JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

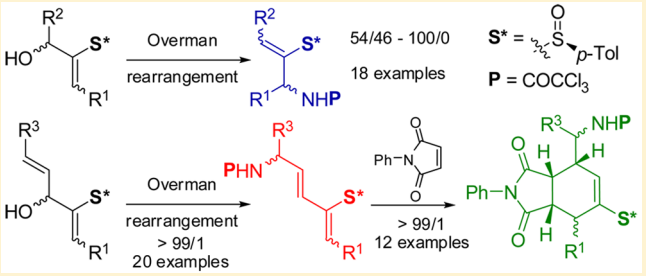
Sulfinyl-Mediated Stereoselective Overman Rearrangements and Diels–Alder Cycloadditions

Ignacio Colomer, Chirag Gheewala, Carmen Simal, Marina Velado, Roberto Fernández de la Pradilla,* and Alma Viso*

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

Supporting Information

ABSTRACT: Sulfinyl trichloroacetamides are readily obtained in excellent yields through a highly stereoselective Overman rearrangement. Related bis-allylic substrates lead to amido 2-sulfinyl butadiene derivatives in excellent yields, with total chemo- and diastereoselectivity. These amido dienyl sulfoxides undergo highly selective Diels–Alder cycloadditions with *N*-phenylmaleimide with remarkable stereocontrol by the sulfoxide moiety.



INTRODUCTION

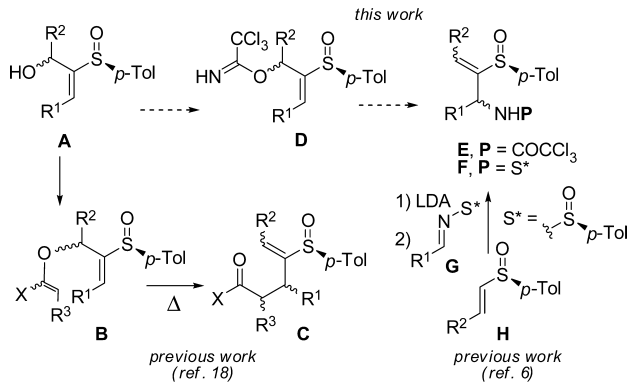
Allylic amines are valuable building blocks in different fields such as synthetic methodology,[1] applications,[2] medicinal chemistry,[3] and synthesis of natural products.[4] This importance has attracted the attention of synthetic chemists to devise routes to produce these compounds efficiently. The addition to imine derivatives of suitable nucleophiles is a popular approach for instance by means of Morita–Baylis–Hillman protocols,[5] generally limited to electron-deficient alkenes unsubstituted at the terminal position. The condensation between sulfinimines and α-lithiated vinyl or dienyl sulfoxides gives rise to enantiopure *N*-sulfinyl allylic amines.[6] The reductive coupling of alkynes with imines is also a valuable variant of the imine electrophile theme.[7]

Another general strategy to allylic amines relies on metal-catalyzed allylic aminations promoted by Ir,[8] Pd,[9] Pt, and Fe.[10] The metal-catalyzed hydroamination of dienes is a valuable related methodology.[11] A different strategy for these useful targets is the aza-Claisen [3,3]-sigmatropic rearrangement of allylic imidates, often referred to as the Overman rearrangement.[12] The reaction is very powerful and proceeds in functionalized molecules by means of a well-defined chair transition state that allows for an oxygen–nitrogen transposition with efficient chirality transfer by using enantiopure allylic alcohols as starting materials.[13] In this paper we provide the full details of our research on the Overman rearrangements of sulfinyl allylic trichloroacetimidates that take place with good diastereoselectivities and yields and complete chemoselectivity and preserve the valuable alkenyl sulfoxide moiety for subsequent chirality transfer operations. This is illustrated by highly selective Diels–Alder cycloadditions of a variety of amido 2-sulfinyl butadiene derivatives with *N*-phenylmaleimide.[14]

RESULTS AND DISCUSSION

Enantiomerically pure sulfoxides are useful and versatile chiral auxiliaries.[15] Our group has pursued new methodologies involving readily available α-hydroxy vinyl sulfoxides **A** (Scheme 1).[16,17] A relevant example of these methodologies

Scheme 1. Proposed Sulfinyl-Mediated Overman Rearrangement

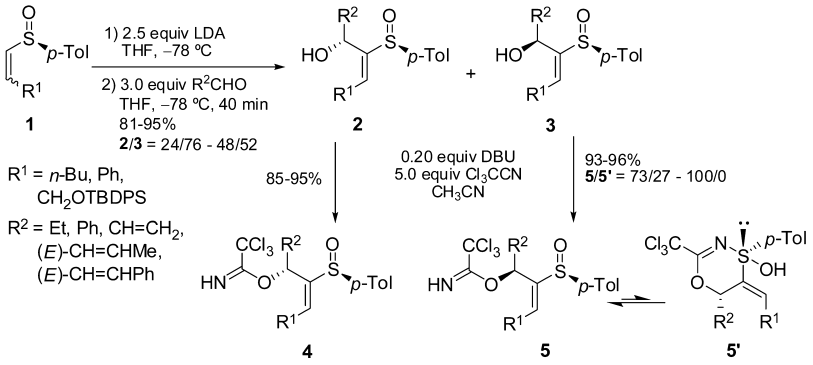


was the highly diastereoselective Claisen rearrangement of enol ethers **B** to carbonyl derivatives **C** that brought about the generation of up to two stereogenic centers with preservation of a useful vinyl sulfoxide and with good control of the geometry of the alkene.[18] Within this context we decided to test the viability of the preparation of trichloroacetimidates **D** and their Overman rearrangement to allylic trichloroacetamides **E** with a stereodefined alkenyl sulfoxide moiety. The main aspects to be examined in this study were the geometry of the starting alkene,

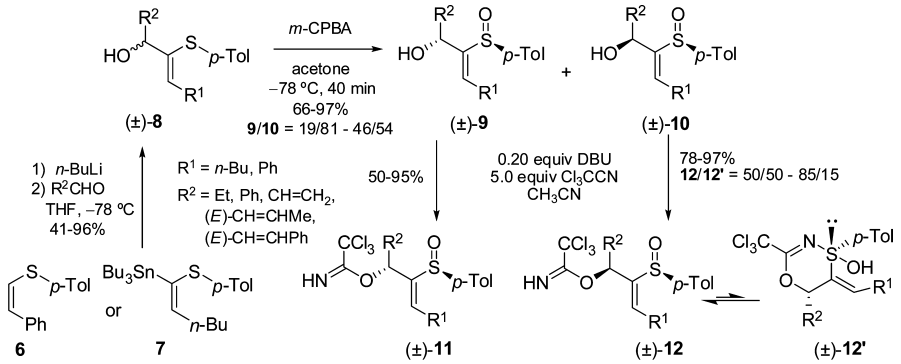
Received: February 19, 2016
Published: April 19, 2016

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081–4097

Scheme 2. Synthesis of *E*-Trichloroacetimidates



Scheme 3. Synthesis of *Z*-Trichloroacetimidates



the relative stereochemistry of the chiral centers, and the nature of representative R^1 and R^2 groups in substrates **A**. If successful, this methodology could complement our previous synthesis of allylic amines by condensation of α-lithio derivatives of sulfoxides **H** and enantiopure sulfinimines **G** to produce *N*-sulfinyl amines **F** with high selectivity and exclusive *E* geometry.[6]

Preparation of Starting Materials. The preparation of enantiopure *E* substrates is summarized in Scheme 2. Lithiation of alkenyl sulfoxides **1**[16] and trapping with a variety of aldehydes gave good yields (81−95%) of hydroxy vinyl sulfoxides **2** and **3**, separable by chromatography on silica gel but with low selectivities (24:76 to 48:52). Treatment of sulfinyl alcohols **2** with catalytic DBU and Cl_3CCN led uneventfully to the desired trichloroacetimidates **4** in excellent yields (85−95%) after column chromatography. Similar treatment of diastereomers **3** afforded imidates **5** in excellent yields after chromatography (93−96%). However, for those examples that had R^1 = alkyl group, the ^{1}H NMR spectra clearly indicated that two inseparable species were present in solution (73:27 to 93:7 mixtures). The major products were assigned the expected trichloroacetimidate structure **5** by comparison of their spectral data with that of diastereomers **4**. The minor products were tentatively assigned sulfurane structures **5′**, presumably in equilibrium with imidates **5**. It should be pointed out that the yields and selectivities of the Overman rearrangements of these cases are not compromised (see below).

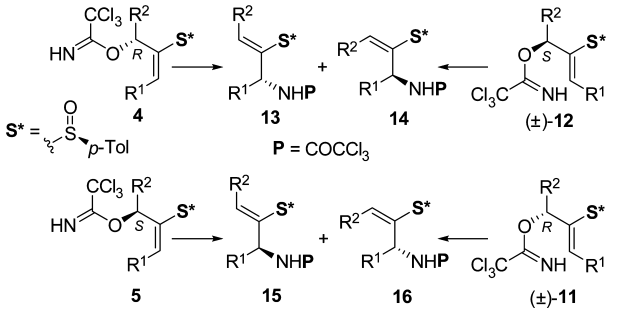
The synthesis of racemic *Z* substrates is summarized in Scheme 3. Lithiation of alkenyl sulfide **6** or tin−lithium exchange of stannane **7** and condensation with a variety of aldehydes led to *Z*-sulfenyl alcohols (±)-**8**.[19,20] Diastereoselective oxidation with *m*-CPBA gave separable mixtures of diastereomeric *Z*-hydroxy alkenyl sulfoxides (±)-**9** and (±)-**10** (19:81 to 46:54) in good yields (66−97%). Treatment with DBU and Cl_3CCN produced the expected trichloroacetimidates (±)-**11** (50−95%) as single species and (±)-**12** (78−97%) as inseparable mixtures in variable ratios (^{1}H NMR, 50:50 to 85:15 mixtures of imidates (±)-**12** and sulfuranes (±)-**12′**) that again led to good yields of rearrangement products (see below).

Overman Rearrangement of Sulfinyl Trichloroacetimidates. The thermal rearrangement of imidate **4a** (Table 1) was then examined in toluene at different temperatures (60−110 °C) with disappointing results. In contrast, switching to DMF, in the presence of a few crystals of BHT to inhibit undesired radical-mediated processes at 100 °C gave an excellent yield of amides **13a**:**14a** with good selectivity (Table 1, entry 1). Under these optimized conditions, we examined the rearrangements of a variety of substrates with different substituents, geometries, and relative configurations and the results are summarized in Table 1.

In the case of *E* substrates with R^1 = *n*-Bu, the rearrangements are high-yielding and the selectivities are high for both diastereomeric imidates (**4a**,**b** and **5a**,**b**) in favor of the *Z* isomers **13** and **15** (Table 1, entries 1−4), with the exception of entry 3 that had modest selectivity. Interestingly, substrates with R^1 = Ph were highly selective substrates leading to single isomers of the transposed amides with complete stereocontrol and good yields in most cases (Table 1, entries 5−8). Thus, it appears that the loss of conjugation in the rearrangement does not hamper the process. The protocol was then extended to substrates with a functionalized R^1 chain with good selectivities and moderate unoptimized yields (Table 1, entries 9 and 10). It should be pointed out that in all cases *Z* amides are obtained from *E* imidates with high selectivity, particularly from isomers **5**, in contrast with a recent report on related unsaturated esters

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

Table 1. Scope of the Sulfinyl-Mediated Overman Rearrangement[a]



entry	SM	R^1	R^2	major product[a]	dr (yield %)[b,c]
1	**4a**	*n*-Bu	Et	**13a**	92/8 (90)
2	**5a**	*n*-Bu	Et	**15a**	96/4 (90)
3	**4b**	*n*-Bu	Ph	**13b**	70/30 (75)
4	**5b**	*n*-Bu	Ph	**15b**	100/0 (92)
5	**4c**	Ph	Et	**13c**	100/0 (83)
6	**5c**	Ph	Et	**15c**	100/0 (91)
7	**4d**	Ph	Ph	**13d**	100/0 (51)
8	**5d**	Ph	Ph	**15d**	100/0 (91)
9	**4e**	$CH_2OTBDPS$	Et	**13e**	90/10 (70)
10	**5e**	$CH_2OTBDPS$	Et	**15e**	95/5 (42)
11	(±)-**11a**	*n*-Bu	Et	(±)-**15a**/(±)-**16a**	50/50 (86)
12	(±)-**12a**	*n*-Bu	Et	(±)-**14a**	80/20 (90)
13	(±)-**11b**	*n*-Bu	Ph	(±)-**16b**	100/0 (85)
14	(±)-**12b**	*n*-Bu	Ph	(±)-**14b**	100/0 (95)
15	(±)-**11c**	Ph	Et	(±)-**15c**/(±)-**16c**	54/46 (81)
16	(±)-**12c**	Ph	Et	(±)-**14c**	100/0 (55)
17	(±)-**11d**	Ph	Ph	-	-
18	(±)-**12d**	Ph	Ph	(±)-**14d**	95/5 (81)

[a]Reactions were performed in DMF with a catalytic amount of BHT at 100 °C. [b]Ratio determined by ^{1}H NMR analysis of crude reaction mixtures. [c]Combined yield after chromatography.

that led mainly to *E* isomers.[21] In this manner this methodology nicely complements our previous efforts on the synthesis of related sulfinyl allylic amines (Scheme 1, **H** to **F**) that afforded exclusively *E* isomers.

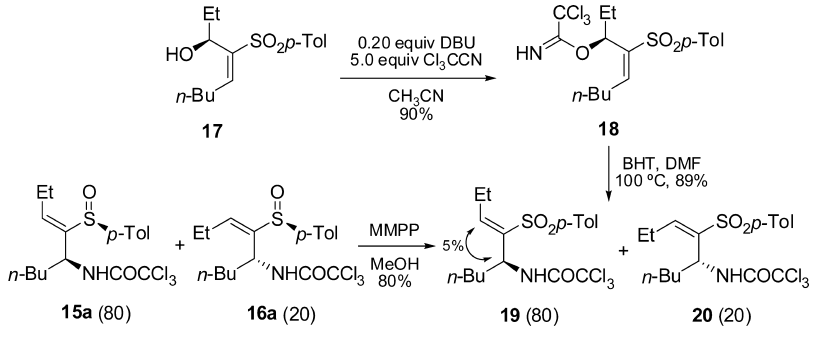
The rearrangements of *Z* substrates with an alkyl R^1 substituent were high-yielding, but the selectivities were remarkably different for the R^2 groups studied (Et and Ph, Table 1, entries 11−14) but favoring the obtention of products with *E* geometry ((±)-**14**, (±)-**16**). The related substrates with R^1 = Ph were also viable in this rearrangement except for (±)-**11d** that decomposed upon heating under the reaction conditions (Table 1, entry 17). Again, substrate (±)-**11c** (*R* configuration at the allylic carbon and R^2 = Et) gave a nonselective mixture of products (±)-**15c**/(±)-**16c** (Table 1, entry 15; compare with entry 11). In contrast the *S* isomers, (±)-**12c,d** gave highly selective rearrangements.

The relative configurations of products **13** and **15** was assigned from their *Z* geometry (NOE's measured between the vinylic and allylic nitrogen-substituted protons were in the range 2−6% for several cases), the known relative configuration of the starting materials **2** and **3**, secured by an X-ray structure of a derivative of **2a**,[19] and the accepted concerted mechanism of the rearrangement that occurs with suprafacial oxygen to nitrogen transposition,[12a] fully consistent with our observation of at most two rearrangement products for each of these substrates, instead of a more complex mixture of isomers derived from an ionization−recombination alternative pathway. Furthermore, some products (**15a**, **14b**) are obtained in sizable amounts from either *E* or *Z* precursors. This mechanism also supports the proposed structures for *E* sulfinyl amides **14** and **16**, the main products obtained from imidates (±)-**11** and (±)-**12**, derived from Z-sulfinyl alcohols (±)-**9** and (±)-**10**.[19]

At this point, we examined the influence of the oxidation state at sulfur on this process and the sulfone analogue of **5a**, **18**, was prepared under standard conditions from **17**.[19] The rearrangement of sulfonyl imidate **18** afforded an 80:20 mixture of *Z* and *E* isomeric amides **19** (NOE between H3−H5 = 5%) and **20** (Scheme 4) that were spectroscopically identical to those obtained by oxidation of an 80:20 mixture of **15a** and **16a**.

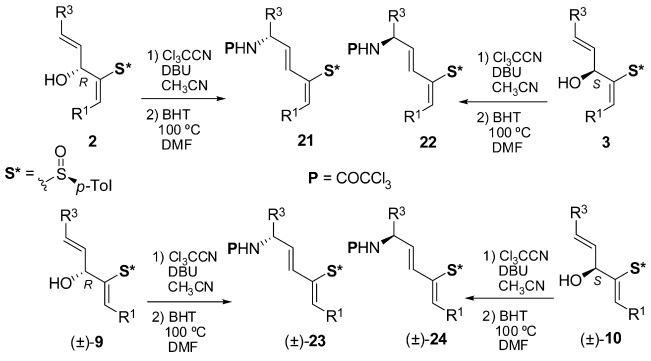
Overman Rearrangement of Bis-allylic Sulfinyl Trichloroacetimidates. Encouraged by the good behavior of our sulfinyl imidates **4**, **5**, **11**, **12**, with trisubstituted alkenes in the Overman rearrangement,[12f] we decided to explore another challenging aspect of this useful methodology, namely the chemoselectivity of the process for bis-allylic substrates that generally takes place with poor selectivity.[12a,e,22] Indeed, we considered that the presence of a sulfinyl substituent on one of the allylic moieties could effectively "deactivate" that alkene in the Overman rearrangement, relative to another allylic moiety and thus provide a synthetically useful level of selectivity. To test this hypothesis, diastereomeric bis-allylic substrates **2f** and **3f** were smoothly transformed to the trichloroacetimidates that, after purification by chromatography on silica gel, were subjected to the standard reaction conditions, to produce excellent yields of amido diene **21f** with complete chemoselectivity (Table 2, entries 1 and 2). Similarly, phenyl-substituted diene **21g** was obtained as a single isomer and in

Scheme 4. Rearrangement of *E* Sulfonyl Imidate 18



DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

Table 2. Overman Rearrangement of Bis-allylic Substrates



entry	SM	R^1	R^3	product[a]	yield (%)
1	**2f**	*n*-Bu	H	**21f**	91
2	**3f**	*n*-Bu	H	**21f**	99
3	**2g**	Ph	H	**21g**	92
4	**3g**	Ph	H	**21g**	98
5	**2h**	*n*-Bu	Me	**21h**	80
6	**3h**	*n*-Bu	Me	**22h**	97
7	**2i**	*n*-Bu	Ph	**21i**	92
8	**3i**	*n*-Bu	Ph	**22i**	95
9	**2j**	Ph	Me	**21j**	83[b]
10	**3j**	Ph	Me	**22j**	77[b]
11	**2k**	Ph	Ph	**21k**	80
12	**3k**	Ph	Ph	**22k**	90
13	(±)-**9h**	*n*-Bu	Me	(±)-**23h**	88
14	(±)-**10h**	*n*-Bu	Me	(±)-**24h**	95
15	(±)-**9i**	*n*-Bu	Ph	(±)-**23i**	85[b]
16	(±)-**10i**	*n*-Bu	Ph	(±)-**24i**	63[b]
17	(±)-**9j**	Ph	Me	(±)-**23j**	60[b]
18	(±)-**10j**	Ph	Me	(±)-**24j**	58[b]
19	(±)-**9k**	Ph	Ph	(±)-**23k**	40[c]
20	(±)-**10k**	Ph	Ph	(±)-**24k**	75[c]

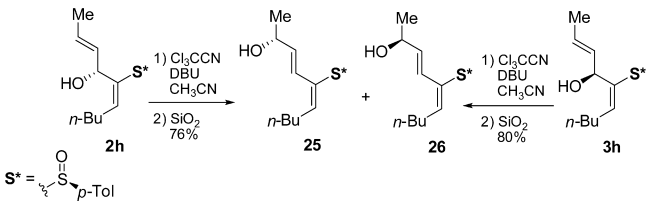
[a]Reactions were performed in DMF with a catalytic amount of BHT at 100 °C. [b]Reactions performed at 60 °C. [c]Reaction performed at 80 °C.

excellent yields from the imidates derived from alcohols **2g** and **3g** (Table 2, entries 3 and 4).

The creation of an additional stereocenter by using a substrate with a more substituted reactive alkene ($R^3 \neq H$) was next examined and, to our dismay, attempted purification by quick chromatography of the trichloroacetimidates derived from **2h** and **3h**, quite clean by ^1H NMR of the crude reaction mixtures, resulted in good yields of hydroxy dienyl sulfoxides **25** and **26** but as inseparable practically equimolecular mixtures (Scheme 5).[23]

At this stage, we decided to test the rearrangement on the trichloroacetimidates as crude products and this gave the desired amido dienes **21h** and **22h** as single isomers, with

Scheme 5. Unselective Preparation of Hydroxy Dienyl Sulfoxides



complete chemo- and stereoselectivity and in excellent overall yields from the starting alcohols (Table 2, entries 5 and 6). The process was readily extended to other derivatives with different R^1 and R^3 groups to produce the expected dienyl trichloroacetamides **21i–k** and **22i–k** in excellent yields (Table 2, entries 7–12). This protocol was also effective for substrates with a *Z* alkenyl sulfoxide moiety (±)-**9h–k** and (±)-**10h–k** that gave the expected dienes (±)-**23h–k** and (±)-**24h–k** as single isomers and in good yields in most cases. It should be mentioned that the geometry of the transposed alkene is always *E*, as expected in most Overman rearrangements.[12]

Rationalization of Stereochemistry. Bis-allylic substrates (Table 2) follow the commonly accepted reaction course for the Overman rearrangement, with the sulfinyl moiety acting just as a powerful controlling element for chemoselectivity. The results found for the allylic sulfinyl imidates (Table 1) can be accommodated by considering diastereomeric transition states of chairlike reactive conformations **I–L** for diastereomers **5** and **11** that lead to the same products **15** and **16** (Figure 1). In the case of *E* vinyl sulfoxides **5a–e**, considering an s-cis arrangement between the alkene and the S=O bonds,[24] approach of the NH fragment to the *re* face would entail reactive conformer **J**, disfavored by an $A^{1,3}$ interaction between R^1 and R^2 and the bulky *p*-Tol group pointing toward the incoming unsaturated fragment. In contrast, reactive conformer **I** has no significant interactions of the kind described above and thus would lead almost exclusively to *Z* isomers **15** due to the favorable arrangement of stereocontrolling elements.

