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Synthesis of Enantioenriched *trans*-Fused Bicyclo[4.4.0]-dec-3-enes and Bicyclo[4.3.0]non-3-enes Bearing a 1,5-Lactone Bridge

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Abstract: The combination of (−)-sparteine-mediated lithiation of (2-methyl-cyclohex-1-enyl)methyl or (2-butyl-cyclopent-1-enyl)methyl carbamate and enantioselective homoaldol reaction with acrolein, transformation to a γ-lactone, enolate allylation, followed by a ring-closing olefin metathesis provides a facile entry to tricyclic lactones of type **7**, bearing a 1,5-lactone bridge.

Keywords: bicyclic lactones; *trans*-bicyclo[4.4.0]decenes; enolate alkylation; homoaldol reactions; ring-closing olefin metathesis

Introduction

trans-Fused bicyclo[4.4.0]decane and bicyclo[4.3.0]nonane moieties are part of the framework of many natural products, such as steroids.[1] Some structures bearing a bridging lactone moiety are also known.[2] These are not directly accessible by the Diels–Alder reaction, which usually is the most important "working horse" in their synthesis.[3] We now report on a novel approach which is based on the asymmetric homoaldol reaction,[4] coupled with diastereoselective γ-lactone enolate alkylation[5] and ring-closing olefin metathesis.[6] Moreover, at both bridgehead positions, stereogenic quaternary carbon centres are created.

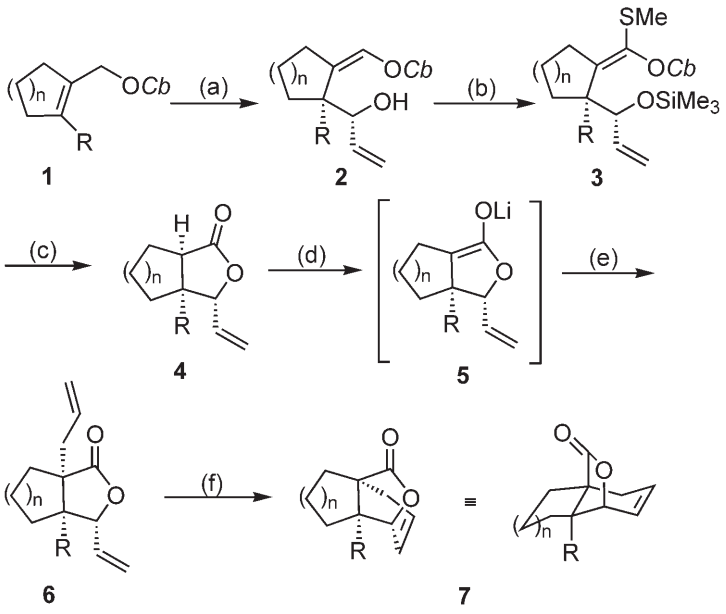
Results and Discussion

1-(2-Alkylcycloalkenyl)methyl *N,N*-diisopropylcarbamates, such as **1**, on (−)-sparteine-assisted lithiation[7] lead to configurationally stable lithium intermediates,[8] which undergo, after lithium-titanium exchange, an addition to alkenals and alkanals (Scheme 1). Similar to the known compound **2b**,[8] the homoaldol product **2a** was prepared from allyl carbamate **1a** and acrolein in 56% yield and 88% ee. Due to the additional double bond, the usual mercuric salt-catalysed solvolysis for removal of the enol carbamate moiety[8] was not applicable here.

Therefore compounds **2**, after transformation into the appropriate *O*-trimethylsilyl ethers, were lithiated at the vinylic position, followed by methanesulfanylation,[8,9a] and the resulting ketene monothioacetals **3a** and **3b**[8] were converted by acid-catalysed methanolysis into the γ-lactones **4a** (yield 75%, 88% ee, based on **2a**) and **4b**[8] (yield 56%, 82% ee), respectively.

