=O), 1615 (lactam C=O); δ_H (200 MHz) 8.16 (br s, 1H, NH), 7.68 (d, 1H, *J* 7.5), 7.38–7.04 (m, 5H, ArH and olefinic), 3.79–3.63 (m, 2H), 3.73 (s, 3H, $COOCH_3$), 3.40–3.25 (m, 1H), 3.18–3.02 (m, 2H), 2.90 (m, 1H), 2.55–1.50 (series of m, 8H); δ_C (50 MHz) 172.0, 167.1, 141.2, 136.3, 131.4, 127.5, 122.0, 121.9, 119.4, 118.8, 113.3, 111.1, 51.6, 48.4, 47.9, 40.8, 32.5, 25.8, 25.7, 23.0, 22.5 (Calc. for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.22; H, 6.71; N, 8.05%).

(1′*R*,2*R*′,3′*R*,6′*S*,7′*S*)-4′,4′-Dimethylspiro([1,3]dioxolane-2,10′-tricyclo[5.2.1.0^{2,6}]dec-8′-en)-3′-ol (+)-36

The α,α-dimethyl ketone (+)-**35**[15] [100 mg, 0.4 mmol, obtained from (+)-**11**] as a solution in dry THF (5 ml) and absolute ethanol (1 ml) was placed in a 100 ml three-necked round-bottomed flask. Ammonia (≈20 ml) was distilled into the reaction flask, and to the rapidly stirred solution was added lithium metal (≈20 mg). After being stirred for 15 min, the reaction mixture was quenched with solid NH_4Cl. After evaporation off of the ammonia, the residue was diluted with water and the reaction mixture was extracted with DCM. The combined extracts were washed and dried. The crude product obtained after removal of the solvent was purified over a silica gel column to furnish the alcohol (+)-**36** (70 mg, 70%), $[\alpha]_D^{25}$ +8.6 (*c* 1, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3425 (OH); δ_H (200 MHz) 6.30–6.23 (m, 2H, olefinic), 3.96–3.75 (m, 4H, ketal), 3.15 (d, 1H, C*H*OH), 2.85–2.52 (series of m, 4H), 1.45 (dd, 1H, *J* 11.8, 8), 0.93 (s, 3H, Me), 0.90 (s, 3H, Me), 1.05–0.80 (m, 1H). The ^{1}H NMR data of (+)-**36** were found to be identical with those reported for the racemic compound.[27]

(1′*R*,2′*R*,3′*R*,6′*S*,7′*S*)-3′-Benzyloxy-4′,4′-dimethylspiro([1,3]-dioxolane-2,10′-tricyclo[5.2.1.0^{2,6}]dec-8′-ene) (−)-37

A solution of *exo*-alcohol (+)-**36** (46 mg, 0.2 mmol) in dry THF (4 ml) was added to a suspension of KH (≈50 mg, 0.3 mmol) in dry THF (2 ml) under N_2. The reaction mixture was stirred at rt for 30 min and then a catalytic amount of *n*-Bu_4NI and benzyl bromide (60 mg, 0.3 mmol) were added. After being stirred for 1 h at rt, the reaction mixture was quenched with water, extracted with diethyl ether, and the extract was washed and dried. The residue obtained after removal of the solvent was passed through a short silica gel column to furnish (−)-**37** (55 mg, 90%), $[\alpha]_D^{25}$ −7.5 (*c* 1.1, $CHCl_3$); δ_H (200 MHz) 7.30 (m, 5H), 6.20–6.04 (m, 2H, olefinic), 4.66 (1/2 ABq, 1H, *J* 12.5, benzylic), 4.50 (1/2 ABq, 1H, *J* 12.5, benzylic), 3.94–3.75 (m, 4H, ketal), 2.92 (d, 1H, *J* 7.7, C*H*OBn), 2.85–2.45 (series of m, 4H), 1.44 (dd, 1H, *J* 12, 9), 1.02 (s, 3H, Me), 0.95 (s, 3H, Me), 0.85 (m, 1H); δ_C (50 MHz) 139.3, 134.7 (2C), 134.3, 128.2 (2C), 127.4 (3C), 87.0, 71.8, 64.8, 64.2, 49.9, 49.5, 48.7, 44.2, 40.8, 40.3, 26.8, 22.6.

(1′*R*,3′*S*,3a′*R*,4′*R*,6a′*S*)-4′-Benzyloxy-5′,5′-dimethylspiro-([1,3]dioxolane-2,2′-perhydropentane)-1′,3′-diyldimethanol (+)-38

Osmium tetraoxide (2 mg) was added to a stirred solution of compound (−)-**37** (50 mg, 1.15 mmol) and NMMO (210 mg,

1.8 mmol) in a mixture of acetone (2 ml), water (2 ml) and *t*-BuOH (1 ml). After 15 h, the osmate ester was hydrolyzed with saturated aq. $NaHSO_3$ and the product was extracted with ethyl acetate. The combined extracts were washed and dried. The crude diol (≈50 mg) obtained after removal of the solvent was dissolved in 10% aq. THF (4 ml) and $NaIO_4$ (32 mg, 0.15 mmol) was added with stirring. The residue obtained after the usual work-up (ethyl acetate) and evaporation off of the solvent was dissolved in dry methanol (5 ml). $NaBH_4$ (≈30 mg) was added and, after stirring of the mixture for 3 h, methanol was removed under reduced pressure. The residue was diluted with water (3 ml) and extracted with ethyl acetate (10 ml × 2). The organic layer was washed and dried. Evaporation of the mixture and purification through a silica gel column (60% ethyl acetate–hexane) furnished the diol (+)-**38** (25 mg, 50% for 3 steps), $[a]_D^{25}$ +59.1 (*c* 1, $CHCl_3$); ν_{max} (neat)/cm^{-1} 3428 (OH); δ_H (200M Hz) 7.33 (m, 5H), 4.80 (1/2 ABq, 1H, *J* 10.6, benzylic), 4.48 (1/2 ABq, 1H, *J* 10.6, benzylic), 3.98–3.56 (m, 9H), 2.80–2.58 (m, 2H), 2.50–2.28 (m, 3H), 1.60–1.44 (m, 3H), 1.25 (s, 3H, Me), 1.01 (s, 3H, Me); δ_C (50 MHz) 137.9, 128.5 (2C), 128.0 (2C), 127.9, 117.8, 88.1, 72.9, 66.8, 65.0, 59.1 (2C), 51.0, 50.6, 45.9, 41.9, 39.2, 34.9, 28.7, 19.9. The ^{1}H NMR spectrum of (+)-**38** was identical with the advanced intermediate prepared by Schuda *et al.*[27] in their synthesis of (+)-coriolin.

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