

Catalytic enantioselective addition of terminal alkynes to aromatic aldehydes using zinc-hydroxyamide complexes†

Gonzalo Blay,^a Luz Cardona,^a Isabel Fernández,^a Alicia Marco-Aleixandre,^a M. Carmen Muñoz^b and José R. Pedro^{*a}

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A mandelamide ligand, derived from (*S*)-mandelic acid and (*S*)-phenylethanamine, catalyzes the addition of aryl-, alkyl- and silyl-alkynylzinc reagents to aromatic and heteroaromatic aldehydes with good yields and good to high enantioselectivities.

Introduction

The enantioselective alkynylation of aldehydes is one of the most convenient methods for the synthesis of chiral nonracemic secondary propargylic alcohols, as a new C-C bond is formed concomitantly with the creation of a stereogenic center in a single transformation.¹ These kinds of compounds serve as precursors for a variety of chiral materials since the heteroatom and alkyne are handles for further transformations. For this reason, propargylic alcohols have been used as intermediates in the efficient synthesis of many natural products and pharmaceuticals.²

A number of catalytic protocols for this enantioselective reaction have been developed in the last years. In most of them, bisalkynylzinc or alkylalkynylzinc species are used as nucleophiles because these reagents feature a high functional group tolerance and a slow rate of addition to carbonyl groups in the absence of a Lewis basic ligand.³ After the pioneering work by Carreira *et al.*⁴ on the alkynylation of aldehydes with zinc acetylides generated *in situ* from terminal alkynes and Zn(OTf)₂ using ephedrine as chiral inductor, a number of *N,O* ligands have been employed as catalysts or pre-catalysts in these reactions. Examples include amino alcohols,⁵ imino alcohols,⁶ oxazolidines,⁷ hydroxy sulfonamides⁸ and hydroxy carboxyamides.⁹ Furthermore, some catalysts based on the axially chiral 1,1'-bi-2-naphthol ligand and Ti(IV) have been developed.¹⁰ Based on the same kinds of ligands, Shibasaki has described the asymmetric alkynylation of aldehydes promoted by the In(III)/BINOL complex and Cy₂NMe.¹¹

The design of new chiral ligands to be used in catalytic enantioselective reactions is an area of permanent interest. Easy preparation by short pathways from readily available non expensive starting materials, modularity and structural variation, low molecular weight, availability in both enantiomeric forms and stability are desirable features in any ligand of practical use. According to these premises, our group has been developing hydroxy

amide chiral ligands that are conveniently synthesized in simple, short sequences and from cheap, easily available chiral resources.¹² Recently we disclosed that simple (*S*)-mandelamides (Fig. 1) in combination with Ti(O^{*i*}Pr)₄ could be used to effectively catalyze the addition of dialkylzinc reagents to aldehydes with moderate to good enantioselectivity.¹³ In absence of Ti(O^{*i*}Pr)₄, these ligands also catalyze the addition of dimethylzinc to α -ketoesters,¹⁴ and we have advanced the alkynylation of heteroaromatic aldehydes,¹⁵ with good yields and enantioselectivities for both reactions.

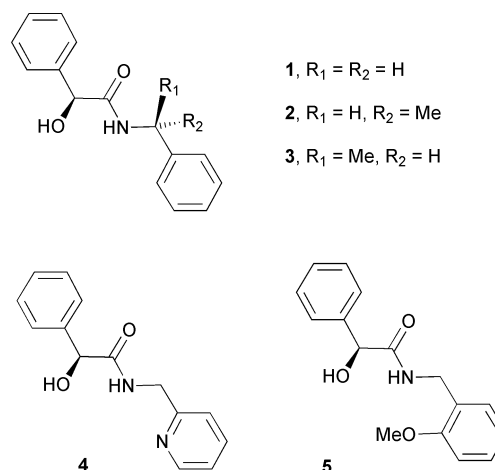


Fig. 1 Mandelamide ligands used in this study.

In this paper, we report the enantioselective addition of a variety of terminal alkynes to aromatic and heteroaromatic aldehydes using simple mandelamide ligands and dimethylzinc, with high yields and good to high enantioselectivities.

