Synthesis of Endo or Exo Norbornenic Lactones via Highly Diastereoselective Lactonization of Bicyclic Vinyl Sulfoxides

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During the last several years we have been engaged in developing new regio- and stereoselective functionalizations of norbornenic[1] and particularly oxanorbornenic[2] substrates, synthetic intermediates of well-established versatility.[3] Within this field, we have devoted many efforts to the development of new methodology to effect the cleavage of the oxygen bridge[4] and the application of these methodologies in synthesis.[5]

Another largely unresolved problem is the endo functionalization of bicyclo[2.2.1]heptane derivatives. To this end, we reported the unique behavior of 7-oxanorbornen-2-one with organocuprate reagents to produce *exo*-oxanorbornenic alcohols.[6] In this regard, and, in connection with our broader interest in vinyl sulfoxide chemistry,[7,8] we envisioned that Marino's lactonization,[9] an extremely powerful method to transfer chirality from sulfur to carbon,[10] could be applied to bicyclo[2.2.1]heptane vinyl sulfoxides and result in efficient synthesis of enantiomerically pure endo or exo tricyclic lactones, not readily available by other routes.

Our initial studies involved readily available norbornadienyl sulfoxides **1** and **10**[11] (Scheme I); when the reaction between **1** and freshly distilled Cl_3CCOCl in the presence of an excess of Zn–Cu couple (−60 °C to rt) was examined, a complex mixture of products was obtained. After considerable experimentation,[12] we found that the major product of the reaction was not the desired dichloro lactone, but instead it was tentatively characterized as the unexpected nortricyclene **6**[13] (43%). We hypothesized that **6** was produced by protonation of the proposed zwitterion intermediate,[14] prior to sigmatropic rearrangement, followed by nucleophilic attack by Cl^- ions, with homoallylic rearrangement in one case.[15]

Thorough removal of HCl from Cl_3CCOCl,[16] surprisingly, gave rise to a complex mixture of monochloro lactones,[17] but we only detected trace amounts of **6** in the ^1H NMR spectrum of the crude reaction mixture. Subsequent chromatography and recrystallization produced a fair yield of chloro lactone **2** (52%; $[\alpha]_D = +44.2°$, $c = 0.62, CHCl_3$). Dehalogenation[18] of the mixture of lactones **2, 3–5** afforded a 86:14 mixture of **7** and **8** (83%). In this fashion, we could determine the overall diastereoselectivity of the process by integration of the ^1H NMR spectrum of the crude reaction mixture. Recrystallization (hexane) of the mixture of **7** and **8** gave pure endo-lactone **7** (40% from **1**; $[\alpha]_D = +109.0°$, $c = 0.80, CHCl_3$). To explore the reactivity of these systems we carried out the desulfurization[19] of endo-lactone **7** and we obtained an excellent yield of pure **9** (80%; $[\alpha]_D = +17.6°$, $c = 0.88, CHCl_3$) after chromatography.

Encouraged by these results we examined the lactonization–dehalogenation sequence for diastereomer **10**, which produced a good yield of chlorolactone **11** ($[\alpha]_D = -3.6°$, $c = 1.22, CHCl_3$) and then pure exo-lactone **15** (45% from **10**; $[\alpha]_D = +6.21°$, $c = 0.29, CHCl_3$) after recrystallization of the 91:9 mixture of **15** and **16**. Thus it appears that our initial hypothesis was correct and that Marino's lactonization was indeed highly stereoselective even in these challenging cases.

The structural assignments of these tricyclic lactones were derived from their spectral features, particularly from

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(12) Under identical reaction conditions (solvent, reagents, etc), commercially available phenyl vinyl sulfoxide produced excellent yields of the expected dichloro lactone.

(13) All new products had satisfactory spectral data including ^1H NMR selective decoupling experiments. Yields refer to pure products isolated by chromatography or recrystallization.

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(15) The reaction between norbornadienes and sulfenyl halides often occurs with homoallylic participation and results in nortricyclene derivatives. See: *The Chemistry of Sulphenic Acids and their Derivatives*; Patai, S.; Ed.; John Wiley & Sons: New York, 1990.

