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Note

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Reformatsky Reaction to Alkynyl N-*tert*-Butanesulfinyl Imines: Lewis Acid Controlled Stereodivergent Synthesis of β-Alkynyl-β-Aminoacids

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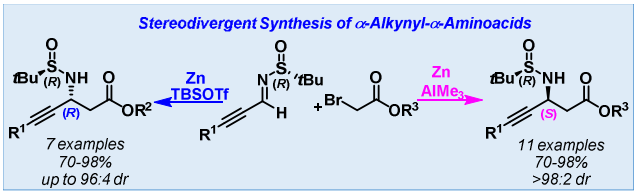
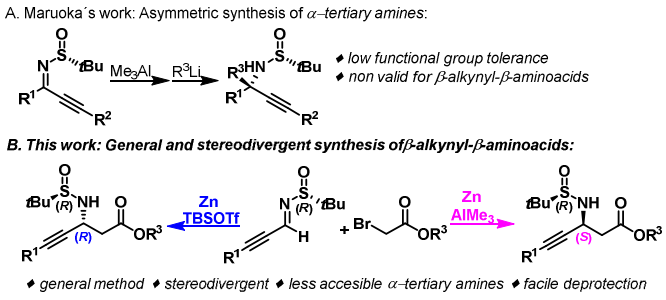
KEYWORDS. Asymmetric synthesis, N-sulfinyl imines, β-aminoacids, Reformatsky reaction, stereodivergent



ABSTRACT: A highly diastereoselective Refortmatsky reaction to *N-tert*-butanesulfinyl propargylaldimines and ketimines is presented. The reaction proceeded with excellent yields and diastereoselectivities provided by the sulfinyl group in the presence of Me3Al. The use of TBSOTf as Lewis acid promoter switched the sense of the stereoinduction. Thus, this methodology allowed the stereodivergent asymmetric synthesis of *β*-alkynyl *β*-amino acid derivatives, from the same sulfinyl configuration by simply changing the Lewis acid promoter.

The development of efficient and practical strategies for the stereoselective construction of privileged structures is an ongoing objective and still holds a preferred position in organic chemistry research.[1] *β*-Amino acids constitute a fundamental class of building-blocks for the synthesis of significant molecules with interesting pharmacological applications, showing hypoglycemic and antiketogenic properties as well as antibacterial and antifungal activities.[2] Besides their intrinsic relevance, β-amino acids are precursors for *β*-lactams, which are important building blocks present in a large number of antibiotics.[3] On the other hand, the corresponding *β*-peptides display high tendency towards the formation of stable secondary structures of notable biological transcendence.[4] Moreover, *β*-amino acids have been widely used in modern organic chemistry as chiral templates for asymmetric synthesis.[2a] Therefore, several groups have focused their attention on the development of efficient methods for the asymmetric synthesis of *β*-amino acids.[2a,5] Addition to imines,[5] including *N*-sulfinyl imines,[6] of ester enolates or silyl ketene acetals[4g,4i,4k,5f] and Reformatsky-type reagents[7] have been the approaches of choice to face this challenge. Although significant efforts have been devoted to synthesis of *β*-amino acids, a number of challenges in connection with its substrate generality still persist, being the synthesis of challenging *γ,δ*–alkynyl-*β*-amino acid derivatives one of them. Propargyl *β*-amino acids are a special class of non-proteinogenic amino acids. In addition to potentially changing biological properties , these amino acids are key intermediates for interesting compounds with pharmacological activity, such as Xemilofiban, which has proven to be a platelet aggregation inhibitor that can prevent ischemia, heart attacks and other major adverse cardiac events.[8] In this regard, asymmetric synthesis of propargylamines have been well established,[9] featuring the alkynylation of imines as the preferred approach. Despite remarkable progress, the enolizable moiety makes the synthesis of related *γ,δ*-alkynyl-*β*-aminoacids[10] inaccessible following this strategy. To circumvent this limitation, the use of alkynyl imines or their precursors[11] as substrates in Mannich-type stereoselective reactions has emerged in the last decades.[12] Snapper and Hoveyda described an efficient silver-catalyzed asymmetric Mannich reaction with chiral ligands of silyl ketene acetal, to *N-ortho*-methoxyphenyl alkynyl imine.[12a] However, the *ortho*-methoxyphenyl directing group is difficult to remove, requiring an oxidative procedure incompatible with many functional groups. The diastereoselective synthesis of *β*-alkynyl β-amino acids has also been addressed using a chiral auxiliary in either the imine ((*S*)-phenylglycinol)[12c] or the nucleophile (chiral phenol derivative).[12d] Both methods only disclosed the reactivity of one

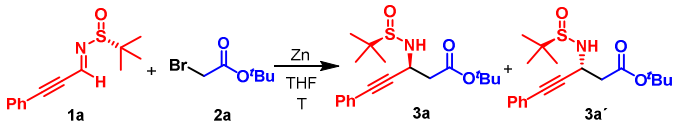
α,β-unsaturated imine and a multistep oxidative cleavage protocol for the amino acid deliverance is required. Recently, Maruoka and coworkers have followed a similar approach pursuing the synthesis of very challenging chiral α-tertiary amines by using alkynyl sulfinyl ketimines as platforms, though β-amino acids synthesis is not compatible with this methodology (A, Scheme 1).[13] Taking all these precedents into consideration, the development of an efficient and general method for the asymmetric synthesis of β-alkynyl β-amino acid derivatives would be highly desirable. The great progress in the field of asymmetric synthesis over the past decades has allowed high control over the selectivity of a given reaction. However, access to the opposite diastereoisomer is not usually possible by using the same set of starting materials under similar reaction conditions. Thus, development of new methodologies that allow access to both stereoisomers by using the same configuration of the starting materials are highly desirable.[5f,14] Herein, we describe a Reformatsky reaction to readily accessible *N*-sulfinyl alkynyl imines as chiral templates. Facile sulfinyl cleavage would lead to the synthesis of enantiopure β-alkynyl β-amino acid derivatives. This straightforward approach gives access to both stereoisomers of the desired γ,δ-alkynyl β-amino acids using the same configuration at the sulfur atom of the sulfinyl group. This stereodivergent approach relies on the use of different Lewis acids (B, Scheme 1), which efficiently switches the reactivity of the imine.



Scheme 1. Previous works (A), present work (B).

We began our studies investigating the Reformatsky reaction of the α-bromo ester derivative **2a** and the alkynyl *N*-sulfinyl imine bearing a phenyl ring **1a** as model substrate (Table 1). After optimizing the amount of Reformatsky reagent (**2a**) and the temperature (entries 1-6), the reaction showed a good efficiency when carried out at -10 °C in presence of 4 equivalents of the α-bromo ester (entry 6). At -40 °C the reaction did not take place and the starting imine was recovered (entry 7). Gratifyingly, in the presence of AlMe3 at -78 °C,[15] the desired γ,δ–alkynyl-β-amino ester derivative **3a** was obtained with complete diastereoselectivity (>98:2) in 88% isolated yield (entry 9).

