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Stereocontrolled Addition of Scrambling *ortho*-Sulfinyl Carbanions: Easy Access to Homopropargylamines and α-Allenylamines

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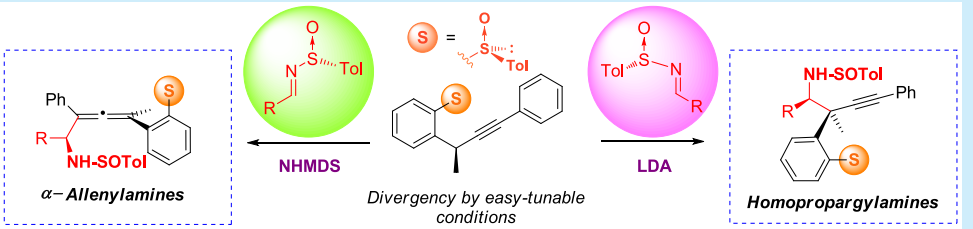

ABSTRACT: An unprecedented behavior of *ortho*-sulfinylpropargyl carbanions in the presence of optically active sulfinylimines affords two different families of compounds: this peculiar chemodivergency is importantly affected by the nature of the employed base, and assisted by the configuration of the electrophile, displaying no alteration in the stereocontrol of both reactions. α-Allenylamines are formed exclusively, using *R*-sulfinyl aldimines as electrophiles, while homopropargylamines result when *S*-sulfinyl aldimines are employed.

Homopropargyl amines hold a preferred position in organic synthesis, because of their versatility as building blocks in the synthesis of terpenoid derivatives and other biologically active compounds.[1] Meanwhile, allenyl derivatives in their optically active form have received great attention in the synthetic chemistry community, because of their ubiquitous presence among different natural products and pharmaceuticals.[2] However, the asymmetric construction of axially chiral allene derivatives and the design of acyclic molecules containing vicinal quaternary carbon centers represent some of the most challenging modern synthetic transformations. Unsurprisingly, a powerful arsenal of strategies that lead to these architectures continuously enriches the synthetic chemist's toolbox, as a consequence of its trending demand. According to the literature,[3a] the most invoked methodologies that enable the synthesis of enantio-enriched allenes consist of the resolution of racemates[3] and chirality transfer from optically pure propargyl derivatives,[4] among others.[5] Related to the present work, Yin and co-workers have described an asymmetric copper-catalyzed alkynylogous aldol addition of propargyl esters to aldehydes, giving access to the corresponding enantio-enriched α-allenyl alcohols.[6] Regarding the preparation of homopropargyl amines,[7] the most frequently employed procedures rely on the use of Schiff bases in the presence of propargyl or allenyl moieties.[7] In this regard, earlier this year, Qiu and Hu[8] reported an enantioselective multicomponent strategy, enabling the preparation of optically active homopropargyl amines.

In a different context, the use of optically active sulfoxides as chiral auxiliaries has been exploited over the last decades; this exploitation is due to their great stability and high stereocontrol in several synthetic transformations. Over the last years, our group has highlighted the peculiar behavior of the *ortho*-sulfinyl carbanions generated by the use of bases, such as LDA or diverse MHMDS, toward the stereocontrolled generation of new C−C single bonds between sterically hindered nucleophile−electrophile pairs.[9] Taking this information into account, we considered the possibility of taking advantage of the delicate equilibrium of *ortho*-sulfinyl propargyl carbanions, designing a chemodivergent procedure based on a remotely controlled activation, to selectively achieve the γ-functionalization (Scheme 1, pathway A, top) or the ε-functionalization (Scheme 1, pathway B, bottom) of the described benzyl-propargyl scaffolds in the presence of the same electrophile. Sulfinyl aldimines[10] were chosen as the amino source in this process, considering (a) its easy preparation, (b) their successful use in numerous asymmetric transformations, (c) the latent possibility of modulating the chiral information at the S atom, and (d) the facile reported

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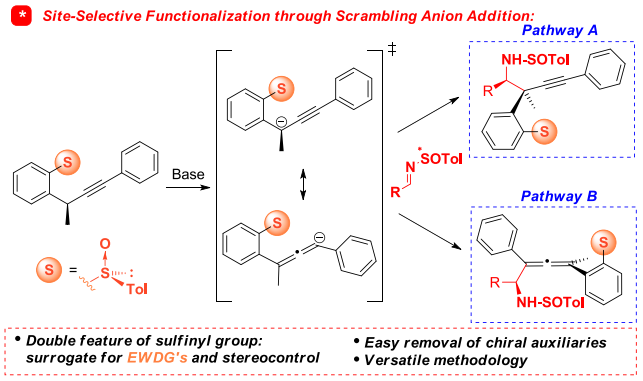
Scheme 1. Proposed Strategy



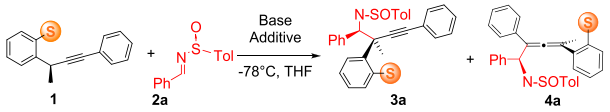
procedures to remove the chiral auxiliary after transformation, leading to two different families of amine derivatives.

