Combining Ring-Closing Metathesis and Hydroformylation Strategies: A Novel Approach to Spirocyclic γ-Butyrolactones

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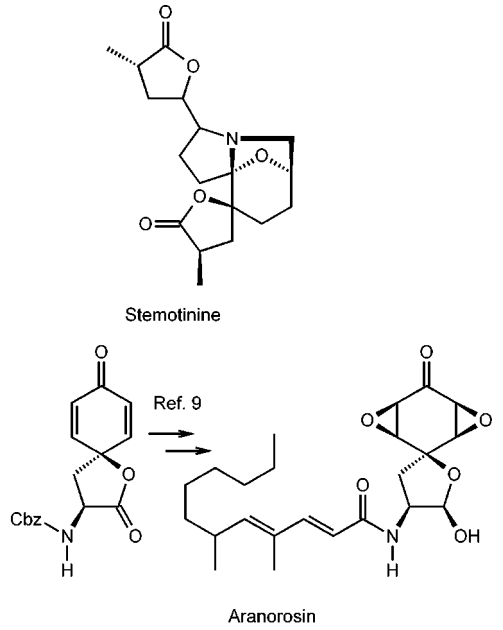
Di- or tetrahydropyrans with a vinyl side chain are obtained by diastereoselective ring-closing metathesis or by addition of vinylmagnesium chloride to an appropriately functionalized tetrahydropyranone. The resulting allylic alcohols are converted to spirocyclic hemiacetals under hydroformylation conditions. Oxidation yields the corresponding lactones.

Introduction

Spirocyclic γ-butyrolactones not only are widespread in nature[1−4] but have also played a key role as synthetic intermediates.[5−7] One example of a natural product with a spirocyclic γ-butyrolactone moiety is the alkaloid stemotinine,[8] and the antitumor antibiotic aranorosin may serve as an example where a spirocyclic lactone has been used as a key intermediate in the total synthesis[9] (Chart 1). Furthermore, a variety of methods are available for the conversion of γ-butyrolactones into α-methylene-γ-butyrolactones.[10] Spirocyclic, steroidal derivatives of these compounds often show outstanding biological properties.[3,4] In principle, one can imagine two different strategies for the construction of spiro compounds: (i) the conversion of a tetrafunctional acyclic compound into a spirocyclic system in a one-pot reaction or (ii) the stepwise formation of two carba- or heterocycles via a monocyclic intermediate. A variety of methods for the synthesis of lactones is available, for example, lactonization after asymmetric dihydroxylation, iodolactonization, palladium-catalyzed cyclization of allenic or homopropargylic carboxylic acids, or samarium-mediated addition of ketones to acrylates. This subject has been reviewed several times over the past few years.[11−14]

Chart 1



In this contribution, we present a novel concept for the synthesis of spirocyclic lactones, which is based on a ruthenium-catalyzed olefin metathesis and a rhodium-catalyzed hydroformylation−acetalation sequence (Scheme 1).

We demonstrate the utility of our approach for the example of di- or tetrahydropyrans linked to lactones in a spirocyclic fashion. Although this class of substances might be interesting in itself,[5,6] they may also serve, after cleavage of the lactone, as intermediates in the synthesis of pyran derivatives with functionalized side chains. This structural element is found in several natural products such as the pseudomonic acids.[15]

The ring-closing olefin metathesis[16−18] has become one of the most powerful cyclization reactions since the

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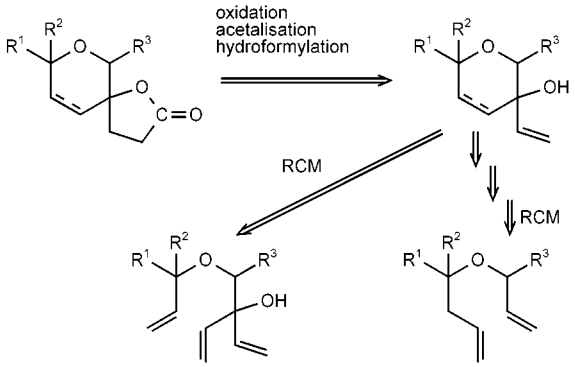
Scheme 1



introduction of highly efficient precatalysts by Schrock[19] and Grubbs.[20] The RCM reaction has been used in the synthesis of spirocycles, either for cyclization of two rings by double-ring-closing metathesis[21−27] or by single-ring-closing metathesis starting from an appropriately functionalized monocyclic precursor.[28−33]

Hydroformylation of olefins not only is a well-established method for the industrial production of aldehydes but has also found interesting applications in organic synthesis.[34] The incorporation of a hydroformylation step in sequential reactions has proven to be a particularly valuable concept.[35] For example, the hydroformylation of an allylic or homoallylic alcohol yields hemiacetals via formation of the primarily formed aldehydes.[36−38] The hemiacetals may be converted into cyclic enol ethers by elimination[39] or into lactones by oxidation.[40]

Results and Discussion

Preparation of Monocyclic Precursors. Starting from the protected allyl-homoallyl ether **2** (obtained by benzylation of alcohols **1**),[26] we obtained the dihydropyrans **3** by ring-closing metathesis. Epoxidation was moderately diastereoselective for the methyl derivative **3a** (diastereomeric ratio = 2:1), whereas the phenyl derivative **3b** was obtained as a 6:1 mixture of diastereoisomers. Compound **4a** was treated as a mixture of diastereomers with benzylic alcohol in the presence of borontrifluoride etherate. Upon chromatography, the major isomer (3*S**,4*S**,6*R**)-**5a** was isolated, which was used for further transformations. In the case of epoxide **4b**, the minor diastereomer was removed by flash chromatography. Epoxide cleavage under the same conditions gave (3*S**,4*S**,6*S**)-**5b** and (2*S**,4*R**,5*R**)-**5b** as a 4.5:1 mixture of regioisomers. Oxidation of the hydroxyl functionality was achieved using TPAP/NMO[41] to yield the ketones **6a**,**b**. Attack of vinylmagnesium chloride occurred from the face opposite to the benzyloxy substituent to give the tertiary allylic alcohols **7a**,**b** with high diastereoselectivity (only one diastereomer was detected in the ^{1}H NMR spectrum) (Scheme 2).

We have recently devised an alternative synthesis for pyran derivatives with an *exo*-vinyl moiety. Ring-closing metathesis of divinyl carbinols **8a** and **8b** gives dihydropyrans **9a** and **9b** in diastereomeric ratios of 3:1 and 4:1, respectively.[27,42] Ring-closing metathesis of triene **10** yields dihydropyrans (5*R**,8*S**)-**11** and (5*S**,8*S**)-**11** as an easily separable mixture of diastereomers (Scheme 3).

Preparation of Spirocyclic Products. Allylic alcohols **7a**,**b** were subjected to hydroformylation in the presence of Rh(acac)(CO)$_2$ (1.0 mol %) and BIPHEPHOS (4.0 mol %)[43] under 10 bar of carbon monoxide and 10 bar of hydrogen at 60 °C. Under these mild conditions, hemiacetals **12a**,**b** result as mixtures of anomers, which is indicated by signals at approximately 99 ppm in the carbon NMR spectrum. Side products resulting from formation of the branched aldehyde could not be detected. The crude hemiacetals were oxidized to the lactones **13a**,**b** using TPAP/NMO. Compound (5*R**,8*R**,10*S**)-**13a** was obtained from **7a** (single isomer), and **7b** (mixture of regioisomers) was converted to (5*R**,8*R**,10*S**)-**13b** and (5*S**,6*R**,9*S**)-**13b**. The regioisomers were separated by column chromatography and fully characterized (Scheme 4).

Hydroformylation of dihydropyrans **9a**, **9b**, (5*R**,8*S**)-**11**, and (5*S**,8*S**)-**11** is highly regio- and chemoselective, with only the *exo*-vinyl moiety being attacked under the reaction conditions. The hemiacetals **12**, **14**, and **16** were obtained as inseparable mixtures of anomers, which were immediately oxidized to the corresponding lactones **13**, **15**, and **17** using the TPAP/NMO reagent combination. Compounds **9a**,**b** were employed as 3:1 and 4:1 mixtures of diastereoisomers. The resulting lactones (5*S*,6*S*)- and (5*R*,6*S*)-**15a** and (5*S**,6*S**)- and (5*R**,6*S**)-**15b** could be easily separated by flash chromatography on silica. Compounds (3*R**,6*S**)-**11** and (3*S**,6*S**)-**11** were employed as single diastereomers. In these cases, single isomers of the corresponding lactones (5*R**,8*S**)-**17** and (5*S**,8*S**)-**17** were obtained (Scheme 5).

