Diastereodivergent Synthesis of the C9-Cyclopentanone Chiral Building Blocks

Hiroshi Nagata, Mitsuhiro Kawamura, Kunio Ogasawara*

Pharmaceutical Institute, Tohoku University, Aobayama, Sendai 980-8578, Japan
Fax +81(22)217-6845; E-mail: konol@mail.cc.tohoku.ac.jp

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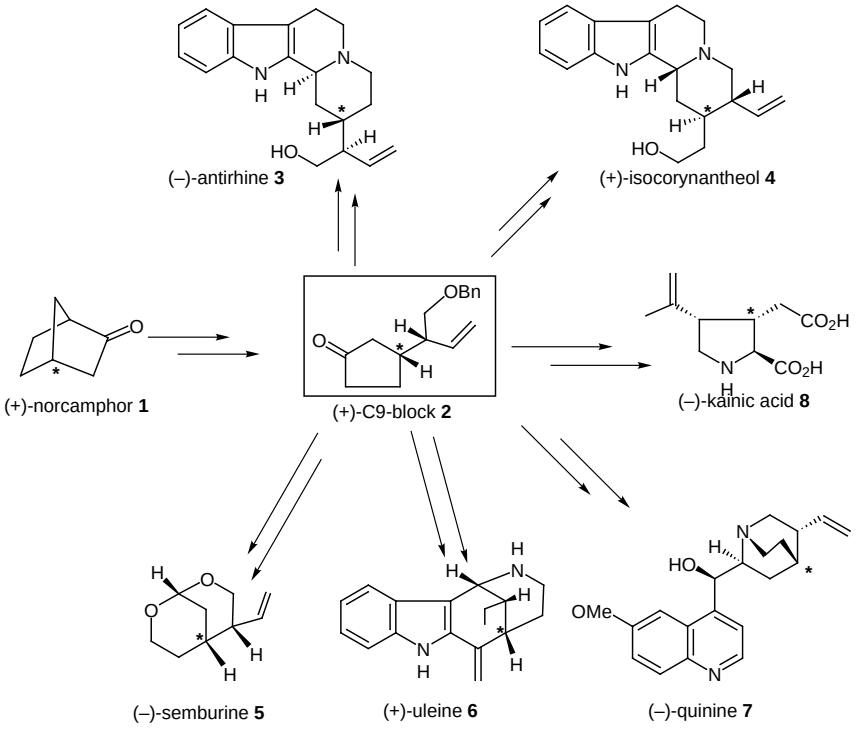
Abstract: Diastereodivergent synthesis the C9-cyclopentanone chiral building block, serving as the non-tryptamine moiety of the Corynanthe type indole alkaloids and the related natural products, and its diastereomer has been developed from racemic norcamphor by employing lipase-mediated resolution via an allylic acetate intermediate having a bicyclo[3.2.1]octane framework. A potential of the latter diastereomer has been demonstrated by its conversion into (−)-semburin, a monoterpene isolated from *Swertia japonica* previously and obtained from the C9-block.

Key words: lipase-mediated kinetic resolution, enantioconvergent synthesis, diastereoconvergent synthesis, enantiodivergent synthesis, diastereodivergent synthesis, chiral building block, ring expansion

Recently we have disclosed an unified enantiocontrolled route to the Corynanthe type indole alkaloids[1] and its biogenetically related natural products as well as a structurally related compound[2] starting from (+)-norcamphor [(+)-**1**] through the C9-cyclopentanone intermediate (+)-**2** after diastereocontrolled introduction of a vinyl functionality (Scheme 1). Although the conversion of the key C9-block (+)-**2** into the target molecules shown could be efficiently carried out without difficulty, the synthesis of the block (+)-**2** itself was accompanied by two difficulties which still remain unsolved. One is the acquisition of the block **2** in both enantiomeric forms. In the above syntheses, we used (+)-norcamphor [(+)-**1**] generated by the oxidation of (+)-norborneol.[3] Since (+)-norborneol precursor is practically produced through a reiterative lipase-mediated kinetic resolution with loss of the (−)-enantiomer, the enantiomeric (−)-norcamphor [(−)-**1**], therefore, could not be obtained which prevents the preparation of the enantiomeric C9-block (−)-**2**. The other one is the lability of the stereochemistry of the second stereogenic center introduced at the vicinal carbon to the carbo-



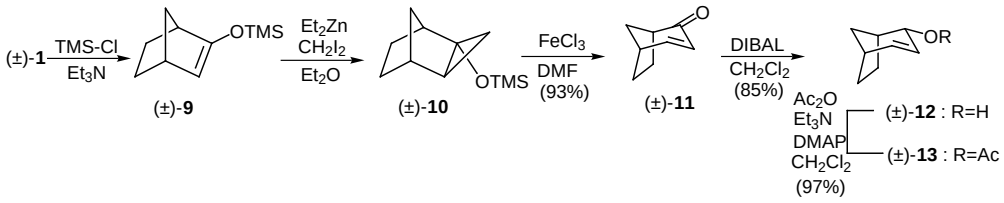
Scheme 1

nyl functionality under basic conditions. This makes preservation of the newly introduced stereogenic center extremely difficult though the introduction itself may be carried out in a diastereocontrolled manner on the basis of the inherent convex-face selectivity of the intermediate lactone having a biased bicyclo[3.2.1]octane framework. This stereochemical lability also prevents the diastereodivergent synthesis of the diastereomer of the C9-block **2** at the second stereogenic center. In oder to circumvent these two difficulties, we explored an alternative procedure being capable of producing the building block **2** and its diastereomer in both enantiomerically pure forms by employing a different methodology. We report here an alternative synthesis of the C9-block **2** and its diastereomer **29** in both enantiomeric forms in a diastereocontrolled manner from racemic norcamphor [(±)-**1**] by a sequence involving ring-expansion to the enone system, lipase-mediated kinetic resolution of an allylic acetate intermediate, and the non-epimerizable introduction of second stereogenic center.[4]

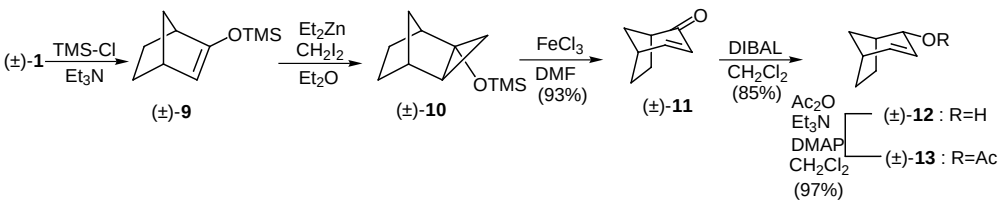
Thus, racemic norcamphor (±)-**1** was first transformed into the silyl enol ether[5] **9** which was then converted into the enone[6] (±)-**11** having a bicyclo[3.2.1]octenone framework via the cyclopropane **10** by sequential Simmons–Smith reaction and oxidative ring-expansion.[7] The enone (±)-**11** was transformed into the *endo*-allyl alcohol[6,8] (±)-**12** which was further transformed into the allyl acetate[6] (±)-**13**, both to be used as substrates for lipase-mediated resolution. The reduction of **11** proceeded in a completely diastereoselective manner owing to the inherent convex-face selectivity exerted by its bicyclo[3.2.1]enone background (Scheme 2).