Despite the brilliant strategies that are currently employed to synthesize α-allenylamines and homopropargyl amines, the lack of a general procedure that enables the selective preparation of each of these skeletons, starting from a common substrate, encouraged us to design a tunable methodology to tackle this challenge in a stereoselective fashion. Herein, we present the first chemodivergent functionalization of aryl propargyl moieties *remotely controlled* by a chiral sulfoxide to the best of our knowledge, which provides efficient access to two different families of amine-bearing compounds exhibiting high stereocontrol in both cases.

We started our studies with the optimization of the addition of alkyne **1** to aldimines **2**. In previous reports,[9] we have established the use of LDA as an efficient deprotonating reagent, triggering the formation of the corresponding benzyl carbanion. Therefore, we performed the reaction of **1** in front of aldimine (***S***)-**2a**, observing the formation of **3a** as the only product with an extraordinary diastereomeric ratio (Table 1, entry 1). Considering this result, and aiming to improve the yield, the temperature was increased. Despite multiple efforts, any attempt led to complete degradation of the starting materials, as −78 °C proved to be the optimal temperature to perform this reaction. Screening different metal−organic bases with lower coordinative character, namely, KHMDS and NHMDS, afforded **3a** in lower yields (Table 1, entries 2 and 3). In order to gather more information about the role of the cation (Li, Na, K), 12-crown-4 ether was evaluated as an additive, recovering the entire unreacted starting materials (Table 1, entry 4). Interestingly, the use of HMPA afforded **3a**, along with the corresponding allene, as a major product for the first time (Table 1, entry 5). This result suggested an important contribution from a plausible association between the base and the recently generated carbanion,[9] favoring the generation of one product over another. Subsequently, we decided to change the configuration of the aldimine to the corresponding (***R***)-**2a**, rendering **4a** with high diastereoselectivity when LHMDS or KHMDS were used (Table 1, entries 7 and 8), while no conversion with LDA was observed (Table 1, entry 6). Nevertheless, NHMDS was remarkably efficient, in terms of yield and diastereomeric ratio (dr) (compare entries 3 and 9 in Table 1), and, to our delight, complete suppression of **3a** was observed, showing a synergistic behavior between the base and the configuration of the imine. With these optimized conditions in our hands, we proceeded to explore the scope of the propargylation reaction (see Scheme 2).

As expected, the reaction was proven to work faster when electron-poor aromatic rings were present in the aldimines (**3c**, **3d**, and **3g**), in contrast to electron-rich ones. The experimental trials disclosed that, when bulkier substituents were used (**3e** and **3j**), the yield severely diminished, enhancing the formation of the allenyl adducts. Nonetheless, the diastereoselectivity remained unaltered in the desired products. Conversely, the use of a *tert*-butyl substituted aldimine suppressed the formation of the target amine. The reaction conditions also proved to be successful when using an aliphatic aldimine (*n*-Pr) leading to **3f**, and heterocyclic substrates also gave good results, giving rise to the products **3h** and **3i**. To our delight, compound **3a** resulted to be a crystalline solid that allowed its study by X-ray diffraction (XRD) in order to elucidate the absolute configuration of the two stereogenic centers, wherein the α-amino center has the *R* configuration and *S* at the benzylic position. Considering that the products were obtained under the same reaction conditions (see the Supporting Information for further details), we

Table 1. Optimization of the Reaction[a]



				Yield[b] (%)		
entry	base	2	additive	3a	4a	diastereomeric ratio, dr
1	LDA	(*S*)-**2a**	–	67	0	>98:<2
2	KHMDS	(*S*)-**2a**	–	<20	0	–
3	NHMDS	(*S*)-**2a**	–	40	15[c]	>98:<2
4[d]	LDA	(*S*)-**2a**	12-crown-4	<10	0	–
5[e]	LDA	(*S*)-**2a**	HMPA	22	43[c]	90:10
6	LDA	(*R*)-**2a**	–	0	0	–
7	LHDMS	(*R*)-**2a**	–	0	18	90:10
8	KHMDS	(*R*)-**2a**	–	0	45	90:10
9	NHMDS	(*R*)-**2a**	–	0	73	>98:<2

