1,2- and 1,5-Stereocontrols in 5-Hexenyl Radical Cyclizations: Cooperative or Antagonist Effect. Confrontation of Experimental Results with MM2 Calculations of Transition States

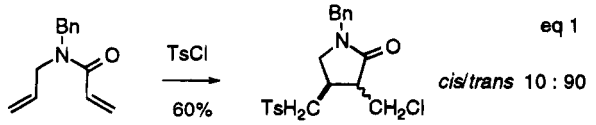
M. P. Bertrand,*,† I. De Riggi,† C. Lesueur,† S. Gastaldi,† R. Nouguier,*,† C. Jaime,‡ and A. Virgili‡

Laboratoire de Chimie Moléculaire Organique–URA 1412, B 562–Faculté des Sciences St Jérôme, Université d'Aix-Marseille III, Av. Escadrille Normandie-Niemen, 13397 Marseille Cedex 20, France, and Departament de Quìmica, Universitat Autònoma de Barcelona, 08193 Bellaterra, Spain

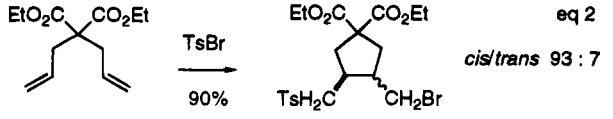
Received March 1, 1995®

The cyclofunctionalization of 1,6-dienes **1** and **2** *via* the addition of tosyl radical allows the analysis of the combined effects of 1,2- and 1,5-stereocontrols on the outcome of 5-hexenyl radical cyclizations. MM2 calculations of transition states agree quite well with the experimental selectivity, *i.e.*, exclusive 1,2-*trans* control, and predominance of 1,5-*cis* over 1,5-*trans* relationship. The addition of TsBr to carbohydrate-derived epimeric dienes **3a** and **3b** shows that the stereochemistry of the newly formed C–C bond is controlled by the configuration of the C2 center of the radical. 1,5-*trans* or 1,5-*cis* selectivity can be achieved depending on the configuration of C2.

The radical addition of various sulfonyl radical precursors to dienes and enynes is now well documented, through the works of our group[1] and of other research groups.[2] These reactions are synthetically interesting for three main reasons: firstly, this strategy allows in one simple step the introduction of two useful functionalities; secondly, the use of sulfonyl radical as the chain carrier allows the chemoselective cyclofunctionalization of unsymmetrical dienes (eq 1);[1f] and thirdly, the stereoselectivity is often high (eq 2).[1b,2]



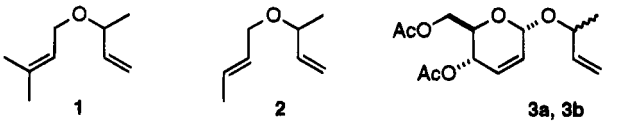
eq 1



eq 2

We investigated the influence of a substituent in position 2 with respect to the radical center upon the diastereoselectivity of the overall process involving three stereogenic centers.

Chart 1



1 **2** **3a, 3b**

We describe herein the results obtained for the addition of TsX (X = Br or Cl) or TsSePh to dienes **1**–**3** (Chart 1).

Results and Discussion

Chronologically, we started studying the reactivity of 3,7-dimethyl-4-oxa-1,6-octadiene (**1**). This substrate—which possesses a prenyl chain—was selected so that only the addition of tosyl radical to the monosubstituted double bond would lead to adducts. With unsymmetrical dienes, where two different double bonds compete with respect to the addition of tosyl radical, we previously showed that the reversibility of the addition of sulfonyl radical to double bonds plays a crucial part in favoring the formation of the adducts which result from the one intermediate radical that cyclizes faster. Furthermore, the atom transfer in the very last step would not introduce a supplementary stereogenic center. In our first experiments we used tosyl bromide as the precursor of tosyl radical but stereochemical information was lost due to the dehydrobromination of the tertiary bromides formed under the reaction conditions. Then the reaction was conducted with tosyl chloride, using a 5-fold excess of chloride with respect to the diene, in order to make the chlorine transfer step efficient. The results (Scheme 1) were actually those expected with regard to the chemoselectivity. Furthermore, among the four possible diastereoisomeric adducts (**4ab**, **5ab**), only two were isolated in a 75:25 ratio. Adducts **4a** and **4b** possessed a 1,2-*trans* configuration, the major one also presenting a 1,5-*cis* relationship (numbering refer to the intermediate 5-hexenyl radical). No traces of the diastereoisomers **5a,b**—resulting from a 1,2-*cis* stereocontrol—were detected.

Stereochemical assignments followed from ^1H and ^{13}C NMR data. A 2D NOESY sequence gave clear evidence for the spatial proximity of the equivalent geminated methyl groups (s, 1.48 ppm) and of the third methyl group

† Université d'Aix-Marsaille III.

‡ Universitat Autònoma de Barcelona.

® Abstract published in *Advance ACS Abstracts,* August 15, 1995.

