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Sulfoxide-controlled S_N2' displacements between cuprates and vinyl and alkynyl epoxy sulfoxides

Roberto Fernández de la Pradilla,* Alma Viso,* Sonia Castro, Jorge Fernández, Pilar Manzano and Mariola Tortosa

Instituto de Química Orgánica, CSIC, Juan de la Cierva, 3, 28006 Madrid, Spain

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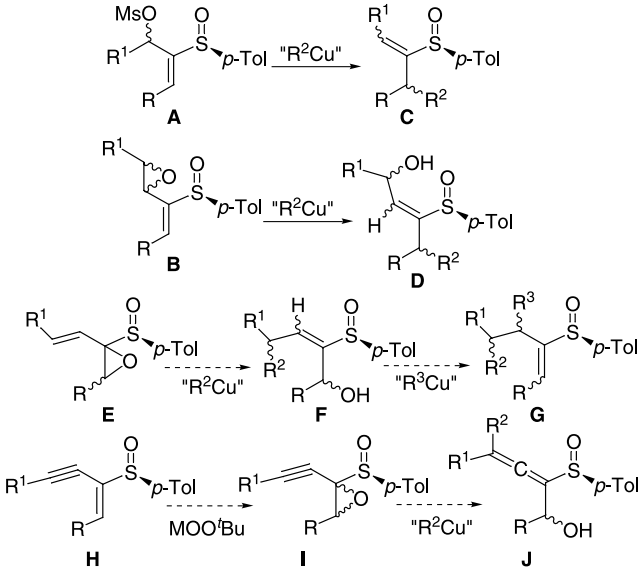
Dedicated to the memory of Dr. Juan Carlos del Amo deceased in Madrid (11 March 2004)

Abstract—The S_N2' displacement of readily available vinyl epoxy sulfoxides with organocopper reagents takes place in good yields with high *anti* selectivity and a good degree of *E*/*Z* stereocontrol to produce enantiopure α-hydroxy vinyl sulfoxides. A second allylic displacement on the related mesyloxy vinyl sulfoxides allows for the asymmetric construction of two adjacent chiral centers. In addition, cuprate mediated S_N2' addition to alkynyl epoxy sulfoxides affords α-hydroxy allenyl sulfoxides in good yields.

1. Introduction

Notwithstanding the advances in the past years, the asymmetric construction of carbon–carbon bonds remains a crucial challenge for the development of organic synthesis. Among the existing methodology, allylic substitution, namely S_N2' displacement of acetates, epoxides and other leaving groups, has been recognized as a powerful tool in the asymmetric synthesis of a number of complex molecules.[1] Within this field and in connection with our interest in the development of sulfur-directed methodology,[2] previous research from our group has been focused on the sulfoxide-controlled S_N2' displacements between cyanocuprates and mesyloxy and epoxy vinyl sulfoxides **A** and **B**. Indeed, we have demonstrated that allylic mesylates **A**, activated with a chiral sulfoxide, undergo copper mediated S_N2' displacements with high asymmetric induction and *Z*/*E* selectivity to produce enantiomerically pure trisubstituted vinyl sulfoxides **C**.[3] Additionally, we have extended the scope of this methodology to enantiopure epoxy vinyl sulfoxides **B** that produce densely functionalised allylic alcohols **D** through a highly regio- and stereoselective S_N2' process.[4] Moreover, further applications of these products could be envisioned due to the presence of the vinyl sulfoxide that should allow for subsequent synthetic manipulations of the molecules (Scheme 1).[5]

To extend this study, vinyl epoxy sulfoxides **E**, now available through nucleophilic epoxidation of vinyl and dienyl sulfoxides,[6] were considered. At the inception of this research, we were aware of previous studies on the somewhat anomalous behavior of simple sulfinyl oxiranes



Scheme 1.

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* Corresponding authors. Fax: +34-91-564-4853; e-mail addresses: iqov379@iqog.csic.es; iqofp19@iqog.csic.es

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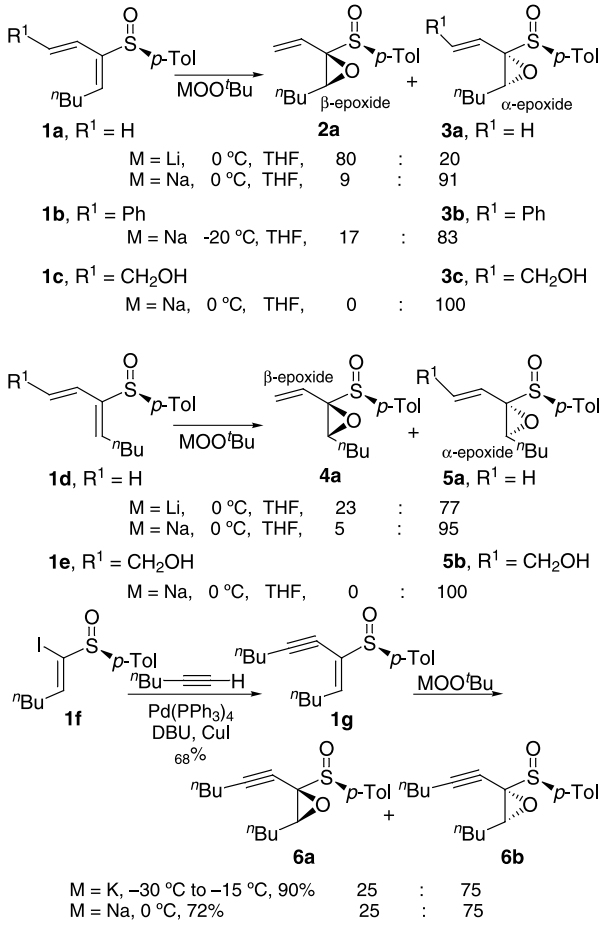
with organocuprates that rendered enolates in good yield without incorporation of the alkyl residue on copper. At any rate we chose to pursue this chemistry with the expectation that an alternative reaction pathway would be operative for our unsaturated oxiranes.[7] In fact, this new class of epoxides could undergo two consecutive asymmetric S_N2' reactions. First, allylic displacement on epoxides **E** would lead to allylic alcohols **F** that maintain the vinyl sulfoxide group and second, S_N2' substitution on a mesylate of **F** would render trisubstituted vinyl sulfoxides **G** with two adjacent newly created chiral centers. In addition, we planned the study of the nucleophilic epoxidation of sulfinyl enynes **H** to produce epoxides **I** that incorporate an alkyne at the electrophilic terminus[8] and could lead to the asymmetric synthesis of hydroxy sulfinyl allenes **J**.[9] In this paper, we present a full account of our results.

2. Synthesis of starting materials

The synthesis of the enantiopure starting oxiranes was performed through the nucleophilic epoxidation of readily available dienyl sulfoxides with LiOO^{t}Bu and NaOO^{t}Bu.[10] We have previously observed that the process takes place in good yields, with complete regiocontrol and preservation of the double bond geometry. Additionally, the diastereofacial selectivity varies from moderate to excellent, depending on the nature of the dienyl sulfoxide **1a-e** and the metalated peroxide (Li or Na).[10c] On the other hand, as an extension of the above methodology, alkynyl vinyl sulfoxide **1g**, available from Sonogashira coupling of *Z* iodovinyl sulfoxide **1f** and 1-hexyne, was submitted to epoxidation with KOO^{t}Bu and NaOO^{t}Bu. Both reagents rendered alkynyl epoxy sulfoxides **6a** and **6b** with good yield, complete regiocontrol and moderate stereoselectivity (25:75) (Scheme 2).[11–13]



Scheme 2.