The introduction of the allyl residue into position 1 was then required. Lactones **4** were converted to the appropriate lactone enolates **5** by means of lithium hexamethyldisilazide (LiHMDS), followed by addition of allyl bromide from the *exo*-face to furnish the pentasubstituted γ-lactones **6a** (71%, dr = 95:5) and **6b** (75%, dr = 95:5). Diastereomeric ratios were determined by ^{1}H NMR. Finally, the formation of the cyclohexene ring was accomplished by ring-closing olefin metathesis using 10 mol % of bis(triphenylphosphine)benzylideneruthenium(II) dichloride, the Grubbs catalyst, to yield the tricyclic lactones **7a** (88% yield, 88% ee[9b]) and **7b** (87% yield, 82% ee[9b]).[10,11]

The relative configuration of **7b** was determined by an X-ray crystal structure analysis[12] (Figure 1); the absolute configurations at C-5 and C-6 are known from previous investigations, carried out on the precursors [8] and further advanced compounds.[13,14]



(a) i. *n*-BuLi/(–)-sparteine, toluene, –78 °C, 1.5 h; ii. ClTi(NEt$_2$)$_3$ (used for **2a**); ClTi(*i*-PrO)$_3$ (used for **2b**), –78 °C, 2 h; iii 2-propenal, –78 °C, 1 h; yield of **2a** = 56% (88% ee); **2b** = 34% (82% ee).[7]
(b) i. NEt$_3$, CH$_2$Cl$_2$, 0 °C; ii. TMSCl, CH$_2$Cl$_2$, 15 h rt; iii. *n*-BuLi/TMEDA, THF, –78 °C, 2 h; iv. MeSSMe, –78 °C, 3 h; yield of **3a** = 69%.
(c) MeSO$_3$H (1.1 equivs.), MeOH/H$_2$O, 50 °C, 15 h; yield of **4a** = 75% (88% ee); **4b** = 56%, from **2b**[7] (82% ee).
(d) LiHMDS, –78 °C, 1 h.
(e) Allyl bromide, THF, –78 °C, 1 h; yield of **6a** = 71%; **6b** = 75% (dr = 95:5 for both **6a** and **6b**).
(f) 10 Mol % Grubbs catalyst, CH$_2$Cl$_2$, rt, 15 h; yield of **7a** = 88% (88% ee); **7b** = 87% (82% ee).[8b]

1 – 7	**a**	**b**
n	1	2
R	*n*-C$_4$H$_9$	CH$_3$

Scheme 1. Synthesis of tricyclic lactones **7**.

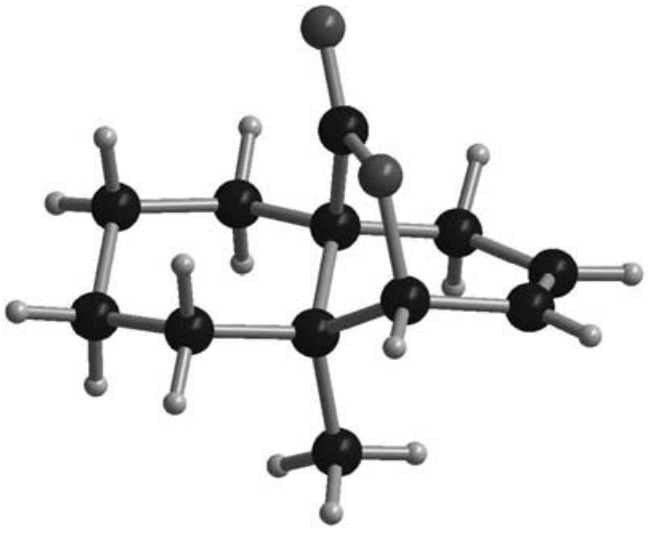


Figure 1. Solid-state structure of **7b**.[12]

Conclusion

The methodology provides a reliable and highly stereoselective access to tricyclic δ-lactones of type **7**, offering several reactive sites for further chemical manipulation. The method has also been applied to simpler analogues.[15]