(16) Trichloroacetyl chloride was sequentially distilled twice under dry argon and then argon was bubbled through the reagent (ca. 5 min) prior to use. We found later that periodic distillation (approximately every month) and another distillation just prior to use generally sufficed.

(17) In some cases we isolated small amounts of the expected dichloro lactones. It appears that these lactones are unusually prone to dehalogenation by the excess Zn–Cu. The selectivity of these dehalogenations is noteworthy and probably related with steric hindrance around the tricyclic skeleton. For example, the lactonization of **1** yielded a mixture of **2**, **3**, **4**, and **5** in 32:4:1:1 ratio (^1H NMR). In most cases, the minor lactones could not be isolated but the ^1H NMR spectra of purified mixtures was sufficiently indicative.

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Scheme I

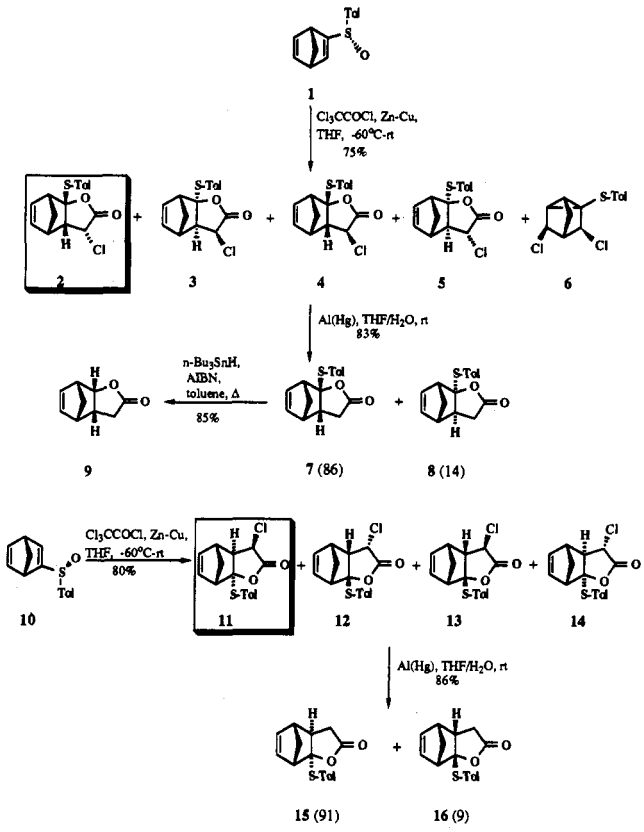
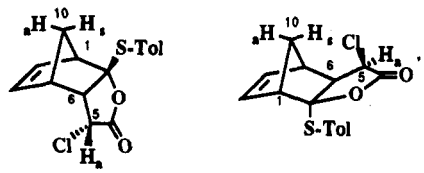


Table I. Selected ^{1}H NMR Data for Monochloro Lactones 2 and 11 ($CDCl_3$, δ in ppm, J in hertz)



	2	11
H-10s	1.99 (br d, 9.4)	1.55 (br d, 10.4)
H-10a	1.82 (dt, 9.4, 1.8)	1.73 (dm, 10.4)
H-6	3.12 (dd, 9.9, 3.8)	2.52 (dd, 10.1, 2.2)
H-5a	3.59 (d, 9.9)	3.93 (d, 10.1)

their ^{1}H NMR[20] data. Table I gathers some selected data for monochloro lactones **2** and **11**. The different chemical shifts for H-6, deshielded for endo-lactone **2** relative to the exo isomer, and the lack of coupling between H-6 and the vicinal bridgehead hydrogen[21] for exo isomer **11** establish the stereochemistry of the tricycle; furthermore, **11** shows a long-range coupling between H-6 and H-10a, which is also very characteristic.[22] The large values found for the coupling between H-5 and H-6 indicate a cis relationship for these protons. The enantiomeric purity of norbornenic lactones **7** and **15** derives from the diastereomeric character of its precursors **1** and **10** and was secured by ^{1}H NMR experiments (300 MHz) in the presence of Eu(hfc)$_3$.