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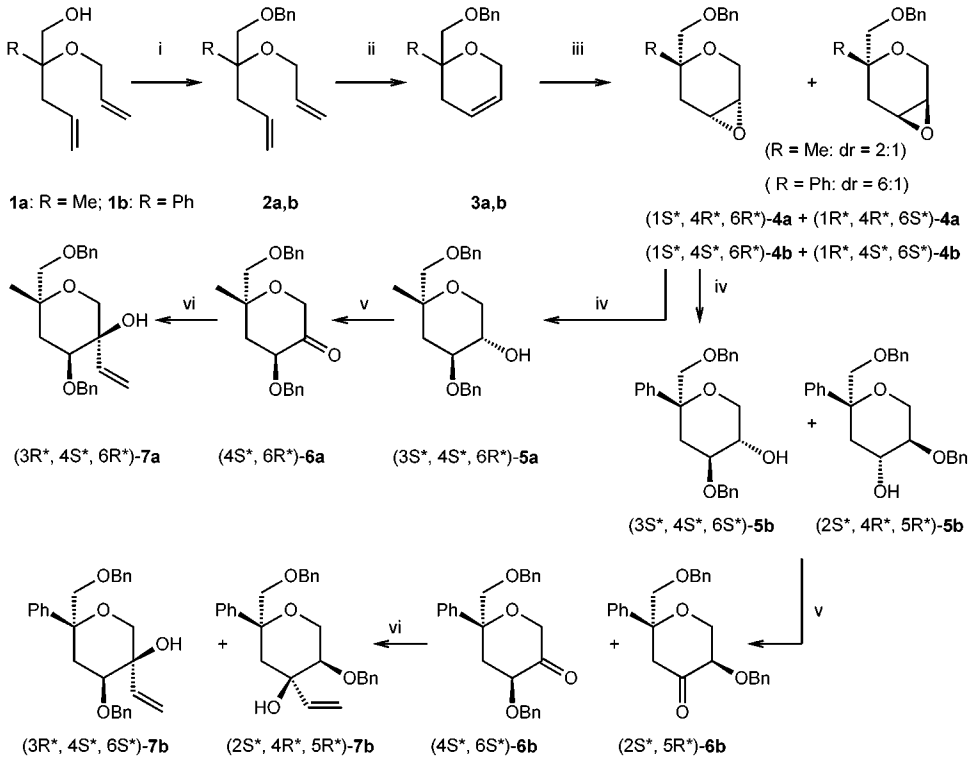
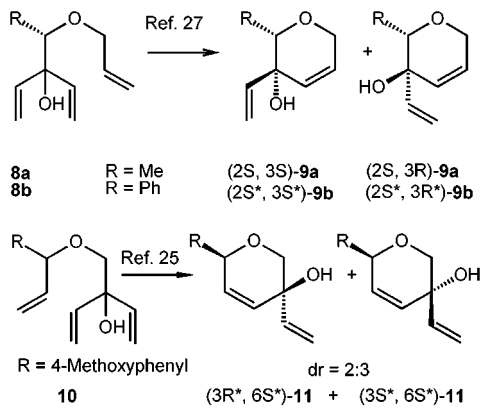
Scheme 2[a]



[a] Key: (i) NaH, BnBr, THF (90% of **2a**, 91% of **2b**); (ii) $Cl_2(Cy_3P)_2Ru{=}CHPh$ (1 mol %), DCM (81% of **3a**, 88% of **2b**); (iii) MCPBA, DCM (91% of **4a**, 99% of **4b**); (iv) BnOH, BF_3OEt_2 (10 mol %), DCM, 0 °C, chromatography (57% of (3*S**,4*S**,6*R**)-**5a**, 78% of (3*S**,4*S**,6*S**)-**5b** and (2*S**,4*R**,5*R**)-**5b**) (4.5:1); (v) TPAP (5 mol %), NMO, 4 Å molecular sieve, DCM (84% of **6a**, 82% of **6b**); (vi) $H_2C{=}CHMgCl$, ether, −78 °C (66% of **7a**, 89% of **7b**).

Scheme 3



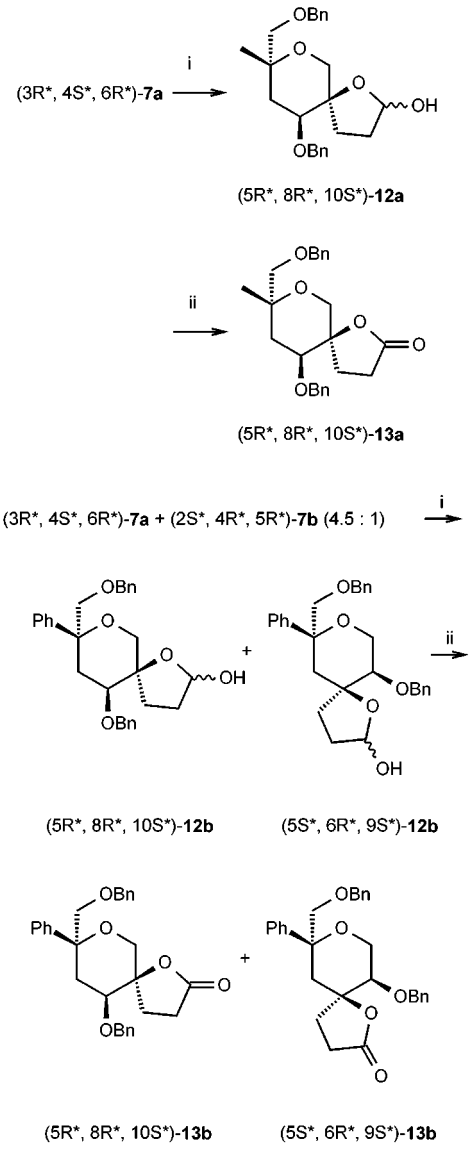
NOE Experiments. The relative configuration of all spirocyclic products was investigated by one- or two-dimensional NOE experiments conducted at 600 or 500 MHz, respectively. For spirocyclic tetrahydropyran **13a**, NOE interactions between the methyl group in the 2-position and the proton H3ax and between the $-CH_2$-OBn moiety and the proton H6ax indicate that the molecule preferably adopts the conformation depicted in Scheme 6. One proton of the CH_2 group of the lactone moiety shows NOE interactions with both protons H6, whereas the other proton of this CH_2 group shows a NOE interaction with H4. The phenyl analogue (5*R**,8*R**,-10*S**)-**13b** shows similar NOE interactions. Its regioisomer (5*S**,6*R**,9*S**)-**13b** adopts a conformation with the phenyl substituent in an axial position: NOE interactions between the *ortho*-H of the phenyl moiety and H6ax as well as H3eq are observed. A NOE interaction between the axially oriented H5 and one proton of the methylene moiety of the lactone ring is indicative of the relative configuration shown in Scheme 6.

NOE interactions for spirocyclic dihydropyrans **15** are summarized in Scheme 7. A NOE interaction between H6ax and H2 indicates that the phenyl moiety adopts a pseudoequatorial position. In the case of (5*S**,6*S**)-**15b**, a NOE interaction between H2 and one proton of the methylene group of the lactone moiety is observed, which is missing for the other diastereomer. For the (5*R**,6*S**)-isomer, a NOE interaction between the ortho protons of the phenyl group and one proton of the methylene group is indicative for the proposed relative configuration. For the methyl derivative **15a**, analogous NOE interactions were observed for the protons of the methyl group.

For dihydropyrans **17** with the spirocyclic junction in the 5-position, NOE interactions of the protons H6ax and H6eq with the methylene group of the lactone ring are most indicative of the relative configuration. For both diastereomers, a NOE effect is observed between the singlet of H2 and one doublet of the H6-AB-system; assignment of the corresponding signals to H6ax and H6eq, respectively, is made on the basis of this interaction. In (5*S**,8*S**)-**17**, a NOE interaction between H6ax and one proton of the methylene group of the lactone is observed, whereas in (5*R**,8*S**)-**17**, H6eq interacts with this CH_2 group (Scheme 8).