Experimental Section

General Remarks

All reactions, which are sensitive to moisture or air, were carried out under Ar using the septum and syringe techniques. All solvents were purified by distillation or dried (Et$_2$O over sodium/benzophenone, CH$_2$Cl$_2$ over CaH$_2$) prior to use. Flash chromatography was carried out with silica gel (40–63 μm) using an Ar pressure of 1.2–1.4 bar. Chiral HPLC was carried out with a chiral column chiragrom-2, 60 × 2 mm, purchased from Grom Analytic and HPLC GmbH, Herrenberg. The solvent

system used for the measurement was hexane:*i*-PrOH (200:1). Chiral GC was carried out with a Beta-Dex™ 120 capillary column, 30 m, Supelco. ^{1}H and ^{13}C NMR spectra were recorded on ARX 300 and AMX 400 Bruker spectrometers. 2D NMR experiments for complete assignment of the signals were carried out on a Varian Unity Plus 600. $CDCl_3$ was used as solvent for NMR measurements, all signals are expressed as ppm downfield from TMS, used as an internal standard. IR absorption spectra were recorded using an IFS 28 purchased from Bruker and a PE 298 purchased from Perkin-Elmer & Co GmbH, Überlingen. The specific optical rotations were measured in a 10 cm cuvette on a polarimeter 241 purchased from Perkin-Elmer & Co GmbH, Überlingen. Elemental analysis was performed at the Microanalytical Section of the Organisch-Chemisches Institut, WWU Münster, on a Vario El III, purchased from Elementar-Analysen-Systeme GmbH. Exact mass measurements were carried out on Micro Tof (Brer Daltronics, Bremen), calibrations were done directly before the measurements of samples with sodium formate clusters.

{1*Z*,1(2*S*),1[2(1*R*)]}-[2-Butyl-2-(1-hydroxyprop-2-enyl)cyclopentylidene]methyl *N*,*N*-Diisopropylcarbamate (2a)

To a solution of **1a** (588 mg, 2.10 mmol) and (−)-sparteine (537 mg, 2.30 mmol) in toluene (10 mL) at −78 °C, *n*-BuLi (1.6 M, 1.43 mL, 2.30 mmol) was added dropwise under vigorous stirring. Then a precooled (−78 °C) solution of chlorotris(diethylamino)titanium [$ClTi(NEt_2)_3$, 1.88 g, 6.30 mmol] in toluene (2 mL) was added after 1.5 h. The reaction mixture was stirred for 2 h at −78 °C and subsequently 2-propenal (351 mg, 6.30 mmol) in toluene (2 mL) was added. Finally, the reaction mixture was stirred for 1 h at −78 °C before it was allowed to warm to room temperature. The solution was poured into an ice-cooled mixture of Et_2O (15 mL) and aqueous 2 N HCl (15 mL). The aqueous layer was extracted with Et_2O (3 × 15 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, petroleum ether:EtOAc = 10:1) and compound **2a** was obtained as a yellow oil; yield: 396 mg (56%); R_f = 0.25 (petroleum ether:EtOAc = 10:1); $[\alpha]_D^{20}$: +16.5 (*c* 1.05, $CHCl_3$). Chiral HPLC: chiragrom-2, hexane:*i*-PrOH = 200:1, 88% ee, major enantiomer appears at lower retention time.

rac-**2a** was prepared by applying the analogous procedure with *sec*-BuLi/TMEDA (1.1 equivs.) and **1a** (588 mg, 2.10 mmol); yield: 408 mg (58%); IR (film): ν = 3460 (OH), 1695 cm^{-1} (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.84 (t, 3H, CH_3), 0.95 (m, 2H, CH_2), 1.22–1.44 (m, 14H, CH_2 and CH_3), 1.53 (m, 2H, CH_2), 1.65 (m, 2H, CH_2), 1.73 (m, 2H, CH_2), 2.18 (m, 2H, CH_2), 3.85 (br s, 2H, CH), 5.03 (d, *J* = 6.7 Hz, 1H, CH), 5.07 (dd, *J* = 10.6 Hz, *J* = 1.6 Hz, 1H, CH_2), 5.18 (dd, *J* = 17.4 Hz, *J* = 1.6 Hz, 1H, CH_2), 5.74 (ddd, *J* = 10.6 Hz, *J* = 17.4 Hz, *J* = 6.7 Hz, 1H, CH), 6.85 (br s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.4 (CH_3), 20.6 (CH_3), 22.8 (CH_2), 24.9 (CH_2), 25.4 (CH_2), 27.7 (CH_2), 30.8 (CH_2), 32.5 (CH_2), 45.9 (CH), 46.6 (C_q), 75.7 (CH), 114.6 (CH_2), 129.9 (C_q), 132.2 (CH), 138.2 (CH), 153.8 (C=O); anal. calcd. for $C_{20}H_{35}NO_3$ (337.50): C 71.18, H 10.45, N 4.15; found: C 71.02, H 10.60, N 4.11; HR-MS: *m/z* calcd. for $C_{20}H_{35}NO_3Na$: 360.2509; found: 360.2530 $[M+Na]^+$.