Resolution of (±)-**12** under transesterification conditions was first investigated. The reaction was found to proceed when (±)-**12** was treated with vinyl acetate in *tert*-butyl methyl ether in the presence of an immobilized lipase [Lipase PS (*Pseudomonas* sp., Amano)] which furnished the enantiomerically enriched acetate (–)-**13** in 47% yield leaving the enantiomerically enriched alcohol (+)-**12** in 40% recovery yield after three days at room temperature. Moreover, the same reaction proceeded within two days to give (–)-**13** in 48% yield and (+)-**12** in 46% recovery yield when a different immobilized lipase, Chirazyme L-2 (*Candida antarctica*, Roche), was used in place of Lipase PS. However, as the enantiomeric excess of the products were still less than satisfactory for practical use, 85% ee for the former and ~81% ee for the latter, we gave up the transesterification method in the present study.

On the other hand, when the racemic acetate (±)-**13** was treated under hydrolysis conditions in a mixture of phosphate buffer and acetone (10:1) in the presence of the same Lipase PS, the enantiopure alcohol (–)-**12** was obtained in 46% yield leaving the highly enantioenriched acetate (>95% ee) (+)-**13** in 50% yield though it took 2 weeks at room temperature. Moreover, we found that the same reaction could be carried out in much shorter time using Chirazyme L-2 to give the alcohol[6] (–)-**12** and the acetate[6] (+)-**13** both in enantiomerically pure forms in yields of 39% and 40%, respectively, within two days in the same phosphate buffer-acetone (10:1) solution. We used the hydrolysis products thus obtained for practical purpose. The enantiopure products obtained were next transformed into the enone[6] **11**. Thus, the alcohol **12** was oxidized under Dess–Martin conditions[9] to afford the enantiopure enone **11**, while the acetate **13** was converted



Scheme 2



Reagents and conditions: a) for **12**: vinyl acetate, *t*-BuOMe, Lipase PS or Chirazyme L-2; b) for **13**: phosphate buffer-acetone (10:1), Chirazyme L-2

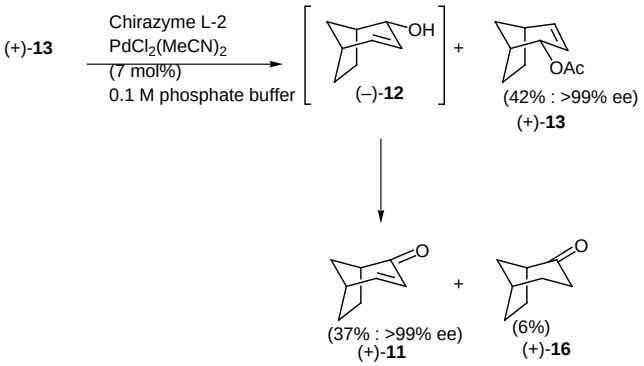
Scheme 3

into the enantiopure enone **11** by sequential alkaline methanolysis and Dess–Martin oxidation (Scheme 3).

In order to make use of both enantiomers of the enone **11** as the single enantiomer, (+)-**11** was first treated with alkaline hydrogen peroxide to give diastereoselectively the *exo*-epoxide (+)-**14** which, on treatment with hydrazine, gave the *exo*-alcohol (–)-**15** epimeric to the *endo*-alcohol (–)-**12**. Diastereoselective generation of (–)-**15** also confirmed the convex-face selectivity exerted by (+)-**11** in the epoxidation. On oxidation under Dess–Martin conditions, (–)-**15** afforded the inverted enone (–)-**11**. Although we did not carry out the same reaction using the enantiomer (–)-**11**, the present conversion constitutes its inversion in a formal sense[5a] (Scheme 4).

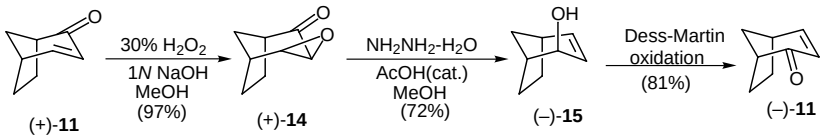
Stimulated by the finding of Williams and co-workers[10] that a certain racemic 2-substituted cyclohex-3-enyl acetate was resolved dynamically under lipase-mediated hydrolysis conditions in the presence of a palladium catalyst to give rise to a single enantiomeric 2-substituted cyclohex-3-enol, we also examined the dynamic resolution of the racemic *endo*-acetate (±)-**13** under the same lipase-palladium-mediated conditions, as **13** has the same symmetric element to those Williams and co-workers had used with respect to its cyclohexenyl acetate system. The expected dynamic resolution did not take place, but instead, concomitant resolution of the racemate (±)-**13** and oxidation of the resulting resolved alcohol (+)-**12** occurred under these conditions in the presence of Novozyme and a palladium catalyst [$PdCl_2(MeCN)_2$, 7 mol%] to give the enone (+)-**11** and the acetate (+)-**13** in yields of 37% and 42%, respectively, both in enantiomerically pure forms[11] accompanied with 7% yield of the enantiopure ketone (+)-**16**. When Lipase PS was used in place of Novozyme, the reaction proceeded very slow and a complex mixture was generated. Although actual mechanism generating two oxidation products from the allyl alcohol (+)-**12** was uncertain, it is apparently due to the presence of palladium catalyst and oxygen in the medium, while a similar palladium-mediated oxidation of allylic alcohols has been reported[12] (Scheme 5).

Having overcome the first difficulty, we next tackled the second problem in the utilization of the enantiopure enone **11** thus obtained. To obtain the C9-building block (–)-**2**, the enantiomer which was not so-far been prepared, one carbon unit was introduced to (–)-**11** as a benzyloxymethyl functionality by diastereoselective 1,4-addition. Thus, treatment of (–)-**11** with a cuprate,[13] generated in situ from benzyl tributylstannylmethyl ether and butyllithium in the presence of a copper(I)-dimethyl sulfide complex

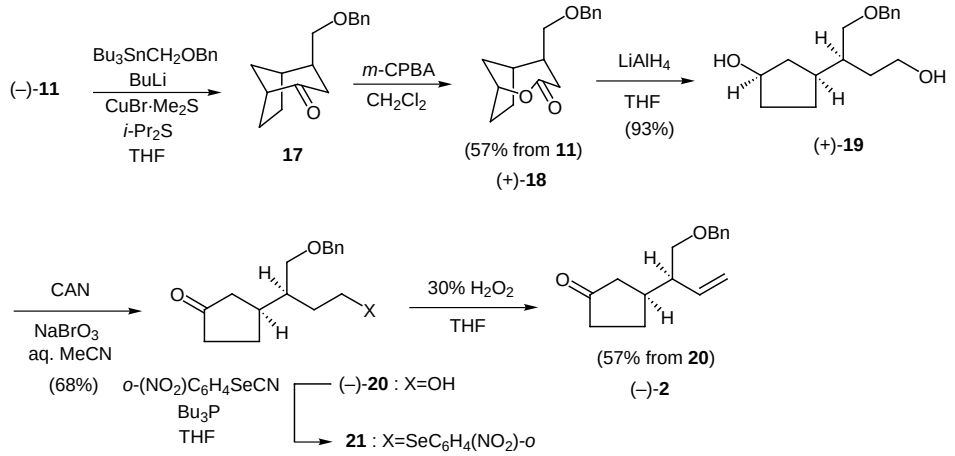


Scheme 5

and diisopropyl sulfide in THF, furnished diastereoselectively the ketone **17** with generation of a tertiary stereogenic center as a single stereoisomer, though a minor amount of the unreacted starting enone could not be separated. In contrast to the previous electrophilic diastereocontrolled construction of a new tertiary stereogenic center at the vicinal carbon to the carbonyl functionality, the present introduction by a nucleophilic 1,4-addition did not bring about epimerization, though both of the procedures rely their stereocontrol on the inherent convex-face selectivity exerted by their biased bicyclo[3.2.1]octane framework, respectively. The ketone **17**, without separation, was next treated with *m*-chloroperbenzoic acid to give the single lactone (+)-**18** via a regioselective Baeyer–Villiger pathway after separation of the contaminated enone (–)-**11**. To obtain the the C9-block (–)-**2**, the lactone (+)-**18** was first reduced with lithium aluminum hydride to give the diol (+)-**19**. Applying Oshima conditions[14] reported for chemoselective oxidation of secondary alcohols, the diol (+)-**19** was treated with a catalytic amount of cerium(IV) ammonium nitrate (CAN) in the presence of sodium bromate to furnish cleanly the keto alcohol (–)-**20** leaving the primary hydroxy functionality intact. Finally, dehydration of (–)-**20** was carried out under Grieco conditions[15] to give the C9-cyclopentanone building block[1] (–)-**2** via the selenide **21**. Thus, the first acquisition of the enantiomer (–)-**2**, which could not be obtained previously, as well as an alternative acquisition of (+)-**2** in a formal sense, has been made with overcoming the second difficulty. Overall yield of (–)-**2** from the enone (–)-**11** was 21% in 6 steps (Scheme 6).



