Available online at www.sciencedirect.com
SCIENCE DIRECT
Tetrahedron
Tetrahedron 61 (2005) 3335–3347

Nucleophilic additions of lithiated allylphenylsulfone to nitrones: experimental and theoretical investigations

Pedro Merino,* Vanni Mannucci and Tomás Tejero

Departamento de Quimica Organica, Facultad de Ciencias-ICMA, Universidad de Zaragoza, E-50009 Zaragoza, Aragon, Spain

Received 23 September 2004; revised 27 October 2004; accepted 6 January 2005

Available online 1 February 2005

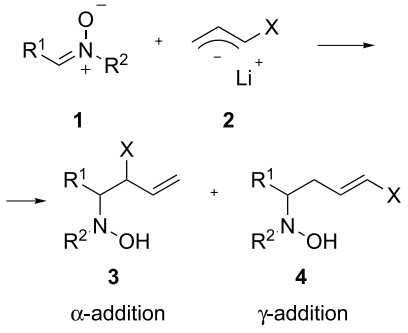
Abstract—The nucleophilic addition of lithiated allylphenylsulfone to nitrones at −80 °C proceeds exclusively α to the phenylsulfonyl group affording *anti* adducts in high yield. At 0 °C isoxazolidines are obtained with complete all-*trans* selectivity. The formation of these compounds involves isomerization of the allylsulphonyl moiety to give a transient vinylsulfone that then undergoes a subsequent intramolecular Michael addition. The addition to several nitrones has been studied and theoretical calculations have been refined to accurately explain the selectivity of the allylation reaction.

1. Introduction

Allylmetalations of imines and related compounds have proven to be of a great importance for the efficient synthesis of acyclic and cyclic amine derivatives.[1] Although the reaction of several allylic metals, including allyllithium derivatives, with imines has been extensively investigated,[2] little attention has been directed toward the allylation of nitrones Wuts and Jung[3] have reported the reaction of allylsilanes and nitrones with trimethylsilyl-triflate as a catalyst. Similarly, Trombini and co-workers[4] found that the same catalyst served to promote the condensation of allyltributylstannane with nitrones. The same authors[5] have also described the reaction of allylic magnesium and zinc reagents with nitrones to form homoallylic hydroxylamines. More recently, allylation of nitrones in aqueous media have been reported using indium[6] and samarium[7] allylic derivatives.

To date, no general studies have appeared in the literature concerning allyllithiation of nitrones **1**. A particular example has been described by Trombini and co-workers regarding the addition of a substituted lithiated derivative **2** (X=OSiMe$_2^t$Bu); however, it was reported that low chemical yields were obtained (Scheme 1).[8]

The introduction of a functional group into the allylic moiety (leading to functionalized allyllithiums **2**) would allow the preparation of hydroxyamino-containing subunits **3** or **4**, depending on the type of addition (α vs γ). In particular, α-substituted homoallylic hydroxylamines **3** should find use as important fundamental building blocks in many biologically active compounds. In extending our previous investigations on nucleophilic additions to nitrones[9] we now focus on the allylsulfonylation of nitrones. Allylic carbanions formed from the corresponding allylsulfones (X=SO$_2$R) have been widely used in organic synthesis.[10] The presence of the sulfonyl group in **3** strongly increases the synthetic potential of these compounds to be used as building blocks.[11]

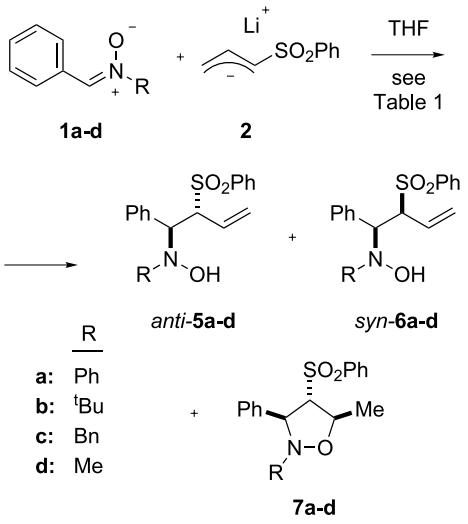


Scheme 1.

In this paper, we describe reaction of the lithiated allylphenylsulfone **2** (X=SO$_2$Ph) with nitrones **1** and the dependence of the reaction on the reaction conditions and on the substrate. The nitrones were subjected to several allylsulfonylation conditions with the purpose of finding reaction conditions suitable for the preparation of allylation

Keywords: Nitrones; Allylation; Hydroxylamines; Isoxazolidines; Allyllithium.
* Corresponding author. Tel.: +34 976 762075; fax: +34 976 762075; e-mail: pmerino@unizar.es

0040–4020/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2005.01.043



Scheme 2.

products in good regio- and stereoselective ways. Furthermore, we also describe herein a theoretical study of the possible reaction pathways associated with the addition of allylic anions to nitrones.

2. Results and discussion

For our initial studies we selected C-phenyl nitrones **1a–d** (Scheme 2) as the substrates and varied both the reaction conditions and the nature of the N-substituent. Some pertinent data are collected in Table 1.

As illustrated, the reaction of lithiated allylphenylsulfone **2** with nitrone **1a** at −80 °C and in THF as a solvent (entry 1) afforded a 54:46 mixture of products consisting of the expected hydroxylamine **5a**, coming from a α-addition to the allylic moiety and the unexpected isoxazolidine **7a**. Each compound was obtained as one stereoisomer possessing the indicated relative configuration and no traces of γ-addition were detected in the reaction mixture.[12] Compound **7** can be seen as the product of a formal [3+2] cycloaddition between the nitrone and a propenyl sulfone; however, it is possible to explain its formation in terms of a nucleophilic addition as discussed below. The addition of pre-complexing agents of the nitrone such as Et_2AlCl (entry 2) or $BF_3\cdot Et_2O$ (entry 3) did not affect the selectivity of the reaction but lower yields were obtained.

On the other hand, when the reaction was performed in the presence of a lithium coordinating agent (entries 4 and 5) the amount of isoxazolidine decreased considerably. Indeed, in the presence of HMPA the hydroxylamine **5a** was the only product of the reaction. Again, only one diastereoisomer could be detected. Interestingly, when the reaction was carried out at 0 °C only the cyclic compound **7a** was obtained (entries 6 and 7) in a complete regio- and stereoselective manner. The isoxazolidine **7a** was obtained in almost quantitative chemical yield in the absence of any additive. Replacement of the *N*-phenyl group by a *tert*-butyl group led to similar results although considerably lower chemical yields were observed (entries 8 and 9). In the case of the *N*-benzyl nitrone **1c** only one compound having an *anti* configuration was obtained at −80 °C (entry 10); at 0 °C (entry 11) a mixture of three compounds was isolated from the reaction mixture. Even though the isoxazolidine **7c** was the major product; the *anti*/*syn* selectivity was only 3:2. A similar result was observed with *N*-methyl nitrone **1d** (entries 12 and 13). Whereas the reaction at low temperature afforded a 4:1 mixture of hydroxylamines **5d** and **6d**, respectively, the reaction at 0 °C gave isoxazolidine **7d** preferentially, the hydroxylamines being obtained in a non-stereoselective way.

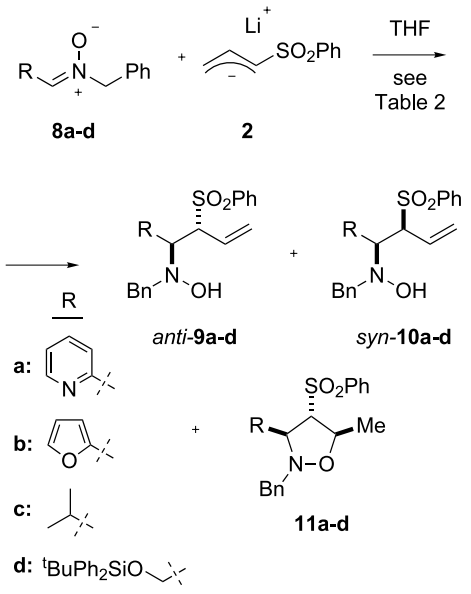
In order to establish the range of application of the allylsulfonylation of nitrones, the addition of lithiated allylphenylsulfone to other C-substituted nitrones was investigated (Scheme 3, Table 2). We chose the benzyl group for N-substitution because it can be easily eliminated by hydrogenation methods during further elaborations with synthetic purposes.

As in the case of C-phenyl nitrones **1a–d** the reaction at −80 °C in the presence of HMPA afforded exclusively hydroxylamines having an *anti* relative configuration (entries 1, 3, 5 and 7). With non-aromatic C-substituents (entries 5 and 7) lower *anti*/*syn* selectivity was observed.

Table 1. Addition of lithiated allylphenylsulfone to nitrones **1a–d**[a]

Entry	Nitrone	*T* (°C)	Additive[b]	(**5**+**6**):**7**[c]	**5**:**6**[c]	Yield (%)[d]
1	**1a**	−80	None	54:46	>20:1	80
2	**1a**	−80	Et_2AlCl[e]	40:60	>20:1	53
3	**1a**	−80	$BF_3\cdot Et_2O$[e]	55:45	>20:1	55
4	**1a**	−80	TMEDA	80:20	>20:1	63
5	**1a**	−80	HMPA	100:0	>20:1	80
6	**1a**	0	None	0:100	—	98
7	**1a**	0	HMPA	0:100	—	70
8	**1b**	−80	HMPA	100:0	>20:1	52
9	**1b**	0	None	0:100	—	46
10	**1c**	−80	HMPA	100:0	>20:1	88
11	**1c**	0	None	30:70	3:2	91
12	**1d**	−80	HMPA	100:0	4:1	80
13	**1d**	0	None	30:70	1:1	91

[a] The reaction was performed with 1.2 equiv of lithiated allylphenylsulfone, formed from 1.2 equiv of BuLi and 1.2 equiv of allylphenylsulphone, in THF.
[b] 1.0 equiv with respect to allylphenylsulfone was added unless otherwise indicated.
[c] Measured by ^{1}H NMR from the isolated reaction mixture.
[d] Referred to the isolated reaction mixture.
[e] 1.0 equiv with respect to the nitrone was added.