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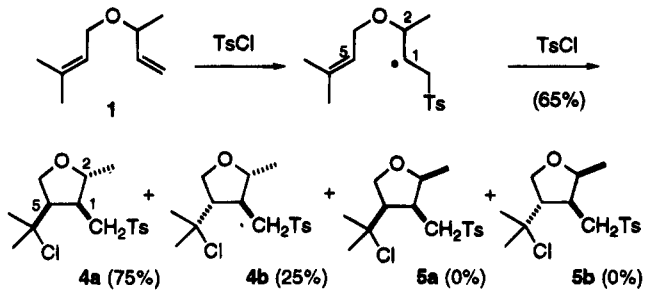
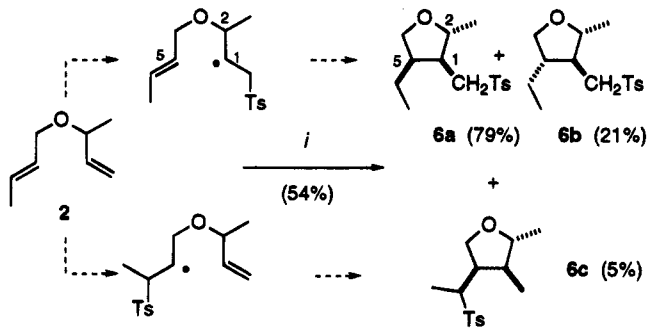
Scheme 1



Scheme 2[a]

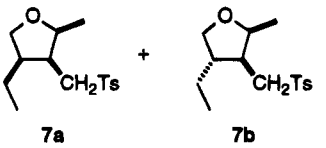


[a] Key: (*i*) TsSePh, AIBN, C_6H_6, 80 °C, 15 h, then *n*-Bu_3SnH, C_6H_6, AIBN, 80 °C, 4h.

(d, 1.38 ppm) in compound **4b**. No similar effect could be observed in the NOESY spectrum of **4a**. ^{13}C NMR spectra showed that the chemical shifts of the primary carbon β to the oxygen were similar in **4a** and **4b** (20.63 and 19.36, respectively), whereas the secondary carbon bearing the sulfone group and the quaternary carbon bearing the chlorine atom were significantly shielded in **4a** due to the γ gauche effect (55.02 and 68, 33 ppm, respectively, in **4a**, versus 61.08 and 71.34 ppm, respectively, in **4b**). Furthermore, all the secondary carbons were more shielded in **4a** than in **4b** (cf. Experimental Section).

All these data went to prove that 1,2-stereocontrol was total whereas 1,5-stereocontrol was only partial. The chemoselectivity was total. In spite of the fact that the reaction might not be chemoselective when a *trans*-disubstituted alkene competed with a monosubstituted one, the same experiment was conducted later on (*E*)-3-methyl-4-oxa-1,6-octadiene (**2**). Substrate **2** allowed *a priori* the competition between tandem addition–cyclization *via* the initial addition of tosyl radical to the monosubstituted double bond and *via* the initial addition of tosyl radical to the disubstituted double bond (Scheme 2). In order to avoid too complex an analysis, the crude adducts were immediately reduced with tributyltin hydride at reflux of benzene. The addition reaction was carried out first with TsBr and then with TsSePh. This last reagent is nearly as reactive as tosyl bromide as a transfer agent, and the overall yield was far better for the thermal addition of TsSePh (54%) than for the photochemically induced addition of TsBr (20%). Again, the reaction was chemo- and stereoselective. The 1,2-*trans* products, **6a** and **6b**, resulting from the initial addition of Ts• to the less substituted double bond were identified in a 75:20 ratio; they contributed to 95% of the reaction products for the addition of TsSePh. As in the previous case, no traces of the 1,2-*cis* isomers (**7a,b**) were detected. A minor product (**6c**), identified as resulting from the initial addition of Ts• to the disubstituted double bond, was also isolated (5%) (Scheme 2).

Chart 2



The products ratio[3] was slightly different for the addition of TsBr, possibly due to the effect of the reaction temperature on both the rate of fragmentation of the intermediate β-sulfonyl radicals[4] and the stereoselectivity of the cyclization step.

The structural assignments were deduced from the analysis of NMR data. Compound **6c** was unambiguously identified by the observation of the signals corresponding to four different methyl groups (three doublets at 0.96, 1.15, and 1.21 ppm; one singlet, at 2.45 ppm). The stereochemistry of **6a** and **6b** followed from the ^{13}C chemical shifts of the primary carbon α to the oxygen (20.19 and 19.92 in **6a** and **6b**, respectively). The secondary carbon bearing the tosyl group, like the secondary carbon of the ethyl group, was more shielded in **6a** than in **6b** (54.60 and 20.61 ppm in **6a** versus 59.7 and 26.27 ppm in **6b**). In regard to **6c**, the chemical shifts of the primary carbon β to the oxygen atom (21.89 ppm) and the chemical shifts of the secondary carbons of the ring (cf. Experimental Section) were consistent with the proposed stereochemistry, analogous to that of **6a** (Chart 2).

The stereochemical outcome of the radical cyclization of numerous substituted 5-hexenyl radicals is well known. It is rationalized on the basis of the relative contribution of chairlike and boatlike transition states.[5] The above cyclizations are typical cases where taking qualitatively into account only chairlike transition states would have led to a wrong prediction concerning the stereochemistry of the minor product (**4b** or **6b**). MM2 calculations of the transition states for the cyclization of the 5-hexenyl radicals involved in the above reactions were performed using the MM2PRIME program.[6a] Whereas transition states had already been calculated for the cyclization of mono-[5a–c] or 1,3-disubstituted[1] 5-hexenyl radicals, no calculations had been performed previously to check the validity of the model for predicting the outcome of 1,2-disubstitution on the stereochemical course of the reaction. Allinger's MM2 (77) force field, together with all MM2 (85) parameters, was used throughout this work.[6b,c] Since not all the parameters involving the S–C(sp^2) bond were available, a mesyl group was used to replace the tosyl group. The parameters of the incoming radical center (C1) and the alkene atom under attack (C5) were

(3) The products ratio was determined by means of ^1H NMR.