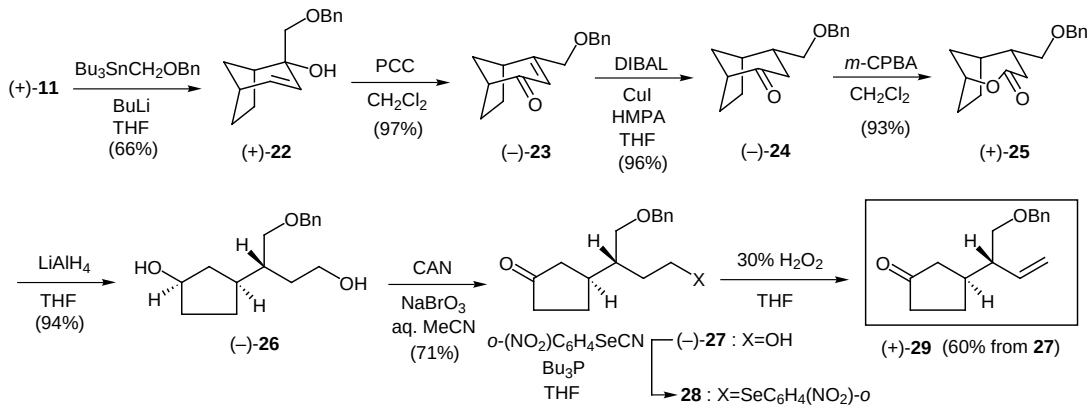
Scheme 4



Scheme 6

As we have solved the second problem for the construction of a new stereogenic center in the C9-block **2** without epimerization, we next examined the introduction of a tertiary stereogenic center in an alternative way so as to construct the diastereomer of the C9-block (−)-**2** starting with the enantiomeric enone (+)-**11**. Treatment of (+)-**11** with a carbanion generated in situ from benzyl tributylstannylmethyl ether and butyllithium in THF[16] afforded the tertiary alcohol (+)-**22**, diastereoselectively, by an 1,2-addition. This was oxidized with pyridinium chlorochromate[5b] (PCC) to give the β-substituted enone (−)-**23**. As expected 1,4-reduction using a complex[17] generated in situ from diisobutylaluminum hydride (DIBAL) and copper(I) iodide in THF containing hexamethylphosphorus triamide (HMPA) proceeded diastereoselectively from the convex-face to give the ketone (−)-**24**, the diastereomer of the ketone (+)-**18**. Baeyer−Villiger oxidation of (−)-**24** with *m*-chloroperbenzoic acid took place regioselectively to give the single lactone (+)-**25** which afforded the diol (−)-**26** on reduction with lithium aluminum hydride. Chemoselective oxididation of (−)-**26** under the same conditions[14] as for (−)-**20** furnished the keto alcohol (−)-**27** without affecting the primary hydroxy group. This compound, after transformation into the selenide **28**, afforded the C9-cyclopentanone (+)-**29**, the diastereomer of the C9-block[1] (+)-**2**. Overall yield of (+)-**29** the from the enone (+)-**11** was 23% in 8 steps. Thus, diastereocontrolled route to both enantiomers of the C9-building block **2** and its diasteromer **29** has been established at this stage in a formal sence (Scheme 7).

To demonstrate a potential of the newly obtained C9-ketone (+)-**29**, the diastereomer of (+)-**2**, its conversion into (−)-sembrin[18] (**5**), a monoterpene principle of *Swertia japonica* which has been previously obtained from (+)-**2**, was examined on the basis of its functionality and stereochemical background. Thus, (+)-**29** was first transformed into the α-diketone monothioketal (+)-**30** by reaction with trimethylene dithiotosylate[19] via the enamine intermediate,[20] whose benzyl ether was cleaved at this stage with boron tribromide[1] to give the primary alcohol **31**. Cleavage of the α-diketone monothioketal functionality of (+)-



Scheme 7

31 with potassium hydroxide in *tert*-butyl alcohol[21] followed by acid treatment furnished the δ-lactone (+)-**32** which was reduced to give the diol (+)-**33**. Finally, the dithiane moiety of (+)-**33** was hydrolysed[22] to give (−)-semburin (**5**) after acidic workup with concomitant cyclization under the conditions. The product obtained was identical with that obtained from norcamphor [(+)-**1**] via the diastereomeric C9-building block[1] (+)-**2**. We have, thus, completed a synthesis of (−)-semburin (**5**) from both enantiomers of the enone **11** in the diastereo- and enantioconvergent manner in a formal sense (Scheme 8).

In conclusion, we have overcome two difficulties which have been encountered previously in the exploitation of (+)-norcamphor, only practically accessible enantiomer at present, for the diastereocontrolled synthesis of the Corynanthe indole alkaloids and the related natural products. The first problem, acquisition of the key C9-chiral block in both enantiomeric forms, has been solved by converting racemic norcamphor into the enantiopure enone having a bicyclo[3.2.1]octane framework by employing lipase-mediated resolution. The second problem, preservation of the labile stereogenic center, has been solved by introducing a new stereogenic center by diastereoselective 1,4-addition at the nonenolizable carbonyl β-position on the basis of the inherent convex-face selectivity exerted by a bicyclo[3.2.1]octane background of the substrate enone. Not only an alternative route to the C9-chiral block through a more enzyme-discriminable allylic acetate intermediate was established, but a route to its enantiomer and its diastereomer which are so far unable to obtain from (+)-norcamphor was also achieved. Moreover, we have demonstrated a potential of the presently obtained diastereomer by converting it into (−)-sembrin which has so far been obtained from (+)-norcamphor.

Melting points are uncorrected. IR spectra were recorded on a JASCO-IR-700 spectrometer. ^{1}H NMR spectra were recorded on a Gemini 2000 (300 MHz) spectrometer. Mass spectra were recorded on a Jenol JMS-DX 303 instrument. Enantiomeric purities were determined on a Gilson Model-307 instrument equipped with a column with a chiral stationary phase. Optical rotations were measured with a JASCO-DIP-370 digital polarimeter.

Bicyclo[3.2.1]oct-3-en-2-one [(±)-11] from (±)-Norcamphor [(±)-1]

To a stirred solution of $FeCl_3$ (23.2 g, 173.98 mmol) in DMF (140 mL) was added the cyclopropane **10** (prepared from racemic norcamphor **[**(±)-**1]** by the reported procedure[5]) (15.5 g, 79.08 mmol) in DMF (50 mL) at 0 °C and the stirring was continued for 12 h at r.t. The reaction was quenched by addition of H_2O (100 mL) and was extracted with Et_2O (3 × 500 mL). The extract was washed with brine (30 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 400 g, eluent: Et_2O/hexane, 1:1 v/v) to give the enone (±)-**11** as a colorless oil (9.01 g, 93%).