Scheme 3.

in a complete agreement with previous nucleophilic additions of organometallic reagents to **12**.[9b]

The formation of isoxazolidines **7**, **11** and **14** can be explained in terms of equilibrium between the hydroxyamino anion **15**, immediately formed after the addition, and the corresponding vinylsulfone **17** as displayed in Scheme 5. The isomerization between allyl and vinyl sulfones in a basic medium is well-known[13] and it has been evidenced in tandem sequences involving intramolecular Michael additions.[14]

According to the reaction pathway shown in Scheme 5, at low temperature (−80 °C) the initially formed adduct **15** is stable enough to afford the corresponding hydroxylamine after aqueous work-up. At 0 °C the equilibrium takes place and the reaction proceeds via the anionic intermediate **17** which ultimately produces **18** through an intramolecular Michael addition.[15] The presence of HMPA is crucial for avoiding isomerization of **15** even at −80 °C (compare entries 1 and 5 in Table 1). Presumably, the coordinating capabilities of HMPA block the equilibration between **15**

Table 2. Addition of lithiated allylphenylsulfone to nitrones **8a–d**[a]

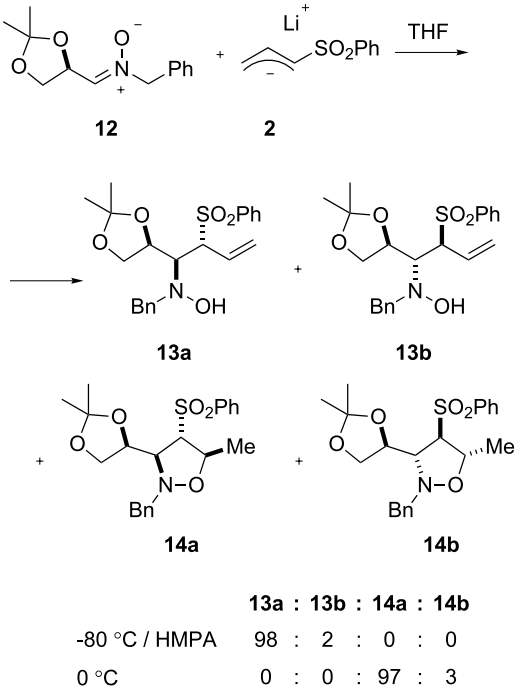
Entry	Nitrone	*T* (°C)	Additive[b]	(**9**+**10**):**11**[c]	**9**:**10**[c]	Yield (%)[d]
1	**8a**	−80	HMPA	100:0	>20:1	86
2	**8a**	0	None	15:85	2:1	87
3	**8b**	−80	HMPA	100:0	>20:1	80
4	**8b**	0	None	20:80	2:1	74
5	**8c**	−80	HMPA	100:0	6:1	69
6	**8c**	0	None	30:70	2:1	73
7	**8d**	−80	HMPA	100:0	>20:1	72
8	**8d**	0	None	0:100	—	69

[a] The reaction was performed with 1.2 equiv of lithiated allylphenylsulfone, formed from 1.2 equiv of BuLi and 1.2 equiv of allylphenylsulphone, in THF.
[b] 1.0 equiv with respect to allylphenylsulfone was added unless otherwise indicated.
[c] Measured by ^{1}H NMR from the isolated reaction mixture.
[d] Referred to the isolated reaction mixture.

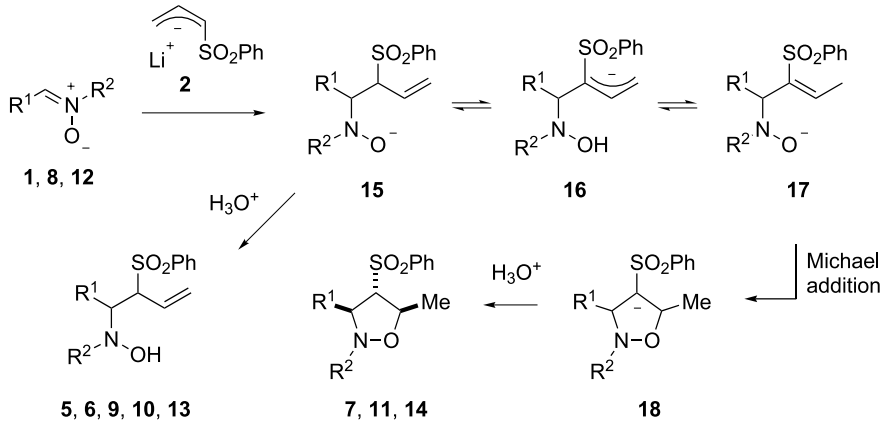
Following the same trend that nitrones **1a–d**, the reaction at 0 °C, in the absence of HMPA, gave rise to isoxazolidines **11** as major products (entries 2, 4, 6 and 8). The modest *anti*/*syn* selectivity observed for hydroxylamines **9** and **10** under these conditions was probably due to the higher temperature. Only in the case of nitrone **8d** the corresponding isoxazolidine **11d** was obtained as the only product of the reaction. It is noteworthy that in all cases only one stereoisomer of isoxazolidines **7** and **11** was obtained thus showing a complete stereoselectivity in the formation of such compounds.

Finally, we decided to explore the reactivity of a chiral substrate. For this purpose nitrone **12**, derived from D-glyceraldehyde and widely used in our laboratory,[9b] was chosen. As expected (Scheme 4), the allylsulfonylation of **12** at −80 °C afforded hydroxylamine **13a** as the main product of the reaction. At 0 °C only isoxazolidines **14a** and **14b** were obtained. The diastereofacial selectivity was also excellent; the *syn* adducts (with respect to the dioxolane ring being obtained with high levels of diastereoselectivity. Indeed, stereoisomers **13b** and **14b** were detected in minor amounts (2–3%).

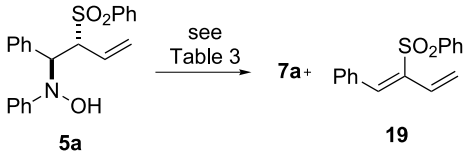
The diastereofacial selectivity observed in the reaction was



Scheme 4.



Scheme 5.



Scheme 6.

although some elimination product **19** was obtained. This product corresponds to the elimination of the *N*-benzyl hydroxyamino moiety. An excess of BuLi (entry 4) dramatically increased the amount of elimination product.

On the other hand, when hydroxylamine **5a** was treated with 1.0 equiv of potassium *tert*-butoxide (entry 5) only a minor amount of **19** was obtained, the main product of the reaction being the isoxazolidine **7a**. This behavior was also observed for other hydroxylamines. Under elimination conditions, compounds **20**–**23** were preferentially obtained and fully characterized (Chart 1). The geometry of the alkene group was established in all cases by NOESY experiments which showed cross-peaks between the terminal vinyl group and the vinylic proton of the trisubstituted alkene. In a similar way to **5a**, deprotonation with 1.0 equiv of either BuLi in the presence of 1.0 equiv of HMPA or potassium *tert*-butoxide at 0 °C afforded the corresponding

Table 3. Deprotonation of **5a**[a]

Entry	*T* (°C)	Base	Equiv[b]	**19**:**7a**[c]	Yield (%)[d]
1	−80	BuLi	1.0	—[e]	—[e]
2	−80	BuLi	1.5	—[f]	—[f]
3	0	BuLi	1.0	8:92	77
4	0	BuLi	1.5	90:10	90
5	0	^{t}BuOK[g]	1.0	4:96	85

[a] The reaction was carried out in THF in the presence of 1.0 equiv of HMPA unless otherwise indicated.
[b] With respect to **5a**.
[c] Measured by ^{1}H NMR from the isolated reaction mixture.
[d] Referred to the isolated reaction mixture.
[e] Pure hydroxylamine **5a** was recovered.
[f] A mixture of *anti* and *syn* hydroxylamines were recovered.
[g] The reaction was conducted without HMPA.

and **17** at low temperature. At 0 °C it has no effect since formation of isoxazolidine is observed anyway (Table 1, entry 7). The formation of isoxazolidines through a concerted cycloaddition reaction between the nitrone and a propenyl sulfone is not very likely since in a basic medium the latter is not present but exists as the corresponding allylic anion.[16]

In order to assess the mechanistic proposal illustrated in Scheme 5 we decided to study the deprotonation of hydroxylamine **5a** (Scheme 6, Table 3). Treatment of **5a** with 1.0 equiv of BuLi in THF at −80 °C in the presence of 1.0 equiv of HMPA, stirring for 2 h and then aqueous work-up afforded the starting compound without traces of any other stereoisomer or isoxazolidine (entry 1). This experiment clearly demonstrates the stability of **5a** at low temperature. The same experiment carried out with 1.5 equiv of BuLi (entry 2) afforded a mixture of *anti*/*syn* diastereomers proving that although a second deprotonation takes place at the α-phenylsulfonyl carbon atom no isomerization to **17** is produced. When the reaction was carried out at 0 °C (entry 3) cyclization to **7a** was observed

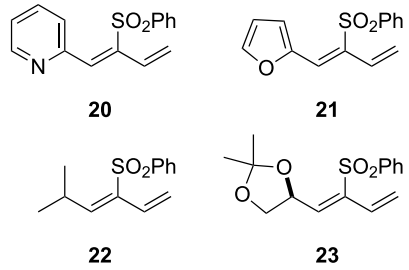


Chart 1.

Table 4. Selected coupling constants for **5a–d**, **6a–d**, **9a–c** and **10a–c**

Entry	R^1	R^2	*anti*	*syn*	$^3J_{H,H}$ (*anti*)	$^3J_{H,H}$ (*syn*)
1	Ph	Ph	**5a**	**6a**	10.0	—[a]
2	Ph	Bn	**5b**	**6b**	9.9	9.1
3	Ph	Me	**5c**	**6c**	9.8	8.5
4	Ph	^{t}Bu	**5d**	**6d**	10.0	—[a]
5	Py[b]	Bn	**9a**	**10a**	9.1	9.6
6	Fu[c]	Bn	**9b**	**10b**	10.1	9.1
7	^{i}Pr	Bn	**9c**	**10c**	10.0	8.8

[a] Not obtained.
[b] 2-Pyridyl.
[c] 2-Furyl.

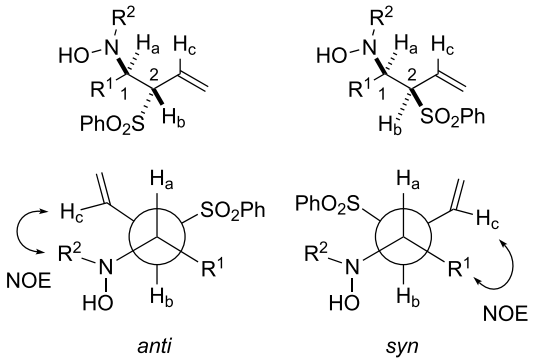


Figure 1. Preferred conformations for compounds **5a–d**, **6a–d**, **9a–c** and **10a–c**.

isoxazolidines thus confirming the mechanism outlined in Scheme 5.

The observed geometry of the newly generated double bond is in agreement with a stereospecific *syn* elimination following a concerted path for the loss of the alkylhydroxyamino unit. Such a reaction represents a retro-Michael addition of a hydroxylamine. Indeed, the corresponding direct reaction has been demonstrated to be a concerted process by Ortuño and co-workers.[17]

3. Determination of configuration

The stereochemical assignments of hydroxylamines **5a–d**, **6a–d**, **9a–c** and **10a–c** were based on NMR evidence In all cases the $^3J_{H,H}$ coupling constants between H_a and H_b (Table 4, Fig. 1) were in the range of 8.5–10.1 Hz. Those values are in agreement with the depicted *anti* and *syn* arrangements in which protons H_a and H_b adopt an antiperiplanar disposition.

Support for that conformation was secured upon cooling to −40 and −80 °C, no significant changes being observed for the ^{1}H NMR coupling patterns. This observation indicated that the solution contained almost exclusively, one single conformer with respect to the C1–C2 bond. Indeed, semiempirical calculations[18] also supported the conformational disposition shown in Figure 1 for *anti* and *syn* isomers. These observations, coupled with the 2D NOESY spectra, which showed strong NOE between the vinylic protons H_c and groups R^2 (Ph, Me, ^{t}Bu, Bn) for *anti* adducts, and between the same proton (H_c) and groups R^1 (Ph, 2-Py, 2-Fu, ^{i}Pr) for *syn* adducts indicated the assigned setereochemistry. In the case of α-alkoxyhydroxylamines **9d**, **13a** and **13b** the observed coupling constants were 4.0, 3.3 and 2.8 Hz, respectively. For these compounds the assigned relative configurations were deduced from 2D COSY, NOESY and HMQC experimental data.

Even though these assignments cannot be considered unambiguous, they are in accordance with earlier reports by Hassner and co-workers[13,19] concerning allylsulfonylation of imines and are also further supported by theoretical calculations (see below).

