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Synthesis of Enantiopure 3-Hydroxypiperidines from Sulfinyl Dienyl Amines by Diastereoselective Intramolecular Cyclization and [2,3]-Sigmatropic Rearrangement

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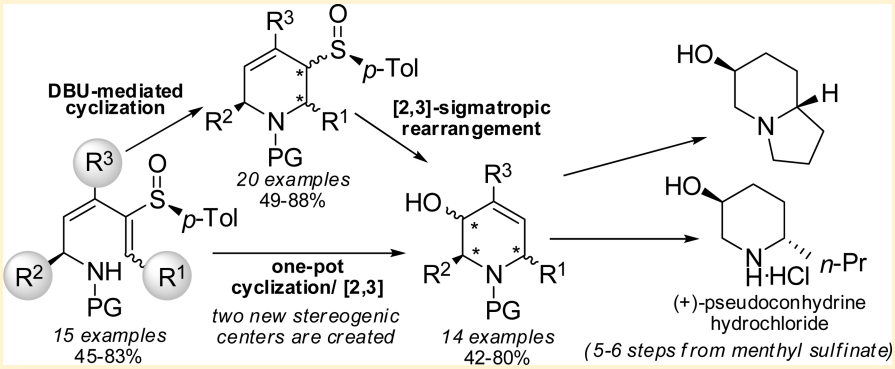
Supporting Information



ABSTRACT: The highly diastereoselective base-promoted intramolecular cyclization of a variety of enantiopure sulfinyl dienyl amines provides novel sulfinyl tetrahydropyridines that are readily converted to 3-hydroxy tetrahydropyridines via sigmatropic rearrangement. The influence of N- and C- substituents on the process has been studied. Procedures to shorten the sequence such as the tandem cyclization followed by [2,3]-sigmatropic rearrangement, as well as cyclization of the free amine, under Boc- or ArSO- deprotection conditions have been examined. Good to excellent levels of selectivity are generally observed for the reported transformations (dr: 75/25 to >98/2). A novel protocol to access substituted amino dienyl sulfoxides is also reported.

INTRODUCTION

The piperidine ring is one of the more frequently encountered substructure of biologically important natural products.[1] Their presence in conformationally restricted peptidomimetics,[2] medicinally important drugs,[3] as well as in numerous compounds with significant pharmacological properties has attracted considerable synthetic efforts to achieve the stereoselective or asymmetric synthesis of these targets.[4] The strategies used to access this privileged scaffold include the aza-Diels−Alder reaction using either aza-dienes or aza-dienophiles,[5] the addition-cyclization to imines,[6] the ring expansion of furan derivatives,[7] the reduction of pyridine scaffolds,[8] the ring-closing metathesis of suitable nitrogen-containing dienes,[9] and various approaches that rely on the nucleophilic attack of nitrogen onto different acceptors.[10]

Many of these protocols employ amino acids or other chiral auxiliaries to obtain these products. The sulfinyl group, broadly used in organic synthesis as stereodirecting functionality,[11] has also been examined within this field by using sulfinimines,[12] and alkenyl sulfoxides as substrates.[13] Nonetheless, the development of new synthetic approaches to access structurally diverse and enantiopure piperidine derivatives through simple and general experimental protocols remains a challenge.

RESULTS AND DISCUSSION

In the past years we have been engaged in the development of novel and efficient chirality transfer methodologies based on the sulfinyl chiral auxiliary.[14] Within this context we envisioned two complementary approaches to synthetically useful functionalized tetrahydropyridin-3-ols, **E**, from amino sulfinyl dienes **C** and **H** (Scheme 1). We considered that readily available amino-1-sulfinyl diene derivatives **C**, prepared in 1−3 steps from the condensation between a lithio sulfinyl diene derived from **A** and sulfinimine **B**,[14d] could undergo a base-promoted intramolecular cyclization to generate an allylic sulfinyl intermediate **D** that would suffer a [2,3]-sigmatropic rearrangement to the desired targets **E**. Alternatively, the cyclization of isomeric amino 2-sulfinyl dienes **H**, similarly to our findings for the related hydroxy 2-sulfinyl dienes,[15] would produce ultimately the desired hydroxy piperidines **E** through

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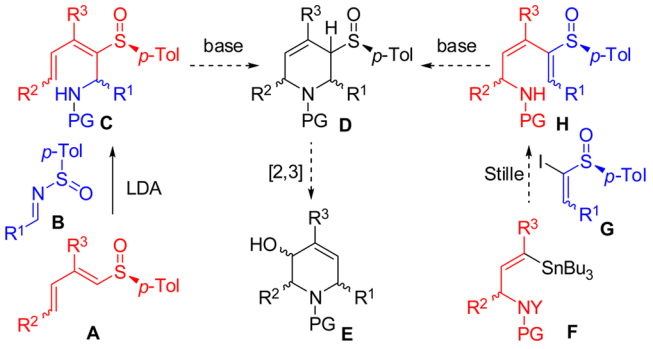
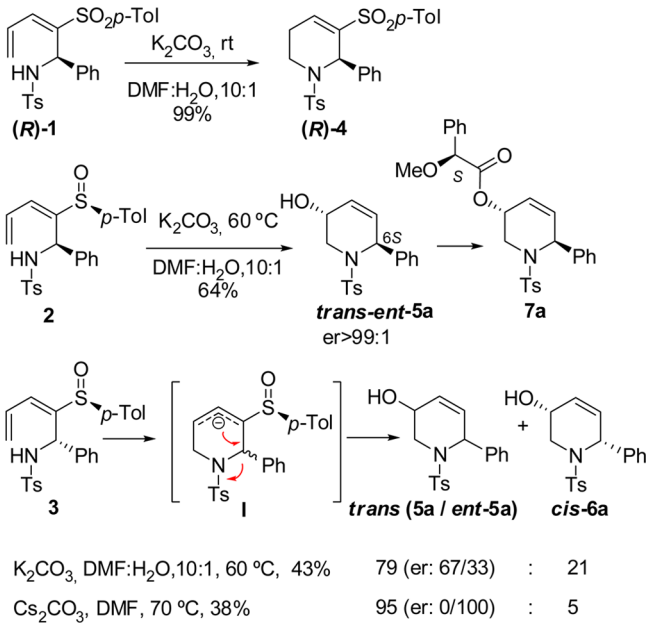
Scheme 1. Proposed Sulfinyl-Mediated Synthesis of Functionalized Tetrahydropyridines



allylic sulfoxide intermediates **D**. Dienes **H** could be prepared by Stille coupling between iodo vinyl sulfoxides **G** and amino stannanes **F**, in analogy with other sulfinyl dienes prepared in our group.[16]

Piperidinols from 1-Sulfinyl Dienes. To establish the viability of the process (**C** → **E**) we selected readily available dienyl sulfone (*R*)-**1** and diastereomeric dienyl sulfoxides **2** and **3**,[14d] and the results obtained are shown in Scheme 2. Similarly

Scheme 2. Base-Promoted Cyclization of Amino 1-Sulfonyl and 1-Sulfinyl Dienes

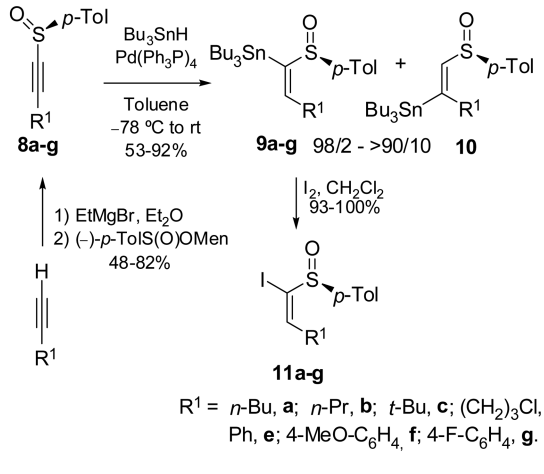


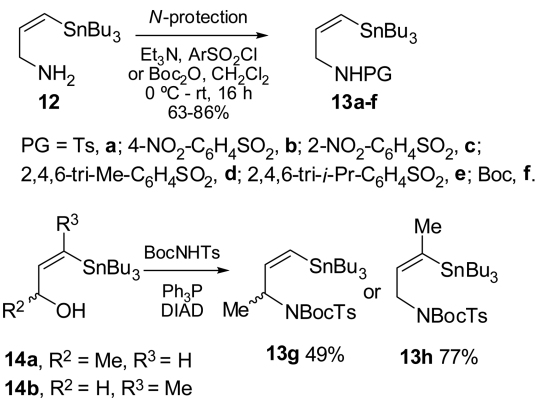
to Back's findings,[17] the intramolecular cyclization of dienyl sulfone (*R*)-**1** took place in excellent yield (99%) to produce enantiopure piperidine (*R*)-**4**. In contrast, the less electron withdrawing sulfoxide group (**2**, **3**) required an excess of base and higher temperatures (50−70 °C) to promote similar cyclizations. Diastereomer **2** was treated with K_2CO_3 leading to a clean crude reaction mixture that contained essentially ***ent*-5a** in moderate unoptimized yield. Unfortunately, **2** (1-(*R*), PG = Ts) derives from the minor diastereomeric product from the addition of lithiated **A** ($R^2 = R^3 = H$) to **B** ($R^1 = Ph$)[14d] (**C**; dr: 13:87, PG = SO*p*-Tol, Scheme 1) after a change of PG, which undermines the efficiency of this route.[18] In contrast, major diastereomer **3** (1-(*S*)) was particularly sluggish providing mixtures of *trans* and *cis* tetrahydropyridin-3-ols (**5a**/**6a**) in low yield or er (K_2CO_3). Furthermore, variable amounts of allylic sulfenates and vinyl sulfoxide intermediates were detected in the crude mixture. These results indicated that our preliminary hypothesis was correct (Scheme 1, **C** → **E**), however, diastereomer **3** was not well-behaved and we tested a number of different reaction parameters such as reaction time, solvents, bases and the nature of the group attached to nitrogen (PG = Ts, SO*p*Tol, Boc, H) with fruitless results. Introducing other substituents on **C** (R^1 = *i*-Pr) did not provide any improvement and we did not envision any advantage for reactivity in attaching substituents, R^2, in these 1-sulfinyl dienes.

The relative and absolute configuration of piperidinol ***ent*-5a** (from **2**) was established by a detailed study of their spectral features including NOE experiments and derivatization to the methoxyphenylacetate **7a**. Surprisingly, a similar study for *trans*-piperidinols from **3** revealed that the enantiomeric ratio was low or completely opposite to our expectations providing ***ent*-5a**. This finding suggests that an alternative reaction pathway entailing a loss of stereoselectivity (C-6*S*/C-6*R*) through a ring-cleavage/ring-closure of allylic sulfinyl anion (**I**) followed by sigmatropic rearrangement to *trans*-piperidinol (**5a** or ***ent*-5a**) is operative in this case.

Piperidinols from 2-Sulfinyl Dienes. *Preparation of Amino 2-Sulfinyl Dienes.* The required iodo alkenyl sulfoxides **11** (Scheme 3) were prepared from alkynyl sulfoxides **8** by our Pd-catalyzed regioselective hydrostannylation, separation by chromatography of major stannane **9** and tin−iodine exchange.[16] The synthesis of *N*-protected amino vinyl

Scheme 3. Synthesis of Iodo Alkenyl Sulfoxides and Amino Vinyl Stannanes





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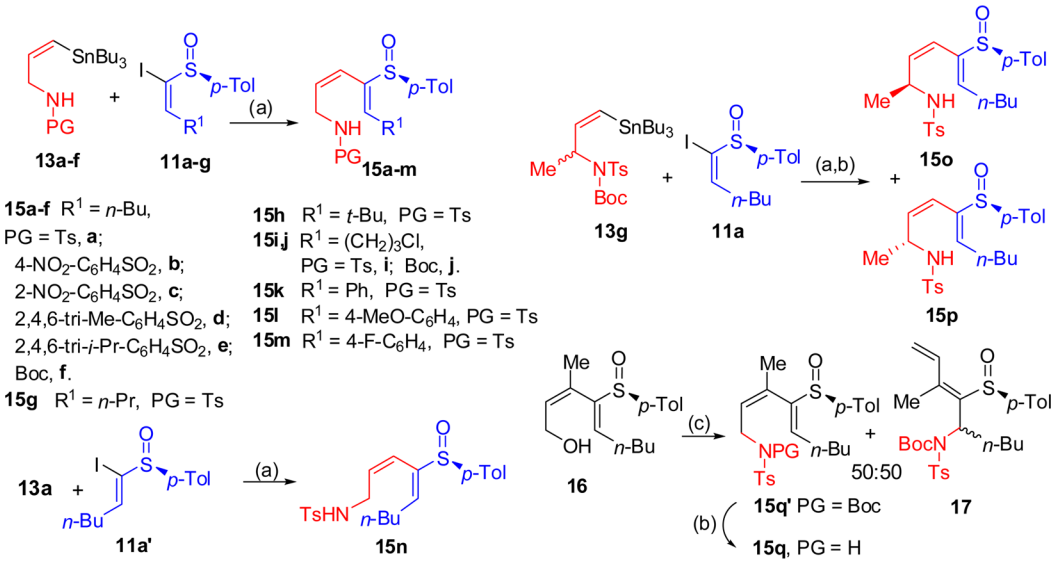
Scheme 4. Synthesis of Protected Amino 2-Sulfinyl Dienes[a]



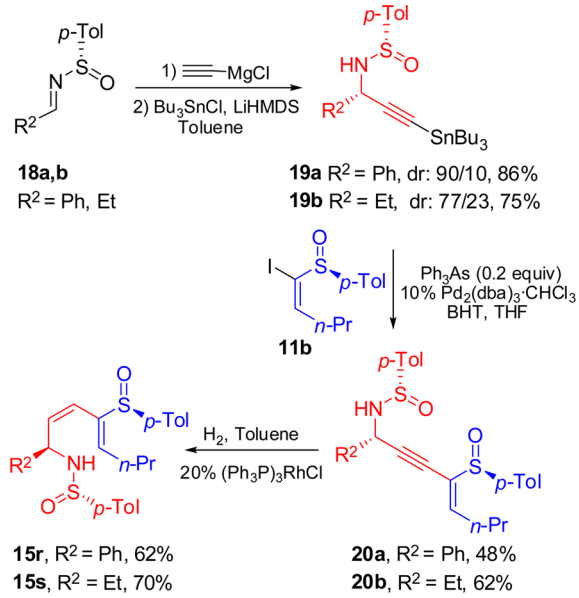
[a]Reaction conditions: (a) $Pd(CH_3CN)_2Cl_2$, BHT, DMF, rt, 16 h, 45−83%; (b) (i) TFA, CH_2Cl_2, (ii) NaOH, 62−79%; (c) BocNHTs, Ph_3P, DEAD, Toluene, 0 °C to rt, 38%.

stannanes **13** is outlined in Scheme 3. The known stannane with a free amino group **12**,[19] was protected uneventfully with a variety of sulfonamides and Boc groups (PG) as representative examples of amine protection, **13a−f**. Alternatively, a Mitsunobu reaction with BocNHTs and hydroxy stannanes **14a,b**[15a] produced the substituted precursors **13g** and **13h**.

At the early stage of the project we examined the synthesis of an unprotected amino dienyl sulfoxide by Stille coupling between stannane **12** and iodide **11a**. A variety of standard Stille conditions including different solvents, temperatures and catalysts ($Pd_2(dba)_3{\cdot}CHCl_3$, $Pd(PPh_3)_4$, $Pd(CH_3CN)_2Cl_2$) were tested with fruitless results. In all cases the majority of the iodide was recovered and the stannane was consumed. It was decided then to address the coupling of iodides **11a−g** with protected stannanes **13a−f** to produce *Z,Z*-amino sulfinyl dienes **15a−m** in fair unoptimized yields. Similarly, the coupling of isomeric iodide **11a′**[15a] with stannane **13a** led to *Z,E*-diene **15n** (Scheme 4). To access more substituted substrates,[15c] the coupling between iodide **11a** and racemic stannane **13g** led to a separable mixture of *N*-Boc dienes that were transformed to the target *N*-tosyl aminodienes **15o** and **15p** by removal of the Boc group with TFA under standard conditions. The coupling between iodide **11a** and stannane **13h** did not give rise to diene **15q**. After considerable experimentation we could obtain the desired diene **15q** by a Mitsunobu reaction on the known hydroxy sulfinyl diene **16**,[15a] and Boc deprotection. It should be pointed out that the efficiency of the route was compromised by the unexpectedly low regioselectivity of the Mitsunobu reaction since an equimolecular mixture of **17** and **15q′** was formed.

To develop a more general route to amino sulfinyl dienes substituted at C-1 (R^2) we explored the addition of ethynylmagnesium chloride to (*S*)-*p*-toluenesulfinimine **18a**[20] followed by treatment with LiHMDS and Bu_3SnCl, to produce a 90/10 separable mixture of diastereomeric sulfinamides that provided a good yield of sulfinamide (3*S*)-**19a** as major diastereomer. Purification on silica gel of (3*S*)-**19a** had to be carried out rapidly to minimize destannylation. Similarly, from sulfinimine **18b**, major stannane (3*S*)-**19b** was obtained in 75% isolated yield. Subsequent Stille coupling of diastereomerically pure stannanes (3*S*)-**19a** and (3*S*)-**19b** with vinyl iodide **11b** gave rise to amino 1,3-enynes **20a** and **20b** in fair isolated yields.[21a] Stereoselective hydrogenation of **20a,b** with Wilkinson's catalyst produced the desired *N*-sulfinyl amino dienes **15r** and **15s** as single diastereomers and in acceptable overall yields.[16,21b]

Scheme 5. Stereoselective Synthesis of *N*-Sulfinylamino 2-Sulfinyl Dienes



Diastereoselective Cyclization of Amino Dienyl Sulfoxides. Initial studies probed the viability of this base-promoted conjugate addition using sulfinyl diene **15a** as a model substrate in the presence of strong non-nucleophilic bases such as LDA or NaH giving allylic sulfoxide **21a** with good diastereoselectivity but in low yields (27% and 19% respectively) along with uncharacterized byproducts. Further

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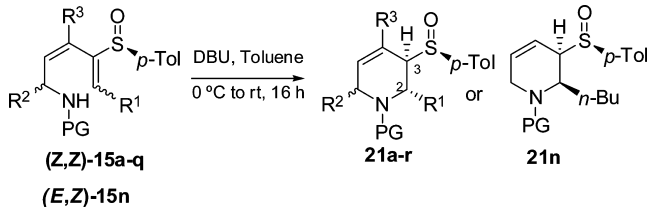
Table 1. DBU-Promoted Cyclization of *Z,Z* and *E,Z* Amino Dienyl Sulfoxides



(Z,Z)-15a-q

(E,Z)-15n

21a-r

21n

entry	SM	PG	R^1	R^2	*trans*/*cis*[a]	**21**[b] (yield %)[c]
1	**15a**	Ts	*n*-Bu	H	97/3	**21a**[d] (60)
2	**15a**	Ts	*n*-Bu	H	>98/2	**21a**[e] (69)
3	**15a**	Ts	*n*-Bu	H	>98/2	**21a** (78)
4	**15b**	*p*NBS	*n*-Bu	H	>98/2	**21b** (64)
5	**15c**	*o*NBS	*n*-Bu	H	>98/2	**21c** (62)
6	**15d**	Ar^1SO_2[f]	*n*-Bu	H	>98/2	**21d** (62)
7	**15e**	Ar^2SO_2[f]	*n*-Bu	H	>98/2	**21e** (76)
8	**15f**	Boc	*n*-Bu	H	90/10	**21f**[g] (81)
9	**15g**	Ts	*n*-Pr	H	>98/2	**21g** (85)
10	**15h**	Ts	*t*-Bu	H	–	–
11	**15i**	Ts	$(CH_2)_3Cl$	H	>98/2	**21i** (84)
12	**15j**	Boc	$(CH_2)_3Cl$	H	80/20	**21j**[g] (63)
13	**15k**	Ts	Ph	H	>98/2	**21k** (71)
14	**15l**	Ts	4-MeO-C_6H_4	H	>98/2	**21l** (68)
15	**15m**	Ts	4-F-C_6H_4	H	97/3	**21m** (70)
16	**15n**	Ts	*n*-Bu	H	2/98	**21n**[h] (51)
17	**15o**	Ts	*n*-Bu	(*S*)-Me	>98/2	**21o** (77)
18	**15p**	Ts	*n*-Bu	(*R*)-Me	>98/2	**21p**[i] (56)
19	**15r**	S(O)*p*-Tol	*n*-Pr	(*R*)-Ph	>98/2	**21r** (68)
20	**15q**	Ts	*n*-Bu	H	96/4	**21q** (64)

[a]2,3-*trans*/*cis* ratio determined by ^{1}H NMR analysis of crude reaction mixtures. [b]R^3 = H unless otherwise stated. [c]Yield of isolated major diastereoisomer of **21**. [d]In THF. [e]In CH_2Cl_2. [f]Ar^1 = 2,4,6-$Me_3C_6H_4$; Ar^2 = 2,4,6-*i*-Pr_3-C_6H_4. [g]NaH/THF; **21j** was isolated along with a 20% of 2,3-*cis*-**21j**. [h]72 h at rt for **21n** and **21q** (R^3 = Me). [i]3 h at 70 °C.

optimization (Table 1, entries 1−3) led to the use of DBU in toluene for the synthesis of the desired *N*-tosyl sulfinyl tetrahydropyridine **21a** as a single isomer, in 78% isolated yield that could be stored for months without noticeable loss of diastereomeric purity.

The influence of the *N*-protecting group on the process was next addressed by performing the reaction with different sulfonamides **15b−e** (Table 1, entries 4−7) that behaved largely as the simple Ts group both in yields and stereoselectivities. In contrast, *N*-Boc dienyl sulfoxide **15f** was unreactive to DBU and required the use of NaH in THF to promote the cyclization (Table 1, entry 8) in good yield and selectivity. It should be pointed out that the presence of rotamers in this case required additional transformations to determine the diastereomeric ratio accurately.[22] Therefore, to facilitate the analysis of the data, the majority of the ensuing study was carried out on *N*-tosyl amino dienyl sulfoxides.

Subsequent studies focusing on variation of substitution (R^1) showed the generality of the DBU-promoted cyclization for *N*-tosyl amino dienyl sulfoxides **15g,i** and the use of NaH for *N*-Boc substrates, **15j**. The protocol readily accommodates alkyl substituents, except for the bulky *t*-Bu group **15h** (Table 1, entries 9−12), as well as substituted aryl groups (Table 1, entries 13−15) with good yields and selectivities. The influence of the geometry of the diene was then briefly examined, and the less reactive diene **15n** required longer reaction times to give a moderate yield of *cis*-tetrahydropyridine **21n**, along with a substantial amount of the undesired cyclic vinyl sulfoxide,[23] resulting from isomerization of the allylic double bond in the final product (Table 1, entry 16).