Table 1. Reformatsky reaction with alkynyl sulfinyl imines: Optimization.[a]



Ent	L. Acids (eq.)	2a (eq.)	T (°C)	t (h)	Conv.[b,c] (%)	d.r.[b] (3a:3a')
1	-	2.5	rt	1.25	100 (75)	87:13
2[d]	-	2	0	15	-	-
3	-	2.5	0	4	90	-
4	-	3.5	0	20	100 (72)	90:10
5	-	3.5	-10	5	20	-
6	-	4	-10	5	100 (84)	91:9
7	-	4	-40	18	-	-
8	$Cu(OTf)_2$ (1.1)	4	rt	22	-	-
9	$AlMe_3$ (1.1)	**4**	**-78**	**3**	**100 (88)**	**>98:2**
10	$BF_3{\cdot}OEt_3$ (2.1)	4	rt	22	100 (80)	86:14
11	TMSOTf (2.1)	4	-78	6	65 (62)	14:86
12	TBSOTf (2.1)	**4**	**-78**	**6**	**100 (86)**	**7:93**

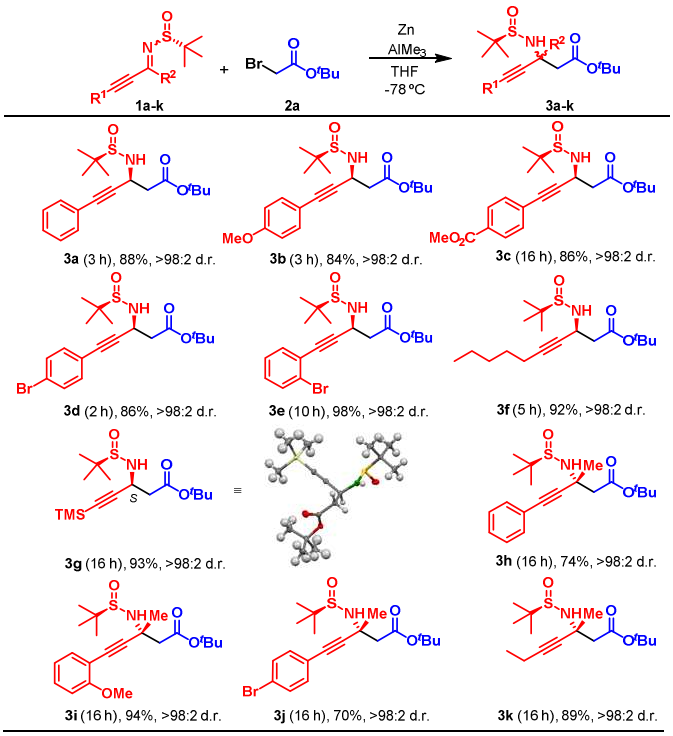
[a] All reactions were carried out with 1a (0.1 mmol) and Zn (0.4 mmol) in 0.25 mL of THF. [b] Determined by ^{1}H-NMR. [c] Isolated yield of the major diastereoisomer in brackets. [d] Reaction carried out with 2 equiv. of Zn.

With the aim of developing a new stereodivergent procedure, which would allow us to synthesize both enantiomers of the corresponding alkynyl β-amino acid derivative starting from the same configuration at the sulfinyl group, we used a highly oxophilic Lewis acid which could potentially modify the transition state through which the reaction takes place. Consequently, when the reaction was performed in the presence of $BF_3{\cdot}OEt_2$, compound with the *S* configuration (**3a**) was still obtained as major diastereoisomer (entry 10). TMSOTf reverses the selectivity of the reaction, leading to *R*-configured isomer with a reasonably high stereocontrol (entry 11). To our delight, when a more sterically hindered silyl derivative was used,

the diastereoselectivity was improved up to 93:7, since the facial discrimination increased as well (entry 12).

After optimizing the reaction conditions, we studied the scope of the reaction regarding the synthesis of the *S* isomer. The results were summarized in Scheme 1. Firstly, different substitution in the aryl unit was considered. Arenes bearing an electron-rich (OMe) and an electron-deficient group (CO_2Me) as well as a bromo group in both *ortho* and para position were well tolerated and the desired products were obtained with complete diastereoselectivity and from good to excellent yields (**3b**-**3e**). Aliphatic alkynyl imine **1f** led to the *β*-amino ester product in high yield and only one diastereomer was observed (**3f**). Similarly, imine **1g**, bearing a TMS-substituted alkyne, underwent efficient Reformatsky reaction to give versatile product **3g**.

Table 2. Highly diastereoselective Reformastky reaction to alkynyl *N*-sulfinyl imines: AlMe3.[a]

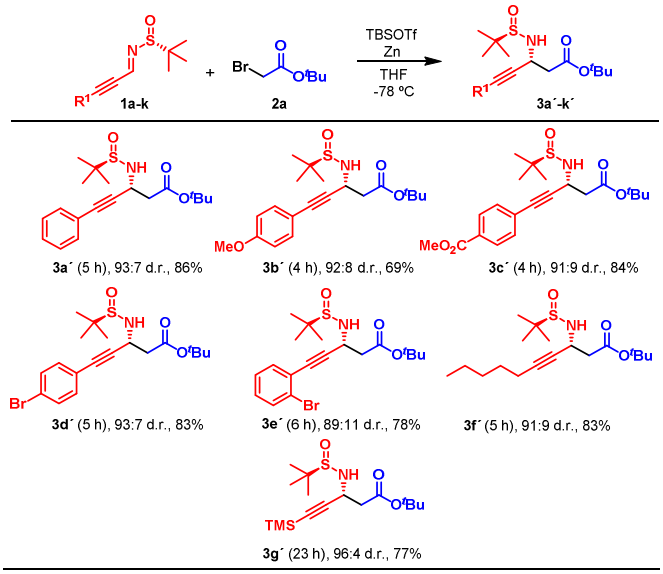


[a] All reactions were carried out with **1** (0.1 mmol), **2a** (0.4 mmol), Zn (0.4 mmol) and AlMe3 (0.11 mmol) in 0.25 mL of THF. The diastereomeric ratio was determined by ^{1}H NMR. Isolated yields.

In addition to sulfinyl aldimines, the corresponding less reactive and challenging ketimines proved to be suitable substrates in the Me3Al-promoted Reformatsky reaction. Thus, differently substituted aryl and alkyl terminus acetylene ketimines led to the desired *β*-amino ester with a α-tertiary amine moiety with complete diastereselectivity (**3h**-**3k**). It should be noted, that chiral α-tertiary amines are fundamental and recurrent motifs in naturally occurring and synthetic bioactive compounds and their synthesis still stands as an important challenge in organic chemistry.[13a] To the best of our knowledge, the synthesis of such *β*-alkynyl *β*-tertiary amino acid derivatives has never been described. The absolute configuration of the asymmetric centers of **3g** were unequivocally assigned as (*Rs*, *S*) by X-ray crystallographic analysis.[16]

We then studied the Reformatsky reaction to alkynyl *N*-sulfinyl imines mediated by TBSOTf in order to evaluate the scope of reaction (Table 3). Regarding the aldimines, these new reaction conditions tolerated electron-rich (OMe) and electron-deficient groups (CO_2Me) as well as a bromo substituent in both ortho and para position of the phenyl group, leading to the desired *β*-amino ester products in good yields and diastereoselectivities (**3a'**-**e'**). Imines bearing alkyl and TMS substituted alkynes underwent efficient Reformatsky reaction, to give adducts **3f'** and **3g'** in good yields and very good diastereoselectivities. No reaction was observed with methyl ketimine **1h**.

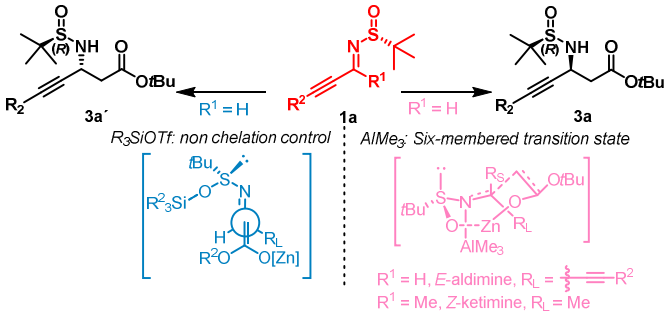
Table 3. Highly diastereoselective Reformastky reaction to alkynyl *N*-sulfinyl imines: TBSOTf.[a]



[a] All reactions were carried out with **1** (0.1 mmol), **2a** (0.4 mmol), Zn (0.4 mmol) and TBSOTf (0.21 mmol) in 0.25 mL of THF. The diastereomeric ratio was determined by ^{1}H NMR. Isolated yields of the major diastereoisomer.