[a]Reaction conditions: **1** (0.1 mmol), **2** (0.12 mmol), base (0.12 mmol), 0.15 M. [b]Isolated yield is shown in all cases. The diastereomeric ratio of the major product is indicated and calculated by NMR crude. [c]Epimer of **4a** at the sulfur atom (*N*-S). [d]12-crown-4 (0.4 mmol). [e]HMPA (0.4 mmol),

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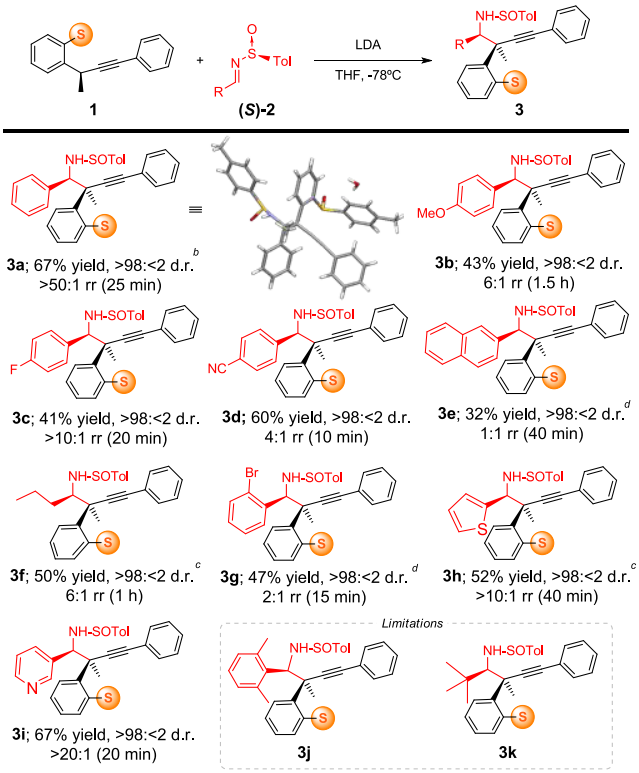
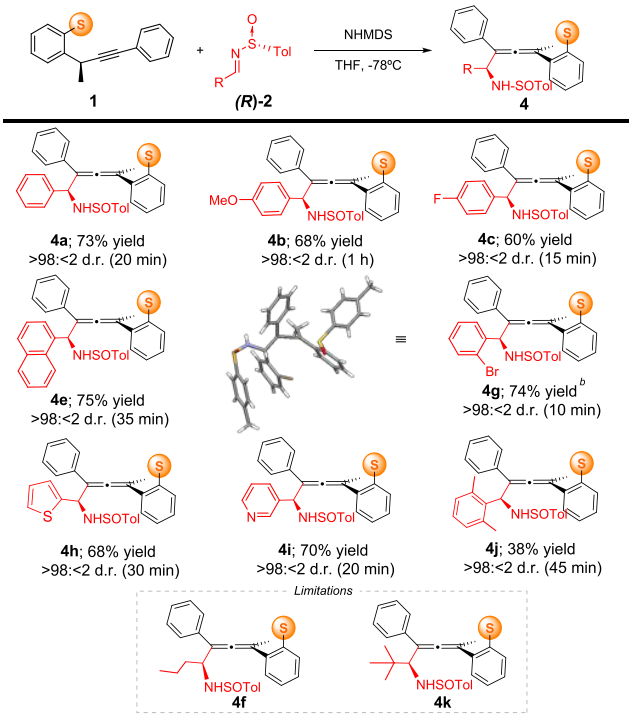
Scheme 2. Scope of the Propargylation Reaction[a]



[a]Reaction conditions: **1** (0.1 mmol), (*S*)-**2** (0.12 mmol), LDA (0.15 mmol), 0.015 M. Isolated yields shown in all cases, unless otherwise noted. Diastereomeric ratio (dr) and regioisomer ratio (rr) were measured via NMR. [b]Reaction was run in 1.2 mmol scale. [c]Yield measured by NMR crude.