The transformation is also compatible with the presence of an additional stereocenter in the dienamine skeleton (R^2). Thus, C-1 methyl substituted substrates **15o** and **15p** were converted into the expected products **21o** and **21p** in good yield and selectivity although the cyclization of **15p** required heating at 70 °C. Moreover, the cyclization of *N*-sulfinyl dienamine **15r**, with a bulky Ph substituent took place similarly. Further investigations demonstrated that the methodology can also tolerate an additional substituent on the diene skeleton (R^3), as shown by the transformation of **15q**, with a Me group at C-3, into sulfinyl piperidine **21q** that underwent a slight epimerization at sulfur upon standing in solution (Table 1, entries 17−20).[15,24]

Finally we pursued the direct cyclization of free amino functionalities that took place smoothly upon one pot treatment of *N*-Boc (**15f**) or *N*-sulfinyl dienyl sulfoxides (**15r**, **15s**) with TFA followed by basification with NaOH to produce **21s**, **21t** and **21u** respectively (Table 2).[25] In this manner, the cyclization of **15j**, with a functionalized side chain (R^1 = $(CH_2)_3Cl$), resulted in a concurrent second cyclization to afford bicyclic allylic sulfoxide **21v** with an indolizidine skeleton, identical to that obtained from *N*-Boc sulfinyl piperidine **21j** under similar conditions but in a shorter and more diastereoselective sequence (98/2 vs 80/20), (Table 2, entry 4 vs Table 1, entry 12).

The high stereoselectivity found for these cyclizations and the configurational stability at sulfur of the resulting allylic

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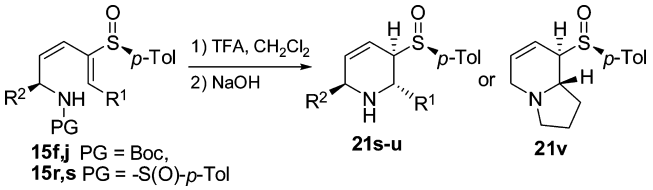
Table 2. TFA/NaOH-Promoted Cyclization of *Z,Z*-Amino Dienyl Sulfoxides

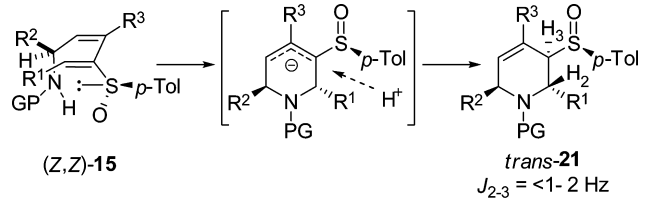


entry	SM	R^1	R^2	**21** (yield %)[a,b]
1	**15f**	*n*-Bu	H	**21s** (59)
2	**15r**	*n*-Pr	(*R*)-Ph	**21t** (88)
3	**15s**	*n*-Pr	(*S*)-Et	**21u** (60)
4	**15j**	$(CH_2)_3Cl$	H	**21v** (49)

[a]2,3-*trans*/*cis* ratio >98/2 determined by ^{1}H NMR analysis of crude reaction mixtures. [b]Yield of isolated major diastereoisomer of **21**.

sulfoxides are noteworthy. This process proceeds with complete stereoselectivity since 2,3-*trans* (**21a**) or 2,3-*cis* (**21n**) cyclic allylic sulfoxides were obtained from (*Z,Z*)- and (*Z,E*)-dienes **15a** and **15n** (R^1 = *n*-Bu, R^2 = R^3 = H), respectively (Table 1, entries 3 and 16). While these sulfinyl allylic tetrahydropyridines **21** were fully characterized by standard techniques, the 2,3-*trans* or 2,3-*cis* stereochemistry could not be firmly established; therefore, stereochemical assignments were secured by an X-ray crystal structure determination of **21o** and subsequent comparison of the data.[15c] In addition, the results of the [2,3]-sigmatropic rearrangements of these allylic sulfoxides to produce allylic alcohols (see below) provided further evidence supporting these assignments. We rationalize the formation of 2,3-*trans* or 2,3-*cis* tetrahydropyridines **21**, by assuming that (*Z,Z*) or (*Z,E*) dienes adopt an *S-cis* eclipsed conformation C═C/S—:, forcing the nucleophilic attack of nitrogen on the α-face of dienamines **15** (Scheme 6).

Scheme 6. Stereochemical Outcome of 2,3-*trans* 21

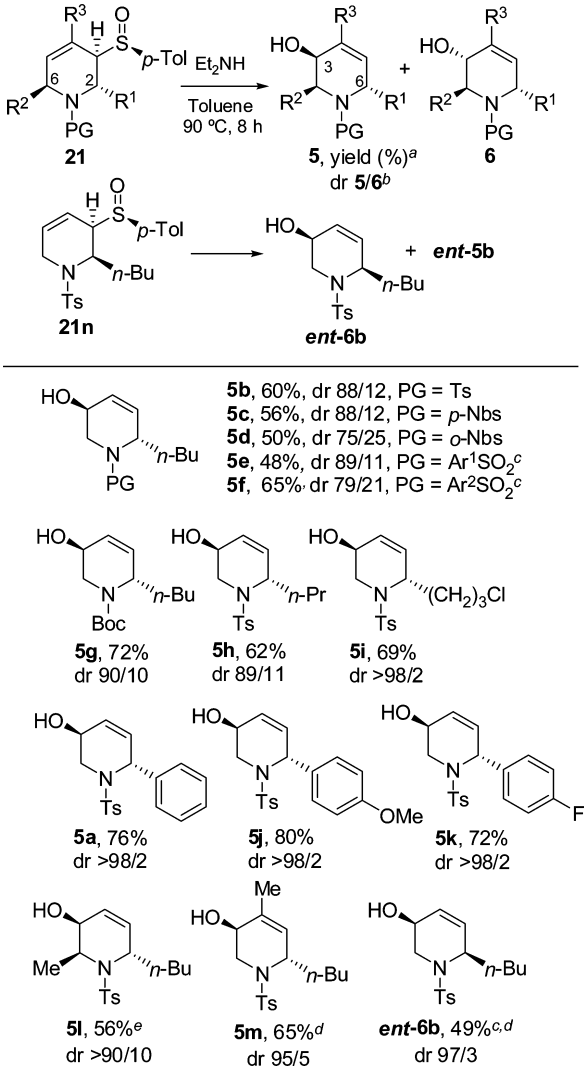


Subsequent protonation of the allylic sulfinyl anion on the same face would lead to 2,3-*trans*-**21** or 2,3-*cis*-**21** cyclic products. It should be pointed out that this stereochemical outcome is parallel to our findings on the cyclization of hydroxy dienyl sulfoxides,[15] as well as other literature precedents.[26,13b]

Sigmatropic Rearrangement of Allylic Sulfinyl Tetrahydropyridines. The [2,3]-sigmatropic rearrangement of allylic sulfoxides leads reversibly to allylic sulfenates that, with an appropriate thiophile, produce allylic alcohols. However, the intrinsic configurational stability of the sulfur center in **21** suggests that the sigmatropic rearrangement might not be a favored pathway.[27]

Substrate **21a** (R^1 = *n*-Bu, R^2 = R^3 = H) was selected as a representative example to examine the feasibility of the sigmatropic process. Treatment of **21a** under standard conditions, $P(OMe)_3$ in MeOH, gave a complex mixture of unidentified products. Performing the reaction in the presence of inorganic bases such as K_2CO_3/DMF-H_2O or Cs_2CO_3/DMF required longer reaction times (48 h) and led to a reduced selectivity (**5b**/**6b**, ca. 70/30) that suggests a possible epimerization at C3 in **21a**.[28] Screening of a range of thiophiles in toluene at 70 °C, showed that DABCO, Et_2NH as well as phosphazene bases (BEMP) could trigger the sigmatropic rearrangement in 24 h. Finally, an excess of Et_2NH (10 equiv) at higher temperature (90 °C) proved optimal, in terms of reaction time (8 h), isolation and yield (60%) with a reasonable high diastereomeric ratio (**5b**/**6b**, 88/12; Scheme 7).

Scheme 7. Sigmatropic Rearrangement of 2,3-*trans* and 2,3-*cis* 3-Sulfinyl Tetrahydropyridines 21[a]



[a]Yield of isolated major diastereoisomer 3,6-*trans* **5**. [b]dr refers to **5**/**6** ratio determined by ^{1}H NMR analysis of crude reaction mixtures. [c]Ar^1 = 2,4,6-$Me_3C_6H_4$; Ar^2 = 2,4,6-*i*-Pr_3-C_6H_4; variable small amounts of regioisomeric 2-alkyl-3-hydroxy-tetrahydropyridines were also detected. [d]3 h, 70–90 °C. [e]24 h, 110 °C.

Further studies probed the scope and generality of this transformation and the results are summarized in Scheme 7. Not too unexpectedly, small amounts of products arising from pyrolytic *syn* elimination of the sulfinyl moiety or formal allylic hydroxyl isomerization were detected in some cases.[15] Nevertheless, under the optimized reaction conditions, this protocol accommodates a range of sulfinyl tetrahydropyridines

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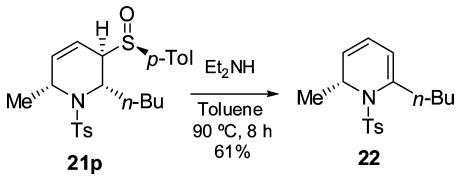
21 with alkyl and aryl substituents at C-2, C-6 and even at C-4, giving the corresponding 3-hydroxy tetrahydropyridines **5a−m** in moderate to good yields (up to 80%) and high diastereoselectivity (up to >98/2 dr). Notable reactivity trends within these series indicate that C(2)-aryl substituted (R^1 = Ph, 4-MeO-C_4H_6, 4-F-C_4H_6) gave higher product conversion and selectivity (**5a**, **5j** and **5k**, dr >98/2), than their C(2)-alkyl substituted counterparts (R^1 = *n*-Bu, *n*-Pr, $(CH_2)_3Cl$, **5b−i**, dr: 75/25−98/2); in particular, aryl units containing electron rich groups exhibit an increased reactivity relative to those with electron deficient substituents (**5j** vs **5k**). The process is compatible with different sulfonamide groups (PG) but with decreased stereoselectivity for **5d**, or with the production of considerable amounts of regioisomeric 2-alkyl-3-hydroxy-tetrahydropyridines in the cases of **5e**,**f**.[29]

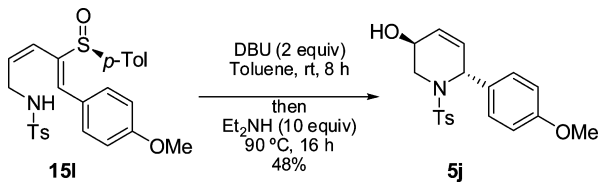
The rearrangement of allylic sulfoxide **21o**, with *S* configuration at C-6, under the standardized reaction conditions rendered a modest 46% conversion into product **5l**; raising the temperature to 110 °C led to an increased 56% isolated yield. We observed an increased reactivity of the C-4 methyl substituted **21q** and 2,3-*cis* diastereoisomer **21n** that provided the related alcohols **5m** (65%) and ***ent*-6b** (49%),[29] in shorter reaction times (3 h). In contrast, the (*R*)-C6 stereoisomer **21p** gave the (2*R*)-methyl substituted dihydropyridine **22** as a major product (61% yield), arising from the pyrolytic *syn*-elimination of the sulfoxide moiety, along with minor byproducts in the crude mixture where the expected 3-hydroxy tetrahydropyridine was barely detected (Scheme 8).

Scheme 8. Pyrolytic *syn*-Elimination of 21p



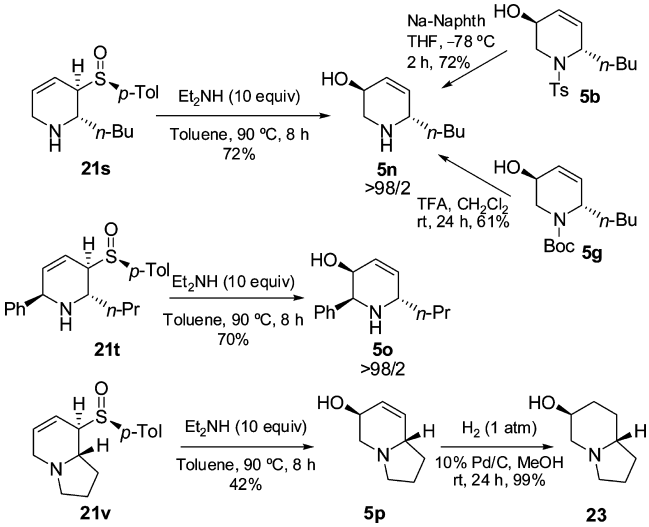
Interestingly, it was possible to perform the cyclization and [2,3]-sigmatropic rearrangement in one step (DBU, then Et_2NH). Amino dienyl sulfoxide **15l** was selected as representative example to give access to tetrahydropyridin-3-ol **5j** in slightly lower unoptimized yield (48%) than the standard two step sequence (54%) and without compromising the diastereocontrol of this transformation (Scheme 9).[30]

Scheme 9. Tandem Cyclization-Sigmatropic Rearrangement for 15l



The results indicate that the nature of the protecting group on nitrogen influences the outcome of these processes, either by conformational biases or by facilitating the ring-opening/ring-closing pathway. To test this hypothesis we examined the sigmatropic rearrangement on *N*-unprotected substrates **21s** and **21t** that took place in increased yields and excellent selectivity (>98/2 dr) with regard to *N*-protected substrates, to afford tetrahydropyridin-3-ol **5n** (72% yield) and **5o** (70% yield) (Scheme 10). It should be mentioned that **5n** was also

Scheme 10. Sigmatropic Rearrangement of Sulfinyl Piperidines with Unprotected Nitrogen



prepared in good yields by deprotection of **5b** with sodium naphthalenide[31] or of **5g** with TFA. The rearrangement of bicyclic sulfoxide **21v** led to unsaturated alcohol **5p** in moderate yield. Hydrogenation of **5p**, under standard conditions, gave an excellent yield of indolizidine alcohol **23**, with identical spectral data to that reported in the literature.[32] Notably the *N*-unprotected substrates provide a more efficient route to 2,3-tetrahydropyridines **5n−p** in terms of yields and selectivities (6−7 linear steps from menthyl sulfinate).

Considering the [2,3]-sigmatropic rearrangement of allylic sulfoxides as a concerted process where the facial selectivity is determined by the configuration of the sulfur-bearing center, 3,6-*trans* and 3,6-*cis* alcohols (**5**, **6**) would be obtained from 2,3-*trans* and 2,3-*cis* tetrahydropyridines, respectively. The relative configuration of these allylic alcohols **5** was assigned through NMR spectroscopic investigations using a combination of NOE and coupling constant analysis measured between H_3−H_{2eq} and H_3−H_{2ax}, typically small (1−3.3 Hz) for *trans*-isomers **5a−p** and larger (6.4, 9.9 Hz) for *cis*-isomer ***ent*-6b**. In addition **5b** was transformed smoothly into **6b** via the Mitsunobu protocol.[33]

The absolute configuration of allylic alcohols *trans*-**5b** and *cis*-**6b** was determined by the preparation of the methoxyphenyl acetates **7** and careful comparison of the spectral data (Scheme 11).[34] Derivatization of **5b** with (*S*)-(+)-MPA (2-methoxy-2-phenylacetic acid) afforded **7b** and **7c** (98/2 dr) and with (*R*)-(−)-MPA gave ***ent*-7b** and ***ent*-7c** (2/98 dr), indicating an excellent enantioselectivity in the sigmatropic rearrangement (96% ee). Shielding effects observed on H_4 and H_{2eq} of **7b** (δH_4 5.91, δH_{2eq} 4.01 ppm) and **7c** (δH_4 5.61, δH_{2eq} 4.16 ppm) showed that the assignment for the alcohols was in agreement with the results observed. The crude reaction mixture of **5b** and **6b** (88/12 dr), obtained from the cyclization-rearrangement sequence of **21a** was also functionalized with (+)-MPA to afford an 88/12 mixture of *trans* and *cis* diastereomers **7b** and **7d** (epimer of **7b** at C-3, δH_4 5.30, δH_{2eq} 4.12 ppm). Comparison of the spectral features of ester **7d** thus obtained, with an identical sample derived by esterification with (+)-MPA

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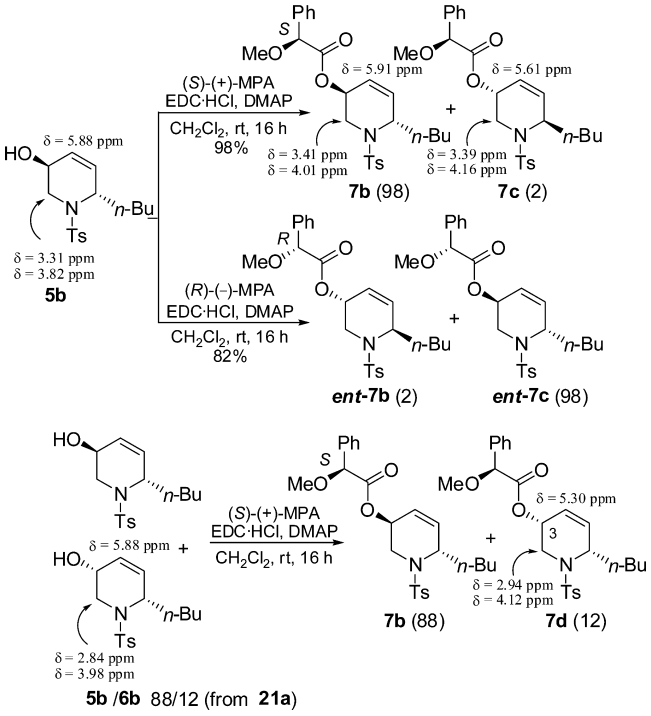
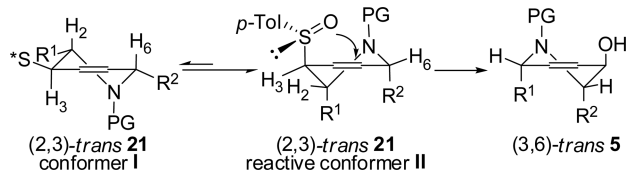
Scheme 11. Derivatization of 5b and 6b with (*S*)- and (*R*)-MPA



of pure **6b** obtained by Mitsunobu inversion of **5b**, indicated that the optical integrity of minor product **6b** was not compromised under these conditions (DBU), in contrast to the findings with Cs_2CO_3.[28] All other tetrahydropyridin-3-ols **5** were assigned by analogy.

A qualitative rationalization of these results considers the relative ease of attaining the reactive conformations of **21** that place the sulfoxide in a pseudoaxial position with the oxygen oriented toward the double bond, that maintain the bulky *p*-tolyl group pointing toward the tetrahydropyridine ring for this absolute configuration (Scheme 12, conformers **I** and **II**).[27a]

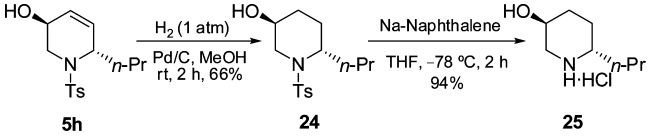
Scheme 12. Proposed Reactive Conformations for 21



This unfavorable scenario could justify the unusual stability of the starting allylic sulfoxides **21** that require high temperatures (90−110 °C) to promote the rearrangement leading ultimately to allylic alcohols **5**. In this rationale, we may assume that the reactive conformer would be more accessible for those substrates with increased size of the substituent at C-2 (R^1) that could force the adjacent sulfinyl moiety at C-3 to adopt a pseudoaxial position to minimize 1,2-strain between the adjacent substituents (sulfoxide/R^1/PG). Then, conformations **I** and **II** would be in slow equilibrium for substrates with alkyl substituents at C-2, **21a−j**, and that might prompt, under reaction conditions, either a base-mediated epimerization at the sulfur bearing center C-3 of **21**, or a ring-opening-closing sequence with diminished selectivity of **5b−i** (R^1 = alkyl) in relation to improved outcome for **5a,j,k** (R^1 = aryl). Likewise, the presence of an additional substituent (R^2 = (*R*)-Me) in **21p** would disfavor conformer **II** due to 1,3-diaxial interactions Me/*n*-Bu and that might explain the decreased reactivity observed (Scheme 8). On the other hand, the rearrangement of *N*-unprotected substrates is more facile and displays a higher stereoselectivity (Scheme 10); this underlines the subtle balance of stereodirecting effects that govern this process.

Synthesis of Natural Product (+)-Pseudoconhydrine. Having demonstrated the suitability of this methodology for the preparation of tetrahydropyridin-3-ols **5** in good yields and selectivities, we further applied this process to the synthesis of Hemlock alkaloid (+)-pseudoconhydrine hydrochloride **25** to exemplify the synthetic utility of these synthetic strategies (Scheme 13). Hydrogenation of **5h**, obtained uneventfully on a

Scheme 13. Synthesis of (+)-Pseudoconhydrine Hydrochloride 25



1 g scale, over Pd/C gave **24** in good yield. Subsequent removal of the *N*-tosyl group with sodium naphthalenide[31] provided **25** as a single isomer with identical spectroscopic data to those in the literature.[35,1i] Moreover, the synthesis of natural product **25** lent further support to the assignment of the absolute configuration of our tetrahydropyridin-3-ols **5**.

CONCLUSIONS

In summary, a general strategy to prepare stereodefined 4-sulfinyl dienyl amine derivatives, with a broad range of substituents, has been described. These substrates undergo a base-promoted intramolecular cyclization to afford novel sulfinyl tetrahydropyridines, thus setting two new stereogenic centers in one step with good yields and selectivities under mild reaction conditions. Subsequent [2,3]-sigmatropic rearrangement of these configurationally stable allylic sulfoxides yields a variety of tetrahydropyridin-3-ols with good to excellent levels of selectivity that were markedly dependent on the nature of the *N*-protecting group. The application of this methodology to the synthesis of enantiopure Hemlock alkaloid (+)-pseudoconhydrine is also detailed herein.

EXPERIMENTAL SECTION

Materials and Methods. Reactions involving moisture sensitive reagents were carried out under an argon atmosphere. Anhydrous solvents were purified by filtration on a solvent purification system. Through this section, the volume of solvents is reported in mL/mmol of starting material. All reactions were carried out under an argon atmosphere. Diethylamine and DBU were purified by distillation from CaH_2. Alkynes were purified by distillation under reduced pressure. Crude products were purified by chromatography on 230−400 mesh silica gel. Analytical TLC was performed on silica gel plates with detection by ultraviolet light (254 nm), followed by staining with iodine/silica and 10% phosphomolybdic acid solution in ethanol. Nuclear magnetic resonance (NMR) spectra were acquired on 300, 400, or 500 MHz (^{1}H) spectrometers at room temperature. Chemical shifts are quoted in parts per million (ppm) and coupling constants, *J*, are quoted in Hz. Infrared spectra (ν max) were recorded using either thin films on NaCl plates or KBr discs. High resolution mass spectra (HRMS) were recorded using Accurate Mass Q-TOF spectrometer. Optical rotations were measured in $CHCl_3$ unless other solvent is

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stated. Compounds **15a,g,k,l,n−q**; **21a,f,g,k,l,o,p,s**; **5a,b,h,j,n**; **24** and **25** were described in the Supporting Information of our preliminary communication.[15c]

Synthesis of Piperidinols from 1-Sulfinyl Dienes. *General Procedure for the Synthesis of Piperidinols and Piperidines from 1-Sulfinyl and Sulfonyl Dienes. Method A.* To a solution of sulfonamide **1**−**3**[14d] in DMF:H_2O 10:1 (10 mL/mmol) in a kimble vial, K_2CO_3 (1.0 equiv for **1**, 4 equiv for **2** and **3**) was added. Argon was bubbled through the mixture and it was sealed. The reaction was stirred at rt for **1** and at 50−60 °C for **2** and **3** (1 day), monitored by TLC. The solvent was removed under reduced pressure and the crude mixture was purified by column chromatography using the appropriate mixture of eluents.