IR (film): ν = 1679 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.49−1.78 (m, 3 H), 1.91−2.21 (m, 3 H), 2.87−2.97 (m, 2 H), 5.84 (dd, 1 H, *J* = 9.8, 1.9 Hz), 7.26 (ddd, 1 H, *J* = 9.8, 6.8, 1.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.4 (t), 29.3 (t), 37.8 (d), 40.2 (t), 50.0 (d), 127.4 (d), 157.0 (d), 204.0 (s).

MS: *m*/*z* = 122 (M^+), 81 (100%).

HRMS: *m*/*z* Calcd for $C_8H_{10}O$ 122.0732. Found 122.0693.

***endo*-Bicyclo[3.2.1]oct-3-en-2-ol [(±)-12]**

To a stirred solution of (±)-**11** (2.00 g, 16.39 mmol) in CH_2Cl_2 (60 mL) was added DIBAL (1.5 M in toluene, 13.1 mL, 19.67 mmol) at −78 °C and the stirring was continued for 1 h at the same temperature. The reaction was quenched by addition of H_2O (13 mL) and the mixture was filtered through a Celite pad. The filtrate was dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 80 g, eluent: Et_2O/hexane, 1:1 v/v) to give the racemic allyl alcohol (±)-**12** (1.73 g, 85%).

IR (film): ν = 3302 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.53−1.71 (m, 5 H), 1.79−1.83 (m, 1 H), 2.40−2.44 (m, 2 H), 4.56 (s, 1 H), 5.30 (dd, 1 H, *J* = 9.9, 3.3 Hz), 5.97 (ddd, 1 H, *J* = 10.0, 6.3, 3.3 Hz).

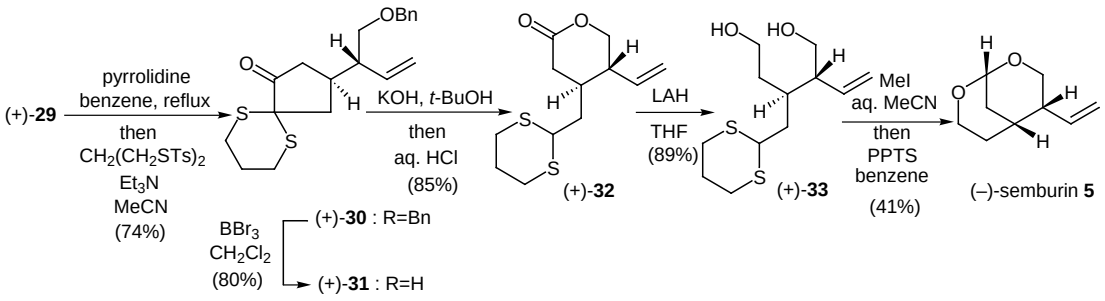
MS: *m*/*z* = 124 (M^+), 83 (100%).

HRMS: *m*/*z* Calcd for $C_8H_{12}O$ 124.0888. Found 124.0852.

Preparation of 4-Acetoxybicyclo[3.2.1]oct-2-ene [(±)-13]

A mixture of (±)-**12** (1.70 g, 13.71 mmol), Et_3N (5.3 mL, 41.13 mmol), 4-(*N*,*N*-dimethylamino)pyridine (16.7 mg, 1.4 mmol), and Ac_2O (2.1 mmol, 20.57 mmol) was stirred at r.t. for 10 h. The mixture was diluted with Et_2O (200 mL) and washed with brine (20 mL), dried ($MgSO_4$), evaporated under reduced pressure. The residue was chromatographed (SiO_2, eluent: Et_2O/hexane, 1:3 v/v) to give the racemic allyl acetate (±)-**13** as a colorless oil (2.20 g, 97%).

IR (film): ν = 1738 cm^{-1}.



Scheme 8

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.60−2.01 (m, 6 H), 2.06 (s, 3 H), 2.40−2.41 (m, 1 H), 2.56−2.58 (m, 1 H), 5.25 (dd, 1 H, *J* = 9.6, 2.4 Hz), 5.57 (ddd, 1 H, *J* = 9.6, 6.2, 3.0 Hz).

MS: *m*/*z* = 166 (M^+), 124 (100%).

HRMS: *m*/*z* Calcd for $C_{10}H_{14}O_2$ 166.0993. Found 166.0990.

Lipase-Meadiated Kinetic Resolution

(a) Resolution of the Racemic Alcohol (±)-12 in the Presence of Lipase PS

A suspension of (±)-**12** (40 mg, 0.32 mmol), vinyl acetate (0.06 mL, 0.64 mmol), and Lipase PS (32 mg) in *tert* butyl methyl ether (5.0 mL) was stirred at r.t. for 3 d. After filtration, the mixture was evaporated under reduced pressure and chromatographed (SiO_2, 4 g, eluent: Et_2O/hexane, 1:3 v/v) to give the acetate (−)-**13** (25 mg, 47%) as a colorless oil and the alcohol (+)-**12** (16 mg, 40%) (from Et_2O/hexane, 1:1 v/v eluent) as a colorless oil. Optical purity of the products were determined by HPLC using a column with a chiral stationary phase (CHIRALCEL OB, eluent: *i*-PrOH/hexane, 1:200 v/v) as 85% ee for (−)-**13** and 71% ee for (+)-**12**. Spectroscopic data are identical with the racemates.

(b) Resolution of the Racemic Alcohol (±)-12 in the Presence of Novozyme

A suspension of (±)-**12** (160 mg, 1.29 mmol), vinyl acetate (0.24 mL, 2.58 mmol), and Chirazymel-2 (128 mg) in *tert* butyl methyl ether (10 mL) was stirred at r.t. for 2 d. After filtration, the mixture was evaporated under reduced pressure and chromatographed (SiO_2, 10 g, eluent: Et_2O/hexane, 1:3 v/v) to give the acetate (−)-**13** (103 mg, 48%) as a colorless oil and the alcohol (+)-**12** (73 mg, 46%) (eluent: Et_2O/hexane, 1:1 v/v) as a colorless oil. Optical purity of the product was determined as above using HPLC as 85% ee for (−)-**13** and 81% ee for (+)-**12**.

(c) Resolution of the Racemic Acetate (±)-13 in the Presence of Lipase PS

A suspension of (±)-**13** (100 mg, 0.06 mmol) and Lipase PS (60 mg) in a mixture of phosphate buffer (0.1 M, 5 mL) and acetone (0.5 mL) was stirred at r.t. for 2 weeks. The mixture was diluted with Et_2O (20 mL) and filtered through a Celite pad. The organic layer was washed with brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2 10g, eluent: Et_2O/hexane, 1:3 v/v) to give the acetate (+)-**13** (50 mg, 50%) and the alcohol (−)-**12** (34 mg, 46%), (eluent: Et_2O/hexane, 1:1 v/v eluent) both as colorless oils. Optical purity of the products were determined as above which revealed (+)-**13** as 94% ee and (−)-**12** as 95% ee.

(d) Resolution of the Racemic Acetate (±)-13 in the Presence of Novozyme

A suspension of (±)-**13** (100 mg, 0.60 mmol) and Novozyme (100 mg) in phosphate buffer (0.1 M, 3 mL) was stirred at r.t. for 48 h. The mixture was diluted with Et_2O (20 mL) and filtered through a Celite pad. The organic layer was washed with brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 5 g, eluent: Et_2O/hexane, 1:5 v/v) to give the acetate (+)-**13** (40 mg, 40%) and the alcohol (−)-**12** (29 mg, 39%) (elunet: Et_2O/hexane, 1:2 v/v) both as colorless oils. Optical purity of the products were determined as above.