Results and discussion

Addition of phenylacetylene

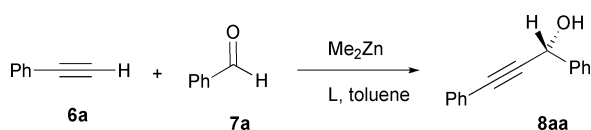
The reaction between benzaldehyde and phenylacetylene in the presence of Me₂Zn and mandelamides **1-5** in toluene was used for the optimization process (Scheme 1, Table 1). Ti(O^{*i*}Pr)₄ was not used to avoid addition of dimethylzinc to the aldehyde.¹³ The study of this reaction revealed the following results:¹⁵

a) Mandelamides (*S*)-**1** and (*S,S*)-**3** gave the best results in terms of enantioselectivity.

^aDepartament de Química Orgànica, Facultat de Química, Universitat de València, Dr. Moliner 50, E-46100-Burjassot (València), Spain. E-mail: jose.r.pedro@uv.es; Fax: +34 963544328

^bDepartamento de Física Aplicada, Universidad Politécnica de Valencia, E-46071, Valencia, Spain

† Electronic supplementary information (ESI) available: NMR spectra and HPLC chromatograms for compounds **8be**, **8cd**, **8ce**, **8de**, **8ds**, **8dt**, **8du** and **9**. CCDC reference numbers 734711. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/b911592g



Scheme 1 Addition of phenylacetylene to benzaldehyde.

Table 1 Alkynylation of benzaldehyde (**7a**) with phenylacetylene (**6a**) in the presence of dimethylzinc and mandelamides as chiral ligands^a

Entry	L	T/°C	8aa Yield ^b (%)	Ee ^c (%)
1	1	0	65	51
2	2	0	80	29
3	3	0	85	50
4	4	0	85	4
5	5	0	87	31
6	1	50	90	42
7	3	50	86	65
8	1	70	84	40
9	3	70	90	70
10 ^d	3	70/0	81	3
11 ^e	3	70/0	95	89
12 ^{e,f}	3	70/0	87	79
13 ^{e,g}	3	70/0	68	64
14 ^{e,h}	3	70/0	90	79

^a All the reactions were carried out in toluene under nitrogen, **7a** (1 mmol), **L** (0.2 mmol), Me₂Zn (6 mmol), **6a** (7.2 mmol). ^b Isolated product after column chromatography. ^c Determined by HPLC on a Chiralcel OD-H column. ^d Reaction according Scheme 2, equation 2. ^e Reaction according Scheme 2, equation 1. ^f Me₂Zn (5 mmol). ^g Me₂Zn (4 mmol). ^h Et₂Zn (6 mmol)

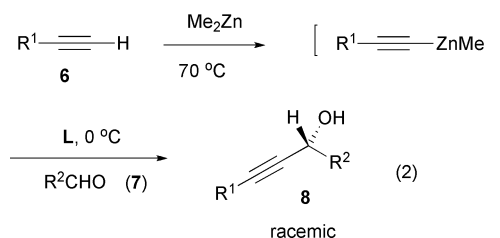
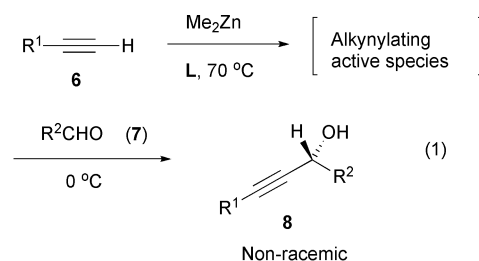
b) The enantioselectivity of the reaction was dependent on the temperature of reaction between the alkyne and dimethylzinc.

c) The enantioselectivity of the reaction was dependent on the order of addition of the mandelamide ligand.

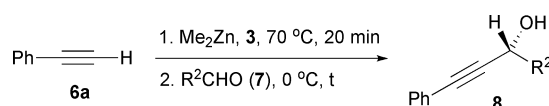
d) The enantioselectivity of the reaction was dependent on the number of equivalents of Me₂Zn

The optimal reaction conditions required pre-formation of the alkynylzinc reagent by heating the alkyne and Me₂Zn at 70 °C in the presence of the mandelamide ligand (until the formation of an abundant white precipitate), followed by addition of the aldehyde at 0 °C (Scheme 2, equation 1). Pre-formation of the alkynylzinc reagent in the absence of the ligand followed by the addition of ligand and aldehyde at 0 °C resulted in a racemic product (Scheme 2, equation 2). Although we do not have a clear explanation for this fact, we believe that the formation of the catalytic complex involves deprotonation of the mandelamide, which can be achieved by Me₂Zn at high temperature but not by the less basic pre-formed alkynylzinc reagent at 0 °C. The reduction in the number of equivalents of Me₂Zn (entries 12 and 13), as well as the use of Et₂Zn (entry 14) gave rise to a reduction in the enantioselectivity.