Method B. To a solution of sulfonamide **3** in anhydrous DMF (10 mL/mmol) in a kimble vial, Cs_2CO_3 (2.0 equiv) was added. Argon was bubbled through the mixture and it was sealed. The reaction was stirred at 60−70 °C and monitored by TLC. The solvent was removed under reduced pressure and the crude mixture was purified by column chromatography using the appropriate mixture of eluents.

*Synthesis of (−)-(**6R**)-[1,5-Bis(p-tolylsulfonyl)-6-phenyl-1,2,3,6-tetrahydro]-pyridine, 4. Method A.* Sulfonamide **1** (8 mg, 0.02 mmol) gave **4** (8 mg, 99%) as a colorless oil after purification by chromatography (10−40% EtOAc-hexane). Data for **4**: R_f 0.14 (30% EtOAc-hexane); $[\alpha]^{20}_D$ −50.7 (*c* 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03−2.29 (m, 2 H), 2.33 (s, 3 H), 2.39 (s, 3 H), 2.99 (ddd, 1 H, *J* = 15.2, 11.2, 5.5 Hz), 3.70 (ddd, 1 H, *J* = 15.4, 6.7, 0.9 Hz), 5.93 (s, 1 H), 6.98−7.16 (m, 8 H), 7.19 (m, 2 H), 7.39 (dt, 2 H, *J* = 8.4, 1.8 Hz), 7.54 (dt, 2 H, *J* = 8.3, 1.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 21.6, 24.1, 35.7, 55.1, 127.1 (2 C), 127.9, 128.2 (2 C), 128.3 (2 C), 128.7 (2 C), 129.4 (2 C), 129.7 (2 C), 136.2, 136.5, 137.3, 138.4, 139.9, 143.6, 144.3; IR (film) 3026, 2920, 1594, 1491, 1452, 1320, 1302, 1161, 1147, 1082, 811, 755, 697, 676 cm^{-1}. MS (ESI): 490 $[M + Na]^+$ (100%), 468 $[M + 1]^+$.

*Synthesis of (−)-(3R,6S)-6-Phenyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-ol, ent-**5a**. Method A.* Sulfonamide **2** (36 mg, 0.08 mmol) after 4 days gave ***ent*-5a** (17 mg, 64%) as a colorless oil after purification by chromatography (30−80% Et_2O-hexane). Derivatization with (+)-(*S*)-2-methoxy-2-phenylacetic acid revealed essentially pure ***ent*-5a**. Data for ***ent*-5a**: R_f 0.30 (15% Et_2O−CH_2Cl_2); $[\alpha]^{20}_D$ −227.4 (*c* 0.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.36 (s, 3 H), 2.40 (d, 1 H, *J* = 10.5 Hz), 3.21 (dd, 1 H, *J* = 15.0, 3.4 Hz), 3.67 (dd, 1 H, *J* = 15.0, 0.8 Hz), 3.99 (dt, 1 H, *J* = 10.5, 3.3 Hz), 5.65 (d, 1 H, *J* = 4.0 Hz), 6.08 (ddd, 1 H, *J* = 10.4, 4.0, 0.5 Hz), 6.15 (ddt, 1 H, *J* = 10.2, 4.7, 1.2 Hz), 7.18 (dd, 2 H, *J* = 8.5, 0.6 Hz), 7.27 (m, 5 H), 7.59 (dd, 2 H, *J* = 8.2, 1.9 Hz). NOE-1D between H-2*ax*/Ph (1.13%); H-2*ax*/H-3 (3.07%); H-3/(H-4+H-5) (1.06%); H-6/(H-4+H-5) (1.79%); H-3/Ph (0.15%); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 46.2, 55.1, 62.0, 127.6 (2 C), 127.9, 128.2 (3 C), 128.5 (2 C), 129.5 (2 C), 130.1, 136.4, 137.2, 143.6; IR (film) 3496, 3061, 3032, 2920, 2867, 1597, 1491, 1454, 1333, 1158, 1067, 1005, 814, 700, 671 cm^{-1}. MS (ESI): 681 $[2M + Na]^+$ (100%), 352 $[M + Na]^+$, 330 $[M + 1]^+$. HPLC: Daicel Chiralcel OD, 15% ^{i}PrOH-hexane, 0.75 mL/min, t_{Rminor} = 16.7 min, t_{Rmajor} = 19.3 min, 95.2% ee.

*Synthesis of (3S,6R)-6-Phenyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-ol, **5a**/ent-**5a** and **6a**. Method A.* Sulfonamide **3** (51 mg, 0.1 mmol) gave after 12 days a 79:21 mixture of **5a**/***ent*-5a** and **6a** (16 mg, 43%) as colorless oil after purification by chromatography (20−80% Et_2O-hexane). Derivatization of **5a**/***ent*-5a** with (+)-(*S*)-2-methoxy-2-phenylacetic acid revealed a 67:33 mixture of **5a** and ***ent*-5a**. *Method B*: sulfonamide **3** (44 mg) gave after 1 day a 95:5 mixture of **5a**/***ent*-5a** and **6a** (12 mg, 38%).[15c] Derivatization with (+)-(*S*)-2-methoxy-2-phenylacetic acid revealed a 0:100 mixture of **5a** and ***ent*-5a**. A 12% of 6-phenylpyridin-3-ol was found in the crude mixture with identical data to that found in the literature.[36]

Preparation of Starting Materials. Alkynyl sulfoxides **8a,e**;[15a] **8b,c**;[37] stannyl sulfoxides **9a,e**;[15a] iodo vinyl sulfoxides **11a,e** and **11′a**[15a] were prepared as described in the literature; amino vinyl stannane **12** has been reported.[19]

*Synthesis of Alkynyl Sulfoxides **8**. Method C.*[15a] A dry two-necked round-bottomed flask fitted with reflux condenser, septum and magnetic stirrer was charged with dry Mg turnings (1.6 equiv) under an argon atmosphere and anhydrous Et_2O was added (0.1 mL/mmol Mg) and 5−10 drops of freshly distilled EtBr. The mixture was heated slowly until the formation of the Grignard reagent was initiated. Then a solution of EtBr (1.7 equiv) in Et_2O (0.4 mL/mmol Mg) was added dropwise, maintaining a moderate reflux, and after the addition was complete, the mixture was heated to reflux until complete disappearance of Mg was observed. To the solution of EtMgBr at rt the alkyne (R—C≡C—H, 1.7 equiv) was added and the mixture was heated to reflux for 2 h. The alkynyl Grignard was added (via syringe) to a cold solution (−20 °C) of (−)-menthyl *p*-toluenesulfinate (1.0 equiv) in anhydrous toluene (5 mL/mmol sulfoxide) and the reaction was stirred at the same temperature until disappearance of starting material was observed (TLC). The mixture was quenched by addition of a saturated NH_4Cl solution (4 mL/mmol sulfoxide) and H_2O (4 mL/mmol sulfoxide) and diluted with EtOAc. The layers were separated, the aqueous layer was extracted with EtOAc and 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 combination of solvents.

*Synthesis of (+)-(S)-5-Chloropentynyl p-tolyl sulfoxide, **8d**. Method C.* 5-Chloropentyne (3.60 mL, 34.0 mmol) gave after chromatography (20−30% EtOAc-hexane) **8d** as a clear oil (2.80 g, 58%). Data for **8d**: R_f 0.50 (30% EtOAc-hexane); $[\alpha]^{20}_D$ +60.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96−2.05 (m, 2 H), 2.42 (s, 3 H), 2.62 (t, 2 H, *J* = 6.9 Hz), 3.59 (t, 2 H, *J* = 6.2 Hz), 7.34 (d, 2 H, *J* = 8.1 Hz), 7.68 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 16.9, 21.2, 30.0, 43.0, 79.2, 103.1, 124.8, 130.0, 140.8, 142.2; IR (film) 3052, 2960, 2923, 2183, 1595, 1492, 1441, 1087, 1056, 810 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{12}H_{14}ClOS$ $[M + H]^+$ 241.0448, found 241.0441.

*Synthesis of (+)-(S)-4-Methoxyphenyl-1-ethynyl p-tolyl sulfoxide, **8f**. Method C.* 4-Methoxyphenylacetylene (2.24 mL, 17.0 mmol) gave after chromatography (20−30% EtOAc-hexane) **8f** as a pale yellow solid (1.72 g, 64%). Data for **8f**: R_f 0.45 (30% EtOAc-hexane); mp 98−100 °C; $[\alpha]^{20}_D$ +49.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (s, 3 H), 3.82 (s, 3 H), 6.86 (d, 2 H, *J* = 8.9 Hz), 7.36 (d, 2 H, *J* = 8.1 Hz), 7.45 (d, 2 H, *J* = 8.9 Hz), 7.76 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 55.4, 85.3, 103.0, 111.6, 114.2 (2 C), 125.2 (2 C), 130.2 (2 C), 134.1 (2 C), 141.0, 142.3, 161.4; IR (KBr) 2965, 2874, 2181, 1493, 1462, 1087, 1058, 1015, 810, 622 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{16}H_{15}O_2S$ $[M + H]^+$ 271.0787, found 271.0789.

*Synthesis of (+)-(S)-4-Fluorophenyl-1-ethynyl p-tolyl sulfoxide, **8g**. Method C.* 4-Fluorophenylacetylene (1.40 mL, 12.2 mmol) gave after chromatography (15−20% EtOAc-hexane) **8g** as a pale yellow solid (1.04 g, 56%). Data for **8g**: R_f 0.30 (15% EtOAc-hexane); mp 58−60 °C; $[\alpha]^{20}_D$ +19.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.44 (s, 3 H), 7.05 (t, 2 H, *J* = 8.7 Hz), 7.37 (d, 2 H, *J* = 8.0 Hz,), 7.50 (dd, 2 H, *J* = 8.5, 6.0 Hz), 7.76 (d, 2 H, *J* = 8.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 86.2, 101.0, 116.1 (d, $^2J_{C-F}$ = 22.4 Hz), 125.2, 130.1, 130.3, 134.5, 140.6, 142.5, 163.8; IR (film) 3061, 2923, 2164, 1599, 1505, 1451, 1235, 1087, 1059, 776 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{15}H_{12}FOS$ $[M + H]^+$ 259.0587, found 259.0582.

*Synthesis of (E)-Stannyl Sulfoxides **9**. Method D.*[15a] To a solution of alkynyl sulfoxide **8** in anhydrous toluene (6.6 mL/mmol sulfoxide) at rt under an argon atmosphere, $Pd(Ph_3P)_4$ (0.02 equiv) was added. Argon was bubbled through the solution for 10 min and the mixture was then cooled to −78 °C. A solution of Bu_3SnH (1.1 equiv) in toluene (1.1 mL/mmol sulfoxide) was added and the reaction mixture was stirred and warmed up to rt until disappearance of starting material (TLC). The solvent was removed in vacuo and the crude product was purified by column chromatography on silica gel with the appropriate combination of solvents.

*Synthesis of (−)-(S)-[(E)-1-(p-Tolylsulfinyl)pent-1-enyl]-tributylstannane, **9b**. Method D.* Alkynyl sulfoxide **8b** (4.04 g, 19.6 mmol) gave a 98:2 mixture of regioisomers **9b** and **10b**. Chromatography (5−15% EtOAc-hexane) afforded **9b** (5.75 g, 59%) as a yellow oil. Data for **9b**: R_f 0.32 (5% EtOAc-hexane); $[\alpha]^{20}_D$ −79.0

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(c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.77−0.97 (m, 15 H), 0.95 (t, 3 H, J = 7.3 Hz), 1.14−1.53 (m, 14 H), 2.25−2.40 (m, 1 H), 2.33 (s, 3 H), 2.62−2.69 (m, 1 H), 6.14 (dd, 1 H, J = 8.4, 5.7 Hz), 7.21 (d, 2 H, J = 8.3 Hz), 7.37 (d, 2 H, J = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.2, 13.5, 13.5, 21.2, 22.4, 27.1, 28.6, 34.7, 124.2 (2 C), 129.4 (2 C), 139.8, 142.4, 148.7, 156.3; IR (film) 2924, 2870, 1638, 1463, 1376, 1079, 1037, 803, 670, 534 cm^{-1}.

*Synthesis of (−)-(S)-[(E)-1-(p-Tolylsulfinyl)-3,3-dimethylbut-1-enyl]tributylstannane, **9c**. Method D.* Alkynyl sulfoxide **8c** (220 mg, 1.00 mmol) gave a >90:10 mixture of regioisomers **9c** and **10c**. Chromatography (20−30% EtOAc-hexane) afforded **9c** as a yellow oil (270 mg, 53%). Data for **9c**: R_f 0.70 (20% EtOAc-hexane); $[\alpha]^{20}_D$ −42.7 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.69−0.84 (m, 15 H), 1.16−1.34 (m, 12 H), 1.26 (s, 9 H), 2.38 (s, 3 H), 6.23 (s, 1 H), 7.26 (d, 2 H, J = 8.1 Hz), 7.45 (d, 2 H, J = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.7, 13.5, 21.0, 27.0, 28.6, 31.3, 31.3, 125.2, 129.3, 139.7, 142.1, 151.4, 158.0; IR (film) 3049, 2958, 2925, 2855, 1579, 1464, 1078, 1029, 807, 704 cm^{-1}.

*Synthesis of (−)-(S)-[(E)-5-Chloro-1-(p-tolylsulfinyl)pent-1-enyl]-tributylstannane, **9d**. Method D.* Alkynyl sulfoxide **8d** (534 mg, 2.22 mmol) gave a >90:10 mixture of regioisomers **9d** and **10d**. Chromatography (20−30% EtOAc-hexane) afforded **9d** as a yellow oil (737 mg, 62%). Data for **9d**: R_f 0.65 (15% EtOAc-hexane); $[\alpha]^{20}_D$ −11.3 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.75−0.93 (m, 15 H), 1.14−1.42 (m, 12 H), 1.87−2.02 (m, 2 H), 2.36 (s, 3 H), 2.48−2.60 (m, 1 H), 2.79−2.91 (m, 1 H), 3.49−3.63 (m, 2 H), 6.13 (dd, 1 H, J = 8.6, 5.7 Hz), 7.24 (d, 2 H, J = 8.2 Hz), 7.39 (d, 2 H, J = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.3, 13.5, 21.1, 27.1, 28.7, 30.0, 31.9, 43.9, 124.3 (2 C), 129.5 (2 C), 140.1, 142.2, 146.3, 158.2; IR (film) 2955, 2922, 1586, 1492, 1456, 1080, 1037, 1016, 805, 658 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{24}H_{41}ClNaOSSn$ $[M + Na]^+$ 555.1477, found 555.1474.

*Synthesis of (−)-(S)-[(E)-2-(4-Methoxyphenyl)-1-(p-tolylsulfinyl)-vinyl]tributylstannane, **9f**. Method D.* Alkynyl sulfoxide **8f** (1.30 g, 4.80 mmol) gave a 94:6 mixture of regioisomers **9f** and **10f**. Chromatography (20−30% EtOAc-hexane) afforded **9f** (2.49 g, 92%) as a yellow oil. Data for **9f**: R_f 0.76 (30% EtOAc-hexane); $[\alpha]^{20}_D$ −318.0 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.82−1.00 (m, 15 H), 1.18−1.50 (m, 12 H), 2.38 (s, 3 H), 3.83 (s, 3 H), 6.90 (d, 2 H, J = 8.8 Hz), 7.10 (s, 1 H), 7.25 (d, 2 H, J = 8.4 Hz), 7.42−7.45 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.9, 13.6, 21.2, 27.3, 28.8, 55.3, 113.9 (2 C), 124.8 (2 C), 129.1, 129.6 (2 C), 131.4 (2 C), 140.0, 141.9, 144.3, 156.4, 159.9; IR (film) 2955, 2923, 2870, 1604, 1508, 1254, 1177, 1033, 807, 552 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{28}H_{43}O_2SSn$ $[M + H]^+$ 563.2006, found 563.2027.

*Synthesis of (−)-(S)-[(E)-2-(4-Fluorophenyl)-1-(p-tolylsulfinyl)-vinyl]tributylstannane, **9g**. Method D.* Alkynyl sulfoxide **8g** (258 mg, 1.00 mmol) gave a >90:10 mixture of regioisomers **9g** and **10g**. Chromatography (5−15% EtOAc-hexane) afforded **9g** as a pale yellow oil (319 mg, 58%). Data for **9g**: R_f 0.43 (5% EtOAc-hexane); $[\alpha]^{20}_D$ −206.6 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.82−0.97 (m, 15 H), 1.00−1.49 (m, 12 H), 2.37 (s, 3 H), 7.06 (t, 2 H, J = 8.7 Hz), 7.11 (s, 1 H), 7.22 (d, 2 H, J = 8.2 Hz), 7.38 (d, 2 H, J = 8.2 Hz), 7.44 (dd, 2 H, J = 8.7, 5.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.9, 13.6, 21.2, 27.3, 28.8, 115.6 (d, $^2J_{C-F}$ = 21.3 Hz, 2 C), 124.8 (2 C), 129.7 (2 C), 131.5 (d, $^3J_{C-F}$ = 8.3 Hz, 2 C), 132.5 (d, $^4J_{C-F}$ = 3.4 Hz), 140.3, 141.5, 143.5, 159.6, 162.6 (d, $^1J_{C-F}$ = 250.0 Hz); IR (film) 2956, 2923, 2871, 1600, 1506, 1237, 1038, 807, 730, 550 cm^{-1}.

*Synthesis of Iodo Vinyl Sulfoxides **11**. Method E.*[15a] To a solution of iodine (1.3 equiv) in CH_2Cl_2 (6 mL/mmol sulfoxide) at rt under an argon atmosphere was added a solution of stannyl sulfoxide (1.0 equiv) in CH_2Cl_2 (5 mL/mmol sulfoxide). The mixture was stirred at rt until disappearance of starting material (TLC), and then it was quenched with an aqueous solution of $Na_2S_2O_4$ (2 mL/mmol, 1 M). The layers were separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4) and concentrated in vacuo. The crude mixture was purified by column chromatography on silica gel with the appropriate combination of solvents.

*Synthesis of (−)-(S)-(E)-1-Iodo-1-(p-tolylsulfinyl)pentene, **11b**. Method E.* Stannyl sulfoxide **9b** (4.58 g, 9.23 mmol) and I_2 (3.05 g, 12.0 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **11b** as a white solid (3.08 g, 100%). Data for **11b**: R_f 0.70 (5% EtOAc-CH_2Cl_2); mp 82−85 °C; $[\alpha]^{20}_D$ −102.6 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.01 (t, 3 H, J = 7.4 Hz), 1.51−1.63 (m, 2 H), 2.38 (s, 3 H), 2.49−2.61 (m, 1 H), 2.71−2.84 (m, 1 H), 6.85 (dd, 1 H, J = 8.7, 7.1 Hz), 7.29 (d, 2 H, J = 8.2 Hz), 7.42 (d, 2 H, J = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.6, 21.4, 22.2, 35.4, 114.4, 124.3 (2 C), 129.7 (2 C), 139.8, 141.6, 151.7; IR (KBr) 2954, 1594, 1490, 1452, 1082, 1057, 906, 811, 732, 523 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{12}H_{16}IOS$ $[M + H]^+$ 334.9961, found 334.9973.

*Synthesis of (−)-(S)-(E)-3,3-Dimethyl-1-iodo-1-(p-tolylsulfinyl)-butene, **11c**. Method E.* Stannyl sulfoxide **9c** (255 mg, 0.50 mmol) and I_2 (165 mg, 0.65 mmol) gave after chromatography (5−20% EtOAc-CH_2Cl_2) **11c** as a yellow oil (174 mg, 100%). Data for **11c**: R_f 0.58 (30% EtOAc-hexane); $[\alpha]^{20}_D$ −75.7 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.38 (s, 9 H), 2.40 (s, 3 H), 7.06 (s, 1 H), 7.31 (d, 2 H, J = 8.3 Hz), 7.45 (d, 2 H, J = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.4, 31.7, 39.4, 113.7, 124.6, 129.7, 140.1, 141.4, 162.3; IR (film) 3051, 2965, 2870, 1492, 1463, 1365, 1085, 1058, 819, 703 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{13}H_{18}IOS$ $[M + H]^+$ 349.0118, found 349.0121.

*Synthesis of (−)-(S)-(E)-5-Chloro-1-iodo-1-(p-tolylsulfinyl)-pentene, **11d**. Method E.* Stannyl sulfoxide **9d** (631 mg, 1.19 mmol) and I_2 (392 mg, 1.58 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **11d** as a clear oil (407 mg, 93%). Data for **11d**: R_f 0.63 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −59.4 (c 1.0, $CHCl_3$); ^1H NMR, COSY (300 MHz, $CDCl_3$) δ 1.95−2.05 (m, 2 H), 2.39 (s, 3 H), 2.70−2.82 (m, 1 H), 2.91−3.04 (m, 1 H), 3.61 (ddd, 2 H, J = 6.4, 6.4, 2.5 Hz), 6.82 (dd, 1 H, J = 8.7, 7.0 Hz), 7.30 (d, 2 H, J = 8.1 Hz), 7.44 (d, 2 H, J = 8.1 Hz); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.4, 30.7, 31.3, 43.6, 116.2, 124.3 (2 C), 129.8 (2 C), 139.7, 141.8, 149.3; IR (film) 2957, 2921, 1595, 1492, 1443, 1303, 1087, 1059, 1016, 809 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{12}H_{15}ClIOS$ $[M + H]^+$ 368.9571, found 368.9573.

*Synthesis of (−)-(S)-(E)-2-(4-Methoxyphenyl)-1-iodo-1-(p-tolylsulfinyl)ethene, **11f**. Method E.* Stannyl sulfoxide **9f** (2.50 g, 4.45 mmol) and I_2 (2.02 g, 5.79 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **11f** as a pale yellow solid (1.77 g, 100%). Data for **11f**: R_f 0.60 (5% EtOAc-CH_2Cl_2); mp 90−94 °C; $[\alpha]^{20}_D$ −457.5 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 3.84 (s, 3 H), 6.95 (d, 2 H, J = 8.8 Hz), 7.29 (d, 2 H, J = 8.1 Hz), 7.46 (d, 2 H, J = 8.1 Hz), 7.53 (d, 2 H, J = 8.8 Hz), 7.81 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.2, 55.1, 113.9 (2 C), 114.6, 124.1 (2 C), 127.8, 129.6 (2 C), 131.1 (2 C), 140.1, 141.3, 149.0, 160.4; IR (KBr) 3002, 2954, 2837, 1602, 1505, 1254, 1178, 1057, 811, 729 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{16}H_{16}IO_2S$ $[M + H]^+$ 398.9910, found 398.9915.

*Synthesis of (−)-(S)-(E)-2-(4-Fluorophenyl)-1-iodo-1-(p-tolylsulfinyl)ethene, **11g**. Method E.* Stannyl sulfoxide **9g** (160 mg, 0.29 mmol) and I_2 (96 mg, 0.38 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **11g** as a yellow oil (178 mg, 100%). Data for **11g**: R_f 0.50 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −317.3 (c 1.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (s, 3 H), 7.12 (t, 2 H, J = 8.7 Hz), 7.30 (d, 2 H, J = 8.4 Hz), 7.40 (d, 2 H, J = 8.4 Hz), 7.53 (dd, 2 H, J = 8.7, 5.2 Hz), 7.85 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.5, 116.0 (d, $^2J_{C-F}$ = 21.9 Hz), 118.2, 124.4, 129.9, 131.4 (d, $^3J_{C-F}$ = 8.4 Hz), 131.8 (d, $^4J_{C-F}$ = 3.6 Hz), 140.1, 141.9, 148.2, 163.2 (d, $^1J_{C-F}$ = 251.8 Hz); IR (film) 3057, 2924, 2855, 1599, 1505, 1455, 1237, 1161, 1086, 1059 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{15}H_{13}FIOS$ $[M + H]^+$ 386.9710, found 386.9720.