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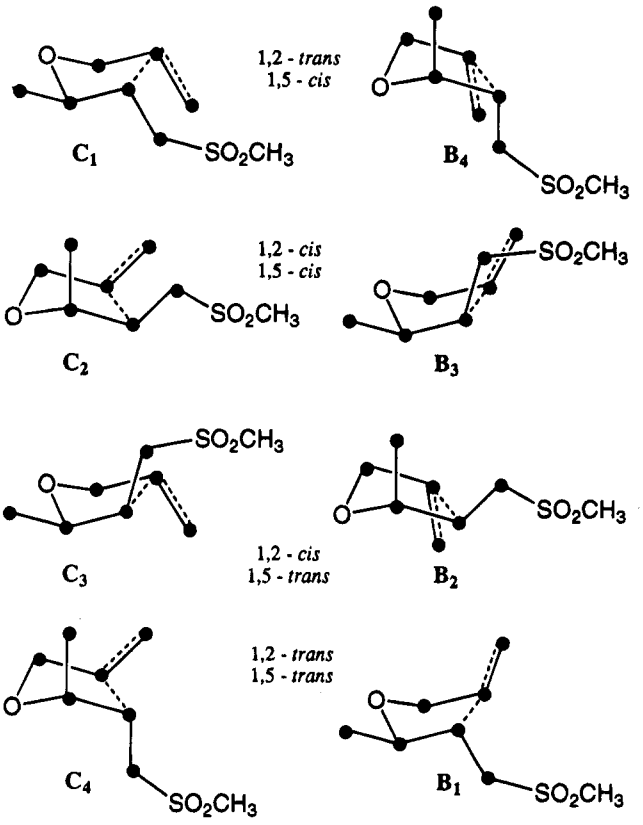

Figure 1. Transition states leading to cyclic products. Hydrogen atoms and methyl groups on the double bond have been omitted for the sake of clarity.

Table 1. Computational Results for the Cyclication of 1 and 2

	cyclization of **1**				cyclization of **2**			
	N_a[a]	E_R[b]	Σ%	product	N_a[a]	E_R[b]	Σ%	product
C_1	7	0.00	59.98	4a	7	0.00	68.32	6a
C_2	5	4.07	0.05	5a	5	4.09	0.06	7a
C_3	7	2.94	0.51	5b	7	2.59	1.18	7b
C_4	8	1.49	4.48	4b	8	1.54	4.93	6b
B_1	7	0.57	27.44	4b	7	0.90	19.71	6b
B_2	8	4.11	0.09	5b	8	4.44	0.06	7b
B_3	6	2.13	1.74	5a	7	2.81	0.64	7a
B_4	7	1.58	5.71	4a	6	1.51	5.10	6a

[a] Na: number of contributing conformers. [b] ER: averaged relative energies (kcal/mol).

added according to Houk,[5c] considering C1 and C5 equivalent to sp^3 carbons (MM2 type 1).

Each possible diastereoisomer can be obtained *via* one boat and one chairlike transition state (the eight conformers are represented in Figure 1). For each simulated transition state, the calculations of the conformational energy surface were achieved by performing rotations around the C1−C7 and the C7−S σ bonds, using the option TREE within the MM2PRIME program.[6]

The total number of the contributing energy minima are given in Table 1. Each of these conformers participates in the overall reaction process. Their individual contributions were analyzed by a Boltzmann distribution at +20 °C (assuming $\Delta G = \Delta H$). It follows that each chairlike or boatlike transition state is described as the sum of several low energy conformers. The global contribution and the average energy of these different transition structures are reported in Table 1.

It can be noticed that all the conformers that present a gauche interaction between the methyl and the tosylmethyl substituents (C_2, C_3, B_2, B_3) are highly destabilized regardless of their boat or chair conformation; as a consequence, 1,2-*trans* stereocontrol is total. Among the others, the most stable chair conformer has no axial substituent.

Table 2. Calculated and Experimental Selectivities for the Cyclization of 1 and 2

	cyclization of **1**				cyclization of **2**			
selectivity %	**4a**	**4b**	**5a**	**5b**	**6a**	**6b**	**7a**	**7b**
calcd	65.7	31.9	1.8	0.6	73.4	24.6	0.7	1.2
exptl	75	25	0	0	79	21	0	0

Table 3. Selected ^{13}C Chemical Shifts (δ, ppm) for 8*endo*, 8*exo*, and 9*endo*

product	C_9	C_8	CH_3
8*endo*	53.41	36.54	18.68
8*exo*	59.73	43.74	20.67
9*endo*	52.61	42.53	19.67

The calculations clearly justify that the main contribution to the formation of the major isomer originates from the chair transition state C_1 which is the most stable in the series, whereas the destabilized boat conformer B_4 contributes very little. Contrastingly, the minor stereoisomer originates mainly from the boatlike transition state B_1 which is only 0.5 (or 0.9 kcal) per mole less stable than C_1. The chair conformer C_4 bearing two pseudoaxial substituents is involved for less than 5% in the formation of **4b** and **6b**. A detailed examination of the structural parameters shows that conformers B_4 and C_4 are not pure boat or chairlike conformers, they are rather twist boats due to the dihedral angle 1−2−4−5 superior to 20°.