In conclusion, we have developed a synthetic approach toward bicyclic spiro compounds with a lactone moiety linked to a six-membered oxacycle on the basis of ring-closing metathesis and a hydroformylation−acetalation sequence. Use of the BIPHEPHOS ligand system allows the differentiation between exocyclic and endocyclic C−C

Scheme 4[a]



[a] Key: (i) $Rh(acac)(CO)_2$ (1.0 mol %), BIPHEPHOS (4.0 mol %), CO (10 bar), H_2 (10 bar), dioxane; (ii) TPAP (5 mol %), NMO, 4 Å molecular sieve, DCM (80% of **13a**, 54% of **13b**).

double bonds under hydroformylation conditions, making spirocyclic dihydropyrans accessible. Further synthetic applications for the combination of olefin metathesis and hydroformylation strategies are currently under investigation in our laboratory.

Experimental Section

Instrumentation, product identification, and general experimental methods have been described previously.[44] Hydroformylation reactions were conducted in steel pressure vessels with a PTFE insert. Signal assignment for NMR spectra is made on the basis of 2D methods (H, H−COSY) or NOE experiments. Signal assignment for cyclic products follows a numbering scheme where the oxygen atom is numbered 1 and the α-carbon atom bearing a substituent is C2. The number of coupled protons was analyzed by DEPT experiments and is denoted by a number in parantheses following the δ_C value. One-dimensional, gradient-selected NOE spectra were obtained at 600 MHz with a mixing time of 800 ms. Two-dimensional NOESY spectra were obtained at 500 MHz with a mixing time of 1.5 s.

2-Allyloxy-2-methyl-pent-4-enyloxymethylbenzene (2a). To a solution of the primary alcohol **1a** (8.65 g, 55 mmol) in THF (150 mL) was added NaH (60% dispersion in mineral oil, 6.65 g, 166 mmol). The mixture was heated to reflux for 30 min and cooled to ambient temperature. Benzyl bromide (9.9 mL, 83 mmol) was added, and the mixture was again refluxed until the starting material was fully consumed as indicated by TLC. After aqueous workup, the solvent was evaporated and the residue was distilled (bp 130 °C, 0.4 mbar) to give 12.23 g (90%) of the benzyl ether **2a**. IR (neat): 698 s, 1103 s, 1454 m, 2859 m, 2982 m. MS *m*/*z* (relative (rel) intensity): 247 ($M^+ + 1$, <5), 131 (60), 91 (100). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27−7.17 (5H), 5.83 (dddd, 1H, J = 17.1, 10.5, 5.3, 5.3 Hz), 5.73 (dddd, 1H, J = 17.5, 10.5, 7.0, 7.0 Hz), 5.18 (dddd, 1H, J = 17.1, 1.5, 1.5, 1.5 Hz), 5.03 (dddd, 1H, J = 10.5, 1.5, 1.5, 1.5 Hz), 4.98 (dddd, 1H, J = 17.5, 1.5, 1.5, 1.5 Hz), 4.94 (dddd, 1H, J = 10.5, 1.5, 1.5, 1.5 Hz), 4.45 (s, 2H), 3.93 (m, 1H), 3.89 (dddd, 1H, J = 11.8, 5.3, 1.5, 1.5 Hz), 3.32 (d, 1H, J = 9.8 Hz), 3.25 (d, 1H, J = 9.8 Hz), 2.30 (dddd, 1H, J = 14.8, 7.0, 1.5, 1.5 Hz), 2.27 (dddd, 1H, J = 14.8, 7.0, 1.5, 1.5 Hz), 1.10 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 138.2 (0), 135.8 (1), 134.0 (1), 128.2 (1), 127.5 (1), 127.4 (1), 117.5 (2), 115.6 (2), 76.6 (0), 74.5 (2), 73.2 (2), 63.2 (2), 40.4 (2), 20.9 (3). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.0; H, 9.0. Found: C, 77.6; H, 8.8.

2-Allyloxy-2-phenyl-pent-4-enyloxymethylbenzene (2b). Following the procedure for the methyl analogue, we obtained **2b** (16.0 g, 91%) from primary alcohol **1b** (12.5 g, 57 mmol) as a colorless liquid (bp 130 °C, 0.4 mbar). IR (neat): 699 s, 1072 s, 1103 s, 1496 m, 3075 m. MS *m*/*z* (rel intensity): 308 ($M^+ - 1$, <5), 267 (5), 187 (25), 145 (25), 131 (80), 105 (80), 91 (100), 77 (25). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.32−7.13 (10H), 5.82 (dddd, 1H, J = 17.3, 10.3, 5.3, 5.3 Hz), 5.63 (dddd, 1H, J = 17.3, 10.3, 7.0, 7.0 Hz), 5.20 (dddd, 1H, J = 17.3, 1.5, 1.5, 1.5 Hz), 5.04 (dddd, 1H, J = 10.3, 1.5, 1.5, 1.5 Hz), 4.97 (dm, 1H, J = 17.3 Hz), 4.94 (dm, 1H, J = 10.3 Hz), 4.42 (d, 1H, J = 12.8 Hz), 4.39 (d, 1H, J = 12.8 Hz), 3.76 (dddd, 1H, J = 12.8, 5.3, 1.5, 1.5 Hz), 3.73 (m, 1H), 3.70 (d, 1H, J = 9.5 Hz), 3.59 (d, 1H, J = 9.5 Hz), 2.75 (ddm, 1H, J = 14.3, 7.0 Hz), 2.64 (ddm, 1H, J = 14.3, 7.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 142.2 (0), 138.2 (0), 135.2 (1), 133.5 (1), 128.2 (1), 128.0 (1), 127.5 (1), 127.5 (1), 127.1 (1), 126.6 (1), 117.9 (2), 115.7 (2), 80.3 (0), 73.3 (2), 73.3 (2), 63.8 (2), 40.3 (2). Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.8; H, 7.8. Found: C, 82.1; H, 7.8.

2-Benzyloxymethyl-2-methyl-3,6-dihydro-2*H*-pyran (3a). To a solution of **2a** (5.00 g, 20 mmol) in DCM (50 mL) was added Grubbs' catalyst (167 mg, 1 mol %). The reaction mixture was stirred at ambient temperature until the starting material was fully consumed as indicated by TLC. The solvent was evaporated, and the residue was purified by flash chromatography on silica using 5:1 (v/v) cyclohexane/MTBE as the eluent to give the dihydropyran **3a** (3.60 g, 81%). IR (neat): 746 m, 1091 s, 1454 m, 2829 m, 3033 m. MS *m*/*z* (rel intensity): 219 ($M^+ + 1$, 40), 201 (30), 181 (60), 153 (70), 129 (100). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27−7.16 (5H), 5.67 (dm, 1H, J = 10.3 Hz), 5.61 (dm, 1H, J = 10.3 Hz), 4.53 (d, 1H, J = 12.5 Hz), 4.48 (d, 1H, J = 12.5 Hz), 4.11 (dm, 1H, J = 16.8 Hz), 4.06 (dm, 1H, J = 16.8 Hz), 3.33 (d, 1H, J = 9.8 Hz), 3.24 (d, 1H, J = 9.8 Hz), 2.13 (dm, 1H, J = 17.5 Hz), 1.77 (dm, 1H, J = 17.5 Hz), 1.18 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.3 (0), 128.2 (1), 127.5 (1), 127.4 (1), 125.1 (1), 122.6 (1), 75.7 (2), 73.4 (2), 71.7 (0), 61.0 (2), 31.7 (2), 20.9 (3). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.0; H, 8.3. Found: C, 76.0; H, 8.1.