The *cis*/*trans* relative configuration of isoxazolidines was assigned by NOE experiments (Fig. 2). Irradiation of H_a for all obtained compounds, only produced enhancement of H_c (5–7%) and irradiation of H_b in the same experiment, produced enhancement of the methyl group (8–11%). Irradiation of the methyl group produced enhancements of H_b (8–10%) and, as expected, of H_c (15–17%). These relationships were confirmed by 2D NOESY experiments in which no interesting cross-peaks were detected between H_a and H_b, and H_b and H_c.

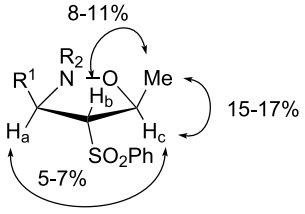


Figure 2. Selected NOE observed for **7a–d**, **11a–d** and **14** (η_{obs} is given as percent of η_{max}).

The observed pattern for the described NOE is in agreement with previous observations for substituted isoxazolidines.[20]

The structures of **7c** and **14a** were confirmed by single-crystal X ray structure determination (Fig. 3).[21] This crystallographic analysis also served to assign unambiguously the absolute configuration of both **13a** and **14a** thus confirming the *syn* diastereofacial preference in the addition to nitrone **12**

4. Theoretical study

In order to evaluate the importance of electronic and steric

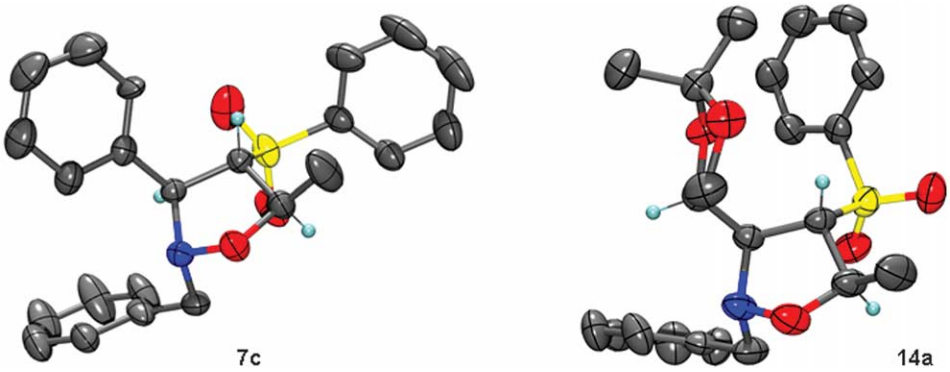
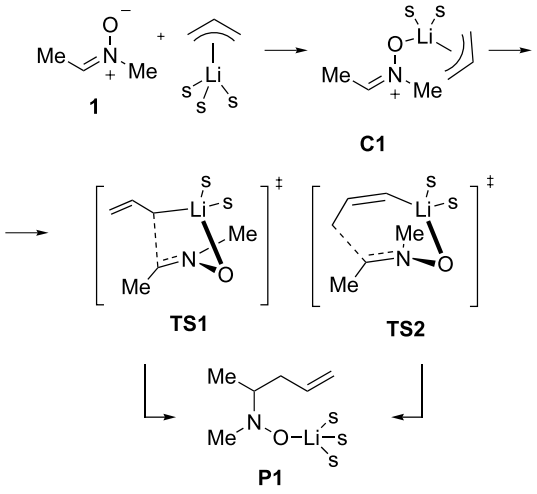


Figure 3. Perspective views (ORTEP) of **7c** and **14a**. Non-hydrogen atoms are drawn as 50% thermal ellipsoids while hydrogens are drawn at an arbitrary size. Only the atoms refined with anisotropic thermal parameters are drawn with the principal axes indicated; the isotropic atoms are represented as simple circles. Some hydrogens have been omitted for clarity.

effects in the outcome of the allylation reactions of nitrones **1** and **8** with lithiated allylphenylsulfone **2**, the reaction has been studied by ab initio molecular orbital calculations We aimed to clarify what is the preferred attack to the substituted allylic metal (α vs γ) and to rationalize the experimentally observed differences in *anti*/*syn* selectivities.

Geometry optimizations of the stationery points (reactants, transition structures and products) were carried out by using ab initio Hartree–Fock calculations with the 6-31G(d) basis set.[22] All transition structures were found to have only one negative eigenvalue with the corresponding eigenvector involving the formation of the newly created C–C bonds. Vibrational frequencies were calculated (1 atm, 298.15 K) for all HF/6-31G(d) optimized structures and used unscaled, to compute ZPVE and activation energies. The transition states reported were shown to belong to the studied reaction by intrinsic reaction coordinate (IRC). All calculations were performed using the Gaussian 03 revision B.05 suite of programs.[23]

We began our study by examining the reaction profile for the nucleophilic addition of unsubstituted allylic lithium to nitrone **1** ($R^1=R^2=Me$). In order to simulate the presence of solvent, water molecules were added when needed. The reaction proceeds through the initial formation of a starting complex without energy barrier. The formation of stable complexes without energy barriers prior to the addition step has been proposed and demonstrated previously for nucleophilic additions to nitrones[24] and carbonyls.[25] After the formation of the complex, the two possible pathways illustrated in Scheme 7 and corresponding to α and γ attacks should be considered. Thus, the reaction is expected to proceed through 'closed' transition states in which the lithium atom is transferred to the nitrone oxygen concomitant with C–C bond formation.



Scheme 7.

We found two minima corresponding to the starting complex **C1** and the product **P1**. Two transition states **TS1** and **TS2**, corresponding to α and γ attacks, respectively, connecting **C1** with **P1** were also located. The calculated free energies for reactants, complex, transition states and product are collected in Table 5, and the geometry of **TS1** and **TS2** is given in Figure 4. As shown by the energy barrier values (Table 5) the preferred transition state corresponds to the γ attack. Based upon these simplified calculations it is obvious that the presence of the sulfonyl group must be considered in order to achieve valid conclusions.

Table 5. Calculated free energies (HF/6-31G(d)) and relative free energies for the stationery points of the allylation of **1**

	Total energy[a]	Relative energy[b]
Nitrone	−246.812390	
Allyllithium·$3H_2O$	−351.913262	
C1	−522.722565	−1.43[c,d]
TS1	−522.693904	17.99[d,e]
TS2	−522.707354	9.55[d,e]
P1	−598.793418	−42.52[e]

[a] Hartrees.
[b] kcal/mol.
[c] Referred to nitrone + allyllithium·$3H_2O$.
[d] The energy corresponding to a molecule of water (−76.005368 au) has been included for comparison of relative energies.
[e] Referred to complex **C1**.

Anders and co-workers[26] have studied the structure of sulfur-stabilized allyllithium derivatives, including lithiated allylphenylsulfone **2**. These authors found three possible structures in the range of 1 kcal/mol as the more stable for **2**. Such structures correspond to the expected η^1 C_α–Li **A** and

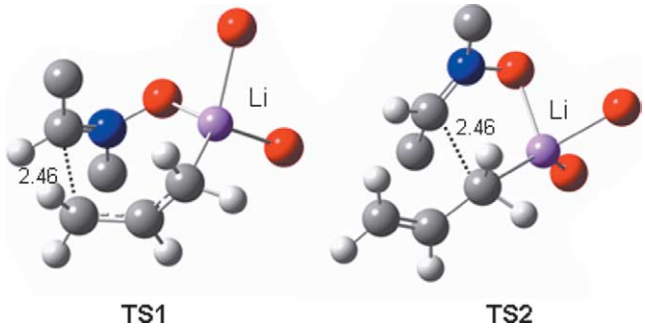


Figure 4. Optimized geometries at HF/6-31G(d) level for the transition structures **TS1** and **TS2**. Some hydrogen atoms have been omitted for clarity. Distances of forming bonds are given in angstroms.

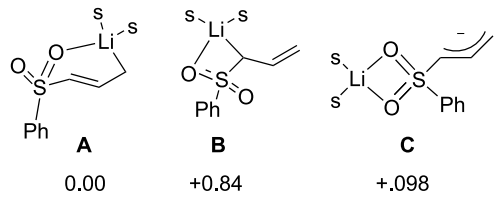


Figure 5. Energetically stable conformers found for lithiated allylphenylsulfone **2**. Relative energies are given in kcal/mol. (Data taken from Ref. 26).

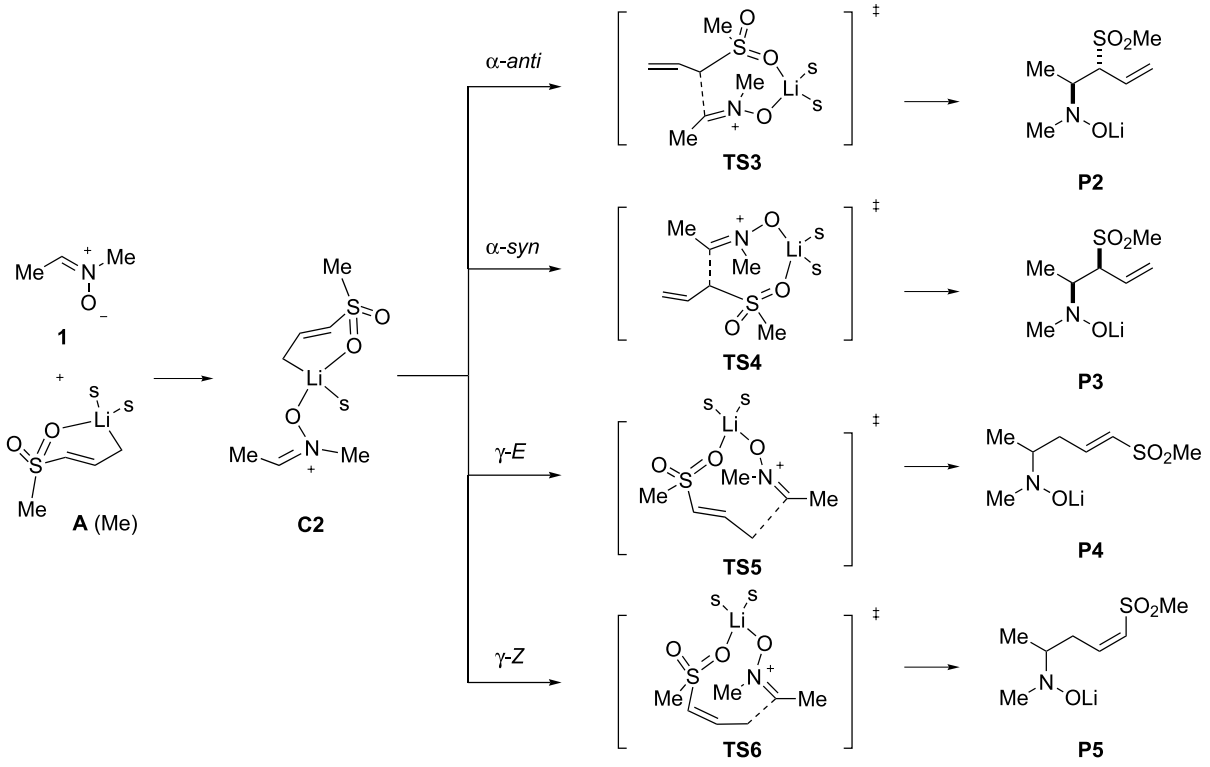
η^1C_γ–Li **B** contacted ion pairs (Fig. 5) and, in addition, an intramolecular OLiO scissor contact ion pair **C** that is defined by the authors as a 'naked' allyl anion.

We initially use in our studies structure **A** as the nucleophile to be added to **1**.[27] The calculated reaction paths are depicted in Scheme 8. The total and relative free energies are summarized in Table 6.