In conclusion, we have shown that Marino's lactonization is a valuable tool to achieve the endo or exo functionalization of bicyclo[2.2.1]heptane derivatives in a predictable and selective manner, ultimately controlled by the absolute configuration of the substrates.

Experimental Section

General Methods. All reactions were carried out under a positive pressure of dry argon, using freshly distilled solvents under anhydrous conditions unless otherwise stated. Reagents and solvents were handled by using standard syringe techniques. Tetrahydrofuran and toluene were distilled from calcium hydride and hexane and ethyl acetate from phosphorus pentoxide. Analytical TLC was carried out on 0.20-mm E. Merck precoated silica gel plates (60F-254), with detection by UV light, iodine, acidic vanillin solution or 10% solution of phosphomolybdic acid in ethanol. Column chromatography was performed with SDS or E. Merck 230–400-mesh silica gel. Melting points were determined on a Köfler apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 681 spectrophotometer. ^{1}H NMR spectra were recorded on a Brüker AM-200 or a Varian XL-300 instrument using $CDCl_3$ as solvent unless otherwise noted. ^{13}C NMR spectra were measured on a Brüker AM-200, using $CDCl_3$ as solvent and are completely decoupled. In both ^{1}H NMR and ^{13}C NMR, chemical shifts are reported in δ units downfield from tetramethylsilane. The following abbreviations are used to describe peak patterns when appropriate: br, broad; s, singlet; d, doublet; t, triplet; q, quartet; quint, quintuplet; m, multiplet. Optical rotations were measured in $CHCl_3$ at 20 °C using the sodium lamp of a Perkin-Elmer 241 polarimeter.

General Procedure for the Lactonization of Bicyclic Vinyl Sulfoxides. Under an atmosphere of argon, a THF (20 mL/mmol of sulfoxide) solution of 5 equiv of freshly distilled trichloroacetyl chloride[16] was added dropwise over a 15-min period to a cold (−60 °C), rapidly stirred suspension of 20 equiv of zinc–copper couple in THF (30 mL/mmol of sulfoxide) containing 1 equiv of the substrate. After addition of the acid chloride, the cooling bath was removed and the mixture was stirred at rt for 15 min. The excess zinc was removed by filtration and the resulting yellow solution was poured into cold (0 °C), saturated $NaHCO_3$ (50 mL/mmol of sulfoxide). After stirring vigorously for 30 min, the layers were separated and the aqueous portion was extracted with ether (50 mL/mmol of sulfoxide). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated in vacuo after removal of the drying agent. The crude product was purified by column chromatography on silica gel with the appropriate eluent.