The stereochemical outcome for *Z* sulfinyl imidates (±)-**11** involves a delicate conformational balance between conformers **L**/**L′** and **K**/**K′**, with **L** being preferred when R^2 = Ph to minimize $A^{1,2}$ interactions, thus leading exclusively to *E* isomer **16** (Table 1, entry 13), and **L** and **K′**, providing mixtures of **15** and **16** for the sterically less demanding scenario when R^2 = Et (Table 1, entries 11 and 15). It should be pointed out that for the simple *Z* propenyl sulfoxide the energy difference between C=C/S=O and C=C/S-: s-cis arrangements is very small, and therefore both types of conformers could participate in the process.[24b]

The rationalization for the stereochemical outcome of diastereomeric *E* sulfinyl imidates **4** is not straightforward because conformer **M** presents severe $A^{1,2}$ interactions, and conformer **N** displays $A^{1,3}$ diaxial interactions, that appear to determine the reaction course to produce *Z* sulfinyl amides **13** predominantly, albeit with lower yields and selectivities than diastereomeric substrates **5**. Similarly, in the case of *Z* sulfinyl imidates (±)-**12**, conformer **P** places the tolyl moiety above the chair, and for conformer **O**, the tolyl is away from the reactive center but the sulfinyl moiety is in close proximity to the R^2 substituent. Nonetheless, as discussed previously for *Z* substrates (±)-**11**, alternative conformers **O′**, with severe $A^{1,2}$ interactions, and **P′**, substantially more stable, should be examined and may account for the predominant obtention of *E* sulfinyl amides **14** in these cases.

Survey of Reactivity of Amido Alkenyl Sulfoxides. At this point, we set out to examine the viability of intramolecular cyclizations with selected amido alkenyl sulfoxides, as well as the behavior of our sulfinyl amido dienes in Diels–Alder processes. Regarding the possible cyclizations, we tested the deprotection of silyl ether **15e** that led to oxazolidinone **27** in excellent yield (Scheme 6). We then explored the dihydroxylation of amido diene **21g** under standard Upjohn conditions that led cleanly to sulfonyl amido diol (±)-**28**.[25] Subsequent

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081–4097

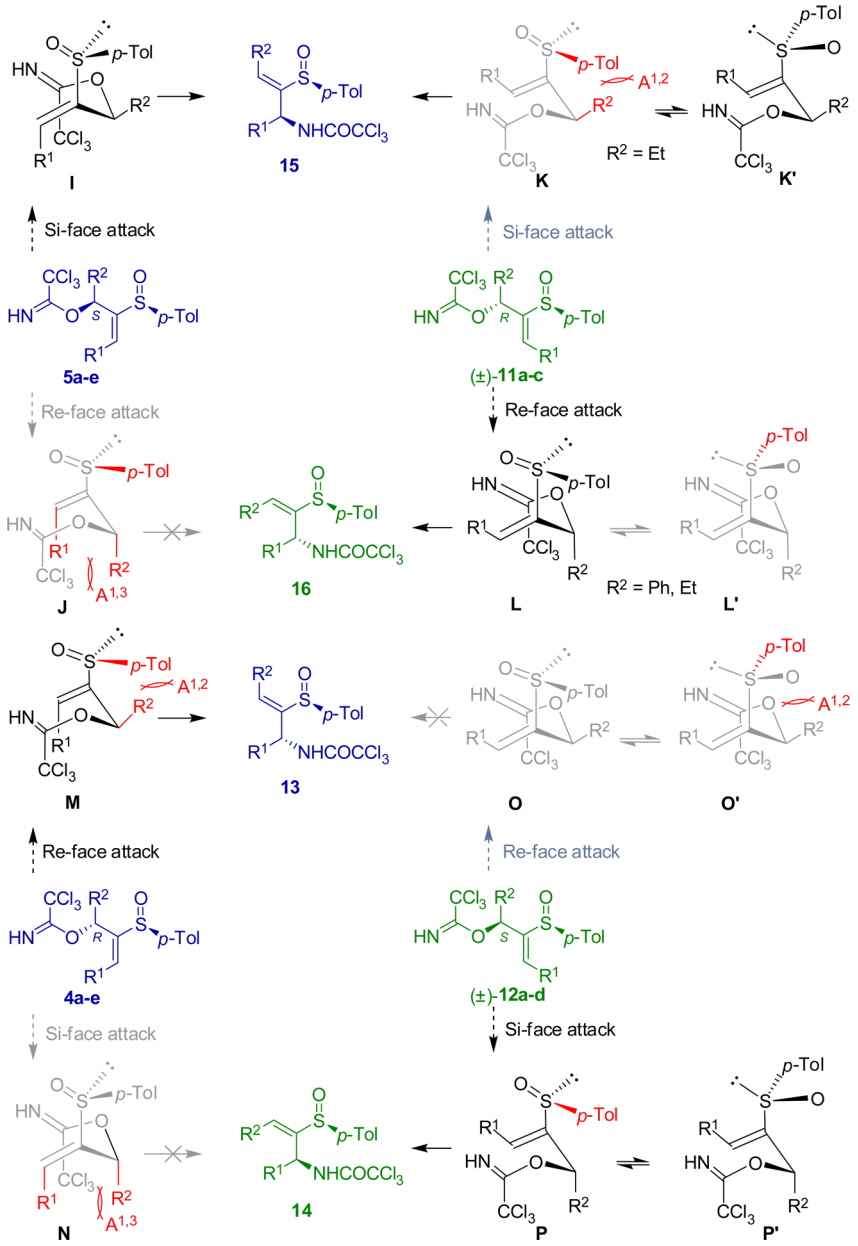
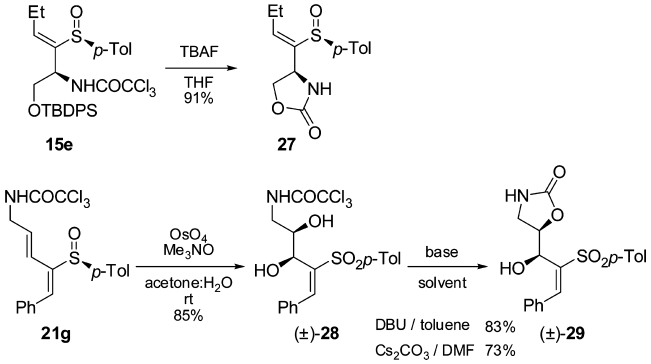


Figure 1. Stereochemical outcome.

Scheme 6. Synthesis of Oxazolidinones (±)-27 and (±)-29



treatment under basic conditions afforded hydroxy oxazolidinone (±)-**29** in good yields.[26] While it is possible that other conditions and/or protection−deprotection strategies could produce the desired cyclizations, the concurrent results obtained on the Diels−Alder chemistry of our amido dienes (see below) prompted us to shift our efforts to this field.

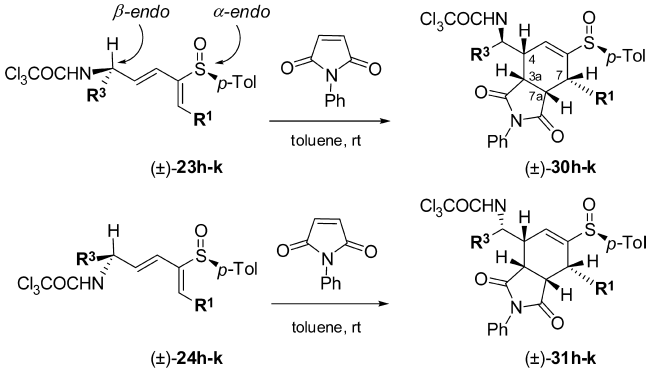
The diastereoselectivity of Diels−Alder cycloadditions of acyclic chiral dienes with a nitrogen substituent at the allylic position has been studied, and while the results are dependent on the diene structure and the nature of the dienophile,[27] it was established that for maleic anhydride, an endo approach *syn* to the protected nitrogen functionality on a conformer that eclipses the allylic hydrogen and the diene was operative.[27c] On the other hand, our group has a long-standing interest in the development of the Diels−Alder chemistry of 2-sulfinyl butadienes to produce adducts that preserve the useful vinyl sulfoxide moiety and often with high diastereoselectivities that even override the powerful directing effect of an allylic oxygen substituent.[28,29] Typically, for S_S sulfinyl dienes as drawn in this paper, simple *Z* or unsubstituted 2-sulfinyl dienes undergo highly selective Diels−Alder processes with maleimides and

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

maleic anhydride with an endo approach to the bottom face of the diene moiety (α-endo), as shown by X-ray crystallography[29g,h] or chemical correlations.[29i] In this context, we were intrigued about the viability and, particularly, the selectivity of the cycloadditions of our amido sulfinyl dienes, especially for diastereomers (±)-**23**, with opposing elements of stereocontrol.

At the early stage of the study we selected *E,Z* dienes (±)-**23h** and (±)-**24h** and *N*-phenylmaleimide (NPM) as dienophile. To our delight, the cycloadditions took place smoothly in toluene at rt to produce the expected isoindoles (±)-**30h** and (±)-**31h** respectively as single isomers and in excellent yields (Table 3, entries 1 and 2). Cycloadducts

Table 3. Sulfinyl-Directed Diels-Alder Cycloadditions (*E,Z*-Dienes)[a]



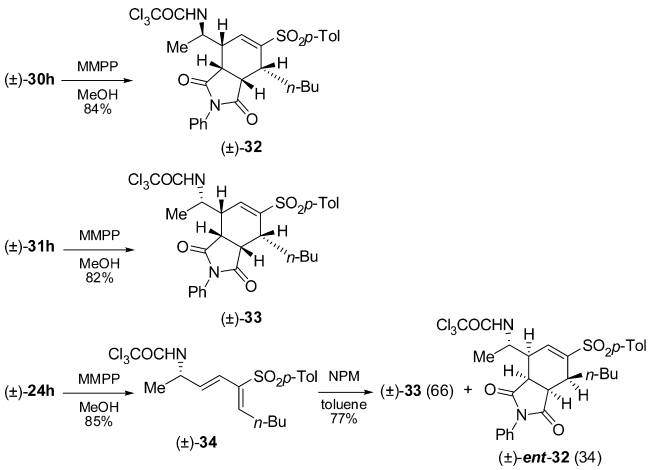
entry	SM	R^1	R^3	product[a]	yield (%)
1	(±)-**23h**	*n*-Bu	Me	(±)-**30h**	84
2	(±)-**24h**	*n*-Bu	Me	(±)-**31h**	82
3	(±)-**23i**	*n*-Bu	Ph	(±)-**30i**	75
4	(±)-**24i**	*n*-Bu	Ph	(±)-**31i**	71
5	(±)-**23j**	Ph	Me	(±)-**30j**	80
6	(±)-**24j**	Ph	Me	(±)-**31j**	76
7	(±)-**23k**	Ph	Ph	(±)-**30k**	73[b]
8	(±)-**24k**	Ph	Ph	(±)-**31k**	80[b]

[a]Reactions were performed in toluene at rt. [b]Reactions performed in toluene at 70 °C.

(±)-**30h** and (±)-**31h** had spectral features, including NOE's (H3a-H4 = 8% and 6%; H4−H7 = 5% and 7%; H7−H7a = 4% and 5%, respectively), compatible with the proposed structures derived from the known reaction pathway of these dienes discussed above. Encouraged by these results, the generality of the methodology was explored for substrates with different R^1 (*n*-Bu, Ph) and R^3 (Ph, Me) groups and the results found were parallel to the first examples with the cycloadditions taking place under mild conditions in good yields and with complete diastereoselectivities (Table 3, entries 3−8).

To evaluate the stereodirecting importance of each chiral element in these molecules, we examined the cycloaddition of amido sulfonyl diene (±)-**34**, prepared by oxidation with MMPP of (±)-**24h**, with NPM that afforded a 66/34 mixture of (±)-**33** and (±)-*ent*-**32**.[30] The ^{1}H and ^{13}C NMR features of these adducts were compared to those of (±)-**32** and (±)-**33** obtained upon straightforward oxidation of the sulfinyl adducts with MMPP (Scheme 7). These results indicate that the stereochemical outcome of the Diels−Alder cycloaddition of these acyclic *E,Z* amido sulfinyl dienes is primarily controlled by the chiral sulfoxide moiety. Indeed, should the amido group have been the main source of stereocontrol of the cyclo-

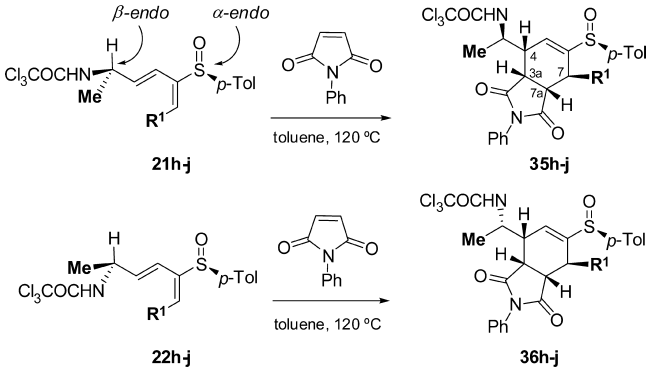
Scheme 7. Oxidation and Diels−Alder with *E,Z* Sulfonyl Diene



addition, the oxidation of (±)-**30h** and (±)-**31h** would have afforded products with identical NMR spectral features.

Encouraged by these results that allow for the generation of four stereogenic centers in a single step while preserving the versatile alkenyl sulfoxide fragment and with an "external" protected amino group, amenable to serve as a handle for carbonyl differentiation, we decided to examine the behavior of the related *E,E* amido sulfinyl dienes **21** and **22**, and the results obtained are gathered in Table 4. Not unexpectedly, the

Table 4. Sulfinyl-Directed Diels−Alder Cycloadditions (*E,E*-Dienes)[a]



entry	SM	R^1	product[a]	yield (%)
1	**21h**	*n*-Bu	**35h**	52
2	**22h**	*n*-Bu	**36h**	55
3	**21j**	Ph	**35j**	49
4	**22j**	Ph	**36j**	62

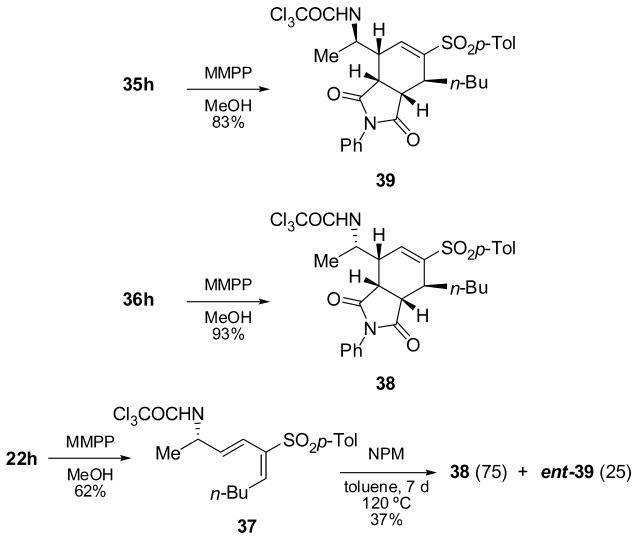
[a]Reactions were performed in toluene at 120 °C.

cycloaddition of these dienes required harsher conditions (120 °C, 4−11 days) and were not as high-yielding as those of the *E,Z* isomers discussed above. Nevertheless, moderate yields of the desired sulfinyl isoindoles were isolated as single isomers without significant optimization.[31] The structures of these adducts were based on the proposed reaction course discussed above and confirmed with a detailed study of their NMR features including the observed couplings between H7−H7a for **35j**/**36j**, in comparison with diastereomers **30j**/**31j**, as well as an observed 5% NOE between H4 and an *n*-Bu methylene for **36h**.

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

Parallel to the *E,Z* isomers we examined the oxidation of dienyl sulfoxide **22h** that gave dienyl sulfone **37** in moderate yield (Scheme 8). The cycloaddition between **37** and NPM

Scheme 8. Oxidation and Diels–Alder with *E,E* Sulfonyl Diene



produced a 75/25 mixture of diastereomeric sulfonyl isoindoles **38** and *ent*-**39**. The NMR features of these adducts were compared to those of **38** and **39** obtained by oxidation of the sulfinyl adducts **35h** and **36h** with MMPP (Scheme 8). These results suggest that for these *E,E* sulfinyl dienes, the chiral sulfur is the main element of stereocontrol in the Diels–Alder processes examined.

CONCLUSIONS

In summary, the thermal Overman rearrangement of simple allylic sulfinyl trichloroacetimidates takes place with high yields and selectivities in most cases. For bis-allylic substrates, the rearrangement is completely chemoselective, involving just the alkene that does not bear the sulfinyl moiety and producing amido 2-sulfinyl butadienes as single isomers and in good to excellent yields. Subsequent highly diastereoselective Diels–Alder cycloadditions, with facial control by the sulfinyl chiral center, lead to densely functionalized sulfinyl isoindoles. Further applications of these methodologies are being explored in our laboratories.

EXPERIMENTAL SECTION

Materials and Methods. Reagents and solvents were handled using standard syringe techniques. All reactions were carried out under an argon atmosphere. Diisopropylamine (*i*-Pr_2NH) was purified by distillation from CaH_2. Aldehydes were purified by distillation and stored over Na_2SO_4. Anhydrous solvents were purified by filtration on a solvent purification system (SPS). Crude products were purified by flash chromatography on 230–400 mesh silica gel with distilled solvents. Analytical TLC was carried out on silica gel plates with detection by UV light or 10% phosphomolybdic acid solution in ethanol. All reagents were commercial products. Through this section, the volume of solvents is reported in mL/mmol of starting material. ^1H and ^{13}C NMR spectra were recorded at 300, 400, or 500 MHz (^1H) and with the residual solvent signal as internal reference ($CDCl_3$, 7.26 and 77.0 ppm) unless otherwise noted. Optical rotations were measured at 20 °C using a sodium lamp. High resolution mass spectra (HRMS) were recorded using an Accurate Mass Q-TOF spectrometer. Vinyl sulfoxides **1** were prepared as *E/Z* mixtures that completely isomerized to the *E* isomer upon lithiation. Compounds **1a,b**, **2f–i**, **3f–i**, **4a–d**, **4f,g**, **5a–d**, **5f,g**, **8h**, (±)-**9h**, (±)-**10h**, (±)-**11b**, (±)-**12b**, **13a–d**, **14a,b**, **15a–d**, **16a**, **18**, **19**, **20**, **21f–i**, **22h,i**, (±)-**23h**, (±)-**24h**, **25**, **26**, **28**, **29**, (±)-**30h**, (±)-**31h**, (±)-**32**, (±)-**33**, and (±)-**34** are described in the Supporting Information of our preliminary communication.[14]

General Procedure for the Synthesis of (*E*)-Hydroxy Vinyl Sulfoxides. To a cold (−78 °C) solution of freshly distilled *i*-Pr_2NH (2.6 equiv) in anhydrous THF (3.5 mL/mmol) was added 1.6 M *n*-BuLi (2.5 equiv), and the resulting LDA solution was stirred at the same temperature. After 10 min, a solution of a *Z/E* mixture of vinyl sulfoxides (1 equiv) in anhydrous THF (2 mL/mmol) was added dropwise slowly to produce a pale yellow solution. After the mixture was stirred for an additional 10 min at −78 °C, freshly distilled aldehyde (3.0 equiv) was added dropwise and the resulting colorless solution was stirred at this temperature for 10 min. The reaction mixture was quenched with a saturated solution of NH_4Cl, and the aqueous layer was extracted with EtOAc. The combined organic layers were washed with brine, dried (Na_2SO_4), and concentrated in vacuo. The crude product was purified by column chromatography on silica gel with the appropriate mixture of solvents to afford (*E*)-hydroxy vinyl sulfoxides **2** and **3**.

Synthesis of (+)-(3R,4E,S$_S$)-6-(tert-Butyldiphenylsilyloxy)-4-(p-tolylsulfinyl)hex-4-en-3-ol, ***2e****, and (+)-(3S,4E,S$_S$)-6-(tert-Butyldiphenylsilyloxy)-4-(p-tolylsulfinyl)hex-4-en-3-ol,* ***3e****.* From ***E/Z*-1c**[32] (640 mg, 1.47 mmol) in THF (3.0 mL), LDA, and propionaldehyde (256 mg, 4.42 mmol) following the general procedure, a 39:61 mixture of **2e** and **3e** was obtained. Chromatographic purification (10–30% EtOAc–hexane) gave **2e** (229 mg, 32%) and **3e** (358 mg, 49%) as yellow oils. Data for **2e**: R_f 0.30 (30% EtOAc–hexane). $[\alpha]^{20}_D$ +2.70 (*c* 1.16, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.73 (t, 3 H, *J* = 7.4 Hz), 1.06 (s, 9 H), 1.28–1.38 (m, 1 H), 1.48–1.59 (m, 1 H), 2.16 (d, 1 H, *J* = 5.3 Hz), 2.41 (s, 3 H), 4.09 (dt, 1 H, *J* = 8.7, 5.3 Hz), 4.47 (d, 2 H, *J* = 5.6 Hz), 6.60 (t, 1 H, *J* = 5.6 Hz), 7.26–7.28 (m, 2 H), 7.35–7.47 (m, 6 H), 7.50 (d, 2 H, *J* = 8.2 Hz), 7.64–7.67 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.5, 19.3, 21.7, 26.9 (3 C), 30.2, 60.9, 70.7, 125.5 (2 C), 128.1 (4 C), 130.1 (2 C), 130.2 (2 C), 132.9, 133.0, 134.5, 135.80 (2 C), 135.83 (2 C), 140.8, 141.8, 147.3. IR (film): 3400, 3071, 3050, 2962, 2931, 2857, 1636, 1590, 1492, 1472, 1463, 1428, 1391, 1374, 1304, 1260, 1179, 1112, 1081, 1029, 1013, 823, 809, 740, 703, 614 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{29}H_{37}O_3SSi$ [M + H]$^+$ 493.2227, found 493.2210. Data for **3e**: R_f 0.20 (30% EtOAc–hexane). $[\alpha]^{20}_D$ +31.4 (*c* 3.67, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 0.70 (t, 3 H, *J* = 7.4 Hz), 1.06 (s, 9 H), 1.09–1.14 (m, 1 H), 1.32–1.43 (m, 1 H), 2.40 (s, 3 H), 2.88 (s, 1 H), 4.02 (dd, 1 H, *J* = 8.8, 4.6 Hz), 4.45 (dd, 1 H, *J* = 14.9, 6.0 Hz), 4.57 (dd, 1 H, *J* = 14.9, 5.0 Hz), 6.51 (dd, 1 H, *J* = 5.9, 5.0 Hz), 7.28 (d, 2 H, *J* = 8.0 Hz), 7.37–7.47 (m, 6 H), 7.49 (d, 2 H, *J* = 8.2 Hz), 7.66–7.68 (m, 4 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 19.1, 21.4, 26.7 (3 C), 30.0, 60.9, 69.8, 125.6 (2 C), 127.81 (2 C), 127.82 (2 C), 129.86 (2 C), 129.9 (2 C), 132.7, 132.8, 133.4, 135.5 (2 C), 135.6 (2 C), 139.6, 141.8, 147.3. IR (film): 3368, 3072, 3051, 2962, 2931, 2857, 1590, 1492, 1472, 1463, 1428, 1373, 1265, 1112, 1082, 1014, 823, 810, 739, 703, 614 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{29}H_{37}O_3SSi$ [M + H]$^+$ 493.2227, found 493.2229.