The optimized conditions were applied to a number of aromatic and aliphatic aldehydes (Scheme 3). The results are gathered in Table 2. In general, the reaction took place with high yields and enantiomeric excesses from good to high for most aromatic aldehydes (Table 2, entries 1–15). There is not a clear relationship between enantioselectivity and the electronic features of the substituents on the aromatic ring, although for *p*-halobenzaldehydes it can be observed an increase of the *ee* with the electronegativity of the halogen atom (entries 2–4). The presence of strong electron-



Scheme 2 Pre-formation of the alkynylzinc species and effect on the enantioselectivity of the reaction.



Scheme 3 Enantioselective addition of phenylacetylene to aldehydes.

withdrawing (NO₂) or electron-releasing (MeO) groups in *ortho* brought about a decrease in the enantioselectivity of the reaction. Remarkably, bulky naphthyl-aldehydes (entries 14 and 15) and, especially, heteroaromatic aldehydes bearing electron-rich five membered heterocycles provided the corresponding propargylic alcohols with high yields and enantioselectivities (entries 16–19). Aliphatic aldehydes reacted fast under the reaction conditions,

Table 2 Enantioselective addition of phenylacetylene (**6a**) to aldehydes according to Scheme 3^a

Entry	7	R ²	t (h)	8	Yield ^b (%)	Ee ^c (%)	Config.
1	7a	Ph	1	8aa	93	89	<i>R</i>
2	7b	4-BrC ₆ H ₄	2	8ab	70	63	<i>R</i>
3	7c	4-ClC ₆ H ₄	2	8ac	90	82	<i>R</i>
4	7d	4-FC ₆ H ₄	1	8ad	96	88	<i>R</i>
5	7e	4-MeC ₆ H ₄	1	8ae	70	79	<i>R</i>
6	7f	4-MeOC ₆ H ₄	1.5	8af	80	76	<i>R</i>
7	7g	3-ClC ₆ H ₄	2	8ag	91	76	<i>R</i>
8	7h	3-MeC ₆ H ₄	2	8ah	90	80	<i>R</i>
9	7i	3-MeOC ₆ H ₄	2	8ai	96	83	<i>R</i>
10	7j	2-ClC ₆ H ₄	2	8aj	93	64	<i>R</i>
11	7k	2-NO ₂ C ₆ H ₄	2.5	8ak	87	32	<i>R</i>
12	7l	2-MeC ₆ H ₄	1.5	8al	90	81	<i>R</i>
13	7m	2-MeOC ₆ H ₄	3.5	8am	89	59	<i>R</i>
14	7p	1-naphthyl	1	8ap	86	80	<i>R</i>
15	7q	2-naphthyl	1	8aq	91	89	<i>R</i>
16	7r	2-furyl	1	8ar	88	83	<i>S</i>
17	7s	3-furyl	1	8as	94	89	<i>S</i>
18	7t	2-thienyl	1.5	8at	91	90	<i>S</i>
19	7u	3-thienyl	2	8au	86	88	<i>S</i>
20	7n	PhCH ₂ CH ₂	0.5	8an	99	34	<i>R</i>
21	7o	cyclohexyl	1	8ao	64	47	<i>R</i>

^a All the reactions were carried out in toluene under nitrogen, **7** (1 mmol), **3** (0.2 mmol), Me₂Zn (6 mmol), **6a** (7.2 mmol). ^b Isolated product after column chromatography. ^c Determined by HPLC.

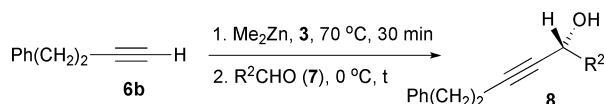
although with variable yields and low enantioselectivities (entries 20 and 21).

The absolute stereochemistry of the products was assigned by comparison of the optical rotation signs and HPLC retention times with values described in the literature for known compounds, and for the rest of the compounds it was assigned on the assumption of a uniform mechanistic pathway. According to this, the configuration of the stereogenic center was *R* in aromatic and aliphatic propargylic alcohols **8aa–8aq** and **8an–ao**, and *S* in heteroaromatic propargylic alcohols **8ar–8au**.¹⁶

Addition of aliphatic alkynes

Although a relatively large number of catalysts have been described for the alkynylation of aldehydes with phenylacetylene, the addition of other aliphatic alkynes has been less studied. For instance, only four examples of catalytic alkynylations of benzaldehyde with 4-phenyl-1-butyne (**6b**) have been reported so far.^{4b,5h,6c,11}

We studied the addition of this alkyne to aldehydes under our catalytic conditions (Scheme 4). In this case, the pre-formation of the alkynylzinc reagent required a little bit longer time until the formation of the white precipitate (30 min). Several aromatic and heteroaromatic aldehydes were alkynylated with good yields and enantiomeric excesses (Table 3). Again the absolute configuration of the stereogenic center was assigned to be *R* in aromatic propargylic alcohols and *S* in heteroaromatic propargylic alcohols after comparison.



