Synthesis of Enantiomerically Pure Allenes with Central and Axial Chirality Mediated by a Remote Sulfinyl Group

José Luis García Ruano,* Vanesa Marcos, José Alemán*

Departamento de Química Orgánica (C-I), Universidad Autónoma de Madrid, Cantoblanco, 28049 Madrid, Spain
Fax +34(914)973966; E-mail: joseluis.garcia.ruano@uam.es; E-mail: jose.aleman@uam.es

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Abstract: Enantiomerically pure 2-(*p*-tolylsulfinyl)benzylcopper reagents react with propargyl bromides and mesylates, affording enantiomerically pure allenes with central and axial chirality. Both regioselectivity (S_N2' processes) and configuration at the chiral axis are completely controlled by the sulfinyl group. The stereoselectivity at the benzylic position is very high. Complete kinetic resolution and moderate dynamic resolution of racemic propargylic mesylates can be achieved. This stereochemical behavior can be explained by assuming the stabilization of the benzylcopper by the sulfinyl oxygen and the association of the triple bond to the metal as a previous step of the intramolecular S_N2' nucleophilic attack.

Key words: allenes, sulfinyl group, axial chirality, central chirality, asymmetric synthesis

In 2000, we reported the first highly stereoselective reactions of lithium 2-(*p*-tolylsulfinyl)benzyl carbanions with different electrophiles (Scheme 1),[1] which demonstrated the ability of the remote sulfinyl group in controlling the configuration of a benzylic chiral center. Thus, in reactions with prochiral carbonyl groups (two chiral centers are formed in the same step), the control of the sulfinyl group on the new hydroxylic chiral center was also significant and became complete when the electrophile also contained a chiral auxiliary in a double induction process. A similar behavior was observed in reactions of lithium 2-(*p*-tolylsulfinyl)benzyl carbanions with imines. The reactions of enantiomerically pure *N*-sulfinylimines with benzyl carbanions containing carbon,[2] oxygen,[3] and sulfur[4] as benzylic substituents evolved in a completely stereoselective way, only yielding one diastereomer in a double-induction process (Scheme 1). However, a mixture of epimers at the nitrogenated carbon was obtained in reactions with *N*-arylimines, without a second chiral auxiliary, in a single induction process.[5] However, in the latter reactions the strong influence of electronic factors on the stereoselectivity was evident, which was quite important in the proposal of a stereochemical model. After removal of the sulfinyl group, these reactions provided one of the best reported methods for obtaining enantiomerically pure *anti*- and *syn*-1,2-disubstituted propylamines. This methodology has been applied to the synthesis of enantiomerically pure piperidines and pyrrolidines,[6] fluoroindolines,[7] β-fluoroamino acids,[8] epoxides,[9] and aziridines[10] (Scheme 1).

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Despite these good results, all attempts at conjugated addition of the lithium benzyl carbanions to deactivated double bonds were unsuccessful and only 1,2-addition products were usually observed. Similar behavior was found in reactions with propargylic halides, which only afforded the S_N2 products (instead of allenes resulting in a S_N2' process). Therefore, it prompted us to evaluate the behavior of their corresponding copper reagents. In this paper, we will describe in detail the results obtained by reaction of propargyl derivatives with copper 2-(*p*-tolylsulfinyl)benzyl carbanions[11] and the mechanistic proposal for explaining these results.

These reactions are interesting because of the importance of allenes, which are a class of unique compounds exhibiting axial chirality and that are present in a large number of medicinal and natural products.[12] Despite the large number of methods for preparing allenes,[13] the number of references allowing their preparation in enantiomerically pure form is rather low. One of the most often used methods for achieving this goal involves the S_N2' reaction of an organocopper reagent with an enantiomerically pure propargylic derivative[14] (Scheme 2, equation 1). As the main limitation of this methodology is the availability of the enantiomerically pure propargylic alcohols,[15] the search for organocopper reagents able to kinetic resolve racemic propargylic derivatives remains a highly desirable challenge.

By assuming that the efficiency of this resolution would be higher when the chiral elements at substrate and reagent, involved in the asymmetric induction, are close in proximity, the use of enantiomerically pure organocopper reagents with a chiral center directly joined to the metal should presumably provide the best results. Thus, we reasoned that organocopper reagents, obtained by transmetalation of our lithium 2-(*p*-tolylsulfinyl)benzyl carbanions, could be appropriated because they would generate allenes bearing a chiral carbon directly connected to the allenic system and exhibiting axial chirality (Scheme 2, equation 2[16]).

We first performed studies to find the optimal conditions for the transmetalation. Reactions of sulfoxide **1a** with propargyl bromide (**2a**) were used as the control experiment. Lithium carbanion [Li]-**1a** only gave the terminal alkyne **3a** (90% yield) as the result of an S_N2 process (Scheme 3). As we presumed that the copper carbanion [Cu]-**1a** would yield the allene **4a**, as the result of a S_N2' process, the observed regioisomeric ratio **3a**/**4a** obtained by treating [Li]-**1a** with different copper sources before

reacting with **2a** could be used as a criterion to gain knowledge of the efficiency of the transmetalation process.

After trying different copper sources (CuTc, CuCl, CuI, CuCN), we found that the best transmetalation conditions were obtained by addition of CuCN–LiCl (2.5 equiv) in tetrahydrofuran at –10 °C to the enantiomerically pure lithium 2-(*p*-tolylsulfinyl)benzyl carbanion [Li]-**1a** at –78 °C (Scheme 3). Under these conditions, [Cu]-**1a** reacts with propargyl bromide (**2a**) in a completely regioselective manner, only affording the allene **4a** in 92% yield. A similar result was obtained by using the propargyl mesylate (**2b**) instead of the bromide **2a** as the starting material.

Reactions of [Cu]-**1a** with C3-substituted propargylic systems **2c–f** under similar conditions also took place with complete regioselectivity and good yields, affording the 1,1-disubstituted allenes **4b–e** (Scheme 4). Similar efficiency was observed when this reaction was performed on a larger scale (up to 5.0 mmol).

We then studied reactions of the copper benzyl carbanion derived from 1-ethyl-2-(*p*-tolylsulfinyl)benzene, [Cu]-**1b**, with propargyl derivatives. The reaction of [Cu]-**1b** with propargyl bromide (**2a**) was completely regioselective, but yielded a 94:6 mixture of the S_N2' products **4f** and **4f′**, epimers at the benzylic position (Scheme 5 and Table 1, entry 1). Identical results were obtained starting from the propargyl mesylate (**2b**) (Scheme 5 and Table 1, entry 2). This fact reveals the scarce influence of the leaving group on the stereoselectivity control. Moreover, the efficiency of the sulfinyl group in controlling the configuration at the benzylic position of copper benzyl carbanions was similar to that exerted in reactions with lithium carbanions (Scheme 1).[1–11] The potential interest in asymmetric synthesis of the allenes such as **4f**, with a chiral center directly joined to the π-system, prompted us to check the scope of this reaction (Table 1).