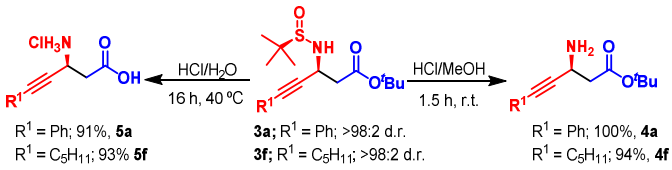
We propose that the Reformatsky reaction proceeded *via* a chair-like transition state[17] where both the bulky *tert*-butyl ester group and the substituent in the sulfinyl imine could occupy equatorial positions. The reaction with aldimines (*E* isomer) and ketimines (*Z* isomer) takes place through a common transition state, although the *E*/*Z* isomeric distribution of the starting imine should be considered. Me3Al would be simply acting as Lewis acid, enhancing the reactivity of the imine.[18] In this context, Me3Al could also be involve in differentiating the two Me3Al imine isomers reaction rates, which are in rapid equilibrium.[13a,17a,19] Highly oxophilic Lewis acid (R3SiOTf) could potentially coordinate to the oxygen atom of the sulfinyl group, disengaging the six-membered chair-like

transition state. Thus, the reaction would take place under non-chelation control. The *tert*-butyl group of the sulfinyl group would direct the approach of the nucleophile to the less hindered re-face of the imine, leading to the opposite configuration (*R*) at the carbon atom that bears the amino group (Scheme 2).



Scheme 2. Proposed transition states for AlMe3- and R3SiOTf-mediated Reformatsky reactions

As mentioned above, apart from the high stereoinduction provided, the *tert*-butane sulfinyl group is an easily removable auxiliary (Scheme 3). Treatment of sulfinamides **3a** and **3f** with HCl in methanol allows the efficient deprotection to the amino ester (**4a** and **4f**) in high yields without erosion in the enantiomeric purity, whereas deliverance of the optically pure *β*-alkynyl *β*-amino acid (**5a** and **5f**) was efficiently accomplished in the presence of H2O.



Scheme 3. Sulfinyl group cleavage. Synthesis of β-alkynyl β-amino esters and β-amino acids

In conclusion, we have described a highly diastereoselective Reformatsky reaction to enantiopure alkynyl *N*-sulfinylimines. The methodology tolerates a reasonably high range of aldimines and ketimines bearing differently substituted alkynyl groups. In addition, by simply changing the Lewis acid promoter, the reactivity switched, and allowed to prepare selectively both epimers from *N*-sulfinylimines with the same configuration at the sulfur atom. Finally, the sulfinyl group can be easily removed, leading to the desired enantiomerically pure *β*-alkynyl *β*-amino acids.

EXPERIMENTAL SECTION

General considerations: All solvents were dried using activated 4Å molecular sieves and stored under nitrogen. 4Å molecular sieves, 1.6-2.5 mm of particle size, were activated by microwave (700W) (3 x 60 sec) and subsequent cycles of vacuum/nitrogen. For thin layer chromatography (TLC) silica gel plates with fluorescence indicator 254 nm were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of potassium permanganate in water followed by heating. Flash column chromatography was performed using silica gel (230−400 mesh) and compressed air. Hexane, ethyl acetate, dichloromethane and diethyl ether for flash chromatography were acquired from commercial sources and were used without previous purification. Optical rotation was recorded in cells with 10 cm path length; the specific solvents and concentrations (in g/100 mL) are indicated. NMR spectra were acquired on a Bruker Avance 300 MHz spectrometer, running at 300, 75 and 282 MHz for ^{1}H, ^{13}C and ^{19}F respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals (CDCl3, 7.26 ppm for ^{1}H NMR and 77.2 ppm for ^{13}C NMR respectively). ^{13}C NMR spectra were acquired on a broad band decoupled mode. The following abbreviations are used to describe peak patterns when appropriate: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), bs (broad singlet). Mass spectra (MS) were obtained by ESI ionization mode. High resolution mass spectra (HRMS) were performed by ESI ionization mode using a time of-flight (TOF) mass analyzer, as indicated for each compound. Zn, dust; <10μ (2.5g). Zinc was previously activated by washing successively with HCl 5% (3 x 3ml), H_2O (3 x 3ml), acetone (3 x 3 ml) and anhydrous Et_2O (3 x 3 ml). Then, it was carefully dried under high vacuum.

***N*-sulfinyl imine synthesis.**

General procedure A: Synthesis of N-sulfinyl aldimines (1a-g): To a solution of (*R*)-*tert*-butane sulfinamide (2.5 mmol) in anhydrous THF (6.5 mL) under argon atmosphere, a solution of the corresponding aldehyde (3 mmol) in anhydrous THF (1 mL) was added. Subsequently, $Ti(OEt)_4$ (10 mmol) was added and the mixture was stirred at 40-45 ºC. After 16h, MeOH (2.5 mL) and a solution of saturated $NaHCO_3$ were added until formation of a yellow precipitate was observed. The crude of reaction was filtered over celite, dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by flash-column chromatography.

General procedure B. Synthesis of N-sulfinyl ketimines (1h-1k): To a solution of (*R*)-*tert*-butane sulfinamide (0.43 mmol) in anhydrous CH_2Cl_2 (5.6 mL) under argon atmosphere, a solution of the corresponding ketone (0.52 mmol) in anhydrous CH_2Cl_2 (1mL) was added. Subsequently, $Ti(OEt)_4$ (1.7 mmol) was added and the mixture was heated at reflux. After 4 hours $Ti(OEt)_4$ (1.72 mmol) was added. After 16h, MeOH (2.5 mL) and a solution of saturated $NaHCO_3$ were added until a formation of yellow precipitate was observed. The crude of reaction was filtered through celite, dried with $MgSO_4$ and the solvent was evaporated under reduced pressure. The residue was purified by flash-column chromatography.

(R_S,E)-2-Methyl-N-(3-phenylprop-2-ynylidene)propane-2-sulfinamide (**1a**)

Following the general procedure A, 3-phenylpropiolaldehyde (3 mmol), gave **1a** (636 mg, 2.73 mmol, 91% yield). Eluent: *n*-hexane/AcOEt (8/1). $[\alpha]^{20}_{D}$ -242.0 (*c* 1.00, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.03 (s, 1H), 7.60-7.57 (m, 2H), 7.46-7.35 (m, 3H), 1.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 147.8, 132.6, 130.4, 128.6, 120.9, 100.1, 85.6, 58.4, 22.6. IR (NaCl): 2961, 2868, 2204, 1727, 1563, 1364, 1179, 1090 cm^{-1}. MS (ESI+) *m/z* (%): 489

(2M+Na) $^+$ (61), 256 $(M+Na)^+$ (87), 234 $(M+H)^+$ (37), 178 (100), 115 (35). HRMS (ESI): *m/z* calcd for $C_{13}H_{16}NOS$ $[M+H]^+$: 234.0947, found: 234.0949.

(R_S,E)-N-[3-(4-Methoxyphenyl)prop-2-ynylidene]-2-methylpropane-2-sulfinamide (**1b**)

Following the general procedure A, 3-(4-methoxyphenyl)propiolaldehyde (3 mmol), gave **1b** (731 mg, 2.76 mmol, 92% yield). Eluent: *n*-hexane/AcOEt (6/1). $[\alpha]^{20}_D$ -168.5 (*c* 0.82, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.01 (s, 1H), 7.54-7.51 (m, 2H), 6.90-6.87 (m, 2H), 3.83 (s, 3H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 161.4, 147.9, 134.6, 114.4, 113.2, 101.2, 85.3, 58.3, 55.4, 22.6. IR (NaCl): 2983, 2961, 2868, 2846, 2197, 1603, 1560, 1509, 1459, 1296, 1174, 1085, 1033 cm^{-1}. MS (ESI+) *m/z* (%): 549 $(2M+Na)^+$ (60), 286 $(M+Na)^+$ (8), 264 $(M+1)^+$ (52), 208 (100), 180 (18), 139 (36). HRMS: *m/z* calcd for $C_{14}H_{18}NO_2S$ $[M+H]^+$: 264.1052, found: 264.1060.