Scheme 4 Enantioselective addition of 4-phenyl-1-butyne to aldehydes.

Then, we studied the addition of the highly sterically hindered *tert*-butylacetylene (**6c**). This is a very challenging substrate on account of its bulkiness and lower reactivity. The addition of *t*-butylacetylene (**6c**) to benzaldehyde with an 80% yield and 53% *ee* reported by Jiang⁵ⁱ is the only successful example in the literature with aromatic aldehydes so far. Besides, Dahmen has reported the addition of **6c** to cyclohexanecarbaldehyde in the presence of a paracyclophane-based imino phenol with 52% yield and 82% *ee*,^{5f} while Jiang reported 93% yield and 96% *ee* for the same reaction using an amino alcohol as ligand.^{5h} In our conditions, the pre-formation of the alkynylzinc species required

Table 3 Enantioselective addition of 4-phenyl-1-butyne (**6b**) to aldehydes according to Scheme 4^a

Entry	7	R ²	<i>t</i> (h)	8	Yield ^b (%)	Ee ^c (%)	Config.
1	7a	Ph	3	8ba	96	88	<i>R</i>
2	7d	4-FC ₆ H ₄	3	8bd	95	90	<i>R</i>
3	7e	4-MeC ₆ H ₄	3	8be	94	87	<i>R</i>
4	7r	2-furyl	1.5	8br	96	90	<i>S</i>
5	7s	3-furyl	2.5	8bs	93	92	<i>S</i>
6	7t	2-thienyl	3.5	8bt	90	91	<i>S</i>
7	7u	3-thienyl	1.7	8bu	94	89	<i>S</i>

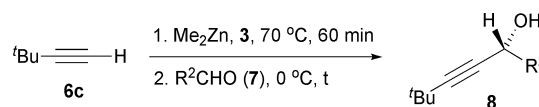
^a All the reactions were carried out in toluene under nitrogen, **7** (1 mmol), **3** (0.2 mmol), Me₂Zn (6 mmol), **6b** (7.2 mmol). ^b Isolated product after column chromatography. ^c Determined by HPLC.

Table 4 Enantioselective addition of *tert*-butylacetylene (**6c**) to aldehydes according to Scheme 5^a

Entry	7	R ²	<i>t</i> (h)	8	Yield ^b (%)	Ee ^c (%)	Config.
1	7a	Ph	3	8ca	93	67	<i>R</i>
2	7d	4-FC ₆ H ₄	3	8cd	91	65	<i>R</i>
3	7e	4-MeC ₆ H ₄	3	8ce	93	66	<i>R</i>
4	7r	2-furyl	1.5	8cr	79	85	<i>S</i>
5	7s	3-furyl	2.5	8cs	98	90	<i>S</i>
6	7t	2-thienyl	3.5	8ct	95	90	<i>S</i>
7	7u	3-thienyl	1.7	8cu	90	77	<i>S</i>

^a All the reactions were carried out in toluene under nitrogen, **7** (1 mmol), **3** (0.2 mmol), Me₂Zn (6 mmol), **6c** (7.2 mmol). ^b Isolated product after column chromatography. ^c Determined by HPLC.

heating the alkyne and ligand **3** with dimethylzinc for 1 h until the apparition of the white precipitate (Scheme 5). In general the reaction required short times to completion (from 1 to 2.5 h) and the corresponding propargylic alcohols were obtained in very high yields and enantiomeric excesses from good to excellent, especially with heteroaromatic aldehydes (Table 4). These are the highest enantioselectivities described so far for the addition of *tert*-butylacetylene to aromatic aldehydes.



Scheme 5 Enantioselective addition of *tert*-butylacetylene to aldehydes.