Lactonization of (1*Rc*,4*Sc*,*Rs*)-2-(Bicyclo[2.2.1]heptan-2,5-dienyl) *p*-Tolyl Sulfoxide, 1. From **1** (60 mg, 0.26 mmol), CCl_3COCl (0.15 mL, 1.30 mmol), and Zn–Cu according to the general procedure was obtained a 32:4:1:1 mixture of monochloro lactones **2**, **3**, **4**, and **5**. Column chromatography (hexane–EtOAc, 7:1) allowed for the separation of **2** and **3** (57 mg, 71%) from **4** and **5** (3 mg, 4%). Pure **2** was obtained by recrystallization from hexane (52%). Data of (1*R*,2*R*,5*R*,6*R*,7*S*)-5-Chloro-2-(*p*-tolylthio)-3-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-4-one, **2**: white solid, mp 84–85 °C (hexane); R_f = 0.33 (hexane–EtOAc, 7:1); [α] = +44.2° (*c* 0.62, $CHCl_3$); ^{1}H NMR 1.82 (dt, 1 H, J = 9.4, 1.8 Hz, H-10a), 1.99 (brd, 1 H, J = 9.4 Hz, H-10s), 2.37 (s, 3 H, CH_3-*p*-Tol), 3.12 (dd, 1 H, J = 9.9, 3.8 Hz, H-6), 3.16 (m, 1 H, H-1), 3.26 (m, 1 H, H-7), 3.59 (d, 1 H, J = 9.9 Hz, H-5), 6.12 (dd, 1 H, J = 5.7, 3.2 Hz, H-7 or H-8), 6.35 (dd, 1 H, J = 5.6, 2.8 Hz, H-7 or H-8), 7.19 (d, 2 H, J = 7.9 Hz, ArH), 7.47 (d, 2 H, J = 8.0 Hz, ArH); ^{13}C NMR 21.3, 47.0, 47.9, 52.8, 53.1, 53.5, 102.2, 126.3, 130.4, 135.9, 136.0, 136.1, 140.4, 171.2; IR ($CHCl_3$) 3020, 2980, 1790, 1495, 1455, 1345, 1200, 1170, 1160, 1125, 940, 820, 795, 775. Anal. Calcd for $C_{16}H_{15}ClO_2S$: C, 62.64; H, 4.93; Cl, 11.56. Found: C, 62.40; H, 4.67; Cl, 11.33. Data of (1*R*,2*S*,5*S*,6*S*,7*S*)-5-Chloro-2-(*p*-tolylthio)-3-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-4-one, **3**: R_f = 0.33 (hexane–

(20) While we could not obtain pure samples of the minor products of these reactions, for instance **8** and **16**, their structures were assigned by comparison on the ^{1}H NMR spectra of enriched mixtures with those of the pure major products (**7** and **15**), considering that products arising from two diastereomeric precursors, **1** and **10**, and exhibiting identical spectroscopic data (within experimental error) must be enantiomeric (for instance **8** and **15**) since the norbornene chiral centers are not affected under the reaction conditions. Similar comparisons allowed for the assignment of the minor monochloro lactones **3**–**5** and **12**–**14**.

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EtOAc, 7:1); ^{1}H NMR 1.57 (brd, 1 H, J = 10.5 Hz, H-10s), 1.75 (dm, 1 H, J = 10.5 Hz, H-10a), 2.36 (s, 3 H, CH_3-p-Tol), 2.54 (dd, 1 H, J = 10.2, 2.2 Hz, H-6), 3.20 (m, 1 H, H-1 or H-7), 3.96 (d, 1 H, J = 10.1 Hz, H-5), 6.28 (dd, 1 H, J = 5.7, 3.1 Hz, H-7 or H-8). The remaining signals could not be measured accurately. Data of (1*R*,2*R*,5*S*,6*R*,7*S*)-5-Chloro-2-(p-tolylthio)-3-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-4-one, **4**, and of (1*R*,2*S*,5*R*,6*S*,7*S*)-5-chloro-2-(p-tolylthio)-3-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-4-one, **5**: R_f = 0.21 (hexane–EtOAc, 7:1); ^{1}H NMR 1.46 (brd, 1 H, J = 10.4 Hz), 1.76–1.82 (m, 2 H), 2.09 (brd, 1 H, J = 9.5 Hz), 2.36 (s, 6 H, CH_3-p-Tol), 2.49 (t, 1 H, J = 2.3 Hz), 2.97 (m, 1 H), 3.00 (dd, 1 H, J = 4.1, 2.4 Hz), 3.13 (m, 1 H), 3.24 (m, 1 H), 3.28 (m, 1 H), 3.78 (d, 1 H, J = 2.6 Hz), 4.07 (d, 1 H, J = 2.4 Hz), 6.16–6.37 (m, 4 H), 7.16–7.20 (m, 4 H, ArH), 7.46–7.51 (m, 4 H, ArH).