{1*Z*,1(2*S*),1[2(1*R*)]}-1-[2-Butyl-2-(1-trimethylsilyloxyprop-2-enyl)-cyclopentylidene]-1-methylsulfanylmethyl *N*,*N*-Diisopropylcarbamate (3a)

To a solution of **2a** (340 mg, 1.00 mmol) in CH_2Cl_2 (5 mL), triethylamine (192 mg, 1.90 mmol) was added dropwise at 0 °C and stirred at 0 °C for 5 min. Subsequently, chlorotrimethylsilane (172 mg, 1.59 mmol) was added slowly and the reaction mixture was stirred for 15 h at room temperature. Then the mixture was extracted with Et_2O (3 × 20 mL) and a saturated solution of sodium hydrogen carbonate (10 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, petroleum ether:Et_2O = 4:1).

After dissolving the resulting product (335 mg, 0.82 mmol) and TMEDA (97 mg, 0.82 mmol) in THF (5 mL) at −78 °C, *n*-BuLi (0.55 mL, 0.90 mmol) was added dropwise and the solution was stirred for 2 h at −78 °C. Then dimethyl disulfide (85 mg, 0.90 mmol) was added slowly and the reaction mixture was stirred for further 3 h at −78 °C. The solution was allowed to warm to room temperature and extracted with Et_2O (3 × 20 mL) and saturated aqueous ammonium chloride (10 mL). The combined organic phases were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by flash column chromatography (petroleum ether:Et_2O = 4:1) to give **3a** as a colourless oil; yield: 313 mg (69% overall); R_F = 0.83 (silica gel, petroleum ether:Et_2O = 4:1).

rac-**3a** was prepared by applying the analogous procedure from *rac*-**2a** (340 mg, 1.00 mmol) as a colourless oil; yield: 320 mg (70%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.05 [s, 9H, $SiCH_3)_3$], 0.95 (t, 3H, CH_3), 1.19 (d, 12H, CH_3), 1.15–2.13 (m, 12H, CH_2), 2.26 (s, 3H, SCH_3), 3.82 (br s, 1H, CH), 3.91, (br s, 1H, CH), 4.97 (d, *J* = 6.7 Hz, 1H, CH), 5.11 (dd, *J* = 10.5 Hz, *J* = 1.7 Hz, 1H, CH_2), 5.17 (dd, *J* = 17.3 Hz, *J* = 1.6 Hz, 1H, CH_2), 5.59 (ddd, *J* = 17.3 Hz, *J* = 10.5 Hz, *J* = 6.7 Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 0.20 (CH_3), 13.8 (CH_3), 15.8 (CH_3), 20.3 (CH_3), 21.3 (CH_2), 23.2 (CH_2), 26.7 (CH_2), 28.9 (CH_2), 29.1 (CH_2), 32.1 (CH_2), 41.8 (C_q), 48.4 (CH), 73.0 (CH), 115.6 (CH_2), 114.6 (C_q), 138.4/140.5 (CH/C_q), 152.5 (C=O).