*Synthesis of Amino Vinyl Stannanes **13**. Method F.* To a solution of **12**[19] (1.0 equiv) in anhydrous CH_2Cl_2 (3.0 mL/mmol stannane) at 0 °C under an argon atmosphere was added triethylamine (2.0 equiv). After stirring for 5 min, the corresponding electrophile (1.0−1.2 equiv) was added and the reaction mixture was allowed to warm to rt and then stirred until disappearance of starting material (TLC). Then, it was quenched with 0.1 N HCl aqueous solution and the aqueous layer was extracted with CH_2Cl_2. The organic extracts were dried (Na_2SO_4) and concentrated in vacuo. The crude mixture was purified

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by column chromatography on silica gel with the appropriate combination of solvents to afford *N*-protected vinyl stannanes **13**.

Method G. To a cold solution (0 °C) of *N*-(*tert*-butoxycarbonyl)-*p*-toluenesulfonamide (1.0 equiv), PPh_3 (1.3−3.0 equiv) in toluene (8 mL/mmol alcohol) was added **14** (1.0 equiv). DEAD or DIAD (1.2−3.0 equiv) was then added and the reaction mixture was stirred and warmed up to rt until disappearance of starting material (TLC). The solvent was evaporated and the crude mixture was purified by column chromatography on silica gel with the appropriate combination of solvents.

*Synthesis of (Z)-N-Tosyl-3-(tributylstannyl)prop-2-en-1-amine, **13a**. Method F.* Amino vinyl stannane **12** (15.3 g, 44.3 mmol), Et_3N (12.3 mL, 88.6 mmol) and TsCl (10.1 g, 53.6 mmol) gave after chromatography (10% EtOAc-hexane) **13a** as a clear oil (19.0 g, 86%). Data for **13a**: R_f 0.30 (50% CH_2Cl_2-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76−0.89 (m, 15 H), 1.18−1.44 (m, 12 H), 2.44 (s, 3 H), 3.46−3.53 (m, 2 H), 4.19 (t, 1 H, J = 6.0 Hz), 6.04 (br d, 1 H, J = 12.6 Hz), 6.37 (dt, 1 H, J = 12.6, 6.6 Hz), 7.33 (d, 2 H, J = 8.4 Hz), 7.76 (d, 2 H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.4, 13.5, 21.4, 27.1, 29.0, 48.6, 127.2 (2 C), 129.7 (2 C), 134.7, 137.2, 142.2, 143.4; IR (film) 3274, 2957, 1667, 1599, 1457, 1331, 1163, 1095, 814, 664 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{22}H_{40}NO_2SSn$ $[M + H]^+$ 502.1799, found 502.1793.

*Synthesis of (Z)-N-(4-Nitrobenzenesulfonyl)-3-(tributylstannyl)-prop-2-en-1-amine, **13b**. Method F.* Amino vinyl stannane **12** (1.07 g, 3.09 mmol), Et_3N (0.86 mL, 6.18 mmol) and *p*-nitrobenzenesulfonyl chloride (822 mg, 3.71 mmol) gave after chromatography (25% EtOAc-CH_2Cl_2) **13b** as a pale yellow oil (1.08 g, 66%). Data for **13b**: R_f 0.70 (25% EtOAc-CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80−0.88 (m, 15 H), 1.19−1.49 (m, 12 H), 3.57−3.61 (m, 2 H), 4.60 (t, 1 H, J = 5.7 Hz), 6.08 (br d, 1 H, J = 12.6 Hz), 6.32 (dt, 1 H, J = 12.6, 6.3 Hz), 8.07 (d, 2 H, J = 9.0 Hz), 8.37 (d, 2 H, J = 9.0 Hz); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 10.3, 13.6, 27.2, 29.0, 48.4, 124.4 (2 C), 128.4 (2 C), 135.9, 141.1, 146.0, 150.1; IR (film) 3289, 2957, 1606, 1532, 1349, 1165, 1093, 854, 736 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{21}H_{36}N_2NaO_4SSn$ $[M + Na]^+$ 555.1306, found 555.1330.

*Synthesis of (Z)-N-(2-Nitrobenzenesulfonyl)-3-(tributylstannyl)-prop-2-en-1-amine, **13c**. Method F.* Amino vinyl stannane **12** (691 mg, 2.00 mmol), Et_3N (0.56 mL, 4.00 mmol) and 2-nitrobenzenesulfonyl chloride (532 mg, 2.40 mmol) gave after chromatography (25% EtOAc-CH_2Cl_2) **13c** as a yellow oil (897 mg, 84%). Data for **13c**: R_f 0.70 (0.25% EtOAc-CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.80−0.88 (m, 15 H), 1.20−1.46 (m, 12 H), 3.67 (ddt, 2 H, J = 7.3, 5.8, 0.8 Hz), 5.26 (t, 1 H, J = 5.8 Hz), 6.08 (d, 1 H, J = 12.6 Hz), 6.37 (dm, 1 H, J = 12.6 Hz), 7.73−7.78 (m, 2 H), 7.85−7.91 (m, 1 H), 8.11−8.17 (m, 1 H); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 10.3, 13.6, 27.2, 29.0, 49.0, 125.4, 131.1, 132.7, 133.6, 133.7, 135.4, 141.3, 148.1; IR (film) 3349, 2957, 1595, 1543, 1359, 1171, 1061, 854, 591 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{21}H_{37}N_2O_4SSn$ $[M + H]^+$ 533.1493, found 533.1504.

*Synthesis of (Z)-3-(Tributylstannyl)-N-(2,4,6-trimethylbenzenesulfonyl)prop-2-en-1-amine, **13d**. Method F.* Amino vinyl stannane **12** (691 mg, 2.00 mmol), Et_3N (0.56 mL, 4.00 mmol) and 2,4,6-trimethylbenzenesulfonyl chloride (525 mg, 2.40 mmol) gave after chromatography (10% EtOAc-hexane) **13d** as a clear oil (936 mg, 86%). Data for **13d**: R_f 0.40 (10% EtOAc-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.77−0.89 (m, 15 H), 1.21−1.45 (m, 12 H), 2.30 (s, 3 H), 2.64 (s, 6 H), 3.45 (td, 2 H, J = 6.2, 1.2 Hz), 4.39 (t, 1 H, J = 6.2 Hz), 6.04 (dt, 1 H, J = 12.5, 1.2 Hz), 6.37 (dt, 1 H, J = 12.5, 6.2 Hz), 6.97 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 13.6, 20.9, 23.0 (2 C), 27.1, 29.0, 48.0, 132.2 (2 C), 133.4, 134.5, 139.1 (2 C), 142.0, 142.2; IR (film) 3293, 2956, 1604, 1463, 1326, 1156, 1072, 851, 655 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{24}H_{44}NO_2SSn$ $[M + H]^+$ 530.2112, found 530.2099.

*Synthesis of (Z)-3-(Tributylstannyl)-N-(2,4,6-triisopropylbenzenesulfonyl)prop-2-en-1-amine, **13e**. Method F.* Amino vinyl stannane **12** (691 mg, 2.00 mmol), Et_3N (0.56 mL, 4.00 mmol) and 2,4,6-triisopropylbenzenesulfonyl chloride (727 mg, 2.40 mmol) gave after chromatography (5−10% EtOAc-hexane) **13e** as a clear gum (772 mg, 63%). Data for **13e**: R_f 0.40 (5% EtOAc-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.82−0.88 (m, 15 H), 1.24−1.47 (m, 30 H), 2.86−2.95 (m, 1 H), 3.55 (t, 2 H, J = 6.3 Hz), 4.12−4.25 (m, 3 H), 6.05 (br d, 1 H, J = 12.8 Hz), 6.37 (dt, 1 H, J = 12.8, 6.3 Hz), 7.17 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3, 13.6, 23.5 (2 C), 24.9 (4 C), 27.2, 29.1, 29.6 (2 C), 34.1, 48.0, 123.8 (2 C), 132.2, 134.4, 142.3, 150.3 (2 C), 152.8; IR (film) 3294, 2958, 1600, 1463, 1321, 1151, 1072, 881, 659 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{30}H_{56}NO_2SSn$ $[M + H]^+$ 614.3077, found 614.3053.

*Synthesis of (Z)-N-(tert-Butoxycarbonyl)-3-(tributylstannyl)prop-2-en-1-amine, **13f**. Method F.* Amino vinyl stannane **12** (9.84 g, 28.4 mmol), Et_3N (7.90 mL, 56.8 mmol) and Boc_2O (6.20 g, 28.4 mmol) gave after chromatography (50% CH_2Cl_2-hexane) **13f** as a clear oil (19.0 g, 79%). Data for **13f**: R_f 0.60 (50% CH_2Cl_2-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86−0.95 (m, 15 H), 1.24−1.53 (m, 21 H), 3.69 (t, 2 H, J = 5.4 Hz), 4.44 (br s, 1 H), 6.01 (br d, 1 H, J = 12.6 Hz), 6.49 (dt, 1 H, J = 12.6, 6.5 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.3, 13.7, 27.2, 28.4, 29.1, 45.9, 79.3, 132.4, 144.1, 155.5; IR (film) 3356, 2958, 1710, 1600, 1505, 1366, 1249, 1172, 865, 666 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{20}H_{42}NO_2Sn$ $[M + H]^+$ 448.2236, found 448.2218.

*Synthesis of (Z)-N-(tert-Butoxycarbonyl)-N-tosyl-4-(tributylstannyl)but-3-en-2-amine, **13g**. Method G.* Hydroxy vinyl stannane **14a**[15a] (185 mg, 0.51 mmol), Ph_3P (175 mg, 0.07 mmol), BocNHTs (139 mg, 0.51 mmol) and DIAD (0.12 mL, 0.61 mmol) gave after chromatography (50% CH_2Cl_2-hexane) **13g** as a clear oil. (115 mg, 49%). Data for **13g**: R_f 0.40 (50% CH_2Cl_2-hexane); ^{1}H NMR, (300 MHz, $CDCl_3$) δ 0.85−1.01 (m, 15 H), 1.24−1.36 (m, 15 H), 1.45−1.56 (m, 6 H), 1.60 (d, 3 H, J = 7.0 Hz), 2.42 (s, 3 H), 4.88−4.98 (m, 1 H), 6.09 (br d, 1 H, J = 12.7 Hz), 7.05 (dd, 1 H, J = 12.7, 8.9 Hz), 7.26 (d, 2 H, J = 8.3 Hz), 7.74 (d, 2 H, J = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 13.7, 21.5, 21.5, 27.3, 27.9, 29.1, 60.1, 84.1, 127.6 (2 C), 129.0 (2 C), 132.8, 138.3, 143.5, 147.7, 150.7; IR (film) 2957, 1727, 1356, 1280, 1154, 985, 812, 673, 589, 549 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{28}H_{50}NO_4SSn$ $[M + H]^+$ 616.2481, found 616.2497.

*Synthesis of (Z)-N-(tert-Butoxycarbonyl)-N-tosyl-3-(tributylstannyl)but-2-en-1-amine, **13h**. Method G.* Hydroxy vinyl stannane **14b**[15a] (115 mg, 0.32 mmol), Ph_3P (109 mg, 0.42 mmol), BocNHTs (87.0 mg, 0.32 mmol) and DEAD (0.18 mL of 40% solution in toluene, 0.38 mmol) gave after chromatography (50% CH_2Cl_2-hexane) **13h** as a clear oil (150 mg, 77%). Data for **13h**: R_f 0.33 (50% CH_2Cl_2-hexane); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87−1.05 (m, 15 H), 1.27−1.40 (m, 15 H), 1.47−1.57 (m, 6 H), 1.96 (d, 3 H, J = 1.4 Hz), 2.43 (s, 3 H), 4.39 (dd, 2 H, J = 6.1, 1.4 Hz), 6.07 (td, 1 H, J = 6.1, 1.4 Hz), 7.27 (d, 2 H, J = 8.4 Hz), 7.77 (d, 2 H, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.0, 13.6, 21.5, 26.8, 27.3, 27.8, 29.1, 49.4, 84.0, 128.9 (2 C), 129.0 (2 C), 136.0, 137.6, 143.1, 143.8, 150.7; IR (film) 2956, 2927, 1728, 1457, 1363, 1157, 1089, 734, 674, 580 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{28}H_{50}NO_4SSn$ $[M + H]^+$ 616.2481, found 616.2454.

*Preparation of Amino 4-Sulfinyl Dienes **15**. Method H.*[16] To a solution of vinyl stannane **13** (1.2 equiv), in anhydrous DMF (12 mL/mmol stannane) at rt was added 2,6-di-*tert*-butyl-4-methylphenol (BHT, 1.0 equiv) and sulfinyl vinyl iodide **11** (1.0 equiv) in anhydrous DMF (12 mL/mmol sulfoxide). Argon was bubbled through the solution for 10 min and $Pd(CH_3CN)_2Cl_2$ (0.1 equiv) was added. The reaction mixture was stirred at the required temperature until disappearance of starting material was observed (TLC). Then, it was quenched with brine and the aqueous layer was extracted with Et_2O. The organic extracts 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.

Method I. To a solution of **18** (1.0 equiv) in anhydrous toluene (10 mL/mmol imine) at rt was added a 0.5 M solution of ethynylmagnesium chloride in THF (1.7 equiv), under an argon atmosphere. The mixture was stirred at rt until disappearance of starting material was observed (TLC). Subsequently, it was cooled to 0 °C and tributyltin chloride (1.7 equiv) and a 1.0 M solution of lithium hexamethyldisilazide in hexane (1.7 equiv) were added dropwise. The

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reaction mixture was stirred and warmed up to rt for 2 h, it was then quenched with saturated $NaHCO_3$ solution and the aqueous layer was extracted with Et_2O. 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 amino ethynyl stannanes **19**. The column chromatography should be done as quickly as possible to prevent destannylation.

Method J. To a solution of alkynyl stannane **19** (1.2 equiv), in anhydrous THF (12 mL/mmol stannane) at rt was added 2,6-di-*tert*-butyl-4-methylphenol (BHT, 1.0 equiv), triphenylarsine (0.4 equiv) and sulfinyl vinyl iodide **11** (1.0 equiv) in anhydrous THF (12 mL/mmol sulfoxide). Argon was bubbled through the solution for 10 min and $Pd_2(dba)_3{\cdot}CHCl_3$ (0.1 equiv) was added. The reaction mixture was monitored and quenched according to Method H.

Method K. To a solution of amino 1,3-enyne **20** in anhydrous toluene (20 mL/mmol stannane) was added Wilkinson's catalyst ($(Ph_3P)_3RhCl$, 0.2 equiv). The mixture was stirred under H_2 (10 bar) for 24 h. After filtration through Celite, the solvent was evaporated in vacuo and the residue was chromatographed on silica gel with the appropriate mixture of solvents.

Synthesis of (+)-(2Z,4Z,R_S)-N-(4-Nitrobenzenesulfonyl)-4-(p-tolylsulfinyl)nona-2,4-dienyl-1-amine, ***15b****. Method H.* Sulfinyl vinyl iodide **11a** (296 mg, 0.85 mmol) and (*Z*)-*N*-(4-nitrobenzenesulfonyl)-3-(tributylstannyl)prop-2-en-1-amine **13b** (587 mg, 1.11 mmol) gave diene **15b** (240 mg, 61%) as single isomer after chromatography (50% EtOAc-hexane) as a pale yellow gum. Data for **15b**: R_f 0.50 (50% EtOAc-hexane); $[\alpha]^{20}_D$ +11.8 (*c* 1.0, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.90 (t, 3 H, *J* = 7.1 Hz, H-9), 1.28−1.46 (m, 4 H, H-7, H-8), 2.40 (s, 3 H, CH_3 *p*-Tol), 2.40−2.69 (m, 2 H, H-6), 3.32−3.39 (m, 1 H, H-1a), 3.46−3.55 (m, 1 H, H-1b), 5.50 (d, 1 H, *J* = 10.9 Hz, H-3), 5.79−5.92 (m, 2 H, H-2, H-5), 6.14 (d, 1 H, *J* = 6.4 Hz, NH), 7.27−7.35 (m, 4 H, *p*-Tol), 8.08 (d, 2 H, *J* = 9.0 Hz, Ar), 8.34 (d, 2 H, *J* = 9.0 Hz, Ar); ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.7 (C-9), 21.4 (CH_3 *p*-Tol), 22.3 (CH_2), 28.4 (C-6), 31.4 (CH_2), 40.0 (C-1), 124.2 (2 × CH *p*-Tol, 2 × CH Ar), 124.5 (C-3), 128.5 (2 × CH Ar), 129.9 (2 × CH *p*-Tol), 133.0 (C-2), 137.3 (C), 140.0 (C), 141.4 (C), 142.3 (C-5), 146.3 (C Ar), 149.8 (C Ar); IR (film) 3105, 2959, 2871, 1606, 1531, 1348, 1166, 1013, 854, 737 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{22}H_{27}N_2O_5S_2$ $[M + H]^+$ 463.1356, found 463.1353.

Synthesis of (−)-(2Z,4Z,R_S)-N-(2-Nitrobenzenesulfonyl)-4-(p-tolylsulfinyl)nona-2,4-dienyl-1-amine, ***15c****. Method H.* Sulfinyl vinyl iodide **11a** (369 mg, 1.06 mmol) and (*Z*)-*N*-(2-nitrobenzenesulfonyl)-3-(tributylstannyl)prop-2-en-1-amine **13c** (680 mg, 1.28 mmol) gave diene **15c** (248 mg, 51%) as single isomer after chromatography (15−20% EtOAc-CH_2Cl_2) as a pale orange solid. Data for **15c**: R_f 0.60 (15% EtOAc-CH_2Cl_2); mp 118−122 °C; $[\alpha]^{20}_D$ −28.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, 3 H, *J* = 7.1 Hz), 1.33−1.52 (m, 4 H), 2.40 (s, 3 H), 2.48−2.60 (m, 1 H), 2.66−2.78 (m, 1 H), 3.63 (t, 2 H, *J* = 6.1 Hz), 5.60−5.75 (m, 3 H), 5.92 (ddd, 1 H, *J* = 8.3, 7.1, 1.3 Hz), 7.29 (d, 2 H, *J* = 8.3 Hz), 7.36 (d, 2 H, *J* = 8.3 Hz), 7.69−7.72 (m, 2 H), 7.81−7.84 (m, 1 H), 8.04−8.07 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.3, 22.3, 28.6, 31.4, 41.2, 123.8, 124.0 (2 C), 125.6, 129.8 (2 C), 130.7, 132.3, 132.6, 133.4, 134.2, 138.5, 140.4, 141.2, 141.5, 148.0; IR (KBr) 3225, 2960, 2871, 1539, 1343, 1164, 1082, 1031, 805, 739 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{22}H_{27}N_2O_5S_2$ $[M + H]^+$ 463.1356, found 463.1368.

Synthesis of (−)-(2Z,4Z,R_S)-4-(p-Tolylsulfinyl)-N-(2,4,6-trimethylbenzenesulfonyl)nona-2,4-dienyl-1-amine, ***15d****. Method H.* Sulfinyl vinyl iodide **11a** (380 mg, 1.09 mmol) and (*Z*)-3-(tributylstannyl)-*N*-(2,4,6-trimethylbenzenesulfonyl)prop-2-en-1-amine **13d** (692 mg, 1.31 mmol) gave diene **15d** (309 mg, 62%) as single isomer after chromatography (20% EtOAc-CH_2Cl_2) as a pale orange oil. Data for **15d**: R_f 0.50 (20% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −67.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.85 (t, 3 H, *J* = 7.1 Hz), 1.22−1.41 (m, 4 H), 2.20 (s, 3 H), 2.30 (s, 3 H), 2.35−2.68 (m, 2 H), 2.53 (s, 6 H), 3.27 (t, 2 H, *J* = 6.3 Hz), 5.01 (t, 1 H, *J* = 6.3 Hz), 5.53−5.64 (m, 2 H), 5.76 (ddd, 1 H, *J* = 8.4, 7.0, 1.2 Hz), 6.84 (s, 2 H), 7.18 (d, 2 H, *J* = 8.3 Hz), 7.26 (d, 2 H, *J* = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 20.8, 21.3, 22.2, 22.9 (2 C), 28.4, 31.3, 39.6, 123.1, 124.0 (2 C), 129.7 (2 C), 131.8 (2 C), 133.1, 134.1, 138.5, 138.9 (2 C), 140.3, 141.0, 141.3, 141.8; IR (film) 3207, 2957, 2859, 1604, 1329, 1166, 1037, 809, 655 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{25}H_{34}NO_3S_2$ $[M + H]^+$ 460.1975, found 460.1989.

Synthesis of (−)-(2Z,4Z,R_S)-4-(p-Tolylsulfinyl)-N-(2,4,6-triisopropylbenzenesulfonyl)nona-2,4-dienyl-1-amine, ***15e****. Method H.* Sulfinyl vinyl iodide **11a** (400 mg, 1.15 mmol) and (*Z*)-3-(tributylstannyl)-*N*-(2,4,6-triisopropylbenzenesulfonyl)prop-2-en-1-amine **13e** (845 mg, 1.38 mmol) gave diene **15e** (318 mg, 51%) as single isomer after chromatography (15−20% EtOAc-CH_2Cl_2) as a pale orange gum. Data for **15e**: R_f 0.40 (15% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −73.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, 3 H, *J* = 7.1 Hz), 1.25 (d, 18 H, *J* = 6.2 Hz), 1.35−1.54 (m, 4 H), 2.39 (s, 3 H), 2.39−2.47 (m, 1 H), 2.59−2.80 (m, 1 H), 2.82−2.96 (m, 1 H), 3.44−3.48 (m, 2 H), 4.04−4.18 (m, 2 H), 4.61 (t, 1 H, *J* = 6.4 Hz), 5.69−5.79 (m, 2 H), 5.87 (t, 1 H, *J* = 7.7 Hz), 7.14 (s, 2 H), 7.28 (d, 2 H, *J* = 8.3 Hz), 7.37 (d, 2 H, *J* = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.7, 21.2, 22.2, 23.5 (2 C), 24.8 (4 C), 28.4, 29.5 (2 C), 31.3, 34.0, 39.7, 123.1, 123.6 (2 C), 124.0 (2 C), 129.7 (2 C), 132.6, 133.1, 138.7, 140.5, 141.0, 141.1 (2 C), 150.2, 152.4; IR (film) 3199, 2959, 2870, 1600, 1461, 1321, 1152, 1040, 910, 733 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{31}H_{46}NO_3S_2$ $[M + H]^+$ 544.2914, found 544.2927.