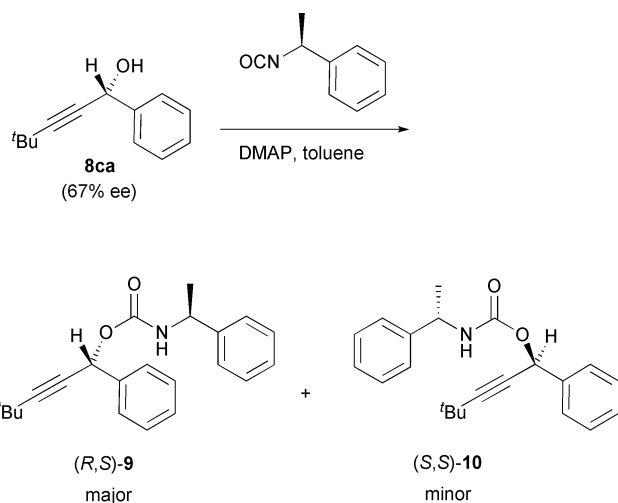
In this case, an assignment of the absolute stereochemistry of the products with literature data was not possible. To determine the absolute stereochemistry of compound **8ca** (67% *ee*) we prepared a carbamate derivative. Upon reaction with (*S*)-phenylethyl isocyanate, a mixture of two diastereomeric carbamates was obtained (Scheme 6).¹⁷ The major diastereomer (*R,S*)-**9** could be separated by crystallization and its relative stereochemistry was determined by X-ray analysis[‡] of the crystals. Knowing the absolute stereochemistry at C9 was *S* from the method of synthesis, the *R* absolute stereochemistry at the propargylic carbon C2 then follows (Fig. 2). This result shows that *tert*-butylacetylene follows the same stereochemical pathway as phenylacetylene and 4-phenyl-1-butyne.

Addition of trimethylsilylacetylene

Finally we studied the addition of trimethylsilylacetylene (**6d**) to aldehydes. This alkyne is a synthetic equivalent of acetylene and allows obtaining terminal propargylic alcohols after removal of the trimethylsilyl group. A few examples on the enantioselective addition of trimethylsilylacetylene to some aromatic^{5b,f,g,j,8f,10i} and aliphatic^{4c,5g,h} aldehydes has been described.

The addition of **6d** was carried out by following the described procedure. Formation of the white precipitate required heating

[‡] **Crystal data:** C₂₂H₂₅NO₂, *M* = 335.43, monoclinic, *a* = 9.9740(3), *b* = 8.8110(3), *c* = 12.1490(5) Å, β = 108.2480(10), *V* = 1013.97(6), *Z* = 2, 8581 reflections measured, 4178 reflections independent (*R*_{int} = 0.0957, *R* = 0.0683, *R*_{all} = 0.1258), Flack parameter = −1(2). CCDC 734711 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.



Scheme 6 Synthesis of carbamate derivatives of compound **8ca**.

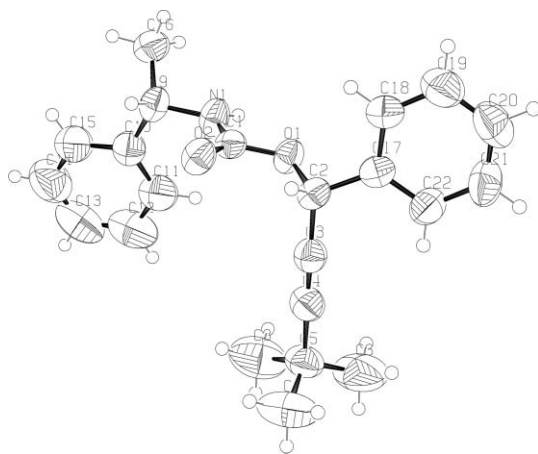
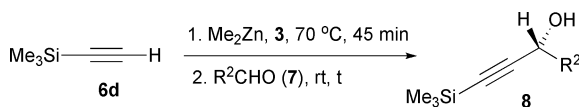


Fig. 2 ORTEP diagram for (R,S)-**9** with ellipsoids drawn at 40% probability.

with Me₂Zn at 70 °C for 45 min. The resulting alkynylzinc reagent was less reactive and the reaction with the aldehydes was carried out at rt (Scheme 7). Yields between 67–90% were obtained with all tested aldehydes (Table 5). Again, heterocyclic aldehydes gave higher enantiomeric excesses, from 80 to 90% *ee* (entries 4–7), than benzaldehyde derivatives (entries 1–3), which provided the expected products with *ee* in the range of 50%.



Scheme 7 Enantioselective addition of trimethylsilylacetylene to aldehydes.