Synthesis of (+)-(3R,1E,4E,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)hexa-1,4-dien-3-ol, ***2j****, and (−)-(3S,1E,4E,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)-hexa-1,4-dien-3-ol,* ***3j****.* From ***E/Z*-1b**[33] (540 mg, 2.23 mmol) in THF (7.8 mL), LDA, and crotonaldehyde (0.55 mL, 6.69 mmol), following the general procedure, a 24:76 mixture of **2j** and **3j** was obtained. Chromatographic purification (10–50% Et_2O–CH_2Cl_2) gave **2j** (140 mg, 20%) and **3j** (432 mg, 62%) as yellow oils. Data for **2j**: R_f 0.20 (30% EtOAc–hexane). $[\alpha]^{20}_D$ +133.1 (*c* 2.00, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.60 (dt, 3 H, *J* = 6.1, 1.0 Hz), 2.40 (s, 3 H), 3.11 (d, 1 H, *J* = 5.5 Hz), 5.28 (t, 1 H, *J* = 5.1 Hz), 5.52–5.67 (m, 2 H), 7.28 (d, 2 H, *J* = 8.5 Hz), 7.34–7.51 (m, 6 H), 7.62 (d, 2 H, *J* = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.4, 21.3, 69.4, 125.8 (2 C), 128.2, 128.4 (2 C), 128.6, 129.5 (2 C), 129.61 (2 C), 129.63, 132.7, 133.7, 140.8, 141.5, 145.8. IR (film): 3337, 3051, 3027, 2917, 2855, 1668,

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081–4097

1627, 1596, 1492, 1447, 1399, 1378, 1265, 1081, 1028, 809, 736, 700, 625 cm^{-1}. HRMS (ES) m/z Calcd for $C_{19}H_{19}OS$ $[M + H - (H_2O)]^+$ 295.1151, found 295.1169. Data for **3j**: R_f 0.15 (30% EtOAc−hexane). $[\alpha]^{20}_D$ −20.4 (*c* 1.94, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (dt, 3 H, *J* = 6.6, 1.5 Hz), 2.40 (s, 3 H), 4.37 (d, 1 H, *J* = 3.9 Hz), 5.08−5.14 (m, 1 H), 5.33−5.41 (m, 2 H), 7.26 (d, 2 H, *J* = 8.4 Hz), 7.33−7.48 (m, 6 H), 7.62 (d, 2 H, *J* = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.3, 21.2, 68.8, 126.3 (2 C), 127.8, 128.2 (2 C), 128.4, 129.2, 129.4 (2 C), 129.7 (2 C), 131.1, 133.8, 140.0, 141.5, 146.8. IR (film): 3338, 3052, 2981, 2938, 2855, 1623, 1596, 1576, 1492, 1448, 1265, 1124, 1082, 1028, 1013, 966, 810, 737, 702, 626 cm^{-1}. HRMS (ES) m/z Calcd for $C_{19}H_{19}OS$ $[M + H - (H_2O)]^+$ 295.1151, found 295.1171.

Synthesis of (+)-(3R,1E,4E,S$_S$)-1,5-Diphenyl-2-(p-tolylsulfinyl)-penta-1,4-dien-3-ol, ***2k****, and (−)-(3S,1E,4E,S$_S$)-1,5-Diphenyl-2-(p-tolylsulfinyl)penta-1,4-dien-3-ol,* ***3k****.* From *E*/*Z*-**1b**[33] (412 mg, 1.70 mmol) in THF (13.0 mL), LDA, and cinnamaldehyde (0.60 mL, 5.10 mmol), following the general procedure, a 43:57 mixture of **2k** and **3k** was obtained. Chromatographic purification (10−50% Et_2O−CH_2Cl_2) gave **2k** (254 mg, 40%) as a colorless oil and **3k** (318 mg, 50%) as a white solid. Data for **2k**: R_f 0.35 (20% Et_2O−CH_2Cl_2). $[\alpha]^{20}_D$ +89.4 (*c* 2.10, $CHCl_3$). ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 2.31 (s, 3 H, CH_3 *p*-Tol), 3.34 (d, 1 H, *J* = 6.8 Hz, OH), 5.52 (ddd, 1 H, *J* = 8.8, 5.1, 1.8 Hz, H-3), 6.06 (dd, 1 H, *J* = 15.9, 5.0 Hz, H-4), 6.44 (dd, 1 H, *J* = 15.9, 1.7 Hz, H-5), 7.10−7.12 (m, 2 H, Ar), 7.20−7.26 (m, 5 H, Ar), 7.35−7.41 (m, 3 H, Ar), 7.47−7.49 (m, 2 H, Ar), 7.55−7.58 (m, 3 H, H-1 and Ar). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 21.3 (CH_3 *p*-Tol), 70.3 (C-3), 125.7 (2 C), 126.5 (2 C), 127.7, 128.2, 128.3 (2 C), 128.7 (2 C), 129.1, 129.6 (2 C), 129.9 (2 C), 131.0, 133.6, 134.6, 136.1, 140.1, 141.8, 144.9. IR (film): 3339, 3081, 3057, 3026, 2979, 2922, 2867, 1626, 1597, 1577, 1493, 1448, 1399, 1304, 1266, 1207, 1180, 1157, 1081, 1028, 967, 809, 751, 737, 695 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{23}O_2S$ $[M + H]^+$ 375.1419, found 375.1393. Data for **3k**: R_f 0.20 (20% Et_2O−CH_2Cl_2). $[\alpha]^{20}_D$ −50.4 (*c* 1.50, $CHCl_3$). mp 117−120 °C. ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 2.25 (s, 3 H, CH_3 *p*-Tol), 3.90 (d, 1 H, *J* = 4.4 Hz, OH), 5.56 (td, 1 H, *J* = 5.4, 1.1 Hz, H-3), 5.70 (dd, 1 H, *J* = 15.9, 5.3 Hz, H-4), 6.25 (dd, 1 H, *J* = 15.9, 1.6 Hz, H-5), 6.97−6.99 (m, 2 H, Ar), 7.17−7.21 (m, 5 H, Ar), 7.33−7.38 (m, 3 H, Ar), 7.41 (s, 1 H, H-1), 7.44−7.47 (m, 2 H, Ar), 7.60 (m, 2 H, *J* = 8.2 Hz, *p*-Tol). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 21.3 (CH_3 *p*-Tol), 69.0 (C-3), 126.40 (2 C), 126.43 (2 C), 127.6, 127.9, 128.2 (2 C), 128.5 (2 C), 128.7, 129.7 (2 C), 129.8 (2 C), 131.0, 132.0, 133.8, 136.2, 139.9, 142.2, 146.8. IR (KBr): 3338, 3081, 3056, 3025, 2921, 1634, 1597, 1577, 1493, 1447, 1400, 1304, 1082, 1027, 1012, 968, 808, 753, 694 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{23}O_2S$ $[M + H]^+$ 375.1419, found 375.1396.

General Procedure for the Synthesis of (*Z*)-Hydroxy Vinyl Sulfides. To a cold solution (−78 °C) of the vinyl stannane or sulfide in anhydrous THF (5.0 mL/mmol) was added a solution 1.6 M of *n*-BuLi (1.2−2.0 equiv), and the mixture was stirred at this temperature. After 10 min, freshly distilled aldehyde (2.0−3.0 equiv) was added dropwise and the resulting solution was stirred at this temperature for 10 min. The reaction mixture was quenched with a saturated solution of NH_4Cl, and the aqueous layer was extracted with EtOAc. The combined organic extracts were washed with a saturated solution of NaCl, dried ($MgSO_4$), and concentrated under reduced pressure to give a crude product that was purified by column chromatography using the appropriate mixture of solvents.

*Synthesis of (±)-(2Z)-1,3-Diphenyl-2-(p-tolylsulfenyl)prop-2-en-1-ol, (±)-****8d****.* From **6**[34] (337 mg, 1.49 mmol), *n*-BuLi (1.86 mL, 2.98 mmol), and benzaldehyde (0.46 mL, 4.47 mmol) in THF, following the general procedure and after chromatographic purification (10−30% EtOAc−hexane), (±)-**8d** (379 mg, 77%) was obtained as a yellow oil. Data for (±)-**8d**: R_f 0.30 (30% EtOAc−hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 2.17 (d, 1 H, *J* = 0.2 Hz), 2.31 (s, 3 H), 5.26 (s, 1 H), 7.06 (dd, 2 H, *J* = 8.6, 0.8 Hz), 7.19 (d, 2 H, *J* = 8.2 Hz), 7.18−7.38 (m, 9 H, H-3), 7.63−7.65 (m, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.0, 76.4, 125.9, 126.9 (2 C), 127.9, 127.98, 128.0 (2 C), 128.4 (2 C), 129.6 (2 C), 129.9 (2 C), 130.1 (2 C), 130.4, 133.8, 135.6, 136.5, 136.8. IR (film): 3406, 3055, 2987, 1492, 1422, 1266, 896, 749, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{20}NaOS$ $[M + Na]^+$ 355.1127, found 355.1122.

*Synthesis of (±)-(3R,1E,4Z)-1-Phenyl-4-(p-tolylsulfenyl)nona-1,4-dien-3-ol, (±)-****8i****.* From **7**[19] (347 mg, 0.70 mmol), *n*-BuLi (0.53 mL, 0.84 mmol), and cinnamaldehyde (0.26 mL, 2.10 mmol) in THF, following the general procedure and after chromatographic purification (10−30% EtOAc−hexane), (±)-**8i** (206 mg, 87%) was obtained as a yellow oil. Data for (±)-**8i**: R_f 0.40 (30% EtOAc−hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 0.89 (t, 3 H, *J* = 7.2 Hz), 1.29−1.44 (m, 4 H), 2.30 (s, 3 H), 2.35−2.41 (m, 2 H), 4.76 (d, 1 H, *J* = 6.0 Hz), 6.19 (dd, 1 H, *J* = 15.9, 6.0 Hz), δ 6.35 (td, 1 H, *J* = 7.2, 0.8 Hz), 6.55 (dd, 1 H, *J* = 15.9, 1.3 Hz), 7.07 (d, 2 H, *J* = 8.0 Hz), 7.20−7.30 (m, 7 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 21.0, 22.4, 29.5, 31.1, 75.6, 126.6 (2 C), 127.6, 128.5 (2 C), 129.0 (2 C), 129.8 (2 C), 129.9, 130.0, 131.7, 134.9, 136.1, 136.6, 139.4. IR (film): 3435, 3054, 2959, 2928, 2859, 1723, 1635, 1600, 1449, 1492, 1422, 1379, 1399, 1265, 1085, 1018, 968, 896, 808, 739, 704 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{25}OS$ $[M - H]^-$ 337.1632, found 337.1621.

*Synthesis of (±)-(1Z,4E)-1-Phenyl-2-(p-tolylsulfenyl)hexa-1,4-dien-3-ol, (±)-****8j****.* From **6**[34] (585 mg, 2.59 mmol), *n*-BuLi (1.94 mL, 3.10 mmol) and crotonaldehyde (0.64 mL, 7.75 mmol) in THF, following the general procedure and after chromatographic purification (10−30% Et_2O−hexane), (±)-**8j** (314 mg, 41%) was obtained as a yellow oil. Data for (±)-**8j**: R_f 0.30 (20% Et_2O−hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 1.71 (d, 3 H, *J* = 6.5 Hz), 2.08 (br s, 1 H), 2.30 (s, 3 H), 4.62 (br d, 1 H, *J* = 6.3 Hz), 5.58 (ddd, 1 H, *J* = 15.3, 6.5, 1.5 Hz), 5.70 (dqd, 1 H, *J* = 15.2, 6.5, 1.0 Hz), 7.06 (d, 2 H, *J* = 7.9 Hz), 7.22−7.33 (m, 6 H), 7.64 (d, 2 H, *J* = 7.9 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.8, 21.0, 75.4, 127.8, 128.0 (2 C), 128.6, 129.5 (2 C), 129.8 (2 C), 129.9 (2 C), 130.7, 131.6, 133.5, 135.8, 136.3, 136.6. IR (film): 3430, 3055, 2987, 2686, 2306, 1645, 1606, 1552, 1422, 1266, 896, 748, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{19}H_{20}NaOS$ $[M + Na]^+$ 319.1127, found 319.1123.

*Synthesis of (±)-(1Z,4E)-1,5-Diphenyl-2-(p-tolylsulfenyl)penta-1,4-dien-3-ol, (±)-****8k****.* From **6**[34] (349 mg, 1.54 mmol), *n*-BuLi (1.16 mL, 1.85 mmol), and cinnamaldehyde (0.39 mL, 3.08 mmol) in THF, following the general procedure and after chromatographic purification (5−10% EtOAc−hexane), (±)-**8k** (397 mg, 72%) was obtained as a yellow oil. Data for (±)-**8k**: R_f 0.15 (10% EtOAc−hexane). ^1H NMR (500 MHz, $CDCl_3$) δ 2.31 (s, 3 H), 4.88 (d, 1 H, *J* = 6.3 Hz), 6.27 (dd, 1 H, *J* = 15.9, 6.4 Hz), 6.59 (d, 1 H, *J* = 15.9 Hz), 7.08 (d, 2 H, *J* = 8.0 Hz), 7.25−7.36 (m, 11 H), 7.69 (d, 2 H, *J* = 7.6 Hz). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.0, 75.6, 126.6 (2 C), 127.7, 128.0, 128.1 (2 C), 128.5 (2 C), 129.6 (2 C), 129.8, 129.9 (2 C), 130.1 (2 C), 130.6, 131.4, 134.1, 135.6, 135.9, 136.5, 136.8. IR (film): 3393, 3057, 3024, 2922, 2856, 1598, 1492, 1446, 1399, 1084, 1068, 1030, 1017, 965, 807, 753, 692 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{21}S$ $[M + H - (H_2O)]^+$ 341.1359, found 341.1362.

General Procedure for the Synthesis of (*Z*)-Hydroxy Vinyl Sulfoxides by Oxidation. To a cold solution (−78 °C) of the starting material (1.0 equiv) in acetone (8.0 mL/mmol) was added *m*-CPBA (2.0 equiv, 77% w/w) and K_2CO_3 (3.0 equiv). The solution was stirred at this temperature for 10 min and then allowed to warm slowly while being monitored by TLC. The reaction mixture was quenched with a 1.0 M aqueous solution of $Na_2S_2O_4$, a saturated solution of $NaHCO_3$, and H_2O. The aqueous layer was extracted with EtOAc, and the combined organic extracts were washed with a saturated aqueous solution of NaCl, dried (Na_2SO_4), and concentrated under reduced pressure. The crude product was purified by column chromatography using the appropriate mixture of solvents.

*Synthesis of (±)-(1R,2Z,S$_S$)-1,3-Diphenyl-2-(p-tolylsulfinyl)prop-2-en-1-ol, (±)-****9d****, and (1S,2Z,S$_S$)-1,3-Diphenyl-2-(p-tolylsulfinyl)prop-2-en-1-ol, (±)-****10d****.* From (±)-**8d** (195 mg, 0.59 mmol), *m*-CPBA (263 mg, 1.17 mmol), and K_2CO_3 (243 mg, 1.76 mmol) in acetone, according to the general procedure, a 19:81 mixture of (±)-**9d** and (±)-**10d** was obtained. Chromatographic purification (1−10% Et_2O−CH_2Cl_2) gave (±)-**9d** (30 mg, 15%) as a yellow oil and (±)-**10d** (130 mg, 64%) as a white solid. Data for (±)-**9d**: R_f 0.30 (5% Et_2O−CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 2.38 (s, 3 H), 3.05 (d, 1 H, *J* = 4.5 Hz), 5.91 (d, 1 H, *J* = 4.5 Hz), 6.93 (s, 1 H), 7.22−7.45 (m, 14

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 71.1, 124.9 (2 C), 126.5 (2 C), 127.5, 128.3 (2 C), 128.5 (2 C), 129.0, 129.3 (2 C), 129.6 (2 C), 133.6, 138.8, 139.8, 141.1, 147.5. IR (film): 3369, 3059, 3030, 2923, 1623, 1597, 1493, 1448, 1401, 1312, 1302, 1266, 1184, 1144, 1084, 1029, 1012, 926, 895, 811, 752, 736, 557 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{21}O_2S$ $[M + H]^+$ 349.1257, found 349.1264. Data for (±)-**10d**: R_f 0.30 (10% Et_2O–CH_2Cl_2). mp 153–155 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3 H), 4.41 (s, 1 H), 5.69 (s, 1 H), 6.73 (s, 1 H), 7.15 (d, 2 H, J = 6.5 Hz), 7.44–7.50 (m, 10 H), 7.51 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 71.3, 124.5 (2 C), 126.5 (2 C), 127.6, 128.2 (2 C), 128.5 (2 C), 129.1, 129.6 (2 C), 130.1 (2 C), 133.4, 138.6, 138.8, 139.6, 141.3, 147.2. IR (KBr): 3414, 3059, 2965, 2926, 1642, 1492, 1448, 1397, 1324, 1269, 1180, 1079, 1039, 1013, 927, 808, 752, 715, 697 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{19}OS$ $[M + H - (H_2O)]^+$ 331.1151, found 331.1171.

*Synthesis of (±)-(1E,3R,4Z,S$_S$)-1-Phenyl-4-(p-tolylsulfinyl)nona-1,4-dien-3-ol, (±)-**9i**, and (1E,3S,4Z,S$_S$)-1-Phenyl-4-(p-tolylsulfinyl)-nona-1,4-dien-3-ol, (±)-**10i**.* From (±)-**8i** (103 mg, 0.304 mmol), *m*-CPBA (136 mg, 0.609 mmol), and K_2CO_3 (126 mg, 0.913 mmol) in acetone, according to the general procedure, a 33:67 mixture of (±)-**9i** and (±)-**10i** was obtained. Chromatographic purification (5–20% EtOAc–hexane) gave (±)-**9i** (35 mg, 32%) and (±)-**10i** (70 mg, 65%) as yellow oils. Data for (±)-**9i**: R_f 0.30 (20% EtOAc–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.94 (t, 3 H, J = 7.1 Hz), 1.35–1.55 (m, 4 H), 2.32–2.41 (m, 1 H), 2.35 (s, 3 H), 2.60–2.69 (m, 1 H), 5.24 (d, 1 H, J = 5.4 Hz), 6.04 (dd, 1 H, J = 15.9, 5.4 Hz), 6.30 (dd, 1 H, J = 8.8, 6.6 Hz), 6.59 (dd, 1 H, J = 15.9, 1.4 Hz), 7.18–7.27 (m, 7 H), 7.53 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.1, 21.5, 22.6, 29.1, 31.3, 72.6, 125.0 (2 C), 126.8 (2 C), 127.8, 128.6 (2 C), 130.0, 130.2 (2 C), 130.3, 136.7, 139.8, 141.2, 141.3, 144.0. IR (film): 3378, 3058, 3026, 2957, 2927, 2859, 1636, 1598, 1476, 1493, 1448, 1430, 1396, 1380, 1290, 1253, 1135, 1080, 1024, 1011, 971, 808, 755, 693 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{26}NaO_2S$ $[M + Na]^+$ 377.1546, found 377.1534. Data for (±)-**10i**: R_f 0.20 (20% EtOAc–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 3 H, J = 7.2 Hz), 1.38–1.56 (m, 4 H), 2.40 (s, 3 H), 2.44–2.53 (m, 1 H), 2.69–2.79 (m, 1 H), 5.09 (d, 1 H, J = 5.6 Hz), 5.92 (dd, 1 H, J = 15.9, 5.6 Hz), 6.36 (dd, 1 H, J = 8.8, 6.8 Hz), 6.48 (dd, 1 H, J = 15.9, 1.5 Hz), 7.20–7.34 (m, 7 H), 7.50 (d, 2 H, J = 8.3 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.3, 22.3, 28.7, 31.2, 68.5, 124.2 (2 C), 126.4 (2 C), 127.6, 128.1, 128.4 (2 C), 130.0 (2 C), 130.9, 136.4, 138.4, 140.6, 141.3, 144.8. IR (film): 3417, 3055, 2987, 2962, 2931, 2874, 2861, 1637, 1599, 1493, 1422, 1266, 1099, 1081, 1012, 1013, 896, 809, 741, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{26}NaO_2S$ $[M + Na]^+$ 377.1546, found 377.1547.

*Synthesis of (±)-(1Z,3R,4E,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)hexa-1,4-dien-3-ol, (±)-**9j**, and (±)-(1Z,3S,4E,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)hexa-1,4-dien-3-ol, (±)-**10j**.* From (±)-**8j** (283 mg, 0.96 mmol), *m*-CPBA (428 mg, 1.91 mmol), and K_2CO_3 (396 mg, 2.87 mmol) in acetone, according to the general procedure, a 32:68 mixture of (±)-**9j** and (±)-**10j** was obtained. Chromatographic purification (30–40% Et_2O–hexane) gave (±)-**9j** (70 mg, 24%) and (±)-**10j** (146 mg, 49%) as yellow oils. Data for (±)-**9j**: R_f 0.30 (40% Et_2O–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.68 (ddd, 3 H, J = 6.5, 1.6, 1.2 Hz), 2.39 (s, 3 H), 2.99 (br s, 1 H), 5.16 (t, 1 H, J = 5.5 Hz), 5.58 (ddq, 1 H, J = 15.3, 5.5, 1.6 Hz), 5.80 (dqd, 1 H, J = 15.3, 6.5, 1.2 Hz), 7.25–7.27 (m, 3 H), 7.36–7.47 (m, 7 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 21.3, 70.7, 124.9 (2 C), 127.7, 128.5 (2 C), 128.9, 129.6 (2 C), 129.8 (2 C), 131.3, 133.7, 137.4, 139.8, 140.9, 146.0. IR (film): 3368, 3053, 3026, 2963, 2917, 2856, 1622, 1596, 1576, 1492, 1446, 1266, 1210, 1119, 1080, 1027, 1012, 971, 926, 809, 753, 735, 697, 638 cm^{-1}. HRMS (ES) m/z Calcd for $C_{19}H_{20}NaO_2S$ $[M + Na]^+$ 335.1076, found 335.1075. Data for (±)-**10j**: R_f 0.20 (40% Et_2O–hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.65 (d, 3 H, J = 6.5 Hz), 2.41 (s, 3 H), 4.09 (br s, 1 H), 5.04 (d, 1 H, J = 6.0 Hz), 5.42 (dd, 1 H, J = 15.1, 6.0 Hz), 5.61 (dq, 1 H, J = 15.1, 6.5 Hz), 7.29–7.53 (m, 10 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 17.6, 21.3, 69.1, 124.6 (2 C), 128.2, 128.5 (2 C), 129.0, 129.6 (2 C), 129.7, 129.9 (2 C), 133.6, 137.5, 138.4, 141.1, 145.9. IR (film): 3293, 3024, 2917, 1618, 1595, 1491, 1449, 1299, 1175, 1121, 1072, 1022, 974, 946, 928, 905, 876, 834, 801, 750, 693, 623 cm^{-1}. HRMS (ES) m/z Calcd for $C_{19}H_{20}NaO_2S$ $[M + Na]^+$ 335.1076, found 335.1081.