Scheme 3. Scope of the Allenylation Reaction[a]



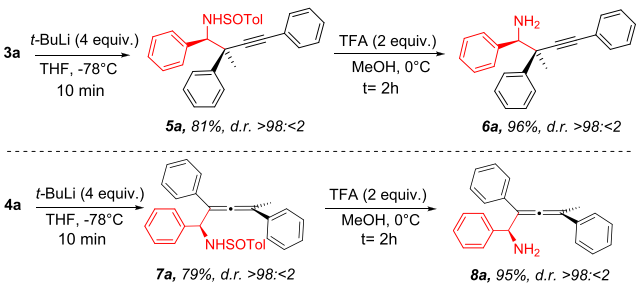
[a]Reaction conditions: **1** (0.1 mmol), (*R*)-**2** (0.12 mmol), NHMDS (0.15 mmol), 0.015 M. Isolated yields are shown in all cases, unless otherwise noted. Diastereomeric ratio (dr) values were measured by NMR, and the regioisomer ratio (rr) is not indicated; in all cases, these values were observed to be >50:1. [b]The reaction was run in 1.2 mmol scale.

assumed the same stereocourse of the reaction, and stereochemical outcome for the compounds.

After studying the synthetic scope of the above-described homopropargylation reaction, we replaced the chiral information of the electrophile by inverting the configuration from the (*S*)-*p*-tolylsulfinyl aldimines to their enantiomeric forms: (*R*)-*p*-tolylsulfinyl aldimines. Taking into account the previously screened parameters, we formed the diastereomeric enriched allenes. Various aromatic aldimines were shown to undergo the desired transformation, affording the products with high levels of diastereoselectivity (Scheme 3). In addition, substrates containing electron-donating substituents (**4b**) and electron-withdrawing substituents (**4c** and **4g**) were tested, proving that the reaction works smoothly, regardless of the electronic nature of the aryl motif. Moreover, the use of thienyl and pyridyl aldimines led to the corresponding allenes **4h** and **4i**, showing efficient results overall. Unfortunately, aliphatic aldimines were found to be unsuitable in this transformation (**4f** and **4k**), affording only complex reaction crudes. As previously stated, the use of bulky substituted aromatic rings produced deleterious results under the quaternization conditions. Therefore, in order to gather more information about this trend, a 2,6-disubstituted aromatic ring under these reaction conditions was tested, furnishing product **4j** in low yield, although maintaining high stereocontrol. To our convenience, suitable crystals of compound **4g** were obtained, allowing the determination of the architecture at the axially chiral allenes (R_a) and absolute configuration of the new stereogenic center via X-ray analysis.

In addition, to fulfill the role of the chiral auxiliaries in the described transformations, the treatment of **3a** and **4a** (independently) with *t*-BuLi furnished the cleavage of the sulfoxide at the aromatic ring, leading to **5a** and **7a**, respectively, in good yield (Scheme 4). Subsequently, the

Scheme 4. Removal of the Chiral Auxiliaries



acidolysis of the *N*-sulfinyl group gave the corresponding free amino group in each case: the homopropargylamine **6a** and the α-allenylamine **8a** in excellent yield, without observing erosion of the optical purity.[11]

In light of the experimental data presented herein, and taking into account previously described theoretical evidence,[9c,d] we propose a plausible mechanism for the present asymmetric transformations. The chemodivergent behavior of the generated benzyl carbanions derived from **1** may be correlated with the nature of the employed base (LDA vs NHMDS), unshackling a different disposition of the *ortho*-sulfinyl motif at an early transition state, and a "match–

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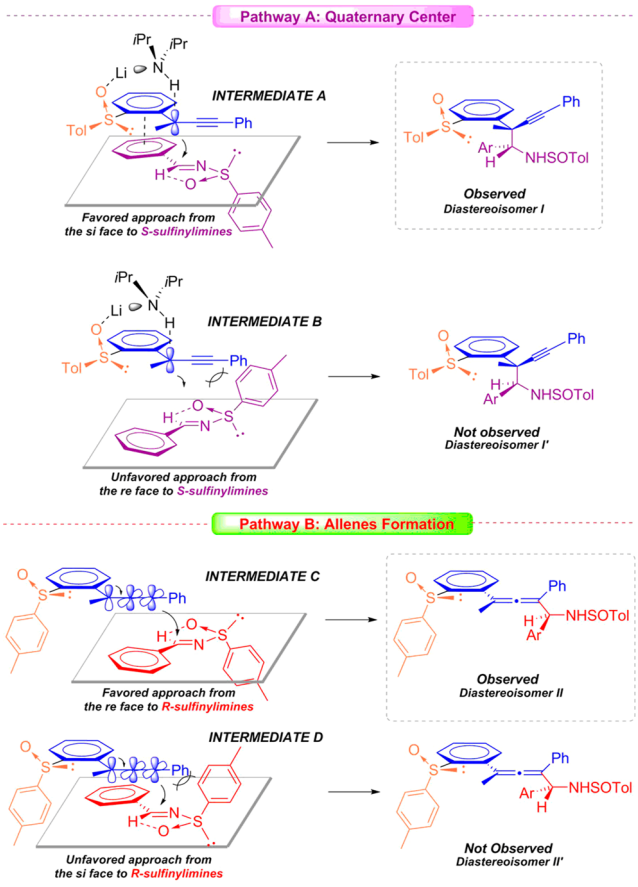
mismatch" relationship with the *N*-sulfinylimines. When lithium diisopropylamide is used, the resulting planar sp^2 benzyl carbanion is stabilized by an intramolecular association with the oxygen atom of the sufoxide (Scheme 5, Pathway A),