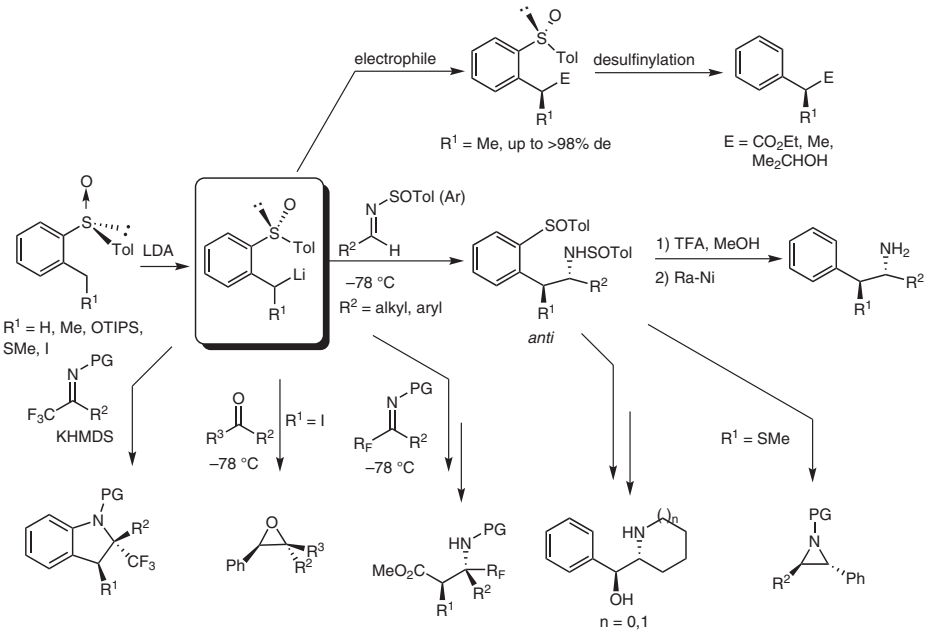
The reaction of [Cu]-**1b** with **2c** afforded a 88:12 mixture of **4g** and **4g′** (Table 1, entry 3), epimers at the benzylic carbon. The total observed regioselectivity in this reaction

Biographical Sketches

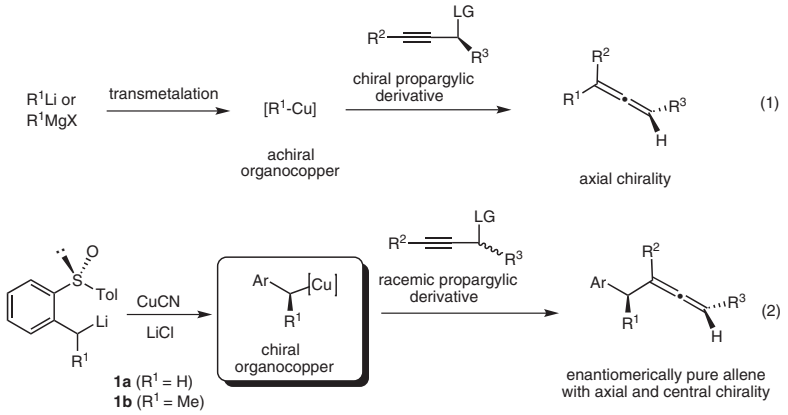
José Luis García Ruano (right) received his Ph.D. at the Universidad Complutense (Madrid, 1973). He has held appointments as a Visiting Professor at Florida State (1992) and Emory (2003) Universities and received a fellowship with JSPS in 2006. He was appointed Full Professor in Organic Chemistry at Universidad Autónoma de Madrid in 1982 and has served as vice-president of the Spanish Royal Society of Chemistry for four years. His research interests are centered in the chemistry of sulfoxides and related compounds and their applications in asymmetric synthesis. In these fields, he has published more than 300 papers and supervised 35 Ph.D. theses.

Vanesa Marcos (middle) received her B.Sc. in chemistry at the Universidad Autónoma of Madrid (Spain) in 2005. She started her thesis on 2005 on the synthesis and reactivities of sulfinyl-allenes, under the supervision of Professor García Ruano and Dr. Alemán. In 2008 she spent six months in the laboratory of Professor Karl Anker Jørgensen working in the area of organocatalysis.

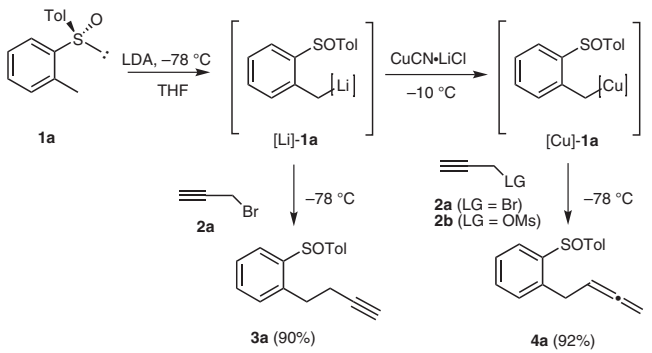
José Alemán (left) received his B.Sc. in chemistry at the Universidad Autónoma of Madrid (Spain) in 2000. In 2003 he spent six months in the laboratory of Professor Albert Padwa at Emory University (Atlanta, USA) working on Pummerer rearrangements. In 2005 he received the Lilly Research Award for Ph.D. students and presented his Ph.D. thesis, which was focused on remote stereocontrol by sulfinyl groups and supervised by Professor Jose Luis García Ruano. He carried out his postdoctoral research (2006–2008) in the group of Professor Karl Anker Jørgensen (Aarhus, Denmark). He is currently working (2009) in García Ruano's lab on new asymmetric methods with sulfur compounds. His research interests include asymmetric synthesis, sulfur chemistry, and organocatalysis.



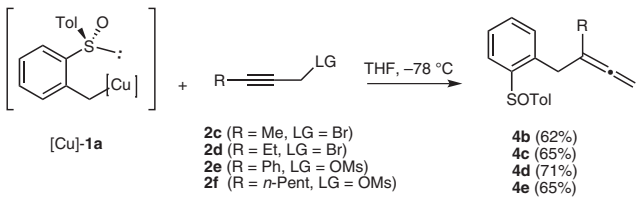
Scheme 1 Different reactions with carbonyl and imines groups towards lithium sulfinylbenzyl carbanions



Scheme 2 Approaches for synthesizing chiral allenes

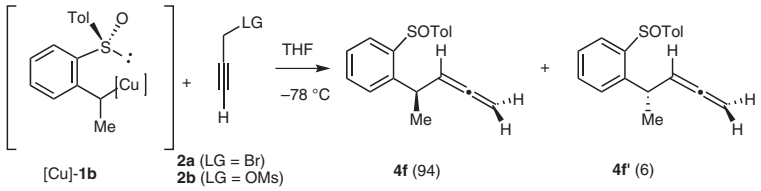


Scheme 3 Regioselectivity in reactions of **2a** with [Li]-**1a** and [Cu]-**1a** (LG = leaving group)



Scheme 4 Reaction with C3-substituted propargylic systems (LG = leaving group)

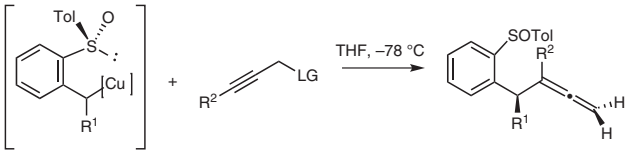
was remarkable despite the fact that the carbon to be attacked was substituted and, therefore, more sterically hindered. Interestingly, the allene **4h** is the only epimer detected by ^{1}H NMR in the reaction of the sulfoxide **1b** with **2e** (>96% de, Table 1, entry 4). Complete stereoselective control was also achieved in reactions of **1c** with **2a** and **2c** which afforded **4i** and **4j**, respectively (Table 1, entries 5 and 6). The reaction of propargylic bromides **2a** and **2c** with allylic carbanion [Cu]-**1d** gave the corresponding 1,2,6-trienes **4k** and **4l**, respectively, in high yields and good diastereomeric ratio (Table 1, entries 7 and 8). These results allow us to conclude that the remote sulfinyl group is quite efficient in controlling the configuration of the benzylic centers in the organocopper reagents.