*Synthesis of (±)-(1Z,3R,4E,S$_S$)-1,5-Diphenyl-2-(p-tolylsulfinyl)-penta-1,4-dien-3-ol, (±)-**9k**, and (±)-(1Z,3S,4E,S$_S$)-1,5-Diphenyl-2-(p-tolylsulfinyl)penta-1,4-dien-3-ol, (±)-**10k**.* From (±)-**8k** (397 mg, 1.11 mmol), *m*-CPBA (497 mg, 2.22 mmol), and K_2CO_3 (459 mg, 3.33 mmol) in acetone, according to the general procedure, a 36:64 mixture of (±)-**9k** and (±)-**10k** was obtained. Chromatographic purification (40–60% Et_2O–hexane) gave (±)-**9k** (100 mg, 24%) as a yellow oil and (±)-**10k** (175 mg, 42%) as a white solid. Data for (±)-**9k**: R_f 0.40 (50% Et_2O–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.34 (s, 3 H), 3.30 (d, 1 H, J = 5.3 Hz), 5.39 (app t, 1 H, J = 5.3 Hz), 6.20 (dd, 1 H, J = 15.9, 5.3 Hz), 6.68 (dd, 1 H, J = 15.9, 1.6 Hz), 7.22–7.51 (m, 15 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 72.2, 124.8 (2 C), 126.6 (2 C), 127.6, 128.4 (2 C), 128.6 (2 C), 129.2, 129.8 (2 C), 130.0 (2 C), 130.3, 133.6, 136.4, 138.3, 139.5, 141.1, 145.20, 145.21. IR (film): 3370, 3054, 2985, 2926, 1599, 1492, 1447, 1421, 1265, 1030, 1013, 971, 896, 810, 750, 702 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{22}NaO_2S$ $[M + Na]^+$ 397.1233, found 397.1230. Data for (±)-**10k**: R_f 0.30 (50% Et_2O–hexane). mp 120–122 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 4.08 (app d, 1 H, J = 2.1 Hz), 5.27 (td, 1 H, J = 5.6, 2.1 Hz), 6.03 (dd, 1 H, J = 15.9, 5.6 Hz), 6.56 (dd, 1 H, J = 15.9, 1.6 Hz), 7.23–7.53 (m, 15 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 68.7, 124.5 (2 C), 126.4 (2 C), 127.6, 128.2, 128.4 (2 C), 128.6 (2 C), 129.1, 129.7 (2 C), 130.0 (2 C), 131.1, 133.5, 136.3, 137.9, 138.4, 141.2, 145.9. IR (KBr): 3368, 3055, 3027, 2923, 1621, 1599, 1492, 1447, 1265, 1080, 1041, 966, 808, 754, 694 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{22}NaO_2S$ $[M + Na]^+$ 397.1233, found 397.1257.

General Procedure for the Synthesis of Vinyl Sulfinyl Trichloroacetimidates. To a cold solution (0 °C) of the starting material (1.0 equiv) in anhydrous CH_3CN (10.0 mL/mmol) were added DBU (0.20 equiv) and trichloroacetonitrile (5.0 equiv). The mixture was allowed to warm to rt and monitored by TLC (15 min). The solvent was evaporated, and the crude product was purified by column chromatography on silica gel using a gradient of the appropriate solvents.

*Synthesis of (+)-(3R,4E,S$_S$)-6-(tert-Butyldiphenylsilyloxy)-4-(p-tolylsulfinyl)hex-4-en-3-yl 2,2,2-trichloroacetimidate, **4e**.* From **2e** (50 mg, 0.10 mmol), DBU (3 μL, 0.02 mmol), and Cl_3CCN (50 μL, 0.50 mmol) in CH_3CN, according to the general procedure, and after chromatographic purification (5–20% EtOAc–hexane), **4e** (54 mg, 85%) was obtained as a yellow oil. Data for **4e**: R_f 0.40 (20% EtOAc–hexane). $[\alpha]^{20}_D$ +48.1 (*c* 0.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.72 (t, 3 H, J = 7.4 Hz), 1.07 (s, 9 H), 1.14–1.23 (m, 1 H), 1.59–1.70 (m, 1 H), 2.39 (s, 3 H), 4.57 (dd, 1 H, J = 15.2, 4.5 Hz), 4.66 (dd, 1 H, J = 15.2, 6.7 Hz), 5.11 (dd, 1 H, J = 9.2, 4.7 Hz), 6.80 (dd, 1 H, J = 6.7, 4.6 Hz), 7.24–7.26 (m, 2 H), 7.36–7.581 (m, 8 H), 7.66–7.68 (m, 4 H), 8.06 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 10.3, 19.4, 21.7, 27.0 (3 C), 27.1, 61.5, 75.9, 77.4, 126.1 (2 C), 127.99 (2 C), 128.0 (2 C), 130.1 (2 C), 133.35, 133.4, 135.81, 135.84, 137.77, 137.8, 139.9, 142.1, 142.5, 161.2. IR (film): 3344, 3072, 3050, 2960, 2931, 2857, 1667, 1472, 1463, 1428, 1378, 1315, 1285, 1112, 1081, 981, 824, 796, 739, 703, 647 cm^{-1}. HRMS (ES) m/z Calcd for $C_{31}H_{37}Cl_3NO_3SSi$ $[M + H]^+$ 636.1324, found 636.1316.

*Synthesis of (+)-(3S,4E,S$_S$)-6-(tert-Butyldiphenylsilyloxy)-4-(p-tolylsulfinyl)hex-4-en-3-yl 2,2,2-trichloroacetimidate, **5e**.* From **3e** (100 mg, 0.2 mmol), DBU (6 μL, 0.04 mmol), and Cl_3CCN (100 μL, 1.0 mmol) in CH_3CN, according to the general procedure, **5e** was obtained. Purification by column chromatography (5–20% EtOAc–hexane) afforded **5e** (118 mg, 93%) as a white solid, in equilibrium with sulfurane **5e′** in an 83:17 ratio. Data for **5e** (from the mixture): R_f 0.40 (20% EtOAc–hexane). $[\alpha]^{20}_D$ +25.4 (*c* 1.0, $CHCl_3$). ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 0.67 (t, 3 H, J = 7.4 Hz, H-1), 0.83–0.91 (m, 1 H, H-2a), 1.07 (s, 9 H, 3 × CH_3 *t*-Bu), 1.07–1.15 (m, 1 H, H-2b), 2.40 (s, 3 H, CH_3 *p*-Tol), 4.56 (dd, 1 H, J = 15.1, 4.7 Hz, H-6b), 4.63 (dd, 1 H, J = 15.1, 6.5, H-6a), 5.44 (dd, 1 H, J = 8.9, 5.2 Hz, H-3), 6.79 (dd, 1 H, J = 6.5, 4.7 Hz, H-5), 7.25–7.70 (m, 14 H, Ar), 8.22 (s, 1 H, NH). ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.8, 10.7, 19.1, 21.5, 26.7, 27.0 (3 C), 53.4, 61.3, 76.0, 77.2, 124.0, 126.1 (2 C), 127.77 (2 C),

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081–4097

127.8, 127.9, 129.8 (2 C), 129.9 (2 C), 130.2, 133.1, 134.9, 135.5, 135.6 (4 C), 139.9, 142.1, 142.5, 160.9. IR (film): 3343, 3071, 3050, 2961, 2931, 2858, 1668, 1590, 1472, 1463, 1428, 1284, 1187, 1112, 1082, 983, 824, 796, 703, 646, 623, 615 cm^{-1}. HRMS (ES) m/z Calcd for $C_{31}H_{37}Cl_3NO_3SSi$ $[M + H]^+$ 636.1324, found 636.1302. Partial data for **5e′** (from the mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 0.60 (t, 3 H, J = 7.3 Hz, H-1), 2.44 (s, 3 H, CH_3 *p*-Tol), 9.58 (s, 1 H, SOH).

*Synthesis of (±)-(3R,4Z,S$_S$)-4-(p-Tolylsulfinyl)non-4-en-3-yl 2,2,2-trichloroacetimidate, (±)-**11a**.* From (±)-**9a**[19] (44 mg, 0.16 mmol), DBU (5 μL, 0.03 mmol), and Cl_3CCN (79 μL, 0.79 mmol) in CH_3CN, according to the general procedure, (±)-**11a** (63 mg, 94%) was obtained after purification by column chromatography (10−60% EtOAc−hexane) as a colorless oil. Data for (±)-**11a**: R_f 0.36 (50% Et_2O−hexane). ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 0.93 (t, 3 H, J = 7.4 Hz, H-1), 0.94 (t, 3 H, J = 7.2 Hz, H-9), 1.35−1.43 (m, 2 H, H-8), 1.45−1.53 (m, 2 H, H-7), 1.83−2.05 (m, 2 H, H-2), 2.38 (s, 3 H, CH_3 *p*-Tol), 2.49−2.58 (m, 1 H, H-6a), 2.69−2.78 (m, 1 H, H-6b), 5.38 (dd, 1 H, J = 7.6, 4.9 Hz, H-3), 6.40 (dd, 1 H, J = 8.6, 7.1 Hz, H-5), 7.26 (d, 2 H, J = 8.2 Hz, *p*-Tol), 7.46 (d, 2 H, J = 8.2 Hz, *p*-Tol), 7.90 (s, 1 H, NH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 9.5 (C-1), 13.8 (C-9), 21.3 (CH_3 *p*-Tol), 22.2 (C-8), 28.3 (C-6), 29.5 (C-2), 31.4 (C-7), 74.8 (C-3), 91.4 (CCl_3), 124.7 (2 C), 129.5 (2 C), 138.9 (*p*-Tol), 140.2 (C-5), 140.6 (*p*-Tol), 142.4 (C-4), 160.4 (C═NH). IR (film): 3346, 3055, 2964, 2933, 2875, 1667, 1493, 1283, 1080, 1044, 1015, 978, 830, 794 cm^{-1}. HRMS (ES) m/z Calcd for $C_{18}H_{25}Cl_3NO_2S$ $[M + H]^+$ 424.0666, found 424.0663.

*Synthesis of (±)-(3S,4Z,S$_S$)-4-(p-Tolylsulfinyl)non-4-en-3-yl 2,2,2-trichloroacetimidate, (±)-**12a**.* From (±)-**10a**[19] (40 mg, 0.16 mmol), DBU (5 μL, 0.03 mmol), and Cl_3CCN (79 μL, 0.79 mmol) in CH_3CN, according to the general procedure, (±)-**12a** (65 mg, 97%) was obtained after purification by column chromatography (20−80% Et_2O−hexane) as a colorless oil, in equilibrium with sulfurane (±)-**12a′** in a 50:50 ratio. Data for (±)-**12a** (from the mixture): R_f 0.32 (50% Et_2O−hexane). ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 0.72 (t, 3 H, J = 7.3 Hz, H-1), 0.90 (t, 3 H, J = 7.2 Hz, H-9), 1.06−1.24 (m, 2 H, H-2), 1.30−1.40 (m, 2 H, H-8), 1.43−1.48 (m, 2 H, H-7), 2.39 (s, 3 H, CH_3 *p*-Tol), 2.42−2.52 (m, 1 H, H-6a), 2.70−2.81 (m, 1 H, H-6b), 5.75 (dd, 1 H, J = 7.8, 4.0 Hz, H-3), 6.35 (t, 1 H, J = 6.3 Hz, H-5), 7.27 (d, 2 H, J = 8.0 Hz, *p*-Tol), 7.43 (d, 2 H, J = 7.9 Hz, *p*-Tol), 8.40 (s, 1 H, NH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 9.2 (C-1), 13.8 (C-9), 21.4 (CH_3 *p*-Tol), 22.1 (C-7), 28.4 (C-2), 31.0 (C-6), 31.3 (C-8), 72.6 (C-3), 91.6 (CCl_3), 123.9 (2 C), 129.8 (2 C), 139.1 (C-5), 140.7, 141.6, 143.1, 160.5 (C═NH). IR (film): 3448, 3220, 2962, 2932, 2874, 1679, 1643, 1492, 1463, 1381, 1288, 1081, 1036, 1015, 984, 837, 795, 714, 637 cm^{-1}. HRMS (ES) m/z Calcd for $C_{18}H_{25}Cl_3NO_2S$ $[M + H]^+$ 424.0666, found 424.0684. Partial data for (±)-**12a′** (from the mixture): ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 0.54−0.61 (m, 1 H, H-2a), 0.64 (t, 3 H, J = 7.3 Hz, H-1), 0.92 (t, 3 H, J = 7.3 Hz, H-9), 1.30−1.40 (m, 3 H, H-8 and H-2b), 1.43−1.48 (m, 2 H, H-7), 2.37 (s, 3 H, CH_3 *p*-Tol), 2.42−2.52 (m, 1 H, H-6a), 2.70−2.81 (m, 1 H, H-6b), 4.78 (dd, 1 H, J = 9.8, 2.5 Hz, H-3), 6.41 (t, 1 H, J = 6.6 Hz, H-5), 7.31 (d, 2 H, J = 8.0 Hz, *p*-Tol), 7.42 (d, 2 H, J = 7.8 Hz, *p*-Tol), 9.57 (s, 1 H, SOH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 10.4 (C-1), 13.77 (C-9), 21.3 (CH_3 *p*-Tol), 22.1, 28.5, 31.0, 31.2, 70.3 (C-3), 91.6 (CCl_3), 123.6 (2 C), 130.2 (2 C), 137.8, 139.9, 141.4 (C-5), 143.2 (C-4), 157.5 (C═N). NOESY 1D (400 MHz, $CDCl_3$): between SOH-H3 11.0%.

*Synthesis of (±)-(3R,1Z,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)pent-1-en-3-yl 2,2,2-trichloroacetimidate, (±)-**11c**.* From (±)-**9c**[19] (24 mg, 0.12 mmol), DBU (3 μL, 0.02 mmol), and Cl_3CCN (57 μL, 0.57 mmol) in CH_3CN, according to the general procedure, (±)-**11c** (25 mg, 50%) was obtained after purification by column chromatography (1−10% Et_2O−CH_2Cl_2) as an oil. Data for (±)-**11c**: R_f 0.40 (5% Et_2O−CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 1.00 (t, 3 H, J = 7.3 Hz), 1.91−2.05 (m, 1 H), 2.04−2.21 (m, 1 H), 2.36 (s, 3 H), 5.51 (dd, 1 H, J = 7.8, 4.4 Hz), 7.20−7.25 (m, 2 H), 7.31−7.48 (m, 6 H), 7.49−7.57 (m, 2 H), 7.96 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.5, 21.4, 30.0, 75.4, 91.4, 124.9 (2 C), 128.6 (2 C), 129.1, 129.6 (2 C), 129.9 (2 C), 133.7, 137.3, 138.5, 140.8, 143.5, 160.5. IR (film): 3334, 3055, 3025, 2971, 2923, 2877, 1667, 1492, 1447, 1348, 1311, 1286, 1079, 1046, 1016, 979, 829, 794, 752, 696 cm^{-1}. HRMS (ES) m/z Calcd for $C_{20}H_{21}Cl_3NO_2S$ $[M + H]^+$ 444.0353, found 444.0359.

*Synthesis of (±)-(3S,1Z,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)pent-1-en-3-yl 2,2,2-trichloroacetimidate, (±)-**12c**.* From (±)-**10c**[19] (16 mg, 0.077 mmol), DBU (2 μL, 0.02 mmol), and Cl_3CCN (38 μL, 0.38 mmol, 5.0 equiv) in CH_3CN, according to the general procedure, (±)-**12c** (28 mg, 83%) was obtained after purification by column chromatography (5−20% EtOAc−hexane) as a colorless oil, in equilibrium with sulfurane (±)-**12c′** in a 50:50 ratio. Data for (±)-**12c** (from the mixture): R_f 0.40 (5% Et_2O−CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, 3 H, J = 6.8 Hz), 1.12−1.41 (m, 1 H), 1.45−1.58 (m, 1 H), 2.44 (s, 3 H), 5.98 (dd, 1 H, J = 8.1, 3.7 Hz), 7.26−7.55 (m, 10 H), 8.51 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.3, 10.6, 21.3, 21.4, 29.0, 29.7, 70.7, 72.6, 124.1 (2 C), 124.2 (3 C), 128.6 (2 C), 128.7, 129.0, 129.8, 129.91 (2 C), 129.94 (2 C), 129.96 (2 C), 130.1, 130.3 (2 C), 132.9, 133.7, 136.5, 138.7, 141.2, 142.0, 157.7, 160.5. IR (film): 3342, 3216, 3054, 2973, 2926, 2878, 2851, 1679, 1597, 1492, 1448, 1290, 1266, 1080, 1034, 1015, 984, 923, 904, 838, 809, 796, 737, 714, 703, 639, 628 cm^{-1}. HRMS (ES) m/z Calcd for $C_{20}H_{21}Cl_3NO_2S$ $[M + H]^+$ 444.0353, found 444.0345. Data for (±)-**12c′** (from the mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 0.76 (t, 3 H, J = 7.3 Hz), 1.12−1.41 (m, 1 H), 1.45−1.58 (m, 1 H), 2.39 (s, 3 H), 5.01 (dd, 1 H, J = 9.8, 2.3 Hz), 7.26−7.55 (m, 10 H), 9.75 (s, 1 H).

*Synthesis of (±)-(1R,2Z,S$_S$)-1,3-Diphenyl-2-(p-tolylsulfinyl)prop-2-en-1-yl 2,2,2-trichloroacetimidate, (±)-**11d**.* From (±)-**9d** (10 mg, 0.03 mmol), DBU (2 μL, 0.006 mmol), and Cl_3CCN (14 μL, 0.93 mmol) in CH_3CN, according to the general procedure, (±)-**11d** (8 mg, 76%) was obtained after purification by column chromatography (1−5% EtOAc−hexane) as a colorless oil. Data for (±)-**11d**: R_f 0.40 (5% Et_2O−CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 2.36 (s, 3 H), 7.00 (s, 1 H), 7.25−7.55 (m, 15 H), 8.12 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 72.2, 91.1, 124.8 (2 C), 126.0 (2 C), 127.9, 128.6 (4 C), 129.5, 129.9 (2 C), 130.0 (2 C), 133.4, 138.7, 141.0, 142.3, 144.4, 160.1. IR (film): 3692, 3055, 2987, 2686, 1422, 1266, 896, 746, 702 cm^{-1}. HRMS (ES) m/z Calcd for $C_{22}H_{19}OS$ $[M - C_2HCl_3NO]^+$ 331.1151, found 331.1169.

*Synthesis of (±)-(1S,2Z,S$_S$)-1,3-Diphenyl-2-(p-tolylsulfinyl)prop-2-ene-1-yl 2,2,2-trichloroacetimidate, (±)-**12d**.* From (±)-**10d** (65 mg, 0.18 mmol), DBU (6 μL, 0.04 mmol), and Cl_3CCN (94 μL, 0.93 mmol) in CH_3CN, according to the general procedure, (±)-**12d** (40 mg, 78%) was obtained after purification by column chromatography (5−20% EtOAc−hexane) as a colorless oil, in equilibrium with sulfurane (±)-**12d′** in an 83:17 ratio. Data for (±)-**12d** (from the mixture): R_f 0.30 (30% EtOAc−hexane). ^1H NMR (400 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 6.91 (s, 1 H), 6.98−7.57 (m, 15 H), 8.48 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 73.1, 91.3, 124.5 (2 C), 126.9 (2 C), 127.9, 128.1 (2 C), 128.6 (2 C), 129.3, 129.6 (2 C), 130.0 (2 C), 133.5, 137.6, 138.6, 138.8, 140.7, 144.2, 160.2. IR (film): 3691, 3054, 2987, 1666, 1603, 1551, 1421, 1265, 745, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{21}Cl_3NO_2S$ $[M + H]^+$ 492.0353, found 492.0329. Partial data for (±)-**12d′** (from the mixture): ^1H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 3 H), 6.17 (s, 1 H), 6.84−6.86 (m, 2 H), 6.98−7.57 (m, 12 H), 7.76 (s, 1 H), 9.76 (s, 1 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.2, 70.9, 124.6 (2 C), 128.2 (2 C), 128.8, 129.9 (2 C), 130.1 (2 C), 132.7 (2 C), 132.7, 136.9, 140.1, 141.4, 142.0, 157.2.

General Procedure for the [3,3]-Sigmatropic Rearrangement. To a solution of the starting material in anhydrous DMF (10.0 mL/mmol), at room temperature, was added a crystal of 2,6-di-*tert*-butyl-4-methylphenol (BHT). The mixture was stirred at 100 °C and monitored by TLC until completion (approximately 1 d). Then the solvent was evaporated under reduced pressure to give the corresponding trichloroacetamide that was purified by chromatography on silica gel using the appropriate mixture of solvents.

*Synthesis of (−)-N-[(2R,3Z,S$_S$)-1-(tert-Butyldiphenylsilyloxy)-3-(p-tolylsulfinyl)hex-3-en-2-yl]-2,2,2-trichloroacetamide, **13e**, and N-[(2S,3E,S$_S$)-1-(tert-Butyldiphenylsilyloxy)-3-(p-tolylsulfinyl)hex-3-en-2-yl]-2,2,2-trichloroacetamide, **14e**.* From **4e** (10.0 mg, 0.02 mmol)

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

in DMF, according to the general procedure and after chromatographic purification (10−20% EtOAc−hexane), a 90:10 mixture of **13e**:**14e** was obtained as a colorless oil (8.0 mg, 70%). Data for **13e** (from the mixture): R_f 0.40 (25% EtOAc−hexane). $[\alpha]^{20}_D$ −46.9 (*c* 0.90, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (s, 9 H, 3 × CH_3 *t*-Bu), 1.15 (t, 3 H, *J* = 7.5 Hz, H-6), 2.36 (s, 3 H, CH_3 *p*-Tol), 2.36−2.43 (m, 1 H, H-5a), 2.68−2.79 (m, 1 H, H-5b), 3.61 (dd, 1 H, *J* = 10.4, 5.1 Hz, H-1), 3.89 (dd, 1 H, *J* = 10.4, 5.1 Hz, H-1), 4.71 (dt, 1 H, *J* = 7.7, 5.1 Hz, H-2), 6.35 (dd, 1 H, *J* = 8.2, 7.0 Hz, H-4), 7.24 (d, 2 H, *J* = 8.0 Hz, Ar), 7.33−7.58 (m, 12 H, Ar), 8.02 (d, 1 H, *J* = 7.7 Hz, NH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 14.0 (C-6), 19.4 (C *t*-Bu), 21.6 (CH_3 *p*-Tol), 22.9 (C-5), 27.0 (3 × CH_3 *t*-Bu), 54.8 (C-2), 64.9 (C-1), 124.5 (2 C), 127.9 (2 C), 128.0 (2 C), 130.06, 130.1, 130.2 (2 C), 132.7, 133.0, 135.7 (2 C), 135.8 (2 C), 138.7, 141.3, 143.9, 160.5 (C═O). IR (film): 3414, 3054, 2961, 2931, 2858, 1717, 1493, 1472, 1462, 1428, 1265, 1113, 1080, 1040, 1013, 895, 823, 809, 739, 705 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{31}H_{37}Cl_3NO_3SSi$ [M + H]$^+$ 636.1324, found 636.1323. Partial data for **14e** (from the mixture): ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.01 (s, 9 H), 2.35 (s, 3 H), 3.64−3.66 (m, 1 H), 4.00 (dd, 1 H, *J* = 10.8, 9.6 Hz), 5.18−5.24 (m, 1 H), 6.14 (ddd, 1 H, *J* = 7.9, 7.1, 1.0 Hz).