3. Results and discussion

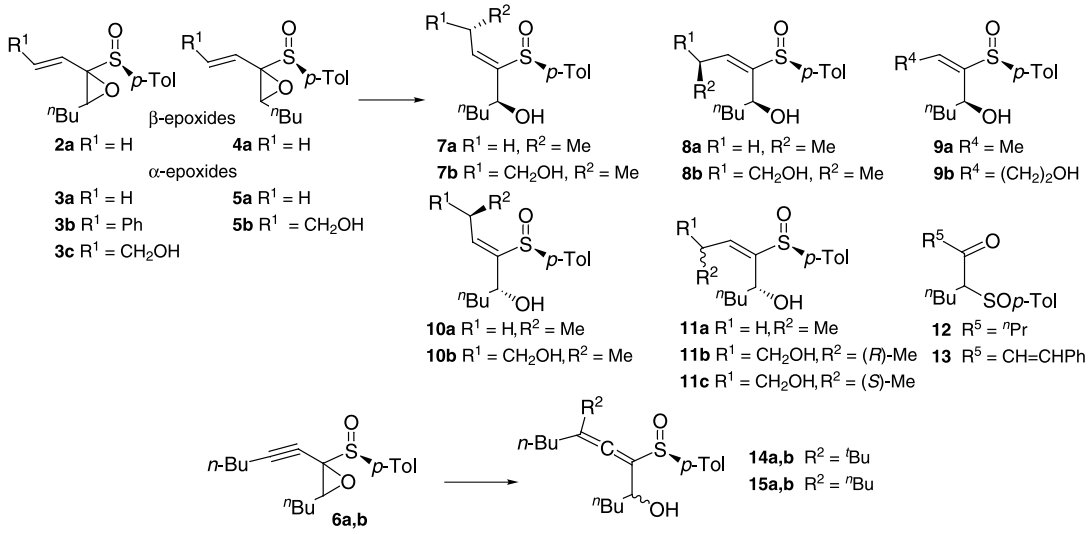
To establish the experimental conditions for the allylic displacement, we initially focused our efforts on β,trans-oxirane **2a** (Table 1). The lack of substituents at the double bond would preclude creation of new chiral centers but also simplify the analysis of the results. Treatment of **2a** with an excess of MeCuCNLi in Et_2O rendered a highly selective mixture of *Z* and *E* S_N2' displacement products **7a** and **8a** (95:2) along with a minor amount (3%) of **9a**. The structure of **9a** indicated that upon quenching, protonation instead of the slower reductive elimination was taking place at the S_N2'–Cu (III) intermediate. Indeed, shortening the reaction time [from 2 h 30 min (0 °C to rt) to 5 min (0 °C)] led to isolation of **9a** as the only product (entries 1 and 2).

The influence of the stereochemistry of the epoxide ring regarding the sulfoxide moiety was examined next.[13] However, we observed that upon treatment with MeCuCNLi α-oxirane **3a** gave a non-selective mixture of displacement products **10a** and **11a** along with 47% of ketone **12** presumably derived from S_N2 attack to the epoxide (see below). The presence of a phenyl group on the double bond, **3b** (R^1=Ph) increased the regioselectivity towards S_N2 attack affording exclusively ketone **13** upon using MeCuCNLi or BuCuCNLi as nucleophiles (entries 3–5). The formation of ketones **12** and **13** (Scheme 3) can be tentatively rationalized as an oxidative S_N2 addition of the cyanocopper reagent to give **K**. Rearrangement to a ketone, followed by migration of the sulfinyl group to the adjacent carbon and simultaneous loss of copper would lead to enone **L**. Then, in situ conjugate addition of excess of MeCuCNLi to **L**, followed by protonation of the enolate upon quenching would produce **12**. Alternatively, the presence of a phenyl ring attached to the enone would prevent the second conjugate addition affording **13**.

Interestingly, the low S_N2' reactivity of these α-epoxides can be partially overcome by placing a hydroxymethyl group at the double bond. Thus, the treatment of **3c** with MeCuCNLi afforded a moderately selective mixture of *Z* and *E* S_N2' compounds **10b**, **11b** and **11c** (70:26:4) (entry 6) although with a low conversion (50%).

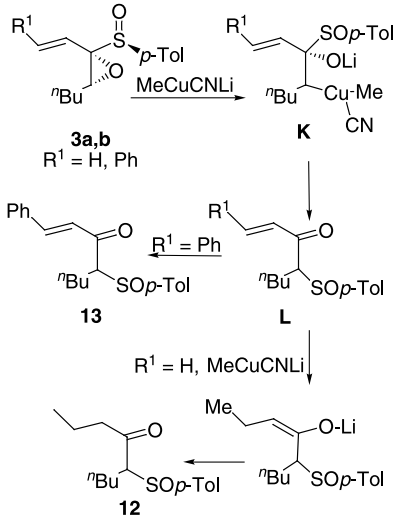
In contrast, *cis* epoxides **4** and **5** display a more selective behavior towards the S_N2' addition of cyanocuprates (entries 7–9) and we have obtained fairly selective mixtures of S_N2' products with high yields. In fact, β-epoxide **4a** underwent allylic displacement with MeCuCNLi affording a 14:86 mixture of **10a** and **11a**. Additionally, treatment of α-oxirane **5a** with MeCuCNLi afforded a remarkably selective mixture of *E* (**8a**) and *Z* (**7a**) displacement products (94:6), along with a small amount of reduction product **9a** (16%). However, sulfinyl epoxide **5b** did not

Table 1. S_N2' displacements between cyanocuprates and vinyl and alkynyl epoxy sulfoxides



Entry	Subs	Cuprate	Z-S_N2'[a]	E-S_N2'[a]	Reduction product[a]	S_N2[a]	Allene	Yield (%)[b]
1	**2a**	MeCuCNLi[c]	**7a** (95)	**8a** (2)	**9a** (3)	—	—	79
2[d]	**2a**	MeCuCNLi	—	—	**9a**	—		45
3	**3a**	MeCuCNLi	**10a** (29)	**11a** (24)	—	**12** (47)[e]		75
4	**3b**	MeCuCNLi	—	—	—	**13**[e]		76
5	**3b**	BuCuCNLi	—	—	—	**13**[e]		57
6[f]	**3c**	MeCuCNLi	**10b** (70)	**11b** (26) **11c** (4)	—	—		31
7	**5a**	MeCuCNLi	**7a** (5)	**8a** (79)	**9a** (16)	—		38
8[g]	**5b**	Me_2CuLi	**7b** (7)	**8b** (81)	**9b** (12)	—		52
9[h]	**4a**	MeCuCNLi	**10a** (14)	**11a** (86)				55
10[i]	**6a**,**b**	^{t}BuCuCNLi					**14a**,**b**	87
11[j]	**6a**,**b**	^{n}Bu$_2$CuLi					**15a**,**b**	64

[a] Ratios from ^{1}H NMR spectra of the crude mixtures shown in parentheses.
[b] Isolated yields for the major compound except for entries 3, 6, 10 and 11 where combined yields are given.
[c] All experiments were conducted in Et_2O.
[d] The mixture was quenched 5 min after addition of **2a**.
[e] As a 60:40 mixture of diastereomers.
[f] 50% of starting material was recovered.
[g] THF was used as solvent.
[h] 8% of starting material was recovered.
[i] **14** was obtained as a 39:61 mixture of diastereoisomers from a 59:41 mixture of **6a** and **6b**.
[j] **15** was obtained as a 37:63 mixture of diastereoisomers from a 34:66 mixture of **6a** and **6b**.

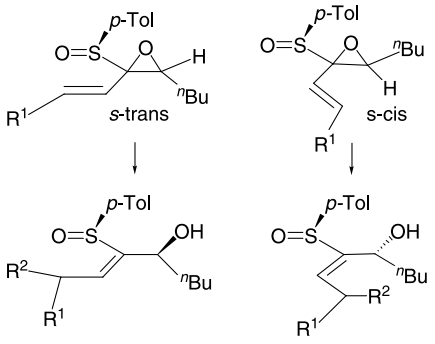


Scheme 3.

react with MeCuCNLi leading to starting material exclusively. At this point we explored different reaction conditions and found that **5b** behaved similarly to **5a** upon treatment with Gilman's cuprate (Me_2CuLi) affording a good selectivity of S_N2' products (**8b/7b**, 92:8) and a 12% of **9b**.