2-Benzyloxymethyl-2-phenyl-3,6-dihydro-2*H*-pyran (3b). Following the procedure for the methyl analogue, we obtained **3b** (4.0 g, 88%) from **2b** (5.0 g, 16 mmol) after flash chromatography as a colorless liquid. IR (neat): 699 s, 1097 s, 2851 m, 2936 m. MS *m*/*z* (rel intensity): 281 ($M^+ + 1$, 10), 207 (40), 159 (50), 105 (100), 91 (40), 77 (40). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38−7.34 (d, 2H, J = 7.5 Hz), 7.29−7.09 (8H), 5.78 (ddddd, 1H, J = 10.3, 2.5, 2.5, 2.5, 2.5 Hz), 5.46 (ddddd, 1H, J = 10.3, 2.5, 2.5, 2.5, 2.5 Hz), 4.49 (d, 1H, J = 12.5 Hz), 4.36 (d, 1H, J = 12.5 Hz), 4.11 (ddddd, 1H, J = 17.0, 2.5, 2.5, 2.5, 2.5 Hz), 3.86 (ddddd, 1H, J = 17.0, 2.5, 2.5, 2.5, 2.5 Hz), 3.52

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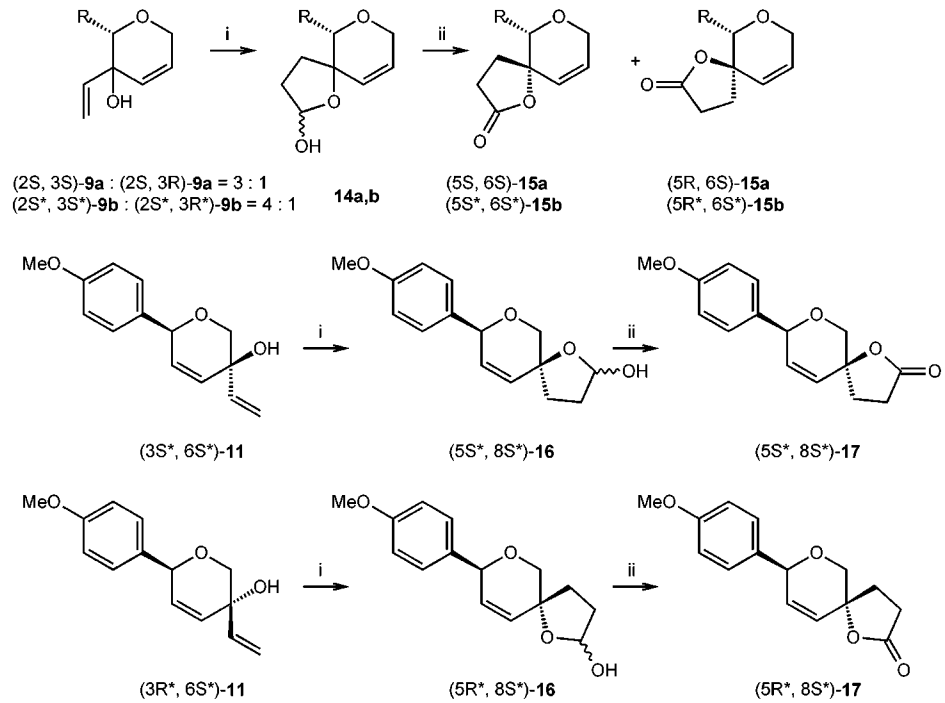
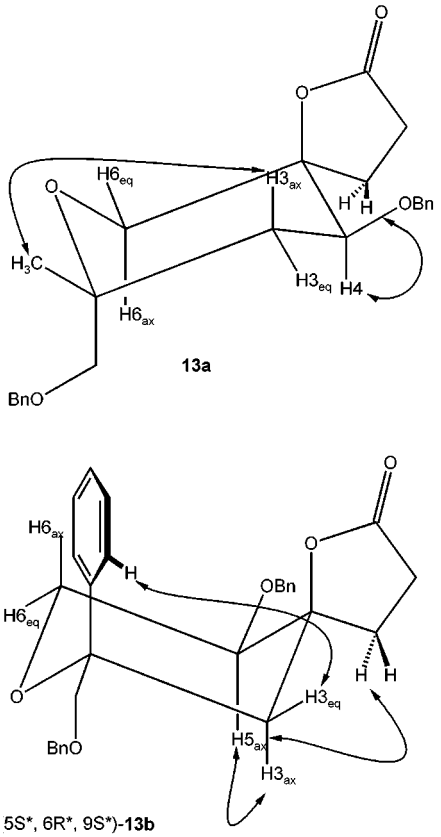
Scheme 5[a]

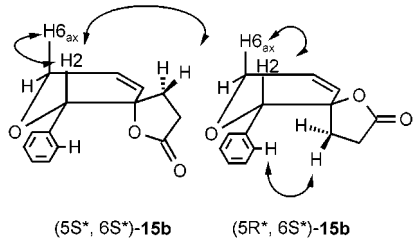


[a] Key: (i) $Rh(acac)(CO)_2$ (1.0 mol %), BIPHEPHOS (4.0 mol %), CO (10 bar), hydrogen (10 bar), dioxane; (ii) TPAP (5 mol %), NMO, 4 Å molecular sieve, DCM (52−81% over two steps).

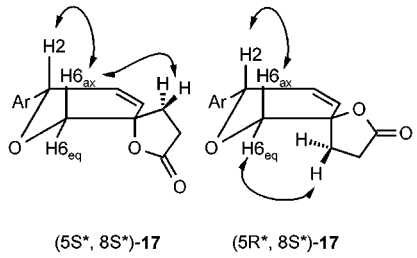
Scheme 6



Scheme 7



Scheme 8



(d, 1H, J = 10.0 Hz), 3.37 (d, 1H, J = 10.0 Hz), 2.70 (ddddd, 1H, J = 17.8, 2.5, 2.5, 2.5, 2.5 Hz), 2.55 (ddddd, 1H, J = 17.8, 2.5, 2.5, 2.5, 2.5 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 140.9 (0), 138.2 (0), 128.2 (1), 128.1 (1), 127.5 (1), 127.4 (1), 127.3 (1), 126.8 (1), 125.7 (1), 122.8 (1), 76.3 (0), 77.1 (2), 73.4 (2), 61.7 (2), 28.3 (2). Anal. Calcd for $C_{19}H_{20}O_4$: C, 81.4; H, 7.2. Found: C, 81.1; H, 7.2.

4-Benzyloxymethyl-4-methyl-3,7-dioxabicyclo[4.1.0]-heptane (4a). To a solution of the dihydropyran **3a** (2.65 g, 12.1 mmol) in DCM (50 mL) was added MCPBA (70% dispersion in water, 3.14 g, 18.2 mmol). The mixture was stirred until the starting material was completely consumed as indicated by TLC. The reaction mixture was diluted with MTBE and washed with Na_2SO_3 solution and then Na_2CO_3 solution. The organic layer was dried, filtered, and evaporated, and the residue was purified by flash chromatography on silica to give epoxide **4a** (2.75 g, 97%) as a 2:1 mixture of diastereoisomers. Spectroscopic data for the major (1*S**,4*R**,6*R**)-isomer. IR (neat): 739 s, 1110 s, 1454 m, 2862 m. MS *m*/*z* (rel intensity): 235 ($M^+ + 1$, 10), 181 (10), 143 (15), 113 (85), 91 (100), 65 (20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.34−7.22 (5H), 4.52 (d, 1H, J = 12.3 Hz), 4.45 (d, 1H, J = 12.3 Hz), 4.02 (d, 1H, J = 13.8 Hz), 3.95 (d, 1H, J = 13.8 Hz), 3.32 (d, 1H, J = 9.5 Hz), 3.29 (dd, 1H, J = 9.8, 4.8 Hz), 3.20 (d, 1H, J = 9.5 Hz), 3.04 (m, 1H), 1.89 (d, 1H, J = 15.3 Hz), 1.63 (dd, 1H, J = 15.3, 5.7 Hz),

1.21 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.2 (0), 128.2 (1), 127.6 (1), 127.5 (1), 76.6 (2), 73.4 (2), 70.4 (0), 58.8 (2), 49.4 (1), 48.7 (1), 30.7 (2), 20.7 (3). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.8; H, 7.7. Found: C, 72.1; H, 7.6.

(1*S,4*S**,6*R**)-4-Benzyloxymethyl-4-phenyl-3,7-dioxabicyclo[4.1.0]heptane (4b).** Following the procedure for the methyl analogue, we obtained **4b** (2.50 g, 99%) from **3b** (2.39 g, 8.5 mmol) as a 6:1 mixture of diastereomers. The major isomer was separated by flash chromatography as a colorless solid (mp 69 °C). IR (KBr, disk): 699 m, 1104 s, 2858 m, 3028 m. MS *m*/*z* (rel intensity): 297 ($M^+ + 1$, 10), 279 (15), 175 (100), 145 (20), 105 (30), 91 (40). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38−7.10 (10H), 4.49 (d, 1H, J = 12.5 Hz), 4.35 (d, 1H, J = 12.5 Hz), 3.96 (d, 1H, J = 13.5 Hz), 3.61 (d, 1H, J = 13.5 Hz), 3.50 (d, 1H, J = 10.0 Hz), 3.40 (d, 1H, J = 6.5 Hz), 3.37 (d, 1H, J = 10.0 Hz), 2.79 (d, 1H, J = 4.3 Hz), 2.68 (dd, 1H, J = 16.1, 6.0 Hz), 2.37 (d, 1H, J = 16.1 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.4 (0), 138.1 (0), 128.5 (1), 128.2 (1), 127.7 (1), 127.5 (1), 127.4 (1), 127.4 (1), 77.7 (2), 75.2 (0), 73.3 (2), 59.4 (2), 48.6 (1), 48.5 (1), 27.6 (2). Anal. Calcd for $C_{19}H_{20}O_3$: C, 77.0; H, 6.8. Found: C, 76.8; H, 6.8.