Conclusions

In conclusion, simple mandelamides and dimethylzinc catalyze the enantioselective addition of terminal alkynes to aromatic and heteroaromatic aldehydes affording high yields and enantioselectivities of the corresponding propargylic alcohols. Terminal alkynes substituted with aromatic, aliphatic or trimethylsilyl

Table 5 Enantioselective addition of trimethylsilylacetylene (**6d**) to aldehydes according to Scheme 7^a

Entry	7	R ²	<i>t</i> (h)	8	Yield ^b (%)	Ee ^c (%)	Config.
1	7a	Ph	23	8da	67	52	<i>R</i>
2	7d	4-FC ₆ H ₄	23	8dd	79	57	<i>R</i>
3	7e	4-MeC ₆ H ₄	23	8de	72	51	<i>R</i>
4	7r	2-furyl	2	8dr	87	78	<i>S</i>
5	7s	3-furyl	6.5	8ds	84	74	<i>S</i>
6	7t	2-thienyl	21	8dt	81	72	<i>S</i>
7	7u	3-thienyl	7	8du	90	69	<i>S</i>

^a All the reactions were carried out in toluene under nitrogen, **7** (1 mmol), **3** (0.2 mmol), Me₂Zn (6 mmol), **6d** (7.2 mmol). ^b Isolated product after column chromatography. ^c Determined by HPLC.

groups can be used as nucleophilic partners in the reaction. An advantage of our catalytic system is that mandelamide ligands are easily prepared in a one step procedure, and a modular design of the catalyst is possible by varying the starting hydroxy acid and amine; also, both enantiomers of the catalyst are available from the corresponding mandelic acid and α-methylbenzylamine enantiomers. Furthermore, the reaction times are short and, unlike most other described procedures, the use of additional Lewis acid such as Ti(O^{*i*}Pr)₄ is not required.

Experimental

General experimental

Glassware was oven-dried overnight at 120 °C. Reactions were monitored by TLC analysis using Merck Silica Gel 60 F-254 thin layer plates. Flash column chromatography was performed on Merck silica gel 60, 0.040–0.063 mm. Specific optical rotations were recorded on a Perkin-Elmer 241 polarimeter using sodium light (D line 589 nm), values are given in 10^{−1} deg cm² g^{−1}. IR spectra were recorded in a Nicolet Avatar 320 FT-IR spectrometer. NMR spectra were recorded on Bruker Advance spectrometers in the deuterated solvents as stated, using residual non-deuterated solvent as internal standard and CFC₃ as internal standard for ¹⁹F NMR. *J* values are given in Hz. The carbon type was determined by DEPT experiments. Mass spectra were recorded on a Fisons Instruments VG Autospec GC 8000 series. Mass spectra (EI) were run at 70 eV. Mass spectra (FAB) were carried out at 30 kV in a MNBA matrix. Chiral HPLC analyses were performed in an Agilent 1100 series instrument equipped with a refraction index detector using chiral stationary columns from Daicel. Retention times are given in min. All alkynes and aldehydes were commercially available and used as purchased without further purification. Toluene was distilled from CaH₂ and stored on 4 Å molecular sieves. Mandelamides were prepared according to procedures described in the literature.^{13,15}

General Procedure for the catalytic asymmetric alkynylation of aldehydes

A 2 M solution of Me₂Zn in toluene (3 mL, 6 mmol) was added to a solution of alkyne **6** (7.2 mmol) in dry toluene (5 mL), under argon at room temperature. After 15 min, a solution of ligand **3** (83 mg, 0.2 mmol) in dry toluene (2 mL) was added and, after 15 min at room temperature, the solution was heated at 70 °C until the

formation of an abundant white precipitate in the solution (20 min for alkyne **6a**, 30 min for alkyne **6b**, 60 min for alkyne **6c** and 45 min for alkyne **6d**). Then, the reaction mixture was cooled to 0 °C and aldehyde **7** (1 mmol) was added. After the reaction was complete (TLC), 1M HCl (20 mL) was added (CAUTION! Gas evolution) and the reaction extracted with diethyl ether (3 × 15 mL). The organic layer was washed with brine, dried, concentrated and chromatographed on silica gel to give compound **8**.

(R)-1,3-Diphenyl-2-propyn-1-ol (8aa)^{4a,10,15}

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer (*R*) *t_r* = 13.1 min, minor enantiomer (*S*) *t_r* = 21.7 min, to be 89%; [α]_D²⁵ +6.7 (*c* 0.54 in CHCl₃).