(1*R*,4*R*,5*S*)-5-Butyl-4-ethenyl-3-oxabicyclo[3.3.0]octan-2-one (4a)

A solution of **3a** (309 mg, 0.68 mmol), methanesulfonic acid (72 mg, 0.75 mmol), water (20 mg, 1.10 mmol), and MeOH (5 mL) was stirred at 50 °C for 15 h. Then the mixture was extracted with Et_2O (3 × 20 mL) and saturated aqueous sodium hydrogen carbonate (10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, petroleum ether:Et_2O = 4:1) to give **4a** as a colourless oil; yield:106 mg (75%); R_F = 0.21 (petroleum ether:Et_2O = 4:1); $[\alpha]_D^{20}$: −28.3 (*c* 0.61, $CHCl_3$). Chiral HPLC: chiragrom-2, hexane:*i*-PrOH = 200:1, 88% ee, major enantiomer appears at lower retention time.

rac-**4a** was obtained from **3a** (309 mg, 0.68 mmol) as a colourless oil; yield: 104 mg (74%); IR (film): ν = 2958, 2923, 2853 (C_{aliph}-H), 1773 cm^{-1} (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.95 (t, 3H, CH_3), 1.13–2.01 (m, 12H, CH_2), 2.23 (t, *J* = 5.3 Hz, 1H, CH), 5.07 (m, 1H, CH), 5.14 (m, 1H, CH_2),

5.21 (m, 1H, CH_2), 5.85 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.5 (CH_3), 21.8 (CH_2), 22.2 (CH_2), 22.2 (CH_2), 22.3 (CH_2), 26.3 (CH_2), 30.1 (CH_2), 42.5 (C_q), 43.9 (CH), 87.5 (CH), 114.4 (CH_2), 139.0 (CH), 178.1 (C=O); HR-MS: *m/z* calcd. for $C_{13}H_{20}O_2$: 209.1541; found: 209.1549 $[M+H]^+$.

(1*R*,4*R*,5*S*)-5-Butyl-4-ethenyl-1-(prop-2-enyl)-3-oxabicyclo[3.3.0]octan-2-one (6a)

To a solution of 1,1,1,3,3,3-hexamethyldisilazane (290 mg, 1.80 mmol) in THF (3 mL) was added *n*-BuLi (1.6 M, 0.60 mL, 0.95 mmol) at 0 °C. After stirring for 5 min, the solvent was removed under vacuum and the remaining crystals were dissolved in THF (5 mL) and, subsequently, **4a** (100 mg, 0.48 mmol) was added dropwise at −78 °C. After the reaction mixture had been stirred for 1 h at −78 °C, allyl bromide (180 mg, 1.70 mmol) was added dropwise and the reaction mixture was stirred for further 15 h at room temperature. Then the solution was extracted with Et_2O (3 × 20 mL) and saturated aqueous ammonium chloride (10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by silica gel flash column chromatography (petroleum ether:EtOAc = 20:1) to give **6a** as a colourless oil; yield: 85 mg (71%); R_F = 0.30 (petroleum ether:Et_2O = 20:1); $[\alpha]_D^{20}$: −20.9 (*c* 0.55, $CHCl_3$), 88% ee.

rac-**6a** was obtained from **4a** (100 mg, 0.43 mmol) as a colourless oil; yield: 87 mg (73%); IR (film): ν = 3073, 3012, 2958, 2926, 2859 (C-H), 1773 (C=O), 1644 cm^{-1} (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, 3H, CH_3), 1.16–2.11 (m, 12H, CH_2), 2.14 (m, 2H, CH_2), 4.83 (d, *J* = 6.8 Hz, 1H, CH), 4.89 (dm; 1H, *J* = 17.1 Hz, CH_2), 4.97 (dm, 1H, *J* = 10.1 Hz, CH_2), 5.05 (dt, *J* = 10.9 Hz, *J* = 1.4 Hz, 1H, CH_2), 5.15 (dt, *J* = 17.3 Hz, *J* = 1.4 Hz, 1H, CH_2), 5.67 (ddd, *J* = 17.3 Hz, *J* = 10.9 Hz, *J* = 6.8 Hz, 1H, CH), 5.83 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.8 (CH_3), 20.2 (CH_2), 21.3 (CH_2), 25.2 (CH_2), 26.2 (CH_2), 28.9 (CH_2), 29.9 (CH_2), 35.1 (CH_2), 44.8 (C_q), 48.4 (C_q), 73.0 (CH), 114.6 (CH_2), 135.6 (CH_2), 138.4 (CH), 140.5 (CH), 178.3 (C=O). HR-MS: *m/z* calcd. for $C_{16}H_{25}O_2$: 249.1854; found: 249.1861 $[M+H]^+$.