Synthesis of (−)-N-[(4S,2Z,S$_S$)-1-(tert-Butyldiphenylsilyloxy)-3-(p-tolylsulfinyl)hex-3-en-2-yl]-2,2,2-trichloroacetamide, ***15e****, and N-[(4R,2E,S$_S$)-1-(tert-Butyldiphenylsilyloxy)-3-(p-tolylsulfinyl)hex-3-en-2-yl]-2,2,2-trichloroacetamide,* ***16e****.* From an 83:17 mixture of **5e**:**5e**′ (31 mg, 0.05 mmol) in DMF, according to the general procedure and after chromatographic purification (10−20% EtOAc−hexane), a 95:5 mixture of **15e**:**16e** was obtained as a colorless oil (13 mg, 42%). Data for **15e** (from the mixture): R_f 0.25 (20% EtOAc−hexane). $[\alpha]^{20}_D$ −72.4 (*c* 1.10, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.02 (s, 9 H, 3 × CH_3 *t*-Bu), 1.04 (t, 3 H, *J* = 7.6 Hz, H-6), 2.24−2.31 (m, 1 H, H-5a), 2.34 (s, 3 H, CH_3 *p*-Tol), 2.44−2.53 (m, 1 H, H-5b), 3.71−3.78 (m, 2 H, H-1), 4.89 (dddd, 1 H, *J* = 8.3, 6.5, 5.7, 0.8 Hz, H-2), 6.15 (ddd, 1 H, *J* = 8.5, 6.8, 0.8 Hz, H-4), 7.20−7.22 (m, 2 H, Ar), 7.36−7.63 (m, 12 H, Ar), 7.98 (d, 1 H, *J* = 8.3 Hz, NH). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 13.4 (C-6), 19.1 (C *t*-Bu), 21.3 (CH_3 *p*-Tol), 22.9 (C-5), 26.8 (3 × CH_3 *t*-Bu), 55.4 (C-2), 65.9 (C-1), 92.3 (CCl_3), 124.6 (2 C), 127.7 (2 C), 127.8 (2 C), 129.8, 129.9, 130.2 (2 C), 132.81, 132.84, 135.5 (2 C), 135.6 (2 C), 138.3, 139.6, 141.1, 143.0 (C-4), 160.9 (C═O). IR (film): 3220, 3047, 2961, 2930, 2856, 1714, 1525, 1428, 1113, 1030, 823, 703, 613 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{31}H_{37}Cl_3NO_3SSi$ [M + H]$^+$ 636.1324, found 636.1307. Partial data for **16e** (from the mixture): ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.22 (dd, 1 H, *J* = 10.6, 6.1 Hz, H-1a), 3.65 (dd, 1H, *J* = 10.6, 8.0 Hz, H-1b), 5.16 (td, 1 H, *J* = 7.9, 6.1 Hz, H-2), 6.52 (t, 1 H, *J* = 7.6 Hz, H-4), 8.27 (d, 1 H, *J* = 7.9 Hz, NH).

*Synthesis of (±)-N-[(2S,1Z,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)pent-2-en-1-yl]-2,2,2-trichloroacetamide, (±)-****15c****, and (±)-N-[(2R,1E,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)pent-2-en-1-yl]-2,2,2-trichloroacetamide, (±)-****16c****.* From (±)-**11c** (20 mg, 0.05 mmol) in DMF, according to the general procedure and after chromatographic purification (10−30% EtOAc−hexane), a 54:46 mixture of (±)-**15c**:(±)-**16c** was obtained as a colorless oil (18 mg, 81%). Data for (±)-**16c** (from the mixture): R_f 0.30 (20% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.17 (t, 3 H, *J* = 7.5 Hz), 2.29 (s, 3 H), 2.39−2.67 (m, 2 H), 6.37 (d, 1 H, *J* = 8.2 Hz), 6.70 (t, 1 H, *J* = 7.9 Hz), 6.92−7.49 (m, 9 H), 8.70 (d, 1 H, *J* = 7.9 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.4, 21.2, 22.4, 52.8, 124.2 (2 C), 125.7, 127.1 (2 C), 128.3 (2 C), 129.6 (2 C), 136.0, 138.2, 141.1, 141.3, 142.9, 160.8. IR (film): 3405, 3243, 3055, 2989, 2935, 1713, 1494, 1455, 1266, 1081, 1046, 1028, 1013, 823, 810, 703 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{20}H_{21}Cl_3NO_2S$ [M + H]$^+$ 444.0353, found 444.0367. Data for (±)-**15c** is identical to that found before.

*Synthesis of (±)-N-[(1S,2E,S$_S$)-1-Phenyl-2-(p-tolylsulfinyl)pent-2-en-1-yl)]-2,2,2-trichloroacetamide, (±)-****14c****.* From a 50:50 mixture of (±)-**12c**:(±)-**12c**′ (20 mg, 0.05 mmol) in DMF, according to the general procedure and after chromatographic purification (10−30% EtOAc−hexane), (±)-**14c** was obtained as a colorless oil (11 mg, 55%). Data for (±)-**14c**: R_f 0.30 (20% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 3 H, *J* = 7.5 Hz), 2.08−2.31 (m, 1 H), 2.38 (s, 3 H), 6.16 (td, 1 H, *J* = 7.6, 1.1 Hz), 6.26 (d, 1 H, *J* = 8.6 Hz), 7.29−7.49 (m, 9 H), 8.98 (d, 1 H, *J* = 8.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 12.8, 21.3, 22.4, 54.9, 125.2 (2 C), 127.1 (2 C), 128.1, 128.9 (2 C), 130.2 (2 C), 138.9, 139.2, 141.0, 141.6, 142.0, 161.0. IR (film): 3416, 3055, 2987, 2928, 1717, 1493, 1446, 1422, 1266, 1180, 1081, 1041, 896, 822, 811, 738 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{20}H_{21}Cl_3NO_2S$ [M + H]$^+$ 444.0353, found 444.0391.

*Synthesis of (±)-N-[(1R,2Z,S$_S$)-1,3-Diphenyl-2-(p-tolylsulfinyl)-prop-2-en-1-yl)]-2,2,2-trichloroacetamide, (±)-****13d****, and (±)-N-[(1S,2E,S$_S$)-1,3-Diphenyl-2-(p-tolylsulfinyl)prop-2-en-1-yl)]-2,2,2-trichloroacetamide, (±)-****14d****.* From (±)-**12d** (16 mg, 0.03 mmol) in DMF, according to the general procedure and after chromatographic purification (10−20% EtOAc−hexane), a 5:95 mixture of (±)-**13d**:(±)-**14d** was obtained as a colorless oil (13 mg, 85%). Data for (±)-**14d** (from the mixture): R_f 0.30 (30% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3 H), 6.58 (d, 1 H, *J* = 8.8 Hz), 7.07 (s, 1 H), 7.28−7.37 (m, 12 H), 7.58 (d, 2 H, *J* = 8.2 Hz), 8.90 (d, 1 H, *J* = 8.7 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.4, 54.4, 92.2, 125.8 (2 C), 126.6 (2 C), 128.1, 128.8 (2 C), 128.9 (2 C), 129.1 (2 C), 129.4, 130.3 (2 C), 133.1, 135.8, 138.1, 139.3, 142.3, 143.5, 161.0. IR (film): 3397, 3270, 3056, 2985, 2926, 2854, 1712, 1597, 1494, 1448, 1422, 1399, 1380, 1305, 1266, 1182, 1083, 1030, 895, 822, 748, 699, 661 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{24}H_{21}Cl_3NO_2S$ [M + H]$^+$ 492.0353, found 492.0375. Spectroscopic data for (±)-**13d** is identical to that found before.

Synthesis of (2R,3E,5E,S$_S$)-5-(p-Tolylsulfinyl)deca-3,5-dien-2-ol, ***25****, and (2S,3E,5E,S$_S$)-5-(p-Tolylsulfinyl)deca-3,5-dien-2-ol,* ***26****.* From **2h** (46 mg, 0.23 mmol), DBU (7 μL, 0.05 mmol), and Cl_3CCN (115 μL, 1.15 mmol), in CH_3CN, according to the general procedure (15 min), the corresponding acetimidate was obtained. After chromatographic purification on silica gel (50% Et_2O−CH_2Cl_2−Et_2O), a 50:50 mixture of sulfinyl dienols **25**:**26** (35 mg, 76%) was obtained as a colorless oil. Similarly from **3h** (30 mg, 0.03 mmol) and after chromatographic purification on silica gel, a 50:50 mixture of sulfinyl dienols **25**:**26** (42 mg, 80%) was obtained as a colorless oil. The structural assignments for **25** and **26** are arbitrary; the structures could be exchanged. Data for **25** (from the mixture): R_f 0.45 (40% Et_2O−CH_2Cl_2). ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 0.89 (t, 3 H, *J* = 7.3 Hz, H-10), 1.13 (d, 3 H, *J* = 6.4 Hz, H-1), 1.34 (sext, 2 H, *J* = 7.2 Hz, H-9), 1.46 (quint, 2 H, *J* = 7.0 Hz, H-8), 1.75 (br s, 1 H, OH), 2.29 (q, 2 H, *J* = 7.4 Hz, H-7), 2.35 (s, 3 H, CH_3 *p*-Tol), 4.23 (br m, 1 H, H-2), 5.92 (dd, 1 H, *J* = 16.2, 5.5 Hz, H-3), 6.12 (d, 1 H, *J* = 6.6 Hz, H-4), 6.47 (t, 1 H, *J* = 7.6 Hz, H-6), 7.22 (d, 2 H, *J* = 8.0 Hz, *p*-Tol), 7.45 (d, 2 H, *J* = 8.2 Hz, *p*-Tol). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 13.8 (C-10), 21.4 (C-1), 22.3 (CH_3 *p*-Tol), 23.1 (C-9), 28.03 (C-7), 31.1 (C-8), 68.46 (C-2), 118.3 (C-4), 125.5 (2 C), 129.68 (2 C), 135.4 (C-6), 139.4 (C-3), 140.4, 140.5, 141.4. IR (film): 3391, 2965, 2929, 2872, 1646, 1597, 1493, 1456, 1401, 1366, 1303, 1145, 1082, 1035, 965, 809 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{17}H_{25}O_2S$ [M + H]$^+$ 293.1570, found 293.1570. Partial data for **26** (from the mixture): R_f 0.45 (40% Et_2O−CH_2Cl_2). The NMR signals overlapped with those of **25**, except for ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 1.16 (d, 3 H, *J* = 6.9 Hz, H-1), 6.08 (d, 1 H, *J* = 6.5 Hz, H-4). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 28.05 (C-7), 68.50 (C-2), 125.47 (2 C), 129.66 (2 C), 134.6 (C-6), 139.5 (C-3), 140.4, 140.5, 141.4.

Synthesis of (+)-N-[(2R,3E,5E,S$_S$)-6-Phenyl-5-(p-tolylsulfinyl)hexa-3,5-dien-2-yl]-2,2,2-trichloroacetamide, ***21j****.* From **2j** (80 mg, 0.26 mmol), DBU (8 μL, 0.05 mmol), and Cl_3CCN (128 μL, 1.28 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (20−30% EtOAc−hexane), **21j** was obtained as a white gum (98 mg, 83%). Data for **21j**: R_f 0.25 (30% EtOAc−hexane). $[\alpha]^{20}_D$ +101.7 (*c* 1.00, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.28 (d, 3 H, *J* = 6.9 Hz, H-1), 2.37 (s, 3 H, CH_3 *p*-Tol), 4.46−4.55 (m, 1 H, H-2), 6.06 (dd, 1 H, *J* = 16.3, 6.0 Hz, H-3), 6.32 (dt, 1 H, *J* = 16.3, 1.4 Hz, H-4), 6.60 (d, 1 H, *J* = 7.4 Hz, NH), 7.24 (d, 2 H, *J* = 8.0 Hz, *p*-Tol), 7.23−7.45 (m, 6 H, H-6, Ar), 7.53 (d, 2 H, *J* = 8.0 Hz, *p*-Tol). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 20.0 (C-1), 21.4 (CH_3 *p*-Tol), 49.1 (C-2), 92.4 (CCl_3), 122.1 (C-4), 125.8 (2 C), 128.7 (2 C), 128.9, 129.6 (2 C), 129.9 (2 C), 131.5, 134.3, 135.4 (C-3), 140.1,

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

140.2, 142.0, 160.9 (C═O). IR (film): 3623, 3418, 3054, 2985, 2929, 1711, 1509, 1493, 1448, 1421, 1265, 1082, 1029, 1016, 895, 823, 811, 739, 704 cm^{-1}. HRMS (ES) m/z Calcd for $C_{21}H_{21}Cl_3NO_2S$ $[M + H]^+$ 456.0353, found 456.0378.

*Synthesis of (+)-N-[(2S,3E,5E,S$_S$)-6-Phenyl-5-(p-tolylsulfinyl)hexa-3,5-dien-2-yl]-2,2,2-trichloroacetamide, **22j**.* From **3j** (160 mg, 0.51 mmol), DBU (15 μL, 0.05 mmol), and Cl_3CCN (0.26 mL, 2.56 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (20−30% EtOAc−hexane), **22j** was obtained as a yellow oil (177 mg, 77%). Data for **22j**: R_f 0.25 (30% EtOAc−hexane). $[\alpha]^{20}_D$ +79.0 (c 1.30, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.25 (d, 3 H, J = 6.9 Hz, H-1), 2.35 (s, 3 H, CH_3 p-Tol), 4.40−4.55 (m, 1 H, H-2), 6.02 (dd, 1 H, J = 16.4, 6.1 Hz, H-3), 6.31 (dt, 1 H, J = 16.4, 1.4 Hz, H-4), 6.60 (d, 1 H, J = 7.9 Hz, NH), 7.23 (d, 2 H, J = 7.9 Hz, p-Tol), 7.27−7.46 (m, 6 H, H-6, Ar), 7.51 (d, 2 H, J = 8.2 Hz, p-Tol). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 20.1 (C-1), 21.6 (CH_3 p-Tol), 49.2 (C-2), 92.6 (CCl_3), 122.6 (C-4), 126.0 (2 C), 128.8 (2 C), 129.1 (C-6), 129.8 (2 C), 130.1 (2 C), 131.9, 134.4, 135.5 (C-3), 140.2, 140.4 (C-5), 142.2, 161.1 (C═O). IR (film): 3417, 3325, 3025, 2977, 2927, 1704, 1596, 1515, 1492, 1447, 1378, 1304, 1234, 1158, 1082, 1037, 1015, 823, 668, 624 cm^{-1}. HRMS (ES) m/z Calcd for $C_{21}H_{21}Cl_3NO_2S$ $[M + H]^+$ 456.0353, found 456.0380.

*Synthesis of (+)-N-[(1S,2E,4E,S$_S$)-1,5-Diphenyl-4-(p-tolylsulfinyl)-penta-2,4-dien-1-yl]-2,2,2-trichloroacetamide, **21k**.* From **2k** (63 mg, 0.17 mmol), DBU (5 μL, 0.03 mmol), and Cl_3CCN (84 μL, 0.84 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure and after chromatographic purification (20−100% Et_2O−hexane), **21k** was obtained as a colorless oil (70 mg, 80%). Data for **21k**: R_f 0.25 (60% Et_2O−hexane). $[\alpha]^{20}_D$ +40.5 (c 1.50, $CHCl_3$). ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 2.38 (s, 3 H, CH_3 p-Tol), 5.51 (ddd, 1 H, J = 7.7, 6.5, 1.3 Hz, H-1), 6.27 (dd, 1 H, J = 16.3, 6.5 Hz, H-2), 6.41 (dt, 1 H, J = 16.3, 1.3 Hz, H-3), 7.04 (d, 1 H, J = 7.7 Hz, NH), 7.09−7.11 (m, 2 H, Ar), 7.19 (d, 2 H, J = 8.4 Hz, p-Tol), 7.31−7.48 (m, 11 H, H-5, Ar). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 21.4 (CH_3 p-Tol), 57.0 (C-1), 92.4 (CCl_3), 123.8 (C-3), 125.9 (2 C), 126.8 (2 C), 128.4, 128.7 (2 C), 128.99, 129.0 (2 C), 129.7 (2 C), 129.9 (2 C), 132.5, 133.4 (C-2), 134.1, 138.1, 139.9, 140.0, 141.9, 161.0 (C═O). IR (film): 3244, 3057, 3028, 2923, 1709, 1596, 1515, 1494, 1449, 1265, 1082, 1038, 1015, 965, 928, 824, 755, 737, 697 cm^{-1}. HRMS (ES) m/z Calcd for $C_{26}H_{23}Cl_3NO_2S$ $[M + H]^+$ 518.0510, found 518.0528.

*Synthesis of (+)-N-[(1R,2E,4E,S$_S$)-1,5-Diphenyl-4-(p-tolylsulfinyl)-penta-2,4-dien-1-yl]-2,2,2-trichloroacetamide, **22k**.* From **3k** (72 mg, 0.19 mmol), DBU (6 μL, 0.04 mmol), and Cl_3CCN (97 μL, 0.961 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure and after chromatographic purification (50−100% Et_2O−hexane), **22k** was obtained as a colorless oil (89 mg, 90%). Data for **22k**: R_f 0.25 (60% Et_2O−hexane). $[\alpha]^{20}_D$ +35.8 (c 1.20, $CHCl_3$). ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 2.38 (s, 3 H, CH_3 p-Tol), 5.52 (t, 1 H, J = 7.3 Hz, H-1), 6.22 (dd, 1 H, J = 16.3, 5.7 Hz, H-2), 6.39 (dt, 1 H, J = 16.3, 1.3 Hz, H-3), 6.80 (d, 1 H, J = 7.6 Hz, NH), 7.02−7.04 (m, 2 H, Ar), 7.21 (d, 2 H, J = 8.3 Hz, p-Tol), 7.27−7.36 (m, 6 H, Ar), 7.40−7.43 (m, 3 H, H-5, Ar), 7.49 (d, 2 H, J = 8.2 Hz, p-Tol). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 21.5 (CH_3 p-Tol), 56.9 (C-1), 92.4 (CCl_3), 123.0 (C-3), 126.2 (2 C), 127.2 (2 C), 128.5, 128.7 (2 C), 128.9, 129.1 (2 C), 129.7 (2 C), 130.0 (2 C), 132.2, 133.0 (C-5), 134.2 (C-2), 137.9, 139.8, 140.1, 142.1, 161.0 (C═O). IR (film): 3418, 3244, 3057, 3028, 2923, 1709, 1596, 1515, 1494, 1449, 1082, 1038, 1015, 965, 928, 824, 755, 737, 697 cm^{-1}. HRMS (ES) m/z Calcd for $C_{26}H_{23}Cl_3NO_2S$ $[M + H]^+$ 518.0510, found 518.0522.

*Synthesis of (±)-N-[(1S,2E,4Z,S$_S$)-1-Phenyl-4-(p-tolylsulfinyl)-nona-2,4-dien-1-yl]-2,2,2-trichloroacetamide, (±)-**23i**.* From (±)-**9i** (35 mg, 0.10 mmol), DBU (3 μL, 0.02 mmol), and Cl_3CCN (50 μL, 0.50 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (10−30% EtOAc−hexane), (±)-**23i** was obtained as a yellow oil (42 mg, 85%). Data for (±)-**23i**: R_f 0.20 (20% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (t, 3 H, J = 7.2 Hz), 1.38−1.56 (m, 4 H), 2.40 (s, 3 H), 2.50−2.59 (m, 1 H), 2.69- 2.79 (m, 1 H), 5.44 (app t, 1 H, J = 7.3 Hz), 6.08 (d, 1 H, J = 15.9), 6.20 (dd, 1 H, J = 15.9, 6.3 Hz), 6.26 (t, 1 H, J = 8.0 Hz), 6.86 (d, 1 H, J = 8.2 Hz), 6.99−7.01 (m, 2 H), 7.24−7.39 (m, 7 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.4, 22.4, 28.8, 31.5, 56.7, 92.6, 124.2 (2 C), 125.0, 126.8 (2 C), 128.1, 128.8 (2 C), 128.9 (2 C), 129.8, 131.4, 138.5, 139.5, 140.6, 141.4, 160.8. IR (film): 3417, 3198, 3032, 2960, 2929, 2873, 2859, 1713, 1599, 1494, 1466, 1455, 1265, 1179, 1105, 1082, 1040, 1014, 970, 839, 823, 810, 740, 702 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{27}Cl_3NO_2S$ $[M + H]^+$ 498.0823, found 498.0853.

*Synthesis of (±)-N-[(1R,2E,4Z,S$_S$)-1-Phenyl-4-(p-tolylsulfinyl)-nona-2,4-dien-1-yl]-2,2,2-trichloroacetamide, (±)-**24i**.* From (±)-**10i** (59 mg, 0.17 mmol), DBU (5 μL, 0.03 mmol), and Cl_3CCN (83 μL, 0.83 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (10−30% EtOAc−hexane), (±)-**24i** was obtained as a yellow oil (53 mg, 63%). Data for (±)-**24i**: R_f 0.20 (20% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, 3 H, J = 7.2 Hz), 1.36−1.54 (m, 4 H), 2.38 (s, 3 H), 2.50−2.59 (m, 1 H), 2.66−2.76 (m, 1 H), 5.46 (ddd, 1 H, J = 7.9, 5.5, 1.6 Hz), 6.04 (dm, 1 H, J = 15.8 Hz), 6.20−6.27 (m, 2 H), 6.85 (d, 1 H, J = 7.9 Hz), 7.11−7.30 (m, 7 H), 7.37 (d, 2 H, J = 8.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 21.4, 22.4, 28.7, 31.5, 56.5, 123.6, 124.2 (2 C), 127.2 (2 C), 127.3, 128.3 (2 C), 128.9 (2 C), 129.8, 131.3, 138.4, 139.4, 140.7, 141.5, 160.7 (C═O). IR (film): 3208, 3066, 3030, 2959, 2928, 2873, 2860, 1710, 1599, 1515, 1494, 1466, 1456, 1302, 1265, 1247, 1106, 1082, 1034, 1014, 967, 838, 824, 810, 738, 699, 670, 624 cm^{-1}. HRMS (ES) m/z Calcd for $C_{24}H_{27}Cl_3NO_2S$ $[M + H]^+$ 498.0823, found 498.0837.