(3*S,4*S**,6*R**)-4-Benzyloxy-6-benzyloxymethyl-6-methyl-tetrahydropyran-3-ol (5a).** To a solution of the epoxide **4a** (2:1 mixture of diastereomers, 2.09 g, 8.9 mmol) and benzylic alcohol (9.3 mL, 89.4 mmol) was added borontrifluoride etherate (0.1 mL, 0.8 mmol) at 0 °C. The mixture was stirred at this temperature until the starting material was completely consumed as indicated by TLC and diluted with MTBE. The reaction was quenched with Na_2CO_3 solution, and the mixture was dried with $MgSO_4$, filtered, and evaporated. Upon flash chromatography on silica, only the (3*S**,4*S**,6*R**)-isomer of **5a** was isolated in pure form (1.73 g, 57%). IR (neat): 698 s, 737 s, 1094 s, 1454 m, 2867 m, 2929 m, 3436 br s. MS *m*/*z* (rel intensity): 341 ($M^+ - 1$, <5), 221 (40), 167 (20), 91 (100), 65 (20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.36−7.26 (10H), 4.63 (d, 1H, J = 11.5 Hz), 4.57 (d, 1H, J = 12.3 Hz), 4.51 (d, 1H, J = 12.3 Hz), 4.44 (d, 1H, J = 11.5 Hz), 3.92 (dd, 1H, J = 11.8, 4.0 Hz), 3.62 (ddd, 1H, J = 7.5, 7.5, 4.0 Hz), 3.58 (ddd, 1H, J = 9.0, 7.5, 4.0 Hz), 3.48 (dd, 1H, J = 11.8, 7.5 Hz), 3.41 (d, 1H, J = 9.5 Hz), 3.36 (d, 1H, J = 9.5 Hz), 2.40 (bs, 1H), 2.21 (dd, 1H, J = 13.8, 4.0 Hz), 1.42 (dd, 1H, J = 13.8, 9.0 Hz), 1.29 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 138.2 (0), 138.1 (0), 128.5 (1), 128.4 (1), 127.8 (1), 127.7 (1), 127.6 (1), 127.5 (1), 77.2 (0), 77.0 (1), 73.7 (2), 73.5 (2), 70.8 (2), 69.5 (1), 64.0 (2), 34.8 (2), 25.0 (3). Anal. Calcd for $C_{21}H_{26}O_4$: C, 73.7; H, 7.7. Found: C, 73.3; H, 7.4.

(3*S,4*S**,6*S**)-4-Benzyloxy-6-benzyloxymethyl-6-phenyltetrahydropyran-3-ol (5b).** Following the procedure for the methyl analogue, we obtained **5b** (2.90 g, 78) from **4b** (2.73 g, 9.2 mmol) as a 4.5:1 mixture of regioisomers. Spectroscopic data were obtained from the mixture. IR (neat): 699 s, 1075 s, 1096 s, 2866 m, 3426 br s. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.37 (d, 2H, J = 7.5 Hz), 7.27−7.10 (6H), 7.02 (d, 2H, J = 8.0 Hz), 4.49 (d, 1H, J = 11.8 Hz), 4.42 (d, 1H, J = 12.5 Hz), 4.35 (d, 1H, J = 11.8 Hz), 4.31 (d, 1H, J = 12.5 Hz), 3.97 (dd, 1H, J = 11.8, 3.5 Hz), 3.68 (ddd, 1H, J = 7.3, 6.3, 4.3 Hz), 3.62 (dd, 1H, J = 11.8, 6.0 Hz), 3.54 (ddd, 1H, J = 6.3, 6.0, 3.5 Hz), 3.48 (d, 1H, J = 10.0 Hz), 3.40 (d, 1H, J = 10.0 Hz), 2.76 (bs, 1H), 2.60 (dd, 1H, J = 14.3, 7.3 Hz), 1.92 (dd, 1H, J = 14.3, 4.3 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.2 (0), 138.2 (0), 137.9 (0), 128.3 (1), 128.2 (1), 127.9 (1), 127.5 (1), 127.5 (1), 127.3 (1), 126.9 (1), 126.0 (1), 78.1 (0), 76.4 (1), 75.8 (2), 73.4 (2), 70.7 (2), 68.6 (1), 64.3 (2), 32.2 (2). Anal. Calcd for $C_{26}H_{28}O_4$: C, 77.2; H, 7.0. Found: C, 76.8; H, 7.0.

(4*S,6*R**)-4-Benzyloxy-6-benzyloxymethyl-6-methyl-dihydropyran-3-one (6a).** To a solution of the alcohol (3*S**,4*S**,6*R**)-**5a** (2.12 g, 6.2 mmol) in DCM (20 mL) were added NMO (1.09 g, 9.3 mmol) and powdered 4 Å molecular sieves (3.10 g). TPAP (0.11 g, 5 mol %) was added, and the mixture was stirred at ambient temperature until the starting material was completely consumed as indicated by TLC. The solvent was evaporated, and the residue was filtered through a small pad of silica. The organics were eluted with MTBE, and the solvent was evaporated to give the ketone **6a** (1.76 g, 84%). IR (neat): 699 m, 1101 s, 1725 s. MS *m*/*z* (rel intensity): 341 ($M^+ + 1$, 10), 323 (60), 233 (70), 181 (100), 144 (55), 113 (55). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.29−7.19 (10H), 4.73 (d, 1H, J = 11.8 Hz), 4.49 (d, 1H, J = 12.3 Hz), 4.46 (d, 1H, J = 11.8 Hz), 4.43 (d, 1H, J = 12.3 Hz), 4.43 (dd, 1H, J = 12.5, 6.5 Hz), 4.13 (d, 1H, J = 18.5 Hz), 4.08 (d, 1H, J = 18.5 Hz), 3.38 (d, 1H, J = 9.5 Hz), 3.29 (d, 1H, J = 9.5 Hz), 2.45 (dd, 1H, J = 13.5, 6.5 Hz), 1.67 (dd, 1H, J = 13.5, 12.5 Hz), 1.16 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 209.9 (0), 137.8 (0), 137.6 (0), 128.4 (1), 128.3 (1), 127.8 (1), 127.8 (1), 127.7 (1), 127.6 (1), 76.7 (2), 76.5 (1), 75.6 (0), 73.5 (2), 72.2 (2), 68.6 (2), 36.9 (2), 22.7 (3).

(4*S,6*S**)-4-Benzyloxy-6-benzyloxymethyl-6-phenyldihydropyran-3-one (6b).** Following the procedure for the methyl analogue, we obtained **6b** (0.90 g, 82%) from **5b** (1.10 g, 2.7 mmol, 4.5:1 mixture of regioisomers). IR (neat): 699 s, 1101 s, 1746 s, 2852 m, 3030 m. MS *m*/*z* (rel intensity): 403 ($M^+ + 1$, <5), 292 (5), 264 (5), 219 (15), 189 (20), 115 (15), 91 (100), 65 (20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.33−7.11 (15H), 4.82 (dd, 1H, J = 13.0, 6.3 Hz), 4.79 (d, 1H, J = 11.8 Hz), 4.52 (d, 1H, J = 11.8 Hz), 4.46 (d, 1H, J = 12.3 Hz), 4.34 (d, 1H, J = 12.3 Hz), 4.14 (d, 1H, J = 18.0 Hz), 3.95 (d, 1H, J = 18.0 Hz), 3.50 (d, 1H, J = 10.0 Hz), 3.33 (d, 1H, J = 10.0 Hz), 2.99 (dd, 1H, J = 13.0, 6.3 Hz), 2.20 (dd, 1H, J = 13.0, 13.0 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 210.3 (0), 141.9 (0), 137.7 (0), 137.7 (0), 128.5 (1), 128.4 (1), 127.9 (1), 127.8 (1), 127.7 (1), 127.5 (1), 125.6 (1), 79.9 (0), 79.2 (2), 76.7 (1), 73.6 (2), 72.6 (2), 69.3 (2), 35.5 (2). Anal. Calcd for $C_{26}H_{26}O_4$: C, 77.6; H, 6.5. Found: C, 77.3; H, 6.3.