[Cu]-**1b** **2a** (LG = Br) **2b** (LG = OMs) **4f** (94) **4f'** (6)

Scheme 5 Reaction of [Cu]-**1b** with **2a** and **2b** (LG = leaving group)

Table 1 The Reaction of **1b–d** with Propargylic Derivatives **2a–c**,**e**[a]



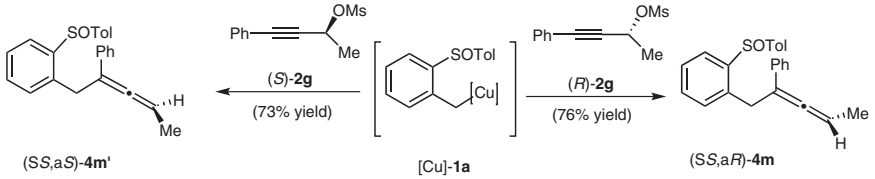
[Cu]-**1b–d** **2a–e** **4f–l**

Entry	Reagent	Electrophile			Product	Yield[b] (%)	dr[c]
	R^1		R^2	LG			
1	{Cu}-**1b**	Me	**2a**	H	Br	**4f**	76	94:6
2	{Cu}-**1b**	Me	**2b**	H	OMs	**4f**	72	94:6
3	{Cu}-**1b**	Me	**2c**	Me	Br	**4g**	51	88:12
4	{Cu}-**1b**	Me	**2e**	Ph	OMs	**4h**	69	>98:2
5	{Cu}-**1c**	Bn	**2a**	H	Br	**4i**	(40)[d]	>98:2
6	{Cu}-**1c**	Bn	**2c**	Me	Br	**4j**	68	>98:2
7	{Cu}-**1d**	$CH_2CH{=}CH_2$	**2a**	H	Br	**4k**	64	85:15
8	{Cu}-**1d**	$CH_2CH{=}CH_2$	**2c**	Me	Br	**4l**	75	95:5

[a] All reactions were performed in a 0.2 mmol scale. LG = leaving group.
[b] Combined isolated yield.
[c] Determined by ^{1}H NMR spectroscopy on the crude mixture.
[d] Conversion measured by ^{1}H NMR spectroscopy, in which allene **4i** was inseparable from sulfoxide **1c**.

We then investigated the synthesis of allenes with axial chirality. In this sense, we prepared the enantiomerically pure mesylates (*R*)-**2g** and (*S*)-**2g**, derived from 4-phenylbut-3-yn-2-ol, by an enzymatic resolution of the racemic alcohol.[15b] Reactions of [Cu]-**1a** with both enantiomers are completely stereoselective, and respectively afforded enantiomerically pure (S*S*,a*R*)-**4m** and (S*S*,a*S*)-**4m′** in 76% and 73% isolated yields (Scheme 6). Configurational assignment of the chiral axis was performed by assuming the predominance of the *anti* attack observed in most of the reactions of the copper anions with the propargylic esters.[14] As expected from the similar rate and the complete stereoselectivity observed for these two reactions, [Cu]-**1a** is not appropriated for getting the kinetic resolution of the racemic mesylate **2g**.

Much more interesting were the reactions of [Cu]-**1b** with propargylic derivatives because they would provide allenes with axial and central chirality and mainly because would allow to confirm our initial assumption about the possible kinetic resolution of the propargylic electrophiles. We first studied reaction of [Cu]-**1b** with (*R*)-**2g**. Under mild conditions (–78 °C), a 95:5 mixture of two diastereomers was almost instantaneously formed (**4n** and **4n′**) in 88% isolated yield (Scheme 7). This result evidences that the configurational control of the axis is completed whereas it is very high at the benzylic center. We initially assumed that **4n** and **4n′** were epimers at the benzylic position, based on the complete *anti*-stereoselectivity observed for reactions in Scheme 6 and the high, but incomplete stereoselectivity shown at Table 1. The con-



(S*S*,a*S*)-**4m'** [Cu]-**1a** (S*S*,a*R*)-**4m**

Scheme 6 Reaction of [Cu]-**1a** with enantiomerically pure propargylic mesylates

figuration of the epimers was further confirmed (see later). Reaction of [Cu]-**1b** with (*S*)-**2g** also gave a 95:5 mixture of **4n** and **4n′**. However, reaction times were longer and the yield was much lower (18%) than those obtained from (*R*)-**2g** (Scheme 7). These results suggested that reaction of [Cu]-**1b** with (*S*)-**2g** is not taking place. Moreover, this mesylate must be partially racemized under the reaction conditions, thus explaining the formation of **4n** and **4n′** resulting from (*R*)-**2g**.

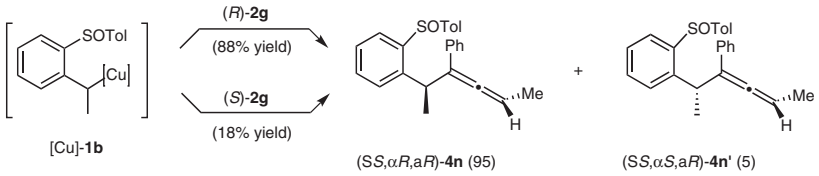
As expected from previous results, the reaction of [Cu]-**1b** with *rac*-**2g** also gave a 95:5 mixture of **4n** and **4n′** (58%) (Table 2, entry 1). Additionally, unreacted **1b** (33%) and the propargylic alcohol resulting in the hydrolysis of *rac*-**2g** (42%) could also be isolated (Table 2, entry 1).

These results pointed out that no reaction of [Cu]-**1b** with (*S*)-**2g** took place and suggested racemization of this mesylate derivative under this reaction conditions. Therefore, we reached a complete kinetic resolution of *rac*-**2g** with this reaction and a partial dynamic kinetic resolution. In order to know the scope of this reaction, we studied the behavior of other racemic mesylates *rac*-**2h–k** in the presence of [Cu]-**1b**. In all the cases, the organocopper reagent only reacts with the *R*-enantiomer yielding the enantiomerically pure allenes **4o–r** (Table 2) which exhibit the a*R*-configuration at their chiral axis. The fact that the isolated yields are always slightly higher than 50%, suggests that partial dynamic kinetic resolution has occurred to some extent.

The main conclusion deduced from these results is that the use of [Cu]-**1b** allows the synthesis of allenes with axial and/or central chirality in high enantiomerical purity from racemic propargyl derivatives, thus avoiding the tedious synthesis of enantiomerically pure propargylic alcohols.[15]

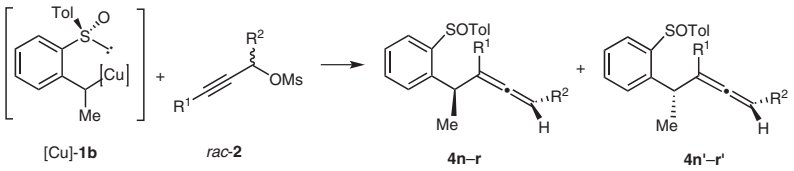
The unequivocal configurational assignment of the obtained allenes was performed in two different ways. Hydrogenation of the 90:10 mixture of **4o** and **4o′** (Table 2, entry 2) with Adam's catalyst afforded a 90:10 mixture of two diastereomers **5** and **5′** (Scheme 8). Thus, we demonstrated that **4o** and **4o′** were epimers at the benzylic position (which remains unaltered after hydrogenation). Desulfinylation of the mixture **5/5′** gave 2-phenylhexane, whose specific rotation unequivocally indicates that the major enantiomer was the *R*-configuration at the benzylic carbon.[17]

The second correlation was based on the well-known stereochemical course of the lithium carbanions with alkyl halides[18] and other electrophiles.[1–11] Reaction of [Li]-**1b** with propargyl bromide (**2a**) afforded a mixture of **3b** and **3b′** in 89% yield. Subsequent hydrogenation of this mixture led alkylsulfinyl derivatives **7/7′** in 85% yield and 90:10 diastereomeric ratio (Scheme 8). The configuration at the benzylic position of these substrates shown in Scheme 8 is identical to those predicted on the basis of the well-established stereochemical course of these reactions.[18] On the other hand, reaction of [Cu]-**1b** with the bromide **2a** gave a 94:6 mixture of allenes **4f/4f′**, whose reduction also gives a mixture of **7** (94) and **7′** (6)