Scheme 5. Proposed Stereochemical Outcome of the Reactions



thus generating a coordination through the O—[LDA]$^+$—benzyl carbanion, that blocks the upper face of the planar system, favoring the approachment of the aldimines from the bottom face, as it was previously supported by DFT calculations.[9c] In the case where NHMDS is used, the resulting "naked" anion, is prompted to delocalize more easily (compared to the coordination proposal) throughout the aromatic ring and the triple bond system (Scheme 5, Pathway B). Therefore, the more compromised the charge is, the less reactive the anion will be. Because of this high conjugation phenomenom, the so-called "scrambling" anion is observed, enabling two activated sites, the propargylic C(sp^3) and the alkynylic C_β(sp), with the latter one being more prompt to perform the nucleophilic attack on the "matched" imine. This previous statement can be supported with the fact that, when using HMPA as an additive and LDA as a base, the major product of the reaction was the allenyl derivative. However, the dr was not entirely satisfactory, because of the "mismatched" imine used (recall Table 1, entry 5).

Regarding the high stereoselectivity observed for both families of products, we propose that, in the case of the homopropargyl amines (as shown in Scheme 5, intermediate **A**), the nucleophilic attack is executed by the *si* face of the aldimine, as the tolyl group of the electrophile is oriented at the bottom face, avoiding any type of steric hindrance. Moreover, a plausible $\pi-\pi$ stabilization could be contributing to this model (not feasible in intermediate **B**), leading to the formation of diastereoisomer **I**. This proposal is in accordance with the observed diminished yields when a bulkier substituent was employed (see Scheme 2, **3g**) and the failure when using the 2,6-disubstituted aromatic ring **3j** and the aliphatic *tert*-Bu **3k**. Regarding the allenylamines, the stereoselectivity can be explained mainly by a desymmetrization process of the two π-bonds forming the triple bond produced by the conjugation with the recently generated carbanion, because only the π-bond oriented in parallel, with respect to the orbital containing the lone electron pair, will be suitable to perform a nucleophilic attack. In order to avoid steric interactions between the nucleophile and the electrophile, the approach is favored by the *re* face of the imine (Scheme 5, intermediate **C**), leading to the observed diastereoisomer **II**. As a complementary reactivity test, both procedures were performed using the racemic sulfinylimine (±)-**2a** as an electrophile. When LDA was used, the yield of **3a** decreased from 67% (as depicted in Scheme 3) to 30%, isolating unreacted starting material **1** and optically enriched *N*-sulfinylimine (−)-**2a**. In agreement with the previous observation, NHMDS conducted to the formation of **4a** in 33% yield,[12] and, in this case, obtaining optically enriched (+)-**2a** with opposite configuration. This fact displays the importance of the right base−imine combination to achieve the targeted amine selectively.

To conclude, we have developed a stereocontrolled chemodivergent strategy that selectively enables the generation of propargylic or allenylic intermediates, starting from a common substrate in front of optically active sulfinylimines. The nature of the employed base proved to be crucial to trigger one activated species over another, because the configuration of the imine played a synergistic role to enhance the diastereoselectivity in the presented transformations. This method represents an elegant approach for the synthesis of two different families of amino compounds and is intended to inspire the development of new procedures to extend its scope and complete its limitations.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c00625.