(R_S,E)-Ethyl 4-[3-(tert-butylsulfinylimino)prop-1-ynyl]benzoate (**1c**)

Following the general procedure A, ethyl 4-(3-oxoprop-1-yn-1-yl)benzoate (3 mmol), gave **1c** (631 mg, 2.07 mmol, 69% yield). Eluent: *n*-hexane/AcOEt (6/1). $[\alpha]^{20}_D$ -154.1 (*c* 0.85, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.04 (s, 1H), 8.06-8.04 (m, 2H), 7.65-7.62 (m, 2H), 4.39 (c, *J*= 7.1 Hz, 2H), 1.39 (t, *J*= 7.1 Hz, 3H), 1.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 165.6, 147.5, 132.4, 132.4, 131.8, 129.6, 125.2, 98.5, 87.4, 61.4, 58.6, 22.6, 14.3. IR (NaCl): 2981, 2929, 2870, 2206, 1721, 1564, 1274, 1176, 1092 cm^{-1}. MS (ESI+) *m/z* (%): 633 $(2M+Na)^+$ (55), 306 $(M+1)^+$ (69), 250 (100), 187 (9). HRMS: *m/z* calcd for $C_{16}H_{20}NO_3S$ $[M+H]^+$: 306.1158, found: 306.1165.

(R_S,E)-N-[3-(4-Bromophenyl)prop-2-ynylidene]-2-methylpropane-2-sulfinamide (**1d**)

Following the general procedure A, ethyl 3-(4-bromophenyl)propiolaldehyde (3 mmol), gave **1d** (758 mg, 2.43 mmol, 81% yield). Eluent: *n*-hexane/AcOEt (5/1). $[\alpha]^{20}_D$ -130.6 (*c* 0.96, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.00 (s, 1H), 7.54-7.50 (m, 2H), 7.45-7.41 (m, 2H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 147, 133.9, 132.0, 125.1, 119.8, 98.7, 86.4, 58.5, 22.6. IR (NaCl): 2961, 2926, 2868, 2205, 1562, 1486, 1179, 1090, 1011 cm^{-}1. MS (ESI+) *m/z* (%) 647 $(2M+Na)^+$ (28), 314 $(M+3)^+$ (66), 312 $(M+1)^+$ (64), 258 (100), 256 (100). HRMS: *m/z* calcd for $C_{13}H_{14}BrNOS$ $[M+H]^+$: 312.0052, found: 312.0036.

(R_S,E)-N-[3-(2-Bromophenyl)prop-2-ynylidene]-2-methylpropane-2-sulfinamide (**1e**)

Following the general procedure A, 3-(2-bromophenyl)propiolaldehyde (3 mmol), gave **1e** (727 mg, 2.34 mmol, 78% yield). Eluent: *n*-hexane/AcOEt (5/1); $[\alpha]^{20}_D$ -171.1 (*c* 1.03, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 8.08 (s, 1H), 7.64-7.58 (m, 2H), 7.34-7.24 (m, 2H), 1.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 147.6, 134.4, 132.8, 131.4, 127.2, 126.4, 123.3, 97.8, 89.1, 58.6, 22.6. IR (NaCl): 2961, 2926, 2867, 2206, 1561, 1470, 1179, 1090 cm^{-}1. MS (ESI+) *m/z* (%): 647 $(2M+Na)^+$ (16), 312 $(M+1)^+$ (53), 258 (100), 256 (100); HRMS: *m/z* calcd for $C_{13}H_{14}BrNOS$ $[M+H]^+$: 312.0052, found: 312.0045.

(R_S,E)-2-Methyl-N-(oct-2-ynylidene)propane-2-sulfinamide (**1f**)

Following the general procedure A, oct-2-ynal (3mmol), gave **1f** (361 mg, 1.59 mmol, 53% yield). Eluent: *n*-hexane/AcOEt (6/1). The spectroscopic data are in accordance with the literature.[20]

(*R_S,E*)-2-Methyl-*N*-[3-(trimethylsilyl)prop-2-ynylidene]propane-2-sulfinamide (**1g**)

Following the general procedure A, 3-(trimethylsilyl)propiolaldehyde (3 mmol), gave **1g** (543 mg, 2.37 mmol, 79% yield). Eluent: n-hexane/AcOEt (from 7/1 to 3/1). $[\alpha]^{20}_D$ -268.9 (c 0.85, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.78 (s, 1H), 1.22 (s, 9H), 0.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 148.4, 108.4, 100.3, 59.0, 23.2, 0.0. IR (NaCl): 2962, 2928, 2902, 2869, 2202, 1563, 1365, 1250, 1098, 1070 cm^{-1}. MS (ESI+) m/z (%): 545 (68), 481 $(2M^+$+Na) (16), 284 (26), 252 $(M+Na)^+$ (22), 230 $(M+1)^+$ (46), 174 (100), 156 (15). HRMS: m/z calcd for $C_{10}H_{20}NOSSi$ $[M+H]^+$: 230.1029, found: 230.1021.

(R_S,Z)-2-methyl-N-(4-phenylbut-3-yn-2-ylidene)propane-2-sulfinamide (**1h**)[13a]

Following the general procedure B, 4-phenylbut-3-yn-2-one (0.43 mmol), gave **1h** (80 mg, 0.3225 mmol, 75% yield) as a mixture of isomers *Z:E* (93:7). Eluent: *n*-hexane/AcOEt (5/1). $[\alpha]^{20}_D$ -208.3 (*c* 0.70, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.57-7.54 (m, 2H), 7.46-7.35 (m, 3H), 2.46 (s, 3H), 1.27 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 162.1, 132.5, 130.5, 128.6, 120.7, 102.2, 84.2, 56.9, 29.4, 22.2. IR (NaCl): 2982, 2926, 2865, 2209, 2158, 1563, 1365, 1178, 1081 cm^{-1}. MS (ESI+) *m/z* (%): 517 $(2M^+$+Na) (90), 270 $(M+Na)^+$ (17), 248 $(M+1)^+$ (23), 192 (100). HRMS: *m/z* calcd for $C_{14}H_{18}NOS$ $[M+H]^+$: 248.1103, found: 248.1108.

(R_S,Z)-N-[4-(2-Methoxyphenyl)but-3-yn-2-ylidene]-2-methylpropane-2-sulfinamide (**1i**)

Following the general procedure B, 4-(2-methoxyphenyl)but-3-yn-2-one (0.43 mmol), gave **1h** (103 mg, 0.37 mmol, 86% yield). Eluent: *n*-hexane/AcOEt (from 4/1 to 3/1). $[\alpha]^{20}_D$ -212.9 (*c* 0.70, $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.49 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 6.96-6.88 (m, 2H), 3.88 (s, 3H), 2.46 (s, 3H), 1.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 162.4, 161.1, 134.6, 132.4, 120.6, 110.9, 109.8, 99.4, 88.3, 57.0, 55.8, 29.2, 22.2.; IR (NaCl): 2961, 2210, 2118, 1568, 1491, 1463, 1280, 1249, 1087cm^{-1}. MS (FAB+) *m/z* (%): 555 $(2M+1)^+$ (18), 278 $(M+1)^+$ (100), 222 (58), 57 (21). HRMS: *m/z* calcd for $C_{15}H_{20}NO_2S$ $[M+H]^+$: 278.1215, found: 278.1219.

(R_S,Z)-N-[4-(4-Bromophenyl)but-3-yn-2-ylidene]-2-methylpropane-2-sulfinamide (**1j**)

Following the general procedure B, 4-(2-methoxyphenyl)but-3-yn-2-one (0.43 mmol), gave **1j** (129 mg, 0.4 mmol, 92% yield) as a mixture of isomers *Z:E* (92:8). Eluent: *n*-hexane/AcOEt (from 8/1 to 2/1). $[\alpha]^{20}_D$ -311.9 (*c* 0.61, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.53-7.40 (AA´BB´ system, 4H), 2.45 (s, 3H), 1.26 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 161.4, 133.91, 132.0, 125.3, 119.5, 100.9, 85.2, 57.1, 29.3, 22.2. IR (NaCl): 2968, 2924, 2865, 2211, 1558, 1471, 1081 cm^{-1}. MS (FAB+) *m/z* (%): 651 $(2M+1)^+$ (9), 326 $(M+1)^+$ (96), 272 (56), 270 (59), 57 (86). HRMS: *m/z* calcd for $C_{14}H_{17}NOSBr$ $[M+H]^+$: 326.0214, found: 326.0218.