(1*S*,6*R*,9*R*)-9-Ethenyl-1-methyl-6-(prop-2-enyl)-8-oxabicyclo[4.3.0]nonan-7-one (6b)

Compound **6b** was prepared by applying the analogous procedure from **4b** (97 mg, 0.54 mmol); yield: 89 mg (75%); R_f = 0.29 (petroleum ether:EtOAc = 20:1); $[\alpha]_D^{20}$: −15.4 (*c* 0.35, $CHCl_3$), 82% ee.

rac-**6b** was prepared by applying the analogous procedure from *rac*-**4b** (158 mg, 0.88 mmol); yield: 139 mg (72%); IR (film): ν = 3076, 3018, 2979, 2936, 2863 (C_{aliph}-H), 1772 (C=O), 1639 cm^{-1} (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85 (s, 3H, CH_3), 1.28–1.39 (m, 2H, $2CH_2$), 1.44–1.52 (m, 3H, $3CH_2$), 1.52–1.60 (m, 1H, CH_2), 1.61–1.68 (m, 1H, CH_2), 1.70–1.76 (m, 1H, CH_2), 2.12 (dd, *J* = 14.4 Hz, *J* = 9.3 Hz, 1H, CH_2), 2.43 (dd, *J* = 14.4 Hz, *J* = 5.6 Hz, 1H, CH_2), 4.84 (d, *J* = 6.5 Hz, 1H, CH), 5.05 (dm, 1H, *J* = 17.2 Hz, CH_2), 5.08 (dm, 1H, *J* = 10.2 Hz, CH_2), 5.29 (dt, *J* = 10.9 Hz, 1H, CH_2), 5.34 (dt, *J* = 17.3 Hz, 1H, CH_2), 5.81 (ddd, *J* = 17.3 Hz, *J* = 10.9 Hz, *J* = 6.5 Hz, 1H, CH), 6.11 (dddd, *J* = 17.2 Hz, *J* = 10.2, *J* = 9.3 Hz, *J* = 5.6 Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 18.8 (CH_3), 20.3 (CH_2), 21.2 (CH_2), 27.9 (CH_2), 31.1 (CH_2), 35.4 (CH_2), 44.6 (C_q), 47.8 (C_q), 82.7 (CH), 117.7 (CH_2), 118.7 (CH_2), 132.4 (CH), 134.2 (CH), 180.0 (C=O); HR-MS: *m/z* calcd. for $C_{14}H_{20}O_2$: 220.14633; found: 220.14624 $[M+H]^+$.

(1*S*,5*R*,6*S*)-6-Butyl-11-oxatricyclo[4.3.2.0^{1,5}]undec-3-ene-10-one (7a)

The mixture of **6a** (80 mg, 0.32 mmol) and, bis(triphenylphosphine)benzylideneruthenium(II) dichloride (Grubbs catalyst) (26 mg, 0.032 mmol) in CH_2Cl_2 (5 mL) was stirred for 15 h at room temperature. Then the mixture was extracted with Et_2O (3 × 20 mL) and ammonium chloride solution (10 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and concentrated under vacuum. The residue was purified by flash column chromatography (silica gel, petroleum ether:Et_2O = 4:1) to give **7a** as a colourless oil; yield: 62 mg (88%); R_F = 0.25 (petroleum ether: Et_2O = 4:1); $[\alpha]_D^{20}$: −25.4 (*c* 0.53, $CHCl_3$), 88% ee.