The first step corresponds to the formation of a stable complex **C2** (6.97 kcal/mol below the reactants) through the displacement of a molecule of solvent by the nitrone. This complex can then evolve in two ways: (i) to give an α addition affording *anti* and *syn* diastereomers **P2** and **P3**, respectively, and (ii) to give a γ addition which, in principle, could led to *E* and *Z* isomers **P4** and **P5**, respectively. The geometries of the corresponding transition structures **TS3**, **TS4**, **TS5** and **TS6** are given in Figure 6.

Contrary to the obtained data for unsubstituted allyllithium and in an excellent agreement with experimental results, the most stable transition structure corresponds to the α attack. Moreover, calculations correctly predict the preferential formation of the corresponding *anti* adduct since **TS3** presented the lowest free activation energy (13.01 kcal/mol). The calculated energy differences between α and γ attacks (**TS3** is 5.52 kcal/mol lower in energy than **TS5**) as well as the differences between *anti* and *syn* approaches (**TS3** is 8.79 kcal/mol lower in energy than **TS4**) for the α attack justify the obtention of only one isomer. The final products are lower in energy than complex **C2**, indicating an exothermic transformation.

The geometries of the transition states are similar regardless of the approach. It is noteworthy that although we started from the most stable isomer of lithiated methylsulfone (**A**, Fig. 5), all transition states present a geometry (Fig. 6) nearest to the 'naked' anion defined by Anders and coworkers[25] (**C**, Fig. 5) thus evidencing the crucial role of the



Scheme 8.

Table 6. Calculated free energies and relative free energies (HF/6-31G(d)) for the stationery points of the allylphenylsulfonylation of **1**

	Total energy[a]	Relative energy[b]
Nitrone	−246.812390	
A (Me)	−862.118716	
C2	−1032.936849	−6.97[c,d]
TS3	−1108.921484	13.010154[d,e]
TS4	−1108.907476	21.800308[d,e]
TS5	−1108.914279	17.531360[d,e]
TS6	−1108.911434	19.316625[d,e]
P2	−1108.945702	−2.18687[e]
P3	−1108.950959	−5.485688[e]
P4	−1108.954456	−7.680089[e]
P5	−1108.948299	−3.816513[e]

[a] Hartrees.
[b] kcal/mol.
[c] Referred to nitrone + lithiated allylmethylsulfone **A**·$3H_2O$.
[d] The energy corresponding to a molecule of water (−76.005368 au) has been included for comparison of relative energies.
[e] Referred to complex **C2**.

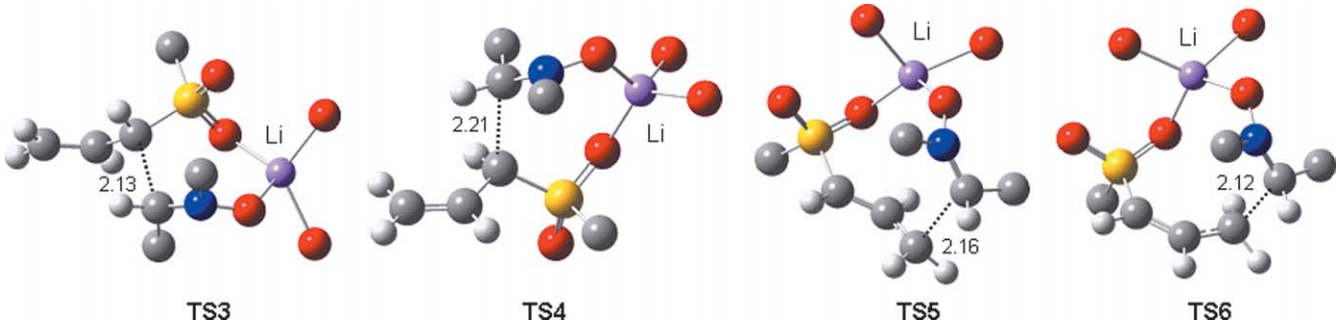


Figure 6. Optimized geometries at HF/6-31G(d) level for the transition structures **TS3**, **TS4**, **TS5** and **TS6**. Some hydrogen atoms have been omitted for clarity. Distances of forming bonds are given in angstroms.

phenylsulfonyl group in favoring the α-addition. The bond lengths of the C–C forming bonds do not change significantly, whether the approach is α-*anti* (**TS3**, 2.13 Å), γ-*E* (**TS5**, 2.16 Å), or γ-*Z* (**TS6**, 2.12 Å). Only a slightly longer forming bond is found for the α-*syn* approach (**TS4**, 2.21 Å).

5. Conclusions

In conclusion, we have studied in detail the nucleophilic addition of lithiated allylphenylsulfone **2** to nitrones The reaction only leads to α-adducts. Thus α-sulfonyl homoallyl hydroxylamines having an *anti* relative configuration are exclusively obtained when the reaction is carried out at −80 °C and in the presence of HMPA. These products are stable, but upon treatment with BuLi at 0 °C they cyclized to isoxazolidines in a process involving isomerization of the double bond and an intramolecular Michael addition. Indeed, it is possible to obtain such isoxazolidines by carrying out the addition of **2** at 0 °C. On the contrary, an excess of base favors a side reaction consisting of elimination of the hydroxyamino group, giving rise to 2-phenylsulfonyl dienes. The observed regio- and stereochemical results are well explained by means of computational methods, which correctly predict both the α-attack and the preferential *anti* selectivity.

6. Experimental

6.1. General

The reaction flasks and other glass equipment were heated in an oven at 130 °C overnight and assembled in a stream of Ar. All reactions were monitored by TLC on silica gel 60 F254; the position of the spots were detected with 254 nm UV light or by spraying with one of the following staining systems: 50% methanolic sulfuric acid, 5% ethanolic phosphomolybdic acid and iodine Preparative centrifugally accelerated radial thin-layer chromatography (radial chromatography) was performed with a Chromatotron® Model 7924 T (Harrison Research, Palo Alto, CA, USA) and with solvents that were distilled prior to use; the rotors (1 or 2 mm layer thickness) were coated with silica gel Merck grade type 7749, TLC grade, with binder and fluorescence indicator (Aldrich 34,644-6) and the eluting solvents were delivered by the pump at a flow-rate of 0.5–1.5 mL min^{-1}. Melting points were uncorrected. IR spectra were recorded on a Perkin–Elmer FT IR instrument in $CHCl_3$. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance 400 instrument in $CDCl_3$. Chemical shifts are reported in ppm (δ) relative to $CHCl_3$ ($\delta=7.26$) in $CDCl_3$. Optical rotations were taken at 25 °C on a Perkin–Elmer 241 polarimeter. Elemental analysis were performed on a Perkin–Elmer 240B microanalyzer. Nitrones **1**, **8** and **12** were prepared from the corresponding aldehydes as described.[28]

6.2. General procedure for the allylphenylsulfonylation of nitrones at −80 °C. Synthesis of homoallyl hydroxylamines

To a cooled (−80 °C) solution of *n*-BuLi (1.33 mL of a 1.6 M solution in hexanes, 1.2 mmol) in anhydrous THF (5 mL) a solution of allylphenylsulfone (0.218 g, 1.2 mmol) and HMPA (0.215 g, 1.2 mmol) in THF (5 mL) was added dropwise. After 30 min a solution of nitrone (1 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred at −80 °C for 2 h at which time the reaction was quenched by adding saturated aq NH_4Cl (1 mL). The reaction mixture was extracted with EtOAc (3×30 mL). The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated. The crude material was purified by radial chromatography using 4:1 hexane/ethyl acetate as an eluent.

6.2.1. (3*R,4*S**)-4-Phenyl-4-(*N*-phenylhydroxyamino)-3-(phenylsulfonyl)-1-butene 5a.** Oil; δ_H (400 MHz, $CDCl_3$) 4.70 (dd, 1H, $J=9.4$, 10.0 Hz), 4.81 (d, 1H, $J=11.0$ Hz), 4.89 (d, 1H, $J=17.0$ Hz), 5.03 (d, 1H, $J=10.0$ Hz), 5.52 (ddd, 1H, $J=9.4$, 11.0, 17.0 Hz), 5.90 (bs, 1H, ex. D_2O), 6.80 (m, 1H), 6.84 (m, 2H), 7.10 (m, 7H), 7.56 (m, 2H), 7.62 (m, 1H), 7.98 (m, 2H); δ_C (100 MHz, $CDCl_3$) 69.3, 71.4, 116.8, 121.8 (2C), 125.4, 127.9 (2C), 128.1, 128.4, 128.5 (2C), 128.8 (2C), 129.3 (4C), 133.8, 134.2, 138.3, 149.7. IR ν 1140, 1230, 1300 cm^{-1}. Anal. Calcd for $C_{22}H_{21}NO_3S$ (379.47): C, 69.63; H, 5.58; N, 3.69. Found: C 69.45, H, 5.80, N, 3.70.

6.2.2. (3*R,4*S**)-4-(*N*-*tert*-Butylhydroxyamino)-4-phenyl-3-(phenylsulfonyl)-1-butene 5b.** Oil; δ_H (400 MHz, $CDCl_3$) 1.12 (s, 9H), 4.02 (d, 1H, $J=10.0$ Hz), 4.52 (t, 1H, $J=9.9$ Hz), 4.68 (d, 1H, $J=17.0$ Hz), 5.00 (d, 1H, $J=10.1$ Hz), 5.20 (bs, 1H, ex. D_2O), 5.25 (dt, 1H, $J=$ 10.0, 17.0 Hz), 7.29 (m, 5H), 7.58 (m, 2H), 7.70 (m, 1H), 7.88 (m, 2H); δ_C (100 MHz, $CDCl_3$) 25.4, 59.6, 70.5, 71.5, 122.1, 128.2, 128.3 (2C), 128.5 (2C), 129.0 (2C), 128.9, 129.9 (2C), 132.1, 133.0, 139.3. IR ν 1135, 1220, 1290 cm^{-1}. Anal. Calcd for $C_{20}H_{25}NO_3S$ (359.48): C, 66.82; H, 7.01; N, 3.90. Found: C 66.70, H, 7.16, N, 3.77.

6.2.3. (3*R,4*S**)-4-(*N*-Benzylhydroxyamino)-4-phenyl-3-(phenylsulfonyl)-1-butene 5c.** Oil; δ_H (400 MHz, $CDCl_3$) 3.57 (s, 2H), 4.28 (d, 1H, $J=9.9$ Hz), 4.51 (t, 1H, $J=$ 9.9 Hz), 4.64 (d, 1H, $J=16.9$ Hz), 4.83 (d, 1H, $J=10.4$ Hz), 5.37 (dt, 1H, $J=9.9$, 16.9 Hz), 5.55 (bs, 1H, ex. D_2O), 7.30 (m, 10H), 7.45 (m, 2H), 7.59 (m, 1H), 7.84 (m, 2H); δ_C (100 MHz, $CDCl_3$) 61.0, 69.5, 71.9, 124.7, 128.1, 128.2 (2C), 128.3 (2C), 128.7 (2C), 128.9, 129.0 (2C), 129.1 (2C), 130.0 (2C), 133.2, 134.8, 137.5, 138.7, 138.9. IR ν 1145, 1230, 1310 cm^{-1}. Anal. Calcd for $C_{23}H_{23}NO_3S$ (393.50): C, 70.20; H, 5.89; N, 3.56. Found: C 70.33, H, 5.91, N, 3.38.