The overall selectivity agrees rather well with the calculations (cf. Table 3).

This series of results clearly demonstrate that 1,2-*trans* stereocontrol outweighs 1,5-*cis* control. This observation agrees with other data from the literature.[7]

In the carbohydrates series, we got evidence for an interesting consequential effect of the predominance of 1,2-stereocontrol. The addition of tosyl bromide to 1-methyl-3-propenyl 4,6-di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2-enopyranoside (**3a,b**), readily prepared as a 50:50 mixture of epimers starting from tri-*O*-acetyl-D-glucal and racemic 3-buten-2-ol *via* a Ferrier reaction,[8] led to a mixture of three products, 8*endo*, 8*exo*, and 9*endo*, in 12:38:50 relative proportions (Scheme 3). Therefore, the *R* epimer led to a mixture of 8*endo* and 8*exo* in a 1:3 ratio, whereas the *S* epimer led to a single *endo* adduct (**9**).

The three isomeric products were difficult to isolate as pure samples from liquid chromatography. Only 8*endo* was available as a satisfactorily pure sample. The assignments of 8*exo* and 9*endo* issued from the spectral data of a mixed chromatographic fraction containing both compounds. The structural assignments were based on NMR data (^1H, COSY HH, ^{13}C, and DEPT experiments). The characteristic signals of selected carbons are given in Table 3.

The shielding of the secondary carbon bearing the sulfone strongly supported the *endo* position of the tosylmethyl group in 8*endo* and 9*endo*. A similar trend

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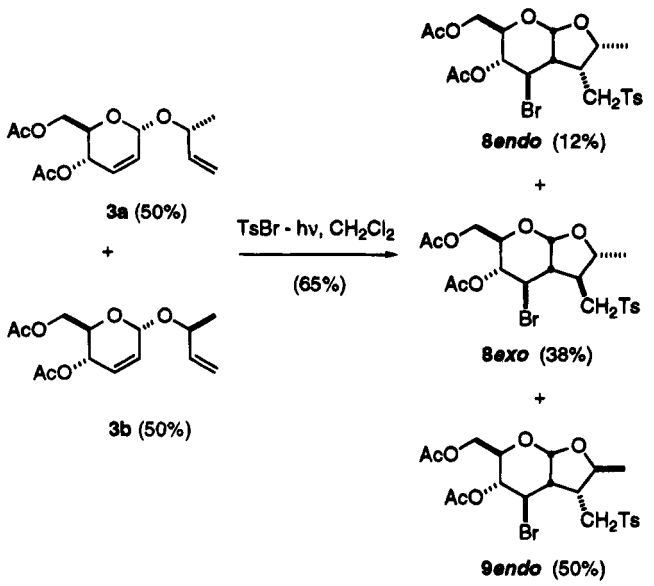
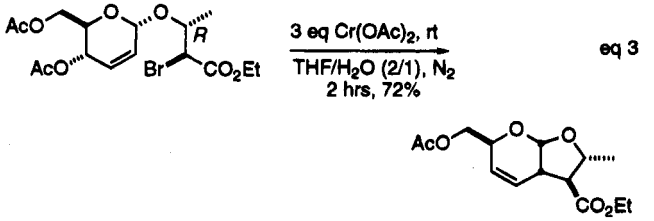
Scheme 3



influenced the chemical shift of C8 and the chemical shift of the primary carbon of the methyl group. Furthermore, the two protons α to the tosyl group (H9) were equivalent in **8***exo*. The stereochemistry was definitely assigned after the measurements of nuclear Overhauser enhancements, which are summarized in Figure 2.

The ratio of **8***endo* versus **8***exo* (*R* configuration at C7), both resulting from **3a**, is the reversal of the *endo:exo* selectivity observed for the cyclization of the *O*-allyl analogue of diene **3**.[1e] These results are well rationalized on the basis of 1,2-*trans* control governing the selectivity. The formation of **8***exo* as the major adduct to **3a** demonstrates that, when opposed to each other, 1,2-*trans* stereocontrol prevails (up to 76%) over 1,5-*cis* stereocontrol and thereby forces the substituents on C7 and C8 (Scheme 3) to be *trans* to each other. On the contrary, the exclusive formation of **9***endo* from **3b** results from the cooperative effects of the two stereochemical controls. This result should be compared to the closely related example of a bromide reductive cyclization published by Schäfer,[9] where the stereoselectivity observed starting from the optically pure *R* substrate is total (eq 3). The



eq 3

origin of 1,2-stereoinduction in radical reactions is now well rationalized.[10] The total control observed for the cyclization of the α-alkoxycarbonyl radical indicates that the conformation of the conjugated radical is strictly governed by allylic $A^{1,3}$-strain.[7c,10]

In conclusion, it must be emphasized that there is a close analogy between the above results concerning the combined effects of 1,2- and 1,5-stereocontrols on the outcome of 5-hexenyl radicals cyclizations and the studies