(R)-1-(4-Bromophenyl)-3-phenyl-2-propyn-1-ol (8ab)^{8b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 10.1 min, minor enantiomer (*S*) *t_r* = 33.3 min, to be 62% *ee*; [α]_D²⁵ +8.8 (*c* 0.54 in CHCl₃).

(R)-1-(4-Chlorophenyl)-3-phenyl-2-propyn-1-ol (8ac)^{8b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 9.6 min, minor enantiomer (*S*) *t_r* = 27.2 min, to be 82%; [α]_D²⁵ +6.2 (*c* 0.53 in CHCl₃).

(R)-1-(4-Fluorophenyl)-3-phenyl-2-propyn-1-ol (8ad)^{8b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 9.5 min, minor enantiomer (*S*) *t_r* = 27.4 min, to be 88%; [α]_D²⁵ +5.2 (*c* 0.51 in CHCl₃).

(R)-1-(4-Methylphenyl)-3-phenyl-2-propyn-1-ol (8ae)^{7c}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 9.9 min, minor enantiomer (*S*) *t_r* = 20.6 min, to be 79%; [α]_D²⁵ +2.8 (*c* 0.47 in CHCl₃).

(R)-1-(4-Methoxyphenyl)-3-phenyl-2-propyn-1-ol (8af)^{8b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 15.0 min, minor enantiomer (*S*) *t_r* = 31.1 min, to be 76%; [α]_D²⁵ +24.1 (*c* 0.31 in CHCl₃).

(R)-1-(3-Chlorophenyl)-3-phenyl-2-propyn-1-ol (8ag)^{6b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 9.8 min, minor enantiomer (*S*) *t_r* = 30.1 min, to be 76%; [α]_D²⁵ +12.6 (*c* 0.54 in CHCl₃).

(R)-1-(3-Methylphenyl)-3-phenyl-2-propyn-1-ol (8ah)^{6b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 11.5 min, minor

enantiomer (*S*) *t_r* = 23.5 min, to be 80%; [α]_D²⁵ +3.1 (*c* 0.54 in CHCl₃).

(R)-1-(3-Methoxyphenyl)-3-phenyl-2-propyn-1-ol (8ai)^{6b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 18.0 min, minor enantiomer (*S*) *t_r* = 26.7 min, to be 83%; [α]_D²⁵ +5.4 (*c* 0.51 in CHCl₃).

(R)-1-(2-Chlorophenyl)-3-phenyl-2-propyn-1-ol (8aj)^{7c}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 10.5 min, minor enantiomer (*S*) *t_r* = 11.5 min, to be 64%; [α]_D²⁵ -37.9 (*c* 0.51 in CHCl₃).

(R)-1-(2-Nitrophenyl)-3-phenyl-2-propyn-1-ol (8ak)^{5g}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 14.6 min, minor enantiomer (*S*) *t_r* = 17.0 min, to be 32%; [α]_D²⁵ -12.4 (*c* 0.53 in CHCl₃).

(R)-1-(2-Methylphenyl)-3-phenyl-2-propyn-1-ol (8al)^{10h}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 9.9 min, minor enantiomer (*S*) *t_r* = 22.2 min, to be 81%; [α]_D²⁵ -12.4 (*c* 0.53 in CHCl₃).

(R)-1-(2-Methoxyphenyl)-3-phenyl-2-propyn-1-ol (8am)^{8b}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 16.1 min, minor enantiomer (*S*) *t_r* = 18.1 min, to be 59%; [α]_D²⁵ -5.8 (*c* 0.55 in CHCl₃).

(R)-1,5-Diphenyl-2-pentyn-3-ol (8an)^{5d}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 15.6 min, minor enantiomer (*S*) *t_r* = 28.9 min, to be 34%; [α]_D²⁵ -22.3 (*c* 0.53 in CHCl₃).

(R)-1-Cyclohexyl-3-phenyl-2-propyn-1-ol (8ao)¹⁸

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 6.2 min, minor enantiomer (*S*) *t_r* = 12.8 min, to be 49%; [α]_D²⁵ -4.0 (*c* 0.54 in CHCl₃).

(R)-3-Phenyl-1-(naphth-1-yl)-2-propyn-1-ol (8ap)^{10h}

Ee was determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 22.9 min, minor enantiomer (*S*) *t_r* = 17.1 min, to be 80%; [α]_D²⁵ -19.8 (*c* 0.48 in CHCl₃).

(R)-3-Phenyl-1-(naphth-2-yl)-2-propyn-1-ol (8aq)^{5g}

Ee was determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) *t_r* = 22.9 min, minor

enantiomer (*S*) $t_r = 17.1$ min, to be 80%; $[\alpha]_D^{25} -19.8$ (c 0.48 in CHCl_3).