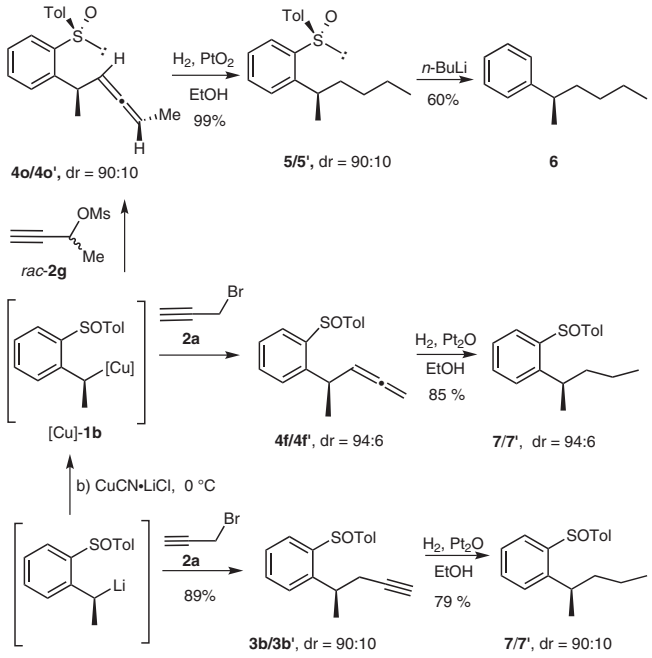
Scheme 7 Reaction of [Cu]-**1b** with optically pure (*R*)- and (*S*)-**2g**

Table 2 Reactions of **1b** with Racemic Propargylic Derivatives[a]



Entry	Electrophile	R^1	R^2	Product	Yield[b] (%)[b]	dr
1	*rac*-**2g**	Ph	Me	**4n**	58	95:5[d]
2	*rac*-**2h**	H	Me	**4o**	53	90:10[c]
3	*rac*-**2i**	4-BrC_6H_4	Me	**4p**	56	85:15[c]
4	*rac*-**2j**	Bu	Me	**4q**	53	93:7[d]
5	*rac*-**2k**	Ph	Et	**4r**	56	96:4[d]

[a] All reactions were performed on a 0.2 mmol scale.
[b] Combined isolated yield.
[c] Diastereomeric ratio determined by ^{1}H NMR on the crude reaction.
[d] Diastereomeric ratio was also determined by chiral HPLC.



Scheme 8 Chemical correlations

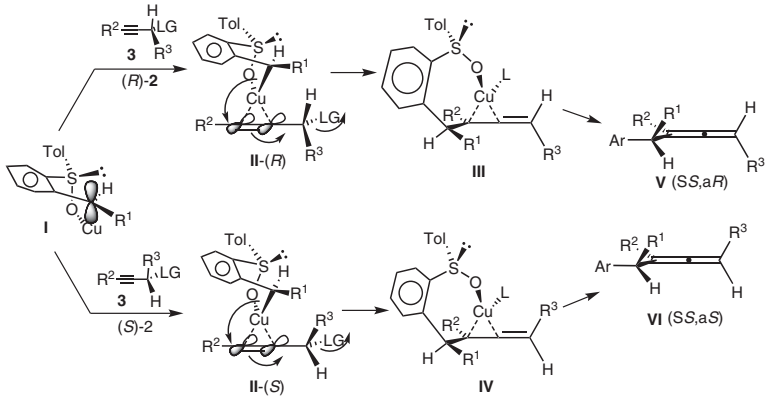
(Scheme 8), which indicated that the stereochemical course at benzylic carbons of organocopper and organolithium reagents is identical in reactions with propargylic derivatives.

In order to explain the stereochemical results we propose the initial formation of a benzylcopper intermediate **I**, stabilized by the *ortho*-sulfinyl oxygen. These species **I** (Scheme 9) must exhibit the *p*-tolyl group at the sulfur atom in a pseudoequatorial arrangement in a half-boat conformation of the six-membered ring.[5] The approach of each enantiomer of the propargyl bromine or mesylate could take place by coordination of one of the π-system at the triple bond with the benzylcopper **I**, respectively forming **II**-(*R*) and **II**-(*S*). The conformation depicted in Scheme 9 for these intermediates shows the leaving group adopting a pseudo-*anti*-periplanar arrangement with respect to the remaining π-double bond acting as nucleophile in the subsequent S_N2' reaction. The intermediates **III** and **IV**, formed when the leaving group has been shifted by the electrons of the π-system, respectively evolve into allenes **V** and **VI** (Scheme 9) by reduction of Cu(III) to Cu(I).

In all the cases, **II**-(*R*) will be favored with respect to **II**-(*S*) by steric interactions (H/R^1 vs R^1/R^3). In reactions from [Cu]-**1a** (R^1 = H), the evolution of both intermediates would be possible. This assumption was confirmed by reacting [Cu]-**1a** with *rac*-**2g**. The use of one equivalent of both reagents determines the formation of a 1:1 mixture of **4m** and **4m′**, which is the expected from results depicted in Scheme 6. In this sense, [Cu]-**1b** is much more efficient. The spatial arrangement corresponding to **II**-(*S*), when [Cu]-**1b** (R^1 = Me) is used as reagent, must be strongly destabilized by the R^1/R^3 interactions (Scheme 9), thus precluding this intermediate can be reached it. As a consequence, [Cu]-**1b** would only react with the *R*-enantiomer towards **II**-(*R*), determining a complete kinetic resolution.

The fact that in all these reactions we observe dynamic resolution in some extent could be explained by assuming the epimerization of the propargyl mesylate under reaction conditions (the recovered propargylic alcohol in reactions of Table 2 are racemic). In order to confirm this assumption we treated the mesylate (*S*)-**2g** with lithium diisopropylamide at –78 °C for five minutes. After work up with saturated aqueous ammonium chloride, we isolated the corresponding propargylic alcohol almost completely racemized. The low dynamic resolution observed in these reactions (ca. 10%) could be due to the formation of species like **II**-(*S*) but in a different conformation to that depicted in Scheme 9, which is not able to evolve into the allene or easily transformed into the starting mesylate and it finally will be transformed in the workup of the reaction to the corresponding alcohol.

In summary, we have demonstrated that the reactions of enantiomerically pure 2-(*p*-tolylsulfinyl)benzylcopper reagents with propargyl bromides and mesylates take place in a completely regioselective S_N2' manner and follow a totally *anti*-stereoselective pathway when a chiral axis is formed. The sulfinyl group is very efficient in controlling the configuration of the α-alkylbenzyl–copper reagents, providing the first method to obtain enantiomerically pure allenes with a chiral center directly joined to the allenic system, in which the chiral axis can also have a defined



Scheme 9 Stereochemical proposal for the S_N2' reaction

configuration. Additionally, a complete kinetic resolution of racemic propargylic mesylates can be achieved with sulfinylated α-alkylbenzyl–copper reagents, which in their turn are moderately efficient for the dynamic kinetic resolution of the propargylic mesylates.

NMR spectra were acquired on a Bruker 200, 300 or a Varian AS 400 spectrometer, running at 200, 300 or 400 and 50, 75, or 100 MHz for ^{1}H and ^{13}C, respectively, referenced to residual solvent signals [$CHCl_3$, δ = 7.26 (^{1}H), $CDCl_3$, δ = 77.0 (^{13}C). ^{13}C NMR spectra were acquired on a broad band decoupled mode. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. All reactions were carried out in anhydrous solvents and under an argon atmosphere. THF and Et_2O were distilled from Na/benzophenone under argon and CH_2Cl_2 was distilled from P_2O_5. Flash column chromatography was performed using silica gel Merck-60 (230–400 mesh). 2.5 M *n*-BuLi in hexanes was purchased from Aldrich.