Experimental details, supplementary figures, characterization of ^{1}H and ^{13}C spectra for all compounds and X-ray data for **3a** and **4g** (PDF)

Accession Codes

CCDC 1969083 and 1969084 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Cui, L.; Li, C.; Zhang, L. A Modular, Efficient, and Stereoselective Synthesis of Substituted Piperidin-4-ols. *Angew. Chem., Int. Ed.* **2010**, *49*, 9178−9181.

(2) For selected reviews, see: (a) Hoffmann-Röder, A.; Krause, N. Synthesis and Properties of Allenic Natural Products and Pharmaceuticals. *Angew. Chem., Int. Ed.* **2004**, *43*, 1196−1216. (b) Rivera-Fuentes, P.; Diederich, F. Allenes in Molecular Materials. *Angew. Chem., Int. Ed.* **2012**, *51*, 2818−2828. (c) Lu, T.; Lu, Z.; Ma, Z.-X.; Zhang, Y.; Hsung, R. P. Allenamides: A Powerful and Versatile Building Block in Organic Synthesis. *Chem. Rev.* **2013**, *113*, 4862−4904. (d) Ye, J.; Ma, S. Palladium-Catalyzed Cyclization Reactions of Allenes in the Presence of Unsaturated Carbon-Carbon Bonds. *Acc. Chem. Res.* **2014**, *47*, 989−1000.

(3) For selected examples, see: (a) Wan, B.; Ma, S. Enantioselective Decarboxylative Amination: Synthesis of Axially Chiral Allenyl Amines. *Angew. Chem., Int. Ed.* **2013**, *52*, 441−445. (b) Wang, Y.; Zhang, W.; Ma, S. A Room- Temperature Catalytic Asymmetric Synthesis of Allenes with ECNU-Phos. *J. Am. Chem. Soc.* **2013**, *135*, 11517−11520.

(4) For selected examples, see: (a) Ohmiya, H.; Yokobori, U.; Makida, Y.; Sawamura, M. General Approach to Allenes through Copper-Catalyzed γ-Selective and Stereospecific Coupling between Propargylic Phosphates and Alkylboranes. *Org. Lett.* **2011**, *13*, 6312−6315. (b) Pu, X.; Ready, J. M. Direct and Stereospecific Synthesis of Allenes via Reduction of Propargylic Alcohols with $Cp_2Zr(H)Cl$. *J. Am. Chem. Soc.* **2008**, *130*, 10874−10875. (c) Lo, V. K-Y.; Zhou, C.-Y.; Wong, M.-K.; Che, C.-M. Silver(I)- mediated highly enantioselective synthesis of axially chiral allenes under thermal and microwave-assisted conditions. *Chem. Commun.* **2010**, *46*, 213−215. (d) Yang, M.; Yokokawa, N.; Ohmiya, H.; Sawamura, M. Synthesis of Conjugated Allenes through Copper-Catalyzed γ-Selective and Stereospecific Coupling between Propargylic Phosphates and Aryl- or Alkenylboronates. *Org. Lett.* **2012**, *14*, 816−819.

(5) For pioneering works, see: (a) Elsevier, C. J.; Vermeer, P.; Gedanken, A.; Runge, W. Synthesis and Absolute Configurations of Halogenoallenes. *J. Org. Chem.* **1985**, *50*, 364−367. (b) Elsevier, C. J.; Vermeer, P. Synthesis and Stereochemistry of Allenes. Part 3. Highly Stereoselective Synthesis of Chiral Alkyl Allenes by Organocopper(I)-Induced anti 1,3-Substitution of Chiral Propynyl Esters. *J. Org. Chem.* **1989**, *54*, 3726−3730. For recent selected examples, see: (c) Hoffmann-Röder, A.; Krause, N. Enantioselective Synthesis of and with Allenes. *Angew. Chem., Int. Ed.* **2002**, *41*, 2933−2935. (d) Hölzl-Hobmeier, A.; Bauer, A.; Silva, A. V.; Bach, T.; Huber, S. M.; Bannwarth, C. Catalytic Deracemization of Chiral Allenes by Sensitized Excitation with Visible Light. *Nature* **2018**, *564*, 240−243. (e) Isomura, M.; Petrone, D. A.; Carreira, E. M. Coordination-Induced Stereocontrol over Carbocations: Asymmetric Reductive Deoxygenation of Racemic Tertiary Alcohols. *J. Am. Chem. Soc.* **2019**, *141*, 4738−4748.