*Synthesis of (±)-N-[(2R,3E,5Z,S$_S$)-6-Phenyl-5-(p-tolylsulfinyl)hexa-3,5-dien-2-yl]-2,2,2-trichloroacetamide, (±)-**23j**.* From (±)-**9j** (42 mg, 0.13 mmol), DBU (4 μL, 0.03 mmol), and Cl_3CCN (67 μL, 0.67 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (20−30% EtOAc−hexane), (±)-**23j** was obtained as a pale yellow oil (35 mg, 60%). Data for (±)-**23j**: R_f 0.25 (30% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.27 (d, 3 H, J = 6.8 Hz), 2.39 (s, 3 H), 4.51 (dd, 1 H, J = 10.4, 6.9, 3.4 Hz), 6.18−6.26 (m, 2 H), 6.64 (d, 1 H, J = 7.9 Hz), 7.24−7.54 (m, 10 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 21.3, 48.8, 92.6, 123.3, 124.4 (2 C), 128.6 (2 C), 129.2, 129.9 (2 C), 130.0 (2 C), 133.7, 134.5, 136.6, 139.4, 140.9, 142.5, 160.9. IR (film): 3412, 3054, 2985, 1712, 1689, 1513, 1446, 1265, 1080, 1021, 1006, 896, 821, 747, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{21}H_{21}Cl_3NO_2S$ $[M + H]^+$ 456.0353, found 456.0355.

*Synthesis of (±)-N-[(2S,3E,5Z,S$_S$)-6-Phenyl-5-(p-tolylsulfinyl)hexa-3,5-dien-2-yl]-2,2,2-trichloroacetamide, (±)-**24j**.* From (±)-**10j** (75 mg, 0.24 mmol), DBU (7 μL, 0.048 mmol), and Cl_3CCN (120 μL, 1.20 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (20−30% EtOAc−hexane), (±)-**24j** was obtained as a yellow oil (62 mg, 58%). Data for (±)-**24j**: R_f 0.25 (30% EtOAc−hexane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.30 (d, 3 H, J = 6.9 Hz), 2.34 (s, 3 H), 4.45−4.54 (m, 1 H), 6.14 (d, 1 H, J = 15.8, 1.1 Hz), 6.22 (dd, 1 H, J = 15.8, 4.8 Hz), 6.65 (d, 1 H, J = 7.9 Hz), 7.21−7.53 (m, 10 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 21.6, 49.0, 92.8, 122.5, 124.7 (2 C), 128.9 (2 C), 129.4, 130.1 (2 C), 130.2 (2 C), 134.0, 135.3, 136.6, 139.5, 141.1, 142.8, 161.1. IR (film): 3419, 3055, 2987, 1713, 1640, 1508, 1422, 1266, 1040, 896, 739, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{21}H_{21}Cl_3NO_2S$ $[M + H]^+$ 456.0353, found 456.0339.

*Synthesis of (±)-N-[(1S,2E,4Z,S$_S$)-1,5-Diphenyl-4-(p-tolylsulfinyl)-penta-2,4-dien-1-yl]-2,2,2-trichloroacetamide, (±)-**23k**.* From (±)-**9k** (36 mg, 0.096 mmol), DBU (3 μL, 0.02 mmol), and Cl_3CCN (48 μL, 0.48 mmol), in CH_3CN the corresponding

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (80 °C) and after chromatographic purification (20−30% EtOAc−hexane), (±)-**23k** (20 mg, 40%) was obtained as a white solid. Data for (±)-**23k**: R_f 0.35 (30% EtOAc−hexane). mp 68−70 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.41 (s, 3 H), 5.51 (ddd, 1 H, J = 7.8, 6.3, 1.2 Hz), 6.26 (dt, 1 H, J = 15.8, 1.2 Hz), 6.39 (dd, 1 H, J = 15.8, 6.3 Hz), 6.97 (br s, 1 H), 7.02−7.05 (m, 2 H), 7.24−7.55 (m, 13 H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.6, 57.0, 92.7, 124.7 (2 C), 125.6, 127.1 (2 C), 128.4, 128.8 (2 C), 129.1 (2 C), 129.5, 130.1 (2 C), 130.2 (2 C), 133.0, 133.9, 138.2, 138.6, 139.6, 141.0, 142.3, 161.1. IR (KBr): 3397, 3267, 3054, 2986, 1711, 1622, 1493, 1449, 1422, 1275, 1255, 1081, 1013, 823, 751, 736, 693 cm^{-1}. HRMS (ES) m/z Calcd for $C_{26}H_{23}Cl_3NO_2S$ $[M + H]^+$ 518.0510, found 518.0495.

*Synthesis of (±)-N-[(1R,2E,4Z,S$_S$)-1,5-Diphenyl-4-(p-tolylsulfinyl)-penta-2,4-dien-1-yl]-2,2,2-trichloroacetamide, (±)-**24k**.* From (±)-**10k** (57 mg, 0.15 mmol), DBU (4.5 μL, 0.03 mmol), and Cl_3CCN (75 μL, 0.75 mmol) in CH_3CN, the corresponding acetimidate was obtained. Without purification, from a solution of this crude mixture in DMF, according to the general procedure (60 °C) and after chromatographic purification (5−30% EtOAc−hexane), (±)-**24k** (58 mg, 75%) was obtained as an oil. Data for (±)-**24k**: R_f 0.25 (20% EtOAc−hexane). ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 2.40 (s, 3 H, CH_3 *p*-Tol), 5.55 (ddd, 1 H, J = 7.7, 5.3, 1.5 Hz, H-1), 6.25 (ddd, 1 H, J = 15.8, 1.5, 0.9 Hz, H-3), 6.43 (dd, 1 H, J = 15.8, 5.3 Hz, H-2), 6.88 (d, 1 H, J = 7.7 Hz, NH), 7.18−7.56 (m, 15 H, H-5, Ar). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 21.4 (CH_3 *p*-Tol), 56.6 (C-1), 92.4 (CCl_3), 124.0 (C-3), 124.5 (2 C), 127.3 (2 C), 128.4, 128.6 (2 C), 129.1 (2 C), 129.3, 129.9 (2 C), 130.0 (2 C), 132.7 (C-2), 133.7, 137.1 (C-5), 138.3, 139.4, 140.9, 142.4, 160.8 (C═O). IR (film): 3267, 3054, 2986, 1711, 1596, 1584, 1493, 1422, 1356, 1255, 1181, 1153, 1081, 1028, 896, 694 cm^{-1}. HRMS (ES) m/z Calcd for $C_{26}H_{23}Cl_3NO_2S$ $[M + H]^+$ 518.0510, found 518.0530.

*Synthesis of (−)-(4S,S$_S$)-4-[(1Z)-1-(p-Tolylsulfinyl)but-1-en-1-yl]-oxazolidin-2-one, **27**.* To a solution of **15e** (30 mg, 0.05 mmol, 1.0 equiv) in THF (0.5 mL) was added TBAF (37 mg, 0.12 mmol, 2.5 equiv), and the resulting solution was stirred for 15 min. The solvent was evaporated under reduced pressure and purification by column chromatography (10−50% EtOAc−CH_2Cl_2) afforded **27** (13 mg, 91%) as a white foam. Data for **27**: R_f 0.30 (40% EtOAc−CH_2Cl_2). $[\alpha]^{20}_D$ −89.7 (*c* 1.00, $CHCl_3$). ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 1.20 (t, 3 H, J = 7.5 Hz, CH_3), 2.42 (s, 3 H, CH_3 *p*-Tol), 2.54−2.65 (m, 1 H, CH_2), 2.75- 2.87 (m, 1 H, CH_2), 3.42 (dd, 1 H, J = 8.8, 5.7 Hz, H-5a), 3.79 (t, 1 H, J = 8.8 Hz, H-5b), 4.70 (dd, 1 H, J = 8.8, 5.7 Hz, H-4), 5.26 (br s, 1 H, NH), 6.39 (dd, 1 H, J = 8.5, 7.0 Hz, H-2′), 7.34 (d, 2 H, J = 8.2 Hz, *p*-Tol), 7.40 (d, 2 H, J = 8.2 Hz, *p*-Tol). ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.8, 21.4, 22.4, 47.0, 70.3, 123.6 (2 C), 130.4 (2 C), 138.2, 140.5, 141.8, 143.5, 158.5. IR (film): 3445, 3055, 2986, 2928, 2855, 1765, 1492, 1422, 1266, 1113, 1081, 1035, 1015, 896, 811, 738, 705 cm^{-1}. HRMS (ES) m/z Calcd for $C_{14}H_{18}NO_3S$ $[M + H]^+$ 280.1002, found 280.0989.

*Synthesis of (±)-(2S,3R,4E)-N-(2,3-Dihydroxy-5-phenyl-4-tosyl-pent-4-en-1-yl)-2,2,2-trichloroacetamide, (±)-**28**.* To a cold (0 °C) solution of **21g** (41 mg, 0.10 mmol) and $Me_3NO{\cdot}2H_2O$ (42 mg, 0.38 mmol) in a 9:1 mixture of acetone−H_2O (1 mL) was added OsO_4 (2.5% in *t*-BuOH, 58 μL, 0.005 mmol). The reaction mixture was allowed to warm to rt until disappearance of the starting material (5 h), and after chromatographic purification (5−50% Et_2O−CH_2Cl_2), a pure fraction of (±)-**28** (38 mg, 85%) was obtained as a colorless oil. Data for (±)-**28**: R_f 0.32 (30% Et_2O−CH_2Cl_2). ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 2.46 (s, 3 H, CH_3 *p*-Tol), 3.12 (dt, 1 H, J = 14.3, 5.2 Hz, H-1a), 3.28 (d, 1 H, J = 6.0 Hz, OH-H3), 3.53 (ddd, 1 H, J = 14.3, 6.8, 3.7 Hz, H-1b), 3.65 (d, 1 H, J = 2.9 Hz, OH-H2), 4.13−4.17 (m, 1 H, H-2), 4.64 (dd, 1 H, J = 7.2, 6.0 Hz, H-3), 7.37−7.43 (m, 5 H, Ar), 7.56−7.58 (m, 2 H, Ar), 7.83 (d, 2 H, J = 8.4 Hz, Ar), 8.00 (s, 1 H, H-5). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 21.7 (CH_3 *p*-Tol), 43.1 (C-1), 69.4 (C-3), 70.6 (C-2), 92.2 (CCl_3), 128.0 (2 C), 129.0 (2 C), 130.12 (2 C), 130.14 (2 C), 130.3, 132.2, 136.4, 139.7, 144.2 (C-4), 145.2 (C-5), 163.2 (C═O). IR (film): 3415, 2091, 1693, 1624, 1525, 1286, 1142, 1084, 820, 753, 672 cm^{-1}. HRMS (ES) m/z Calcd for $C_{20}H_{21}Cl_3NO_5S$ $[M + H]^+$ 492.0201, found 492.0230.

*Synthesis of (±)-(5R)-5-[(1S,2E)-1-Hydroxy-3-phenyl-2-tosylprop-2-en-1-yl]oxazolidin-2-one, (±)-**29**.* To a cold solution (0 °C) of (±)-**28** (9.82 mg, 0.02 mmol) in toluene (0.2 mL), DBU (4 μL, 0.03 mmol) was added. This mixture was stirred until disappearance of the starting material (TLC, ∼1 h). The crude was concentrated and purified by chromatography on silica gel (5−50% Et_2O−CH_2Cl_2) to obtain (±)-**29** (6.2 mg, 83%) as a colorless oil. Alternatively, to a cold solution (0 °C) of (±)-**28** (15 mg, 0.03 mmol) in DMF (0.4 mL) was added Cs_2CO_3 (20 mg, 0.06 mmol). This mixture was stirred until disappearance of the starting material (1 d). The crude was concentrated and purified as before to obtain (±)-**29** (8 mg, 73%) as a colorless oil. Data for (±)-**29**: R_f 0.20 (30% Et_2O−CH_2Cl_2). ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 2.46 (s, 3 H, CH_3 Ts), 2.84 (d, 1 H, J = 4.0 Hz, OH), 3.15 (ddd, 1 H, J = 9.0, 6.2, 0.9 Hz, H-4a), 3.49 (td, 1 H, J = 9.0, 0.4 Hz, H-4b), 4.88 (dd, 1 H, J = 9.0, 4.0 Hz, H-1′), 4.94 (s, 1 H, NH), 5.13 (td, 1 H, J = 9.0, 6.2 Hz, H-5), 7.37 (d, 2 H, J = 8.4 Hz, *p*-Tol), 7.43−7.45 (m, 3 H, Ar), 7.56−7.58 (m, 2 H, Ar), 7.83 (d, 2 H, J = 8.4 Hz, *p*-Tol), 8.14 (s, 1 H, H-3′). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 21.7 (CH_3 *p*-Tol), 41.9 (C-4), 70.5 (C-1′), 77.0 (C-5), 128.3 (2 C), 129.1 (2 C), 129.8 (2 C), 130.0 (2 C), 130.5, 132.2, 137.0, 138.0, 144.9, 145.5 (C-3′), 158.2 (C═O). IR (film): 3391, 2960, 2923, 1748, 1622, 1598, 1493, 1447, 1288, 1242, 1146, 1085, 1031, 814, 736, 698, 676 cm^{-1}. HRMS (ES) m/z Calcd for $C_{19}H_{20}NO_5S$ $[M + H]^+$ 374.1057, found 374.1039.

General Procedure for Diels−Alder Reaction. To a solution of dienyl trichloroacetamide in anhydrous toluene (10.0 mL/mmol) and at rt was added *N*-phenylmaleimide (NPM, 1.5−2.0 equiv). The mixture was stirred and monitored by TLC or ^{1}H NMR until completion. Then the solvent was evaporated under reduced pressure to give the corresponding adduct that was purified by chromatography on silica gel using the appropriate mixture of eluents.

*Synthesis of (±)-2,2,2-Trichloro-N-{(S)-[(3aR,4S,7R,7aR,S$_S$)-7-butyl-1,3-dioxo-2-phenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl](phenyl)methyl}acetamide, (±)-**30i**.* From (±)-**23i** (12.0 mg, 0.024 mmol) and NPM (8.0 mg, 0.048 mmol) in toluene, according to the general procedure (1 week) and after chromatographic purification (5−15% Et_2O−CH_2Cl_2), (±)-**30i** was obtained as a white solid (12.0 mg, 75%). Data for (±)-**30i**: R_f 0.20 (10% Et_2O−CH_2Cl_2). mp 115−117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.81 (t, 3 H, J = 7.3 Hz, H-12), 1.09−1.34 (m, 2 H, CH_2), 1.63−1.80 (m, 3 H, CH_2, H-9a), 2.08−2.17 (m, 1 H, H-9b), 2.37 (s, 3 H, CH_3 *p*-Tol), 2.62−2.64 (m, 1 H), 2.99 (dd, 1 H, J = 8.7, 4.8 Hz), 3.24−3.29 (m, 1 H), 3.35 (dd, 1 H, J = 8.7, 6.4 Hz), 5.88 (dd, 1 H, J = 11.4, 8.1 Hz, H-8), 6.92 (s, 1 H, H-5), 7.13 (d, 1 H, J = 8.1 Hz, NH), 7.12−7.26 (m, 4 H, Ar), 7.35−7.48 (m, 8 H, Ar), 7.64 (d, 2 H, J = 7.1 Hz, Ar). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.8 (C-12), 21.5 (CH_3 *p*-Tol), 22.4, 25.1, 29.7, 39.8, 41.5, 42.7, 43.4, 55.8 (C-8), 92.7 (CCl_3), 126.4, 126.7, 127.8, 128.7, 128.9, 129.2, 130.3, 131.4, 132.7, 138.4, 139.1, 142.5, 149.6, 161.3 (C═O), 174.2 (C═O), 175.4 (C═O). IR (KBr): 3415, 3054, 2986, 2961, 2928, 2854, 1713, 1597, 1500, 1421, 1387, 1265, 1196, 1082, 1032, 896, 811, 737, 704 cm^{-1}. HRMS (ES) m/z Calcd for $C_{34}H_{34}Cl_3N_2O_4S$ $[M + H]^+$ 671.1299, found 671.1309.

*Synthesis of (±)-2,2,2-Trichloro-N-{(R)-[(3aR,4S,7R,7aR,S$_S$)-7-butyl-1,3-dioxo-2-phenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl](phenyl)methyl}acetamide, (±)-**31i**.* From (±)-**24i** (18.0 mg, 0.036 mmol) and NPM (13.0 mg, 0.072 mmol) in toluene, according to the general procedure (4 d) and after chromatographic purification (5−15% Et_2O−CH_2Cl_2), (±)-**31i** was obtained as a white solid (17.0 mg, 71%). Data for (±)-**31i**: R_f 0.20 (10% Et_2O−CH_2Cl_2). mp 117−119 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (t, 3 H, J = 7.3 Hz, H-12), 1.10−1.33 (m, 2 H, CH_2), 1.63−1.80 (m, 3 H, H-9a, CH_2), 2.09−2.20 (m, 1 H, H-9b), 2.38 (s, 3 H, CH_3 *p*-Tol), 2.59−2.63 (m, 1 H, H-7a), 3.16 (app q, 1 H, J = 4.8 Hz, H-7), 3.29 (dd, 1 H, J = 8.6, 4.6 Hz, H-3a), 3.39 (dd, 1 H, J = 8.6, 6.8 Hz, H-4), 5.60 (dd, 1 H, J = 9.1, 6.8 Hz, H-8), 6.66 (dd, 1 H, J = 4.6, 2.5 Hz, H-5), 7.23−7.25 (m, 4 H, Ar), 7.32−7.50 (m, 10 H, Ar), 9.26 (d, 1 H, J = 9.1 Hz, NH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.8 (C-12), 21.5 (CH_3 *p*-Tol), 22.4 (CH_2), 25.2 (CH_2), 29.8 (CH_2), 39.7 (C-7a),

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

41.9 (C-3a), 42.0 (C-7), 42.4 (C-4), 54.9 (C-8), 92.7 (CCl_3), 126.5 (2 C), 126.7 (2 C), 126.8 (2 C), 128.3, 129.05 (2 C), 129.08, 129.3 (2 C), 130.3 (2 C), 131.2, 138.0, 138.9, 142.7, 149.0, 162.3 ($COCl_3$), 174.2 (CO), 177.9 (CO). IR (KBr): 3688, 3292, 3054, 2986, 2961, 1704, 1597, 1514, 1500, 1421, 1392, 1264, 1190, 1083, 1035, 896, 824, 812, 735, 702 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{34}H_{34}Cl_3N_2O_4S$ $[M + H]^+$ 671.1299, found 671.1304.

*Synthesis of (±)-2,2,2-Trichloro-N-{(R)-1-[(3aR,4S,7S,7aR,S$_S$)-1,3-Dioxo-2,7-diphenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, (±)-**30j**.* From (±)-**23j** (29.0 mg, 0.064 mmol) and NPM (22.0 mg, 0.127 mmol) in toluene, according to the general procedure (1 week) and after chromatographic purification (10−20% Et_2O−CH_2Cl_2), (±)-**30j** was obtained as a yellow oil (32.0 mg, 80%). Data for (±)-**30j**: R_f 0.10 (10−20% Et_2O−CH_2Cl_2). ^1H NMR (400 MHz, $CDCl_3$) δ 1.67 (d, 3 H, J = 7.1 Hz), 2.39 (s, 3 H), 3.37 (t, 1 H, J = 7.6 Hz), 3.44 (t, 1 H, J = 8.2 Hz), 3.68 (t, 1 H, J = 7.4 Hz), 3.77 (d, 1 H, J = 7.4 Hz), 4.88 (hex, 1 H, J = 7.4 Hz), 6.27 (dd, 2 H, J = 7.7, 2.0 Hz), 6.97 (s, 1 H), 7.05−7.06 (m, 2 H), 7.07−7.31 (m, 10 H), 8.00 (d, 1 H, J = 8.5 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.1, 21.5, 38.4, 38.5, 38.7, 45.9, 49.0, 92.7, 125.6 (2 C), 126.0 (2 C), 127.7, 128.4, 128.8, 128.9 (2 C), 129.0 (2 C), 129.8 (2 C), 130.1 (2 C), 130.5, 135.3, 138.4, 142.7, 144.7, 161.6, 174.3, 176.0. IR (film): 3414, 3055, 1714, 1501, 1422, 1382, 1266, 1177, 1082, 1031, 1015, 896, 829, 809, 739, 705, 666 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{31}H_{28}Cl_3N_2O_4S$ $[M + H]^+$ 629.0830, found 629.0847.

*Synthesis of (±)-2,2,2-Trichloro-N-{(S)-1-[(3aR,4S,7S,7aR,Ss)-1,3-dioxo-2,7-diphenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}-acetamide, (±)-**31j**.* From (±)-**24j** (25.0 mg, 0.055 mmol) and NPM (19.0 mg, 0.110 mmol) in toluene, according to the general procedure (1 week) and after purification by precipitation (50% CH_2Cl_2−hexane), (±)-**31j** was obtained as a white solid (25.0 mg, 76%). Data for (±)-**31j**: R_f 0.50 (50% Et_2O−EtOAc). mp 112−115 °C. ^1H NMR (400 MHz, $CDCl_3$) δ 1.63 (d, 3 H, J = 6.7 Hz), 2.31 (s, 3 H), 3.37 (m, 1 H), 3.47 (t, 1 H, J = 7.4 Hz), 3.55−3.58 (m, 1 H), 4.06 (d, 1 H, J = 7.6 Hz, 1 H), 4.92 (br s, 1 H), 6.21 (dd, 2 H, J = 8.2, 1.6 Hz), 6.91−7.24 (m, 13 H), 8.65 (d, 1 H, J = 8.1 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.5, 21.4, 37.3, 39.2, 41.3, 46.2, 48.9, 92.9, 125.1 (2 C), 126.0 (2 C), 128.1, 128.7 (2 C), 128.8 (2 C), 129.8 (2 C), 130.0 (2 C), 130.4, 134.9, 138.2, 141.9, 145.2, 162.0, 174.1, 176.7. IR (KBr): 3414, 3054, 2986, 1714, 1597, 1501, 1455, 1421, 1381, 1367, 1265, 1177, 1082, 1031, 896, 829, 809, 738, 704, 666 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{31}H_{28}Cl_3N_2O_4S$ $[M + H]^+$ 629.0830, found 629.0831.