Synthesis of (−)-(2Z,4Z,R_S)-N-(tert-Butoxycarbonyl)-4-(p-tolylsulfinyl)nona-2,4-dienyl-1-amine, ***15f****. Method H.* Sulfinyl vinyl iodide **11a** (2.02 g, 5.80 mmol) and (*Z*)-*N*-(*tert*-butoxycarbonyl)-3-(tributylstannyl)prop-2-en-1-amine **13f** (3.11 g, 6.96 mmol) gave diene **15f** as a single isomer after chromatography (20−30% EtOAc-CH_2Cl_2) as a white gum (1.49 g, 68%). Data for **15f**: R_f 0.50 (20% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −348.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.97 (t, 3 H, *J* = 7.1 Hz), 1.35−1.59 (m, 4 H), 1.42 (s, 9 H), 2.40 (s, 3 H), 2.50−2.62 (m, 1 H), 2.72−2.84 (m, 1 H), 3.51−3.68 (m, 2 H), 4.31 (br s, 1 H), 5.73 (dt, 1 H, *J* = 11.4, 6.6 Hz), 5.83 (dd, 1 H, *J* = 11.4, 1.0 Hz), 5.92 (td, 1 H, *J* = 8.4, 1.0 Hz), 7.28 (d, 2 H, *J* = 8.2 Hz), 7.40 (d, 2 H, *J* = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.3, 22.4, 28.4 (3 C), 28.7, 31.5, 38.1, 79.3, 121.9, 124.1 (2 C), 129.7 (2 C), 134.3, 139.4, 140.8, 141.0 (2 C), 155.6; IR (film) 3325, 2960, 2930, 1713, 1505, 1366, 1250, 1172, 1045, 809 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{21}H_{32}NO_3S$ $[M + H]^+$ 378.2097, found 378.2092.

Synthesis of (+)-(2Z,4Z,R_S)-6,6-Dimethyl-4-(p-tolylsulfinyl)-N-tosylhepta-2,4-dienyl-1-amine, ***15h****. Method H.* Sulfinyl vinyl iodide **11c** (157 mg, 0.45 mmol) and (*Z*)-3-(tributylstannyl)-*N*-tosylprop-2-en-1-amine **13a** (270 mg, 0.54 mmol) gave diene **15h** (87.4 mg, 45%) as a single isomer after chromatography (10% EtOAc-CH_2Cl_2) as a yellow gum. Data for **15h**: R_f 0.37 (10% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +11.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 1.27 (s, 9 H, CH_3 *t*-Bu), 2.41 (s, 3 H, CH_3 *p*-Tol), 2.42 (s, 3 H, CH_3 *p*-Tol), 3.26 (dddd, 1 H, *J* = 12.5, 8.8, 3.9, 1.3 Hz, H-1a), 3.40 (dddd, 1 H, *J* = 12.5, 8.8, 6.5, 1.3 Hz, H-1b), 5.37 (dd, 1 H, *J* = 8.8, 3.9 Hz, NH), 5.49 (br dd, 1 H, *J* = 10.8, 1.3 Hz, H-3), 5.78 (ddd, 1 H, *J* = 10.8, 8.8, 6.5 Hz, H-2), 5.87 (d, 1 H, *J* = 1.7 Hz, H-5), 7.27−7.38 (m, 6 H, *p*-Tol), 7.77 (d, 2 H, *J* = 8.3 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.3 (CH_3 *p*-Tol), 21.5 (CH_3 *p*-Tol), 32.0 (CH_3 *t*-Bu), 34.8 (C *t*-Bu), 40.0 (C-1), 124.5 (2 × CH *p*-Tol), 124.8 (C-3), 127.3 (2 × CH *p*-Tol), 129.5 (2 × CH *p*-Tol), 129.7 (2 × CH *p*-Tol), 132.5 (C-2), 136.8 (C), 137.5 (C), 137.8 (C), 141.1 (C), 143.0 (C), 151.7 (C-5); IR (film) 3271, 2964, 2928, 1598, 1463, 1333, 1162, 1093, 813, 737 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{23}H_{30}NO_3S_2$ $[M + H]^+$ 432.1662, found 432.1656.

Synthesis of (−)-(2Z,4Z,R_S)-8-Chloro-4-(p-tolylsulfinyl)-N-tosylocta-2,4-dienyl-1-amine, ***15i****. Method H.* Sulfinyl vinyl iodide **11d** (508 mg, 1.38 mmol) and (*Z*)-3-(tributylstannyl)-*N*-tosylprop-2-en-1-amine **13a** (832 mg, 1.66 mmol) gave diene **15i** as single isomer (405 mg, 65%) after chromatography (10−20% EtOAc-CH_2Cl_2) as an orange gum. Data for **15i**: R_f 0.50 (20% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −34.7 (*c* 2.4, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85−1.95 (m, 2 H, H-7), 2.40 (s, 3 H, CH_3 *p*-Tol), 2.43 (s, 3 H, CH_3 *p*-Tol), 2.62−2.89 (m, 2 H, H-6), 3.27−3.43 (m, 2 H, H-1), 3.54 (t, 2 H, *J* = 6.3 Hz, H-8), 5.19 (br s, 1 H, NH), 5.62 (br dd, 1 H, *J* = 11.0, 1.4 Hz, H-3), 5.74−5.86

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(m, 2 H, H-2, H-5), 7.26−7.37 (m, 6 H, *p*-Tol), 7.73 (d, 2 H, *J* = 8.3 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.3 (CH_3 *p*-Tol), 21.4 (CH_3 *p*-Tol), 26.0 (C-6), 31.7 (C-7), 40.3 (C-1), 43.8 (C-8), 123.3 (C-3), 124.1 (2 × CH *p*-Tol), 127.1 (2 × CH *p*-Tol), 129.5 (2 × CH *p*-Tol), 129.8 (2 × CH *p*-Tol), 133.1 (C-2), 136.9 (C), 138.0 (C), 139.0 (C-5), 141.3 (C), 141.8 (C), 143.1 (C); IR (film) 3151, 2923, 1598, 1446, 1330, 1160, 1037, 812, 754, 661 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{22}H_{27}ClNO_3S_2$ $[M + H]^+$ 452.1115, found 452.1097.

Synthesis of (−)-(2Z,4Z,R$_S$)-N-(tert-Butoxycarbonyl)-8-chloro-4-(p-tolylsulfinyl)octa-2,4-dienyl-1-amine, ***15j****. Method H.* Sulfinyl vinyl iodide **11d** (351 mg, 0.95 mmol) and (*Z*)-*N*-(*tert*-butoxycarbonyl)-3-(tributylstannyl)prop-2-en-1-amine **13f** (511 mg, 1.14 mmol) gave diene **15j** (245 mg, 65%) as single isomer after chromatography (20% EtOAc-CH_2Cl_2) as white solid. Data for **15j**: R_f 0.38 (20% EtOAc-CH_2Cl_2); mp 110−112 °C; $[\alpha]^{20}_D$ −110.0 (*c* 1.0, $CDCl_3$); ^{1}H NMR, COSY (300 MHz, $CHCl_3$) δ 1.43 (s, 9 H, CH_3 Boc), 1.98−2.09 (m, 2 H, H-7), 2.41 (s, 3 H, CH_3 *p*-Tol), 2.72−2.84 (m, 1 H, H-6a), 2.90−3.02 (m, 1 H, H-6b), 3.52−3.67 (m, 4 H, H-1, H-8), 4.34 (br s, 1 H, NH), 5.71−5.94 (m, 3 H, H-2, H-3, H-5), 7.30 (d, 2 H, *J* = 8.1 Hz, *p*-Tol), 7.41 (d, 2 H, *J* = 8.1 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.8 (CH_3 *p*-Tol), 26.7 (C-6), 28.8 (CH_3 Boc), 32.5 (C-7), 38.6 (C-1), 44.4 (C-8), 79.8 (C Boc), 122.1 (C-3), 124.6 (2 × CH *p*-Tol), 130.2 (2 × CH *p*-Tol), 135.1 (C-2), 139.0 (C-5), 139.6 (C), 141.5 (C), 142.9 (C), 156.0 (CO Boc); IR (KBr) 3351, 2920, 1684, 1533, 1436, 1366, 1168, 1038, 803, 749 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{20}H_{29}ClNO_3S$ $[M + H]^+$ 398.1551, found 398.1532.

Synthesis of (−)-(2Z,4Z,S$_S$)-5-(4-Fluorophenyl)-4-(p-tolylsulfinyl)-N-tosylpenta-2,4-dienyl-1-amine, ***15m****. Method H.* Sulfinyl vinyl iodide **11g** (151 mg, 0.390 mmol) and (*Z*)-3-(tributylstannyl)-*N*-tosylprop-2-en-1-amine **13a** (234 mg, 0.47 mmol) gave diene **15m** (148 mg, 67%) as a single isomer after chromatography (10−20% EtOAc-CH_2Cl_2) as a clear oil. Data for **15m**: R_f 0.50 (20% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −137.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.38 (s, 3 H), 2.39 (s, 3 H), 3.42−3.57 (m, 2 H), 5.50 (br t, 1 H, *J* = 5.4 Hz), 5.74 (d, 1 H, *J* = 11.1 Hz), 5.84 (dt, 1 H, *J* = 11.1, 7.2 Hz), 6.86 (s, 1 H), 7.06−7.42 (m, 10 H), 7.73 (d, 2 H, *J* = 8.3 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.3, 21.4, 40.4, 115.7 (d, $^2J_{C-F}$ = 21.8 Hz, 2 C), 123.9, 124.3 (2 C), 127.1 (2 C), 129.4 (d, $^4J_{C-F}$ = 3.4 Hz), 129.5 (2 C), 129.8 (2 C), 131.6 (d, $^3J_{C-F}$ = 8.4 Hz, 2 C), 133.4, 136.9, 137.8, 141.2 (2 C), 141.4, 143.1, 163.0 (d, $^1J_{C-F}$ = 250.7 Hz). ^{19}F NMR (400 MHz, $CDCl_3$) δ −111.2; IR (film) 3271, 2923, 1600, 1507, 1447, 1332, 1232, 1160, 1082, 1039 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{25}H_{25}FNO_3S_2$ $[M + H]^+$ 470.1254, found 470.1247.

Synthesis of (+)-(3S)-3-Phenyl-N-((S)-p-tolylsulfinyl)-1-(tributylstannyl)prop-1-yn-3-amine, ***19a****. Method I.* (*S*)-*N*-Benzylidene-*p*-toluenesulfinamide **18a**[20] (1.07 g, 4.40 mmol), ethynylmagnesium chloride (14.9 mL of 0.5 M solution, 7.47 mmol), Bu_3SnCl (2.03 mL, 7.47 mmol) and LiHMDS (7.47 mL of 1.0 M solution, 7.47 mmol) gave (***S***)-**19a** and (***R***)-**19a** as a 90:10 diastereomeric mixture. Chromatography (50% Et_2O-hexane, 0.5% Et_3N) afforded (***S***)-**19a** (2.11 g, 86%) as a white gum. Data for (***S***)-**19a**: R_f 0.65 (50% Et_2O-hexane); $[\alpha]^{20}_D$ +86.6 (*c* 1.0, $CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 0.89 (t, 9 H, *J* = 7.3 Hz, *n*-Bu), 0.95−0.97 (m, 6 H, *n*-Bu), 1.28−1.36 (m, 6 H, *n*-Bu), 1.50−1.55 (m, 6 H, *n*-Bu), 2.41 (s, 3 H, CH_3 *p*-Tol), 4.48 (d, 1 H, *J* = 5.4 Hz, NH), 5.29 (d, 1 H, *J* = 5.4 Hz, H-3), 7.29−7.39 (m, 5 H, Ph, *p*-Tol), 7.63−7.66 (m, 4 H, Ph, *p*-Tol); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 11.1 (*n*-Bu), 13.7 (*n*-Bu), 21.4 (CH_3 *p*-Tol), 26.9 (*n*-Bu), 28.9 (*n*-Bu), 48.9 (C-3), 89.5 (C), 108.1 (C), 126.1 (2 × CH), 128.1 (CH), 128.1 (2 × CH), 128.6 (2 × CH), 129.5 (2 × CH), 139.3 (C), 141.3 (2 × C); IR (film) 3219, 2956, 2923, 1538, 1493, 1455, 1089, 1044, 810, 698 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{28}H_{42}NOSSn$ $[M + H]^+$ 560.2007, found 560.1987. Partial data for (***R***)-**19a** (from the crude reaction mixture): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.38 (s, 3 H), 4.30 (d, 1 H, *J* = 5.1 Hz), 5.27−5.34 (m, 1 H).

Synthesis of (−)-(3S)-N-((S)-p-Tolylsulfinyl)-1-(tributylstannyl)-pent-1-yn-3-amine, ***19b****. Method I.* (*S*)-*N*-Propylidene-*p*-toluenesulfinamide **18b**[20] (1.54 g, 7.90 mmol), ethynylmagnesium chloride (26.8 mL of 0.5 M solution, 13.4 mmol), Bu_3SnCl (3.63 mL, 13.4 mmol) and LiHMDS (13.4 mL of 1.0 M solution, 13.4 mmol) gave (***S***)-**19b** and (***R***)-**19b** as a 77:23 diastereomeric mixture. Chromatography (10% EtOAc-CH_2Cl_2) afforded (***S***)-**19b** (3.02 g, 75%) as a clear oil. Data for (***S***)-**19b**: R_f 0.55 (10% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −21.2 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86−1.06 (m, 18 H), 1.26−1.38 (m, 6 H), 1.48−1.58 (m, 6 H), 1.72−1.91 (m, 2 H), 2.41 (s, 3 H), 4.04 (ddd, 1 H, *J* = 7.8, 6.4, 5.2 Hz), 4.21 (d, 1 H, *J* = 7.8 Hz), 7.29 (d, 2 H, *J* = 8.1 Hz), 7.62 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.81, 10.9, 13.5, 21.2, 26.7, 28.7, 30.8, 47.4, 87.0, 109.3, 125.9 (2 C), 129.3 (2 C), 140.9, 141.4; IR (film) 3311, 3210, 2957, 2926, 2148, 1536, 1464, 1089, 1061, 811 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{24}H_{42}NOSSn$ $[M + H]^+$ 512.2009, found 512.1999. Partial data for (***R***)-**19b** (from the crude reaction mixture): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.39 (s, 3 H), 3.81−3.87 (m, 1 H), 4.13−4.21 (m, 1 H), 7.17 (d, 2 H, *J* = 7.8 Hz), 7.24 (d, 2 H, *J* = 7.8 Hz).

Synthesis of (−)-(1R,2Z,4Z,R$_S$)-1-Phenyl-4-(p-tolylsulfinyl)-N-((S)-p-tolylsulfinyl)octa-2,4-dienyl-1-amine, ***15r****. Method J.* Sulfinyl vinyl iodide **11b** (1.04 g, 3.12 mmol) and (+)-(3*S*)-3-phenyl-*N*-((*S*)-*p*-tolylsulfinyl)-1-(tributylstannyl)prop-1-yn-3-amine **19a** (2.01 g, 3.74 mmol) gave amino 1,3-enyne **20a** (712 mg, 48%) after chromatography (20% EtOAc-CH_2Cl_2) as a yellow solid. Data for **20a**: R_f 0.25 (20% EtOAc-CH_2Cl_2); mp 112−113 °C; $[\alpha]^{20}_D$ +3.0 (*c* 0.7, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.02 (t, 3 H, *J* = 7.4 Hz, H-8), 1.51−1.61 (m, 2 H, H-7), 2.33 (s, 3 H, CH_3 *p*-Tol), 2.41 (s, 3 H, CH_3 *p*-Tol), 2.54−2.63 (m, 1 H, H-6a), 2.66−2.77 (m, 1 H, H-6b), 4.29 (d, 1 H, *J* = 5.8 Hz, NH), 5.32 (d, 1 H, *J* = 5.8 Hz, H-1), 6.40 (t, 1 H, *J* = 8.0 Hz, H-5), 7.15 (d, 2 H, *J* = 8.4 Hz), 7.26−7.34 (m, 5 H), 7.41−7.44 (m, 4 H), 7.54 (d, 2 H, *J* = 8.2 Hz); ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.8 (C-8), 21.4 (2 × CH_3 *p*-Tol), 22.4 (C-7), 31.2 (C-6), 48.7 (C-1), 77.9 (C), 92.7 (C), 124.5 (2 × CH), 125.9 (2 × CH), 128.0 (2 × CH), 128.3 (CH), 128.7 (2 × CH), 129.5 (2 × CH), 129.6 (2 × CH), 132.1 (C), 138.0 (C), 139.5 (C), 141.1 (C), 141.3 (C), 141.5 (C), 147.4 (C-5); IR (KBr) 3187, 2961, 2928, 1596, 1492, 1455, 1087, 1055, 810, 698 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{28}H_{30}NO_2S_2$ $[M + H]^+$ 476.1712, found 476.1712.

Method K. Amino 1,3-enyne **20a** (524 mg, 1.10 mmol) gave after chromatography (50% EtOAc-hexane) **15r** as a yellow oil (326 mg, 62%). Data for **15r**: R_f 0.33 (50% EtOAc-hexane); $[\alpha]^{20}_D$ −115.2 (*c* 0.83, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.10 (t, 3 H, *J* = 7.4 Hz), 1.60−1.72 (m, 2 H), 2.11 (s, 3 H), 2.41 (s, 3 H), 2.60−2.85 (m, 2 H), 3.33 (d, 1 H, *J* = 2.9 Hz), 5.11 (dd, 1 H, *J* = 9.8, 2.9 Hz), 5.83 (dd, 1 H, *J* = 11.3, 9.8 Hz), 6.07 (d, 1 H, *J* = 11.3 Hz), 6.07 (dd, 1 H, *J* = 8.4, 7.2 Hz), 7.22 (d, 2 H, *J* = 8.4 Hz), 7.28−7.45 (m, 9 H), 7.52 (d, 2 H, *J* = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 21.0, 21.3, 22.8, 31.1, 55.6, 121.9, 124.1 (2 C), 125.3 (2 C), 128.0 (2 C), 128.1, 129.0 (2 C), 129.5 (2 C), 130.1 (2 C), 136.3, 139.4, 139.51, 139.54, 140.6, 140.7, 141.3, 142.0; IR (film) 3178, 3053, 2961, 1597, 1492, 1455, 1085, 1045, 810, 701 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{28}H_{32}NO_2S_2$ $[M + H]^+$ 478.1869, found 478.1877.

Synthesis of (+)-(3S,4Z,6Z,R$_S$)-6-(p-Tolylsulfinyl)-N-((S)-p-tolylsulfinyl)deca-4,6-dienyl-3-amine, ***15s****. Method J.* Sulfinyl vinyl iodide **11b** (789 mg, 2.36 mmol) and (−)-(3*S*)-*N*-((*S*)-*p*-tolylsulfinyl)-1-(tributylstannyl)pent-1-yn-3-amine **19b** (1.45 g, 2.84 mmol) gave amino 1,3-enyne **20b** (608 mg, 62%) after chromatography (40% EtOAc-CH_2Cl_2) as a yellow oil. Data for **20b**: R_f 0.37 (40% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −16.4 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.90 (t, 3 H, *J* = 7.4 Hz), 1.01 (t, 3 H, *J* = 7.4 Hz), 1.49−1.78 (m, 4 H), 2.33 (s, 3 H), 2.41 (s, 3 H), 2.52−2.78 (m, 2 H), 3.98−4.08 (m, 2 H), 6.40 (t, 1 H, *J* = 8.0 Hz), 7.20−7.30 (m, 4 H), 7.44 (d, 2 H, *J* = 8.2 Hz), 7.53 (d, 2 H, *J* = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 9.8, 13.7, 21.3 (2 C), 22.4, 30.3, 31.0, 47.2, 76.2, 93.9, 124.4 (2 C), 125.8 (2 C), 129.5 (4 C), 132.1, 139.5, 141.2 (2 C), 141.3, 147.0; IR (film) 3202, 2964, 2209, 1596, 1492, 1455, 1087, 1054, 810, 754 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{24}H_{30}NO_2S_2$ $[M + H]^+$ 428.1712, found 428.1724.

Method K. Amino 1,3-enyne **20b** (608 mg, 1.42 mmol) gave after chromatography (50−70% EtOAc-hexane) **15s** as an orange oil (427 mg, 70%). Data for **15s**: R_f 0.45 (70% EtOAc-hexane); $[\alpha]^{20}_D$ +76.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 1.00 (t, 3 H, *J* = 7.4 Hz, H-1), 1.09 (t, 3 H, *J* = 7.4 Hz, H-10), 1.54−1.89 (m, 4 H, H-2,

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H-9), 2.22 (s, 3 H, CH_3 *p*-Tol), 2.43 (s, 3 H, CH_3 *p*-Tol), 2.55−2.65 (m, 1 H, H-8a), 2.73−2.86 (m, 1 H, H-8a), 3.44 (d, 1 H, J = 5.2 Hz, NH), 4.08−4.17 (m, 1 H, H-3), 5.61 (dd, 1 H, J = 11.5, 9.7 Hz, H-4), 5.82 (d, 1 H, J = 11.5 Hz, H-5), 6.22 (t, 1 H, J = 7.5 Hz, H-7), 7.21 (d, 2 H, J = 8.1 Hz, *p*-Tol), 7.30 (d, 2 H, J = 8.1 Hz, *p*-Tol), 7.40 (d, 2 H, J = 8.1 Hz, *p*-Tol), 7.55 (d, 2 H, J = 8.1 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 10.0 (C-1), 13.9 (C-10), 21.1 (CH_3 *p*-Tol), 21.3 (CH_3 *p*-Tol), 22.7 (C-9), 28.5 (C-2), 30.9 (C-8), 53.5 (C-3), 121.8 (C-5), 124.1 (2 × CH *p*-Tol), 125.5 (2 × CH *p*-Tol), 129.4 (2 × CH *p*-Tol), 129.8 (2 × CH *p*-Tol), 138.0 (C-4), 139.5 (C), 140.6 (C), 141.1 (2 × C), 141.2 (C-7), 142.7 (C); IR (film) 3202, 3051, 2962, 2930, 1492, 1456, 1086, 1048, 1016, 810 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{24}H_{32}NO_2S_2$ $[M + H]^+$ 430.1869, found 430.1885.

Preparation of 3-(p-Tolylsulfinyl)-1,2,3,6-tetrahydropyridines ***21****. Method L.* To a cold solution (0 °C) of dienyl sulfoxide **15** in anhydrous toluene (20 mL/mmol sulfoxide), was added 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 2.0 equiv), under an argon atmosphere and the mixture was stirred and warmed up to rt. When disappearance of starting material was observed (TLC) the reaction was quenched with saturated NH_4Cl solution 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.

Method M. To a cold suspension (0 °C) of sodium hydride (1.92 mg, 0.08 mmol, 1.3 equiv) in anhydrous THF (5.0 mL/mmol sulfoxide) was added a solution of the corresponding *N*-Boc dienyl sulfoxide (1.0 equiv) in anhydrous THF (5.0 mL/mmol sulfoxide), under an argon atmosphere and the mixture was stirred and warmed up to rt. The reaction was followed and quenched according to Method L.

Method N. To a solution of the corresponding *N*-Boc dienyl sulfoxide in CH_2Cl_2 (10 mL/mmol sulfoxide) at rt was added trifluoroacetic acid (TFA, 10.0−20.0 equiv). The reaction mixture was stirred until disappearance of starting material (TLC). It was then stirred (15 min) with 0.1 N aqueous NaOH solution and the aqueous layer was extracted with CH_2Cl_2. The organic extracts were 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. Basic quenching (0.1 N NaOH) followed by an immediate extraction with CH_2Cl_2 and a rapid ^{1}H NMR of the crude mixture allowed for the detection of the free diene amine prior to cyclization.