Finally, we briefly explored the reactivity of alkynyl epoxy sulfoxides **6a** and **6b** towards organocopper reagents (Table 1, entries 10 and 11). Addition of ^{t}BuCNCuLi to a 59:41 mixture of epoxides led to a diasteromeric mixture (39:61) of hydroxy allenyl sulfoxides **14a**,**b** with good yield (87%). Seeking to improve this result the addition of homocuprate, ^{n}Bu$_2$CuLi, was also carried out and a 37:63 mixture of allenes **15a**,**b** was obtained. These initial results outline the potential versatility of our methodology to produce highly functionalized enantiopure allenes.[14]

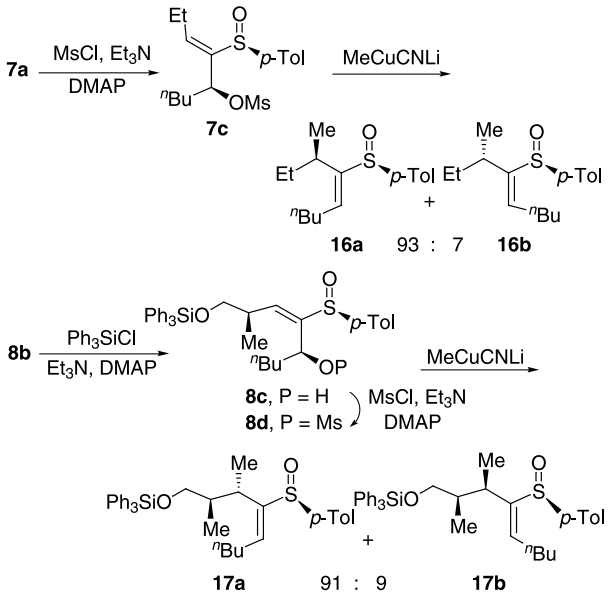
To understand the stereochemical outcome of the S_N2'



Scheme 4.

process we have considered that the major product from *cis* epoxides, [α-(**5a**,**b**) and β-(**4a**)], has an *E* stereochemistry (**8a**, **8b** and **11a**) and from *trans* epoxide [β-(**2a**) and α-(**3c**)] a *Z* vinyl sulfoxide was obtained (**7a**, **10b**). These results indicate that for *cis* and *trans* epoxides a different reactive conformation, *s-cis* or *s-trans*, is operative in these processes (Scheme 4). Indeed, for *trans* epoxides the arrangement of the butyl group would preclude the *s-cis* conformation leading to *Z* stereochemistry in the displacement products.[15] On the other hand, through an inspection of the NMR data of related vinyl sulfoxides, we have tentatively determined that addition of the cyanocuprate to vinyl epoxy sulfoxide **5b** occurs with *anti* stereochemistry for the major product **8b**.[16]

To extend the scope of our methodology we undertook the study of the second S_N2' displacement on allylic mesylates derived from **7a** and **8b**. This process would allow for the asymmetric construction of two adjacent chiral centers through two consecutive copper-mediated S_N2' displacements (Scheme 5). Therefore, α-hydroxy vinyl sulfoxide **7a** was reacted with mesyl chloride and Et_3N affording a good yield of **7c**, that upon treatment with MeCuCNLi gave a mixture of displacement products **16a**[17] and **16b** with high diastereoselectivity (93:7). Although the absence of substitution at the double bond of the precursor epoxy sulfoxide



Scheme 5.

(**2a**, R^1 = H, see scheme of Table 1) excluded the formation of two consecutive chiral centers, a high degree of diastereocontrol was observed for (*Z*)-α-mesyloxy vinyl sulfoxides **7a**. Thus, this result complements our previous studies of the S_N2' displacements of (*E*)-α-mesyloxy vinyl sulfoxides.

Subsequently, compound **8b** was selectively protected at the primary alcohol to give **8c** and then was mesylated at the secondary alcohol under standard conditions to render **8d**. The S_N2' addition of MeCuCNLi to allylic mesylate **8c** proceeds with high regio- and stereocontrol affording a 91:9 mixture of displacement products **17a** and **17b**. Tentative structural assignment of the products was based on an *anti* attack of the cuprate to the mesylate. Additionally, the comparison with the ^1H NMR data of related S_N2' compounds allowed to establish tentatively the structure of the new trisubstituted vinyl sulfoxides.[16,18]

In summary, we have demonstrated that S_N2' displacements of readily available vinyl epoxy sulfoxides using organocopper reagents as nucleophiles occur with high *anti* selectivity and a good degree of *E*/*Z* stereocontrol to produce enantiopure α-hydroxy vinyl sulfoxides in good yields. A subsequent allylic displacement on the related mesyloxy vinyl sulfoxides allows for the asymmetric construction of two adjacent chiral centers in the molecules. In addition, we have briefly explored the cuprate mediated S_N2' addition to alkynyl epoxy sulfoxides that leads to α-hydroxy allenyl sulfoxides in good yield. However, the future studies and applications of this methodology would require the development of alternative routes to alkynyl oxiranes.

4. Experimental

4.1. General

Reagents and solvents were handled by using standard syringe techniques. All reactions were carried out under an argon atmosphere. Hexane, toluene and CH_2Cl_2 were distilled from CaH_2, and THF and Et_2O from sodium. $(MeO)_2P(O)Me$, Et_3N, *i*-Pr_2NH, *i*-Pr_2EtN, *t*-$BuMe_2SiOTf$ were distilled from CaH_2. Crude products were purified by flash chromatography on Merck 230–400 mesh silica gel with distilled solvents. Analytical TLC was carried out on Merck (Kieselgel 60F-254) silica gel plates with detection by UV light, iodine, acidic vanillin solution, 10% phosphomolybdic acid solution in ethanol. All reagents were commercial products purchased from Aldrich, Acros, Fluka or Merck. Organolithium reagents were titrated prior to use by reacting with 3,4-dimethoxybenzaldehyde. NaH and KH (60% in mineral oil) were washed repeatedly with dry hexane and dried prior to use. Through this section, the volume of solvents is reported in mL/mmol of starting material. Infrared spectra (IR) were obtained on a Perkin–Elmer 681 and on a Perkin–Elmer Spectrum one. ^1H and ^{13}C NMR spectra were recorded on a Brüker AM-200 (200 MHz), Varian Gemini-200 (200 MHz), Varian INOVA-300 (300 MHz) and Varian INOVA-400 (400 MHz) using $CDCl_3$ as solvent and with the residual solvent signal as internal reference ($CDCl_3$, 7.24 and

77.0 ppm). The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), br (broad). Melting points were determined on a Reichert Kofler microscope and are uncorrected. Optical rotations were measured on a Perkin–Elmer 241 polarimeter at 20 °C using a sodium lamp and in $CHCl_3$ solution. Low resolution mass spectra were recorded by direct injection on a Hewlett–Packard 5973 MSD instrument using the electronic impact technique with an ionizacion energy of 70 eV or on a Hewlett–Packard 1100 MSD instrument using the atmospheric pressure chemical ionizacion (APCI) or electrospray (ES) chemical ionizacion techniques in its positive or negative modes. High resolution mass spectra (HRMS) were obtained on a VG-250-S spectrometer or on a Finnigan-4201 spectrometer. Elemental analyses were carried out on a Perkin–Elmer 240C and on a Heraus CHN-O-Rapid instruments at Instituto de Química Orgánica, CSIC (Madrid).

4.2. Preparation of starting materials

Vinyl epoxy sulfoxides **2a**, **3a-c**, **4a** and **5a**,**b** were prepared according to procedures previously reported by us.[10]

4.2.1. Synthesis of (±)-6-(*p*-tolylsulfinyl)-dodec-5-en-7-yne, 1g. To a solution of **1f**[17] (642 mg, 1.84 mmol) in benzene (18 mL) at room temperature was added CuI (105 mg, 0.552 mmol), DBU (1,8-diazabicyclo[5.4.0.]-undec-7-ene) (0.55 mL, 561 mg, 3.68 mmol), 1-hexyne (0.63 mL, 450 mg, 5.48 mmol) and $Pd(Ph_3P)_4$ (106 mg, 0.092 mmol). After 45 min the mixture was quenched with a saturated solution of NH_4Cl (5 mL/mmol) and H_2O (5 mL/mmol), and extracted with EtOAc (3×3 mL/mmol). The organic layer was washed with brine (2×4 mL/mmol) dried over anhydrous $MgSO_4$ and evaporated to afford a crude product that was purified by chromatography on silica gel (0–30% EtOAc–hexane). Pure **1g** was obtained (377 mg, 68%) as a yellow oil and was stored in benzene at −17 °C due to unstability of the samples

Data for **1g**. R_f=0.22 (20% EtOAc–hexane). ^{1}H NMR (200 MHz) δ 0.80 (t, 3H, J=7.1 Hz, Me *n*-Bu), 0.92 (t, 3H, J=7.1 Hz, Me *n*-Bu), 1.11–1.49 (m, 8H), 2.21 (t, 2H, J=6.8 Hz, H-9), 2.37 (s, 3H, Me *p*-Tol), 2.45–2.80 (m, 2H, H-4), 6.32 (dd, 1H, J=8.4, 7.7 Hz, H-5), 7.26 (d, 2H, J=7.9 Hz, ArH), 7.47 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.5 (Me *n*-Bu), 13.8 (Me *n*-Bu), 19.0, 21.4 (Me *p*-Tol), 21.7, 22.2, 28.7, 30.3, 31.2, 72.1 (C-7), 96.1 (C-8), 124.5 (2C *p*-Tol), 129.4 (2C *p*-Tol), 132.9, 139.9, 141.0, 145.2 (C-5). IR (film): 2965, 2940, 2300, 1595, 1485, 1460, 1445, 1075, 1050, 795 cm^{-1}. MS (APCI): 303 $[M+1]^+$ (100%).