rac-**7a** was obtained from *rac*-**6a** (80 mg, 0.32 mmol) as a colourless oil; yield: 63 mg (89%); IR (film): ν = 2980, 2965, 2923, 2863, (C_{aliph}-H), 1761 (C=O), 1635 cm^{-1} (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.79 (t, 3H, CH_3), 1.16–1.93 (m, 12H, CH_2), 2.04 (m, 2H, CH_2), 4.39 (m, 1H, CH), 5.89 (m, 1H, CH), 6.05 (m, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13.5 (CH_3), 20.4 (CH_2), 23.2 (CH_2), 25.3 (CH_2), 26.4 (CH_2), 27.9 (CH_2), 28.9 (CH_2), 35.5 (CH_2), 42.8 (C_q), 48.4 (C_q), 79.0 (CH), 128.4 (CH), 132.5 (CH), 180.3 (C=O); anal. calcd. for $C_{14}H_{20}O_2$ (220.31): C 76.33, H 9.15; found: C 76.36, H 9.19.

(1*S*,5*R*,6*S*)-6-Methyl-12-oxatricyclo[4.4.2.0^{1,5}]dodec-3-en-11-one (7b)

Compound **7b** was prepared by applying the analogous procedure from **6b** (75 mg, 0.34 mmol) and Grubbs catalyst (28 mg, 0.034 mmol); yield: 57 mg (87%); R_f = 0.24 (petroleum ether:Et_2O = 4:1), mp 133 °C (petroleum ether:Et_2O); $[\alpha]_D^{20}$: +70.1 (*c* 0.37, $CHCl_3$) 82% ee. IR (KBr): ν = 2997, 2980, 2936, 2860, 2828 (C_{aliph}-H), 1759 (C=O), 1636 cm^{-1} (C=C).

rac-**7b** was prepared by applying the analogous procedure from *rac*-**6b** (21 mg, 0.0095 mmol); yield: 15 mg (87%); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.08 (s, 3H, CH_3), 1.21–1.93 (m, 8H, CH_2), 2.00 (ddd, *J* = 19.1 Hz, *J* = 3.0 Hz, *J* = 2.8 Hz, 1H, CH_2), 2.11 (ddd, *J* = 19.1 Hz, *J* = 3.4 Hz, *J* = 1.7 Hz, 1H, CH_2), 4.09 (dm, *J* = 5.5 Hz, *J* = 1.0 Hz, 1H, CH), 5.83 (dddd, *J* = 9.4 Hz, *J* = 3.4 Hz, *J* = 3.0 Hz, *J* = 1.0 Hz, 1H, CH), 6.07 (dddd, *J* = 9.4 Hz, *J* = 5.5 Hz, *J* = 2.8 Hz, *J* = 1.7 Hz, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 15.0 (CH_3), 21.8 (CH_2), 22.8 (CH_2), 27.7 (CH_2), 33.0 (CH_2), 34.6 (CH_2), 42.3 (C_q), 48.3 (C_q), 79.1 (CH), 127.5 (CH), 131.3 (CH), 180.5 (C=O); anal. calcd. for $C_{12}H_{16}O_2$ (192.25): C 74.97, H 8.39; found: C 74.95, H 8.65.

X-Ray Crystallographic Study[12]

X-ray crystal structure analysis for HOP1392: formula $C_{12}H_{16}O_2$, *M* = 192.25, colourless crystal 0.50 × 0.30 × 0.20 mm, *a* = 6.786(5), *b* = 16.492(8), *c* = 8.990(2) Å, *V* = 1001.9(9) Å^3, ϱ_{calc} = 1.275 g cm^{-3}, μ = 6.78 cm^{-1}, empirical absorption cor-

rection *via* ψ scan data ($0.728 \leq T \leq 0.876$), $Z=4$, monoclinic, space group $P2_1$ (No. 4), $\lambda=1.54178$ E, $T=223$ K, $\omega/2\theta$ scans, 2298 reflections collected ($+h$, $+k$, $\pm l$), $[(\sin\theta)/\lambda]=0.62$ E^{-1}, 2121 independent ($R_{int}=0.111$) and 1816 observed reflections [$I \geq 2\ \sigma(I)$], 255 refined parameters, $R=0.068$, $wR^2=0.173$, Flack parameter 0.2(4), max. residual electron density 0.55 (-0.30) e $Å^{-3}$, two almost identical molecules in the asymmetric unit, hydrogens calculated and refined as riding atoms.

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