Synthesis of (1*S*,2*S*,3*S*,4*R*,5*R*,6*S*)-3,5-Dichloro-2-(p-tolylthio)tricyclo[2.2.1.0^{2,6}]heptane, 6. From **1** (65 mg, 0.28 mmol) and Cl_3CCOCl (0.16 mL, 1.41 mmol) presumably contaminated with trace amounts of HCl and Zn–Cu (368 mg, 5.64 mmol), according to the general procedure, sulfide **6** (31 mg, 43%) was obtained as the major product, along with small amounts of monochloro lactones **2–5**, after chromatography (hexane–EtOAc, 25:1). Data of **6**: mp 75–77 °C (hexane); R_f = 0.40 (hexane–EtOAc, 25:1); [α] = +35.7° (c 1.06, $CHCl_3$); ^{1}H NMR (C_6D_6) 1.57 (dq, 1 H, J = 5.1, 1.3 Hz, H-1), 1.73 (dt, 1 H, J = 5.1, 1.4 Hz, H-6), 1.83 (hept, 1 H, J = 1.5 Hz, H-7a), 1.91 (dt, 1 H, J = 11.6, 1.5 Hz, H-7s) 2.04 (s, 3 H, CH_3-p-Tol), 2.10 (dt, 1 H, J = 11.6, 1.4 Hz, H-4), 3.19 (t, 1 H, J = 1.6 Hz, H-5), 3.39 (d, 1 H, J = 1.8 Hz, H-3), 6.85 (d, 2 H, J = 7.9 Hz, ArH), 7.28 (d, 2 H, J = 8.2 Hz, ArH); ^{1}H NMR ($CDCl_3$) 1.96 (dd, 1 H, J = 5.1, 1.2 Hz), 2.07 (dt, 1 H, J = 5.1, 1.5 Hz), 2.14 (dt, 1 H, J = 11.7, 1.5 Hz), 2.32 (dt, 1 H, J = 11.6, 1.5 Hz), 2.33 (s, 3 H), 2.40 (m, 1 H), 3.84 (d, 1 H, J = 1.8 Hz), 3.93 (t, 1 H, J = 1.6 Hz), 7.12 (d, 2 H, J = 8.0 Hz), 7.34 (d, 2 H, J = 8.2 Hz); ^{13}C NMR 21.1, 23.2, 28.9, 32.4, 38.3, 46.5, 59.3, 63.5, 129.9, 130.5, 132.0, 137.8; IR ($CHCl_3$) 3020, 1495, 1305, 1275, 920, 900. Anal. Calcd for $C_{14}H_{14}Cl_2S$: C, 58.95; H, 4.95; Cl, 24.86. Found: C, 58.61; H, 4.78; Cl, 24.64.