4.2.2. Synthesis of (±)-(2*S*,3*R*,S_S)-3-*n*-butyl-2-(1′-hexynyl)-2-(*p*-tolylsulfinyl)oxirane, 6a and (±)-(2*R*,3*S*,S_S)-3-*n*-butyl-2-(1′-hexynyl)-2-(*p*-tolylsulfinyl)oxirane, 6b. From KH (24 mg, 0.60 mmol), *t*-BuOOH (75 μL, 54 mg, 0.60 mmol) in THF (3.0 mL) and a solution of **1g** (45 mg, 0.15 mmol) in 1.1 mL of THF, from −30 to −15 °C (35 min) following the method reported by us[10] was obtained a 25:75 mixture of **6a** and **6b**. Purification by chromatography on silica gel (0–60% EtOAc–CH_2Cl_2) yielded 43 mg (90%) of the mixture of epoxides as a yellow oil. Due to unstability of the samples rapid manipulation of the products and storage in benzene at −17 °C was necessary. A similar result was obtained from NaH (33 mg, 1.36 mmol) in 7.0 mL of THF, *t*-BuOOH (0.17 mL, 122 mg, 1.35 mmol) and a solution of **1g** (103 mg, 0.34 mmol) in 2.5 mL of THF at 0 °C (1 h 10 min). After chromatography (0–5% Et_2O–CH_2Cl_2) was isolated **6a** (14 mg, 13%), **6b** (31 mg, 29%) and a mixture of both epoxides (32 mg, 30%).

Data for **6a**. R_f=0.26 ($CHCl_3$). ^{1}H NMR (200 MHz) δ 0.82 (t, 3H, J=7.1 Hz, Me *n*-Bu), 0.94 (t, 3H, J=7.1 Hz, Me *n*-Bu), 1.17–1.65 (m, 8H), 1.95–2.19 (m, 4H), 2.40 (s, 3H, Me *p*-Tol), 3.48 (dd, 1H, J=6.8, 5.7 Hz, H-3), 7.30 (d, 2H, J=7.9 Hz, ArH), 7.57 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.5 (Me *n*-Bu), 13.9 (Me *n*-Bu), 18.6, 21.5 (Me *p*-Tol), 21.7, 22.4, 27.7, 28.3, 30.0, 67.5 (C-3), 70.1, 70.2, 92.0 (C-2′ alkyne), 125.2 (2C *p*-Tol), 129.3 (2C *p*-Tol), 136.8, 142.0. IR ($CHCl_3$): 3010, 2980, 2920, 2380, 1620, 1515, 1490, 1400, 1115, 830 cm^{-1}. MS (APCI): 319 $[M+1]^+$.

Data for **6b**. R_f=0.19 ($CHCl_3$). ^{1}H NMR (200 MHz) δ 0.82 (t, 3H, J=7.2 Hz, Me *n*-Bu), 0.93 (t, 3H, J=7.2 Hz, Me *n*-Bu), 1.15–1.59 (m, 8H), 1.90–2.02 (m, 2H), 2.13 (t, 2H, J=6.8 Hz, 2H-1′ *n*-Bu), 2.41 (s, 3H, Me *p*-Tol), 3.34 (m, 1H-3), 7.31 (d, 2H, J=7.9 Hz, ArH), 7.59 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.5 (Me *n*-Bu), 13.9 (Me *n*-Bu), 18.5, 21.5 (Me *p*-Tol), 21.7, 22.2, 27.7, 28.9, 29.9, 66.8 (C-3), 71.0, 71.8, 92.0 (C-2′ alkyne), 125.5 (2C *p*-Tol), 129.5 (2C *p*-Tol), 138.0, 142.3. MS (APCI): 319 $[M+1]^+$.

4.3. General procedure for the S_N2' displacement with cuprates

Argon was bubbled to a suspension of 3–6 equiv. of CuCN or CuI in Et_2O (10 mL×mmol) during 10 min (occasionally THF was employed as solvent). Then, the mixture was cooled to 0 °C and 3–6 equiv. of MeLi or *n*-BuLi was added. After 10 min stirring, 1 equiv. of sulfinyl oxirane in Et_2O (10 mL×mmol) was added dropwise and the yellow solution turned colorless. The reaction mixture was stirred at 0 °C for 30 min and then at room temperature (2–18 h) approximately turning from colorless to black. Then the reaction was quenched with a saturated solution of $Na_2S_2O_4$ (4 mL×mmol) and diluted with EtOAc (8 mL×mmol). The aqueous layer was extracted with EtOAc (3×10 mL×mmol) and the organic extracts were washed with brine (4 mL×mmol), dried over anhydrous $MgSO_4$ and evaporated under vacuum. Chromatography on silica gel using mixtures of EtOAc–hexane as eluent afforded pure displacement products. The ratio of isomers was measured by integration of well resolved peaks of the crude ^{1}H NMR spectra.

4.3.1. Synthesis of (−)-(5*S*,S_S)-(3*Z*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 7a, (−)-(5*S*,S_S)-(3*E*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 8a and (−)-(4*S*,S_S)-(2*E*)-3-(*p*-tolylsulfinyl)-oct-2-en-4-ol, 9a. From CuCN (60.5 mg, 0.675 mmol) in 6.7 mL of Et_2O, MeLi (0.42 mL, 1.6 M, 0.675 mmol) and **2a** (59.5 mg, 0.225 mmol) in 2.2 mL of Et_2O following the above procedure (2 h) was obtained a mixture of **7a**, **8a** and

9a (95:2:3). After chromatography (20–50% EtOAc–hexane) 50 mg (79%) of **7a** was isolated as a pale yellow oil. When the reaction was quenched after 5 min at 0 °C [CuCN (19 mg, 0.21 mmol), MeLi (0.15 mL, 1.4 M, 0.21 mmol), **2a** (11 mg, 0.04 mmol)] was obtained **9a** as a single product (4.9 mg, 45%).

Data for **7a**. R_f=0.14 (30% EtOAc–hexane). $[\alpha]_D^{20}$=−181.1 (c=1.03). ^{1}H NMR (300 MHz) δ 0.72 (t, 3H, J=6.6 Hz, Me), 0.95–1.20 (m, 4H, H-7, H-8), 1.14 (t, 3H, J=7.4 Hz, Me), 1.23–1.32 (m, 1H, H-6), 1.50–1.60 (m, 1H, H-6), 2.38 (s, 3H, Me *p*-Tol), 2.48 (m, 1H, H-2), 2.71 (m, 1H, H-2), 3.53 (d, 1H, J=2.3 Hz, OH), 4.28 (ap td, 1H, J=7.8, 2.2 Hz, H-5), 6.17 (dd, 1H, J=8.2, 7.0 Hz, H-3), 7.28 (d, 2H, J=8.2 Hz, ArH), 7.41 (d, 2H, J=8.3 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.7 (Me), 13.8 (Me), 21.2 (Me *p*-Tol), 22.1, 22.3, 27.5, 34.1 (C-2), 67.2 (C-5), 124.1 (2C *p*-Tol), 129.8 (2C *p*-Tol), 138.9 (2C), 140.9, 144.9. IR (film): 3400 (br), 2960, 2940, 2880, 1650, 1600, 1500, 1460, 1380, 1120, 1090, 1050, 1020, 810 cm^{-1}. MS (CI/CH_4): 282 $[M+2]^+$, 281 $[M+1]^+$ (100%), 263, 247, 139, 123. HRMS calcd for $C_{16}H_{25}O_2S$ $[M+1]^+$: 281.1575. Found: 281.1570.