Synthesis of (−)-(2S,3R,R$_S$)-2-Butyl-1-N-(4-nitrobenzenesulfonyl-3-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine, ***21b****. Method L.* Dienyl sulfoxide **15b** (172 mg, 0.37 mmol) and DBU (0.11 mL, 0.74 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **21b** as a white solid in >98:2 dr (110 mg, 64%). Data for **21b**: R_f 0.30 (5% EtOAc-CH_2Cl_2); mp 114−118 °C; $[\alpha]^{20}_D$ −79.8 (c 1.0, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.87 (t, 3 H, J = 6.9 Hz, CH_3), 1.15−1.70 (m, 6 H, CH_2), 2.39 (s, 3 H, CH_3 *p*-Tol), 3.15 (d, 1 H, J = 5.7 Hz, H-3), 3.68 (dd, 1 H, J = 18.3, 1.8 Hz, H-6a), 4.04 (br d, 1 H, J = 18.3 Hz, H-6b), 4.85 (t, 1 H, J = 7.1 Hz, H-2), 4.94−4.99 (m, 1 H, H-4), 5.89−5.92 (m, 1 H, H-5), 7.27 (d, 2 H, J = 8.0 Hz, *p*-Tol), 7.42 (d, 2 H, J = 8.0 Hz, *p*-Tol), 8.19 (d, 2 H, J = 8.8 Hz, Ar), 8.36 (d, 2 H, J = 8.8 Hz, Ar); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 13.8 (CH_3), 21.4 (CH_3 *p*-Tol), 22.3 (CH_2), 28.4 (CH_2), 30.7 (CH_2), 41.3 (C-6), 50.4 (C-2), 67.4 (C-3), 117.5 (C-4), 124.2 (2 × CH Ar), 125.1 (2 × CH *p*-Tol), 128.8 (2 × CH Ar), 128.9 (C-5), 129.9 (2 × CH *p*-Tol), 138.4 (C), 142.4 (C), 145.7 (C), 150.0 (C Ar); IR (KBr) 2958, 1606, 1531, 1350, 1166, 1092, 1048, 855, 740, 607 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{22}H_{27}N_2O_5S_2$ $[M + H]^+$ 463.1356, found 463.1339.

Synthesis of (−)-(2S,3R,R$_S$)-2-Butyl-1-N-(2-nitrobenzenesulfonyl)-3-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine, ***21c****. Method L.* Dienyl sulfoxide **15c** (50.0 mg, 0.11 mmol) and DBU (0.03 mL, 0.22 mmol) gave after chromatography (5−10% EtOAc-CH_2Cl_2) **21c** as a pale yellow gum in >98:2 dr (30.9 mg, 62%). Data for **21c**: R_f 0.40 (10% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −247.2 (c 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, J = 7.0 Hz), 1.23−1.43 (m, 4 H), 1.52−1.64 (m, 1 H), 1.70−1.82 (m, 1 H), 2.39 (s, 3 H), 3.05 (dd, 1 H, J = 5.5, 1.2 Hz), 3.82 (dq, 1 H, J = 18.9, 2.4 Hz), 3.82 (app dq, 1 H, J = 18.9, 2.1 Hz), 4.62 (t, 1 H, J = 7.3 Hz), 4.84−4.90 (m, 1 H), 6.00 (dm, 1 H, J = 10.3 Hz), 7.27 (d, 2 H, J = 8.2 Hz), 7.42 (d, 2 H, J = 8.2 Hz), 7.64−7.78 (m, 3 H), 8.34−8.37 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 21.5, 22.4, 28.4, 30.7, 41.4, 50.7, 67.9, 116.7, 124.0, 125.2 (2 C), 129.8 (2 C), 130.1, 132.1, 132.5, 133.6, 133.7, 138.6, 142.2, 147.7; IR (film) 2956, 1543, 1371, 1167, 1127, 1076, 1046, 851, 659, 581 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{22}H_{27}N_2O_5S_2$ $[M + H]^+$ 463.1356, found 463.1369.

Synthesis of (−)-(2S,3R,R$_S$)-2-Butyl-3-(p-tolylsulfinyl)-1-N-(2,4,6-trimethylbenzenesulfonyl)-1,2,3,6-tetrahydropyridine, ***21d****. Method L.* Dienyl sulfoxide **15d** (53.4 mg, 0.12 mmol) and DBU (0.03 mL, 0.23 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **21d** as a white solid in >98:2 dr (33.0 mg, 62%). Data for **21d**: R_f 0.40 (5% EtOAc-CH_2Cl_2); mp 126−128 °C; $[\alpha]^{20}_D$ −78.7 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.87 (t, 3 H, J = 6.8 Hz), 1.15−1.42 (m, 4 H), 1.53−1.64 (m, 1 H), 1.92−2.03 (m, 1 H), 2.29 (s, 3 H), 2.39 (s, 3 H), 2.69 (s, 6 H), 3.04 (d, 1 H, J = 4.2 Hz), 3.81 (app dq, 1 H, J = 18.3, 2.5 Hz), 4.17 (ddd, 1 H, J = 18.3, 4.3, 2.3 Hz), 4.28 (dd, 1 H, J = 10.3, 4.2 Hz), 4.84−4.90 (m, 1 H), 5.97 (dm, 1 H, J = 10.1 Hz), 6.98 (s, 2 H), 7.27 (d, 2 H, J = 8.2 Hz), 7.45 (d, 2 H, J = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 21.0, 21.4, 22.4, 23.2 (2 C), 28.8, 29.4, 40.5, 49.7, 67.6, 117.3, 125.1 (2 C), 129.7 (2 C), 129.9, 132.1 (2 C), 132.3, 139.5, 140.5 (2 C), 142.0, 142.8; IR (KBr) 2957, 1603, 1455, 1327, 1157, 1046, 917, 851, 726, 666 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{25}H_{34}NO_3S_2$ $[M + H]^+$ 460.1975, found 460.1992.

Synthesis of (−)-(2S,3R,R$_S$)-2-Butyl-3-(p-tolylsulfinyl)-1-N-(2,4,6-triisopropylbenzenesulfonyl)-1,2,3,6-tetrahydropyridine, ***21e****. Method L.* Dienyl sulfoxide **15e** (48.9 mg, 0.09 mmol) and DBU (0.03 mL, 0.18 mmol) gave after chromatography (5% EtOAc-CH_2Cl_2) **21e** as a white solid in >98:2 dr (37.0 mg, 76%). Data for **21e**: R_f 0.50 (5% EtOAc-CH_2Cl_2); mp 62−66 °C; $[\alpha]^{20}_D$ −48.4 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.88 (t, 3 H, J = 6.8 Hz), 1.24−1.46 (m, 4 H), 1.25 (d, 6 H, J = 6.7 Hz), 1.32 (d, 6 H, J = 6.6 Hz), 1.33 (d, 6 H, J = 6.7 Hz), 1.58−1.71 (m, 1 H), 1.92−2.05 (m, 1 H), 2.40 (s, 3 H), 2.86−2.95 (m, 1 H), 3.16 (d, 1 H, J = 5.5 Hz), 3.85 (app d, 2 H, J = 1.9 Hz), 4.10−4.19 (m, 2 H), 4.78 (dd, 1 H, J = 10.2, 3.4 Hz), 4.84−4.89 (m, 1 H), 5.92 (dm, 1 H, J = 10.3 Hz), 7.20 (s, 2 H), 7.28 (d, 2 H, J = 8.2 Hz), 7.50 (d, 2 H, J = 8.2 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 21.4, 22.5, 23.5, 23.5, 25.0 (2 C), 25.4 (2), 28.7, 29.6, 29.9 (2 C), 34.1, 40.8, 49.5, 67.3, 117.4, 124.0 (2 C), 125.2 (2 C), 129.4, 129.7 (2 C), 131.3, 139.6, 142.0, 151.8 (2 C), 153.2; IR (KBr) 2958, 1600, 1463, 1316, 1154, 1047, 915, 714, 666, 563 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{31}H_{46}NO_3S_2$ $[M + H]^+$ 544.2914, found 544.2896.

Synthesis of (−)-(2S,3R,R$_S$)-2-(3-Chloropropyl)-3-(p-tolylsulfinyl)-1-N-tosyl-1,2,3,6-tetrahydropyridine, ***21i****. Method L.* Dienyl sulfoxide **15i** (84.8 mg, 0.19 mmol) and DBU (0.06 mL, 0.38 mmol) gave after chromatography (Et_2O) **21i** in 98:2 dr (72.1 mg, 84%). Data for **21i**: R_f 0.42 (Et_2O); mp 138−140 °C; $[\alpha]^{20}_D$ −139.2 (c 1.6, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 1.55−1.80 (m, 2 H, CH_2), 1.88−1.97 (m, 2 H, CH_2), 2.40 (s, 3 H, CH_3 *p*-Tol), 2.41 (s, 3 H, CH_3 *p*-Tol), 3.11 (d, 1 H, J = 5.6 Hz, H-3), 3.56 (td, 2 H, J = 6.2, 2.2 Hz, CH_2Cl), 3.72 (app dq, 1 H, J = 18.8, 2.3 Hz, H-6a), 4.02 (app dt, 1 H, J = 18.8, 3.6 Hz, H-6b), 4.88−4.94 (m, 2 H, H-2, H-4), 5.96 (ddd, 1 H, J = 10.3, 3.6, 2.3 Hz, H-5), 7.09−7.33 (m, 4 H, *p*-Tol), 7.46 (d, 2 H, J = 8.1 Hz, *p*-Tol), 7.88 (d, 2 H, J = 8.2 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.4 (CH_3 *p*-Tol), 21.5 (CH_3 *p*-Tol), 27.9 (CH_2), 29.2 (CH_2), 40.8 (C-6), 44.5 (CH_2Cl), 49.4 (C-2), 68.1 (C-3), 117.2 (C-4), 125.1 (2 × CH *p*-Tol), 127.5 (2 × CH *p*-Tol), 129.2 (C-5), 129.5 (2 × CH *p*-Tol), 129.7 (2 × CH *p*-Tol), 136.9 (C *p*-Tol), 138.7 (C *p*-Tol), 142.2 (C *p*-Tol), 143.5 (C *p*-Tol); IR (KBr) 3051, 2925, 1597, 1446, 1337, 1162, 1102, 1043, 814, 664 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{22}H_{27}ClNO_3S_2$ $[M + H]^+$ 452.1115, found 452.1117.

Synthesis of (−)-(2S,3R,R$_S$)-N-(tert-Butoxycarbonyl)-2-(3-chloropropyl)-3-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine, ***21j****. Method M.* Dienyl sulfoxide **15j** (175 mg, 0.44 mmol) and NaH (13.7 mg, 0.57 mmol) gave an 80:20 mixture of allylic sulfoxides **21j** and **2,3-*cis*-21j** along with a 19% of carbamate 5-((1*E*,3*E*)-hexa-1,3,5-trienyl)-oxazolidin-2-one (**21′**). This cyclic carbamate may be formed by base-mediated allylic proton abstraction of **15j** at C-6, followed by regioselective sigmatropic rearrangement, ring closure and subsequent

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chloride elimination on the alkyl side chain. Chromatography (Et_2O) afforded, an inseparable fraction of **21j**:**2,3-*cis*-21j** (110 mg, 63%) as a clear gum in 80:20 dr and the oxazolidinone **21′** (12.3 mg, 11%) as a white solid in >98:2 dr. Data for **21j**: R_f 0.62 (Et_2O); $[\alpha]^{20}_D$ −199.1 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.54 (s, 9 H, CH_3 Boc), 1.71−1.88 (m, 4 H, CH_2), 2.40 (s, 3 H, CH_3 *p*-Tol), 3.09 (d, 1 H, *J* = 5.7 Hz, H-3), 3.44−3.62 (m, 3 H, CH_2Cl, H-6a), 4.54 (dm, 1 H, *J* = 19.0 Hz, H-6b), 4.91−4.96 (m, 1 H, H-4), 5.08−5.11 (m, 1 H, H-2), 5.92 (ddd, 1 H, *J* = 10.2, 3.9, 2.2 Hz, H-5), 7.29 (d, 2 H, *J* = 8.0 Hz, *p*-Tol), 7.53 (d, 2 H, *J* = 8.0 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.4 (CH_3 *p*-Tol), 28.1 (CH_2), 28.3 (CH_3 Boc), 29.1 (CH_2), 39.5 (C-6), 44.3 (CH_2Cl), 47.5 (C-2), 68.8 (C-3), 80.9 (C Boc), 116.5 (C-4), 125.2 (2 × CH *p*-Tol), 129.7 (2 × CH *p*-Tol), 130.7 (C-5), 138.9 (C *p*-Tol), 142.0 (C *p*-Tol), 154.8 (CO Boc); IR (film) 2975, 1694, 1411, 1364, 1170, 1115, 1083, 1045, 812, 657 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{20}H_{29}ClNO_3S$ $[M + H]^+$ 398.1551, found 398.1550. Partial data for ***cis*-21j** (from the mixture): ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.48 (s, 9 H), 3.23 (d, 1 H, *J* = 5.7 Hz), 4.16−4.23 (m, 1 H), 5.85−5.88 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.7, 40.7, 44.7, 46.2, 67.6, 80.3, 116.8, 125.5, 129.6, 129.9, 141.9. Data for **21′**: R_f 0.20 (Et_2O); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 3.35 (t, 1 H, *J* = 8.4 Hz, H-4a), 3.75 (t, 1 H, *J* = 8.5 Hz, H-4b), 5.08−5.34 (m, 3 H, H-5, CH_2), 5.48 (s, 1 H, NH), 5.74 (dd, 1 H, *J* = 15.0, 7.4 Hz), 6.22−6.44 (m, 4 H); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 46.4 (C-4), 77.1 (C-5), 119.2 (CH_2), 128.4 (CH), 130.9 (CH), 134.3 (CH), 136.0 (CH), 136.3 (CH), 159.6 (CO); HRMS (ESI) *m*/*z* Calcd for $C_9H_{12}NO_2$ $[M + H]^+$ 166.0863, found 166.0855.

*Synthesis of (−)-(2S,3R,R$_S$)-2-(4-Fluorophenyl)-3-(p-tolylsulfinyl)-1-N-tosyl-1,2,3,6-tetrahydropyridine, **21m**. Method L.* Dienyl sulfoxide **15m** (123 mg, 0.26 mmol) and DBU (0.08 mL, 0.52 mmol) gave a 97:3 diastereomeric mixture of allyl sulfoxides **21m** and **2,3-*cis*-21m**. Chromatography (10−20% EtOAc-CH_2Cl_2) afforded **21m** (86.1 mg, 70%) as a clear oil and **2,3-*cis*-21m** (2.46 mg, 2%) as a white gum. Data for **21m**: R_f 0.50 (10% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −65.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.40 (s, 3 H, CH_3 *p*-Tol), 2.41 (s, 3 H, CH_3 *p*-Tol), 3.51 (d, 1 H, *J* = 5.8 Hz, H-3), 3.73 (app dq, 1 H, *J* = 18.6, 2.5 Hz, H-6a), 4.08 (ddd, 1 H, *J* = 18.6, 3.8, 2.5 Hz, H-6b), 5.08−5.13 (m, 1 H, H-4), 5.96 (ddd, 1 H, *J* = 10.2, 3.8, 2.5 Hz, H-5), 6.07 (s, 1 H, H-2), 6.93 (t, 2 H, *J* = 6.6 Hz, Ar), 7.25−7.32 (m, 6 H, Ar, *p*-Tol), 7.51 (d, 2 H, *J* = 8.2 Hz, *p*-Tol), 7.78 (d, 2 H, *J* = 8.3 Hz, *p*-Tol); ^{13}C NMR, HSQC (100 MHz $CDCl_3$) δ 21.48 (CH_3 *p*-Tol), 21.53 (CH_3 *p*-Tol), 41.8 (C-6), 52.0 (C-2), 68.7 (C-3), 115.4 (d, $^2J_{C-F}$ = 21.4 Hz, 2 × CH Ar), 117.6 (C-4), 125.4 (2 × CH *p*-Tol), 127.7 (2 × CH *p*-Tol), 129.4 (d, $^3J_{C-F}$ = 8.0 Hz, 2 × CH Ar), 129.4 (2 × CH *p*-Tol), 129.8 (C-5), 129.9 (2 × CH *p*-Tol), 134.2 (d, $^4J_{C-F}$ = 3.4 Hz, C Ar), 136.4 (C *p*-Tol), 138.6 (C *p*-Tol), 142.4 (C *p*-Tol), 143.6 (C *p*-Tol), 162.4 (d, $^1J_{C-F}$ = 247.2 Hz, C Ar). ^{19}F NMR (400 MHz, $CDCl_3$) δ −114.5; IR (film) 3052, 2924, 2852, 1599, 1509, 1455, 1345, 1227, 1161, 1096 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{25}H_{25}FNO_3S_2$ $[M + H]^+$ 470.1254, found 470.1266. Data for ***cis*-21m**: R_f 0.57 (10% EtOAc-CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 2.48 (s, 3 H), 3.45 (app dq, 1 H, *J* = 18.1, 2.7 Hz), 3.68 (dm, 1 H, *J* = 18.1 Hz), 3.82−3.84 (m, 1 H), 5.92 (s, 1 H), 6.04 (ddt, 1 H, *J* = 10.3, 5.2, 2.3 Hz), 6.16 (dm, 1 H, *J* = 10.3 Hz), 6.83 (t, 2 H, *J* = 8.7 Hz), 7.02 (dd, 2 H, *J* = 8.7, 5.2 Hz), 7.06 (d, 2 H, *J* = 8.2 Hz), 7.39−7.41 (m, 4 H), 7.88 (d, 2 H, *J* = 8.3 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.4, 21.8, 41.3, 52.4, 66.8, 115.5 (d, $^2J_{C-F}$ = 21.5 Hz), 116.6, 127.8 (2 C), 128.8 (d, $^3J_{C-F}$ = 8.2 Hz), 129.1 (2 C), 129.7 (2 C), 129.8 (2 C), 130.5, 133.5, 134.6 (d, $^4J_{C-F}$ = 3.5 Hz), 134.8, 143.5, 145.2, 162.3 (d, $^1J_{C-F}$ = 247.9 Hz). ^{19}F NMR (400 MHz, $CDCl_3$) δ −113.8; IR (film) 3057, 2925, 2852, 1598, 1510, 1266, 1162, 1095, 737, 570 cm^{-1}.

*Synthesis of (−)-(2S,3R,6R,R$_S$)-6-Phenyl-2-propyl-3-(p-tolylsulfinyl)-1-N-((S)-p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine, **21r**. Method L.* Dienyl sulfoxide **15r** (23.6 mg, 0.05 mmol) and DBU (0.02 mL, 0.01 mmol) gave after chromatography (50% EtOAc-hexane) and recrystallization from Et_2O-hexane **21r** (15.9 mg, 68%) as a white solid in >98:2 dr. Data for **21r**: R_f 0.51 (50% Et_2O-hexane); mp 154−156 °C; $[\alpha]^{20}_D$ −41.2 (*c* 0.4, $CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 0.90 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.17−1.40 (m, 2 H, CH_2), 1.76−1.84 (m, 1 H, CH_2), 2.31−2.37 (m, 1 H, CH_2), 2.40 (s, 3 H, CH_3 *p*-Tol), 2.42 (s, 3 H, CH_3 *p*-Tol), 3.02 (dt, 1 H, *J* = 6.0, 2.0 Hz, H-3), 4.06−4.08 (m, 1 H, H-2), 4.84 (dddd, 1 H, *J* = 9.8, 6.0, 2.3, 1.0 Hz, H-4), 5.33 (app q, 1 H, *J* = 2.3 Hz, H-6), 5.86 (dd, 1 H, *J* = 9.8, 2.3 Hz, H-5), 7.27 (d, 2 H, *J* = 8.0 Hz), 7.35−7.41 (m, 3 H), 7.46−7.52 (m, 4 H), 7.58−7.60 (m, 4 H); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 14.0 (CH_3), 20.0 (CH_2), 21.5 (CH_3 *p*-Tol), 21.6 (CH_3 *p*-Tol), 33.3 (CH_2), 51.1 (C-2), 58.9 (C-6), 67.8 (C-3), 116.1 (C-4), 125.2 (2 × CH), 126.1 (2 × CH), 128.4 (CH), 129.0 (2 × CH), 129.3 (2 × CH), 129.7 (2 × CH), 129.8 (2 × CH), 135.9 (C-5), 138.3 (C), 139.3 (C), 139.5 (C), 141.7 (C), 142.0 (C); IR (KBr) 3401, 3045, 2960, 1597, 1493, 1455, 1085, 1066, 1049, 810 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{28}H_{32}NO_2S_2$ $[M + H]^+$ 478.1869, found 478.1865.

*Synthesis of (−)-(2S,3R,6R,R$_S$)-6-Phenyl-2-propyl-3-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine, **21t**. Method N.* Dienyl sulfoxide **15r** (5.3 mg, 0.01 mmol) and TFA (0.02 mL, 0.22 mmol) gave after chromatography (4% MeOH−CH_2Cl_2) **21t** as a white solid in >98:2 dr (3.29 mg, 88%). Data for **21t**: R_f 0.36 (4% MeOH−CH_2Cl_2); mp 113−115 °C; $[\alpha]^{20}_D$ −91.3 (*c* 0.2, $CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 0.94 (t, 3 H, *J* = 7.2 Hz, CH_3), 1.33 (br s, 1 H, NH), 1.33−1.51 (m, 3 H, CH_2), 1.73−1.86 (m, 1 H, CH_2), 2.43 (s, 3 H, CH_3 *p*-Tol), 3.09 (ddt, 1 H, *J* = 5.3, 2.6, 1.1 Hz, H-3), 3.72−3.76 (m, 1 H, H-2), 4.50 (app q, 1 H, *J* = 2.3 Hz, H-6), 5.17−5.23 (m, 1 H, H-4), 5.94 (ddd, 1 H, *J* = 10.1, 2.3, 1.1 Hz, H-5), 7.28−7.40 (m, 7 H, Ar, *p*-Tol), 7.60 (d, 2 H, *J* = 7.9 Hz, *p*-Tol); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 14.0 (CH_3), 19.5 (CH_2), 21.5 (CH_3 *p*-Tol), 33.2 (CH_2), 49.4 (C-2), 54.4 (C-6), 66.9 (C-3), 117.4 (C-4), 125.3 (2 × CH *p*-Tol), 127.6 (CH Ar), 127.8 (2 × CH Ar), 128.6 (2 × CH Ar), 129.7 (2 × CH *p*-Tol), 136.9 (C-5), 139.3 (C *p*-Tol), 141.7 (C *p*-Tol), 143.5 (C Ar). NOESY 1D (400 MHz, $CDCl_3$): between H_6-*n*Pr 2.9%; IR (KBr) 3320, 3049, 2959, 2929, 1597, 1492, 1453, 1083, 1039, 856, 811 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{21}H_{26}NOS$ $[M + H]^+$ 340.1730, found 340.1729.