Lactonization of (1*Sc*,4*Rc*,*Rs*)-2-(Bicyclo[2.2.1]hepta-2,5-dienyl) p-Tolyl Sulfoxide, 10. From **2** (55 mg, 0.24 mmol), Cl_3CCOCl (0.13 mL, 1.19 mmol), and Zn–Cu (310 mg, 4.77 mmol), according to the general procedure, a 107:13:1:39 mixture of monochloro lactones **11**, **12**, **13**, and **14** was obtained (^{1}H NMR). Column chromatography (hexane–EtOAc, 7:1) allowed for the separation of **11** and **12** (48 mg, 65%) from **13** and **14** (11 mg, 15%). Pure **11** and **14** were obtained by recrystallization from hexane. In some runs, we isolated small amounts of the expected dichloro lactone. Data of (1*S*,2*R*,5*R*,6*R*,7*R*)-5-Chloro-2-(p-tolylthio)-3-oxatricyclo[5.2.1.0^{2,6}]dec-8-en-4-one, **11**: white solid, mp = 107–108 °C (hexane); R_f = 0.25 (hexane–EtOAc, 7:1); [α] = –3.6° (c 1.22, $CHCl_3$); ^{1}H NMR 1.55 (brd, 1 H, J = 10.4 Hz, H-10s), 1.73 (dm, 1 H, J = 10.4 Hz, H-10a), 2.34 (s, 3 H, CH_3-p-Tol), 2.52 (dd, 1 H, J = 10.1, 2.2 Hz, H-6), 3.14 (m, 1 H, H-1 or H-7), 3.18 (m, 1 H, H-1 or H-7), 3.93 (d, 1 H, J = 10.1 Hz, H-5), 6.22 (dd, 1 H, J = 5.7, 3.1 Hz, H-8 or H-9), 6.32 (dd, 1 H, J = 5.7, 3.1 Hz, H-8 or H-9), 7.15 (d, 2 H, J = 7.9 Hz, ArH), 7.41 (d, 2 H, J = 8.0 Hz, ArH); ^{13}C NMR 21.2, 44.4, 44.9, 49.8, 51.8, 53.5, 103.0, 126.1, 130.3, 135.2, 136.1, 138.0, 140.3, 172.4; IR ($CHCl_3$) 3060, 2970, 2950, 2910, 1880, 1790, 1490, 1240, 1170, 1160, 1000, 980, 930, 810, 690. Anal. Calcd for $C_{16}H_{15}ClO_2S$: C, 62.64; H, 4.93; Cl, 11.56. Found: C, 62.45; H, 4.72; Cl, 11.37. Data of (1*S*,2*R*,5*S*,6*R*,7*R*)-5-Chloro-2-(p-tolylthio)-3-oxatricyclo[5.2.1.0^{2,6}]-dec-8-en-4-one, **14**: white solid, mp 110–111 °C (hexane); R_f = 0.14 (hexane–EtOAc, 7:1). [α] = +51.0° (c 0.55, $CHCl_3$); ^{1}H NMR 1.43 (brd, 1 H, J = 10.3 Hz, H-10s), 1.76 (dm, 1 H, J = 10.4 Hz, H-10a), 2.34 (s, 3 H, CH_3-p-Tol), 2.47 (t, 1 H, J = 2.3 Hz, H-6), 2.95 (m, 1 H, H-1 or H-7), 3.11 (m, 1 H, H-1 or H-7), 4.04 (d, 1 H, J = 2.3 Hz, H-5), 6.19 (dd, 1 H, J = 5.7, 3.1 Hz, H-8 or H-9), 6.30 (dd, 1 H, J = 5.7, 3.0 Hz, H-8 or H-9), 7.16 (d, 2 H, J = 8.1 Hz, ArH), 7.46 (d, 2 H, J = 8.1 Hz, ArH); ^{13}C NMR 21.2, 44.3, 47.2, 51.0, 53.5, 55.7, 102.9, 126.3, 130.0, 135.3, 136.0, 137.5, 140.0, 172.4. IR ($CHCl_3$) 2950, 2910, 1785, 1490, 1230, 1170, 1155, 1005, 980, 925, 915, 810, 725. Anal. Calcd for $C_{16}H_{15}ClO_2S$: C, 62.64; H, 4.93; Cl, 11.56. Found: C, 62.50; H, 4.81; Cl, 11.41. The structures of **12** and **13** were assigned by comparison of the spectra of enriched mixtures with those of **2** and **4**. Data of (1*S*,2*R*,6*R*,7*R*)-5,5-Dichloro-2-(p-tolylthio)-3-oxatricyclo[5.2.1.0^{2,6}]-dec-8-en-4-one: R_f = 0.34 (hexane–EtOAc, 6:1); ^{1}H NMR 1.43 (dd, 1 H, J = 10.7, 0.6 Hz, H-10s), 1.71 (dq, 1 H, J = 10.7, 1.8 Hz, H-10a), 2.37 (s, 3 H, CH_3-p-Tol), 2.89 (d, 1 H, J = 2.2 Hz, H-6), 3.07 (m, 1 H, H-1 or H-7), 3.31 (m, 1 H, H-1 or H-7), 6.23 (dd, 1 H, J = 5.6, 3.1 Hz, H-8 or H-9), 6.36 (dd, 1 H, J = 5.6, 3.1 Hz, H-8 or H-9), 7.18 (d, 2 H, J = 8.3 Hz, ArH), 7.49 (d, 2 H, J = 8.2 Hz, ArH); ^{13}C NMR 21.3, 44.0, 47.5, 51.3; 62.0, 102.2, 126.1, 130.0, 135.6, 136.4, 137.4, 140.0, 168.7.