Data for **9a**. R_f=0.10 (30% EtOAc–hexane). $[\alpha]_D^{20}$=−16.9 (c=0.80). ^{1}H NMR (500 MHz) δ 0.85 (t, 3H, J=6.7 Hz, Me *n*-Bu), 1.18–1.28 (m, 4H, H-6, H-7), 1.53–1.59 (m, 2H, H-5), 1.92 (d, 3H, J=7.2 Hz, H-1), 2.36 (s, 3H, Me *p*-Tol), 2.36–2.38 (m, 1H, OH), 4.42–4.45 (m, 1H, H-4), 6.37 (q, 1H, J=7.2 Hz, H-2), 7.25 (d, 2H, J=7.9 Hz, ArH), 7.47 (d, 2H, J=8.3 Hz, ArH). DNOE between Me vinyl/H-2: 9%; between Me vinyl/H-4: 3%; between H-2/Me vinyl: 3.3%; between H-2/ArH: 1.2%; between H-4/Me vinyl: 1.7%; between H-4/ArH: 1.1%. ^{13}C NMR (50 MHz) δ 13.8 (Me *n*-Bu), 14.5, 21.3, 22.2, 28.0, 36.6 (C-1), 68.8 (C-4), 125.3 (2C *p*-Tol), 129.8 (2C *p*-Tol), 131.9 (2C), 141.4, 147.6. IR (film): 3400 (br), 2980, 2970, 2940, 2870, 1600, 1500, 1460, 1380, 1120, 1090, 1050, 1020, 810 cm^{-1}. MS (CI/CH_4): 268, 267 $[M+1]^+$ (100%), 249, 233, 109. HRMS calcd for $C_{15}H_{23}O_2S$ $[M+1]^+$: 267.1419. Found: 267.1417. Anal. calcd for $C_{15}H_{22}O_2S$: C, 67.39;H, 8.20; S, 11.96. Found: C, 67.52;H, 8.05; S, 11.87.

4.3.2. Synthesis of (−)-(5*S*,*S*$_S$)-(3*E*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 8a. From CuCN (17.3 mg, 0.20 mmol) in 2 mL of Et_2O, MeLi (0.14 mL, 1.4 M, 0.20 mmol) and **5a** (17 mg, 0.064 mmol) in 0.6 mL of Et_2O following the above procedure (2 h) was obtained a mixture of **7a**, **8a** and **9a** (5:79:16). After chromatography (20–50% EtOAc–hexane) 7 mg (38%) of pure **8a** was isolated as a colorless oil.

Data for **8a**. R_f=0.13 (30% EtOAc–hexane). $[\alpha]_D^{20}$=−25.5 (c=0.64). ^{1}H NMR (200 MHz) δ 0.74 (t, 3H, J=7.0 Hz, Me), 1.08 (t, 3H, J=7.5 Hz, Me), 1.09–1.33 (m, 5H), 1.47–1.63 (m, 1H), 2.25–2.42 (m, 2H), 2.38 (s, 3H, Me *p*-Tol), 2.47 (d, 1H, J=5.3 Hz, OH), 4.42 (m, 1H, H-5), 6.28 (t, 1H, J=7.6 Hz, H-3), 7.27 (d, 2H, J=8.1 Hz, ArH), 7.49 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.5 (Me), 13.8 (Me), 21.3 (Me *p*-Tol), 22.1 (2C), 28.1, 37.0 (C-2), 68.9 (C-5), 125.3 (2C *p*-Tol), 129.8 (2C *p*-Tol), 138.6, 140.3, 141.4, 146.3. IR (film): 3400, 2980, 2960, 2940, 1600, 1490, 1460, 1380, 1090, 1040, 1010, 810 cm^{-1}. MS (CI/NH_3): 281 $[M+1]^+$, 265 (100%), 247, 233, 224, 195, 158, 141, 123, 108, 91, 81. HRMS calcd for $C_{16}H_{25}O_2S$ $[M+1]^+$: 281.1575. Found: 281.1562. Anal. calcd for $C_{16}H_{24}O_2S$: C, 68.53; H, 8.63; S, 11.43. Found: C, 68.74; H, 8.78; S, 11.18.

4.3.3. Synthesis of (+)-(5*R*,*S*$_S$)-(3*E*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 11a. From CuCN (20 mg, 0.22 mmol) in 2.2 mL of Et_2O, MeLi (0.16 mL, 1.4 M, 0.22 mmol) and **4a** (19.7 mg, 0.074 mmol) in 0.7 mL of Et_2O following the above procedure (2 h) was obtained a mixture of **4a**, **11a** and **10a** (8:79:13). After chromatography (20–50% EtOAc–hexane) 11.4 mg (55%) of pure **11a** was isolated as a colorless oil.

Data for **11a**. R_f=0.15 (30% EtOAc–hexane). $[\alpha]_D^{20}$=+23.2 (c=1.09). ^{1}H NMR (200 MHz) δ 0.77 (t, 3H, J=7.3 Hz, Me), 1.10 (t, 3H, J=7.5 Hz, Me), 1.11–1.64 (m, 6H, H-6, H-7, H-8), 2.33 (m, 2H, H-2), 2.38 (s, 3H, Me *p*-Tol), 2.53 (br s, 1H, OH), 4.53 (m, 1H, H-5), 6.43 (t, 1H, J=7.6 Hz, H-3), 7.28 (d, 2H, J=8.9 Hz, ArH), 7.52 (d, 2H, J=8.3 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.5 (Me), 13.8 (Me), 21.3 (Me *p*-Tol), 21.9, 22.3, 27.9, 36.6 (C-2), 70.2 (C-5), 125.0 (2C *p*-Tol), 129.8 (2C *p*-Tol), 139.3, 140.7, 141.2, 144.8. IR (film): 3400 (br), 2980, 2960, 2880, 1650, 1600, 1500, 1460, 1380, 1090, 1040, 810 cm^{-1}. MS (CI/NH_3): 292 $[M+NH_4]^+$, 281 $[M+1]^+$ (100%), 263, 247, 223, 195, 165, 140, 123. HRMS calcd for $C_{16}H_{25}O_2S$ $[M+1]^+$: 281.1575. Found: 282.1566.

Partial data for **10a** *from the mixture*. ^{1}H NMR (200 MHz): δ 4.35 (m, 1H, H-5), 6.21 (dd, 1H, J=8.2, 7.0 Hz, H-3).

4.3.4. Synthesis of (−)-(5*R*,*S*$_S$)-(3*Z*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 10a, and (+)-(5*R*,*S*$_S$)-(3*E*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 11a, and 5-(*p*-tolylsulfinyl)-non-4-one, 12. From CuCN (25 mg, 0.28 mmol) in 20.75 mL of Et_2O, MeLi (0.17 mL, 0.27 mmol) and **3a** (17 mg, 0.064 mmol) in 0.50 mL of Et_2O following the above procedure (2 h) was obtained a mixture of **10a**, **11a** and **12** (29:24:47). After chromatography (5–40% EtOAc–hexane) 3 mg (23%) of pure **10a**, 2 mg (16%) of pure **11a** and 9 mg (36%) of **12** as a 60:40 mixture of diastereoisomers was isolated. Data for isolated **11a** are the same as above.

Data for **10a**. R_f=0.18 (30% EtOAc–hexane). $[\alpha]_D^{20}$=−108.8 (c=1.25). ^{1}H NMR (300 MHz) δ 0.81 (t, 3H, J=7.1 Hz, Me *n*-Bu), 1.12 (t, 3H, J=7.4 Hz, Me Et), 1.10–1-38 (m, 4H, H-7, H-8), 1.52–1.61 (m, 2H, H-6), 2.24 (d, 1H, J=5.1 Hz, OH), 2.34–2.48 (m, 1H, H-2), 2.38 (s, 3H, Me *p*-Tol), 2.58–2.71 (m, 1H, H-2), 4.36 (ap q, 1H, J=6.5 Hz, H-5), 6.22 (dd, 1H, J=8.6, 6.8 Hz, H-3), 7.29 (d, 2H, J=8.1 Hz, ArH), 7.48 (d, 2H, J=8.3 Hz, ArH). IR (CCl_4): 3400 (br), 2960, 2930, 2860, 1740, 1640, 1600, 1495, 1460, 1380, 1260, 1080, 1030, 1015, 810 cm^{-1}. MS (EI): 281 (M+1), 263, 245, 223, 193, 149, 140 (100%), 139, 123, 111, 95, 92, 91, 81, 69, 57, 43, 41.

Partial data for **12** (*major isomer, from the mixture*). R_f=0.26 (30% EtOAc–hexane). ^{1}H NMR (300 MHz) δ 2.39 (s, 3H, Me *p*-Tol), 3.54 (dd, J=9.9, 4.9 Hz, H-5).

Partial data for **12** (*minor isomer, from the mixture*). R_f=0.26 (30% EtOAc–hexane). ^{1}H NMR (300 MHz) δ 2.40 (s, 3H, Me *p*-Tol), 3.67 (dd, J=9.6, 4.6 Hz, H-5).

4.3.5. Synthesis of (*E*)-1-phenyl-4-(*p*-tolylsulfinyl)-1-en-3-octanone, 13. From CuCN (16 mg, 0.18 mmol) in 0.4 mL of Et_2O, MeLi (0.11 mL, 0.18 mmol) and **3b** (10 mg, 0.03 mmol) in 0.3 mL of Et_2O following the above procedure (18 h) was obtained after chromatography (5–30% EtOAc–hexane) 8 mg (76%) of **13** as a 60:40 inseparable mixture of diastereomers. Alternatively, using *n*-BuLi (0.16 mL, 0.18 mmol) instead of MeLi and following the same procedure (5 h) was obtained after chromatography (5–30% EtOAc–hexane) 6 mg (57%) of **13** as a 60:40 mixture of diastereomers.