(R_S,Z)-N-(Hex-3-yn-2-ylidene)-2-methylpropane-2-sulfinamide (**1k**)

Following the general procedure B, hex-3-yn-2-one (0.43 mmol), gave **1k** (63 mg, 0.32 mmol, 73% yield). Eluent: *n*-hexane/AcOEt (4/1). $[\alpha]^{20}_D$ -242.6 (*c* 0.67, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 2.42 (q, *J* = 7.4 Hz, 2H), 2.31 (s, 3H), 1.22-1.17

(m, 3H), 1.20 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 163.4, 106.9, 76.3, 56.5, 29.5, 22.0, 13.3, 12.8. IR (NaCl): 2980, 2215, 1578, 1364, 1252, 1088 cm^{-1}. MS (FAB+) *m/z* (%): 399 $(2M+1)^+$ (10), 200 $(M+1)^+$ (100), 144 (53), 57 (34). HRMS: *m/z* calcd for $C_{10}H_{18}NOS$ $[M+H]^+$: 200.1109, found: 200.1107.

Diastereoselective Reformatsky reaction to imines.

General procedure C. Table 2. $AlMe_3$: To a solution of the corresponding imine (0.086 mmol) in anhydrous THF (0.2 mL) under argon atmosphere at -78 °C, $AlMe_3$ (0.0946 mmol) was added, and the mixture stirred for 5 min. Then, organozinc reagent[21] was dropwise added at -78 °C. After the time indicated at the table 2, NH_4Cl (sat. solution, 1.5 mL) was added. The organic phase was separated, and the aqueous layer was extracted with Et_2O (2 x 10mL) and CH_2Cl_2 (10 mL), dried over $MgSO_4$, filtered and the solvent evaporated under reduced pressure. The residue was purified by flash-column chromatography.

General procedure D. Table 3. TBSOTf: To a solution of the corresponding imine (0.086 mmol) in anhydrous THF (0.2 mL) under argon atmosphere at -78 °C, TBSOTf (0.181 mmol) was added. The mixture was stirred 5 min. To the resulting mixture organozinc reagent[4] was added dropwise at -78 °C. After the time indicated in the table 3, NH_4Cl (sat. solution, 1.5 mL) was added. The organic phase was separated and the aqueous layer was extracted with Et_2O (2 x 10mL) and CH_2Cl_2 (10 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The residue was purified by flash-column chromatography.

tert-Butyl (*S*)-3-[(R_S)-1,1-dimethylethylsulfinamido]-5-phenylpent-4-ynoate (**3a**)

Following the general procedure C, imine **1a** (0.43 mmol) after 3h, gave **3a** as major diastereoisomer (132 mg, 0.38 mmol, 88% yield). Eluent: *n*-hexane/AcOEt, (2/1). $[\alpha]^{20}_D$ -59.4 (*c* 0.63, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.43-7.40 (m, 2H), 7.31-7.27 (2m, 3H), 4.70-4.64 (m, 1H), 4.41 (d, *J*= 6.7 Hz, 1H), 2.88 (dd, *J*= 15.9, 5.2 Hz, 1H), 2.78 (dd, *J*= 15.9, 7.0 Hz, 1H), 1.48 (s, 9H), 1.26 (s, 9H); ^{13}C NMR ($CDCl_3$): δ 169.7, 131.7, 128.5, 128.3, 122.5, 87.1, 85.1, 81.8, 56.0, 45.4, 42.8, 28.1, 22.6. IR (NaCl): 2979, 2928, 2203, 1731, 1367, 1154, 1069 cm^{-1}; MS (ESI+): *m/z* (%): 721 $(2M+Na)^+$ (100), 699 $(2M+1)^+$ (48), 350 $(M+1)^+$ (16), 294 (40). HRMS: *m/z* calcd for $C_{19}H_{28}NO_3S$ $[M+H]^+$: 350.1784; found: 350.1787.

tert-Butyl (*S*)-3-{[(R_S)-tert-butylsulfinyl]amino}-5-(4-methoxyphenyl)pent-4-ynoate (**3b**)

Following the general procedure C, imine **1b** (0.43 mmol) after 3h, gave **3a** as major diastereoisomer (137 mg, 0.36 mmol, 84% yield). Eluent: *n*-hexane/AcOEt, (2/1). 97 % *e.d.* (Chiralcel OD, 1.0 mL/min, hexane/*i*PrOH (95:5), λ=254nm, t_{RR} = 12.0 min, t_{RS} = 19.6 min, . $[\alpha]^{20}_D$ -41.9 (*c* 1.08, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.39-7.32 (m, 2H), 6.84-6.79 (m, 2H), 4.67-4.61 (m, 1H), 4.38 (d, *J*= 6.7 Hz, 1H), 3.80 (s, 3H), 2.87 (dd, *J*= 15.8, 5.2 Hz, 1H), 2.77 (dd, *J*= 15.8, 7.0 Hz, 1H), 1.47 (s, 9H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.8, 159.8, 133.2, 114.6, 113.9, 85.7, 85.1, 81.7, 56.0, 55.3, 45.5, 43.0, 28.1, 22.6. IR (NaCl): 2980, 2924, 2198, 1731, 1366, 1249, 1153 cm^{-1}. MS (ESI+): *m/z* (%): 781 $(2M+Na)^+$ (26), 759 $(2M+1)^+$ (100), 380 $(M+1)^+$ (4). HRMS: *m/z* calcd for $C_{20}H_{30}NO_4S$ $[M+H]^+$: 380.1890, found: 380.1890.

Ethyl 4-((S)-5-(tert-butoxy)-3-[(R_S)-1,1-dimethylethylsulfinamido]-5-oxopent-1-yn-1-yl)benzoate (**3c**)

Following the general procedure C, imine **1c** (0.43 mmol) after 16h, gave **3c** as major diastereoisomer (156 mg, 0.37 mmol, 86% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_D$ -48.6 (*c* 1.48, in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 8.00-7.88 (m, 2H), 7.51-7.39 (m, 2H), 4.70-4.64 (m, 1H), 4.42 (d, *J*= 6.8 Hz, 1H), 4.36 (c, *J*= 7.2 Hz, 2H), 2.89 (dd, *J*= 16.0, 5.1 Hz, 1H), 2.79 (dd, *J*= 15.9, 7.0 Hz, 1H), 1.47 (s, 9H), 1.38 (t, *J*= 7.2 Hz, 3H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.6, 166.0, 131.6, 130.2, 129.4, 127.0, 90.1, 84.4, 81.9, 61.2, 56.1, 45.4, 42.6, 28.1, 22.6, 14.3. IR (NaCl): 2979, 2927, 2205, 1720, 1606, 1458, 1367, 1273, 1163 cm^{-1}. MS (ESI+): *m/z* (%): 865 $(2M+Na)^+$ (15), 843 $(2M+1)^+$ (100), 444 $(M+Na)^+$ (4), 422 $(M+1)^+$ (8), 366 (22). HRMS: *m/z* calcd for $C_{22}H_{32}NO_5S$ $[M+H]^+$: 422.1995, found: 422.1970.

tert-Butyl (S)-5-(4-bromophenyl)-3-[(R_S)-1,1-dimethylethylsulfinamido]pent-4-ynoate (**3d**)