(3*R,4*S**,6*R**)-4-Benzyloxy-6-benzyloxymethyl-6-methyl-3-vinyl-tetrahydropyran-3-ol (7a).** Vinylmagnesium chloride (1.7 M solution in THF, 0.6 mL, 1.0 mmol) was added to a solution of the ketone **6a** (0.11 g, 0.3 mmol) in ether (10 mL) at −78 °C. The mixture was stirred until the starting material was fully converted and warmed to ambient temperature, and the reaction was quenched with saturated NH_4Cl solution. The aqueous layer was extracted with MTBE, and the combined organic extracts were dried with $MgSO_4$. Upon flash chromatography on silica, pure **7a** (82 mg, 66%) was isolated. IR (neat): 698 s, 1096 s, 1454 m, 2867 m, 3446 br s. MS *m*/*z* (rel intensity): 351 ($M^+ - 17$, 10), 333 (40), 243 (50), 153 (90), 91 (100). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.27−7.18 (10H), 5.78 (dd, 1H, J = 17.3, 10.8 Hz), 5.40 (d, 1H, J = 17.3 Hz), 5.14 (d, 1H, J = 10.8 Hz), 4.57 (d, 1H, J = 14.5 Hz), 4.50 (d, 1H, J = 11.3 Hz), 4.46 (d, 1H, J = 14.5 Hz), 4.39 (d, 1H, J = 11.3 Hz), 3.59 (dd, 1H, J = 9.0, 4.8 Hz), 3.52 (d, 1H, J = 12.3 Hz), 3.49 (d, 1H, J = 12.3 Hz), 3.34 (d, 1H, J = 9.5 Hz), 3.29 (d, 1H, J = 9.5 Hz), 2.61 (bs, 1H), 1.92 (dd, 1H, J = 13.8, 4.8 Hz), 1.72 (dd, 1H, J = 13.8, 9.0 Hz), 1.11 (s, 3H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 139.5 (1), 138.1 (0), 137.8 (0), 128.4 (1), 127.8 (1), 127.7 (1), 127.6 (1), 127.4 (1), 126.7 (1), 116.0 (2), 76.4 (1), 74.8 (2), 74.2 (0), 73.4 (2), 71.6 (0), 71.3 (2), 67.5 (2), 33.0 (2), 26.9 (3). Anal. Calcd for $C_{23}H_{28}O_4$: C, 75.0; H, 7.7. Found: C, 74.9; H, 7.8.

(3*R,4*S**,6*S**)-4-Benzyloxy-6-benzyloxymethyl-6-phenyl-3-vinyltetrahydropyran-3-ol (7b).** Following the procedure for the methyl analogue, we obtained **7b** (0.33 g, 89%) from **6b** (0.35 g, 0.9 mmol). IR (neat): 699 m, 1075 s, 1101 s, 1454 m, 3030 m, 3543 br s. MS *m*/*z* (rel intensity): 429 ($M^+ + 1$, 15), 384 (20), 218 (25), 207 (100), 157 (30), 117 (35), 91 (75), 73 (55). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.38 (d, 2H, J = 7.5 Hz), 7.28−7.08 (11H), 6.93 (dd, 2H, J = 7.5, 3.7 Hz), 6.00 (dd, 1H, J = 17.3, 10.8 Hz), 5.48 (dd, 1H, J = 17.3, 1.5 Hz), 5.19 (dd, 1H, J = 10.8, 1.5 Hz), 4.49 (d, 1H, J = 11.3 Hz), 4.43 (d, 1H, J = 12.1 Hz), 4.34 (d, 1H, J = 12.1 Hz), 4.28 (d, 1H, J = 11.3 Hz), 3.68 (d, 1H, J = 12.0 Hz), 3.64 (dd, 1H, J = 7.3, 4.0 Hz), 3.64 (d, 1H, J = 12.0 Hz), 3.44 (d, 1H, J = 10.3 Hz), 3.40 (d, 1H, J = 10.3 Hz), 2.63 (bs, 1H), 2.40 (dd, 1H, J = 14.3, 4.0 Hz), 2.27 (dd, 1H, J = 14.3, 7.3 Hz). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 143.1 (0), 139.1 (1), 138.0 (1), 137.6 (0), 128.2 (1), 128.2 (1), 128.1 (1), 128.0 (1), 127.7 (1), 127.6 (1), 127.5 (1), 127.5 (1), 127.4 (1), 126.8 (1), 125.3 (1), 116.0 (2), 77.6 (0), 77.3 (1), 76.8 (2), 73.4 (2), 71.2 (2), 70.8 (0), 67.3 (2), 31.1 (2).

General Procedure for the Preparation of Spirocyclic Lactones. A solution of the allylic alcohol (3.0 mmol), Rh(acac)$(CO)_2$ (1.0 mol %), and BIPHEPHOS (4.0 mol %) in anhydrous dioxane (10 mL) was heated at 60 °C for 20 h under

an atmosphere of carbon monoxide (10 bar) and hydrogen (10 bar) in an autoclave. The reaction mixture was filtered through basic alumina, and all organics were eluted with MTBE and then ethanol. The solvent was evaporated, and the crude hemiacetals were redissolved in DCM (20 mL). Powdered molecular sieve (4 Å, 2.00 g) and *N*-methyl morpholine-*N*-oxide (0.53 g, 4.5 mmol) were added, followed by TPAP (53 mg, 5 mol %). The mixture was stirred at ambient temperature until the starting material was completely converted as indicated by TLC (3:1 (v/v) hexanes/ethyl acetate). The solvent was evaporated to one-third of the original volume, and the residue was filtered through a 5 cm pad of silica. The products were eluted with MTBE and purified by flash chromatography, if necessary.

(5*R,8*R**,10*S**)-10-Benzyloxy-8-benzyloxymethyl-8-methyl-1,7-dioxaspiro[4.5]decan-2-one (13a).** The title compound was obtained from **7a** (0.19 g, 0.5 mmol) following the general procedure for the preparation of spirocyclic lactones. Yield: 0.16 g (80%). IR (neat): 1077 s, 1218 m, 1454 m, 1727 m, 1770 s, 2930 m. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.37−7.24 (10H), 4.67 (d, 1H, J = 12.2 Hz, −CH(4)OC*H*HPh), 4.53 (d, 1H, J = 12.2 Hz, −CHHOC*H*HPh), 4.50 (d, 1H, J = 12.2 Hz, −CHHOC*H*HPh), 4.41 (d, 1H, J = 12.2 Hz, −CH(4)-OC*H*HPh), 3.73 (d, 1H, J = 12.7 Hz, H6), 3.72 (dd, 1H, J = 10.7, 4.4 Hz, H4), 3.70 (d, 1H, J = 12.2 Hz, H6), 3.50 (d, 1H, J = 9.8 Hz, −CH*H*OCHHPh), 3.37 (d, 1H, J = 9.8 Hz, −CH*H*OCHHPh), 2.69 (ddd, 1H, J = 18.0, 10.5, 9.0 Hz, (O)-CCH*H*CHH−), 2.43 (ddd, 1H, J = 18.0, 10.5, 4.0 Hz, (O)-CCH*H*CHH−), 2.14 (dd, 1H, J = 13.3, 4.4 Hz, H3eq), 1.92 (ddd, 1H, J = 12.8, 10.5, 4.0 Hz, (O)CCHHCH*H*−), 1.82 (dd, 1H, J = 13.3, 10.7 Hz, H3ax), 1.72 (ddd, 1H, J = 12.8, 10.5, 9.0 Hz, (O)CCHHCH*H*−), 1.21 (s, 3H, −C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.8 (0), 138.0 (0), 137.9 (0), 128.4 (1), 128.4 (1), 127.8 (1), 127.7 (1), 127.6 (1), 127.4 (1), 83.4 (0), 76.1 (2), 75.0 (0), 74.7 (2), 73.5 (2), 70.3 (2), 68.3 (2), 33.5 (2), 28.8 (2), 27.5 (2), 26.1 (2). Anal. Calcd for $C_{24}H_{28}O_5$: C, 72.7; H, 7.1. Found: C, 72.4; H, 7.1.