Data for **13** (*major, from the mixture*). R_f=0.37 (30% EtOAc–hexane). ^{1}H NMR (300 MHz) δ 0.86 (m, 3H, Me *n*-Bu), 1.31 (m, 2H), 1.52–1.60 (m, 2H), 2.05–2.13 (m, 2H), 2.26 (s, 3H, Me *p*-Tol), 3.97 (dd, 1H, J=9.9, 4.5 Hz, H-4), 6.49 (d, 1H, J=16.9 Hz, H-2), 7.16–7.49 (m, 10H, Ph, *p*-Tol and H-1). IR (CCl_4, mixture of isomers): 2960, 2930, 2860, 1680, 1650, 1610, 1580, 1495, 1450, 1345, 1080, 1050, 990, 975 cm^{-1}.

Data for **13** (*minor, from the mixture*). R_f=0.37 (30% EtOAc–hexane). ^{1}H NMR (300 MHz) δ 0.86 (m, 3H, Me *n*-Bu), 1.31 (m, 2H), 1.93–1.96 (m, 2H), 2.28–2.40 (m, 2H), 2.32 (s, 3H, Me *p*-Tol), 3.81 (dd, 1H, J=8.3, 6.2 Hz, H-4), 6.73 (d, 1H, J=16.0 Hz, H-2), 7.16–7.49 (m, 10H, Ph, *p*-Tol and H-1).

4.3.6. Synthesis of (−)-(2*S*,5*R*,S_S)-(3*Z*)-2-methyl-4-(*p*-tolylsulfinyl)-non-3-en-1,5-diol, 10b and (2*S*,5*R*,S_S)-(3*E*)-2-methyl-4-(*p*-tolylsulfinyl)-non-3-en-1,5-diol, 11b. From CuCN (27 mg, 0.30 mmol) in 0.75 mL of Et_2O, MeLi (0.18 mL, 0.29 mmol) and **3b** (14 mg, 0.05 mmol) in 0.5 mL of Et_2O following the above procedure (4 h) was obtained a mixture of **10b**, **11b**, and **11c** (70:26:4). After chromatography (20–100% EtOAc–hexane) was isolated 16 mg (22%) of **10b** and 7 mg (9%) of **11b** as colorless oils.

Data for **10b**. R_f=0.27 (75% EtOAc–hexane). $[\alpha]_D^{20}$=−23.6 (c=0.36). ^{1}H NMR (300 MHz) δ 0.84 (t, 3H, J=7.0 Hz, Me *n*-Bu), 1.03 (d, 3H, J=6.4 Hz, Me), 1.15–1.39 (m, 4H), 1.56–1.67 (m, 2H), 2.03 (br s, 1H, OH), 2.16 (br s, 1H, OH), 2.38 (s, 3H, Me *p*-Tol), 3.37–3.48 (m, 2H, H-1), 3.69 (m, 1H, H-2), 4.30 (t, 1H, J=6.6 Hz, H-5), 6.07 (d, 1H, J=10.3 Hz, H-3), 7.28 (d, 2H, J=8.0 Hz, ArH), 7.64 (d, 2H, J=8.3 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.9 (Me), 16.7 (Me), 21.2 (Me *p*-Tol), 22.4, 27.8, 35.8, 37.3, 67.1, 69.8, 124.9, 126.6 (2C *p*-Tol), 129.9 (2C *p*-Tol), 142.1, 147.5, 147.9. MS (EI): 293, 259, 253, 223, 205, 177, 169, 153, 140, 139, 97, 95, 92, 69, 57, 43 (100%).

Data for **11b**. R_f=0.24 (75% EtOAc–hexane). ^{1}H NMR (300 MHz) δ 0.79 (t, 3H, J=6.6 Hz Me *n*-Bu), 0.90 (d, 3H, J=6.8 Hz, Me), 1.09–1.36 (m, 4H), 1.61–1.80 (m, 2H), 2.07 (br s, 1H, OH), 2.33 (br s, 1H, OH), 2.40 (s, 3H, Me *p*-Tol), 3.16–3.37 (m, 2H, H-1), 3.40–3.69 (m, 1H, H-2), 4.19 (dd, 1H, J=9.3, 3.5 Hz, H-5), 6.24 (d, 1H, J=10.7 Hz, H-3), 7.26–7.57 (m, 4H, ArH).

Partial data of **11c** (*from the mixture*). R_f=0.24 (75% EtOAc–hexane). ^{1}H NMR (300 MHz) δ 4.58 (m, 1H, H-5), 6.36 (d, 1H, J=10.5 Hz, H-5).

4.3.7. Synthesis of (+)-(2*R*,5*S*,S_S)-(3*E*)-2-methyl-4-(*p*-tolylsulfinyl)-non-3-en-1,5-diol, 8b, (2*S*,5*S*,S_S)-(3*Z*)-2-methyl-4-(*p*-tolylsulfinyl)-non-3-en-1,5-diol, 7b and (5*S*,S_S)-(3*E*)-4-(*p*-tolylsulfinyl)-non-3-en-1,5-diol, 9b. From CuI (288 mg, 1.51 mmol) in 3.75 mL of THF, MeLi (1.86 mL, 2.98 mmol) and **5b** (73 mg, 0.25 mmol) in 2.5 mL of THF following the above procedure (18 h) was obtained a mixture of **8b**, **7b**, and **9b** (81:7:12). After chromatography (20–100% EtOAc–hexane) was isolated 40 mg (52%) of **8b**, 3 mg (4%) of **7b** and 6 mg (8%) of **9b** as colorless oils.

Data for **8b**. R_f=0.09 (EtOAc). $[\alpha]_D^{20}$=+84.6 (c=2.0). ^{1}H NMR (300 MHz) δ 0.73 (t, 3H, J=7.0 Hz, Me *n*-Bu), 1.03 (d, 3H, J=6.7 Hz, Me), 1.05–1.66 (m, 6H, H-6, H-7, H-8), 2.38 (s, 3H, Me *p*-Tol), 2.93–3.00 (m, 1H, H-2), 3.22 (br s, 1H, OH), 3.45 (dd, 1H, J=10.4, 8.8 Hz, H-1), 3.62 (dd, 1H, J=10.6, 5.0 Hz, H-1), 4.56 (dd, 1H, J=8.9, 4.7 Hz, H-5), 6.15 (d, 1H, J=10.6 Hz, H-3), 7.26 (d, 2H, J=8.1 Hz, ArH), 7.52 (d, 2H, J=8.2 Hz, ArH). DNOE between H-2/Me: 3.5%; between H-2/H-5: 5.9%; between Me/H-2: 1.7%; between Me/H-3: 1.3%; between H-5/H-2: 8.0%; between H-5/Me: 2.7%. ^{13}C NMR (50 MHz) δ 13.7 (Me), 16.3 (Me), 21.4 (Me *p*-Tol), 22.2, 27.9, 35.6, 36.0, 66.8, 68.5, 126.1, 128.3 (2C *p*-Tol), 129.8 (2C *p*-Tol), 141.9, 147.9, 148.6. IR ($CHCl_3$): 3400 (br), 2960, 2930, 2870, 1600, 1395, 1460, 1380, 1305, 1215, 1080, 1030, 1010, 790, 760 cm^{-1}. MS (EI): 293, 253, 171, 153, 140, 139, 97, 95, 92, 71, 57, 55, 41 (100%).

Partial data for **7b**. R_f=0.12 (EtOAc). ^{1}H NMR (300 MHz) δ 1.11 (d, 3H, J=6.5 Hz, Me), 2.38 (s, 3H, Me *p*-Tol), 3.52 (m, 1H, H-2), 3.71 (dd, 1H, J=10.1, 5.1 Hz, H-1), 4.01 (dd, 1H, J=12.3, 4.8 Hz, H-1), 4.26 (dd, 1H, J=8.0, 5.7 Hz, H-5), 6.05 (d, 1H, J=10.1 Hz, H-3), 7.22–7.60 (m, 4H, ArH).