*Synthesis of (−)-(2S,3R,6S,R$_S$)-6-Ethyl-2-propyl-3-(p-tolylsulfinyl)-1,2,3,6-tetrahydropyridine, **21u**. Method N.* Dienyl sulfoxide **15s** (374 mg, 0.87 mmol) and TFA (1.29 mL, 17.4 mmol) gave after chromatography (2−5% MeOH−CH_2Cl_2) **21u** as a yellow oil in >98:2 dr (151 mg, 60%). Data for **21u**: R_f 0.40 (5% MeOH−CH_2Cl_2); $[\alpha]^{20}_D$ −80.1 (*c* 0.45, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.89 (t, 3 H, *J* = 7.1 Hz, CH_3), 0.97 (t, 3 H, *J* = 7.4 Hz, CH_3), 1.29−1.56 (m, 7 H, NH, CH_2), 2.42 (s, 3 H, CH_3 *p*-Tol), 2.95−2−97 (m, 1 H, H-3), 3.26−3.31 (m, 1 H, H-2), 3.63−3.67 (m, 1 H, H-6), 5.09−5.15 (m, 1 H, H-4), 5.93 (d, 1 H, *J* = 10.1 Hz, H-5), 7.31 (d, 2 H, *J* = 8.1 Hz), 7.55 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 9.9 (CH_3), 13.9 (CH_3), 19.6 (CH_2), 21.4 (CH_3 *p*-Tol), 28.4 (CH_2), 33.3 (CH_2), 49.2 (C-6), 50.0 (C-2), 66.9 (C-3), 117.7 (C-4), 125.2 (2 × CH *p*-Tol), 129.7 (2 × CH *p*-Tol), 137.8 (C-5), 139.4 (C *p*-Tol), 141.6 (C *p*-Tol); IR (film) 3321, 3034, 2959, 2872, 1494, 1456, 1380, 1083, 1042, 811 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{17}H_{26}NOS$ $[M + H]^+$ 292.1730, found 292.1720.

*Synthesis of (−)-(8R,8aS,R$_S$)-8-(p-Tolylsulfinyl)-1,2,3,5,8,**8a**-hexahydroindolizine, **21v**. Method N.* Amino dienyl sulfoxide **15j** (130 mg, 0.33 mmol) and TFA (0.48 mL, 6.50 mmol) gave after chromatography (5−10% MeOH−CH_2Cl_2) **21v** as a yellow gum in >98:2 dr (42.2 mg, 49%). Alternatively, 3-sulfinyl tetrahydropyridine **21j** (11.4 mg, 0.03 mmol, 80:20 dr) and TFA (0.04 mL, 0.58 mmol) gave **21v** (7.60 mg, 100%) as a yellow gum in 80:20 dr. Data for **21v**: R_f 0.56 (10% MeOH−CH_2Cl_2); $[\alpha]^{20}_D$ −31.0 (*c* 0.48, $CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 1.48−1.62 (m, 1 H, H-2a), 1.68−1.92 (m, 2 H, H-1), 1.99−2.10 (m, 1 H, H-2b), 2.16 (app q, 1 H, *J* = 8.9 Hz, H-3a), 2.30 (app q, 1 H, *J* = 8.6 Hz, H-8a), 2.42 (s, 3 H, CH_3 *p*-Tol), 2.74 (ddd, 1 H, *J* = 16.8, 4.5, 2.9 Hz, H-5a), 3.16 (td, 1 H, *J* = 8.9, 2.3 Hz, H-3b), 3.42 (app ddt, 1 H, *J* = 16.8, 4.5, 2.2 Hz, H-5b), 3.55 (app ddq, 1 H, *J* = 8.6, 4.4, 2.2 Hz, H-8), 5.60 (dm, 1 H, *J* = 10.0 Hz, H-7), 5.98 (ddt, 1 H, *J* = 10.0, 4.5, 2.2 Hz, H-6), 7.31 (d, 2 H, *J* = 8.0 Hz, *p*-Tol), 7.52 (d, 2 H, *J* = 8.0 Hz, *p*-Tol); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 21.4 (C-2), 21.5 (CH_3 *p*-Tol), 30.1 (C-1), 51.5 (C-5), 53.2 (C-3), 59.7 (C-8a), 68.0 (C-8), 119.4 (C-7), 125.5 (2 × CH *p*-Tol), 129.7 (2 × CH *p*-Tol), 131.5 (C-6), 138.1 (C *p*-Tol), 142.0 (C *p*-Tol); IR (film) 3040, 2958, 2789, 1596, 1493, 1331, 1154,

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1084, 1045, 811 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{15}H_{20}NOS$ $[M + H]^+$ 262.1260, found 262.1262.

General Procedure for the [2,3]-Sigmatropic Rearrangement. *Method O.* To a Kimble tube fitted with a magnetic stir bar and a solution of the corresponding allylic sulfoxide in anhydrous toluene (10 mL/mmol) was added Et_2NH (10.0 equiv) under an argon atmosphere and then was rapidly sealed. The reaction mixture was heated (90−110 °C) and monitored by TLC. It was then cooled to rt and quenched with saturated NH_4Cl solution. The aqueous phase was extracted with EtOAc and the organic extracts 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.

*Synthesis of (+)-(3S,6S)-6-Butyl-1-N-(4-nitrobenzenesulfonyl)-1,2,3,6-tetrahydropyridin-3-ol, **5c**. Method O.* Allylic sulfoxide **21b** (12.0 mg, 0.03 mmol) and Et_2NH (0.03 mL, 0.26 mmol) gave a 65:9:26 mixture of alcohols **5c** and **6c** and 6-butyl-1-(4-nitrobenzenesulfonyl)-1,2-dihydropyridine, analog to **22** (see below). Purification by column chromatography (5% EtOAc-CH_2Cl_2) afforded **5c** (4.98 mg, 56%) as a pale yellow gum in 96:4 dr. Data for **5c**: R_f 0.30 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +96.5 (c 1.0, $CHCl_3$); ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 0.87 (t, 3 H, J = 7.0 Hz, CH_3), 1.25−1.36 (m, 4 H, CH_2), 1.50−1.67 (m, 3 H, OH, CH_2), 3.38 (dd, 1 H, J = 15.1, 3.0 Hz, H-2a), 3.95 (d, 1 H, J = 15.1 Hz, H-2b), 3.98−4.04 (m, 1 H, H-3), 4.30−4.35 (m, 1 H, H-6), 5.85 (ddt, 1 H, J = 10.3, 5.6, 1.6 Hz, H-4), 5.94 (dd, 1 H, J = 10.3, 5.3 Hz, H-5), 8.07 (d, 2 H, J = 8.8 Hz, Ar), 8.32 (d, 2 H, J = 8.8 Hz, Ar); ^{13}C NMR, HSQC (100 MHz, $CDCl_3$) δ 13.9 (CH_3), 22.5 (CH_2), 28.2 (CH_2), 32.9 (CH_2), 46.4 (C-2), 53.5 (C-6), 62.0 (C-3), 124.0 (2 × CH Ar), 126.1 (C-4), 128.8 (2 × CH Ar), 131.7 (C-5), 146.5 (C Ar), 149.58 (C Ar); IR (film) 3435, 2958, 1607, 1531, 1350, 1164, 1007, 855, 740, 600 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{15}H_{19}N_2O_5S$ $[M - H]^+$ 339.1020, found 339.0996. Partial data for **6c** (from the crude mixture): ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.92 (dd, 1 H, J = 14.0, 9.9 Hz), 4.05 (ddd, 1 H, J = 14.0, 4.0, 2.0 Hz), 4.13−4.16 (m, 1 H), 5.61 (dq, 1 H, J = 10.6, 1.6 Hz), 5.75 (ddd, 1 H, J = 10.6, 4.0, 2.0 Hz).

*Synthesis of (+)-(3S,6S)-6-Butyl-1-N-(2-nitrobenzenesulfonyl)-1,2,3,6-tetrahydropyridin-3-ol, **5d**. Method O.* Allylic sulfoxide **21c** (100 mg, 0.22 mmol) and Et_2NH (0.22 mL, 2.20 mmol) gave a 75:25 mixture of alcohols **5d** and **6d**. Purification by column chromatography (5−10% EtOAc-CH_2Cl_2) followed by a second purification (80% EtOAc-hexane) afforded **5d** (37.5 mg, 50%) as pale yellow gum in >98:2 dr. Data for **5d**: R_f 0.29 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +80.6 (c 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (t, 3 H, J = 7.0 Hz), 1.23−1.36 (m, 4 H), 1.57−1.68 (m, 2 H), 1.76 (br s, 1 H), 3.41 (dd, 1 H, J = 14.8, 2.3 Hz), 3.77 (d, 1 H, J = 14.8 Hz), 3.95 (dt, 1 H, J = 5.0, 2.3 Hz), 4.35−4.40 (m, 1 H), 5.92 (dd, 1 H, J = 10.3, 5.0 Hz), 6.02 (dd, 1 H, J = 10.3, 4.4 Hz), 7.60−7.71 (m, 3 H), 8.15−8.17 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.9, 22.5, 28.1, 33.4, 46.5, 54.1, 62.2, 124.1, 125.2, 125.6, 131.7 (2 C), 132.0, 133.6, 147.7; IR (film) 3543, 2958, 1543, 1372, 1165, 1058, 1011, 852, 738, 583 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{15}H_{21}N_2O_5S$ $[M + H]^+$ 341.1166, found 341.1178.

*Synthesis of (+)-(3S,6S)-6-Butyl-1-N-(2,4,6-trimethylbenzenesulfonyl)-1,2,3,6-tetrahydropyridin-3-ol, **5e**. Method O.* Allylic sulfoxide **21d** (114 mg, 0.25 mmol) and Et_2NH (0.26 mL, 2.50 mmol) gave a 57:7:36 mixture of alcohols **5e**, **6e** and regioisomeric (*S*)-2-butyl-1-(2,4,6-trimethylbenzenesulfonyl)-1,2,3,6-tetrahydropyridin-3-ol[38] (tentatively assigned). Column chromatography (5−10% EtOAc-CH_2Cl_2) afforded **5e** (40.6 mg, 48%) as a pale orange oil in >98:2 dr. Data for **5e**: R_f 0.30 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +103.2 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.76 (t, 3 H, J = 7.0 Hz), 0.97−1.25 (m, 4 H), 1.41−1.54 (m, 2 H), 2.30 (s, 3 H), 2.62 (s, 6 H), 3.34 (dd, 1 H, J = 15.0, 3.0 Hz), 3.79 (d, 1 H, J = 15.0 Hz), 3.90 (br s, 1 H), 4.03 (td, 1 H, J = 7.2, 2.4 Hz), 5.97 (m, 2 H), 6.96 (s, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.8, 21.0, 22.3, 22.8 (2 C), 28.0, 32.5, 45.6, 52.5, 61.8, 126.7, 131.6, 131.8, 132.0 (2 C), 140.4 (2 C), 142.9. NOESY 1D (400 MHz, $CDCl_3$): between H_{2ax}-*n*Bu 3.0%; IR (film) 3489, 2957, 1604, 1467, 1315, 1153, 1056, 852, 736, 576 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{18}H_{28}NO_3S$ $[M + H]^+$ 338.1784, found 338.1785.

*Synthesis of (+)-(3S,6S)-6-Butyl-1-N-(2,4,6-triisopropylbenzenesulfonyl)-1,2,3,6-tetrahydropyridin-3-ol, **5f**. Method O.* Allylic sulfoxide **21e** (99.3 mg, 0.18 mmol) and Et_2NH (0.19 mL, 1.80 mmol) gave a 69:19:12 mixture of alcohols **5f**, **6f** and regioisomeric (*S*)-2-butyl-1-(2,4,6-triisopropylbenzenesulfonyl)-1,2,3,6-tetrahydropyridin-3-ol (tentatively assigned). Purification by column chromatography (5−10% EtOAc-CH_2Cl_2) afforded an 85:15 mixture of **5f** and the regioisomer (49.3 mg, 65%) as a clear gum. A pure sample of **5f** was obtained by a second careful chromatography. Data for **5f**: R_f 0.40 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +66.2 (c 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.73 (t, 3 H, J = 7.0 Hz, CH_3), 1.08−1.16 (m, 4 H, CH_2), 1.24−1.28 (m, 18 H, 6 x CH_3 *i*-Pr), 1.37−1.53 (m, 2 H, CH_2), 2.86−2.94 (m, 1 H, CH *i*-Pr), 3.36 (dd, 1 H, J = 15.3, 3.4 Hz, H-2a), 3.94 (dm, 2 H, J = 15.3 Hz, H-2b, H-3), 4.07−4.13 (m, 3 H, H-6, 2 × CH *i*-Pr), 6.00 (m, 2 H, H-4, H-5), 7.18 (s, 2 H, Ar); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 13.7 (CH_3), 22.3 (CH_2), 23.5 (CH_3 *i*-Pr), 23.6 (CH_3 *i*-Pr), 24.8 (2 × CH_3 *i*-Pr), 25.1 (2 × CH_3 *i*-Pr), 28.0 (CH_2), 29.5 (2 × CH *i*-Pr), 32.7 (CH_2), 34.2 (CH *i*-Pr), 45.6 (C-2), 52.0 (C-6), 61.6 (C-3), 124.0 (2 × CH Ar), 127.0 (C-4), 130.6 (C Ar), 131.3 (C-5), 151.5 (2 × C Ar), 153.5 (C Ar). NOESY 1D (400 MHz, $CDCl_3$): between H_{2ax}-*n*Bu 6.0%; IR (film) 3508, 2958, 1601, 1564, 1463, 1311, 1151, 883, 758, 561 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{24}H_{40}NO_3S$ $[M + H]^+$ 422.2723, found 422.2744.

*Synthesis of (+)-(3S,6S)-1-N-(tert-Butoxycarbonyl)-6-butyl-1,2,3,6-tetrahydropyridin-3-ol, **5g**. Method O.* Allylic sulfoxide **21f** (15.0 mg, 0.04 mmol) and Et_2NH (0.04 mL, 0.40 mmol. Purification by column chromatography (20% EtOAc-CH_2Cl_2) provided **5g** (7.37 mg, 0.03 mmol, 72%) as a clear gum. The presence of rotamers made difficult to establish a diastereomeric ratio for **5g**; further *N*-Boc-deprotection of **5g** afforded **5n**[15c] in 90:10 dr. Data for **5g**: R_f 0.40 (20% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +239.0 (c 0.85, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.89 (t, 3 H, J = 6.9 Hz), 1.25−1.47 (m, 6 H), 1.47 (s, 9 H), 1.84 (br s, 1 H), 2.95−3.14 (m, 1 H), 3.95−4.55 (m, 3 H,), 5.92 (br d, 2 H, J = 3.7 Hz); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 14.0, 22.6, 28.4 (3 C), 28.4, 32.0, 43.9, 45.1, 51.3, 52.2, 63.0, 79.8, 127.4, 132.7, 133.3, 155.5; IR (film) 3422, 2931, 1695, 1421, 1365, 1274, 1175, 1130, 1072, 865, 827 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{14}H_{26}NO_3$ $[M + H]^+$ 256.1923, found 256.1907.

*Synthesis of (+)-(3S,6S)-6-(3-Chloropropyl)-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-ol, **5i**. Method O.* Allylic sulfoxide **21i** (103 mg, 0.23 mmol) and Et_2NH (0.24 mL, 2.30 mmol) gave an 80:20 mixture of alcohol **5i** and 6-(3-chloropropyl)-1-tosyl-1,2-dihydropyridine, analog to **22** (see below). Chromatography (70−90% Et_2O-hexane) afforded **5i** (52.7 mg, 69%) as a clear gum in >98:2 dr. Data for **5i**: R_f 0.23 (80% Et_2O-hexane); $[\alpha]^{20}_D$ +145.8 (c 1.0,$CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 1.60−1.88 (m, 4 H, CH_2), 2.12 (br s, 1 H, OH), 2.42 (s, 3 H, CH_3 *p*-Tol), 3.31 (dd, 1 H, J = 15.3, 3.5 Hz, H-2a), 3.53 (td, 2 H, J = 6.3, 1.8 Hz, CH_2Cl), 3.81 (d, 1 H, J = 15.3 Hz, H-2b), 3.89 (td, 1 H, J = 3.5, 1.3 Hz, H-3), 4.42 (ddd, 1 H, J = 8.8, 5.9, 3.1 Hz, H-6), 5.88−5.92 (m, 2 H, H-4, H-5), 7.30 (d, 2 H, J = 8.2 Hz, *p*-Tol), 7.76 (d, 2 H, J = 8.2 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 21.5 (CH_3 *p*-Tol), 29.1 (CH_2), 29.9 (CH_2), 44.5 (CH_2Cl), 46.1 (C-2), 51.9 (C-6), 61.9 (C-3), 126.9 (CH), 127.6 (2 × CH *p*-Tol), 129.7 (2 × CH *p*-Tol), 131.4 (CH), 136.8 (C *p*-Tol), 143.8 (C *p*-Tol); IR (film) 3500, 2924, 1598, 1447, 1330, 1113, 1004, 815, 711, 691 cm^{-1}; HRMS (ESI) m/z Calcd for $C_{15}H_{21}ClNO_3S$ $[M + H]^+$ 330.0925, found 330.0939.

*Synthesis of (+)-(3S,6R)-6-(4-Fluorophenyl)-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-ol, **5k**. Method O.* Allylic sulfoxide **21m** (42 mg, 0.09 mmol) and Et_2NH (0.09 mL, 0.89 mmol) gave after chromatography (70−90% Et_2O-hexane) **5k** (22.3 mg, 72%) as a clear oil in >98:2 dr. Data for **5k**: R_f 0.20 (70% Et_2O-hexane); $[\alpha]^{20}_D$ +228.7 (c 1.0, $CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 1.57 (br s, 1 H, OH), 2.38 (s, 3 H, CH_3 *p*-Tol), 3.19 (dd, 1 H, J = 15.0, 3.3 Hz, H-2a), 3.69 (d, 1 H, J = 15.0 Hz, H-2b), 3.99 (br s, 1 H, H-3), 5.63 (d, 1 H, J = 4.2 Hz, H-6), 6.05 (dd, 1 H, J = 10.3, 4.2 Hz, H-5), 6.16 (dd, 1 H, J = 10.3, 5.2 Hz, H-4), 6.97 (t, 2 H, J = 8.6 Hz, Ar), 7.22 (d, 2 H, J = 8.2 Hz, *p*-Tol), 7.24−7.27 (m, 2 H, Ar), 7.60 (d, 2 H, J = 8.2 Hz, *p*-Tol); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 21.5 (CH_3 *p*-Tol), 46.2 (C-2), 54.4 (C-6), 62.0 (C-3), 115.4 (d, $^2J_{C-F}$ = 21.5 Hz, 2

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× CH Ar), 127.6 (2 × CH *p*-Tol), 128.2 (C-4), 129.6 (2 × CH *p*-Tol), 129.9 (C-5), 130.0 (d, $^{3}J_{C-F}$ = 8.3 Hz, 2 × CH Ar), 133.1 (d, $^{4}J_{C-F}$ = 3.2 Hz, C Ar), 136.5 (C *p*-Tol), 143.7 (C *p*-Tol), 162.6 (d, $^{1}J_{C-F}$ = 247.5 Hz, C Ar). ^{19}F NMR (400 MHz, $CDCl_3$) δ −114.1; IR (film) 3501, 3055, 2925, 2852, 1604, 1509, 1447, 1226, 1159, 738 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{18}H_{19}FNO_3S$ [M + H]$^+$ 348.1064, found 348.1069.

Synthesis of (+)-(2S,3S,6S)-6-Butyl-2-methyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-ol, ***5l****. Method O.* Allylic sulfoxide **21o** (48.4 mg, 0.10 mmol) and Et_2NH (0.11 mL, 1.00 mmol) gave after chromatography a 67:7:26 mixture of alcohols **5l** and **6l** and dihydropyridine (*S*)-6-butyl-2-methyl-1-tosyl-1,2-dihydropyridine (***S***)-**22**. Purification by column chromatography (5% EtOAc-CH_2Cl_2) afforded **5l** (18.1 mg, 56%) as a clear gum in 95:5 dr. Data for **5l**: R_f 0.30 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ +126.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.86 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.24−1.33 (m, 4 H, CH_2), 1.31 (d, 3 H, *J* = 7.0 Hz, CH_3), 1.57−1.67 (m, 2 H, CH_2), 2.42 (s, 3 H, CH_3 *p*-Tol), 2.72 (d, 1 H, *J* = 10.2 Hz, OH), 3.79−3.87 (m, 2 H, H-2, H-3), 4.59−4.65 (m, 1 H, H-6), 5.87 (dd, 1 H, *J* = 10.6, 3.6 Hz, H-4), 5.94 (dd, 1 H, *J* = 10.6, 4.1 Hz, H-5), 7.28 (d, 2 H, *J* = 8.3 Hz, *p*-Tol), 7.75 (d, 2 H, *J* = 8.2 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 13.9 (CH_3), 14.6 (CH_3), 21.5 (CH_3 *p*-Tol), 22.4 (CH_2), 28.2 (CH_2), 35.6 (CH_2), 53.4 (C-2), 55.0 (C-6), 66.5 (C-3), 127.3 (2 × CH *p*-Tol), 128.0 (C-4), 129.4 (2 × CH *p*-Tol), 131.6 (C-5), 140.0 (C *p*-Tol), 143.3 (C *p*-Tol). NOESY 1D (400 MHz, $CDCl_3$): between H_6−CH_3 2.0%; IR (film) 3500, 2931, 1598, 1456, 1319, 1158, 1089, 815, 677, 564 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{17}H_{26}NO_3S$ [M + H]$^+$ 324.1628, found 324.1624. The data obtained for (*S*)-**22** was identical to that of (*R*)-6-butyl-2-methyl-1-tosyl-1,2-dihydropyridine except for the optical rotation: $[\alpha]^{20}_D$ +157.0 (*c* 0.4, $CHCl_3$).

Synthesis of (−)-(R)-6-Butyl-2-methyl-1-tosyl-1,2-dihydropyridine, ***(R)-22****. Method O.* Allylic sulfoxide **21p** (17.4 mg, 0.04 mmol) and Et_2NH (0.04 mL, 0.39 mmol) gave after chromatography (10−20% Et_2O-hexane) (***R***)-**22** as a clear gum (7.30 mg, 61%). Data for (***R***)-**22**: R_f 0.50 (5% EtOAc-CH_2Cl_2); $[\alpha]^{20}_D$ −153.3 (*c* 0.6, $CHCl_3$); ^{1}H NMR, COSY (500 MHz, $CDCl_3$) δ 0.91 (t, 3 H, *J* = 7.3 Hz, CH_3), 1.12 (d, 3 H, *J* = 6.9 Hz, CH_3), 1.30−1.45 (m, 3 H, CH_2), 1.62−1.69 (m, 1 H, CH_2), 2.22 (ddd, 1 H, *J* = 15.0, 9.5, 6.6 Hz, CH_2), 2.38 (s, 3 H, CH_3 *p*-Tol), 2.86 (ddd, 1 H, *J* = 15.0, 9.3, 5.0 Hz, CH_2), 4.79−4.84 (m, 1 H, H-2), 5.32 (dd, 1 H, *J* = 9.3, 5.6 Hz, H-3), 5.45 (dd, 1 H, *J* = 9.3, 5.3 Hz, H-4), 5.55 (app d, 1 H, *J* = 5.3 Hz, H-5), 7.28 (d, 2 H, *J* = 8.3 Hz, *p*-Tol), 7.75 (d, 2 H, *J* = 8.3 Hz, *p*-Tol); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 13.9 (CH_3), 18.8 (CH_3), 21.5 (CH_3 *p*-Tol), 22.4 (CH_2), 29.9 (CH_2), 35.6 (CH_2), 50.8 (C-2), 115.0 (C-5), 120.8 (C-4), 125.1 (C-3), 127.2 (2 × CH *p*-Tol), 128.9 (2 × CH *p*-Tol), 136.9 (C), 137.3 (C), 143.1 (C); IR (film) 2958, 1597, 1455, 1344, 1173, 1152, 1088, 812, 694, 558 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{17}H_{24}NO_2S$ [M + H]$^+$ 306.1522, found 306.1520.