(6) (a) Zhong, F.; Xue, Q.-H.; Yin, L. Construction of Chiral 2,3-Allenols through Copper(I)-Catalyzed Asymmetric Direct Alkynylogous Aldol Reaction. *Angew. Chem., Int. Ed.* **2020**, *59*, 1562−1566. For selected examples, see: (b) *Modern Allene Chemistry*; Krause, N., Hashmi, A. S. K., Ed.; Wiley−VCH: Weinheim, Germany, 2004. (c) Burks, H. E.; Liu, S.; Morken, J. P. Development, Mechanism, and Scope of the Palladium-Catalyzed Enantioselective Allene Diboration. *J. Am. Chem. Soc.* **2007**, *129*, 8766−8773. (d) Zbieg, J. R.; McInturff, E. L.; Leung, J. C.; Krische, M. J. Amplification of Anti-Diastereoselectivity via Curtin-Hammett Effects in Ruthenium-Catalyzed Hydrohydroxyalkylation of 1,1-Disubstituted Allenes: Diastereoselective Formation of All-Carbon Quaternary Centers. *J. Am. Chem. Soc.* **2011**, *133*, 1141−1144. (e) Cooke, M. L.; Xu, K.; Breit, B. Enantioselective Rhodium-Catalyzed Synthesis of Branched Allylic Amines by Intermolecular Hydroamination of Terminal Allenes. *Angew. Chem., Int. Ed.* **2012**, *51*, 10876−10879. (f) Wu, H.; Haeffner, F.; Hoveyda, A. H. An Efficient, Practical and Enantioselective Method for Synthesis of Homoallenylamides Catalyzed by and Aminoalcohol-Derived, Boron-Based Catalyst. *J. Am. Chem. Soc.* **2014**, *136*, 3780−3783.

(7) For catalytic enantioselective synthesis of homopropargylamines, see: (a) Kagoshima, H.; Uzawa, T.; Akiyama, T. Catalytic, Enantioselective Propargyl- and Allenylation Reactions of α-Imino Ester. *Chem. Lett.* **2002**, *31*, 298−299. (b) Wisniewska, H. M.; Jarvo, E. R. Enantioselective Silver-Catalyzed Propargylation of Imines. *Chem. Sci.* **2011**, *2*, 807−810. (c) Vieira, E. M.; Haeffner, F.; Snapper, M. L.; Hoveyda, A. H. A Robust, Efficient, and Highly Enantioselective Method for Synthesis of Homopropargyl Amines. *Angew. Chem., Int. Ed.* **2012**, *51*, 6618−6621. (d) Guo, T.; Song, R.; Yuan, B. H.; Chen, X. Y.; Sun, X.; Lin, G.-Q. Highly Efficient Asymmetric Construction of Quaternary Carbon-containing Homoallylic and Homopropargylic Amines. *Chem. Commun.* **2013**, *49*, 5402−5404. (e) Yuan, B.-H.; Zhang, Z.-C.; Liu, W.-J.; Sun, X.-W. A Highly Practical Approach to Chiral Homoallylic-homopropargylic Amines via Aza-Barbier Reaction. *Tetrahedron Lett.* **2016**, *57*, 2147−2151.

(8) Yu, S.; Hua, R.; Fu, X.; Liu, G.; Zhang, D.; Jia, S.; Qiu, H.; Hu, W. Asymmetric Multicomponent Reactions for Efficient Construction of Homopropargyl Amine Carboxylic Esters. *Org. Lett.* **2019**, *21*, 5737−5741.

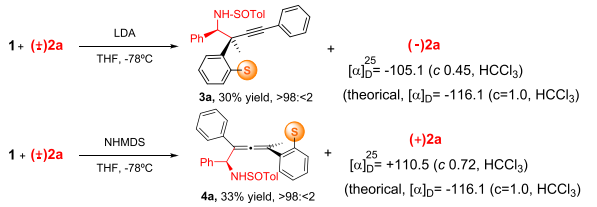
(9) For recent examples, see: (a) Rodríguez, R. I.; Ramírez, E.; Yuste, F.; Sánchez-Obregón, R.; Alemán, J. Asymmetric Synthesis of Secondary and Tertiary Propargylic Alcohols by Umpolung of Acetylenic Sulfones and ortho-Sulfinyl Carbanions. *J. Org. Chem.* **2018**, *83*, 1940−1947. (b) Rodríguez, R. I.; Ramírez, E.; Fernández-Salas, J. A.; Sánchez-Obregón, R.; Yuste, F.; Alemán, J. Asymmetric [2,3]-Wittig Rearrangement: Synthesis of Homoallylic, Allenylic, and Enynyl α-Benzyl Alcohols. *Org. Lett.* **2018**, *20*, 8047−8051. For open