Partial data for **9b**. R_f=0.05 (EtOAc). ^{1}H NMR (200 MHz) δ 0.66 (t, 3H, J=7.0 Hz, Me *n*-Bu), 2.37 (s, 3H, Me *p*-Tol), 3.81 (t, 2H, J=5.6 Hz, H-1), 4.41 (dd, 1H, J=8.9, 4.4 Hz, H-5), 6.51 (t, 1H, J=7.4 Hz, H-3), 7.26 (d, 2H, J=8.0 Hz, ArH), 7.48 (d, 2H, J=8.2 Hz, ArH).

4.3.8. Synthesis of (±)-(5*R*,7*R*,S_S)-8-*tert*-butyl-6-(*p*-tolylsulfinyl)-dodeca-6,7-dien-5-ol, 14a and (±)-(5*S*,7*S*,S_S)-8-*tert*-butyl-6-(*p*-tolylsulfinyl)-dodeca-6,7-dien-5-ol, 14b. From CuCN (29 mg, 0.32 mmol) in 2.6 mL of THF, *t*-BuLi (1.5 M, 0.21 mL, 0.31 mmol) and a mixture of sulfinyl oxiranes **6a** and **6b** 41:59 (25 mg, 0.79 mmol) in 0.4 mL of THF following the above procedure (5 min at −78 °C and 30 min at rt) was obtained a mixture of **14a** and **14b** (39:61). After chromatography (0–30% EtOAc–CH_2Cl_2) was isolated 26 mg (87%) of the mixture of allenes as a colorless oil. Pure compounds were isolated by preparative TLC (3% MeOH–toluene).

Data for **14a**. R_f=0.13 (3% MeOH–toluene). ^{1}H NMR (300 MHz) δ 0.77 (t, 3H, J=6.9 Hz, Me *n*-Bu), 0.88 (t, 3H, J=7.2 Hz, Me *n*-Bu), 1.14 (s, 9H, 3Me *t*-Bu), 1.05–1.47 (m, 10H), 2.03 (t, 2H, J=7.9 Hz), 2.40 (s, 3H, Me *p*-Tol), 3.75 (br s, 1H, OH), 4.30 (dd, 1H, J=7.3, 5.9 Hz, H-5), 7.30 (d, 2H, J=7.9 Hz, ArH), 7.53 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.9 (Me *n*-Bu), 14.0 (Me *n*-Bu), 21.4

(Me *p*-Tol), 22.4, 22.7, 27.4, 27.6, 29.2 (3Me *t*-Bu), 30.8, 34.9, 35.0, 68.6 (C-5), 124.4, 124.6 (2C *p*-Tol), 125.4, 129.7 (2C *p*-Tol), 139.6, 141.4, 197.9 (C-7). IR ($CHCl_3$): 3370, 2960, 2884, 1930, 1585, 1483, 1460, 1230, 1021, 799 cm^{-1}. MS (ES): 775 $[2M+Na]^+$, 399 $[M+Na]^+$ (100%), 377 $[M+1]^+$.

Data for **14b**. R_f=0.09 (3% MeOH–toluene). ^1H NMR (300 MHz) δ 0.89 (s, 9H, 3Me *t*-Bu), 0.84–0.92 (m, 6H, 2Me *n*-Bu), 1.22–1.39 (m, 8H), 1.46–1.66 (m, 2H), 1.88–2.15 (m, 2H), 2.40 (s, 3H, Me *p*-Tol), 2.75 (br s, 1H, OH), 4.52 (br t, 1H, J=6.4 Hz, H-5), 7.28 (d, 2H, J=7.8 Hz, ArH), 7.55 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 13.9 (Me *n*-Bu), 14.0 (Me *n*-Bu), 21.4 (Me *p*-Tol), 22.5, 22.7, 27.5, 27.8, 28.9 (3Me *t*-Bu), 30.4, 34.7, 35.9, 69.1 (C-5), 117.9, 125.4 (2C *p*-Tol), 125.8, 129.6 (2C *p*-Tol), 140.4, 141.6, 195.7 (C-7). IR ($CHCl_3$): 3380, 2998, 2977, 2890, 1935, 1594, 1496, 1472, 1240, 1087, 1038, 812 cm^{-1}.

4.3.9. Synthesis of (±)-(5*R*,S_S)-8-*n*-butyl-6-(*p*-tolylsulfinyl)-dodeca-6,7-dien-5-ol, 15a and (±)-(5*S*,S_S)-8-*n*-butyl-6-(*p*-tolylsulfinyl)-dodeca-6,7-dien-5-ol, 15b. From CuI (57 mg, 0.30 mmol) in 3.0 mL of THF, *n*-BuLi (1.6 M, 0.37 mL, 0.59 mmol) and a mixture of sulfinyl oxiranes **6a** and **6b** 34:66 (19 mg, 0.060 mmol) in 0.6 mL of THF following the above procedure (2 h from −30 °C to rt) was obtained a mixture of **15a** and **15b** (37:63). After chromatography (0–25% EtOAc–CH_2Cl_2) was isolated 14 mg (64%) of the mixture of allenes as a colorless oil.

Data for **15a** (*from the mixture*). ^1H NMR (200 MHz) δ 0.75–0.95 (m, 9H), 1.09–1.70 (m, 12H), 1.83–2.30 (m, 6H), 2.40 (s, 3H, Me *p*-Tol), 3.79 (br s, 1H, OH), 4.27 (t, 1H, J=6.1 Hz, H-5), 7.29 (d, 2H, J=7.9 Hz, ArH), 7.49 (d, 2H, J=8.4 Hz, ArH).

Data for **15b** (*from the mixture*). ^1H NMR (200 MHz) δ 0.75–0.95 (m, 9H), 1.09–1.70 (m, 12H), 1.83–2.30 (m, 6H), 2.38 (s, 3H, Me *p*-Tol), 2.75 (br s, 1H, OH), 4.48 (t, 1H, J=6.1 Hz, H-5), 7.27 (d, 2H, J=7.9 Hz, ArH), 7.53 (d, 2H, J=8.4 Hz, ArH).

4.3.10. Synthesis of the mesylate of (−)-(5*S*,S_S)-(3*Z*)-4-(*p*-tolylsulfinyl)-non-3-en-5-ol, 7c. To a cold solution (0 °C) of **7a** (55 mg, 0.17 mmol) in 3.5 mL of THF was added 3 equiv. of Et_3N (73.3 mL, 53 mg, 0.52 mmol), 3 equiv. of MsCl (40 mL, 59.5 mg, 0.52 mmol) and the mixture was stirred for 1 h. After that time, a saturated solution of $NaHCO_3$ (5 mL) and EtOAc (5 mL) was added to the reaction mixture. The organic layer was washed with a saturated solution of NH_4Cl, dried over $MgSO_4$ and evaporated under vacuum. After chromatography on deactivated silica gel (washed with a 5% solution of $NaHCO_3$ in MeOH and dried) and using as solvent 20–50% EtOAc–hexane was obtained 67.0 mg (95%) of **7c** as a yellow oil.

Data for **7c**. R_f=0.32 (30% EtOAc–hexane). ^1H NMR (200 MHz) δ 0.58 (t, 3H, J=6.5 Hz, Me), 0.70–1.50 (m, 6H), 1.16 (t, 3H, J=7.4 Hz, Me), 2.37 (s, 3H, Me *p*-Tol), 2.58 (m, 1H), 2.76 (m, 1H), 3.07 (s, 3H, Me Ms), 5.07 (dd, 1H, J=9.2, 4.3 Hz, H-5), 6.41 (dd, 1H, J=8.6, 7.1 Hz, H-3), 7.28 (d, 2H, J=8.4 Hz, ArH), 7.38 (d, 2H, J=8.3 Hz, ArH).

4.3.11. Synthesis of (+)-(3*R*,S_S)-(4*E*)-3-methyl-4-(*p*-tolylsulfinyl)-non-4-ene, 16a. From CuCN (52 mg, 0.58 mmol) in 5.8 mL of THF, MeLi (0.36 mL, 1.6 M, 0.58 mmol) and mesylate **7c** (67 mg, 0.19 mmol) in 2 mL of THF following the above procedure (1 h at −78 °C) was obtained a mixture of **16a** and **16b** (93:7). After chromatography (20–50% EtOAc–hexane) was isolated 35 mg (71% from **7a**) of **16a** as a colorless oil.