*Synthesis of (±)-2,2,2-Trichloro-N-{(S)-[(3aR,4S,7S,7aR,S$_S$)-1,3-dioxo-2,7-diphenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl](phenyl)methyl}acetamide, (±)-**30k**.* From (±)-**23k** (17.0 mg, 0.033 mmol) and NPM (11.0 mg, 0.07 mmol) in toluene, according to the general procedure (2 d, 70 °C) and after chromatographic purification (10−20% Et_2O−CH_2Cl_2), (±)-**30k** was obtained as a white solid (16.5 mg, 73%). Data for (±)-**30k**: R_f 0.25 (20% Et_2O−CH_2Cl_2). mp 169−170 °C. ^1H NMR, COSY (500 MHz, $CDCl_3$) δ 2.32 (s, 3 H, CH_3 *p*-Tol), 3.14−3.17 (t, 1 H, J = 7.6 Hz, H-3a), 3.36 (t, 1 H, J = 8.2 Hz, H-7a), 3.72 (m, 1 H, H-4), 3.78 (dt, 1 H, J = 8.2, 2.0 Hz, H-7), 6.16 (dd, 1 H, J = 10.7, 8.4 Hz, H-8), 6.54−6.56 (m, 2 H, Ar), 6.94 (d, 2 H, J = 7.4 Hz, Ar), 7.02−7.07 (m, 4 H), 7.16 (m, 2 H), 7.21−7.26 (m, 4 H), 7.33 (m, 1 H, H-5), 7.35−7.43 (m, 3 H, Ar), 7.53 (d, 1 H, J = 8.4 Hz, NH), 7.54−7.65 (m, 2 H, Ar). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 21.4 (CH_3 *p*-Tol), 40.3 (C-3a, C-7), 40.6 (C-4), 46.6 (C-7a), 56.0 (C-8), 92.7 (CCl_3), 125.5 (2 C), 126.0 (2 C), 127.7 (2 C), 128.2, 128.46, 128.5 (2 C), 128.7, 128.8 (2 C), 129.1 (C-5), 129.2 (2 C), 128.8 (2 C), 130.5 (2 C), 130.8, 134.0, 138.39, 138.4, 142.1, 146.3, 161.5 ($COCl_3$), 173.8 (CO), 174.4 (CO). IR (KBr): 3307, 3054, 2985, 2927, 1782, 1711, 1499, 1383, 1265, 1179, 1148, 1054, 909, 845, 824, 738, 704 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{36}H_{30}Cl_3N_2O_4S$ $[M + H]^+$ 691.0986, found 691.1005.

*Synthesis of (±)-2,2,2-Trichloro-N-{(R)-[(3aR,4S,7S,7aR,S$_S$)-1,3-dioxo-2,7-diphenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl](phenyl)methyl}acetamide, (±)-**31k**.* From (±)-**24k** (15.0 mg, 0.03 mmol) and NPM (10.0 mg, 0.058 mmol) in toluene, according to the general procedure (2 d, 70 °C) and after chromatographic purification (60−70% EtOAc−hexane), (±)-**31k** was obtained as a white solid (16.6 mg, 80%). Data for (±)-**31k**: R_f 0.25 (60% EtOAc−hexane). mp 124−126 °C. ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 2.35 (s, 3 H, CH_3 *p*-Tol), 3.18 (t, 1 H, J = 7.1 Hz, H-3a), 3.39 (t, 1 H, J = 8.3 Hz, H-7a), 3.71 (br s, 1 H, H-4), 3.87 (d, 1 H, J = 8.3 Hz, H-7), 6.06 (dd, 1 H, J = 9.7, 4.6 Hz, H-8), 6.24−6.26 (dm, 2 H, J = 7.8 Hz, Ar), 6.97−6.98 (dm, 2 H, J = 7.8 Hz, Ar), 7.10−7.25 (m, 11 H, H-5, Ar), 7.29−7.41 (m, 3 H, Ar), 7.48−7.50 (m, 2 H, Ar), 9.70 (d, 1 H, J = 9.7 Hz, NH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 21.4 (CH_3 *p*-Tol), 38.6 (C-7), 39.9 (C-3a), 42.1 (C-4), 46.4 (C-7a), 55.6 (C-8), 92.9 (CCl_3), 125.3 (2 C), 125.8 (2 C), 126.0 (2 C), 128.0, 128.4, 128.7, 128.8 (4 C), 129.0 (2 C), 129.5, 129.9 (2 C), 130.2 (2 C), 134.2, 134.7, 137.5, 138.5, 142.2, 146.7, 162.4 ($COCl_3$), 173.7 (CO), 176.7 (CO). IR (KBr): 3307, 3054, 2985, 2927, 1782, 1711, 1499, 1383, 1265, 1148, 1054, 909, 845, 824, 810, 738, 704, 671 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{36}H_{33}Cl_3N_3O_4S$ $[M + NH_4]^+$ 708.1252, found 708.1257.

*Synthesis of (−)-2,2,2-Trichloro-N-{(R)-1-[(3aR,4S,7S,7aR,Ss)-7-butyl-1,3-dioxo-2-phenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, **35h**.* From **21h** (30.0 mg, 0.07 mmol) and NPM (23.9 mg, 0.14 mmol) in toluene, according to the general procedure (7 d, 120 °C) and after purification by column chromatography (10−15% Et_2O−CH_2Cl_2), **35h** (21.8 mg, 52%) was obtained as a white solid. Data for **35h**: R_f 0.38 (10% Et_2O−CH_2Cl_2). mp 116−119 °C. $[\alpha]^{20}_D$ −42.2 (*c* 0.55, $CHCl_3$). ^1H NMR, COSY (400 MHz, $CDCl_3$) δ 0.84 (t, 3 H, J = 7.0 Hz, H-13), 1.13−1.46 (m, 6 H, H-10, H-11, H-12), 1.52 (d, 3 H, J = 6.7 Hz, H-9), 2.23 (s, 3 H, CH_3 *p*-Tol), 2.93−2.97 (m, 1 H, H-7), 3.07 (ddd, 1 H, J = 10.1, 7.1, 3.1 Hz, H-4), 3.30 (dd, 1 H, J = 9.1, 1.3 Hz, H-7a), 3.46 (dd, 1 H, J = 9.1, 7.1 Hz, H-3a), 4.69−4.79 (m, 1 H, H-8), 6.62 (d, 1 H, J = 3.1 Hz, H-5), 7.02−7.05 (dm, 2 H, J = 7.5 Hz, Ar), 7.09 (d, 2 H, J = 8.0 Hz, Ar), 7.23 (d, 1 H, J = 8.9 Hz, NH), 7.37−7.44 (m, 5 H, Ar). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.9 (C-13), 18.1 (C-9), 21.3 (CH_3 *p*-Tol), 22.1 (CH_2), 29.6 (CH_2), 32.0 (CH_2), 34.9 (C-7), 40.6 (C-4), 41.1 (C-3a), 43.7 (C-7a), 48.5 (C-8), 92.7 (CCl_3), 124.6 (2 C), 125.8 (2 C), 128.5, 128.8 (2 C), 130.1 (3 C), 131.3, 138.5, 142.0, 150.7, 161.8 ($COCl_3$), 175.89 (CO), 175.92 (CO). IR (KBr): 3328, 3046, 2957, 2928, 2857, 1712, 1597, 1518, 1500, 1380, 1260, 1190, 1082, 1041, 822, 753, 690, 624 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{29}H_{32}Cl_3N_2O_4S$ $[M + H]^+$ 609.1143, found 609.1157.

*Synthesis of (−)-2,2,2-Trichloro-N-{(S)-1-[(3aR,4S,7S,7aR,Ss)-7-butyl-1,3-dioxo-2-phenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, **36h**.* From **22h** (60.5 mg, 0.139 mmol) and NPM (48.2 mg, 0.278 mmol) in toluene, according to the general procedure (4 d, 120 °C) and after purification by column chromatography (10−15% Et_2O−CH_2Cl_2), **36h** (46.7 mg, 55%) was obtained as a white solid. Data for **36h**: R_f 0.39 (10% Et_2O−CH_2Cl_2). mp 76−80 °C. $[\alpha]^{20}_D$ −55.6 (*c* 0.16, $CHCl_3$). ^1H NMR, COSY (300 MHz, $CDCl_3$) δ 0.87 (t, 3 H, J = 7.0 Hz, H-13), 1.25−1.54 (m, 6 H, H-10, H-11, H-12), 1.61 (d, 3 H, J = 6.9 Hz, H-9), 2.22 (s, 3 H, CH_3 *p*-Tol), 2.96−3.00 (m, 1 H, H-7), 3.24 (td, 1 H, J = 6.7, 3.3 Hz, H-4), 3.30 (dd, 1 H, J = 8.9, 0.9 Hz, H-7a), 3.55 (dd, 1 H, J = 8.9, 6.7 Hz, H-3a), 4.47−4.54 (m, 1 H, H-8), 6.53 (d, 1 H, J = 3.3 Hz, H-5), 6.92−6.95 (dm, 2 H, J = 7.4 Hz, Ar), 7.09 (d, 2 H, J = 8.2 Hz, Ar), 7.36−7.43 (m, 5 H, Ar), 8.25 (d, 1 H, J = 8.7 Hz, NH). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 13.9 (C-13), 17.6 (C-9), 21.3 (CH_3 *p*-Tol), 22.1 (CH_2), 29.5 (CH_2), 33.0 (CH_2), 35.3 (C-7), 39.6 (C-4), 41.3 (C-3a), 43.3 (C-7a), 48.3 (C-8), 92.9 (CCl_3), 124.4 (2 C), 125.9 (2 C), 128.7, 128.8 (2 C), 130.1 (2 C), 131.3, 138.5, 140.2, 151.0 (2 C), 162.3 ($COCl_3$), 176.1 (CO), 177.6 (CO). NOESY 1D (400 MHz, CD_2Cl_2): between H4-$(CH_2)n$-Bu 5%; between H3a-H4 3%; between H7-ArPh 2%; between H7a-$(CH_2)n$-Bu 6%; between H7a-H3a 4%. IR (KBr): 3356, 3311, 2959, 2922, 2852, 1715, 1512, 1467, 1380, 1262, 1189, 1083, 1036, 807, 753, 691, 624 cm^{-1}. HRMS (ES) *m/z* Calcd for $C_{29}H_{32}Cl_3N_2O_4S$ $[M + H]^+$ 609.1143, found 609.1153.

*Synthesis of (+)-2,2,2-Trichloro-N-{(R)-1-[(3aR,4S,7S,7aR,Ss)-1,3-dioxo-2,7-diphenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, **35j**.* From **21j** (93.3 mg, 0.21 mmol) and NPM (71.0 mg, 0.41 mmol) in toluene, according to the general procedure (11 d, 120 °C) and after purification by column

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

chromatography (10−15% Et_2O−CH_2Cl_2), **35j** (64.6 mg, 49%) was obtained as a white solid. Data for **35j**: R_f 0.40 (10% Et_2O−CH_2Cl_2). mp 195−197 °C. $[\alpha]^{20}_D$ +95.7 (*c* 0.65, $CHCl_3$). ^1H NMR (300 MHz, $CDCl_3$) δ 1.53 (d, 3 H, *J* = 6.9 Hz, H-9), 2.14 (s, 3 H, CH_3 *p*-Tol), 2.99 (td, 1 H, *J* = 6.3, 3.6 Hz, H-4), 3.59 (dd, 1 H, *J* = 9.0, 6.3 Hz, H-3a), 3.72 (d, 1 H, *J* = 9.0 Hz, H-7a), 4.52−4.68 (m, 1 H, H-8), 4.58 (s, 1 H, H-7), 6.84 (d, 1 H, *J* = 3.6 Hz, H-5), 6.96 (d, 2 H, *J* = 7.8 Hz, Ar), 7.02−7.05 (m, 2 H, Ar), 7.18−7.49 (m, 10 H, Ar), 8.20 (d, 1 H, *J* = 9.0 Hz, NH). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 18.1 (C-9), 21.2 (CH_3 *p*-Tol), 39.2 (C-7), 40.0 (C-4), 41.2 (C-3a), 47.5 (C-8), 48.0 (C-7a), 92.9 (CCl_3), 124.1 (2 C), 125.9 (2 C), 126.9 (2 C), 127.3, 128.8, 128.9 (2 C), 129.1 (2 C), 129.9 (2 C), 131.1, 132.7 (C-5), 137.4, 138.6, 141.7, 149.1, 162.3 ($COCl_3$), 175.3 (CO), 177.9 (CO). IR (KBr): 3368, 3050, 2957, 2925, 2854, 1705, 1598, 1509, 1384, 1230, 1175, 1083, 1052, 821, 755, 637 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{31}H_{28}Cl_3N_2O_4S$ $[M + H]^+$ 629.0830, found 629.0846.

Synthesis of (−)-2,2,2-Trichloro-N-{(R)-1-[(3aR,4S,7S,7aR,Ss)-1,3-dioxo-2,7-diphenyl-6-(p-tolylsulfinyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, ***36j****.* From **22j** (25.2 mg, 0.055 mmol) and NPM (19.2 mg, 0.110 mmol) in toluene, according to the general procedure (7 d, 120 °C) and after purification by column chromatography (10−15% Et_2O−CH_2Cl_2), **36j** (21.4 mg, 62%) was obtained as a white solid. Data for **36j**: R_f 0.40 (10% Et_2O−CH_2Cl_2). mp 200−202 °C. $[\alpha]^{20}_D$ −90.9 (*c* 0.55, $CHCl_3$). ^1H NMR, COSY (500 MHz, $CDCl_3$) δ 1.52 (d, 3 H, *J* = 6.9 Hz, H-9), 2.13 (s, 3 H, CH_3 *p*-Tol), 2.99 (td, 1 H, *J* = 6.4, 3.5 Hz, H-4), 3.59 (dd, 1 H, *J* = 9.1, 6.4 Hz, H-3a), 3.72 (dd, 1 H, *J* = 9.1, 1.4 Hz, H-7a), 4.57 (s, 1 H, H-7), 4.59−4.63 (m, 1 H, H-8), 6.83 (d, 1 H, *J* = 3.5 Hz, H-5), 6.96 (d, 2 H, *J* = 8.0 Hz, Ar), 7.02−7.04 (m, 2 H, Ar), 7.22−7.47 (m, 10 H, Ar), 8.19 (d, 1 H, *J* = 9.2 Hz, NH). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 17.8 (C-9), 21.2 (CH_3 *p*-Tol), 39.3 (C-7), 41.0 (C-4), 41.2 (C-3a), 47.5 (C-8), 48.0 (C-7a), 92.9 (CCl_3), 124.1 (2 C), 125.9 (2 C), 126.9 (2 C), 127.3, 128.8, 128.9 (2 C), 129.1 (2 C), 129.9 (2 C), 131.1, 132.7 (C-5), 137.4, 138.6, 141.7, 149.1, 162.3 ($COCl_3$), 175.3 (CO), 177.8 (CO). IR (KBr): 3371, 2924, 1705, 1509, 1499, 1384, 1194, 1175, 1083, 1052, 821, 755, 638 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{31}H_{28}Cl_3N_2O_4S$ $[M + H]^+$ 629.0830, found 629.0829.

General Procedure for Oxidation of Sulfoxides to Sulfones with MMPP. To a solution of the starting material in anhydrous MeOH (10 mL/mmol), at 0 °C, was added magnesium bis(monoperoxyphthalate) hexahydrate (MMPP, 2.0 equiv). The mixture was stirred at room temperature and monitored by TLC until completion. Then the solvent was evaporated under reduced pressure to give the corresponding sulfone that was purified by chromatography on silica gel using the appropriate mixture of eluents.

Synthesis of (−)-2,2,2-Trichloro-N-{(S)-1-[(3aR,4S,7S,7aR)-7-butyl-1,3-dioxo-2-phenyl-6-tosyl-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, ***38****.* From **36h** (9.0 mg, 0.015 mmol) and MMPP (14.6 mg, 0.030 mmol) in MeOH according to the general procedure (2 h) and after chromatographic purification (80% Et_2O−hexane), sulfonyl isoindole **38** (8.6 mg, 0.014 mmol, 93%) was obtained as a white solid. Data for **38**: R_f 0.53 (2% Et_2O−CH_2Cl_2). mp 176−177 °C. $[\alpha]^{20}_D$ −53.0 (*c* 0.10, $CHCl_3$). ^1H NMR, COSY (300 MHz, $CDCl_3$) δ 0.91 (t, 3 H, *J* = 7.1 Hz, H-13), 1.25−1.49 (m, 6 H, H-10, H-11, H-12), 1.62 (d, 3 H, *J* = 6.9 Hz, H-9), 2.28 (s, 3 H, CH_3 *p*-Tol), 3.18 (dd, 1 H, *J* = 9.4, 4.9, Hz, H-7), 3.22−3.28 (m, 1 H, H-4), 3.31 (dd, 1 H, *J* = 9.0, 1.1, Hz, H-7a), 3.55 (dd, 1 H, *J* = 9.0, 6.3, Hz, H-3a), 4.35−4.47 (m, 1 H, H-8), 6.87−6.96 (m, 2 H, Ar), 6.95 (d, 1 H, *J* = 3.5 Hz, H-5), 7.15 (d, 2 H, *J* = 8.0 Hz, Ar), 7.38−7.40 (m, 3 H, Ar), 7.65 (d, 2 H, *J* = 8.3 Hz, Ar), 8.06 (d, 1 H, *J* = 8.4 Hz, NH). ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 13.9 (C-13), 17.5 (C-9), 21.6 (CH_3 *p*-Tol), 22.0 (CH_2), 29.6 (CH_2), 32.1 (CH_2), 37.3 (C-7), 39.4 (C-4), 41.0 (C-3a), 43.2 (C-7a), 48.5 (C-8), 92.7 (CCl_3), 126.0 (2 C), 128.3 (2 C), 128.8, 129.1 (2 C), 130.0 (2 C), 131.0, 135.3, 136.6 (C-5), 144.8, 147.3, 162.2 ($COCl_3$), 176.0 (CO), 177.2 (CO). IR (KBr): 3356, 3054, 2959, 2926, 2854, 1706, 1597, 1513, 1458, 1379, 1264, 1148, 1089, 819, 742 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{29}H_{35}Cl_3N_3O_5S$ $[M + NH_4]^+$ 642.1358, found 642.1371.

Synthesis of (−)-2,2,2-Trichloro-N-{(R)-1-[(3aR,4S,7S,7aR)-7-butyl-1,3-dioxo-2-phenyl-6-tosyl-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, ***39****.* From **35h** (14.0 mg, 0.023 mmol) and MMPP (28.0 mg, 0.046 mmol) in MeOH according to the general procedure (16 h) and after chromatographic purification (1−2% Et_2O−CH_2Cl_2), sulfonyl isoindole **39** (12.0 mg, 0.019 mmol, 83%) was obtained as a white solid. Data for **38**: R_f 0.31 (2% Et_2O−CH_2Cl_2). mp 108−110 °C. $[\alpha]^{20}_D$ −103.8 (*c* 0.67, $CHCl_3$). ^1H NMR, COSY (500 MHz, $CDCl_3$) δ 0.92 (t, 3 H, *J* = 7.0 Hz, H-13), 1.24−1.64 (m, 6 H, H-10, H-11, H-12), 1.54 (d, 3 H, *J* = 6.9 Hz, H-9), 2.29 (s, 3 H, CH_3 *p*-Tol), 3.08 (ddd, 1 H, *J* = 10.3, 6.9, 3.3 Hz, H-4), 3.19 (dd, *J* = 10.3, 4.2 Hz, 1 H, H-7), 3.32 (dd, 1 H, *J* = 9.0, 1.2 Hz, H-7a), 3.49 (dd, 1 H, *J* = 9.1, 6.9 Hz, H-3a), 4.70 (ddd, 1 H, *J* = 10.3, 8.7, 6.6 Hz, H-8), 6.91 (dd, 2 H, *J* = 8.0, 1.8 Hz, Ar), 7.02 (d, 1 H, *J* = 3.3 Hz, H-5), 7.06 (d, 1 H, *J* = 8.8 Hz, NH), 7.16 (d, 2 H, *J* = 8.2 Hz, Ar), 7.35−7.41 (m, 3 H, Ar), 7.66 (d, 2 H, *J* = 8.3 Hz, Ar). ^{13}C NMR, HSQC, HMBC (125 MHz, $CDCl_3$) δ 14.1 (C-13), 18.3 (C-9), 21.7 (CH_3 *p*-Tol), 22.2 (CH_2), 29.7 (CH_2), 31.7 (CH_2), 36.9 (C-7), 40.6 (C-4), 40.9 (C-3a), 43.6 (C-7a), 48.6 (C-8), 92.7 (CCl_3), 126.1 (2 C), 128.5 (2 C), 128.8, 129.05 (2 C), 130.25 (2 C), 131.3, 135.3, 136.6, 145.0, 147.5, 161.9 ($COCl_3$), 175.6 (CO), 175.9 (CO). IR (CH_2Cl_2): 3314, 2958, 2931, 1713, 1525, 1499, 1315, 1194, 1144, 1088, 820, 666 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{29}H_{35}Cl_3N_3O_5S$ $[M + NH_4]^+$ 642.1358, found 642.1375.

Synthesis of (−)-2,2,2-Trichloro-N-{(2S,3E,5E)-5-tosyldeca-3,5-dien-2-yl}acetamide, ***37****.* From **22h** (34.0 mg, 0.08 mmol) and MMPP (78.0 mg, 0.16 mmol) in MeOH, according to the general procedure (2 h) and after chromatographic purification (2% Et_2O−CH_2Cl_2), **37** was obtained as a yellowish oil (22.0 mg, 62%). Data for **37**: R_f 0.44 (2% Et_2O−CH_2Cl_2). $[\alpha]^{20}_D$ −32.5 (*c* 0.28, $CHCl_3$). ^1H NMR, COSY (300 MHz, $CDCl_3$) δ 0.90 (t, 3 H, *J* = 7.2 Hz, CH_3), 1.25−1.52 (m, 4 H, 2 CH_2), 1.31 (d, 3 H, *J* = 6.9 Hz, H-1), 2.23−2.30 (m, 2 H, H-7), 2.41 (s, 3 H, CH_3 *p*-Tol), 4.43−4.54 (m, 1 H, H-2), 6.03 (dd, 1 H, *J* = 16.2, 5.5 Hz, H-3), 6.12 (d, 1 H, *J* = 16.2 Hz, H-4), 6.51 (d, 1 H, *J* = 7.6 Hz, NH), 7.00 (t, 1 H, *J* = 7.6 Hz, H-6), 7.28 (d, 2 H, *J* = 8.2 Hz, *p*-Tol), 7.67 (d, 2 H, *J* = 8.2 Hz, *p*-Tol). ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.8 (C-10), 20.0 (C-1), 21.6 (CH_3 *p*-Tol), 22.4 (C-9), 28.3 (C-7), 30.6 (C-8), 49.1 (C-2), 92.5 (CCl_3), 119.5 (C-4), 127.9 (2 C), 129.6 (2 C), 136.8, 137.3 (C-3), 138.1, 143.7 (C-6), 144.1, 160.8 (C═O). IR (film): 3332, 2959, 2928, 2857, 1709, 1597, 1516, 146, 1300, 1288, 1138, 1088, 821, 738, 671 cm^{-1}. HRMS (ES) *m*/*z* Calcd for $C_{19}H_{28}Cl_3N_2O_3S$ $[M + NH_4]^+$ 469.0898, found 469.0881.