(5*R,8*R**,10*S**)-10-Benzyloxy-8-benzyloxymethyl-8-phenyl-1,7-dioxaspiro[4.5]decan-2-one ((5*R**,8*R**,10*S**)-13b) and (5*S**,6*R**,9*S**)-6-Benzyloxy-9-benzyloxymethyl-9-phenyl-1,8-dioxaspiro[4.5]decan-2-one ((5*S**,6*R**,9*S**)-13b).** The title compounds were obtained from **7b** (0.53 g, 1.2 mmol) following the general procedure for the preparation of spirocyclic lactones as a 4:1 mixture of regioisomers that were separated by column chromatography. Data for (5*R**,8*R**,-10*S**)-**13b**. Yield: 0.14 g (44%). IR (neat): 1075 s, 1775 s, 3033 s. MS *m*/*z* (rel intensity): 337 (M^+ − $PhCH_2OCH_2$−, 100%), 229 (32), 91 ($C_7H_7^+$, 98). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.59 (d, 2H, J = 8.0 Hz, Ph), 7.24 (dd, 2H, J = 7.7, 7.7 Hz, Ph), 7.20−7.08 (11H, Ph), 4.39 (d, 1H, J = 12.2 Hz, CH(4)OC*H*$_2$-Ph), 4.22 (d, 1H, J = 12.2 Hz, CH(4)OC*H*$_2$Ph), 4.19 (d, 1H, J = 12.5 Hz, −CH_2OC*H*$_2$Ph), 4.17 (d, 1H, J = 12.5 Hz, −CH_2-OC*H*$_2$Ph), 3.77 (d, 1H, J = 12.2 Hz, H6), 3.61 (dd, 1H, J = 9.7, 4.2 Hz, H4), 3.51 (d, 1H, J = 10.0 Hz, H6), 3.50 (d, 1H, J = 12.2 Hz, −C*H*$_2$OCH_2Ph), 3.40 (d, 1H, J = 12.2 Hz, −C*H*$_2$OCH_2-Ph), 2.44 (dd, 1H, J = 13.5, 4.2 Hz, H3eq), 2.33 (ddd, 1H, J = 17.5, 10.5, 8.2 Hz, (O)CC*H*$_2$CH$_2$−), 2.26 (dd, 1H, J = 13.5, 9.7 Hz, H3ax), 1.94 (ddd, 1H, J = 17.5, 10.7, 4.7 Hz, (O)CC*H*$_2$-CH$_2$−), 1.37 (ddd, 1H, J = 13.0, 10.5, 4.7 Hz, (O)CCH$_2$C*H*$_2$−), 1.20 (ddd, 1H, J = 13.0, 10.5, 8.2 Hz, (O)CCH$_2$C*H*$_2$−). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.7 (0), 143.7 (0), 137.9 (0), 137.8 (0), 128.4 (1), 128.3 (1), 128.0 (1), 127.7 (1), 127.6 (1), 127.5 (1), 127.4 (1), 127.1 (1), 125.1 (1), 83.4 (0), 78.2 (0), 76.4 (1), 75.6 (2), 73.5 (2), 70.6 (2), 67.9 (2), 33.2 (2), 28.7 (2), 27.8 (2). Data for (5*S**,6*R**,9*S**)-**13b**. Yield: 0.03 g (10%). IR (neat): 1096 s, 1454 m, 1778 s, 2928 s. MS *m*/*z* (rel intensity): 336 (M^+ − $PhCH_2OCH_3$, 86%), 91 ($C_7H_7^+$, 100). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.58 (d, 2H, J = 8.6 Hz, Ph), 7.41−7.06 (13H, Ph), 4.48 (d, 1H, J = 12.3 Hz, −CH_2OC*H*$_2$Ph), 4.35 (d, 1H, J = 12.3 Hz, −CH_2OC*H*$_2$Ph), 4.23 (d, 1H, J = 12.3 Hz, −CH(4)OC*H*$_2$-Ph), 4.03 (d, 1H, J = 12.3 Hz, −CH(4)OC*H*$_2$Ph), 3.80 (dd, 1H, J = 10.8, 10.8 Hz, H6ax), 3.71 (dd, 1H, J = 10.8, 4.8 Hz, H6eq), 3.51 (d, 1H, J = 10.0 Hz, −C*H*$_2$OCH_2Ph), 3.32 (d, 1H, J = 10.0 Hz, −C*H*$_2$OCH_2Ph), 3.24 (dd, 1H, J = 10.8, 4.8 Hz, H5), 2.49 (d, 1H, J = 15.0 Hz, H3eq), 2.43 (ddd, 1H, J = 17.6, 10.0, 10.0 Hz, (O)CC*H*$_2$CH$_2$−), 2.31 (d, 1H, J = 15.0 Hz, H3ax), 2.05 (ddd, 1H, J = 17.6, 10.8, 3.3 Hz, (O)CC*H*$_2$CH$_2$−), 1.69 (ddd, 1H, J = 13.1, 10.5, 3.3 Hz, (O)CCH$_2$C*H*$_2$−), 1.36 (ddd, 1H, J = 13.1, 10.8, 10.0 Hz, (O)CCH$_2$C*H*$_2$−). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 175.8 (0), 141.6 (0), 139.6 (0), 139.0 (0), 129.2 (1), 129.1 (1), 128.9 (1), 128.5 (1), 128.4 (1), 128.3 (1), 128.2 (1), 128.1 (1), 127.8 (1), 83.4 (0), 80.3 (2), 79.9 (0), 79.4 (1), 74.4 (2), 72.2 (2), 60.9 (2), 39.8 (2), 33.1 (2), 29.7 (2).

(5*S*,6*S*)-6-Methyl-1,7-dioxaspiro[4,5]dec-9-en-2-one ((5*S*,6*S*)-15a) and (5*R*,6*S*)-6-Methyl-1,7-dioxaspiro[4,5]dec-9-en-2-one ((5*R*,6*S*)-15a). The title compounds were obtained from **9a** (3:1 mixture of diastereoisomers, 1.3 g, 9.3 mmol) as a 3:1 mixture of diastereoisomers. Separation of the diastereoisomers by column chromatography on silica gives (5*S*,6*S*)-**15a** (0.95 g, 61%) and (5*R*,6*S*)-**15a** (0.31 g, 20%). Analytical data for (5*S*, 6*S*)-**15a**. Mp = 103 °C. IR (KBr, disk): 954 s, 1132 s, 1377 s, 1469 s, 1767 s, 2998 s. MS *m*/*z* (rel intensity): 168 (M^+, 100), 108 (20). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.02 (ddd, 1H, J = 10.0, 3.3, 1.8 Hz, H5), 5.74 (ddd, 1H, J = 10.0, 2.0, 2.0 Hz, H4), 4.22 (ddd, 1H, J = 17.1, 3.3, 2.0 Hz, H6eq), 4.09 (ddd, 1H, J = 17.1, 2.0, 2.0 Hz, H6ax), 3.62 (q, 1H, J = 6.5 Hz, H2), 2.64 (ddd, 1H, J = 18.2, 10.5, 7.5 Hz, (O)CC*H*$_2$-CH$_2$−), 2.56 (ddd, 1H, J = 18.2, 9.8, 6.5 Hz, (O)CC*H*$_2$CH$_2$−), 2.12 (m, 1H, (O)CCH$_2$C*H*$_2$−), 2.01 (m, 1H, (O)CCH$_2$C*H*$_2$−), 1.24 (d, 3H, J = 6.5 Hz, −CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2 (0), 130.7 (1), 126.4 (1), 80.9 (0), 75.4 (1), 64.1 (2), 29.9 (2), 28.0 (2), 13.9 (3). $[\alpha]^{20}_D$ = +171° (*c* 1.55, CH_2Cl_2). Anal. Calcd for $C_9H_{12}O_3$: C, 64.3; H, 7.2. Found: C, 64.3; H, 7.2. Analytical data for (5*R*,6*S*)-**15a**. Mp = 102 °C. IR (KBr, disk): 727 m, 959 s, 1069 s, 1227 s, 1759 s, 2999 s. MS *m*/*z* (rel intensity): 168 (M^+, 100). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 5.81 (ddd, 1H, J = 10.3, 2.5, 1.3 Hz), 5.77 (ddd, 1H, J = 10.3 Hz), 4.16 (dm, 1H, J = 16.8 Hz), 4.06 (dm, 1H, J = 16.8 Hz), 3.71 (q, 1H, J = 6.5 Hz), 2.56 (ddd, 1H, J = 18.4, 10.0, 4.8 Hz), 2.47 (ddd, 1H, J = 18.4, 10.0, 8.6 Hz), 2.37 (ddd, 1H, J = 13.3, 10.0, 4.8 Hz), 1.93 (ddd, 1H, J = 13.3, 10.0, 8.6 Hz), 1.14 (d, 3H, J = 6.5 Hz, −CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.7 (0), 129.5 (1), 128.2 (1), 82.5 (0), 73.8 (1), 65.6 (2), 29.2 (2), 27.1 (2), 14.4 (3). $[\alpha]^{20}_D$ = +161° (*c* 1.60, $CHCl_3$). Anal. Calcd for $C_9H_{12}O_3$: C, 64.3; H, 7.2. Found: C, 64.2; H, 7.1.