Commercially available starting materials and solvents were used without further purification. Sulfoxides **1a–d** have been previously described in the literature.[19] The racemic or optically enriched propargylic alcohols were prepared following methods described in the literature.[15b]

2-(But-3-ynyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (3a)

A soln of 2.3 M *n*-BuLi in hexanes (0.60 mmol) was added to *i*-Pr_2NH (0.89 mmol) in THF (3 mL) at 0 °C and the mixture was stirred for 30 min; it was then cooled to –78 °C. A soln of the sulfoxide **1a** (0.50 mmol) in THF (2 mL) was added, the mixture was stirred for 5 min and then propargyl bromide (**2a**, 2.0 equiv) was added at –78 °C. When the reaction was complete (5 min), the mixture was hydrolyzed with sat. NH_4Cl) and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with sat. NH_4Cl soln (2 × 10 mL), dried ($MgSO_4$), and the solvent evaporated. The residue was purified by flash column chromatography (*n*-hexanes–EtOAc, 6:1); yield: 90%.

$[\alpha]_D^{20}$ –96.7 (*c* 0.87, $CHCl_3$).

IR (NaCl): 3306, 2920, 1594, 1493, 1471 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.00–7.90 (m, 1 H), 7.50–7.12 (m, 7 H), 3.50–2.80 (m, 2 H), 2.50–2.32 (m, 2 H), 2.36 (s, 3 H), 2.01 (t, *J* = 2.1 Hz, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 142.9, 141.8, 141.6, 139.6, 136.9, 130.9, 129.9, 129.6, 127.3, 125.9, 124.8, 115.5, 34.5, 31.1, 21.3.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{17}H_{17}OS$: 269.1000; found: 269.0993.

Allenes 4; General Procedure

A soln of 2.3 M *n*-BuLi in hexanes (0.60 mmol) was added to *i*-Pr_2NH (0.89 mmol) in THF (3 mL) at 0 °C and the mixture was stirred for 30 min; it was then cooled to –78 °C. A soln of the corresponding sulfoxide **1a–d** (4.5 mmol) in THF (2 mL) was added, the mixture was stirred for 5 min and then a soln CuCN·LiCl (10.80 mmol) in THF (3.5 mL) (previously cooled to –10 °C) was added at –78 °C. After 5 min, the corresponding propargyl bromide or mesylate **2** (6.5 mmol) in THF (2 mL) at –78 °C was added. When the reaction was complete (5 min), the mixture was hydrolyzed with sat. NH_4Cl soln (2 mL) and extracted with Et_2O (3 × 10 mL). The combined organic extracts were washed with sat. NH_4Cl soln (2 × 10 mL), dried ($MgSO_4$), and the solvent evaporated. The residue was purified by flash column chromatography.

2-(Buta-2,3-dienyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4a)

Following the general procedure starting from sulfoxide **1a** and propargyl bromide (**2a**) with flash chromatography (toluene–EtOAc, 20:1) gave **4a** (92%) as a colorless oil.

$[\alpha]_D^{20}$ –104.9 (*c* 0.6, acetone).

IR (NaCl): 2982, 2922, 1955, 1607, 1439, 1033 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.95–7.90 (m, 1 H), 7.50–7.10 (m, 7 H), 5.11 (sext, *J* = 8.0 Hz, 1 H), 4.70–4.60 (m, 2 H), 3.60–3.30 (m, 2 H), 2.30 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 209.0, 143.2, 141.8, 141.6, 137.9, 131.0, 130.0, 127.7, 126.1, 125.9, 124.9, 88.4, 75.9, 29.7, 18.5.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{17}H_{17}OS$: 269.1012; found: 269.0994.

Anal. Calcd for $C_{17}H_{16}OS$: C, 76.08; H, 6.01; S, 11.95. Found: C, 74.98; H, 6.20; S, 11.26.

2-(2-Methylbuta-2,3-dienyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4b)

Following the general procedure starting from sulfoxide **1a** and 1-bromobut-2-yne (**2c**) with flash chromatography (toluene–EtOAc, 20:1) gave **4b** (62%) as a colorless oil.

$[\alpha]_D^{20}$ –133.6 (*c* 1.0, acetone).

IR (NaCl): 2980, 2920, 1955, 1607, 1439, 1033 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 9.3 Hz, 1 H), 7.50–7.30 (m, 5 H), 7.22 (d, *J* = 8.5 Hz, 2 H), 4.47–4.36 (m, 2 H), 3.42–3.37 (m, 2 H), 2.34 (s, 3 H), 1.61 (t, *J* = 3.1 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 207.3, 143.8, 141.9, 141.4, 137.2, 130.7, 130.4, 129.8, 127.7, 125.7, 124.9, 97.2, 74.8, 36.4, 21.3, 18.2.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{19}OS$: 283.1139; found: 283.1151.

2-(2-Ethylbuta-2,3-dienyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4c)

Following the general procedure starting from sulfoxide **1a** and 1-bromopent-2-yne (**2d**) with flash chromatography (toluene–EtOAc, 20:1) gave **4c** (65%) as a colorless oil.

$[\alpha]_D^{20}$ –87.4 (*c* 0.75, $CHCl_3$).

IR (NaCl): 2966, 1957, 1716, 1457, 1059, 1033 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.87–7.83 (m, 1 H), 7.40–7.14 (m, 7 H), 4.56–4.38 (m, 2 H), 3.43–3.29 (m, 2 H), 2.28 (s, 3 H), 1.86–1.77 (m, 2 H), 0.90 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.9, 144.0, 142.2, 141.8, 137.8, 131.1, 130.9, 130.3, 128.1, 126.2, 125.3, 104.3, 77.8, 35.7, 25.0, 21.7, 12.3.

MS (ESI): *m*/*z* (%) = 297 ([M + H$^+$], 100), 287 (15), 231 (10), 211 (16), 143 (21), 139 (25).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{19}H_{21}OS$: 297.1308; found: 297.1307.

2-(2-Phenylbuta-2,3-dienyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4d)

Following the general procedure starting from sulfoxide **1a** and 3-phenylprop-2-ynyl mesylate (**2e**) with flash chromatography (toluene–EtOAc, 20:1) gave **4d** (71%) as a colorless oil.

$[\alpha]_D^{20}$ –58.0 (*c* 0.83, $CHCl_3$).

IR (NaCl): 2924, 1956, 1716, 1492, 1083, 1033 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.03 (dd, *J* = 7.5, 1.8 Hz, 1 H), 7.49–7.18 (m, 12 H), 4.97–4.68 (m, 2 H), 3.97–3.73 (m, 2 H), 2.38 (s, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 210.2, 143.9, 142.2, 137.5, 135.7, 131.4, 130.9, 130.6, 130.5, 129.0, 128.3, 127.5, 126.7, 126.4, 125.3, 104.1, 79.6, 33.1, 21.9.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{23}H_{21}OS$: 345.1295; found: 345.1307.

2-(2-Vinylideneheptyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4e)
Following the general procedure starting from sulfoxide **1a** and oct-2-ynyl mesylate (**2f**) with flash chromatography (toluene–EtOAc, 20:1) gave **4e** (65%) as a colorless oil.

$[\alpha]_D^{20}$ –127.8 (*c* 1.03, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.00–7.96 (m, 1 H), 7.54–7.42 (m, 4 H), 7.31–7.26 (m, 3 H), 4.46–4.47 (m, 2 H), 3.35–3.38 (m, 2 H), 2.40 (s, 3 H), 1.4–1.34 (m, 8 H), 0.92 (t, *J* = 6.8 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 206.8, 143.7, 141.4, 137.4, 130.7, 130.5, 129.9, 129.8, 127.7, 125.8, 124.8, 102.3, 35.3, 31.5, 27.0, 22.4, 21.3, 14.0.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{22}H_{27}OS$: 339.1777; found: 339.1774.

2-[(*R*)-Penta-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4f)
Following the general procedure starting from sulfoxide **1b** and propargyl bromide (**2a**) with flash chromatography (toluene–EtOAc, 20:1) gave **4f** (76%) as a colorless oil; mixture of diastereomers 94:6.

$[\alpha]_D^{20}$ –206.1 (*c* 0.4, acetone).