(+)-13

$[\alpha]_D^{25}$ +32.1 (*c* = 0.8, $CHCl_3$); >99% ee.

(−)-12

$[\alpha]_D^{29}$ −10.8 (*c* = 0.6, $CHCl_3$); >99% ee.

(e) Resolution of the Racemic Acetate (±)-13 in the Presence of Novozyme and $PdCl_2(MeCN)_2$

A suspension of (±)-**13** (230 mg, 1.39 mmol), Novozyme (230 mg) and $PdCl_2(MeCN)_2$ (18 mg, 0.07 mmol) in phosphate buffer (0.1 M, 9 mL) was stirred at r.t. for 48 h. The mixture was diluted with Et_2O (40 mL) and filtered through a Celite pad. The organic layer was separated, washed with brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 10 g, eluent: Et_2O/hexane, 1:5 v/v) to give the acetate (+)-**13**, the enone (+)-**11** and the ketone (+)-**16**. The spectroscopic data of the enantiopure acetate (+)-**13** and the enone (+)-**11** thus obtained were identical with those of the racemates, respectively.

(+)-13

Yield: 96 mg (42%); >99% ee by HPLC; colorless oil; $[\alpha]_D^{25}$ +32.1 (*c* = 0.8, $CHCl_3$)

(+)-11

Yield: 63 mg (37%); >99% ee by HPLC; colorless oil; $[\alpha]_D^{27}$ +340.5 (*c* = 0.6, $CHCl_3$).

(+)-16

Yield: 10 mg (6%); mp 58−60 °C; $[\alpha]_D^{29}$ +129.6 (*c* = 0.3, $CHCl_3$).

IR (film): ν = 1717 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.64−2.05 (m, 8 H), 2.15−2.25 (m, 1 H), 2.31−2.46 (m, 2 H), 2.70 (t, 1 H, *J* = 5.2 Hz).

MS: *m*/*z* = 124 (M^+), 80 (100%).

HRMS: *m*/*z* Calcd for $C_{10}H_{14}O_2$ 124.0888. Found 124.0868.

The spectral data of (+)-**16** including specific rotation value were identical with those obtained from the enantiopure enone (+)-**11** on catalytic hydrogenation {$[\alpha]_D^{28}$ +127.0 (*c* = 0.7, $CHCl_3$)}.

Conversion of the Allyl Alcohol (−)-12 into the Enone (+)-11

To a stirred solution of (−)-**12** (135 mg, 1.09 mmol) in CH_2Cl_2 (5 mL) was added the Dess−Martin reagent (554 mg, 1.3 mmol) at r.t. and the stirring was continued for 5 min at the same temperature. H_2O (10 mL) was added and the mixture was extracted with Et_2O (2 × 20 mL). The extract was washed with sat. aq $NaHCO_3$ solution (5 mL) and brine (3 mL), dried ($MgSO_4$), evaporated under reduced pressure, and filtered through a Celite pad. The filtrate was dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 5 g, eluent: Et_2O/hexane, 1:2 v/v) to give (+)-**11** (107 mg, 81%); $[\alpha]_D^{28}$ +362.1 (*c* = 1.6, $CHCl_3$) (>99% ee by HPLC), as a colorless oil. Spectroscopic data were indentical with those of (±)-**11**.

Conversion of the Allyl Acetate (+)-13 into the Allyl Alcohol (+)-12

To a stirred solution of (+)-**13** (2.6 mg, 15.66 mmol) in MeOH (50 mL) was added the K_2CO_3 (4.3 mg, 31.33 mmol) at r.t. and the stirring was continued for 1 h. The mixture was diluted with Et_2O (200 mL) and was filtered through a Celile pad. The filtrate was evaporated under reduced pressure and chromatographed (SiO_2, 50 g, eluent: Et_2O/hexane, 1:1 v/v) to give enantiopure (+)-**12** as a colorless oil (1.92 g, 98%).

Conversion of the Allyl Alcohol (+)-12 into the Enone (−)-11

To a stirred solution of (+)-**12** (1.8 mg, 14.75 mmol) in CH_2Cl_2 (50 mL) was added the Dess−Martin reagent (18.8 g, 44.26 mmol) at r.t. After 1 h, the mixture was diluted with H_2O (50 mL) and Et_2O (300 mL), and washed successively with sat.aq $NaHCO_3$ solution (50 mL) and brine (30 mL), dried ($MgSO_4$), evaporated under reduced presure, and chromatographed (SiO_2, 50 g, eluent: Et_2O/hexane, 1:2 v/v) to give (−)-**11** (1.48 g, 82%); $[\alpha]_D^{22}$ −339.0 (*c* = 1.6, $CHCl_3$); >99% ee by HPLC.

(+)-(1*R*,5*S*,6*S*)-5-Benzyloxymethyl-2-oxabicyclo[4.2.1]nonan-3-one (18)

To a stirred solution of Bu_3SnCH_2OBn (588 mg, 1.43 mmol) in THF (5.0 mL) was added BuLi (1.56 M in hexane, 0.92 mL, 1.43 mmol) was added at −78 °C and, after 10 min, CuBr·Me_2S (316 mg, 1.54 mmol) and *i*-Pr_2S (1.5 mL) in THF (2.5 mL), were added and the stirring was continued for 20 min at the same temperature. To this mixture was added the enone (+)-**11** (125 mg, 1.03 mmol) in THF, then after 5 min, BF_3·Et_2O (0.19 mL, 1.54 mmol) and the stirring was continued for 30 min at 0 °C. The reaction was quenched by the addition of sat. aq NH_4Cl solution (10 mL) and extracted with Et_2O (3 × 20 mL). The extract was washed with brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 10 g, eluent: Et_2O/hexane, 1:2 v/v) to give the ketone **17** as a mixture containing a minor amount of the starting enone (−)-**11** which was used for the next reaction. The mixture was dissolved in CH_2Cl_2 (5.0 mL) and was treated with *m*-CPBA (70%, 379 mg, 1.54 mmol) with stirring at 0 °C and the stirring was continued for 12 h at the same temperature. The reaction was quenched by addition of 5% aq Na_2SO_3 solution (5 mL) and the mixture was diluted with EtOAc (20 mL). The organic layer was separated, washed successively with 10% aq NaOH solution (5 mL) and brine (5 mL) dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 10 g, eluent: EtOAc/hexane, 1:2 v/v) to give the lactone **18** (152 mg, 57%); as a colorless oil; $[\alpha]_D^{28}$ +6.7 (*c* = 1.2, $CHCl_3$).

IR (film): ν = 1717 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.58−1.76 (m, 2 H), 1.85−2.08 (m, 4 H), 2.16−2.32 (m, 1 H), 2.63 (dd, 1 H, *J* = 14.8, 4.7 Hz), 2.76 (dd, 1 H, *J* = 14.3, 4.7 Hz), 3.45 (d, 1 H, *J* = 7.5 Hz), 4.52 (d, 2 H, *J* = 11.8 Hz), 4.82 (t, 1 H, *J* = 6.6 Hz), 7.26−7.38 (m, 5 H).

MS: *m*/*z* = 260 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{20}O_3$ 260.1411. Found 260.1410.

(+)-(1*R*,3*S*)-3-[(1*S*)-1-Benzyloxymethyl-3-hydoroxypropyl]cyclopentan-1-ol (19)

To a stirred solution of the lactone (+)-**18** (152 mg, 0.59 mmol) in THF (4.0 mL) was added $LiAlH_4$ (33 mg, 0.88 mmol) at 0 °C. After 10 min the reaction was quenched by addition of 35% NH_4OH (3 mL) and the mixture was diluted with $CHCl_3$ (20 mL) and filtered through a Celite pad. The filtrate was dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 5 g, eluent: $CHCl_3$/MeOH, 10:1 v/v) to give the diol **19** (143 mg, 93%); as a colorless oil; $[\alpha]_D^{29}$ +7.8 (*c* = 1.2, $CHCl_3$).