Following the general procedure C, imine **1d** (0.43 mmol) after 2h, gave **3d** as major diastereoisomer (158 mg, 0.37 mmol, 86% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_D$ -47.6 (*c* 0.70, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.37-7.34 (m, 2H), 7.21-7.18 (m, 2H), 4.67-4.60 (m, 1H), 4.39 (d, *J*= 6.7 Hz, 1H), 2.80 (dd, *J* = 15.9, 5.2 Hz, 1H), 2.71 (dd, *J* = 16.0, 7.0 Hz, 1H), 1.48 (s, 9H), 1.24 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.6, 133.1, 131.5, 122.8, 121.4, 88.3, 84.1, 81.8, 56.0, 45.3, 42.6, 28.1, 22.6. IR (NaCl): 2978, 2923, 2208, 1729, 1486, 1367, 1153, 1070 cm^{-1}. MS (ESI+): *m/z* (%): 879 $(2M^+$+Na) (27), 857 $(2M+1)^+$ (100), 430 $(M+3)^+$ (27), 428 $(M+1)^+$ (24). HRMS: *m/z* calcd for $C_{19}H_{26}NO_3SBr$ $[M+H]^+$: 428.0889, found: 428.0871.

tert-Butyl (S)-5-(2-bromophenyl)-3-[(R_S)-1,1-dimethylethylsulfinamido]pent-4-ynoate (**3e**)

Following the general procedure C, imine **1e** (0.43 mmol) after 10 h, gave **3e** as major diastereoisomer (180 mg, 0.42 mmol, 98% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_D$ -56.9 (*c* 0.50, in $CHCl_3$); ^{1}H NMR ($CDCl_3$): δ 7.56-7.54 (m, 1H), 7.45-7.42 (m, 1H), 7.26-7.21(m, 1H), 7.18-7.12 (m, 1H), 4.74-4.68 (m, 1H), 4.46 (d, *J*= 6.8 Hz, 1H), 2.86 (dd, *J* = 16.1, 5.1 Hz, 1H), 2.76 (dd, *J* = 16.1, 6.8 Hz, 1H), 1.47 (s, 9H), 1.25 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.6, 133.5, 132.4, 129.6, 127.0, 125.6, 124.6, 91.8, 83.6, 81.8, 56.1, 45.5, 42.6, 28.1, 22.6. IR (NaCl): 2979, 2928, 2870, 2206, 1729, 1471, 1367, 1154, 1062 cm^{-1}. MS (ESI+): *m/z* (%): 879 $(2M^+$+Na) (40), 857 $(2M+1)^+$ (100), 428 $(M+1)^+$ (27). HRMS: *m/z* calcd for $C_{19}H_{26}NO_3SBr$ $[M+H]^+$: 428.0889, found: 428.0867.

tert-Butyl (S)-3-[(R_S)-1,1-dimethylethylsulfinamido]dec-4-ynoate (**3f**)

Following the general procedure C, imine **1f** (0.43 mmol) after 5 h, gave **3f** as major diastereoisomer (136 mg, 0.40 mmol, 92% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 1/1). $[\alpha]^{20}_D$ -57.6 (*c* 1.76, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.43-4.37 (m, 1H), 4.25 (d, *J*= 6.2 Hz, 1H), 2.74 (dd, *J* = 15.9, 5.2 Hz, 1H), 2.65 (dd, *J* = 15.9, 7.0 Hz, 1H), 2.16 (dt, *J*= 2.0, 7.0 Hz, 2H), 1.45 (s, 9H), 1.40-1.27 (m, 5H), 1.22 (s, 9H), 0.88 (t, *J*= 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 169.9, 86.0, 81.5, 78.0, 55.8, 44.9, 43.2, 31.0, 28.2, 28.1, 22.6, 22.2, 18.6, 14.0. IR (NaCl): 2959, 2932, 2862, 2204, 1732, 1367, 1156, 1061 cm^{-1}. MS (ESI+): *m/z* (%): 709 $(2M+Na)^+$ (100), 687 $(2M+1)^+$ (34), 344 $(M+1)^+$ (29), 288 (76), 214 (13). HRMS: *m/z* calcd for $C_{18}H_{34}NO_3S$ $[M+H]^+$: 344.2253; found: 344.2259.

tert-Butyl (S)-3-[(R_S)-1,1-dimethylethylsulfinamido]-5-(trimethylsilyl)pent-4-ynoate (**3g**)

Following the general procedure C, imine **1g** (0.43 mmol) after 16 h, gave **3g** as major diastereoisomer (138 mg, 0.4 mmol, 93% yield). Eluent: *n*-hexane/AcOEt, (2/1). $[\alpha]^{20}_{D}$ -56.9 (*c* 0.70, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.43-4.37 (m, 1H), 4.31 (d, *J*= 7.4 Hz, 1H), 2.64 (dd, *J* = 15.9, 5.2 Hz, 1H), 2.53 (dd, *J* = 15.9, 6.6 Hz, 1H), 1.45 (s, 9H), 1.21 (s, 9H), 0.13 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.9, 103.7, 89.9, 81.9, 56.2, 45.8, 43.0, 28.3, 22.8, 0.0. IR (NaCl): 2955, 2929, 2207, 2867, 1737, 1315, 1153, 1055 cm^{-1}. MS (ESI+): *m/z* (%): 713 $(2M+Na)^+$ (100), 691 $(2M+1)^+$ (30), 346 $(M^+ +1)$ (34), 290 (90). HRMS: *m/z* calcd for $C_{16}H_{32}NO_3SSi$ $[M+H]^+$: 346.1866; found: 346.1882.

tert-Butyl (R)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-3-methyl-5-phenylpent-4-ynoate (**3h**)

Following the general procedure C, imine **1h** (0.43 mmol) after 16 h, gave **3h** as major diastereoisomer (116 mg, 0.32 mmol, 74% yield). Eluent: *n*-hexane/AcOEt, (4/1 to 2/1). $[\alpha]^{20}_{D}$ -87.9 (*c* 0.72, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.43-7.40 (m, 2H), 7.26-7.24 (m, 3H), 4.90 (s, 1H), 2.83 (d, *J* = 15.1 Hz, 1H), 2.59 (d, *J* = 15.1 Hz, 1H), 1.63 (s, 3H), 1.44 (s, 9H), 1.21 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.8, 131.8, 128.3, 128.2, 122.6, 90.4, 85.1, 81.9, 55.8, 51.6, 48.3, 29.3, 28.2, 22.6. IR (NaCl): 2980, 2926, 2210, 1720, 1369, 1159, 1070 cm^{-1}. MS (ESI+): *m/z* (%): 749 $(2M+Na)^+$ (100), 727 $(2M+1)^+$ (28), 364 $(M+1)^+$ (51), 308 (66), 187 (74), 122 (45). HRMS: *m/z* calcd for $C_{20}H_{30}NO_3S$ $[M+H]^+$: 364.1940; found: 364.1954.

tert-Butyl (R)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-5-(2-methoxyphenyl)-3-methylpent-4-ynoate (**3i**)

Following the general procedure C, imine **1i** (0.43 mmol) after 16 h, gave **3i** as major diastereoisomer (159 mg, 0.4 mmol, 94% yield). Eluent: *n*-hexane/AcOEt, (2/1). $[\alpha]^{20}_{D}$ -90.1 (*c* 0.80, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.44-7.41 (m, 1H), 7.27-7.21 (m, 1H), 7.88-7.81 (m, 2H), 4.86 (s, 1H), 3.83 (s, 3H), 2.97 (d, *J* = 10.6, 1H), 2.69 (d, *J* = 10.6, 1H), 1.65 (s, 3H), 1.46 (s, 9H), 1.23 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.9, 160.1, 134.0, 129.7, 120.4, 112.0, 110.9, 94.2, 81.7, 55.8, 55.7, 52.0, 48.1, 29.3, 28.1, 22.6, 22.2. IR (NaCl): 2979, 2932, 2210, 17319, 1575, 1494, 1369, 1247, 1161 cm^{-1}. MS (ESI+): *m/z* (%): 416 $(M+Na)^+$ (36), 394 $(M+1)^+$ (72), 217 (100). HRMS: *m/z* calcd for $C_{21}H_{32}NO_4S$ $[M+H]^+$: 394.2046; found: 394.2064.