IR (NaCl): 2920, 1952, 1639 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (major diastereomer) = 7.93–7.90 (m, 1 H), 7.50–7.10 (m, 7 H), 5.28 (q, *J* = 6.4 Hz, 1 H), 4.84–4.79 (m, 2 H), 4.10–3.90 (m, 1 H), 2.35 (s, 3 H), 0.99 (d, *J* = 6.4 Hz, 3 H); δ (minor diastereomer) = 7.93–7.90 (m, 1 H), 7.50–7.10 (m, 7 H), 4.97 (q, *J* = 6.4 Hz, 1 H), 4.69–4.64 (m, 2 H), 4.10–3.90 (m, 1 H), 2.35 (s, 3 H), 1.24 (d, *J* = 6.4 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 207.9, 144.0, 142.3, 141.7, 131.3, 130.0, 129.9, 127.7, 127.6, 126.1, 124.7, 95.1, 76.6, 33.1, 21.6, 20.5.

MS (FAB): *m*/*z* (%) = 283 ([M + H$^+$], 100), 241 (36), 149 (12), 139 (18).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{19}OS$: 283.1146; found: 283.1151.

Anal. Calcd for $C_{18}H_{18}OS$: C, 76.56; H, 6.42; S, 11.35. Found: C, 75.83; H, 6.46; S, 10.98.

2-[(*R*)-3-Methylpenta-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4g)
Following the general procedure starting from sulfoxide **1b** and 1-bromobut-2-yne (**2c**) with flash chromatography (toluene–EtOAc, 20:1) gave **4g** (51%) as a colorless oil; mixture of diastereomers 88:12.

$[\alpha]_D^{20}$ –169.9 (*c* 0.3, acetone).

IR (NaCl): 2971, 2923, 1956, 1680 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ (major diastereomer) = 7.98 (d, *J* = 9.3 Hz, 1 H), 7.50–7.30 (m, 5 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 4.80–4.63 (m, 2 H), 3.80–3.60 (m, 1 H), 2.34 (s, 3 H), 1.53 (t, *J* = 3.5 Hz, 3 H), 0.98 (d, *J* = 6.8 Hz, 3 H); δ (minor diastereomer) = 7.98 (d, *J* = 9.3 Hz, 1 H), 7.50–7.30 (m, 5 H), 7.22 (d, *J* = 8.0 Hz, 2 H), 4.67–4.64 (m, 2 H), 3.80–3.60 (m, 1 H), 2.34 (s, 3 H), 1.53 (t, *J* = 3.5 Hz, 3 H), 0.98 (d, *J* = 6.8 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 206.3, 143.6, 142.8, 142.2, 141.7, 131.3, 130.0, 127.5, 126.3, 125.1, 124.4, 102.8, 76.4, 37.4, 21.4, 20.4, 18.0.

MS (FAB): *m*/*z* (%) = 297 ([M + H$^+$], 57), 255 (5), 158 (100), 157 (16), 143 (36), 139 (12).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{19}H_{21}OS$: 297.1308; found: 297.1307.

Anal. Calcd for $C_{19}H_{20}OS$: C, 76.98; H, 6.80; S, 10.82. Found: C, 76.22; H, 6.97; S, 10.82.

2-[(*R*)-3-Phenylpenta-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4h)
Following the general procedure starting from sulfoxide **1b** and 3-phenylprop-2-ynyl mesylate (**2e**) with flash chromatography (toluene–EtOAc, 20:1) gave **4h** (69%) as a colorless oil; single diastereomer.

$[\alpha]_D^{20}$ –168.4 (*c* 0.6, $CHCl_3$).

IR (NaCl): 2966, 1963, 1735, 1604, 1063, 1034 cm^{-1}.

^{1}H NMR (200 MHz, $CDCl_3$): δ = 8.09–7.99 (m, 1 H), 7.46–6.82 (m, 12 H), 5.25 (d, *J* = 3.0 Hz, 2 H), 4.37–4.29 (m, 1 H), 2.37 (s, 3 H), 0.98 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 209.2, 141.8, 141.6, 135.3, 131.1, 130.1, 129.9, 128.9, 128.4, 127.1, 126.7, 126.4, 126.0, 124.7, 124.6, 109.9, 80.1, 24.8, 21.3, 14.8.

MS (FAB): *m*/*z* (%) = 359 ([M + H$^+$], 100), 349 (24), 245 (17), 243 (7), 220 (36).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{24}H_{23}OS$: 359.1463; found: 359.1464.

2-[(*R*)-1-Phenylpenta-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4i)
Following the general procedure starting from sulfoxide **1c** and propargyl bromide (**2a**) with flash chromatography (toluene–EtOAc, 20:1) gave **4i** (40% conversion) as an inseparable mixture with **1c** as a colorless oil; single diastereomer.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.86–7.85 (m, 1 H), 7.37–7.03 (m, 12 H), 5.25–5.18 (m, 1 H), 4.65–4.62 (m, 2 H), 4.21–4.15 (m, 1 H), 3.07–2.58 (m, 2 H), 2.24 (s, 3 H).

2-[(*R*)-3-Methyl-1-phenylpenta-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4j)
Following the general procedure starting from sulfoxide **1c** and 1-bromobut-2-yne (**2c**) with flash chromatography (toluene–EtOAc, 20:1) gave **4j** (68%) as a colorless oil; single diastereomer.

$[\alpha]_D^{20}$ –35.7 (*c* 0.43, $CHCl_3$).

IR (NaCl): 2960, 1958, 1712, 1593, 1469, 1030 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.4 Hz, 1 H), 7.46–6.92 (m, 12 H), 4.84–4.82 (m, 2 H), 4.16–4.11 (m, 1 H), 3.20–2.74 (m, 2 H), 2.34 (s, 3 H), 1.61 (d, *J* = 3.1 Hz, 3 H).

^{13}C-NRM (75 MHz, $CDCl_3$): δ = 206.6, 144.2, 142.6, 141.1, 139.9, 131.5, 129.8, 129.1, 128.4, 128.2, 128.0, 127.9, 126.1, 125.9, 125.7, 101.9, 77.2, 44.8, 40.7, 21.3, 18.3.

MS (FAB): *m*/*z* (%) = 373 ([M + H$^+$], 100), 234 (7), 143 (6).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{25}H_{25}OS$: 373.1613; found: 373.1620.

2-[(*R*)-Hepta-1,2,6-trien-4-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4k)
Following the general procedure starting from sulfoxide **1d** and propargyl bromide (**2a**) with flash chromatography (toluene–EtOAc, 20:1) gave **4k** (64%) as a colorless oil; mixture of diastereomers 85:15.

$[\alpha]_D^{20}$ –11.6 (*c* 0.4, acetone).

IR (NaCl): 2968, 2925, 1593, 1469, 1030 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 7.99 (d, *J* = 7.5 Hz, 1 H), 7.50–7.20 (m, 7 H), 5.30–5.20 (m, 2 H), 5.00–4.90 (m, 2 H), 4.80–4.70 (m, 2 H), 3.92–3.88 (m, 1 H), 2.50–2.38 (m, 1 H), 2.35 (s, 3 H), 2.30–1.95 (m, 1 H); δ (minor diastereomer) = 7.99 (d, *J* = 7.5 Hz, 1 H), 7.50–7.20 (m, 7 H), 5.30–5.20 (m, 2 H), 5.00–

4.90 (m, 2 H), 4.62–4.58 (m, 2 H), 3.92–3.88 (m, 1 H), 2.50–2.38 (m, 1 H), 2.35 (s, 3 H), 2.30–1.95 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 208.2, 142.6, 142.2, 142.1, 141.7, 135.5, 131.2, 130.0, 127.9, 127.8, 126.3, 125.0, 116.8, 93.3, 77.3, 39.0, 38.8, 21.4.

MS (FAB): *m*/*z* (%) = 309 ([M + H], 100), 271 (36), 211 (29).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{20}H_{21}OS$: 309.1306; found: 309.1307.

Anal. Calcd for $C_{20}H_{20}OS$: C, 77.88; H, 6.54; S, 10.40. Found: C, 76.58; H, 6.63; S, 10.03.