IR (film): ν = 3370 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.18−1.29 (m, 1 H), 1.38−1.96 (m, 9 H), 2.06−2.18 (m, 1 H), 3.40 (dd, 1 H, *J* = 9.3, 5.8 Hz), 3.55 (dd, 1 H, *J* = 9.3, 5.8 Hz), 3.58−3.74 (m, 2 H), 4.24−4.32 (m, 1 H), 4.51 (d, 2 H, *J* = 2.5 Hz), 7.25−7.39 (m, 5 H).

MS: *m*/*z* = 264 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{24}O_3$ 264.1724. Found 264.1718.

(−)-(3*S*)-3-[(1*S*)-1-Benzyloxymethyl-3-hydroxypropyl]cyclopentan-1-one (20)

To a stirred solution of the diol (+)-**19** (143 mg, 0.54 mmol) in aq MeCN (25%, 6.5 mL) were added sequentially, $NaBrO_3$ (82 mg, 0.54 mmol) and $(NH_4)_2Ce(NO_2)_6$ (CAN, 30 mg, 0.05 mmol) at r.t. and the mixture was refluxed for 1 h. After cooling, the mixture was extracted with EtOAc (20 mL) and the extract was washed successively with sat. aq $NaHCO_3$ solution (5 mL) and brine (3 mL), dried ($MgSO_4$), evaprorated under reduced pressure and chromatographed (SiO_2, 10g, eluent: EtOAc/hexane, 1:1 v/v) to give the keto alcohol **20** (95 mg, 68%) as a colorless oil; $[\alpha]_D^{29}$ −97.9 (*c* = 1.2, $CHCl_3$).

IR (film): ν = 3450, 1725 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.46−1.93 (m, 6 H), 2.05−2.44 (m, 5 H), 2.57 (br s, 1 H), 3.49 (dd, 1 H, *J* = 9.0, 3.0 Hz), 3.56 (dd, 1 H, *J* = 9.0, 3.3 Hz), 3.62−3.74 (m, 2 H), 4.53 (d, 2 H, *J* = 2.2 Hz), 7.26−7.40 (m, 5 H).

MS: *m*/*z* = 263 (M^+ + 1), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{23}O_3$ 263.1646. Found 263.1695.

(−)-(3*S*)-3-[(1*S*)-2-Benzyloxy-1-vinylethyl]cyclopentan-1-one [(−)-2]

A solution of (−)-**20** (95 mg, 0.36 mmol) in THF (2 mL) was stirred with *o*-nitrophenyl selenocyanate (99 mg, 0.44 mmol) and Bu_3P (0.1 mL, 0.44 mmol) at r.t. for 30 min. After evaporation of the solvent under reduced pressure, the residue was dissolved in THF (3 mL) and the solution was treated with 30% H_2O_2 (0.3 mL) at 0 °C with stirring and the stirring was continued for 2 h at r.t. The mixture was extracted with Et_2O (20 mL) and the extract was washed successively with H_2O (10 mL) and brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 10 g, eluent: Et_2O/hexane, 5:1 v/v) to give (−)-**2** (51 mg, 57%); $[\alpha]_D^{27}$ −111.7 (*c* = 0.5, $CHCl_3$) {Lit.[1a] $[\alpha]_D^{28}$ +112.3 (*c* = 2.0, $CHCl_3$) for the enantiomer}, as a colorless oil which, except for the sign of the optical rotation, was identical in all respects with an authentic material obtained from norcamphor **[(+)-1]**.

(+)-(1*R*,2*S*,5*R*)-2-Benzyloxymethylbicyclo[3.2.1]oct-3-en-2-ol (22)

To a stirred solution of Bu_3SnCH_2OBn (1.34 g, 3.28 mmol) in THF (20 mL) was added BuLi (1.58 mL, 2.46 mmol) at −78 °C and the mixture was stirred at the same temperature for 20 min. To this stirred mixture was then added (+)-**11** (200 mg, 1.639 mmol) in THF (5 mL) at −78 °C and the mixture was stirred at the same temperature for 10 min. The mixture was diluted with Et_2O (20 mL) and washed successively with H_2O (10 mL) and brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 20g, eluent: Et_2O/hexane, 1:5 v/v) to give the tertiary alcohol **23** (264 mg, 66%) as a colorless oil; $[\alpha]_D^{23}$ +90.5 (*c* = 1.3 $CHCl_3$).

IR (film): ν = 3452 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.39−1.48 (m, 1 H), 1.56−1.82 (m, 5 H), 2.15−2.24 (m, 1 H), 2.38−2.45 (m, 2 H), 3.38 (d, 1 H, *J* = 9.0 Hz), 3.56 (d, 1 H, *J* = 9.0 Hz), 4.57 (d, 1 H, *J* = 4.4 Hz), 5.21 (dd, 1 H, *J* = 9.6, 1.9 Hz), 6.01 (ddd, 1 H, *J* = 9.9, 6.4, 1.4 Hz), 7.26−7.40 (m, 5 H).

MS: *m*/*z* = 244 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{20}O_2$ 244.1462. Found 244.1486.

(−)-(1*R*,5*S*)-4-Benzyloxymethylbicyclo[3.2.1]oct-3-en-2-one (23)

To a stirred solution of **22** (490 mg, 2.01 mmol) in CH_2Cl_2 (15 mL) was added PCC (866 mg, 4.02 mmol) at r.t. and the stirring was continued for 3 h at the same temperature. The mixture was diluted with Et_2O (50 mL) and filtered through a Celite-pad, evaporated under reduced pressure, and chromatographed (SiO_2, 40 g, eluent: Et_2O/hexane, 1:1 v/v) to give the enone **23** (470 mg, 97%) as a colorless oil; $[\alpha]_D^{28}$ −138.5 (*c* = 2.1, $CHCl_3$).

IR (film): ν = 1658 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.53−1.70 (m, 3 H), 1.91−2.05 (m, 2 H), 2.07−2.19 (m, 1 H), 2.73 (t, 1 H, *J* = 5.0 Hz), 2.94 (t, 1 H, *J* = 5.5 Hz), 4.09 (dd, 1 H, *J* = 15.9, 1.7 Hz), 4.26 (dd, 1 H, *J* = 16.2, 1.9 Hz), 4.56 (d, 2 H, *J* = 3.3 Hz), 5.83 (s, 1 H), 7.25−7.40 (m, 5 H).

MS: *m*/*z* = 242 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{18}O_2$ 242.1306. Found 242.1307.

(−)-(1*R*,4*R*,5*S*)-4-Benzyloxymethylbicyclo[3.2.1]octan-2-one (24)

To a stirred suspension of CuI (2.25 g, 11.84 mmol) and HMPA (17.5 mL) in THF (50 mL) was added DIBAL (15.8 mL, 23.68 mmol) at −78 °C and the stirring was continued for 30 min at the same temperature. Then, the enone **23** (1.91 g, 7.89 mmol) in THF (20 mL) was added at the same temperature. After raising the temperature to −20 °C, the mixture was further stirred for 2 h at the same temperature and diluted with Et_2O (100 mL), washed successively with H_2O (20 mL) and brine (10 mL), dried ($MgSO_4$), evaporated under reduced pressure, chromatographed (SiO_2, 80g, eluent: Et_2O/hexane, 1:4 v/v) to give the ketone **24** (1.84 g, 96%) as a colorless oil; $[\alpha]_D^{25}$ −46.9 (*c* = 0.9, $CHCl_3$).