General Procedure for the Dehalogenation of Norbornenic Chloro Lactones. To a solution of the chloro lactone in THF:H_2O, 9:1 (30 mL/mmol of sulfoxide) was added 10 equiv of aluminum amalgam, generated from aluminum foil by the procedure of Corey.[18] The solution was stirred at rt for 4 h after which time the reaction mixture was filtered and the residue was washed with ether (3 × 20 mL/mmol of sulfoxide). The resulting solution was washed with brine, dried ($MgSO_4$), and concentrated in vacuo after removal of the drying agent. The crude product was purified by column chromatography on silica gel with the appropriate eluent.

Synthesis of (1*R*,2*R*,6*R*,7*S*)-2-(p-Tolylthio)-3-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-4-one, 7. From the mixture of **2–5** (116 mg, 0.38 mmol) and aluminum amalgam (102 mg, 3.78 mmol), according to the general procedure, endo-lactone **7** was obtained as the major product of an 86:14 mixture of diastereoisomers (87 mg, 83%), after chromatography of the crude (hexane–EtOAc, 4:1). Pure **7** (40% from **1**) was obtained by recrystallization from hexane. Data of **7**: white solid, mp 92–93 °C; R_f = 0.29 (hexane–EtOAc, 4:1); [α] = +109.0° (c 0.80, $CHCl_3$); ^{1}H NMR 1.76 (dt, 1 H, J = 9.4, 1.8 Hz, H-10a), 1.86 (dd, 1 H, J = 18.7, 3.2 Hz, H-5s), 2.01 (brd, 1 H, J = 9.4 Hz, H-10s), 2.05 (dd, 1 H, J = 18.6, 10.4 Hz, H-5a), 2.36 (s, 3 H, CH_3-p-Tol), 2.80 (ddd, 1 H, J = 10.4, 3.7, 3.5 Hz, H-6), 3.01–3.03 (m, 1 H, H-7), 3.20 (m, 1 H, *H*-1), 6.17 (dd, 1 H, J = 5.6, 3.1 Hz, H-9), 6.22 (dd, 1 H, J = 5.7, 2.8 Hz, H-8), 7.16 (d, 2 H, J = 7.8 Hz, ArH), 7.48 (d, 2 H, J = 8.2 Hz, ArH). An experiment with pure (+)-**7** (20 mg) in $CDCl_3$, in the presence of Eu(hfc)$_3$ (4.8 mg) showed no signal splittings, as observed for racemic **7**, especially for H-5a; ^{13}C NMR 21.2, 33.2, 46.9, 47.0, 48.6, 52.4, 103.4, 127.3, 130.0, 135.2, 135.7, 136.9, 139.6, 176.5; IR ($CHCl_3$) 3025, 2980, 1775, 1495, 1410, 1340, 1190, 1160. Anal. Calcd for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92. Found: C, 70.41; H, 5.78.