2-[(*R*)-3-Methylhepta-1,2,6-trien-4-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4l)

Following the general procedure starting from sulfoxide **1d** and 1-bromobut-2-yne (**2c**) with flash chromatography (toluene–EtOAc, 20:1) gave **4l** (75%) as a colorless oil; mixture of diastereomers 95:5.

$[\alpha]_D^{20}$ –200.6 (*c* 1.0, $CHCl_3$).

IR (NaCl): 2966, 1957, 1716, 1594, 1083, 1030 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 7.98–7.97 (m, 1 H), 7.52–7.24 (m, 7 H), 5.50–5.39 (m, 2 H), 5.00–4.95 (m, 2 H), 4.85–4.72 (m, 2 H), 3.65–3.60 (m, 1 H), 2.50–2.38 (m, 1 H), 2.38 (s, 3 H), 1.99–1.90 (m, 2 H), 1.60 (t, *J* = 3.1 Hz, 1 H); δ (minor diastereomer) = 7.98–7.97 (m, 1 H), 7.52–7.24 (m, 7 H), 5.50–5.39 (m, 2 H), 5.00–4.95 (m, 2 H), 4.85–4.72 (m, 2 H), 3.65–3.60 (m, 1 H), 2.50–2.38 (m, 1 H), 2.38 (s, 3 H), 1.99–1.90 (m, 2 H), 1.03 (t, *J* = 3.1 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.4, 143.1, 141.9, 141.8, 136.0, 131.2, 130.0, 129.9, 127.7, 126.5, 126.4, 124.6, 116.2, 101.2, 76.7, 43.0, 38.4, 21.4, 18.2.

MS (FAB): *m*/*z* (%) = 323 ([M + H$^+$], 100), 322 (18), 321 (79), 311 (19).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{21}H_{23}OS$: 323.1452; found: 323.1464.

Anal. Calcd for $C_{21}H_{22}OS$: C, 78.22; H, 6.88; S, 9.94. Found: C, 76.89; H, 7.07; S, 9.43.

(a*R*)-2-(2-Phenylpenta-2,3-dienyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4m)

Following the general procedure starting from sulfoxide **1a** and (*R*)-4-phenylbut-3-yn-2-yl mesylate [(*R*)-**2g**] with flash chromatography (toluene–EtOAc, 20:1) gave **4m** (76%) as a colorless oil; single diastereomer.

$[\alpha]_D^{20}$ –75.0 (*c* 0.9, CH_2Cl_2).

IR (NaCl): 3058, 2920, 1684, 1117, 1032, 810, 758 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (m, 1 H), 7.48–7.20 (m, 12 H), 5.45–5.40 (m, 1 H), 3.99–3.71 (m, 2 H), 2.38 (s, 3 H), 1.60 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.0, 143.2, 141.6, 137.3, 136.2, 131.6, 130.8, 130.2, 129.9, 128.3, 127.7, 126.7, 126.1, 125.9, 124.6, 103.1, 90.0, 32.8, 21.4, 13.7.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{24}H_{23}OS$: 359.1469; found: 359.1478.

(a*S*)-2-(2-Phenylpenta-2,3-dienyl)phenyl *p*-Tolyl (*S*)-Sulfoxide (4m′)

Following the general procedure starting from sulfoxide **1a** and (*S*)-4-phenylbut-3-yn-2-yl mesylate [(*S*)-**2g**] with flash chromatography (toluene–EtOAc, 20:1) gave **4m′** (73%) as a colorless oil; single diastereomer.

$[\alpha]_D^{20}$ –84.5 (*c* 1.1, CH_2Cl_2).

IR (NaCl): 3058, 2923, 1684, 1117, 1032, 810, 758 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (m, 1 H), 7.48–7.20 (m, 12 H), 5.12–5.07 (m, 1 H), 3.99–3.71 (m, 2 H), 2.38 (s, 3 H), 1.53 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 206.1, 143.1, 141.5, 137.2, 136.2, 131.6, 130.7, 130.1, 129.9, 128.3, 127.6, 126.6, 126.0, 125.8, 124.3, 103.6, 90.1, 32.9, 24.4, 13.8.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{24}H_{23}OS$: 359.1469; found: 359.1474.

(a*R*)-2-[(2*R*)-3-Phenylhexa-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4n)

Following the general procedure starting from sulfoxide **1b** and (*R*)-4-phenylbut-3-yn-2-yl mesylate [(*R*)-**2g**] with flash chromatography (toluene–EtOAc, 20:1) gave **4n** (88%) as a colorless oil; single diastereomer. Starting from racemic 4-phenylbut-3-yn-2-yl mesylate (*rac*-**2g**) gave **4n** (58%); 90% de [HPLC (2 Chiralpak OD columns, hexane–*i*-PrOH, 95:5; flow rate 0.3 mL/min): t_R = 94.3 (major), 106.2 (minor) min].

$[\alpha]_D^{20}$ –45.7 (*c* 0.51, $CHCl_3$).

IR (NaCl): 2970, 1682, 1594, 1449, 1029 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 8.06 (d, *J* = 7.0 Hz, 1 H), 7.38–6.80 (m, 12 H), 5.66–5.64 (m, 1 H), 4.35–4.29 (m, 1 H), 2.39 (d, *J* = 6.0 Hz, 3 H), 2.38 (s, 3 H), 1.69 (d, *J* = 7.0 Hz, 3 H); δ (minor diastereomer) = 8.06 (d, *J* = 7.0 Hz, 1 H), 7.38–6.80 (m, 12 H), 5.48–5.46 (m, 1 H), 4.35–4.29 (m, 1 H), 2.38 (s, 3 H), 1.86 (d, *J* = 6.0 Hz, 3 H), 0.96 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.8, 143.7, 142.0, 141.9, 136.3, 131.3, 130.1, 128.4, 128.0, 127.5, 127.3, 126.8, 126.6, 126.5, 124.5, 109.9, 90.9, 34.8, 21.9, 21.4, 14.2.

MS (ESI): *m*/*z* (%) = 373 ([M + H], 100), 349 (63), 301 (50), 259 (25), 234 (12), 139 (19).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{25}H_{25}OS$: 373.1609; found: 373.1620.

(a*S*)-2-[(2*R*)-Hexa-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4o)

Following the general procedure starting from sulfoxide **1b** and *rac*-but-3-yn-2-yl mesylate (*rac*-**2h**) with flash chromatography (toluene–EtOAc, 20:1) gave **4o** (53%) as a colorless oil; mixture of diastereomers 90:10.

$[\alpha]_D^{20}$ –191.0 (*c* 1.85, $CHCl_3$).

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 7.90–7.88 (m, 1 H), 7.42–7.15 (m, 7 H), 5.16–5.13 (m, 2 H), 3.86–3.81 (m, 1 H), 2.28 (s, 3 H), 1.63–1.55 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.1, 144.3, 142.4, 141.7, 131.3, 130.0, 127.9, 127.8, 127.5, 126.1, 124.6, 95.5, 88.5, 33.8, 21.4, 14.6, 14.2.

(a*R*)-(2-[(2*R*)-3-(4-Bromophenyl)hexa-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4p)

Following the general procedure starting from sulfoxide **1b** and *rac*-4-(4-bromophenyl)but-3-yn-2-yl mesylate (*rac*-**2i**) with flash chromatography (toluene–EtOAc, 20:1) gave **4p** (56%) as a colorless oil; mixture of diastereomers 85:15.

$[\alpha]_D^{20}$ –93.9 (*c* 2.08, $CHCl_3$).