IR (film): ν = 1712 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.56−1.66 (m, 1 H), 1.72−2.01 (m, 6 H), 2.16−2.29 (m, 2 H), 2.50 (br s, 1 H), 2.70 (t, 1 H, *J* = 5.2 Hz), 3.30 (dd, 1 H, *J* = 9.3, 5.5 Hz), 3.42 (dd, 1 H, *J* = 9.3, 5.5 Hz), 4.51 (d, 2 H, *J* = 2.7 Hz), 7.22−7.40 (m, 5 H).

MS: *m*/*z* = 244 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{20}O_2$ 244.1462. Found 244.1443.

(+)-(1*R*,5*R*,6*S*)-5-Benzyloxymethyloxabicyclo[4.2.1]nonan-3-one (25)

To a stirred solution of (−)-**24** (649 mg, 2.66 mmol) in CH_2Cl_2 (20 mL) was added *m*-chloroperbenzoic acid (70%, 1.06 g, 6.65 mmol) at 0 °C and the stirring was continued for 12 h at the same temperature. The reaction wad quenched by addition of 5% aq $Na_2S_2O_3$ solution (5 mL) and the mixture was diluted with EtOAc (50 mL). The organic layer was separated, washed successively with 10% aq NaOH (5 mL) and brine (5mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 60g, eluent: EtOAc/hexane, 1:2 v/v) to give the lactone **25** (641 mg, 93%) as a colorless oil; $[\alpha]_D^{34}$ +33.2 (*c* = 1.4, $CHCl_3$).

IR (film): ν = 1717 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.59−1.74 (m, 1 H), 1.76−1.82 (m, 1 H), 1.84−2.40 (m, 4 H), 2.18−2.35 (m, 2 H), 2.55 (t, 1 H, *J* = 6.6 Hz), 2.71 (m, 1 H), 3.30 (dd, 1 H, *J* = 9.3, 7.7 Hz), 3.36 (dd, 1 H, *J* = 9.3, 7.7 Hz), 4.50 (s, 1 H), 4.85 (t, 1 H, *J* = 6.7 Hz), 7.26−7.40 (m, 5 H).

MS: *m*/*z* = 260 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{20}O_3$ 260.1411. Found 260.1379.

(−)-(1*R*,3*S*)-3-[(1*R*)-1-Benzyloxymethyl-3·hydroxypropyl]cyclopentan-1-ol (26)

To a stirred solution of the lactone (+)-**25** (641 mg, 2.47 mmol) in THF (20 mL) was added $LiAlH_4$ (140 mg, 3.70 mmol) at 0 °C. After 10 min, the reaction was quenched by the addition of 35% NH_4OH (5 mL) and the mixture was diluted with $CHCl_3$ (20 mL) and filtered through a Celite pad. The filtrate was dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 30g, eluent: $CHCl_3$/MeOH, 10:1 v/v) to give the diol **26** (614 mg, 94 %) as a colorless oil; $[\alpha]_D^{27}$ −4.5 (*c* = 1.6, $CHCl_3$).

IR (film): ν = 3342 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.16−1.28 (m, 1 H), 1.40−1.86 (m, 9 H), 2.04−2.18 (m, 1 H), 2.86 (br s, 1 H), 3.46 (dd, 1 H, *J* = 9.1, 6.6 Hz), 3.54 (dd, 1 H, *J* = 9.3, 6.0 Hz), 3.58−3.74 (m, 2 H), 4.23−4.32 (m, 1 H), 4.51 (d, 2 H, *J* = 2.5 Hz), 7.26−7.39 (m, 5 H).

MS: *m*/*z* = 264 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{24}O_3$ 264.1724. Found 264.1705.

(−)-(3*S*)-3-[(1*R*)-1-Benzyloxymethyl-3-hydroxypropyl]cyclopentan-1-one (27)

To a stirred solution of the diol **26** (141 mg, 0.53 mmol) in aq MeCN (25%, 7 mL) was added $NaBrO_3$ (81 mg, 0.53 mmol) and $(NH_4)_2Ce(NO_2)_6$ (29 mg, 0.06 mmol) at r.t. and the mixture was refluxed for 1 h. After cooling, the mixture was extracted with EtOAC (20 mL) and the extract was washed with sat. aq $NaHCO_3$ solution (5 mL) and brine (3 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 10g, eluent: EtOAc/hexane, 1:1 v/v) to give the ketol **27** (100 mg, 71%) as a colorless oil; $[\alpha]_D^{25}$ −95.2 (*c* = 0.9, $CHCl_3$),.

IR (film): ν = 3430, 1739 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.47−1.56 (m, 1 H), 1.58−1.93 (m, 4 H), 2.05−2.40 (m, 5 H), 2.60 (br s, 1 H), 3.42 (dd, 1 H, *J* = 9.3, 3.3 Hz), 3.53 (dd, 1 H, *J* = 9.3, 3.0 Hz), 3.64−3.76 (m, 2 H), 4.50 (d, 1 H, *J* = 3.6 Hz), 7.26−7.40 (m, 5 H).

MS: *m*/*z* = 262 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd. for $C_{16}H_{22}O_3$ 262.1568. Found 262.1555.

(+)-(3*S*)-3-[(1*R*)-2-Benzyloxy-1-vinylethyl]cyclopentan-1-one (29)

A solution of (−)-**27** (282 mg, 1.08 mmol) in THF (7 mL) was stirred with *o*-nitrophenyl selenocyanate (733 mg, 3.23 mmol) and Bu_3P (0.80 mL, 3.23 mmol) at r.t. for 30 min. After evaporation of the solvent under reduced pressure, the residue was treated with 30% H_2O_2 (2.0 mL) at 0 °C with stirring and the stirring was continued for 2 h at r.t. The mixture was extracted with Et_2O (30 mL) and the extract was washed successively with H_2O (5 mL) and brine (3 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 30 g, eluent: Et_2O/hexane, 5:1 v/v) to give (+)-**29** (158 mg, 60%) as a colorless oil; $[\alpha]_D^{31}$ +0.9 (*c* = 1.1, $CHCl_3$),.

IR (film): ν = 1728 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.42−1.58 (m, 1 H), 2.12−2.18 (m, 2 H), 2.20−2.40 (m, 4 H), 3.48 (d, 1 H, *J* = 4.7 Hz), 4.51 (s, 2 H), 5.12 (dd, 1 H, *J* = 17.0, 1.7 Hz), 5.16 (dd, 1 H, *J* = 10.7, 1.9 Hz), 5.75 (ddd, 1 H, *J* = 17.0, 10.4, 8.5 Hz), 7.26−7.39 (m, 5 H).

MS: *m*/*z* = 244 (M^+), 91 (100%).

HRMS: *m*/*z* Calcd for $C_{16}H_{20}O_2$ 244.1462. Found 244.1463.

(+)-(4*R*)-4-[(1*R*)-2-Benzyloxy-1-vinylethyl]-2,2-propanedithiocyclopentan-1-one (30)

A solution of (+)-**29** (420 mg, 1.72 mmol) and pyrrolidine (0.72 mL, 8.61 mmol) in benzene (20 mL) was refluxed with removal of water using a Dean−Stark apparatus. After 1 h, the benzene was replaced by MeCN (12 mL) after evaporation under reduced prossure and to this mixture were added trimethylene dithiotosylate (716 mg, 1.72 mmol) and Et_3N (0.72 mL, 5.16 mmol) and the mixture was refluxed for 1 h. The mixture was diluted with Et_2O (50 mL) and washed successively with H_2O (20 mL) and brine (10 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 100 g, eluent: Et_2O/ hexane, 1:5 v/v) to give the α-diketone monothioketal **30** (442 mg, 74%) as a pale yellow oil; $[\alpha]_D^{31}$ +53.4 (*c* = 0.6, $CHCl_3$),.