Synthesis of (−)-2,2,2-Trichloro-N-{(S)-1-[(3aR,4S,7S,7aR)-7-butyl-1,3-dioxo-2-phenyl-6-tosyl-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide, ***38****, and 2,2,2-Trichloro-N-{(S)-1-[(3aS,4R,7-R,7aS)-7-butyl-1,3-dioxo-2-phenyl-6-tosyl-2,3,3a,4,7,7a-hexahydro-1H-isoindol-4-yl]ethyl}acetamide,* ***ent-39****.* From **37** (8.0 mg, 0.02 mmol) and NPM (17.3 mg, 0.035 mmol) in toluene, according to the general procedure (7 d, 120 °C), a 75:25 mixture of adducts **38** and *ent*-**39** was obtained. Purification by column chromatography (2% Et_2O−CH_2Cl_2) afforded **38** (4.6 mg, 37%) as a white solid. Data for **38**: $[\alpha]^{20}_D$ −41.4 (*c* 0.05, $CHCl_3$). Additional data identical to that found before. Partial data for *ent*-**39**: R_f 0.32 (2% Et_2O−CH_2Cl_2). ^1H NMR (300 MHz, $CDCl_3$) δ 0.90−0.95 (m, 3 H), 1.26−1.69 (m, 9 H), 2.30 (s, 3 H), 3.05−3.12 (m, 1 H), 3.17−3.23 (m, 1 H), 3.31 (d, 1 H, *J* = 9.1 Hz), 3.49 (dd, 1 H, *J* = 9.1, 7.1 Hz), 4.66−4.75 (m, 1 H), 6.90−7.69 (m, 11 H). HRMS (ES) *m*/*z* Calcd for $C_{29}H_{35}Cl_3N_3O_5S$ $[M + NH_4]^+$ 642.1358, found 642.1373.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b00365.

Spectral data (^1H NMR and ^{13}C NMR) for new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: iqofp19@iqog.csic.es.

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

*E-mail: iqov379@iqog.csic.es. Fax: (+34) 915644853.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was supported by MINECO (CTQ2013-46459-C2-2-P) and (CTQ2009-07752) cofunded by FEDER. We also thank MEC for a fellowship to I.C., the U.S. Department of State and Spanish Fulbright Commission for a fellowship to C.G., and Fondo Social Europeo for a JAE-doc contract to C.S. We are grateful to Dr. Carmen de la Torre (IQOG-CSIC) and Dr. Miguel Ángel Sierra (UCM) for encouragement and support.

■ REFERENCES

(1) (a) Nishikawa, T.; Asai, M.; Ohyabu, N.; Isobe, M. *J. Org. Chem.* **1998**, *63*, 188−192. (b) Lee, E. E.; Batey, R. A. *J. Am. Chem. Soc.* **2005**, *127*, 14887−14893. (c) Dugal-Tessier, J.; Dake, G. R.; Gates, D. P. *Organometallics* **2007**, *26*, 6481−6486. (d) Jamieson, A. G.; Sutherland, A. *Tetrahedron* **2007**, *63*, 2123−2131. (e) Jaunzeme, I.; Jirgensons, A. *Tetrahedron* **2008**, *64*, 5794−5799. (f) Swift, M. D.; Sutherland, A. *Tetrahedron* **2008**, *64*, 9521−9527.

(2) (a) Chen, Y. K.; Lurain, A. E.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, *124*, 12225−12231. (b) Singh, O. V.; Han, H. *Org. Lett.* **2004**, *6*, 3067−3070. (c) Gonda, J.; Martinková, M.; Zadrosová, A.; Soteková, M.; Raschmanová, J.; Conka, P.; Gajdosíková, E.; Kappe, C. O. *Tetrahedron Lett.* **2007**, *48*, 6912−6915. (d) Jamieson, A. G.; Sutherland, A. *Org. Lett.* **2007**, *9*, 1609−1611. (e) Swift, M. D.; Sutherland, A. *Org. Lett.* **2007**, *9*, 5239−5242. (f) Wang, B. *J. Org. Chem.* **2010**, *75*, 6012−6015.

(3) (a) Brouwer, A. J.; Elgersma, R. C.; Jagodzinska, M.; Rijkers, D. T. S.; Liskamp, R. M. J. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 78−84. (b) Liu, Q.; Qian, W.; Li, A.; Biswas, K.; Chen, J. J.; Fotsch, C.; Han, N.; Yuan, C.; Arik, L.; Biddlecome, G.; Johnson, E.; Kumar, G.; Lester-Zeiner, D.; Ng, G. Y.; Hungate, R. W.; Askew, B. C. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4593−4597.

(4) (a) Ohyabu, N.; Nishikawa, T.; Isobe, M. *J. Am. Chem. Soc.* **2003**, *125*, 8798−8805. (b) Dickson, D. P.; Wardrop, D. J. *Org. Lett.* **2009**, *11*, 1341−1344. (c) Hama, N.; Matsuda, T.; Sato, T.; Chida, N. *Org. Lett.* **2009**, *11*, 2687−2690. (d) Kitamoto, K.; Sampei, M.; Nakayama, Y.; Sato, T.; Chida, N. *Org. Lett.* **2010**, *12*, 5756−5759. (e) Hama, N.; Aoki, T.; Miwa, S.; Yamazaki, M.; Sato, T.; Chida, N. *Org. Lett.* **2011**, *13*, 616−619. (f) Collett, N. D.; Carter, R. G. *Org. Lett.* **2011**, *13*, 4144−4147. (g) Takahashi, K.; Yamaguchi, D.; Ishihara, J.; Hatakeyama, S. *Org. Lett.* **2012**, *14*, 1644−1647. (h) Calder, E. D. D.; Zaed, A. M.; Sutherland, A. *J. Org. Chem.* **2013**, *78*, 7223−7233. (i) Tsuzaki, S.; Usui, S.; Oishi, H.; Yasushima, D.; Fukuyasu, T.; Oishi, T.; Sato, T.; Chida, N. *Org. Lett.* **2015**, *17*, 1704−1707.

(5) (a) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2009**, *109*, 1−48. (b) Masson, G.; Housseman, C.; Zhu, J. *Angew. Chem., Int. Ed.* **2007**, *46*, 4614−4628. (c) Shi, M.; Xu, Y.-M. *Angew. Chem., Int. Ed.* **2002**, *41*, 4507−4510. (d) Abermil, N.; Masson, G.; Zhu, J. *J. Am. Chem. Soc.* **2008**, *130*, 12596−12597. (e) Shi, M.; Chen, L.-H.; Li, C.-Q. *J. Am. Chem. Soc.* **2005**, *127*, 3790−3800. (f) Matsui, K.; Takizawa, S.; Sasai, H. *J. Am. Chem. Soc.* **2005**, *127*, 3680−3681. (g) Yukawa, T.; Seelig, B.; Xu, Y.; Morimoto, H.; Matsunaga, S.; Berkessel, A.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 11988−11992 and references therein.

(6) (a) Viso, A.; Fernández de la Pradilla, R.; Ureña, M.; Colomer, I. *Org. Lett.* **2008**, *10*, 4775−4778. (b) Viso, A.; Fernández de la Pradilla, R.; Ureña, M.; Bates, R. H.; del Águila, M. A.; Colomer, I. *J. Org. Chem.* **2012**, *77*, 525−542.

(7) (a) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2004**, *43*, 3941−3944. (b) Patel, S. J.; Jamison, T. F. *Angew. Chem., Int. Ed.* **2003**, *42*, 1364−1367. (c) Skucas, E.; Kong, J. R.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 7242−7243. (d) Barchuk, A.; Ngai, M.-Y.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 8432−8433. (e) Ngai, M.-Y.; Barchuk, A.; Krische, M. J. *J. Am. Chem. Soc.* **2007**, *129*, 12644−12645. (f) Skucas, E.; Ngai, M.-Y.; Komanduri, V.; Krische, M. J. *Acc. Chem. Res.* **2007**, *40*, 1394−1401.

(8) (a) Ohmura, T.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 15164−15165. (b) Leitner, A.; Shekhar, S.; Pouy, M. J.; Hartwig, J. F. *J. Am. Chem. Soc.* **2005**, *127*, 15506−15514. (c) Leitner, A.; Shu, C.; Hartwig, J. F. *Org. Lett.* **2005**, *7*, 1093−1096. (d) Shekhar, S.; Trantow, B.; Leitner, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 11770−11771. (e) Pouy, M. J.; Leitner, A.; Weix, D. J.; Ueno, S.; Hartwig, J. F. *Org. Lett.* **2007**, *9*, 3949−3952. (f) Weix, D. J.; Markovic, D.; Ueda, M.; Hartwig, J. F. *Org. Lett.* **2009**, *11*, 2944−2947.

(9) (a) Mancheño, O. G.; Priego, J.; Cabrera, S.; Gómez Arrayás, R.; Llamas, T.; Carretero, J. C. *J. Org. Chem.* **2003**, *68*, 3679−3686. (b) Tonogaki, K.; Itami, K.; Yoshida, J. *J. Am. Chem. Soc.* **2006**, *128*, 1464−1465. (c) Nagano, T.; Kobayashi, S. *J. Am. Chem. Soc.* **2009**, *131*, 4200−4201.

(10) For Pt complexes, see: (a) Utsunomiya, M.; Miyamoto, Y.; Ipposhi, J.; Ohshima, T.; Mashima, K. *Org. Lett.* **2007**, *9*, 3371−3374. For iron-catalyzed allylic amination, see: (b) Plietker, B. *Angew. Chem., Int. Ed.* **2006**, *45*, 6053−6056.

(11) (a) Löber, O.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2001**, *123*, 4366−4367. (b) Pawlas, J.; Nakao, Y.; Kawatsura, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2002**, *124*, 3669−3679. (c) Johns, A. M.; Utsunomiya, M.; Incarvito, C. D.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 1828−1839. (d) Qin, H.; Yamagiwa, N.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2006**, *128*, 1611−1614. (e) Brouwer, C.; He, C. *Angew. Chem., Int. Ed.* **2006**, *45*, 1744−1747.

(12) For recent reviews of allylic trichloroacetimidate or related rearrangements, see: (a) Overman, L. E.; Carpenter, N. E. *Organic Reactions* **2005**, *66*, 1−107. (b) Majumdar, K. C.; Bhattacharyya, T.; Chattopadhyay, B.; Sinha, B. *Synthesis* **2009**, *2009*, 2117−2142. (c) Clayden, J.; Donnard, M.; Lefranc, J.; Tetlow, D. J. *Chem. Commun.* **2011**, *47*, 4624−4639. (d) Nishikawa, T.; Urabe, D.; Adachi, M.; Isobe, M. *Synlett* **2015**, *26*, 1930−1939. See also: (e) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901−2910. (f) Wai, J. S.; Fisher, T. E.; Embrey, M. W. *Tetrahedron Lett.* **1995**, *36*, 3461−3464. (g) Nakayama, Y.; Sekiya, R.; Oishi, H.; Hama, N.; Yamazaki, M.; Sato, T.; Chida, N. *Chem. - Eur. J.* **2013**, *19*, 12052−12058. (h) Howard, J. K.; Amin, C.; Lainhart, B.; Smith, J. A.; Rimington, J.; Hyland, C. J. T. *J. Org. Chem.* **2014**, *79*, 8462−8468. (i) Calder, E. D. D.; Grafton, M. W.; Sutherland, A. *Synlett* **2014**, *25*, 1068−1080.

(13) For recent advances in the catalytic enantiocontrol of the [3,3]-sigmatropic rearrangement of trichloroacetimidates and related substrates, see: (a) Calter, M.; Hollis, T. K.; Overman, L. E.; Ziller, J.; Zipp, G. G. *J. Org. Chem.* **1997**, *62*, 1449−1456. (b) Donde, Y.; Overman, L. E. *J. Am. Chem. Soc.* **1999**, *121*, 2933−2934. (c) Anderson, C. E.; Overman, L. E. *J. Am. Chem. Soc.* **2003**, *125*, 12412−12413. (d) Anderson, C. E.; Donde, Y.; Douglas, C. J.; Overman, L. E. *J. Org. Chem.* **2005**, *70*, 648−657. (e) Wanniarachchi, Y. A.; Kogiso, Y.; Slaughter, L. M. *Organometallics* **2008**, *27*, 21−24. (f) Nomura, H.; Richards, C. J. *Chem. - Asian J.* **2010**, *5*, 1726−1740. (g) Jiang, G.; Halder, R.; Fang, Y.; List, B. *Angew. Chem., Int. Ed.* **2011**, *50*, 9752−9755. (h) Bauer, J. M.; Peters, R. *Catal. Sci. Technol.* **2015**, *5*, 2340−2346.

(14) For a preliminary communication on a portion of this chemistry, see: Fernández de la Pradilla, R.; Colomer, I.; Viso, A. *Org. Lett.* **2012**, *14*, 3068−3071.

(15) (a) Carreño, M. C. *Chem. Rev.* **1995**, *95*, 1717−1760. (b) Fernández, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651−3706. (c) Gnas, Y.; Glorius, F. *Synthesis* **2006**, *2006*, 1899−1930. (d) Pellissier, H. *Tetrahedron* **2006**, *62*, 5559−5601. (e) Mellah, M.; Voituriez, A.; Schulz, E. *Chem. Rev.* **2007**, *107*, 5133−5209. (f) Carreño, M. C.; Hernández-Torres, G.; Ribagorda, M.; Urbano, A. *Chem. Commun.* **2009**, 6129−6144. (g) Wojaczyńska, E.; Wojaczyński, J. *Chem. Rev.* **2010**, *110*, 4303−4356. (h) Smith, L. H. S.; Coote, S. C.; Sneddon, H. F.; Procter, D. J. *Angew. Chem., Int. Ed.* **2010**, *49*, 5832−5844. (i) Choppin, S.; Ferreiro-Medeiros, L.; Barbarottoa, M.; Colobert, F. *Chem. Soc. Rev.* **2013**, *42*, 937−949. (j) Trost, B. M.; Rao, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 5026−5043.

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097

(16) Vinyl sulfoxides **1** are available in one step by the procedure of Craig: Craig, D.; Daniels, K.; MacKenzie, A. R. *Tetrahedron* **1993**, *49*, 11263−11304. Lithiation and trapping with aldehydes leads to the substrates of this study **2**/**3**. In most cases, **2** and **3** are readily interconverted by a Mitsunobu protocol.

(17) (a) Fernández de la Pradilla, R.; Colomer, I.; Ureña, M.; Viso, A. *Org. Lett.* **2011**, *13*, 2468−2471. (b) Fernández de la Pradilla, R.; Castellanos, A.; Osante, I.; Colomer, I.; Sánchez, M. I. *J. Org. Chem.* **2009**, *74*, 170−181. (c) Fernández de la Pradilla, R.; Alhambra, C.; Castellanos, A.; Fernández, J.; Manzano, P.; Montero, C.; Ureña, M.; Viso, A. *J. Org. Chem.* **2005**, *70*, 10693−10700. (d) Fernández de la Pradilla, R.; Manzano, P.; Montero, C.; Priego, J.; Martínez-Ripoll, M.; Martínez-Cruz, L. A. *J. Org. Chem.* **2003**, *68*, 7755−7767.

(18) Fernández de la Pradilla, R.; Montero, C.; Tortosa, M.; Viso, A. *Chem. - Eur. J.* **2009**, *15*, 697−709.

(19) Racemic *Z* sulfinyl alcohols were selected due to their ease of preparation and suitability to the purpose of this study directed to explore the viability and diastereoselectivity of the process. See: Fernández de la Pradilla, R.; Fernández, J.; Manzano, P.; Méndez, P.; Priego, J.; Tortosa, M.; Viso, A.; Martínez-Ripoll, M.; Rodríguez, A. *J. Org. Chem.* **2002**, *67*, 8166−8177 and references cited therein.

(20) For an enantioselective synthesis of *Z* sulfenyl alcohols, see: Berenguer, R.; Cavero, M.; García, J.; Muñoz, M. *Tetrahedron Lett.* **1998**, *39*, 2183−2186.

(21) See ref 11 in Lee, S. I.; Moon, S. Y.; Hwang, G.-S.; Ryu, D. H. *Org. Lett.* **2010**, *12*, 3234−3237.

(22) Chemoselective Overman rearrangement on bis-allylic trichloroacetimidates continues to be a challenge, since poor selectivity (60/40) has been achieved. See: (a) Birtwistle, D. H.; Brown, J. M.; Foxton, M. W. *Tetrahedron* **1988**, *44*, 7309−7318. (b) Commerçon, A.; Ponsinet, G. *Tetrahedron Lett.* **1990**, *31*, 3871−3874.

(23) The leaving group nature of allylic trichloroacetimidates is well known and may be synthetically useful. For a recent review on this topic, see: Arnold, J. S.; Zhang, Q.; Nguyen, H. M. *Eur. J. Org. Chem.* **2014**, *2014*, 4925−4948.

(24) For a discussion of stereoelectronic effects in the reactions of conformationally fixed vinyl sulfoxides, see: (a) Ulshöfer, R.; Podlech, J. *J. Am. Chem. Soc.* **2009**, *131*, 16618−16619. For a theoretical study on the conformations of alkenyl sulfoxides, see: (b) Tietze, L. F.; Schuffenhauer, A.; Schreiner, P. R. *J. Am. Chem. Soc.* **1998**, *120*, 7952−7958.

(25) VanRheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, *17*, 1973−1976. It should be mentioned that we did not study the enantiomeric purity of **28** and **29**, ultimately dependent on the relative rates of dihydroxylation and oxidation at sulfur of enantiopure diene **21g** under these conditions; therefore, we have arbitrarily considered them to be racemic.

(26) (a) Mehmandoust, M.; Petit, Y.; Larchevêque, M. *Tetrahedron Lett.* **1992**, *33*, 4313−4316. (b) Link, J. T.; Raghavan, S.; Gallant, M.; Danishefsky, S. J.; Chou, T. C.; Ballas, L. M. *J. Am. Chem. Soc.* **1996**, *118*, 2825−2842. (c) Haddad, M.; Imogaï, H.; Larchevêque, M. *J. Org. Chem.* **1998**, *63*, 5680−5683. (d) Davies, S. G.; Sanganee, H. J.; Szolcsanyi, P. *Tetrahedron* **1999**, *55*, 3337−3354. (e) Shih, T.-L.; Li, H.-Y.; Ke, M.-S.; Kuo, W.-S. *Synth. Commun.* **2008**, *38*, 4139−4149. (f) Stanková, K.; Martinková, M.; Gonda, J.; Bago, M.; Pilátová, M.; Gönciová, G. *Tetrahedron: Asymmetry* **2015**, *26*, 1394−1407.

(27) (a) Kozikowski, A. P.; Nieduzak, T. R.; Springer, J. P. *Tetrahedron Lett.* **1986**, *27*, 819−822. (b) Kozikowski, A. P.; Nieduzak, T. R.; Konoike, T.; Springer, J. P. *J. Am. Chem. Soc.* **1987**, *109*, 5167−5175. (c) Crisp, G. T.; Gebauer, M. G. *J. Org. Chem.* **1996**, *61*, 8425−8431. (d) Grafton, M. W.; Farrugia, L. J.; Senn, H. M.; Sutherland, A. *Chem. Commun.* **2012**, *48*, 7994−7996. (e) Grafton, M. W.; Farrugia, L. J.; Sutherland, A. *J. Org. Chem.* **2013**, *78*, 7199−7207. (f) Grafton, M. W.; Johnson, S. A.; Farrugia, L. J.; Sutherland, A. *Tetrahedron* **2014**, *70*, 7133−7141.

(28) For related work on Diels−Alder with 2-sulfinyl dienes, see: (a) Fernández de la Pradilla, R.; Montero, C.; Tortosa, M.; Viso, A. *Chem. - Eur. J.* **2005**, *11*, 5136−5145. (b) Fernández de la Pradilla, R.; Tortosa, M.; Castellanos, E.; Viso, A.; Baile, R. *J. Org. Chem.* **2010**, *75*, 1517−1533.

(29) For a review of general aplications of sulfoxides in cycloadditions, see: (a) García Ruano, J. L.; Cid de la Plata, B. *Top. Curr. Chem.* **1999**, 1−126. See also: (b) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P. *Tetrahedron: Asymmetry* **1997**, *8*, 1339−1367. (c) Aversa, M. C.; Barattucci, A.; Bonaccorsi, P.; Giannetto, P. *Arkivoc* **2002**, *xi*, 79−98. See also: (d) Arroyo, Y.; Rodríguez, J. F.; Santos, M.; Sanz Tejedor, M. A.; Vaca, I.; García Ruano, J. L. *Tetrahedron: Asymmetry* **2004**, *15*, 1059−1063. (e) Aversa, M. C.; Bonaccorsi, P.; Faggi, C.; Lamannac, G.; Menichetti, S. *Tetrahedron* **2005**, *61*, 11902−11909. (f) Montaña, A. M.; Grima, P. M.; Batalla, C.; Sanz, F.; Kociok-Köhn, G. *Eur. J. Org. Chem.* **2014**, *2014*, 2726−2746. (g) Chou, S.-S. P.; Liang, P.-W. *Tetrahedron Lett.* **2002**, *43*, 4865−4870. (h) Gosselin, P.; Bonfand, E.; Hayes, P.; Retoux, R.; Maignan, C. *Tetrahedron: Asymmetry* **1994**, *5*, 781−784. (i) Gosselin, P.; Bonfand, E.; Maignan, C. *J. Org. Chem.* **1996**, *61*, 9049−9052.

(30) The *ent* nomenclature is used to facilitate comparison of the data.

(31) Under these harsher conditions, major adducts **35** and **36** were isolated from more complex crude reaction mixtures than those obtained from the isomeric *E*,*Z* amido sulfinyl dienes.

(32) Fernández de la Pradilla, R.; Buergo, M. V.; Manzano, P.; Montero, C.; Priego, J.; Viso, A.; Cano, F. H.; Martínez-Alcázar, M. P. *J. Org. Chem.* **2003**, *68*, 4797−4805.

(33) Kosugi, H.; Kitaoka, M.; Tagani, K.; Takahasi, A.; Uda, H. *J. Org. Chem.* **1987**, *52*, 1078−1082.

(34) Truce, W. E.; Simms, J. A. *J. Am. Chem. Soc.* **1956**, *78*, 2756−2759.

DOI: 10.1021/acs.joc.6b00365
J. Org. Chem. 2016, 81, 4081−4097