IR (NaCl): 2973, 2925, 1628, 1595, 1491, 1083, 1054, 1030 1469, 758 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 7.92–6.99 (m, 12 H), 5.63–5.60 (m, 1 H), 4.33–4.27 (m, 1 H), 2.38 (s, 3 H), 1.77 (d, *J* = 7.0 Hz, 3 H), 0.87 (d, *J* = 7.0 Hz, 3 H); δ (minor diastereomer) = 7.92–6.99 (m, 14 H), 5.53–5.46 (m, 1 H), 4.23–4.17 (m,

1 H), 2.38 (s, 3 H), 1.83 (d, *J* = 7.0 Hz, 3 H), 0.90 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 205.8, 143.8, 142.0, 136.3, 131.2, 131.0, 130.1, 128.3, 128.0, 127.5, 127.4, 126.7, 126.6, 126.5, 124.6, 109.9, 90.8, 34.9, 30.8, 21.4, 14.2.

(a*S*)-2-[(*R*)-3-(Prop-1-enylidene)heptan-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4q)

Following the general procedure starting from sulfoxide **1b** and *rac*-oct-3-yn-2-yl mesylate (*rac*-**2j**) with flash chromatography (toluene–EtOAc, 20:1) gave **4q** (53%) as a colorless oil; mixture of diastereomers 93:7; 86% de [HPLC (2 Chiralpak OD columns, hexane–*i*-PrOH, 95:5; flow rate 0.3 mL/min): t_R = 59.7 (major), 69.7 (minor) min].

$[\alpha]_D^{20}$ –20.9 (*c* 0.50, $CHCl_3$).

IR (NaCl): 2921, 1958, 1690, 1595, 1492, 1032 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 8.00–7.98 (m, 1 H), 7.50–7.21 (m, 7 H), 5.27–5.20 (m, 1 H), 3.66–3.60 (m, 1 H), 2.35 (s, 3 H), 1.76–1.60 (m, 5 H), 1.32–1.19 (m, 4 H), 0.87–0.70 (m, 6 H); δ (minor diastereomer) = 8.00–7.98 (m, 1 H), 7.50–7.21 (m, 7 H), 5.14–5.11 (m, 1 H), 3.66–3.60 (m, 1 H), 2.35 (s, 3 H), 1.76–1.60 (m, 5 H), 1.32–1.19 (m, 4 H), 0.87–0.70 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.8, 144.0, 142.6, 142.2, 141.7, 131.2, 130.0, 127.5, 127.4, 124.1, 108.3, 88.9, 37.1, 31.1, 29.8, 22.2, 21.4, 20.5, 15.1, 13.9.

MS (ESI): *m*/*z* (%) = 353 ([M + H$^+$], 100), 349 (63), 301 (50), 259 (25), 234 (12), 139 (19).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{23}H_{29}OS$: 353.1861; found: 353.1870.

(a*R*)-2-[(2*R*)-3-Phenylhepta-3,4-dien-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (4r)

Following the general procedure starting from sulfoxide **1b** and *rac*-1-phenylpent-1-yn-3-yl mesylate (*rac*-**2k**) with flash chromatography (toluene–EtOAc, 20:1) gave **4r** (56%) as a colorless oil; mixture of diastereomers 96:4; 92% de [HPLC (2 Chiralpak OD columns, hexane–*i*-PrOH, 95:5; flow rate 0.3 mL/min): t_R = 89.1 (major), 106.0 (minor) min].

$[\alpha]_D^{20}$ –53.7 (*c* 0.43, $CHCl_3$).

IR (NaCl): 2972, 1964, 1598, 1492, 1040 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ (major diastereomer) = 7.98–7.97 (m, 1 H), 7.44–7.08 (m, 12 H), 5.72–5.70 (m, 1 H), 4.34–4.27 (m, 1 H), 2.37 (s, 3 H), 2.19–2.12 (m, 2 H), 1.14–1.03 (m, 3 H), 0.92 (d, *J* = 6.7 Hz, 3 H); δ (minor diastereomer) = 7.98–7.97 (m, 1 H), 7.44–7.08 (m, 12 H), 5.59–5.52 (m, 1 H), 4.57–4.53 (m, 1 H), 2.37 (s, 3 H), 1.85–1.78 (m, 2 H), 1.52–1.49 (m, 3 H), 0.92 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 204.4, 143.7, 142.1, 141.9, 141.5, 136.4, 131.7, 130.1, 128.4, 127.4, 126.8, 126.3, 124.5, 111.0, 98.1, 34.7, 22.2, 22.0, 21.5, 13.4.

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{21}H_{25}OS$: 373.1547; found: 373.1548.

2-[(*R*)-Hexan-2-yl]phenyl *p*-Tolyl (*S*)-Sulfoxide (5)

The product was obtained starting from a mixture of **4o** and **4o′** (90:10) following the procedure for hydrogenation with PtO_2.[20] To a soln of a mixture of **4o** and **4o′** (90:10, 0.05 mmol) in EtOH (5 mL) with a hydrogen balloon was added PtO_2 (10 mol%). The reaction was followed by TLC and when the reaction was complete, the mixture was filtered through celite and the solvent was eliminated under reduced pressure, to give a mixture of **5** and **5′** (90:10); yield: 99%.

$[\alpha]_D^{20}$ –71.0 (*c* 0.69, $CHCl_3$).

^{1}H NMR(400 MHz, $CDCl_3$): δ = 7.98–7.90 (m, 1 H), 7.42–7.13 (m, 7 H), 3.12–2.99 (m, 1 H), 2.32 (s, 3 H), 1.58–1.46 (m, 2 H), 1.25–0.98 (m, 7 H), 0.85 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.0, 143.2, 142.1, 131.9, 130.4, 127.9, 127.1, 126.4, 125.2, 122.0, 38.4, 37.1, 34.9, 29.9, 23.2, 21.6, 14.4.

(*R*)-1-(Pentan-2-yl-2-[(*S*)-*p*-tolylsulfinyl)]benzene (7)

The product was obtained starting from a diastereomeric mixture of **4f/4f′** (94:6) or **3b/3b′** (90:10), following the procedure for hydrogenation with PtO_2.[20] To a soln of **4f/4f′** or **3b/3b′** in EtOH (5 mL) with a hydrogen balloon was added PtO_2 (10 mol%). The reaction was followed by TLC and when the reaction was completed, the mixture was filtered through celite and solvent was eliminated under reduced pressure, followed by flash chromatography (*n*-hexane–EtOAc, 8:1) to give **7** as a colorless oil; yield: 85% (**4f/4f′**), 79% (**3b/3b′**).

$[\alpha]_D^{20}$ –84.4 (*c* 1.7, $CHCl_3$).

IR (NaCl): 2958, 2928, 1595, 1493, 1160, 1083, 1033 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88–7.85 (m, 1 H), 7.40–7.14 (m, 7 H), 3.10–3.03 (m, 1 H), 2.28 (s, 3 H), 1.17 (d, *J* = 6.8 Hz, 3 H), 1.17–0.77 (m, 7 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 146.2, 142.0, 141.8, 141.5, 131.2, 129.8, 129.7, 126.9, 126.3, 124.7, 39.1, 34.1, 21.9, 21.2, 20.4, 13.9.

MS (ESI): *m*/*z* (%) = 287 ([M + H$^+$], 100), 229 (53), 207 (10).

HRMS: *m*/*z* [M + H$^+$] calcd for $C_{18}H_{23}OS$: 287.1454; found: 287.146.

(*R*)-2-Phenylhexane (6)[17]

Over a soln of the sulfoxide **5** (+ **5′**) (0.05 mmol) in THF (5 mL) at 0 °C was added *n*-BuLi (0.5 mmol). After 10 min the mixture was hydrolyzed with sat. NH_4Cl (5 mL), extracted with Et_2O (3 × 5 mL) and the solvent was eliminated under reduced pressure. The residue oil was purified by flash chromatography (pentane) to give **6**; yield: 60%.

$[\alpha]_D^{20}$ –97.7 (*c* 0.1, EtOH). The negative sign of the specific optical rotation matched with that described in the literature[4] for the *R*-enantiomer.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.01 (m, 5 H), 2.66–2.58 (m, 1 H), 1.55–1.11 (m, 6 H), 1.22 (m, 3 H), 0.85 (m, 3 H).

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