Synthesis of (1*S*,2*R*,6*R*,7*R*)-2-(p-Tolylthio)-3-oxatricyclo-[5.2.1.0^{2,6}]dec-8-en-4-one, 15. From the mixture of **11–14** (107 mg, 0.35 mmol) and aluminum amalgam (95 mg, 3.5 mmol), according to the general procedure, exo-lactone **15** was obtained as the major product of a 91:9 mixture of diastereoisomers (83 mg, 86%), after chromatography (hexane–EtOAc, 4:1). Pure **15** was obtained by recrystallization from hexane. Data of **15**: white solid, mp 123–124 °C; R_f = 0.34 (hexane–EtOAc, 2:1); [α] = +6.21° (c 0.29, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 1.60 (brd, 1 H, J = 10.2 Hz, H-10s), 1.73 (dm, 1 H, J = 10.1 Hz, H-10a), 2.15 (dd, 1 H, J = 17.9, 2.1 Hz, H-5s), 2.29 (ddd, 1 H, J = 10.2, 2.1, 1.9 Hz, H-6), 2.35 (s, 3 H, CH_3-p-Tol), 2.43 (dd, 1 H, J = 17.9, 10.2 Hz, H-5a), 2.71 (m, 1 H, H-7), 3.13 (m, 1 H, H-1), 6.16 (dd, 1 H, J = 5.7, 3.1 Hz, H-9), 6.30 (dd, 1 H, J = 5.7, 3.0 Hz, H-8), 7.15 (d, 2 H, J = 8.1 Hz, ArH), 7.46 (d, 2 H, J = 8.1 Hz, ArH). An experiment with pure (+)-**15** (20 mg) in $CDCl_3$, in the presence of Eu(hfc)$_3$ (5.1 mg), showed no signal splitting, as observed for racemic **15**, especially for H-5a; ^{1}H NMR (C_6D_6) 1.24–1.26 (m, 2 H, H-10s, H-10a), 1.55 (dd, 1 H, J = 18.3, 2.4 Hz, H-5s), 1.76 (dm, 1 H, J = 10.5 Hz, H-6), 1.86–1.87 (m, 1 H, H-1 or H-7), 1.90 (dd, 1 H, J = 18.3, 10.5 Hz, H-5a), 1.96 (s, 3 H, CH_3-p-Tol), 2.92–2.93 (m, 1 H, H-1 or H-7), 5.84 (dd, 1 H, J = 5.7, 3.1 Hz, H-8 or H-9), 5.93 (dd, 1 H, J = 5.7, 3.1 Hz, H-8 or H-9); ^{13}C NMR 21.2, 33.9, 44.1, 45.3, 47.8, 51.4, 103.2, 126.9, 129.9, 134.4, 135.8, 138.1, 139.5, 176.8; IR ($CHCl_3$) 2995, 2975, 2885, 1750, 1495, 1410, 1230, 1170. Anal. Calcd for $C_{16}H_{16}O_2S$: C, 70.56; H, 5.92. Found: C, 70.41; H, 5.78.

Synthesis of (1*R*,2*S*,6*R*,7*S*)-3-Oxatricyclo[5.2.1.0^{2,6}]dec-8-en-4-one, 9. To a solution of lactone **7** (60 mg, 0.22 mmol) in 3 mL of toluene was added tri-n-butyltin hydride (96 mg, 0.66 mmol, 0.09 mL) and AIBN (10 mg) and the mixture was heated at reflux for 48 h. The solvent was removed in vacuo and the residue was chromatographed (hexane–EtOAc, 3:1) to give pure **9** (28 mg, 85%). Data of **9**: white solid, mp 79–80 °C (hexane); R_f = 0.13 (hexane–EtOAc, 3:1); [α] = +17.6° (c 0.88, $CHCl_3$); ^{1}H NMR 1.37 (dm, 1 H, J = 9.4 Hz, H-10s), 1.66 (dt, 1 H, J = 9.4,

1.9 Hz, H-10a), 1.98 (dd, 1 H, J = 18.7, 3.5 Hz, H-5s), 2.46 (dd, 1 H, J = 18.7, 3.5 Hz, H-5s), 2.46 (dd, 1 H, J = 18.7, 10.9 Hz, H-5a), 2.75–2.88 (m, 1 H, H-6), 2.95–2.99 (m, 1 H, H-7), 3.22–3.28 (m, 1 H, H-1), 5.09 (dd, 1 H, J = 8.1, 4.2 Hz, H-2), 6.13 (ddd, 1 H, J = 5.8, 3.0, 0.6 Hz, H-8 or H-9), 6.27 (dd, 1 H, J = 5.8, 3.0 Hz, H-8 or H-9); ^{13}C NMR 31.7, 38.4, 45.4, 46.6, 47.0, 84.2, 135.2 (2C), 177.9; IR ($CHCl_3$) 3020, 1770, 1415, 1360, 1190, 1180, 1055, 1045. Anal. Calcd for $C_9H_{10}O_2$: C, 71.98; H, 6.71. Found: C, 71.65; H, 6.56.

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