Synthesis of (+)-(3S,6S)-6-Butyl-4-methyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-ol, ***5m****. Method O.* Allylic sulfoxide **21r** (12.7 mg, 0.03 mmol) and Et_2NH (0.03 mL, 0.29 mmol) gave a 95:5 mixture of alcohols **5m** and **6m**. Chromatography (70% Et_2O-hexane) afforded **5m** (6.00 mg, 65%) as a clear gum in 97:3 dr. Data for **5m**: R_f 0.40 (70% Et_2O-hexane); $[\alpha]^{20}_D$ +67.8 (*c* 0.5, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.84 (t, 3 H, *J* = 6.5 Hz), 1.19−1.28 (m, 4 H), 1.42−1.50 (m, 2 H), 1.79 (s, 3 H), 2.15 (dd, 1 H, *J* = 10.8, 1.0 Hz), 2.42 (s, 3 H), 3.25 (ddd, 1 H, *J* = 15.0, 3.0, 1.0 Hz), 3.65 (dd, 1 H, *J* = 10.8, 3.0 Hz), 3.79 (d, 1 H, *J* = 15.0 Hz), 4.31−4.37 (m, 1 H), 5.59 (dt, 1 H, *J* = 4.5, 1.5 Hz), 7.30 (d, 2 H, *J* = 8.1 Hz), 7.77 (d, 2 H, *J* = 8.1 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 13.9, 20.8, 21.5, 22.5, 28.3, 32.9, 46.1, 52.9, 66.1, 125.7, 127.6 (2 C), 129.6 (2 C), 134.0, 137.2, 143.6; IR (film) 3504, 2958, 1598, 1455, 1335, 1155, 1088, 814, 685, 548 cm^{-1}; HRMS (ESI) *m*/*z* calcd for $C_{17}H_{26}NO_3S$ [M + H]$^+$ 324.1628, found 324.1620.

Synthesis of (+)-(3S,6S)-6-Butyl-1,2,3,6-tetrahydropyridin-3-ol, ***5n****. Method O.* Allylic sulfoxide **21s** (22.2 mg, 0.08 mmol) and Et_2NH (0.08 mL, 0.80 mmol). The reaction mixture was placed directly in the column chromatography (20% MeOH−CH_2Cl_2) to yield **5n** (8.95 mg, 0.06 mmol, 72%) as a white solid in >98:2 dr. *Method J:* TFA (0.06 mL, 0.80 mmol) and allylic alcohol **5g** (12.5 mg, 0.04 mmol) after chromatography (20% MeOH−CH_2Cl_2) afforded **5n** (7.60 mg, 61%), as a white gum in >98:2 dr. Alternatively from Na-naphthalene [naphthalene (30.8 mg, 0.24 mmol), sodium metal (7.40 mg, 0.32 mmol) at rt] and allylic alcohol **5b** (24.8 mg, 0.08 mmol) in anhydrous THF (10 mL/mmol) at −78 °C[31] was obtained after chromatography (20% MeOH−CH_2Cl_2) **5n** (9.00 mg, 72%) as a white solid in >98:2 dr. Data for **5n** was identical to that reported.[15c]

Synthesis of (+)-(2S,3S,6S)-2-Phenyl-6-propyl-1,2,3,6-tetrahydropyridin-3-ol, ***5o****. Method O.* Allylic sulfoxide **21t** (7.30 mg, 0.02 mmol) and Et_2NH (0.02 mL, 0.15 mmol). The reaction mixture was placed directly in the column chromatography (5−20% MeOH−CH_2Cl_2) to yield **5o** (2.35 mg, 70%) as a yellow gum in >98:2 dr. Data for **5o**: R_f 0.55 (10% MeOH−CH_2Cl_2); $[\alpha]^{20}_D$ +19.8 (*c* 0.13, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.93 (t, 3 H, *J* = 7.2 Hz, CH_3), 1.25 (br s, 1 H, OH), 1.32−1.46 (m, 2 H, CH_2), 1.48−1.60 (m, 2 H, CH_2), 3.52−3.58 (m, 1 H, H-6), 3.98 (dd, 1 H, *J* = 5.1, 2.5 Hz, H-3), 4.16 (d, 1 H, *J* = 2.5 Hz, H-2), 5.97 (dd, 1 H, *J* = 10.0, 3.8 Hz, H-5), 6.05 (ddd, 1 H, *J* = 10.0, 5.1, 1.6 Hz, H-4), 7.29−7.43 (m, 5 H, Ph); ^{13}C NMR, HSQC (125 MHz, $CDCl_3$) δ 14.0 (CH_3), 20.1 (CH_2), 35.2 (CH_2), 53.8 (C-6), 56.6 (C-2), 65.9 (C-3), 127.0 (C-4), 127.2 (2 × CH Ph), 127.4 (CH Ph), 128.5 (2 × CH Ph), 134.2 (C-5), 140.8 (C Ph); IR (film) 3307, 3029, 2957, 2927, 1604, 1456, 1383, 1076, 1031, 699 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{14}H_{20}NO$ [M + H]$^+$ 218.1539, found 218.1542.

Synthesis of (6S,8aS)-1,2,3,5,6,8a-Hexahydroindolizin-6-ol, ***5p****. Method O.* Allylic sulfoxide **21v** (6.3 mg, 0.02 mmol) and Et_2NH (0.02 mL, 0.24 mmol). The reaction mixture was placed directly on a cation exchange solid support (benzenesulfonic/silica gel) [gradient elution: (i) CH_2Cl_2, (ii) MeOH, (iii) 0.1−1.0% NH_3-MeOH] that afforded slightly impure **5p** (1.40 mg, 42%) as a yellow gum in >98:2 dr. Data for **5p**: R_f 0.10 (70% MeOH−$CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.41−1.54 (m, 1 H), 1.67−2.00 (m, 3 H, H-1), 2.36−2.46 (m, 1 H), 2.56 (dd, 1 H, *J* = 11.8, 4.9 Hz), 2.74−2.90 (m, 2 H), 3.12 (dd, 1 H, *J* = 11.8, 4.9 Hz), 3.15−3.21 (m, 1 H), 4.20−4.25 (m, 1 H), 5.81 (ddd, 1 H, *J* = 10.2, 2.7, 1.7 Hz), 5.87 (dd, 1 H, *J* = 10.2, 2.4 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 29.1, 52.7, 54.4, 59.4, 63.4, 127.8, 131.1; IR (film) 3347, 2958, 1732, 1456, 1463, 1379, 1276, 1263, 1075, 800 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_8H_{14}NO$ [M + H]$^+$ 140.1070, found 140.1065.

Synthesis of (−)-(6S,8aS)-Octahydroindolizin-6-ol, ***23****.*[32] To a solution of allylic alcohol **5p** (5.0 mg, 0.04 mmol) and Pd/C (0.38 mg, 0.004 mmol) in MeOH (10 mL/mmol alcohol) at rt was added H_2 (1 atm). The reaction mixture was stirred until disappearance of starting material (TLC). Filtration by column chromatography (70% MeOH−$CHCl_3$) followed by a cation exchange solid support (benzenesulfonic/silica gel) [gradient elution: (i) CH_2Cl_2, (ii) MeOH, (iii) 0.1−1% NH_3-MeOH], affording **23** (5.07 mg, 99%) as a clear gum in >98:2 dr. Data for **23**: R_f 0.40 (70% MeOH−$CHCl_3$); $[\alpha]^{20}_D$ −45.1 (*c* 0.45, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22−1.41 (m, 3 H), 1.67−1.91 (m, 6 H), 2.03−2.20 (m, 3 H), 3.02 (td, 1 H, *J* = 8.6, 2.3 Hz), 3.29 (ddd, 1 H, *J* = 10.1, 4.7, 1.8 Hz), 3.80−3.90 (m, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 28.9, 29.8, 34.3, 53.9, 60.1, 63.7, 68.5; HRMS (ESI) *m*/*z* Calcd for $C_8H_{16}NO$ [M + H]$^+$ 142.1226, found 142.1226.

Preparation of 2-Methoxy-2-phenyl acetates ***7****. Method P.* To a solution of alcohol (1.0 equiv) in anhydrous CH_2Cl_2 (10 mL/mmol alcohol) under argon was added 2-methoxy-2-phenylacetic acid (1.05−4.0 equiv), EDC·HCl (4.0 equiv) or DCC (1.0 equiv) and DMAP (0.1−0.5 equiv). The mixture was stirred at room temperature until disappearance of starting material was observed (TLC). It was then quenched with 0.1 N HCl aqueous solution and the aqueous layer was extracted with CH_2Cl_2. The combined organic layers were washed with saturated $NaHCO_3$ aqueous solution, dried (Na_2SO_4) and concentrated in vacuo. In the case of DCC the crude mixture was filtered through silica gel (3 mg/mmol), using CH_2Cl_2 (2 × 10 mL/mmol). The crude product was then purified by column chromatography on silica gel with the appropriate mixture of solvents.

Synthesis of (−)-(3R,6S)-6-Phenyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-yl (2S)-methoxy-2-phenylacetate, ***7a****. Method P.* Allylic

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alcohol *ent*-**5a** (7 mg, 0.021 mmol), (+)-(*S*)-2-methoxy-2-phenylacetic acid (4 mg, 0.022 mmol), DCC (4 mg, 0.021 mmol) and DMAP (1.2 mg, 0.01 mmol) gave after chromatography (5−30% EtOAc-hexane) **7a** as a colorless oil (6 mg, 60%). Data for **7a**: R_f 0.31 (30% EtOAc-hexane); $[\alpha]^{20}_D$ −184.4 (*c* 0.48, $CHCl_3$); ^{1}H NMR, COSY (400 MHz, $CDCl_3$) δ 2.35 (s, 3 H, CH_3 *p*-Tol), 3.34 (dd, 1 H, *J* = 15.3, 3.0 Hz, H-2a), 3.44 (s, 3 H, OCH_3), 4.08 (d, 1 H, *J* = 15.3 Hz, H-2b), 4.66 (s, 1 H, PhCH), 5.16 (td, 1 H, *J* = 3.3, 0.9 Hz, H-3), 5.50 (dd, 1 H, *J* = 4.6, 2.0 Hz, H-6), 5.82 (ddd, 1 H, *J* = 10.2, 4.6, 1.3 Hz, H-4), 6.10 (ddd, 1 H, *J* = 10.2, 4.6, 0.7 Hz, H-5), 7.13−7.18 (m, 4 H, Ar), 7.21−7.25 (m, 3 H, Ar), 7.31−7.41 (m, 5 H, Ar), 7.52 (dt, 2 H, *J* = 8.4, 1.8 Hz, Ar); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.5, 43.4, 55.9, 57.6, 64.6, 82.0, 122.6, 127.1 (2 C), 127.4 (2 C), 128.1 (2 C), 128.2, 128.6 (4 C), 129.3 (2 C), 133.4, 136.1, 136.8, 137.7, 142.9 (2 C), 170.5; IR (film) 3026, 2926, 1746, 1597, 1491, 1454, 1339, 1273, 1157, 999, 697, 664 cm^{-1}. MS (ESI): 500 $[M + Na]^+$ (100%). Alternatively from allylic alcohol *ent*-**5a** (8 mg, 0.024 mmol) and (±)-2-methoxy-2-phenylacetic acid (5 mg, 0.026 mmol) was obtained a 50:50 mixture of esters (9 mg, 78%) as a colorless oil after purification by column chromatography (5−30% EtOAc-hexane). Data from the 50:50 mixture of (*R*,*S*)-2-methoxy-2-phenyl acetates: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 6 H), 3.31 (dd, 1 H, *J* = 15.0, 3.1 Hz), 3.35 (dd, 1 H, *J* = 15.0, 3.1 Hz), 3.39 (s, 3 H), 3.44 (s, 3 H), 3.91 (d, 1 H, *J* = 15.6 Hz), 4.08 (d, 1 H, *J* = 16.0 Hz), 4.60 (s, 1 H), 4.66 (s, 1 H), 5.09 (td, 1 H, *J* = 3.5, 1.6 Hz), 5.16 (m, 1 H), 5.48 (d, 1 H, *J* = 3.5 Hz), 5.50 (dd, 1 H, *J* = 4.3, 2.0 Hz), 5.82 (dddd, 1 H, *J* = 10.1, 5.1, 3.1, 1.9 Hz), 6.08−6.16 (m, 3 H), 7.13−7.20 (m, 6 H), 7.20−7.26 (m, 8 H), 7.29−7.44 (m, 10 H), 7.52 (d, 4 H, *J* = 8.2 Hz). MS (ESI): 500 $[M + Na]^+$ (100%).

*Synthesis of (+)-(3S,6S)-6-Butyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-yl (2S)-methoxy-2-phenylacetate, **7b**. Method P.* Allylic alcohol **5b** (59.5 mg, 0.19 mmol), (+)-(*S*)-2-methoxy-2-phenylacetic acid (128 mg, 0.77 mmol), EDC·HCl (147 mg, 0.77 mmol) and DMAP (11.7 mg, 0.10 mmol) gave a 98:2 diastereomeric mixture of esters **7b** and **7c** that proved a 96% ee of the starting alcohol **5b**. Column chromatography (40−60% Et_2O-hexane) afforded **7b** as a clear gum (86.5 mg, 98%). Data for **7b**: R_f 0.53 (60% Et_2O-hexane); $[\alpha]^{20}_D$ +143.6 (*c* 1.0, $CDCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.82 (t, 3 H, *J* = 7.0 Hz, CH_3), 1.19−1.32 (m, 4 H, CH_2), 1.53−1.61 (m, 2 H, CH_2), 2.41 (s, 3 H, CH_3 *p*-Tol), 3.37 (s, 3 H, OCH_3), 3.38−3.44 (m, 1 H, H-2a), 4.01 (d, 1 H, *J* = 15.4 Hz, H-2b), 4.24 (tdd, 1 H, *J* = 6.7, 4.5, 1.6 Hz, H-6), 4.52 (s, 1 H, PhCH), 4.97−5.00 (m, 1 H, H-3), 5.91 (ddd, 1 H, *J* = 10.3, 3.8, 1.6 Hz, H-4), 6.06 (ddd, 1 H, *J* = 10.3, 4.5, 0.6 Hz, H-5), 7.27 (d, 2 H, *J* = 8.4 Hz, *p*-Tol), 7.32−7.39 (m, 5 H, Ph), 7.75 (d, 2 H, *J* = 8.4 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 13.8 (CH_3), 21.5 (CH_3 *p*-Tol), 22.5 (CH_2), 27.9 (CH_2), 32.6 (CH_2), 43.0 (C-2), 53.1 (C-6), 57.3 (OCH_3), 65.4 (C-3), 82.2 (PhCH), 121.9 (C-4), 127.0 (2 × CH Ph), 127.5 (2 × CH *p*-Tol), 128.6 (2 × CH Ph), 128.7 (CH Ph), 129.3 (2 × CH *p*-Tol), 134.4 (C-5), 135.8 (C), 138.2 (C), 142.9 (C), 170.3 (CO); IR (film) 2931, 1747, 1599, 1495, 1456, 1338, 1160, 998, 816, 696 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{25}H_{35}N_2O_5S$ $[M + NH_4]^+$ 475.2261, found 475.2249.

*Synthesis of (+)-(3S,6S)-6-Butyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-yl (2R)-methoxy-2-phenylacetate, ent-**7c**. Method P.* Allylic alcohol **5b** (59.5 mg, 0.19 mmol), (*R*)-2-methoxy-2-phenylacetic acid (128 mg, 0.77 mmol), EDC·HCl (147 mg, 0.77 mmol) and DMAP (11.7 mg, 0.10 mmol) gave a 98:2 diastereomeric mixture of esters *ent*-**7c** and *ent*-**7b** (**5b**, 96% ee). Purification by column chromatography (40−60% Et_2O-hexane) afforded *ent*-**7c** (86.5 mg, 98%) as a clear oil. Data for *ent*-**7c**: R_f 0.33 (40% Et_2O-hexane); $[\alpha]^{20}_D$ +137.3 (*c* 1.0, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.81 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.13−1.29 (m, 4 H, CH_2), 1.49−1.57 (m, 2 H, CH_2), 2.41 (s, 3 H, CH_3 *p*-Tol), 3.39 (dd, 1 H, *J* = 15.5, 3.0 Hz, H-2a), 3.42 (s, 3 H, OCH_3), 4.16 (d, 1 H, *J* = 15.5 Hz, H-2b), 4.27 (tdd, 1 H, *J* = 7.0, 4.5, 1.8 Hz, H-6), 4.56 (s, 1 H, PhCH), 5.06−5.08 (m, 1 H, H-3), 5.61 (ddt, 1 H, *J* = 10.3, 5.2, 1.8 Hz, H-4), 6.02 (dd, 1 H, *J* = 10.3, 4.5 Hz, H-5), 7.27 (d, 2 H, *J* = 8.0 Hz, *p*-Tol), 7.31−7.35 (m, 5 H, Ph), 7.75 (d, 2 H, *J* = 8.0 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 13.8 (CH_3), 21.5 (CH_3 *p*-Tol), 22.5 (CH_2), 28.0 (CH_2), 32.6 (CH_2), 43.2 (C-2), 53.2 (C-6), 57.5 (OCH_3), 64.7 (C-3), 82.0 (PhCH), 121.6 (C-4), 127.0 (2 × CH Ph), 127.4 (2 × CH *p*-Tol), 128.5 (2 × CH Ph), 128.6 (CH Ph), 129.5 (2 × CH *p*-Tol), 134.8 (C-5), 136.1 (C), 138.4 (C), 143.0 (C), 170.5 (CO); IR (film) 2930, 1747, 1599, 1495, 1455, 1159, 816, 696, 545 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{25}H_{35}N_2O_5S$ $[M + NH_4]^+$ 475.2261, found 475.2269.

*Synthesis of (+)-(3R,6S)-6-Butyl-1-N-tosyl-1,2,3,6-tetrahydropyridin-3-yl (2S)-methoxy-2-phenylacetate, **7d**. Method P.* An 88:12 mixture of alcohols **5b** and **6b** (18.8 mg, 0.06 mmol) prepared from **21a**, (+)-(*S*)-2-methoxy-2-phenylacetic acid (40.0 mg, 0.24 mmol), EDC·HCl (47 mg, 0.24 mmol) and DMAP (3.75 mg, 0.03 mmol) gave an 88:12 diastereomeric mixture of esters **7b** and **7d**. Alternatively, from **6b** (11.2 mg, 0.04 mmol) prepared from **5b** via Mitsunobu inversion, (+)-(*S*)-2-methoxy-2-phenylacetic acid (24.0 mg, 0.14 mmol), EDC·HCl (28.0 mg, 0.14 mmol) and DMAP (2.20 mg, 0.02 mmol) was obtained a 95:5 diastereomeric mixture of esters **7d** and **7e** that proved a 90% ee of **6b**. Purification by column chromatography (40% Et_2O-hexane) afforded **7d** as a clear oil (12.0 mg, 73%). Data for **7d**: R_f 0.38 (40% Et_2O-hexane); $[\alpha]^{20}_D$ +11.6 (*c* 0.66, $CHCl_3$); ^{1}H NMR, COSY (300 MHz, $CDCl_3$) δ 0.90 (t, 3 H, *J* = 6.9 Hz, CH_3), 1.25−1.44 (m, 4 H, CH_2), 1.56−1.63 (m, 2 H, CH_2), 2.39 (s, 3 H, CH_3 *p*-Tol), 2.94 (d, 1 H, *J* = 14.0, 9.9 Hz, H-2a), 3.38 (d, 3 H, *J* = 0.8 Hz, OCH_3), 4.12 (d, 1 H, *J* = 14.0, 6.3 Hz, H-2b), 4.25−4.27 (m, 1 H, H-6), 4.70 (s, 1 H, PhCH), 4.70−4.80 (m, 1 H, H-3), 5.30 (d, 1 H, *J* = 10.6 Hz, H-4), 5.72 (dddd, 1 H, *J* = 10.6, 3.9, 2.0, 0.7 Hz, H-5), 7.26 (d, 2 H, *J* = 8.3 Hz, *p*-Tol), 7.33−7.41 (m, 5 H, Ph), 7.70 (d, 2 H, *J* = 8.3 Hz, *p*-Tol); ^{13}C NMR, HSQC (75 MHz, $CDCl_3$) δ 13.9 (CH_3), 21.5 (CH_3 *p*-Tol), 22.5 (CH_2), 28.4 (CH_2), 33.9 (CH_2), 41.3 (C-2), 53.5 (C-6), 57.3 (OCH_3), 64.5 (C-3), 82.4 (PhCH), 124.8 (C-4), 126.9 (2 × CH *p*-Tol), 127.1 (2 × CH Ph), 128.7 (2 × CH Ph), 128.8 (CH Ph), 129.8 (2 × CH *p*-Tol), 131.5 (C-5), 135.8 (C), 137.7 (C), 143.5 (C), 169.9 (CO); IR (film) 2932, 1748, 1599, 1495, 1456, 1348, 1166, 1111, 996, 815 cm^{-1}; HRMS (ESI) *m*/*z* Calcd for $C_{25}H_{35}N_2O_5S$ $[M + NH_4]^+$ 475.2261, found 475.2255. Partial data for **7e** (from the crude mixture): ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.77 (d, 1 H, *J* = 14.1, 9.9 Hz, H-2a), 3.96 (dd, 1 H, *J* = 14.1, 5.9 Hz, H-2b), 5.47 (d, 1 H, *J* = 10.8 Hz, H-4).

■ ASSOCIATED CONTENT

Supporting Information

Spectral data (^{1}H NMR and ^{13}C NMR) for new compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b01307.

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Notes

The authors declare no competing financial interest.

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(18) A separable 50:50 mixture of **2** and **3** can also be prepared by addition of lithiated **A** to the related *p*-toluene sulfonimine.

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(21) (a) In some experiments **19b** was submitted to the Stille coupling as an 80:20 diastereomeric mixture; further chromatographic separation rendered uneventfully pure **20b**. (b) While (*E*)-1-sulfinyl-1-en-3-ynes were smoothly hydrogenated to the dienyl sulfoxides with Wilkinson's catalyst, the transformation of the related (*Z*) isomers was unsuccessful. To our knowledge this transformation is unprecedented to prepare functionalized 2-sulfinyl dienes such as **15**.

(22) Sequential [2,3]-sigmatropic rearrangement of **21f** followed by *N*-Boc deprotection to give **5n** was required to verify the diastereomeric ratio.

(23) A 40% ratio of the related isomeric vinyl sulfoxide was observed in the crude product ^{1}H NMR.

(24) A parallel behavior was observed for the related dihydropyran.

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(25) The corresponding *N*-unprotected amino dienes could be detected by a rapid ^{1}H NMR of the mixture.
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(28) Isomer *cis*-**6b**, isolated from treatment of **21a** with Cs_2CO_3 was derivatized with (*S*)-(+)-MPA to provide a practically 50/50 diastereomeric mixture of 2-methoxy-2-phenylacetates; this reveals an additional epimerization at C-6 for **6b** probably due to a ring-opening−closing sequence for **21a** under the reaction conditions.
(29) Variable amounts (12−36%) of (2,3)-regioisomers (2-butyl-1,2,3,6-tetrahydropyridin-3-ols) were observed in the crude reaction mixtures; this explains the reduced yields.
(30) Amino diene **15l** was also converted into **5j** by treatment with Et_2NH (10 equiv) at 90 °C over 16 h (38% yield).
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