6.2.4. (3*S,4*S**)-4-(*N*-Benzylhydroxyamino)-4-phenyl-3-(phenylsulfonyl)-1-butene 6c.** Oil; δ_H (400 MHz, $CDCl_3$) 3.53 (d, 1H, $J=14.2$ Hz), 3.57 (d, 1H, $J=14.2$ Hz), 4.13 (dd, 1H, $J=9.1$, 10.1 Hz), 4.51 (d, 1H, $J=9.1$ Hz), 4.87 (d, 1H, $J=17.0$ Hz), 4.90 (bs, 1H, ex. D_2O), 5.25 (dd, 1H, $J=$ 1.3, 10.1 Hz), 6.11 (dt, 1H, $J=10.1$, 17.0 Hz), 7.25 (m, 10H), 7.46 (m, 2H), 7.60 (m, 1H), 7.78 (m, 2H); δ_C (100 MHz, $CDCl_3$) 61.2, 69.1, 70.5, 123.7, 128.2 (2C), 128.3, 128.4 (2C), 128.5, 128.6 (2C), 128.9, 129.0 (2C), 129.1, 129.7, 129.9, 133.2 (2C), 137.9, 138.5, 138.9. IR ν 1145, 1225, 1290 cm^{-1}. Anal. Calcd for $C_{23}H_{23}NO_3S$ (393.50): C, 70.20; H, 5.89; N, 3.56. Found: C 70.45, H, 5.68, N, 3.49.

6.2.5. (3*R,4*S**)-4-(*N*-Methylhydroxyamino)-4-phenyl-3-(phenylsulfonyl)-1-butene 5d.** White solid; mp 115–116 °C; δ_H (400 MHz, $CDCl_3$) 2.43 (s, 3H), 4.14 (d, 1H, $J=$ 9.8 Hz), 4.53 (t, 1H, $J=9.8$ Hz), 4.75 (d, 1H, $J=16.8$ Hz), 4.94 (d, 1H, $J=10.2$ Hz), 5.46 (dt, 1H, $J=10.2$, 16.8 Hz), 5.83 (bs, 1H, ex. D_2O), 7.31 (m, 5H), 7.54 (m, 2H), 7.62 (m, 1H), 7.92 (m, 2H); δ_C (100 MHz, $CDCl_3$) 44.7, 71.1, 71.8, 123.8, 128.1 (2C), 128.2, 128.6 (2C), 129.2 (2C), 129.9, 130.4 (2C), 133.2, 133.6, 138.7. IR ν 1140, 1235, 1310 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_3S$ (317.40): C, 64.33; H, 6.03; N, 4.41. Found: C 64.42, H, 5.87, N, 4.63.

6.2.6. (3*S,4*S**)-4-(*N*-Methylhydroxyamino)-4-phenyl-3-(phenylsulfonyl)-1-butene 6d.** Oil; δ_H (400 MHz, $CDCl_3$) 2.38 (s, 3H), 4.06 (dd, 1H, $J=8.6$, 10.1 Hz), 4.31 (d, 1H, $J=8.6$ Hz), 4.84 (d, 1H, $J=17.2$ Hz), 5.1 (bs, 1H, ex. D_2O), 5.25 (dd, 1H, $J=1.3$, 10.1 Hz), 6.07 (dt, 1H, $J=10.1$, 17.2 Hz), 7.21 (m, 5H), 7.34 (m, 2H), 7.46 (m, 1H), 7.63 (m, 2H); δ_C (100 MHz, $CDCl_3$) 45.7, 71.3, 74.4, 124.1, 128.1 (2C), 128.4, 128.6 (2C), 128.9 (2C), 129.4, 129.9 (2C), 133.3, 135.3, 138.8. IR ν 1145, 1230, 1290 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_3S$ (317.40): C, 64.33; H, 6.03; N, 4.41. Found: C 64.51, H, 6.23, N, 4.70.

6.2.7. (3*R,4*S**)-4-(*N*-Benzylhydroxyamino)-4-(2-pyridyl)-3-(phenylsulfonyl)-1-butene 9a.** Oil; δ_H (400 MHz, $CDCl_3$) 3.55, (d, 1H, $J=13.6$ Hz), 3.69 (d, 1H, $J=13.6$ Hz), 4.48 (d, 1H, $J=9.1$ Hz), 4.70 (t, 1H, $J=9.3$ Hz), 4.80 (d, 1H, $J=16.9$ Hz), 4.89 (dd, 1H, $J=1.1$, 10.3 Hz), 5.39 (dt, 1H, $J=10.3$, 16.9 Hz), 6.67 (bs, 1H, ex. D_2O), 7.30 (m, 7H), 7.51 (m, 2H), 7.60 (m, 1H), 7.83 (m, 2H), 7.90 (m, 1H), 8.45 (m, 1H). δ_C (100 MHz, $CDCl_3$) 57.4, 69.3, 70.8, 123.1, 123.5, 123.7, 128.2 (2C), 128.5, 128.6 (2C), 129.4 (2C), 129.6 (2C), 133.4, 136.4, 136.5, 137.4, 138.3, 148.6, 156.2. IR ν 1135, 1235, 1285 cm^{-1}. Anal. Calcd for $C_{22}H_{22}N_2O_3S$ (359.48): C, 66.98; H, 5.62; N, 7.10. Found: C 66.81, H, 5.44, N, 7.32.

6.2.8. (3*S,4*S**)-4-(*N*-Benzylhydroxyamino)-4-(2-pyridyl)-3-(phenylsulfonyl)-1-butene 10a.** Oil; δ_H (400 MHz, $CDCl_3$) 3.44 (d, 1H, $J=13.4$ Hz), 3.75 (d, 1H, $J=13.4$ Hz), 4.51 (d, 1H, $J=9.6$ Hz), 4.67 (t, 1H, $J=9.9$ Hz), 4.94 (d, 1H, $J=17.2$ Hz), 5.21 (dd, 1H, $J=1.2$, 10.1 Hz), 6.01 (dt, 1H, $J=10.1$, 17.2 Hz), 6.70 (bs, 1H, ex. D_2O), 7.29 (m, 7H), 7.48 (m, 2H), 7.58 (m, 1H), 7.81 (m, 2H), 7.90 (m, 1H), 8.44 (m, 1H).; δ_C (100 MHz, $CDCl_3$) 61.0, 66.6, 72.1, 123.2, 123.6, 123.7, 128.2, 128.3 (2C), 128.6 (2C), 128.9 (2C), 129.0 (2C), 133.8, 136.4 (2C), 137.6, 138.2, 148.7, 156.1. IR ν 1145, 1235, 1310 cm^{-1}. Anal. Calcd for $C_{22}H_{22}N_2O_3S$ (359.48): C, 66.98; H, 5.62; N, 7.10. Found: C 66.79, H, 5.83, N, 7.25.

6.2.9. (3*R,4*S**)-4-(*N*-Benzylhydroxyamino)-4-(2-furyl)-3-(phenylsulfonyl)-1-butene 9b.** Oil; δ_H (400 MHz, $CDCl_3$) 3.64 (d, 1H, $J=13.6$ Hz), 3.69 (d, 1H, $J=$ 13.6 Hz), 4.37 (d, 1H, $J=10.1$ Hz), 4.50 (t, 1H, $J=$ 9.8 Hz), 4.81 (d, 1H, $J=17.2$ Hz), 4.94 (dd, 1H, $J=0.9$, 10.1 Hz), 5.46 (dt, 1H, $J=9.9$, 17.2 Hz), 5.50 (bs, 1H, ex. D_2O), 6.27 (dd, 1H, $J=0.8$, 3.2 Hz), 6.30 (dd, 1H, $J=1.8$, 3.2 Hz), 7.30 (m, 5H), 7.32 (dd, 1H, $J=0.8$, 1.8 Hz), 7.40 (m, 2H), 7.51 (m, 1H), 7.79 (m, 2H); δ_C (100 MHz, $CDCl_3$) 60.9, 63.1, 70.5, 110.2, 111.1, 124.4, 127.3 (2C), 128.3 (2C), 128.4, 128.7 (2C), 129.1 (2C), 129.2, 133.5, 137.1, 138.7, 142.6, 148.8. IR ν 1130, 1245, 1310 cm^{-1}. Anal. Calcd for $C_{21}H_{21}NO_4S$ (383.46): C, 65.78; H, 5.52; N, 3.65. Found: C 65.59, H, 5.78, N, 3.44.

6.2.10. (3*S,4*S**)-4-(*N*-Benzylhydroxyamino)-4-(2-furyl)-3-(phenylsulfonyl)-1-butene 10b.** Oil; δ_H (400 MHz, $CDCl_3$) 3.60 (s, 2H), 4.30 (dd, 1H, $J=9.1$, 9.9 Hz), 4.56 (d, 1H, $J=9.1$ Hz), 4.70 (bs, 1H, ex. D_2O), 5.02 (d, 1H, $J=16.8$ Hz), 5.27 (dd, 1H, $J=1.1$, 10.1 Hz), 6.02 (dt, 1H, $J=10.1$, 16.8 Hz), 6.24 (dd, 1H, $J=1.8$, 3.2 Hz), 6.26 (dd, 1H, $J=0.8$, 3.2 Hz), 7.30 (m, 5H), 7.33 (dd, 1H, $J=0.8$, 1.8 Hz), 7.43 (m, 2H), 7.55 (m, 1H), 7.72

(m, 2H); δ_C (100 MHz, $CDCl_3$) 61.1, 61.4, 72.3, 110.6, 111.1, 123.7, 127.5 (2C), 128.4 (2C), 128.7 (2C), 129.0, 129.2 (2C), 129.6, 133.4, 137.1, 138.4, 142.4, 148.5. IR ν 1125, 1240, 1310 cm^{-1}. Anal. Calcd for $C_{21}H_{21}NO_4S$ (383.46): C, 65.78; H, 5.52; N, 3.65. Found: C 65.84, H, 5.41, N, 3.89.

6.2.11. (3*R,4*S**)-4-(*N*-Benzylhydroxyamino)-5-methyl-3-(phenylsulfonyl)-1-hexene 9c.** Oil; δ_H (400 MHz, $CDCl_3$) 0.98 (d, 6H, J=7.0 Hz), 1.80 (m, 1H), 3.52 (t, 1H, J=10.0 Hz), 3.56 (d, 1H, J=13.4 Hz), 3.61 (d, 1H, J=13.4 Hz), 4.30 (t, 1H, J=9.4 Hz), 4.88 (d, 1H, J=16.9 Hz), 5.20 (d, 1H, J=10.1 Hz), 5.40 (bs, 1H, ex. D_2O), 5.47 (dt, 1H, J=10.1, 16.9 Hz), 7.28 (m, 5H), 7.40 (m, 2H), 7.58 (m, 1H), 7.80 (m, 2H); δ_C (100 MHz, $CDCl_3$) 20.1 (2C), 26.1, 61.4, 63.2, 72.1, 123.6, 127.9, 128.6 (2C), 128.8 (2C), 129.0 (2C), 129.4 (2C), 130.1, 133.6, 133.8, 138.2. IR ν 1135, 1240, 1285 cm^{-1}. Anal. Calcd for $C_{20}H_{25}NO_3S$ (359.48): C, 66.82; H, 7.01; N, 3.90. Found: C 66.69, H, 7.17, N, 3.83.