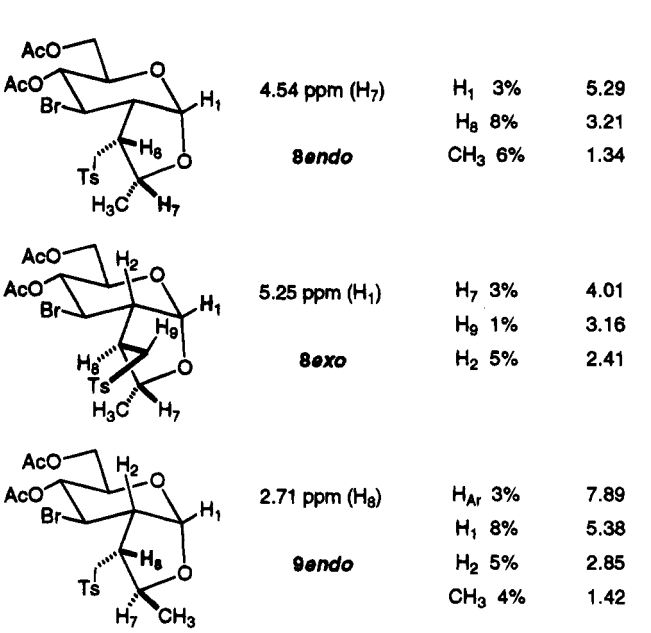


Figure 2. NOE enhancements on irradiation of H_7, H_1, and H_8, observed, respectively, for **8***endo*, **8***exo*, and **9***endo*.

conducted by Rajanbabu[11] about the cooperative or antagonist effects of 4,5- and 1,5-stereocontrols in radical cyclizations on sugar templates.

Experimental Section

NMR spectra were recorded in $CDCl_3$ solutions. *J* values are given in Hz. Homonuclear $^1H\{^1H\}$ NOEs were determined by means of the NOE difference technique, using 8 s low-power (5 mW) presaturation. Five hundred and twelve transients were acquired using 16 K data points and a sweep width of 5000 Hz, in alternate groups of eight, irradiating on/off resonance. A 90° pulse was used during acquisition. Column chromatographies were performed on silica gel 60 (Merck 7734). HPLC analyses were conducted on a Waters Nova-Pak Silica (4 μm) column (3.9 mm i.d. × 15 cm) coupled to a UV detector (254 nm) and a refractometer. TsBr and TsSePh were prepared according to known procedures[12] and were dried under vacuum before use.

3,7-Dimethyl-4-oxa-1,6-octadiene (1). A 100 mL, round-bottom flask was charged with 50% NaOH (4.90 g, 4 equiv), tetrabutylammonium bromide (60 mg, 6 mmol), 3-buten-2-ol (2.23 g, 31 mmol), and 1-bromo-3-methyl-2-butene (4.56 g, 31 mmol). The mixture was stirred at room temperature for 15 h and then extracted with Et_2O. The organic layers were dried over $MgSO_4$ and evaporated to give 3,7-dimethyl-4-oxa-1,6-octadiene (3.1 g, 73%). The crude product was satisfactorily pure and was used without further purification: ^1H NMR δ 1.25 (3 H, d, J = 6.4), 1.66 (3 H, s), 1.74 (3 H, s), 3.78–4.00 (3 H, m), 5.02–5.14 (2 H, m), 5.35 (1 H, t, J = 6.7), 5.75 (1 H, ddd, J = 16.5, 10.3, 7.3).

Addition of TsCl to 1. To a solution of 3,7-dimethyl-4-oxa-1,6-octadiene (**1**) (1.2 g, 8.6 mmol) and tosyl chloride (10 g, 6.1 equiv) in toluene (40 mL), heated at reflux under an inert atmosphere (Ar), was added benzoyl peroxide (30 mg) by portions over 36 h. After the solvent was evaporated, chromatography on silica gel (95:5 to 60:40 pentane/EtOAc) afforded 720 mg of **4a**, 720 mg of a mixture of **4a** and **4b**, and 270 mg of **4b** (65% overall yield). The 75:25 ratio of **4a** to **4b** was determined by HPLC on the crude mixture (70:30 isooctane/EtOAc, 1 mL/mn).

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(10) For reviews see: (a) Porter, N. A.; Giese, B.; Curran, D. P. *Acc. Chem. Res.* **1991**, *24*, 296. (b) Smajda, W. *Synlett* **1994**, 1.
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(12) (a) Truce, W. E.; Heuring, D. L.; Wolf, G. C. *J. Org. Chem.* **1974**, *39*, 238. (b) Gancarz, R. A.; Kice, J. L. *Ibid.* **1981**, *46*, 4899.

(2S*,3R*,4S*) 4-(1-Chloroisopropyl)-2-methyl-3-(tosylmethyl)tetrahydrofuran (4a): ^{1}H NMR δ 1.20 (3 H, d, J = 6.4), 1.56 (3 H, s), 1.59 (3 H, s), 2.46 (3 H, s), 2.53 (1 H, ddt, J = 11.0, 7.1, 1.5), 2.62 (1 H, dt, J = 10.2, 7.6), 3.15 (1 H, dd, J = 14.4, 11.0), 3.81 (1 H, dd, J = 10.2, 8.3), 3.96 (1 H, dd, J = 14.4, 1.5), 4.04 (1 H, t, J = 8.1), 4.37 (1 H, qd, J = 6.4, 1.5), 7.38 (2 H, d, J = 8.2), 7.80 (2 H, d, J = 8.2); ^{13}C NMR δ 20.63 (CH_3), 21.19 (CH_3), 31.56 (CH_3), 34.39 (CH_3), 40.72 (CH), 51.56 (CH), 55.02 (CH_2), 67.39 (CH_2), 68.33 (C), 80.12 (CH), 127.48 (CH), 129.66 (CH), 136.37 (C), 144.47 (C).