Data for **16a**. R_f=0.39 (30% EtOAc–hexane). $[\alpha]_D^{20}$=+29.8 (c=3.12). ^1H NMR (200 MHz) δ 0.71 (d, 3H, J=7.3 Hz, Me), 0.73 (t, 3H, J=7.0 Hz, Me), 0.90 (t, 3H, J=6.9 Hz, Me), 1.22–1.50 (m, 6H), 2.20–2.32 (m, 3H), 2.36 (s, 3H, Me *p*-Tol), 6.35 (t, 1H, J=7.6 Hz, H-5), 7.22 (d, 2H, J=8.8 Hz, ArH), 7.46 (d, 2H, J=8.2 Hz, ArH). ^{13}C NMR (50 MHz) δ 12.3 (Me), 13.9 (Me), 19.8 (Me), 21.4 (Me *p*-Tol), 22.5, 28.5, 29.7, 31.3, 33.0, 125.5 (2C, *p*-Tol), 129.5 (2C, *p*-Tol), 135.0, 140.6, 141.1, 148.4. IR (film): 3060, 2980, 2940, 2880, 1600, 1490, 1460, 1400, 1380, 1305, 1290, 1180, 1150, 1090, 1050, 1020, 920, 910, 810 cm^{-1}. MS (CI/CH_4): 282, 281 $[M+1]^+$ (100%), 263, 247, 139, 123. HRMS calcd for $C_{17}H_{27}OS$ $[M+1]^+$: 281.1575. Found: 281.1570. Anal Calcd for $C_{17}H_{26}OS$: C, 72.60; H, 9.21; S, 11.34. Found: C, 72.89; H, 9.15; S, 11.24.

4.3.12. Synthesis of (2*R*,5*S*,S_S)-(3*E*)-2-methyl-4-(*p*-tolylsulfinyl)-1-triphenylsilyloxy-non-3-en-5-ol, 8c. To a cold (0 °C) solution of **8b** (25 mg, 0.08 mmol) in 1 mL of anhydrous CH_2Cl_2 was added 3.0 equiv. of Et_3N (34 μL, 24 mg, 0.24 mmol), a catalytic amount of DMAP and 1.2 equiv. of Ph_3SiCl (28.5 mg, 0.10 mmol). The mixture was stirred at rt until starting material disappearance (1H, TLC) and then was quenched with 5% solution of $NaHCO_3$ (4 mL/mmol) and diluted with EtOAc (10 mL/mmol). The aqueous layer was washed with EtOAc (3×10 mL/mmol) and the organic extracts were washed with brine, dried over anhydrous $MgSO_4$ and evaporated under vacuum. Chromatography of the crude (10–50% EtOAc–hexane) afforded 26 mg (57%) of **8c** as a colorless oil.

Data for **8c**. R_f=0.18 (30% EtOAc–hexane). ^1H NMR (300 MHz) δ 0.69 (t, 3H, J=7.0 Hz, Me *n*-Bu), 1.00–1.06 (m, 4H), 1.05 (d, 3H, J=6.7 Hz, Me), 1.20–1.60 (m, 2H, H-6), 2.31 (s, 3H, Me *p*-Tol), 2.41 (br s, 1H, OH), 3.01–3.11 (m, 1H, H-2), 3.66 (dd, 1H, J=9.8, 7.7 Hz, H-1), 3.75 (dd, 1H, J=9.8, 5.4 Hz, H-1), 4.39 (m, 1H, H-5), 6.20 (d, 1H, J=10.6 Hz, H-3), 7.08 (d, 2H, J=8.1 Hz, ArH), 7.34–7.57 (m, 17H, ArH).

4.3.13. Synthesis of the mesylate of (2*R*,5*S*,S_S)-(3*E*)-2-methyl-4-(*p*-tolylsulfinyl)-1-triphenylsilyloxy-non-3-en-5-ol, 8d. From **8c** (22 mg, 0.04 mmol), Et_3N (22 μL, 16 mg, 0.15 mmol), MsCl (9 μL, 13 mg, 0.12 mmol) and DMAP in THF following the procedured described for **7c** was obtained after chromatography (5–40% EtOAc–hexane) 16 mg (64%) of **8d** as a colorless oil.

Data for **8d**. R_f=0.20 (30% EtOAc–hexane). ^1H NMR (300 MHz) δ 0.59 (t, 3H, J=7.1 Hz, Me *n*-Bu), 0.72–0.97 (m, 4H), 1.05 (d, 3H, J=6.6 Hz, Me), 1.15–1.30 (m, 1H,

H-6), 1.66–1.80 (m, 1H, H-6), 2.35 (s, 3H, Me *p*-Tol), 2.95 (s, 3H, Me Ms), 3.08–3.18 (m, 1H, H-2), 3.68 (dd, 1H, $J=$ 9.8, 8.2 Hz, H-1), 3.80 (dd, 1H, $J=9.8$, 4.8 Hz, H-1), 5.06 (dd, 1H, $J=10.4$, 3.4 Hz, H-5), 6.50 (d, 1H, $J=11.1$ Hz, H-3), 7.11 (d, 2H, $J=8.1$ Hz, ArH), 7.35–7.58 (m, 17H, ArH).

4.3.14. Synthesis of (2*R*,3*S*,S_S)-(4*E*)-2,3-dimethyl-4-(*p*-tolylsulfinyl)-1-triphenylsilyloxy-non-4-ene, 17a. From CuCN (13.6 mg, 0.15 mmol) in 0.5 mL of THF, MeLi (93 mL, 0.15 mmol) and mesylate **8d** (12 mg, 0.02 mmol) in 0.5 mL of THF following the above procedure (40 h at rt) was obtained a mixture of **17a** and **17b** (91:9) along with a 45% of starting material. After chromatography (5–40% EtOAc–hexane) was isolated 8 mg (76%) of **17a** as a colorless oil.

Data for **17a**. $R_f=0.27$ (30% EtOAc–hexane). $[\alpha]_D^{20}=+56.1$ ($c=0.18$). ^{1}H NMR (400 MHz) δ 0.66 (d, 3H, $J=$ 6.9 Hz, Me-2), 0.79 (d, 3H, $J=7.2$ Hz, Me-3), 0.90 (t, 3H, $J=7.2$ Hz, Me *n*-Bu), 1.22–2.24 (m, 8H, H-2, H-3, H-6, H-7, H-8), 2.36 (s, 3H, Me *p*-Tol), 3.61 (dd, 1H, $J=10.1$, 5.1 Hz, H-1), 3.71 (dd, 1H, $J=10.1$, 3.2 Hz, H-1), 6.36 (t, 1H, $J=7.6$ Hz, H-5), 7.17 (d, 2H, $J=8.0$ Hz, ArH), 7.34–7.57 (m, 17H, ArH). IR (film): 3065, 2961, 2920, 2855, 1454, 1428, 1261, 1216, 1116, 807, 758, 700 cm^{-1}. MS (ES): 1155 $[2M+Na]^+$, 589 $[M+Na]^+$ (100%), 567 $[M+1]^+$.

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11. The stereochemical assignment of diastereomers **6a** and **6b** is tentative since extensive decomposition upon storage at room temperature along with the low stereoselectivity found, could indicate a favourable [2,3]-sigmatropic rearrangement of the propargylic sulfoxides with loss of the stereochemical integrity at sulfur.

12. Sonogashira coupling followed by nucleophilic epoxidation of related (*E*)-1-iodo styryl sulfoxide led to an equimolecular

mixture of unstable alkynyl epoxides therefore we did not examine the S_N2' reactivity of these substrates.

13. Arbitrarily, we termed epoxides β (up) or α (down) regarding the plane of paper.
14. These results seems to indicate a higly stereocontrolled pathway of the allylic displacement. The structural assignment of **14a**,**b** was made on the basis of an *anti* attack, however, we cannot accurately establish the stereochemical outcome since the structural assignment for **6a**,**b** is tentative, see Ref. 11.
15. Structural assignments of the products are based in the comparison of NMR data with that of related hydroxy vinyl sulfoxides from our group previously characterized by X-ray diffraction analysis. The *Z*–*E* stereochemistry is easily established through the chemical shifts of vinyl protons. For example **7a** (H-3): 6.17 ppm; **11a** (H-3): 6.43 ppm. Significant differences are also found for H-2 protons in these compounds.
16. Additional data (i.e., X-ray) will be needed for unequivocal structural assignment of this compound.
17. Spectral data (^{1}H and ^{13}C NMR) of **16a** are almost identical to that encountered for (*E*)-5(*R*)-methyl-4(R_s)-(*p*-tolylsulfinyl) non-3-ene (compd. **8b** in Ref. 3a). As we have previously observed the newly introduced methyl group appears more shielded (0.71 ppm) for that relative stereochemistry.
18. The chemical shifts of vinylic protons usually appear downfield for the *E* double bond (6.35–6.36). Some similarities can be observed for the newly introduced methyl group with the same relative stereochemistry regarding the sulfoxide.
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