6.2.12. (3*S,4*S**)-4-(*N*-Benzylhydroxyamino)-5-methyl-3-(phenylsulfonyl)-1-hexene 10c.** Oil; δ_H (400 MHz, $CDCl_3$) 1.00 (d, 6H, J=6.8 Hz), 1.72 (m, 1H), 3.58 (dd, 1H, J=8.8, 10.0 Hz), 3.60 (s, 2H), 4.47 (dd, 1H, J=4.8, 8.8 Hz), 4.92 (d, 1H, J=17.2 Hz), 5.30 (d, 1H, J=10.4 Hz), 5.62 (bs, 1H, ex. D_2O), 5.94 (dt, 1H, J=10.4, 17.2 Hz), 7.25 (m, 5H), 7.43 (m, 2H), 7.61 (m, 1H), 7.84 (m, 2H); δ_C (100 MHz, $CDCl_3$) 19.8 (2C), 25.2, 61.6, 62.9, 72.4, 123.8, 128.2, 128.4 (2C), 128.7 (2C), 128.9 (2C), 129.3 (2C), 132.4, 133.4, 133.9, 138.4. IR ν 1130, 1220, 1320 cm^{-1}. Anal. Calcd for $C_{20}H_{25}NO_3S$ (359.48): C, 66.82; H, 7.01; N, 3.90. Found: C 66.70, H, 6.88, N, 3.95.

6.2.13. (2*S,3*R**)-2-(*N*-Benzylhydroxyamino)-1-*O*-(*tert*-butyldiphenylsilyl)-3-(phenylsulfonyl)-4-penten-1-ol 9d.** Oil; δ_H (400 MHz, $CDCl_3$) 1.00 (s, 9H), 3.78 (d, 1H, J=13.6 Hz), 3.82 (m, 2H), 3.90 (dd, 1H, J=4.0, 10.4 Hz), 3.95 (d, 1H, J=13.6 Hz), 4.12 (dd, 1H, J=4.3, 9.6 Hz), 4.60 (bs, 1H, ex. D2O), 4.77 (d, 1H, J=17.2 Hz), 5.17 (dd, 1H, J=1.2, 10.1 Hz), 6.02 (dt, 1H, J=10.1, 17.2 Hz), 7.35 (m, 12H), 7.53 (m, 2H), 7.60 (m, 4H), 7.75 (m, 2H); δ_C (100 MHz, $CDCl_3$) 19.2, 26.8 (3C), 59.4, 62.3, 65.3, 71.3, 124.3, 127.6, 127.8 (2C), 127.9 (2C), 128.0, 128.3 (2C), 128.6 (2C), 129.0 (2C), 129.1, 129.9, 130.0, 130.1, 133.4, 135.3, 135.6, 135.7 (4C), 137.8, 138.2. IR ν 1145, 1240, 1315 cm^{-1}. Anal. Calcd for $C_{34}H_{39}NO_4SSi$ (585.83): C, 69.71; H, 6.71; N, 2.39. Found: C 69.93, H, 6.90, N, 2.51.

6.2.14. (2*S*,3*S*,4*R*)-3-(*N*-Benzylhydroxyamino)-1,2-di-*O*-isopropylidene-4-(phenylsulfonyl)-5-hexen-1,2-diol 13a. Oil; $[\alpha]_D^{20}$ = +35 (*c* 0.45, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.31 (s, 3H), 1.39 (s, 3H), 3.59 (dd, 1H, J=3.3, 10.1 Hz), 3.70 (dd, 1H, J=7.3, 8.6 Hz), 3.91 (dd, 1H, J=6.7, 8.6 Hz), 3.96 (dd, 1H, J=3.3, 7.1 Hz), 4.04 (d, 1H, J=13.9 Hz), 4.27 (d, 1H, J=13.9 Hz), 4.61 (pseudo q, 1H, J=7.1 Hz), 4.72 (bs, 1H, ex. D_2O), 4.82 (d, 1H, J=16.9 Hz), 5.22 (dd, 1H, J=1.0, 10.1 Hz), 6.13 (dt, 1H, J=10.1, 16.9 Hz), 7.29 (m, 3H), 7.34 (m, 2H), 7.41 (m, 2H), 7.53 (m, 1H), 7.74 (m, 2H); δ_C (100 MHz, $CDCl_3$) 25.3, 26.8, 63.7, 65.2, 66.6, 71.0, 73.2, 109.1, 124.6, 127.3, 128.3 (2C), 128.7 (2C), 129.2 (2C), 129.4 (2C), 133.5, 138.3 (2C), 143.3. IR ν 1135, 1240, 1300 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_5S$ (417.52): C, 63.29; H, 6.52; N, 3.35. Found: C 63.05, H, 6.36, N, 3.49.

6.2.15. (2*S*,3*S*,4*S*)-3-(*N*-Benzylhydroxyamino)-1,2-di-*O*-isopropylidene-4-(phenylsulfonyl)-5-hexen-1,2-diol 13b. Oil; $[\alpha]_D^{20}$ = −8 (*c* 0.32, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.26 (s, 3H), 1.34 (s, 3H), 3.70 (dd, 1H, J=2.8, 8.4 Hz), 3.89 (d, 1H, J=13.6 Hz), 3.95 (dd, 1H, J=6.6, 8.6 Hz), 4.03 (d, 1H, J=13.6 Hz), 4.07 (dd, 1H, J=6.3, 8.6 Hz), 4.32 (m, 2H), 4.65 (bs, 1H, ex. D_2O), 5.00 (dd, 1H, J=1.2, 17.2 Hz), 5.22 (dd, 1H, J=1.3, 10.1 Hz), 5.97 (dt, 1H, J=10.1, 17.2 Hz), 7.32 (m, 5H), 7.41 (m, 2H), 7.53 (m, 1H), 7.74 (m, 2H); δ_C (100 MHz, $CDCl_3$) 25.5, 26.3, 63.9, 68.2, 69.0, 70.2, 71.3, 109.5, 124.3, 127.4, 128.5 (2C), 128.8 (2C), 129.0 (2C), 129.7 (2C), 133.4, 138.5 (2C), 142.0. IR ν 1140, 1210, 1280 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_5S$ (417.52): C, 63.29; H, 6.52; N, 3.35. Found: C 63.11, H, 6.67, N, 3.52.

6.3. General procedure for the allylphenylsulfonylation of nitrones at 0 °C. Synthesis of isoxazolidines

To a cooled (−80 °C) solution of *n*-BuLi (1.33 mL of a 1.6 M solution in hexanes, 1.2 mmol) in anhydrous THF (5 mL) a solution of allylphenylsulfone (0.218 g, 1.2 mmol) in THF (5 mL) was added dropwise. After 30 min the resulting mixture was warmed to 0 °C and a solution of nitrone (1 mmol) in THF (5 mL) was added dropwise. The reaction mixture was stirred at 0 °C for 2 h at which time the reaction was quenched by adding saturated aq NH_4Cl (1 mL). The reaction mixture was extracted with EtOAc (3×30 mL). The combined organic extract was washed with brine, dried ($MgSO_4$) and concentrated. The crude material was purified by radial chromatography.

6.3.1. (3*S,4*S**,5*R**)-2,3-Diphenyl-4-(phenylsulfonyl)-5-methylisoxazolidine 7a.** Oil; δ_H (400 MHz, $CDCl_3$) 1.34 (d, 3H, J=6.1 Hz), 3.96 (t, 1H, J=5.9 Hz), 4.54 (d, 1H, J=5.6 Hz), 4.80 (pseudo quintuplet, 1H, J=6. 5 Hz), 6.94 (m, 3H), 7.29 (m, 5H), 7.50 (m, 4H), 7.61 (m, 1H), 7.82 (m, 2H); δ_C (100 MHz, $CDCl_3$) 18.4, 71.0, 75.8, 83.2, 114.3 (2C), 122.1, 126.4 (2C), 127.8, 128.8 (2C), 128.9 (2C), 129.0 (2C), 129.5 (2C), 134.3, 137.4, 140.7, 149.8. IR ν 1130, 1240, 1310 cm^{-1}. Anal. Calcd for $C_{22}H_{21}NO_3S$ (379.47): C, 69.63; H, 5.58; N, 3.69. Found: C 69.76, H, 5.72, N, 3.40.

6.3.2. (3*S,4*S**,5*R**)-2-*tert*-Butyl-3-phenyl-4-(phenylsulfonyl)-5-methylisoxazolidine 7b.** Oil; δ_H (400 MHz, $CDCl_3$) 1.01 (s, 9H), 1.32 (d, 3H, J=6.4 Hz), 3.50 (dd, 1H, J=5.5, 6.8 Hz), 4.00 (d, 1H, J=6.8 Hz), 4.10 (dq, 1H, J=5.5, 6.4 Hz), 7.33 (m, 5H), 7.55 (m, 2H), 7.62 (m, 1H), 7.81 (m, 2H); δ_C (100 MHz, $CDCl_3$) 20.4, 26.9 (3C), 59.0, 74.1, 74.8, 82.3, 127.9, 128.2 (2C), 128.5 (2C), 128.8 (2C), 129.1 (2C), 135.2, 137.9, 139.5. IR ν 1140, 1230, 1305 cm^{-1}. Anal. Calcd for $C_{20}H_{25}NO_3S$ (359.5): C, 66.82; H, 7.01; N, 3.90. Found: C 66.75, H, 7.24, N, 4.10.

6.3.3. (3*S,4*S**,5*R**)-2-Benzyl-3-phenyl-4-(phenylsulfonyl)-5-methylisoxazolidine 7c.** White solid; mp 89–90 °C; δ_H (400 MHz, $CDCl_3$) 1.30 (d, 3H, J=6.4 Hz), 3.74 (t, 1H, J=5.9 Hz), 4.05 (d, 1H, J=13.5 Hz), 4.13 (d, 1H, J=13.5 Hz), 4.44 (d, 1H, J=5.9 Hz), 4.85 (pseudo quintuplet, 1H, J=6.4 Hz), 7.20 (m, 10H), 7.52 (m, 2H), 7.65 (m, 1H), 7.88 (m, 2H); δ_C (100 MHz, $CDCl_3$) 20.3, 59.1, 70.7, 74.8, 81.9, 127.2 (2C), 127.3, 127.9, 128.3 (4C), 128.5 (2C), 128.7 (2C), 129.5 (2C), 134.2, 137.0, 138.2, 139.1. IR ν 1135, 1240, 1310 cm^{-1}. Anal. Calcd for

$C_{23}H_{23}NO_3S$ (393.5): C, 70.20; H, 5.89; N, 3.56. Found: C 70.00, H, 5.96, N, 3.39.

6.3.4. (3*S,4*S**,5*R**)-2,5-Dimethyl-3-phenyl-4-(phenylsulfonyl) isoxazolidine 7d.** White solid; mp 68–69 °C; δ_H (400 MHz, $CDCl_3$) 1.36 (d, 3H, $J=6.3$ Hz), 2.62 (s, 3H), 3.75 (dd, 1H, $J=5.1$, 7.0 Hz), 4.02 (d, 1H, $J=7.0$ Hz), 4.75 (dq, 1H, $J=5.1$, 6.3 Hz), 7.28 (m, 5H), 7.54 (m, 2H), 7.65 (m, 1H), 7.84 (m, 2H); δ_C (100 MHz, $CDCl_3$) 20.7, 42.8, 73.7, 73.9, 81.6, 127.7, 128.1 (2C), 128.4 (2C), 128.5 (2C), 129.4 (2C), 134.1, 137.7, 138.2. IR ν 1125, 1250, 1275 cm^{-1}. Anal. Calcd for $C_{17}H_{19}NO_3S$ (317.4): C, 64.33; H, 6.03; N, 4.41. Found: C 64.29, H, 6.28, N, 4.22.