and closed conformations see: (c) Arroyo, Y.; Meana, A.; Sanz-Tejedor, M. A.; Alonso, I.; García Ruano, J. L. 2-(*p*-Tolylsulfinyl)-benzyl Halides as Efficient Precursors of Optically Pure *trans*-2,3-Disubstituted Aziridines. *Chem. - Eur. J.* **2010**, *16*, 9874−9883. (d) García Ruano, J. L.; Martín-Castro, A. M.; Tato, F.; Torrente, E.; Poveda, A. M. Stereodivergent Quaternization of 2-Alkyl-2-*p*-tolylsulfinylacetonitriles: NMR Spectroscopic Evidence of Planar and Pyramidal Benzylic Carbanions. *Chem. - Eur. J.* **2010**, *16*, 6317−6325.

(10) (a) Davis, F. A.; Reddy, R. E.; Szewczyk, J. M.; Reddy, G. V.; Portonovo, P. S.; Zhang, H.; Fanelli, D.; Reddy, T.; Zhou, P.; Carroll, P. J. Asymmetric Synthesis and Properties of Sulfinimines (Thiooxime S-Oxides). *J. Org. Chem.* **1997**, *62*, 2555−2563. (b) Davis, F. A.; Zhang, Y.; Andemichael, Y.; Fang, T.; Fanelli, D. L.; Zhang, H. Improved Synthesis of Enantiopure Sulfinimines (Thiooxime S-Oxides) from *p*-Toluensulfinamide and Aldehydes and Ketones. *J. Org. Chem.* **1999**, *64*, 1403−1406. (c) Davis, F. A.; Chen, B. C. In *Stereoselective Syntheses*; Helmchen, G., Hoffman, R. W., Mulzer, J., Schaumann, E., Houben-Weyl, G., Eds.; Thieme Verlag: Stuttgart, Germany, 1995; Chapter E21e, Part 4, p 4497. (d) Davis, F. A.; ThimmaReddy, R.; Weismiller, M. C. (−)-. Alpha, alpha.-Dichlorocamphorsulfonyloxaziridine: a Superior Reagent for the Asymmetric Oxidation of Sulfides to Sulfoxides. *J. Am. Chem. Soc.* **1989**, *111*, 5964−5965. (e) Davis, F. A.; Reddy, R. E.; Szewczyk, J. M. Asymmetric Synthesis of (*R*)-(+)-.beta.-Phenylalanine from (*S*)-(+)-Benzylidene-*p*-toluenesulfinamide. Regeneration of the Sulfinimine Precursor. *J. Org. Chem.* **1995**, *60*, 7037−7039. (f) Ellman, J. A.; Owens, T. D.; Tang, T. P. *N-tert*-Butanesulfinyl Imines: Versatile Intermediates for the Asymmetric Synthesis of Amines. *Acc. Chem. Res.* **2002**, *35*, 984−995. (g) García Ruano, J. L.; Alemán, J.; Soriano, J. F. Facile Synthesis of Optically Pure 1,2-Diaryl (and 1-Alkyl-2-aryl) Ethyl and Propylamines. *Org. Lett.* **2003**, *5*, 677−680. (h) Davis, F. A. Adventures in Sulfur-Nitrogen Chemistry. *J. Org. Chem.* **2006**, *71*, 8993−9003. (i) Janssen, G. V.; Janssen, E.; Vande Velde, C. M. L.; Ehlers, A. W.; Slootweg, J. C.; Ruijter, E.; Lammertsma, K.; Orru, R. V. A. Chemoselective Addition of Isocyanides to *N-tert*-Butanesulfinimines. *Org. Lett.* **2014**, *16*, 5116−5119.

(11) Steps order of the transformation was inverted, looking for the best global yield from **3a** and **4a** to **6a** and **8a**, respectively. It was found that the most suitable order is the one presented in the manuscript in terms of yield. Note that, in both cases, the diastereoselectivity is preserved.

(12) Standard conditions were employed when performing these tests (0.1 mmol of **1**, and 0.12 mmol of *rac*-**2a**). It was possible to recover the unreacted **2a** after flash column chromatography, in both cases with optical rotation nearly to the optically pure *N*-sulfinylimine, indicating that a kinetic resolution process has occurred. See: Davis, F. A.; Reddy, R. E.; Szewczyk, J. M.; Portonovo, P. S. *Tetrahedron Lett.* **1993**, *34*, 6229−6232.



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