(5*S,6*S**)-6-Phenyl-1,7-dioxaspiro[4,5]dec-9-en-2-one ((5*S**,6*S**)-15b) and (5*R*,6*S*)-6-Phenyl-1,7-dioxaspiro[4,5]-dec-9-en-2-one ((5*R**,6*S**)-15b).** The title compounds were obtained from **9b** (0.60 g, 3.0 mmol) as a 4:1 mixture of diastereoisomers. Separation of the diastereoisomers by column chromatography on silica gives (5*S*,6*S*)-**15b** (0.26 g, 38%) and (5*R**,6*S**)-**15b** (0.10 g, 14%). Analytical data for (5*S**,6*S**)-**15b**. Mp = 164 °C. IR (KBr, disk): 708 s, 1032 s, 1201 s, 1456 m, 1767 s, 2831 m, 2945 m. MS *m*/*z* (rel intensity): 231 (M^+ + 1, 20), 157 (45), 141 (100). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.44 (d, 2H, J = 7.3 Hz, *ortho*-H, Ph), 7.37−7.32 (3H, Ph), 6.16 (ddd, 1H, J = 10.3, 3.5, 1.5 Hz, H5), 5.84 (ddd, 1H, J = 10.3, 2.0, 2.0 Hz, H4), 4.46 (ddd, 1H, J = 17.2, 3.4, 2.0 Hz, H6eq), 4.42 (s, 1H, H2), 4.32 (ddd, 1H, J = 17.2, 1.5, 1.5 Hz, H6ax), 2.24−2.16 (2H, (O)CC*H*$_2$CH$_2$−), 2.01 (m, 1H, (O)CCH$_2$C*H*$_2$−), 1.49 (m, 1H, (O)CCH$_2$CH$_2$−). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2 (0), 135.4 (0), 131.9 (1), 128.9 (1), 128.7 (1), 128.4 (1), 127.5 (1), 83.1 (1), 80.3 (0), 66.1 (2), 30.0 (2), 27.9 (2). Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1. Found: C, 73.0; H, 6.2. Analytical data for (5*R**,6*S**)-**15b**. Mp = 110 °C. IR (KBr, disk): 704 m, 1028 s, 1092 s, 1454 s, 1692 m, 1778 s, 2941 s. MS *m*/*z* (rel intensity): 231 (M^+ + 1, 100), 124 (55), 96 (47). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.41 (d, 2H, J = 7.3 Hz, *ortho*-H, Ph), 7.37−7.29 (3H, Ph), 5.95 (ddd, 1H, J = 10.3, 2.5, 2.0 Hz, H4,5), 5.90 (ddd, 1H, J = 10.3, 2.0, 2.0 Hz, H4,5), 4.67 (s, 1H, H2), 4.40−4.33 (2H, H6), 2.33 (ddd, 1H, J = 13.7, 10.7, 2.4 Hz, (O)-CCH$_2$C*H*$_2$−), 2.03 (ddd, 1H, J = 18.1, 10.7, 2.4 Hz, (O)CC*H*$_2$-CH$_2$−), 1.86 (ddd, 1H, J = 13.7, 10.5, 10.5 Hz, (O)CCH$_2$C*H*$_2$−), 0.92 (ddd, 1H, J = 18.1, 10.5, 10.5 Hz, (O)CC*H*$_2$CH$_2$−). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 177.0 (0), 136.0 (0), 130.0 (1), 128.5 (1), 128.3 (1), 128.0 (1), 126.6 (1), 82.5 (0), 78.5 (1), 66.3 (2), 28.4 (2), 27.9 (2). Anal. Calcd for $C_{14}H_{14}O_3$: C, 73.0; H, 6.1. Found: C, 72.8; H, 6.1.

(5*R,8*S**)-8-(4-Methoxyphenyl)-1,7-dioxaspiro[4,5]dec-9-en-2-one ((5*R**,8*S**)-17).** The title compound was obtained

from (3*R**,6*S**)-**11** (0.50 g, 2.2 mmol) as a colorless solid (0.33 g, 58%). Purification was achieved by flash chromatography on silica and recrystallization from DCM/hexane. Mp = 64 °C. IR (KBr, disk): 1032 s, 1244 s, 1304 s, 1514 s, 1612 s, 1775 s, 2838 m, 2959 s. MS *m*/*z* (rel intensity): 260 (M^+, 76), 162 (61), 135 (100). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.21 (d, 2H, J = 8.3 Hz, *ortho*-H, Ar), 6.87 (d, 2H, J = 8.3 Hz, *meta*-H, Ar), 5.96 (d, 1H, J = 10.7 Hz, H3,4), 5.93 (d, 1H, J = 10.7 Hz, H3,4), 5.10 (s, 1H, H2), 3.86 (d, 1H, J = 11.2 Hz, H6eq), 3.79 (d, 1H, J = 11.2, H6ax), 3.78 (s, 3H, OMe), 2.66−2.56 (2H, (O)CCH_2-CH_2−), 2.45 (ddd, 1H, J = 13.2, 8.3, 5.4 Hz, (O)CCH_2CH_2−), 2.18 (ddd, 1H, J = 13.2, 9.8, 9.3 Hz, (O)CCH_2CH_2−). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.2 (0), 159.7 (0), 132.6 (1), 131.4 (0), 128.7 (1), 128.0 (1), 114.0 (1), 79.3 (0), 76.0 (1), 69.2 (2), 55.3 (3), 31.3 (2), 27.8 (2). Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.2; H, 6.2. Found: C, 68.9; H, 6.2.

(5*S,8*S**)-8-(4-Methoxyphenyl)-1,7-dioxaspiro[4,5]dec-9-en-2-one ((5*R**,8*S**)-17).** The title compound was obtained from (5*S**,8*S**)-**17** (0.80 g, 3.4 mmol) as a colorless solid (0.48 g, 54%). Purification was achieved by flash chromatography on silica and recrystallization from DCM/hexane. Mp = 218 °C. IR (KBr, disk): 967 s, 1173 s, 1437 m, 1594 m, 1774 s, 2960 m. MS *m*/*z* (rel intensity): 260 (M^+, 100), 229 (28), 162 (45), 135 (90). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.29 (d, 2H, J = 8.5 Hz, *ortho*-H, Ar), 6.87 (d, 2H, J = 8.5 Hz, *meta*-H, Ar), 6.03 (d, 1H, J = 10.3, 2.0 Hz, H3), 5.90 (d, 1H, J = 10.3 Hz, H4), 5.03 (s, 1H, H2), 3.97 (d, 1H, J = 11.7 Hz, H6eq), 3.77 (s, 3H, OMe), 3.66 (d, 1H, J = 11.7, H6ax), 2.66 (ddd, 1H, J = 18.1, 10.0, 7.0 Hz, (O)CCH_2CH_2−), 2.59 (ddd, 1H, J = 18.1, 10.0, 7.0 Hz, (O)CCH_2CH_2−), 2.15 (ddd, 1H, J = 13.2, 10.0, 7.0 Hz, (O)CCH_2CH_2−), 2.10 (ddd, 1H, J = 13.2, 10.0, 7.0 Hz, (O)CCH_2CH_2−). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.0 (0), 159.6 (0), 134.0 (1), 131.0 (0), 129.0 (1), 126.0 (1), 113.8 (1), 78.9 (0), 75.9 (1), 69.6 (2), 55.2 (3), 30.1 (2), 28.0 (2). Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.2; H, 6.2. Found: C, 69.0; H, 6.0.

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