6.3.5. (3*S,4*S**,5*R**)-2-Benzyl-3-(2-pyridyl)-4-(phenylsulfonyl)-5-methylisoxazolidine 11a.** Oil; δ_H (400 MHz, $CDCl_3$) 1.17 (d, 3H, $J=6.1$ Hz), 4.20 (d, 1H, $J=13.5$ Hz), 4.33 (d, 1H, $J=13.5$ Hz), 4.60 (d, 1H, $J=4.6$ Hz), 4.64 (dd, 1H, $J=4.6$, 7.1 Hz), 4.90 (dq, 1H, $J=6.1$, 7.1 Hz), 6.98 (m, 1H), 7.13 (m, 1H), 7.21 (m, 1H), 7.27 (m, 2H), 7.45 (m, 5H), 7.50 (m, 1H), 7.87 (m, 2H), 8.26 (m, 1H); δ_C (100 MHz, $CDCl_3$) 19.12, 59.8, 70.39, 75.2, 77.7, 122.5, 122.7, 127.6, 128.5 (2C), 128.6 (2C), 129.3 (2C), 129.6 (2C), 133.9, 136.5, 138.7, 138.9, 148.8, 157.8. IR ν 1145, 1250, 1300 cm^{-1}. Anal. Calcd for $C_{22}H_{22}N_2O_3S$ (394.5): C, 66.98; H, 5.62; N, 7.10. Found: C 67.12, H, 5.78, N, 6.89.

6.3.6. (3*S,4*S**,5*R**)-2-Benzyl-3-(2-furyl)-4-(phenylsulfonyl)-5-methylisoxazolidine 11b.** Oil; δ_H (400 MHz, $CDCl_3$) 1.24 (d, 3H, $J=6.1$ Hz), 3.62 (dd, 1H, $J=4.9$, 6.8 Hz), 4.40 (d, 1H, $J=13.6$ Hz), 4.51 (d, 1H, $J=13.6$ Hz), 4.77 (d, 1H, $J=4.9$ Hz), 4.98 (pseudo quintuplet, 1H, $J=6.5$ Hz), 6.25 (dd, 1H, $J=1.7$, 3.2 Hz), 6.28 (dd, 1H, $J=0.9$, 3.2 Hz), 7.30 (m, 5H), 7.34 (dd, 1H, $J=0.9$, 1.7 Hz), 7.49 (m, 2H), 7.60 (m, 1H), 7.82 (m, 2H); δ_C (100 MHz, $CDCl_3$) 21.2, 60.2, 63.6, 75.2, 81.4, 110.4, 111.3, 127.2, 127.7 (2C), 128.1 (2C), 128.9 (2C), 129.1 (2C), 133.2, 137.3, 138.5, 140.3, 149.0. IR ν 1140, 1240, 1275 cm^{-1}. Anal. Calcd for $C_{21}H_{21}NO_4S$ (383.5): C, 65.78; H, 5.52; N, 3.65. Found: C 65.62, H, 5.36, N, 3.81.

6.3.7. (3*S,4*S**,5*R**)-2-Benzyl-3-(isopropyl)-4-(phenylsulfonyl)-5-methylisoxazolidine 11c.** Oil; δ_H (400 MHz, $CDCl_3$) 0.55 (d, 3H, $J=6.8$ Hz), 0.70 (d, 3H, $J=6.6$ Hz), 0.95 (d, 3H, $J=6.1$ Hz), 2.70 (m, 1H), 3.28 (dd, 1H, $J=3.8$, 7.8 Hz), 3.36 (dd, 1H, $J=3.8$, 6.4 Hz), 4.10 (d, 1H, $J=13.2$ Hz), 4.15 (d, 1H, $J=13.2$ Hz), 4.70 (dq, 1H, $J=6.1$, 7.8 Hz), 7.32 (m, 5H), 7.55 (m, 2H), 7.64 (m, 1H), 7.80 (m, 2H); δ_C (100 MHz, $CDCl_3$) 19.8 (2C), 20.5, 27.3, 59.6, 61.7, 75.8, 80.9, 127.4, 127.5 (2C), 128.3 (2C), 128.5 (2C), 129.2 (2C), 134.1, 138.1, 138.6. IR ν 1160, 1240, 1305 cm^{-1}. Anal. Calcd for $C_{20}H_{25}NO_3S$ (359.48): C, 66.82; H, 7.01; N, 3.90. Found: C 66.65, H, 7.25, N, 4.11.

6.3.8. (3*S,4*S**,5*R**)-2-Benzyl-3-(*tert*-butyldiphenylsiloxymethyl)-4-(phenylsulfonyl)-5-methylisoxazolidine 11d.** Oil; δ_H (400 MHz, $CDCl_3$) 0.93 (s, 9H), 0.95 (d, 3H, $J=6.2$ Hz), 3.36 (dd, 1H, $J=6.1$, 10.6 Hz), 3.52 (dd, 1H, $J=6.2$, 10.6 Hz), 3.55 (dd, 1H, $J=4.3$, 7.4 Hz), 3.70 (dt, 1H, $J=4.3$, 6.1 Hz), 3.99 (d, 1H, $J=13.2$ Hz), 4.12 (d, 1H, $J=13.2$ Hz), 4.66 (dq, 1H, $J=6.2$, 7.4 Hz), 7.25 (m, 7H), 7.33 (m, 4H), 7.45 (m, 6H), 7.59 (m, 1H), 7.80 (m, 2H); δ_C (100 MHz, $CDCl_3$) 18.7, 26.9 (3C), 29.7, 64.8, 67.5, 74.3, 75.5, 79.1, 127.5, 127.8 (2C), 128.4 (4C), 129.1 (2C), 129.5 (2C), 129.6 (2C), 129.8 (2C), 133.9, 134.1 (2C), 135.6 (4C), 136.7, 139.2. IR ν 1145, 1250, 1310 cm^{-1}. Anal. Calcd for $C_{34}H_{39}NO_4SSi$ (585.8): C, 69.71; H, 6.71; N, 2.39. Found: C 69.98, H, 6.83, N, 2.12.

6.3.9. (3*S*,4*S*,5*R*)-2-Benzyl-3-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4-(phenylsulfonyl)-5-methylisoxazolidine 14a. White solid; mp 109–110 °C; $[\alpha]_D^{20}=+10$ (*c* 0.32, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 0.88 (s, 3H), 1.07 (s, 3H), 1.10 (d, 3H, $J=6.1$ Hz), 3.15 (m, 1H), 3.42 (dd, 1H, $J=2.8$, 8.6 Hz), 3.66 (dd, 1H, $J=2.8$, 7.8 Hz), 3.82 (m, 2H), 4.11 (s, 2H), 4.78 (dq, 1H, $J=6.1$, 7.8 Hz), 7.28 (m, 3H), 7.33 (m, 2H), 7.54 (m, 2H), 7.61 (m, 1H), 7.86 (m, 2H); δ_C (100 MHz, $CDCl_3$) 18.9, 25.1, 26.3, 60.0, 68.4, 69.0, 75.4, 77.0 (2C), 109.9, 128.1, 128.8 (2C), 128.9 (2C), 129.9 (2C), 130.2 (2C), 134.5, 137.1, 139.3. IR ν 1130, 1225, 1285 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_5S$ (417.5): C, 63.29; H, 6.52; N, 3.35. Found: C 63.17, H, 6.74, N, 3.49.

6.3.10. (3*R*,4*R*,5*S*)-2-Benzyl-3-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4-(phenylsulfonyl)-5-methylisoxazolidine 14b. Oil; $[\alpha]_D^{20}=-22$ (*c* 0.32, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.01 (d, 3H, $J=6.1$ Hz), 1.05 (s, 3H), 1.09 (s, 3H), 3.41 (dd, 1H, $J=3.8$, 8.1 Hz), 3.66 (dd, 1H, $J=5.8$, 8.8 Hz), 3.72 (dd, 1H, $J=3.8$, 5.8 Hz), 3.79 (dd, 1H, $J=6.8$, 8.8 Hz), 3.93 (pseudoq, 1H, $J=5.8$ Hz), 4.11 (s, 2H), 4.74 (dq, 1H, $J=6.1$, 8.1 Hz), 7.25 (m, 3H), 7.34 (m, 2H), 7.52 (m, 2H), 7.63 (m, 1H), 7.82 (m, 2H); δ_C (100 MHz, $CDCl_3$) 16.7, 23.8, 25.1, 59.4, 64.8, 66.3, 74.1, 74.7, 75.5, 108.4, 126.8, 127.6 (2C), 127.9 (2C), 128.8 (2C), 128.9 (2C), 133.5, 136.0, 137.8. IR ν 1135, 1225, 1310 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_5S$ (417.5): C, 63.29; H, 6.52; N, 3.35. Found: C 63.15, H, 6.39, N, 3.56.

6.4. General procedure for the conversion of hydroxylamines into isoxazolidines

To a cooled (0 °C) solution hydroxylamine (0.5 mmol) in THF (5 mL) *n*-BuLi (0.8 mL of a 1.6 M solution in hexanes, 0.5 mmol) was added dropwise. After 1 h the reaction was quenched by adding saturated aq NH_4Cl (1 mL). The reaction mixture was extracted with EtOAc (3×15 mL). The combined organic extract was washed with brine, dried ($MgSO_4$), concentrated and examined by ^1H NMR. The crude material was purified by radial chromatography.

To obtain elimination products preferentially the reaction was repeated using 1.5 equiv of BuLi (0.47 mL of a 1.6 M solution in hexanes, 0.75 mmol).

6.4.1. (*Z*)-4-Phenyl-3-(phenylsulfonyl)-1,3-butadiene 19. Oil; δ_H (400 MHz, $CDCl_3$) 5.40 (dt, 1H, $J=1.2$, 11.0 Hz), 5.83 (dd, 1H, $J=1.2$, 17.8 Hz), 6.31 (ddd, 1H, $J=1.2$, 11.0, 17.8 Hz), 7.32 (m, 3H), 7.44 (m, 4H), 7.51 (m, 1H), 7.82 (m, 3H), 7.81 (s, 1H); δ_C (100 MHz, $CDCl_3$) 123.9, 126.5, 128.1 (2C), 128.7 (2C), 129.0 (2C), 130.0 (2C), 130.5 (2C), 133.2, 133.4, 138.2, 138.7. IR ν 1125, 1210, 1270 cm^{-1}. Anal. Calcd for $C_{16}H_{14}O_2S$ (270.4): C, 71.08; H, 5.22. Found: C 71.17, H, 5.40.

6.4.2. (*Z*)-4-(2-Pyridyl)-3-(phenylsulfonyl)-1,3-butadiene 20. Oil; δ_H (400 MHz, $CDCl_3$) 5.36 (dt, 1H, $J=1.1$,

11.6 Hz), 5.71 (dd, 1H, J=1.0, 17.4 Hz), 6.50 (ddd, 1H, J=1.1, 11.6, 17.4 Hz), 7.40 (m, 3H), 7.54 (m, 1H), 7.80 (m, 3H), 8.3 (s, 1H), 8.6 (m, 1H); δ_C (100 MHz, $CDCl_3$) 123.8, 124.5, 128.6 (2C), 129.4 (2C), 130.0, 130.6, 132.9, 133.1, 133.3, 138.5, 139.1, 148.3, 150.2. IR ν 1115, 1200, 1275 cm^{-1}. Anal. Calcd for $C_{15}H_{13}NO_2S$ (271.33): C, 66.40; H, 4.83; N, 5.16. Found: C, 66.72; H, 4.56; N, 5.37.