(2S*,3R*,4R*) 4-(1-Chloroisopropyl)-2-methyl-3-(tosylmethyl)tetrahydrofurane (4b): ^{1}H NMR δ 1.38 (3 H, d, J = 6.2), 1.48 (6 H, s), 2.24 (1 H, td, J = 6.4, 5.7), 2.31 (1 H, m), 2.45 (3 H, s), 3.29 (1 H, dd, J = 14.0, 8.8), 3.32 (1 H, dd, J = 14.0, 3.6), 3.78 (2 H, d, J = 6.4), 4.07 (1 H, qd, J = 6.2, 5.2), 7.38 (2 H, d, J = 8.0), 7.79 (2 H, d, J = 8.0); ^{13}C NMR δ 19.36 (CH_3), 21.51 (CH_3), 29,92 (CH_3); 31.09 (CH_3), 42.86 (CH), 59.15 (CH), 61.08 (CH_2), 67.62 (CH_2), 71.34 (C), 81.22 (CH), 127.77 (CH), 129.89 (CH), 136.64 (C), 144.82 (C). Anal. Calcd for $C_{16}H_{23}ClSO_3$(**4a** + **4b**): C, 58.08; H, 7.1; Cl, 10.71; S, 9.69. Found: C, 58.09; H, 7.05; Cl, 10.80; S, 9.40.

***(E)*-3-Methyl-4-oxa-1,6-octadiene (2).** To a suspension of 60% NaH (1.3 g, 32 mmol) in dry THF (15 mL) was added 3-buten-2-ol (2g, 28 mmol). The reaction mixture was stirred at room temperature for 1 h before a solution of *(E)*-1-chloro-2-butene (2.49 g, 28 mmol) in THF (10 mL) was added. Then, the solution was heated at reflux for 20 h. After addition of 50 mL of water, the mixture was extracted three times with Et_2O and the organic layers were dried over Na_2SO_4 and evaporated. Distillation of the crude product provided **2** (860 mg, 25%): bp 80 °C (325 mbar); ^{1}H NMR δ 1.23 (3H, d, J = 6.4), 1.71 (3H, dq, J = 5.9, 1.0), 4.0–3.7 (3H, m), 5.20–5.10 (2H, m), 5.8–5.5 (3H, m); ^{13}C NMR 17.74, 21.32, 68.76, 76.04, 115.69, 127.84, 129.06, 140.35.

Addition of TsBr to 2. A solution containing **2** (300 mg, 2.4 mmol) and TsBr (556 mg, 2.4 mmol) in acetonitrile (140 mL) was placed under inert atmosphere (Ar), immersed in a thermostated bath (15 °C), and submitted to external irradiation with a high pressure mercury lamp. After 8 h, the solvent was evaporated and the residue was dissolved in benzene (20 mL). n-Bu_3SnH (1.18 g, 4 mmol) was added and the solution refluxed under argon, together with AIBN added by portions over 4 h. After evaporation of the solvent, the residue was diluted with CH_3CN, extracted with three portions of pentane, and then concentrated and purified by flash chromatography (100:0 to 50:50 pentane/Et_2O) to give a 71:12:17 mixture of **6a**:**6b**:**6c** (136 mg, 20%).

Addition of TsSePh to 2. To a stirred solution of **2** (300 mg, 2.4 mmol) and TsSePh (740 mg, 2.4 mmol) in degassed benzene (140 mL), at reflux, under Ar atmosphere, was added AIBN (40 mg) by portions over 15 h. After concentration to 20 mL, n-Bu_3SnH (1.10 g, 3.7 mmol) was added and the solution was heated at reflux for 4 h in the presence of AIBN. After evaporation of the solvent, the residue was diluted with CH_3CN and extracted three times with pentane. After evaporation of acetonitrile, purification by flash chromatography (100:0 to 50:50 pentane/Et_2O) afforded a 75:20:5 mixture of **6a**, **6b**, and **6c** (385 mg, 54%). The relative proportions were based on ^{1}H NMR. A second chromatography allowed the separation of a sample of **6a** and of a mixed fraction containing only **6b** and **6c**.

(2S*,3R*,4S*) 4-Ethyl-2-methyl-3-(tosylmethyl)tetrahydrofuran (6a): ^{1}H NMR δ 0.86 (t, J = 7.2, 3H), 1.19 (d, J = 6.1, 3H), 1.35–1.45 (m, 2H), 2.25–2.32 (m, 2H), 2.45 (s, 3H), 2.97 (dd, J = 14.2, 6.2, 1H), 3.19 (dd, J = 14.2, 6.2, 1H), 3.48 (dd, J = 8.6, 5.8, 1H) 3.82–3.98 (superimposed m, 1H), 3.96 (dd, J = 8.6, 6.2, 1H), 7.38 (d, J = 8.0, 2H), 7.79 (d, J = 8.0, 2H), when irradiating at 2.3 ppm the following changes were observed: 3.96 (d, J = 8.6), 3.89 (q, J = 6.1), 3.48 (d, J = 8.6), 3.19 (d, J = 14.2), 2.97 (d, J = 14.2); ^{13}C NMR δ 12.42 (CH_3), 20.19 (CH_2), 20.61 (CH_3), 21.71 (CH_3), 42.67 (CH), 43.76 (CH), 54.60 (CH_2), 71.42 (CH_2), 78.57 (CH), 128.04 (CH), 130.08 (CH), 136.40 (C), 144.9 (C).