tert-butyl (R)-5-(4-bromophenyl)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-3-methylpent-4-ynoate (**3j**)

Following the general procedure C, imine **1j** (0.43 mmol) after 16 h, gave **3j** as major diastereoisomer (132 mg, 0.3 mmol, 70% yield). Eluent: *n*-hexane/AcOEt, (4/1). $[\alpha]^{20}_{D}$ -70.3 (*c* 0.52, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.42-7.39 (m, 2H), 7.31-7.26 (m, 2H), 4.94 (s, 1H), 2.85 (d, *J* = 15.0, 1H), 2.63 (d, *J* = 15.0, 1H), 1.63 (s, 3H), 1.46 (s, 9H), 1.23 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.7, 133.2, 131.4, 122.6, 121.6, 91.6, 84.0, 82.0, 55.9, 51.4, 48.2, 29.1, 28.1, 22.6. IR (NaCl): 3194, 2973, 2953 , 1739, 1488, 1352, 1217, 1156, 1131, 1052 cm^{-1}. MS (ESI+): *m/z* (%):442 $(M+1)^+$ (22), 267 (32), 265 (31), 122 (54), 57 (100). HRMS: *m/z* calcd for $C_{20}H_{29}NO_3SBr$ $[M+H]^+$: 442.1052; found: 442.1038.

tert-Butyl (R)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-3-methylhept-4-ynoate (**3k**)

Following the general procedure C, imine **1k** (0.43 mmol) after 16 h, gave **3k** as major diastereoisomer (121 mg, 0.39 mmol, 89% yield). Eluent: *n*-hexane/AcOEt, (4/1). $[\alpha]^{20}_{D}$ -89.6 (*c* 0.51, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.79 (s, 1H), 2.75 (d, *J* = 15.1 Hz, 1H), 2.52 (d, *J* = 15.1 Hz, 1H), 2.18 (c, *J* = 7.5 Hz, 2H), 1.51 (s, 3H), 1.45 (s, 9H), 1.19 (s, 9H), 1.10 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 170.0, 87.1, 81.6, 80.6, 55.6, 51.1, 48.6, 29.5, 28.1, 22.6, 13.7, 12.4. IR (NaCl): 2979, 1719, 1458, 1236, 1158, 1068 cm^{-1}. MS (ESI+): *m/z* (%): 631 $(2M+1)^+$ (19), 316 $(M+1)^+$ (100), 260 (94), 186 (35), 57 (63). HRMS: *m/z* calcd for $C_{16}H_{30}NO_3S$ $[M+H]^+$: 316.1946; found: 316.1945.

tert-Butyl (R)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-5-phenylpent-4-ynoate (**3a'**)

Following the general procedure D, imine **1a** (0.086 mmol) after 5 h, gave **3a'** as major diastereoisomer (26 mg, 0.074 mmol, 86% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_{D}$ - 26.7 (*c* 0.66, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.43-7.40 (m, 2H), 7.30-7.27 (m, 3H), 4.67-4.60 (m, 1H), 3.98 (d, *J*= 6.7 Hz, 1H), 2.84 (dd, *J* = 15.9, 7.8 Hz, 1H), 2.73 (dd, *J* = 15.9, 5.5 Hz, 1H), 1.46 (s, 9H), 1.23 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.5, 131.8, 128.5, 128.2, 122.4, 87.4, 85.3, 81.6, 56.3, 45.4, 43.2, 28.1, 22.6.

tert-Butyl (R)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-5-(4-methoxyphenyl)pent-4-ynoate (**3b'**)

Following the general procedure D, imine **1b** (23 mg, 0.06 mmol, 0.086 mmol) after 4 h, gave **3b'** as major diastereoisomer (69% yield). Eluent: *n*-hexane/AcOEt, (3/1). $[\alpha]^{20}_{D}$ -24.7 (*c* 1.05, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.35 (d, *J* = 8.7 Hz, 2H), 6.81 (d, *J* = 8.7 Hz, 2H), 4.66-4.59 (m, 1H), 3.92 (d, *J*= 6.6 Hz, 1H), 3.79 (s, 3H), 2.83 (dd, *J* = 15.9, 7.8 Hz, 1H), 2.71 (dd, *J* = 15.8, 5.5 Hz, 1H), 1.46 (s, 9H), 1.22 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.5, 159.8, 133.2, 114.6, 113.9, 86.0, 85.2, 81.5, 56.2, 55.3, 45.5, 43.4, 28.1, 22.6.

Ethyl 4-{(R)-5-(tert-butoxy)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]-5-oxopent-1-yn-1-yl}benzoate (**3c'**)

Following the general procedure D, imine **1c** (31 mg, 0.073 mmol, 0.086 mmol) after 4 h, gave **3c'** as major diastereoisomer (84% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_{D}$ -18.1 (*c* 1.20, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.91-7.82 (m, 2H), 7.42-7.34 (m, 2H), 4.67-4.61 (m, 1H), 4.37-4.24 (m, 2H), 3.93-3.85 (m, 1H), 2.85-2.64 (m, 2H), 1.46 (s, 9H), 1.38 (t, *J*= 6.9 Hz, 3H), 1.22 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.3, 166.0, 131.7, 130.2, 129.4, 127.0, 90.3, 84.5, 81.7, 61.1, 56.4, 45.4, 43.0, 28.1, 22.5, 14.3.

tert-Butyl (R)-5-(4-bromophenyl)-3-[(R$_S$)-1,1-dimethylethylsulfinamido}pent-4-ynoate (**3d'**)

Following the general procedure D, imine **1d** (0.086 mmol) after 5 h, gave **3d'** as major diastereoisomer (31 mg, 0.072 mmol, 83% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_{D}$ - 4.8 (*c* 0.54, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.35 (d, *J* = 8.4 Hz, 2H), 7.21 (d, *J* = 8.4 Hz, 2H), 4.57-4.51 (m, 1H), 3.90 (d, *J*= 7.2 Hz, 1H), 2.76 (dd, *J* = 15.9, 7.7 Hz, 1H), 2.65 (dd, *J* = 15.9, 5.5 Hz, 1H), 1.39 (s, 9H), 1.16 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.4, 133.2, 131.5, 122.8, 121.4, 88.6, 84.2, 81.6, 56.3, 45.4, 43.0, 28.1, 22.5.

tert-Butyl (R)-5-(2-bromophenyl)-3-[(R$_S$)-1,1-dimethylethylsulfinamido]pent-4-ynoate (**3e'**)

Following the general procedure D, imine **1e** (0.086 mmol) after 6 h, gave **3e'** as major diastereoisomer (29 mg, 0.068 mmol, 78% yield). Eluent: *n*-hexane/AcOEt, (3/1 to 2/1). $[\alpha]^{20}_{D}$ - 8.8 (*c* 0.60, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): 7.56-7.53 (m, 1H), 7.48-7.45 (m, 1H), 7.26-7.20 (m, 1H), 7.18-7.12 (m, 1H), 4.73-4.66 (m, 1H), 4.01 (d, *J*= 6.7 Hz, 1H), 2.89 (dd, *J* = 16.2, 7.9 Hz, 1H), 2.79 (dd, *J* = 16.2, 5.4 Hz, 1H), 1.47 (s,

9H), 1.23 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.4, 133.7, 132.3, 129.6, 127.0, 125.6, 124.6, 92.1, 83.8, 81.6, 56.3, 45.3, 43.0, 28.1, 22.6.

tert-Butyl (R)-3-[(R_S)-1,1-dimethylethylsulfinamido]dec-4-ynoate (**3f'**)