6.4.3. (*Z*)-4-(2-Furyl)-3-(phenylsulfonyl)-1,3-butadiene 21. Oil; δ_H (400 MHz, $CDCl_3$) 5.40 (dt, 1H, J=1.0, 12.1 Hz), 5.90 (dd, 1H, J=1.0, 17.9 Hz), 6.46 (dd, 1H, J=2.0, 3.5 Hz), 6.74 (bd, 1H, J=3.5 Hz), 6.83 (ddd, 1H, J=1.2, 12.1, 17.9 Hz), 7.41 (m, 3H), 7.53 (m, 1H), 7.80 (m, 2H), 8.08 (s, 1H); δ_C (100 MHz, $CDCl_3$) 110.1, 122.9, 123.6, 128.5 (2C), 129.6 (2C), 130.2, 131.9, 134.3, 137.9, 139.6, 139.7, 143.0. IR ν 1135, 1225, 1250 cm^{-1}. Anal. Calcd for $C_{14}H_{12}O_3S$ (260.31): C, 64.60; H, 4.65. Found: C 64.71, H, 4.80.

6.4.4. (*Z*)-5-Methyl-3-(phenylsulfonyl)-1,3-hexadiene 22. Oil; δ_H (400 MHz, $CDCl_3$) 1.03 (d, 6H, J=6.6 Hz), 2.70 (dh, 1H, J=6.6, 10.1 Hz), 5.32 (dt, 1H, J=1.0, 11.6 Hz), 5.45 (dd, 1H, J=1.0, 17.9 Hz), 6.18 (ddd, 1H, J=1.0, 11.6, 17.9 Hz), 6.80 (d, 1H, J=10.1 Hz), 7.43 (m, 2H), 7.51 (m, 1H), 7.76 (m, 2H); δ_C (100 MHz, $CDCl_3$) 22.0 (2C), 28.1, 123.1, 125.5, 127.8 (2C), 128.9 (2C), 129.0, 133.1, 140.0, 149.4. IR ν 1110, 1220, 1260 cm^{-1}. Anal. Calcd for $C_{13}H_{16}O_2S$ (236.33): C, 66.07; H, 6.82. Found: C 65.84, H, 6.99.

6.4.5. (*Z*)-4-[(4*S*)-2,2-Dimethyl-1,3-dioxolan-4-yl]-3-(phenylsulfonyl)-1,3-butadiene 23. Oil; $[\alpha]_D^{20}=+28$ (*c* 0.26, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 1.41 (s, 3H), 1.50 (s, 3H), 3.78 (dd, 1H, J=6.9, 8.4 Hz), 4.16 (dd, 1H, J=6.4, 8.4 Hz), 4.83 (td, 1H, J=6.6, 8.3 Hz), 5.50 (m, 2H), 6.28 (dd, 1H, J=11.1, 17.9 Hz), 6.96 (d, 1H, J=8.3 Hz), 7.50 (m, 2H), 7.63 (m, 1H), 7.86 (m, 2H); δ_C (100 MHz, $CDCl_3$) 25.7, 26.6, 69.1, 72.1, 110.6, 125.1, 125.4, 128.2 (2C), 129.1 (2C), 133.4, 138.7, 139.2, 143.2. IR ν 1130, 1235, 1280 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_4S$ (294.4): C, 61.20; H, 6.16. Found: C 61.08, H, 6.30.

Acknowledgements

This work was supported by the Spanish Ministry of Science and Technology (MCYT) and FEDER Program (Project BQU2001-2428), and the Government of Aragon in Spain (Project P116-2001 and Consolidated Research Groups Program). One of us (V. M.) thanks the Spanish Ministry of Education for a grant (F.P.U. program). We also thank Mr. Vincent Terrasson and Mrs. Carole Cabrol for technical assistance and Prof. Fernando Lahoz (ICMA, University of Zaragoza-CSIC) for collecting X-ray data.

References and notes

1. (a) Yamamoto, Y.; Asoa, N. *Chem. Rev.* **1993**, *93*, 2207–2293. (b) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293–1316. (c) Merino, P.; Delso, J. I.; Mannucci, V. *Curr. Org. Synth.* **2005**, in press.
2. For recent and representative examples see (a) Andrews, P. C.; Peatt, A. C.; Raston, C. L. *Tetrahedron Lett.* **2004**, *45*, 243–248. (b) Ollevier, T.; Ba, T. *Tetrahedron Lett.* **2003**, *44*, 9003–9005. (c) Gastner, T.; Ishitani, H.; Akiyama, R.; Kobatashi, S. *Angew. Chem., Int. Ed. Engl.* **2001**, *40*, 1896–1898. (d) Sebellius, S.; Wallner, O. A.; Szabo, K. J. *Org. Lett.* **2003**, *5*, 3065–3068. (e) Cainelli, G.; Giacomini, D.; Galetti, P.; Quintavalla, A. *Eur. J. Org. Chem.* **2002**, 3153–3161. (f) Hirabayashi, R.; Ogawa, C.; Sugiura, M.; Kobayashi, S. *J. Am. Chem. Soc.* **2001**, *123*, 9493–9499. (g) Ogawa, C.; Sugiura, M.; Kobayashi, S. *J. Org. Chem.* **2002**, *67*, 5359–5364. (h) Yamasaki, J.; Fujii, K.; Wada, R.; Kanai, M.; Shibasaki, M. *J. Am. Chem. Soc.* **2002**, *124*, 6536–6537. (i) Wipf, P.; Kendall, C. *Org. Lett.* **2001**, *3*, 2773–2776. (j) Sugiura, M.; Robvieux, F.; Kobayashi, S. *Synlett* **2003**, 1749–1751. (k) Yanada, R.; Okaniwa, M.; Kaieda, A.; Ibuka, T.; Takemoto, Y. *J. Org. Chem.* **2001**, *66*, 1283–1286.
3. Wuts, P. G. M.; Jung, Y.-W. *J. Org. Chem.* **1988**, *53*, 1957–1965.
4. Gianotti, M.; Lombardo, M.; Trombini, M. *Tetrahedron Lett.* **1998**, *39*, 1643–1646.
5. Fiumana, A.; Lombardo, M.; Trombini, M. *J. Org. Chem.* **1997**, *62*, 5623–5626.
6. Kumar, H. M. S.; Anjaneyulu, S.; Reddy, E. J.; Yadav, J. S. *Tetrahedron Lett.* **2000**, *41*, 9311–9314.
7. Laskar, D. D.; Prajapati, D.; Sandhu, J. S. *Tetrahedron Lett.* **2001**, *42*, 7883–7886.
8. Lombardo, M.; Spada, S.; Trombini, C. *Eur. J. Org. Chem.* **1998**, 2361–2364.
9. (a) Merino, P. In Padwa, A., Ed.; Science of Synthesis; Thieme: Stuttgart, 2004; Vol. 27, pp 511–580. (b) Merino, P.; Franco, S.; Merchan, F. L.; Tejero, T. *Synlett* **2000**, 442–454.
10. (a) Hassner, A.; Ghera, E.; Yechezkel, T.; Kleiman, V.; Balasubramanian, T.; Ostercamp, D. *Pure Appl. Chem.* **2000**, *72*, 1671–1683. (b) Alonso, D. A.; Najera, C.; Sansano, J. M. *Tetrahedron* **1994**, *50*, 6603–6620.
11. For reviews and treatises on the synthetic potential of the sulfonyl group see (a) Biellman, J. F.; Ducep, J.-B. *Org. React.* **1982**, *27*, 1–344. (b) Uchida, Y. In *The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C. J. M., Eds.; Wiley: New York, 1988; pp 583–664. (c) Simpkins, N. S. Sulphones in Organic Synthesis; Pergamon: Oxford, 1993. (d) Najera, C.; Yus, M. *Tetrahedron* **1999**, *55*, 10547–10658.
12. It is known that carbanions derived from allylic sulphones undergo α- rather than γ-alkylation. See Ref. 11c.
13. Kumareswaran, A.; Hassner, A. *Tetrahedron: Asymmetry* **2001**, *12*, 3409–3415.
14. Dong, Z.; Pyne, S. G.; Skelton, B. W.; White, A. H. *Synlett* **1997**, 103–104.
15. The corresponding protonated **17** was not detected in any case because of the rapidity of the Michael addition.
16. We have also performed parallel studies that demonstrate the lack of reactivity between nitrone **1** and propenyl sulfone at 0 °C during 1 h. In addition, theoretical calculations show that a concerted process between a nitrone and an allylic anion is clearly disfavored.
17. Moglioni, A. G.; Muray, E.; Castillo, J. A.; Alvarez-Larena, A.; Moltrasio, G. V.; Branchadell, V.; Ortuño, R. M. *J. Org. Chem.* **2002**, *67*, 2402–2410.
18. We generate 73 different conformations by stepwise rotation

of 5° around the C1–C2 bond, and they were optimized. The heat of formation (ΔH_f) was calculated (PM3, MOPAC2000) for all these conformations and the relative and absolute minima were reoptimized. The minimum energy structure obtained in each case was essentially identical to those depicted in Figure 1.

19. (a) Hassner, A.; Kumareswaran, R. *Tetrahedron: Asymmetry* **2001**, *12*, 269–2276. (b) Kumareswaran, R.; Balasubramanian, T.; Hassner, A. *Tetrahedron Lett.* **2000**, *41*, 8157–8162.
20. Merino, P.; Franco, S.; Merchan, F. L.; Romero, P.; Tejero, T.; Uriel, S. *Tetrahedron: Asymmetry* **2003**, *14*, 3731–3743.
21. The authors have deposited the atomic coordinates for these structures with the Cambridge Crystallographic Data Centre. CCDC 250314 and CCDC 250315 contain the supplementary crystallographic data for compounds **7c** and **14a**, respectively. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033. The graphic views shown in Figure 3 were made with ORTEP3 software. Copyright by Farrugia, L. J., University of Glasgow, 1997–2000.
22. Structures were first optimized through step by step calculations using semiempirical methods (PM3) and then fully optimized at the HF/6-31G(d) level of theory.
23. Gaussian 03, revision B.05. Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Montgomery, J. A., Jr.; Vreven, T.; Kudin, K. N.; Burant, J. C.; Millam, J. M.; Iyengar, S. S.; Tomasi, J.; Barone, V.; Mennucci, B.; Cossi, M.; Scalmani, G.; Rega, N.; Petersson, G. A.; Nakatsuji, H.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Klene, M.; Li, X.; Knox, J. E.; Hratchian, H. P.; Cross, J. B.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Ayala, P. Y.; Morokuma, K.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Zakrzewski, V. G.; Dapprich, S.; Daniels, A. D.; Strain, M. C.; Farkas, O.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Ortiz, J. V.; Cui, Q.; Baboul, A. G.; Clifford, S.; Cioslowski, J.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Gonzalez, C.; Pople, J. A. Gaussian, Inc., Pittsburgh PA, 2003.
24. (a) Merino, P.; Tejero, T. *Tetrahedron* **2001**, *57*, 8125–8128. (b) Merino, P.; Tejero, T.; Revuelta, J.; Romero, P.; Cicchi, S.; Mannucci, V.; Brandi, A.; Goti, A. *Tetrahedron: Asymmetry* **2003**, *14*, 367–379.
25. (a) Safont, V. S.; Moliner, V.; Oliva, M.; Castillo, R.; Andres, J.; Gonzalez, F.; Carda, M. *J. Org. Chem.* **1996**, *61*, 3467–3475. (b) Murga, J.; Falomir, E.; Carda, M.; Marco, J. A. *Tetrahedron* **2000**, *57*, 6239–6247.
26. Piffl, M.; Weston, J.; Günter, W.; Anders, E. *J. Org. Chem.* **2000**, *65*, 5942–5950.
27. In order to simplify the calculations the phenyl group was replaced by a methyl group and the solvent was modelized by water molecules.
28. Dondoni, A.; Franco, S.; Merchan, F. L.; Merino, P.; Tejero, T. *Synth. Commun.* **1994**, *22*, 2200–2224.