(2S*,3R*,4R*) 4-Ethyl-2-methyl-3-(tosylmethyl)tetrahydrofuran (6b): ^{1}H NMR δ 0.86 (t, J = 7.2, 3H), 1.29 (d, J = 6.1, 3H), 1.5–1.62 (m, 2H), 2.32–2.52 (m, 2H), 2.45 (s, 3H), 3.03–3.22 (AB part of an ABX, J_{AB} = 14.3, 2H), 3.58 (dd, J = 8.9, 5.7, 1H), 3.70–3.90 (m, 2H), 7.38, (d, J = 8.0, 2H), 7.79 (d, J = 8.0, 2H); ^{13}C NMR δ 12.47 (CH_3), 19.92 (CH_3), 21.65 (CH_3), 26.27 (CH_2), 46.24 (CH), 48.22 (CH), 59.7 (CH_2), 71.12 (CH_2), 80.71 (CH), 127.92 (CH), 130.00 (CH), 136.90 (C), 144.8 (C).

(2S*,3R*,4S*) 4-(2-Tosylpropyl)-2,3-dimethyltetrahydrofuran (6c): ^{1}H NMR δ 0.96 (d, J = 7.1, 3H), 1.15 (d, J = 6.3, 3H); 1.21 (d, J = 6.8, 3H), 2.32–2.51 (m,2H), 2.45 (s, 3H), 3.05 (dq, J = 11.36, 6.8, 1H), 3.70–3.90 m, 1H), 3.74 (dd, J = 10.9, 9.4, 1H), 4.35 (dd, J = 9.4, 7.3, 1H), 7.38 (d, J = 8.0, 2H), 7.77 (d, J = 8.0, 2H); ^{13}C NMR δ 14.06 (CH_3), 15.16 (CH_3), 21.65 (CH_3), 21.89 (CH_3), 41.38 (CH), 41.70 (CH), 59.90 (CH), 69.45 (CH_2), 81.54 (CH), 128.96 (CH), 129.85 (CH), 134.42 (C), 144.8 (C). Anal. Calcd for $C_{15}H_{22}O_3S$ (**6a** + **6b** + **6c**): C, 64.03; H, 7.52; S, 11.39. Found: C, 64.06; H, 7.56; S, 11.30.

1-Methyl-3-propenyl 4,6-Di-*O*-acetyl-2,3-dideoxy-α-D-*erythro*-hex-2- enopyranoside (3a,b). To a stirred solution of 3,4,6-tri-*O*-acetyl-D-glucal (6.81 g, 25 mmol) in dry CH_3CN (125 mL) were rapidly added, at −30 °C, under Ar, BF_3·OEt_2 (3.07 mL, 25 mmol) and 2-buten-1-ol (1.89 g, 1.05 equiv). After 3.5 h, the solution was partially neutralized with 2 equiv of solid $NaHCO_3$ and was allowed to warm to room temperature. After solvant evaporation under reduced pressure, the residue was dissolved in CH_2Cl_2 (100 mL) and washed with a solution of $NaHCO_3$ and then with water until neutrality. The organic layer was dried over Na_2SO_4 and evaporated. The residue, a white powder, was triturated with pentane (50 mL). After filtration, the solid was washed with pentane and the filtrate was concentrated. The isolated syrup (4,26 g, 60%) was a mixture of the two α epimers (**3a,b**) containing also traces of the two β epimers; it was used without further purification: ^{1}H NMR δ 1.37 (d, J = 6.3, 3H), 1.35 (d, J = 6.3, 3H), 2.18–2.15 (s, 6H), 4.40–4.00 (m, 4H), 5.33–5.05 (m, 4H), 6.00–5.60 (m, 3H); ^{13}C NMR δ 19.99, 20.69, 20.87, 21.41, 21.61, 62.83 , 62.02, 63.46, 64.21, 65.19, 65.34, 66.76, 66.80, 72.49 , 73.87, 74.27, 74.74, 91.23, 91.51, 92.67, 114.36, 116.44, 117.42, 125.16, 128.09, 128.91, 130.85, 138.90, 140.33, 170.67, 170.70. Anal. Calcd for $C_{14}H_{20}O_6$: C, 59.15; H, 7.09. Found: C, 59.18; H, 7.18.