IR (film): ν = 1723 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.64 (dd, 1 H, *J* = 15.0, 11.3 Hz), 1.87 (tq, 1 H, *J* = 13.5, 3.1 Hz), 2.08−2.32 (m, 4 H), 2.43−2.72 (m, 4 H), 3.14 (dt, 1 H, *J* = 13.4, 2.2 Hz), 3.43 (d, 2 H, *J* = 5.8 Hz), 3.89 (dt, 1 H, *J* = 13.5, 2.0 Hz), 4.49 (s, 2 H), 5.12 (d, 1 H, *J* = 17.0 Hz), 5.16 (d, 1 H, *J* = 10.2 Hz), 5.68 (dt, 1 H, *J* = 17.0, 10.1 Hz), 7.26−7.39 (m, 5 H).

MS: *m*/*z* = 348 (M^+), 257 (100%).

HRMS: *m/z* Calcd for $C_{19}H_{24}O_2S_2$ 348.1216. Found 348.1245.

(+)-(4*R*)-4-[(1*R*)-2-Hydroxy-1-vinylethyl]-2,2-propanedithiocyclopentan-1-one (31)

To a stirred solution of (+)-**30** (410 mg, 1.18 mmol) in CH_2Cl_2 (15 mL) was added BBr_3 (1 M in CH_2Cl_2, 3.5 mL, 3.53 mmol) at −78 °C and, after 10 min, the mixture was quenched by addition of sat. aq $NaHCO_3$ solution (5 mL) and extracted with Et_2O (30 mL). The extract was washed successively with sat. aq $NaHCO_3$ solution (5 mL) and H_2O (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 20 g, eluent: Et_2O/hexane, 1:1 v/v) to give the primary alcohol **31** (242 mg, 80%) as a colorless needles; mp 77−79 °C; $[\alpha]_D^{27}$ +52.9 (*c* = 1.8, $CHCl_3$).

IR (film): ν = 3438, 1717 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.54 (br s, 1 H), 1.68 (dd, 1 H, *J* = 13.7, 11.8 Hz), 1.87 (tq, 1 H, *J* = 13.4, 3.0 Hz), 2.07−2.24 (m, 4 H), 2.39−2.60 (m, 3 H), 2.73 (ddd, 1 H, *J* = 18.4, 7.7 1.9 Hz), 3.14 (dt, 1 H, *J* = 13.2, 2.5 Hz), 3.46−3.54 (m, 1 H), 3.59−3.69 (m, 1 H), 3.89 (dt, 1 H, *J* = 13.2, 2.5 Hz), 5.20 (d, 1 H, *J* = 17.0 Hz), 5.25 (d, 1 H, *J* = 10.4 Hz), 5.62 (dt, 1 H, *J* = 17.0, 10.0 Hz).

MS: *m/z* = 258 (M^+), 132 (100%).

HRMS: *m/z* Calcd for $C_{12}H_{18}O_2S_2$ 258.0747. Found 258.0729.

(+)-(3*R*,4*R*)-3-[(1,3-Dithian-2-yl)methyl]-4-vinyl-5-pentanolide (32)

A solution of (+)-**31** (242 mg, 0.94 mmol) in *t*-BuOH (9.0 mL) was heated with KOH (194 mg, 3.47 mmol) at 65 °C for 45 min. After evaporation of the solvent under reduce pressure, the residue was treated with 1 N HCl (5 mL) and extracted with Et_2O (30 mL). The extract was washed with brine (5 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 10 g, eluent: Et_2O/hexane, 1.1 v/v) to give the lactone **32** (205 mg, 85%) as a colorless oil; $[\alpha]_D^{25}$ +28.0 (*c* = 1.2, $CHCl_3$),.

IR (film): ν = 1735 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.51−1.62 (m, 1 H), 1.79−1.95 (m 2 H), 2.02 (ddd, 1 H, *J* = 14.3, 10.4, 3.9 Hz), 2.14−2.40 (m, 4 H), 2.79−3.00 (m, 5 H), 4.06 (t, 1 H, *J* = 10.2 Hz), 4.07 (dd, 1 H, *J* = 11.2, 3.3 Hz), 4.28 (dd, 1 H, *J* = 11.6, 3.3 Hz), 5.25 (d, 1 H, *J* = 10.0 Hz), 5.29 (d, 1 H, *J* = 17.3 Hz), 5.58 (ddd, 1 H, *J* = 17.3, 10.0, 7.9 Hz).

MS: *m/z* = 258 (M^+), 132 (100%).

HRMS: *m/z* Calcd for $C_{12}H_{18}O_2S_2$ 258.0747. Found 258.0770.

(+)-(2*R*,3*R*)-3-[(1,3-Dithian-2-yl)methyl]-2-vinylpentane-1,5-diol (33)

To a stirred solution of the lactone (+)-**32** (62 mg, 0.24 mmol) in THF (3.0 mL) was added $LiAlH_4$ (13.7 mL, 0.36 mmol) at 0 °C and, after 10 min, the reaction was quenched by the addition of H_2O (5 mL) and the mixture was diluted with EtOAc (20 mL). After filtration through a Celite pad, the filtrate was dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 5 g, eluent: EtOAc/hexane, 2:1 v/v) to give the diol **33** (56 mg, 89%) as a colorless oil; $[\alpha]_D^{27}$ +10.3 (*c* = 1.3, $CHCl_3$).

IR (film): ν = 3358 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.49−1.70 (m, 3 H), 1.85 (ddd, 1 H, *J* = 14.3, 10.2, 5.7 Hz), 1.80−2.20 (m, 5 H), 2.28−2.40 (m, 1 H), 2.78−3.00 (m, 4 H), 3.55−3.76 (m, 2 H), 3.71 (t, 1 H, *J* = 6.6 Hz), 5.16 (dd, 1 H, *J* = 17.3, 1.9 Hz), 5.22 (dd, 1 H, *J* = 10.4, 1.9 Hz), 5.63 (ddd, 1 H, *J* = 17.3, 10.4, 7.7 Hz).

MS: *m/z* = 262 (M^+), 119 (100%).

HRMS: *m/z* Calcd for $C_{12}H_{22}O_2S_2$ 262.1060. Found 262.1050.

(−)-Semburin (5)

A solution of the diol (+)-**33** (60 mg, 0.23 mmol) and MeI (0.48 mL, 6.9 mmol) in aq MeCN (10%, 5.5 mL) was stirred at r.t. for 12 h. The mixture was diluted with Et_2O (20 mL) and treated with aq 5% $Na_2S_2O_3$ solution (2 mL). The organic layer was separated and was washed with brine (3 mL), dried ($MgSO_4$) and evaporated under reduced pressure to give a hemiacetal mixture. The mixture was then dissolved in benzene (3.0 mL) and refluxed for 5 h in the presence of pyridinim *p*-toluenesulfonate (PPTS, 6 mg, 0.02 mmol). After cooling the mixture was diluted with Et_2O (20 mL) and the solution was washed successively with sat. aq $NaHCO_3$ solution (5 mL) and brine (3 mL), dried ($MgSO_4$), evaporated under reduced pressure, and chromatographed (SiO_2, 5 g, eluent: EtOAc/hexane, 1:5 v/v) to give (−)-semburin (**5**) (14.4 mg, 41%) as a colorless oil; $[\alpha]_D^{29}$ −2.7 (*c* = 0.1, $CHCl_3$) {Lit. $[\alpha]_D^{25}$ −2.0 (*c* = 0.1, $CHCl_3$)}. Spectroscopic data were identical in all respects with those of an authentic material obtained from (+)-norcamphor **[**(+)-**1]**.

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