Following the general procedure D, imine **1f** (0.086 mmol) after 5 h, gave **3f'** as major diastereoisomer (22 mg, 0.062 mmol, 72% yield). Eluent: n-hexane/AcOEt, (2/1). $[\alpha]^{20}_D$ -31.8 (c 0.45, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.41-4.35 (m, 1H), 3.79 (d, J= 6.3 Hz, 1H), 2.71 (dd, J = 15.8, 7.8 Hz, 1H), 2.58 (dd, J= 15.9, 5.5 Hz, 1H), 2.16 (dt, J= 2.0, 6.9 Hz, 2H), 1.44 (s, 9H), 1.38-1.27 (m, 6H), 1.19 (s, 9H), 0.88 (t, J= 6.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 169.7, 86.1, 81.3, 78.3, 56.0, 45.0, 43.6, 31.0, 28.2, 28.1, 22.5, 22.1, 18.7, 13.9.

tert-Butyl (R)-3-[(R_S)-1,1-dimethylethylsulfinamido]-5-(trimethylsilyl)pent-4-ynoate (**3g'**)

Following the general procedure D, imine **1g** (0.086 mmol) after 5 h, gave **3g'** as major diastereoisomer (23 mg, 0.067 mmol, 77% yield). Eluent: *n*-hexane/AcOEt, (4/1 to 2/1). $[\alpha]^{20}_D$ -27.1 (*c* 0.78, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 4.45-4.38 (m, 1H), 3.83 (d, *J*= 6.4 Hz, 1H), 2.74 (dd, *J* = 16.0, 7.8 Hz, 1H), 2.61 (dd, *J* = 15.9, 5.6 Hz, 1H), 1.44 (s, 9H), 1.19 (s, 9H), 0.14 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 169.6, 103.8, 90.2, 81.7, 56.4, 45.4, 43.4, 28.3, 22.7, 0.0.

Sulfinamide deprotection:

General procedure E. The corresponding sulfinamide (0.0815 mmol) was treated with HCl in MeOH (0.163 mmol, 1.15 M). The mixture stirred at room temperature for 90 min. Then, the reaction mixture was concentrated *in vacuo*, and H_2O (5mL) and HCl (1 M) were added (to acid pH). The aqueous layer was washed with AcOEt (2 x 10mL), being the organic layers discarded. The aqueous layer neutralized and extracted with AcOEt (3 x 10mL). The organic phases dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure.

tert-Butyl (S)-3-amino-5-phenylpent-4-ynoate (**4a**)

Following the general procedure E, sulfinamide **3a** (0.086 mmol) after 16 h, gave **4a** (21 mg, 0.086 mmol, 100%). $[\alpha]^{20}_D$ - 8.3 (*c* 0.41, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 7.40-7.37 (m, 2H), 7.29-7.26 (m, 3H), 4.22-4.18 (m, 1H), 2.68 (dd, *J* = 15.6, 5.6 Hz, 1H), 2.61 (dd, *J* = 15.6, 7.5 Hz, 1H), 1.82 (s, 1H), 1.47 (s, 9H). ^{13}C NMR ($CDCl_3$): δ 170.2, 131.6, 128.2, 128.1, 123.0, 82.7, 81.0 (2C), 44.0, 41.0, 28.1. IR (NaCl): 2977, 2926, 2854, 1729, 1600, 1368, 1259, 1149 cm^{-1}. MS (FAB+): *m/z* (%): 246 $(M+1)^+$ (30), 190 (39), 173 (45), 131 (29), 73 (30), 57 (100). HRMS: *m/z* calcd for $C_{15}H_{20}NO_2$ $[M+H]^+$: 246.1494; found: 246.1495.

tert-Butyl (S)-3-aminodec-4-ynoate (**4f**)

Following the general procedure E, sulfinamide **3f** (0.086 mmol) after 16 h, gave **4f** (20 mg, 0.081 mmol, 94%). **$[\alpha]^{20}_D$** - 9.1 (*c* 0.43, in $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ 3.95 (s, 1H), 2.59-2.43 (m, 2H), 2.17-2.12 (m, 2H), 1.83 (s, 2H), 1.45 (s, 9H), 1.38-1.25 (m, 6H), 0.91-0.86 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 170.5, 83.2, 80.8, 44.4, 40.6, 31.0, 29.7, 28.4, 28.1, 22.2, 18.6, 14.0. IR (NaCl): 2959, 2930, 2858, 1731, 1458, 1368, 1256, 1150 cm^{-1}. MS (ESI+): *m/z* (%): 460 (6), 240 $(M+1)^+$ (11), 184 (100), 167 (10). HRMS: *m/z* calcd for $C_{14}H_{26}NO_2$ $[M+H]^+$: 240.1958; found: 240.1969.

***β*-Amino acid synthesis. Ester hydrolysis**

General procedure F. The sulfinamide (0.0815 mmol) was treated with HCl/H_2O (6N). The mixture was stirred at 40°C. After 15 h the solvent was evaporated *in vacuo*.

(S)-3-Amino-5-phenylpent-4-ynoic acid hydrochloride (**5a**)

Following the general procedure F, sulfinamide **3a** (0.086 mmol) after 1.5 h, gave **5a** (15 mg, 0.08 mmol, 91%). $[\alpha]^{20}_D$ -3.7 (*c* 0.66, in MeOH). ^{1}H NMR (CD_3OD): δ 6.15-6.13 (m, 2H), 6.08-6.03 (m, 3H), 3.36-3.32(m, 1H), 1.97 (s, 2H), 1.72-1.63 (m, 2H). ^{13}C NMR (CD_3OD): δ 170.8, 131.4, 129.1, 128.2, 120.9, 86.7, 82.0, 39.8, 37.0. IR (NaCl): 3590, 3421, 2918, 2850, 2243, 1717, 1595, 1490, 1400, 1187 cm^{-1}. MS (FAB+): *m/z* (%): 212 (M^++ Na) (7), 190 $(M+1)^+$ (16), 173 (27), 131 (100). HRMS: *m/z* calcd for $C_{11}H_{12}NO_2$ $[M+H]^+$: 190.0862; found: 190.0871.

(S)-3-Aminodec-4-ynoic acid hydrochloride (**5f**)

Following the general procedure F, sulfinamide **3f** (0.086 mmol) after 1.5 h, gave **5f** (15 mg, 0.08 mmol, 93%). $[\alpha]^{20}_D$ = -10,8 (*c* 0.83, in MeOH). ^{1}H NMR (CD_3OD): δ 2.89-2.83 (m, 2H), 2.32-2.25 (m, 2H), 1.59-1.51 (s, 2H), 1.46-1.34 (m, 6H), 0.94 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (CD_3OD): δ 131.4, 89.7, 75.1, 41.1, 32.0, 30.0, 29.0, 23.2, 19.1, 14.2. MS (FAB+): *m/z* (%): 206 (M+ Na)$^+$ (33), 201 (M+ NH_4)$^+$ (38), 184 $(M+1)^+$ (100), 167 (7), 157 (8), 121 (5). HRMS: *m/z* calcd for $C_{10}H_{18}NO_2$ $[M+H]^+$: 184.1332; found: 184.1362.

Supporting Information Available. The Supporting Information is available free of charge on the ACS Publication website at DOI: 10.1021/acs.joc.7b01211. Copies of ^{1}H and ^{13}C spectra for all new compounds and X-ray data for compound **3g** are included. This material is free of charge via the Internet at http://pubs.acs.org.

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(20) Ferreira, F.; Audouin, M.; Chemla, F. Influence of HMPA on the Stereochemical Outcome of the Addition of a Racemic Allenylzinc onto Enantiopure N-tert-Butanesulfinimines: Stereoselective Access to Enantiopure cis-Ethynylaziridines. *Chem. Eur. J.* **2005**, *11*, 5269-5278.

(21) To a solution of zinc (0.0344 mmol) in THF anhydrous (0.4 mL) under argon atmosphere, *tert*-butyl 2-bromoacetate (0.344 mmol) was added. The mixture was stirred for 30 min at reflux (it gets a greenish color). After the complete dissolution of the metal, the reaction was cooled until the corresponding temperature.