Addition of TsBr to 3a,b. A solution containing **3a,b** (0.56 g, 2 mmol) and TsBr (0.46 g, 1 equiv) in degassed CH_2Cl_2 (125 mL) was submitted in a Pyrex vessel to external irradiation with a high pressure mercury lamp. The flask was immersed in a thermostated bath at 15 °C. After 24 h the solvant was evaporated and the viscous residue was rapidly chromatographed on silica gel (6:4 $CHCl_3$/Et_2O). The purification afforded **8***endo* (90 mg), a mixed fraction containing **8***endo*, **8***exo*, and **9***endo* (60 mg), and a third fraction (350 mg) containing **8***exo* and **9***endo* together with traces of 4,6-di-*O*-acetyl-2,3-dideoxy-D-*erythro*-hex-2-eno-1,5-lactone in 50% combined yields. The relative proportions of the three adducts were determined by 400 MHz NMR analysis of the crude products (it was based on the integration of the corresponding methyl doublets). **8***endo*: ^{1}H NMR δ 1.34 (d, J = 6.7, 3H), 1.94 (s, 3H), 1.96 (s, 3H), 2.33 (s, 3H), 2.65 (ddd, J = 10.2, 6.3, 4.2, 1H), 3.21 (m, 1H), 3.35 (dd, J = 14.1, 11.5, 1H), 3.90 (dd, J = 14.1, 2.3, 1H), 4.02 (dd, J = 12.3, 2.3, 1H), 4.05 (superimposed m, 1H), 4.07 (t, J = 10.2, 1H), 4.31 (dd, J = 12.3, 4.2, 1H), 4.54 (dq, J = 8.6, 6.7, 1H), 5.13 (t, J = 10.1, 1H), 5.29 (d, J = 4.2, 1H), 7.25 (d, J = 8.2, 2H), 7.65 (d, J = 8.2, 2H); ^{13}C NMR δ 18.68, 20.64, 20.76, 21.67, 36.54, 48.14, 49.72, 53.41, 62.03, 69.49, 70.09, 73.73 100.20, 127.92, 130.22, 136.20, 145.32, 162.27, 170.77. **8***exo*: ^{1}H NMR δ 1.35 (d, J = 6.7, 3H), 2.20–2.00 (2 s, 6H), 2.40 (s, 3H), 2.41 (superimposed m, 1H), 3.15 (superimposed m, 1H), 3.16 (d, J = 6.5, 2H), 4.10–3.91 (m, 3H), 4.35–4.20 (m, 2H), 5.13 (t, J = 9.2, 1H), 5.25 (d, J = 4.3, 1H), 7.45 (d, J = 8.2, 2H), 7.89 (d, J = 8.2, 2H; ^{13}C NMR δ 20.67, 20.69, 20.79, 21.69, 43.74, 51.92, 52.40, 59.73, 62.44, 69.45, 70.58, 76.93, 99.09, 127.91, 130.14, 136.38, 145.25, 169.35, 170.73. **9***endo*: ^{1}H NMR δ 1.42 (d, J = 6.7), 2.20–2.00 (2s, 6H), 2.40 (s, 3H), 2.71 (m, 1H), 2.85 (ddd, J = 10.2, 5.5, 4.2, 1H), 2.91 (dd, J = 14.4, 4.4, 2H), 3.81 (t, J = 10.1, 1H), 4.10–3.91 (m, 4H), 4.35–4.20 (m, 1H), 5.16 (t, J = 10.1, 1H), 5.38 (d, J = 4.2, 1H)), 7.46 (d, J = 8.2, 2H), 7.89 (d, J = 8.2, 2H); ^{13}C NMR δ 19.67, 20.69, 20.79, 21.21, 42.53, 48.00, 48.26,

52.61, 62.12, 69.39, 70.11, 76.66, 100.34, 128.09, 130.10, 136.38, 145.25, 169.26, 170.75; HRMS (*8endo* + *8exo* + *9endo*) $[M - OCOCH_3 - HBr]^+$ calcd for $C_{19}H_{23}O_6S$ 379.12152, found 379.1221.

Computational Details. Calculations were performed on a VAX-8820 computer at the Computer Centre of the Universitat Autònoma of Barcelona. MM2 (85) parameters were used throughout this work, except those concerning both the incoming radical center, defined as MM2 type 48, and the alkene atom being attacked, defined as type 49.[5c]

Torsional definitions (V_1, V_2, and V_3, respectively, for the given angle): 0, −25.0, 0, 5−2−49−48; rotation about the double bond, 0, 0, 0.25, 5−2−49−5; 0, 0.2, 0.2, 5−2−49−1; rotation about the forming bond, 0, 0, 0.0267, 5−48−49−5; 0, 0, 0.0273, 1−48−49−5; 0, 0, 0.041, 5−48−49−2; 0, 0, 0.065, 5−48−49−1; −0.241, 0.241, 0.399, 1−48−49−2; 1.364, −1.103, 0.339, 1−48−49−1.

Bond stretching and compression parameters: forming bond, atom type 48−49, $l_o = 2.27$, $K_s = 4.0$; double bond, atom type 49−2, $l_o = 1.375$, $K_s = 4.4$.

Angle-bending parameters (K_B and θ_o, respectively, for the given angle): radical center, 0.32, 116.6, 5−48−5; 0.36, 100.5, 5−48−49; 0.36, 116.6, 5−48−1; 0.45, 116.6, 1−48−1; 0.45, 100.5, 1−48−49; carbon type 49, 0.36, 90.3, 5−49−48; 0.60, 107.0, 2−49−48; 0.36, 120.3, 2−49−5; 0.32, 115.8, 5−49−5; 0.45, 90.3, 1−49−48; 0.45, 120.3, 1−49−2; 0.36, 115.8, 1−49−5; terminal carbon of the double bond, 0.36, 121.4, 5−2−49; 0.32, 117.0, 5−2−5.

Acknowledgment. We are grateful to the CIRIT, which made calculations possible by its financial supports and to CICYT for attributing fellowships to Dr. I. De Riggi.

Supporting Information Available: ^1H NMR spectrum of compound **1**, ^1H and ^{13}C NMR spectra of compound **2**, fully assigned NMR data of *8endo*, *8exo*, and *9endo*, and structural drawings of the calculated transition states and computational data (33 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO950405F