(*S*)-1-(Furan-2-yl)-3-phenyl-2-propyn-1-ol (8ar)^{10j,15}

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 10.3$ min, minor enantiomer $t_r = 21.1$ min, to be 83%; $[\alpha]_D^{25} +34.0$ (c 0.58 in CHCl_3).

(*S*)-1-(Furan-3-yl)-3-phenyl-2-propyn-1-ol (8as)^{11,15}

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 9.6$ min, minor enantiomer $t_r = 24.7$ min, to be 89%; $[\alpha]_D^{25} +3.0$ (c 0.53 in CHCl_3).

(*S*)-3-Phenyl-1-(thiophen-2-yl)-2-propyn-1-ol (8at)¹⁵

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 11.2$ min, minor enantiomer $t_r = 23.2$ min, to be 90%; $[\alpha]_D^{25} +20$ (c 0.53 in CHCl_3).

(*S*)-3-Phenyl-1-(thiophen-3-yl)-2-propyn-1-ol (8au)^{11,15}

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 11.5$ min, minor enantiomer $t_r = 30.8$ min, to be 88%; $[\alpha]_D^{25} +20$ (c 0.53 in CHCl_3).

(*R*)-1,5-Diphenyl-2-pentyn-1-ol (8ba)^{11,15}

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) $t_r = 15.7$ min, minor enantiomer (*S*) $t_r = 27.4$ min, to be 88%; $[\alpha]_D^{25} +13.0$ (c 0.52 in CHCl_3).

(*R*)-1-(4-Fluorophenyl)-5-phenyl-2-pentyn-1-ol (8bd)¹¹

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) $t_r = 12.3$ min, minor enantiomer (*S*) $t_r = 34.8$ min, to be 90%; $[\alpha]_D^{25} +17.6$ (c 0.54 in CHCl_3).

(*R*)-1-(4-Methylphenyl)-5-phenyl-2-pentyn-1-ol (8be)

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) $t_r = 11.4$ min, minor enantiomer (*S*) $t_r = 22.2$ min, to be 87%; $[\alpha]_D^{25} +16.3$ (c 0.56 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3373, 2970, 2222, 1225, 1013, 814 and 762; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.28 (d, J 7.8, 2H), 7.25–7.10 (m, 5H), 7.08 (d, J 7.8, 2H), 5.31 (s, 1H), 2.78 (t, J 7.5, 2H), 2.49 (td, J 7.5 and 1.8, 2H), 2.28 (s, 3H) and 2.00 (br s, 1H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 140.5 (C), 138.2 (C), 138.0 (C), 129.2 (2CH), 128.5 (2CH), 128.4 (2CH), 126.6 (2CH), 126.3 (CH), 86.5 (C), 80.9 (C), 64.6 (CH), 34.9 (CH_2), 21.1 (CH_3) and 21.0 (CH_2); m/z (EI) 250.1353 (M^+ , 27%, $\text{C}_{18}\text{H}_{18}\text{O}$ requires 250.1358), 235 (17), 217 (5), 119 (33) and 91 (100).

(*S*)-1-(Furan-2-yl)-5-phenyl-2-pentyn-1-ol (8br)¹⁵

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 13.9$ min, minor enantiomer $t_r = 21.7$ min, to be 90%; $[\alpha]_D^{25} +14.2$ (c 0.54 in CHCl_3).

(*S*)-1-(Furan-3-yl)-5-phenyl-2-pentyn-1-ol (8bs)¹⁵

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 11.9$ min, minor enantiomer $t_r = 22.6$ min, to be 92%; $[\alpha]_D^{25} +12.3$ (c 0.52 in CHCl_3).

(*S*)-5-Phenyl-1-(thiophen-2-yl)-2-pentyn-1-ol (3bt)¹⁵

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 14.7$ min, minor enantiomer $t_r = 30.6$ min, to be 91%; $[\alpha]_D^{25} +27.5$ (c 0.57 in CHCl_3).

(*S*)-5-Phenyl-1-(thiophen-3-yl)-2-pentyn-1-ol (3bu)¹⁵

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 14.7$ min, minor enantiomer $t_r = 29.9$ min, to be 89%; $[\alpha]_D^{25} +15.4$ (c 0.51 in CHCl_3).

(*R*)-4,4-Dimethyl-1-phenyl-2-pentyn-1-ol (3ca)¹⁵

Ee was determined by HPLC (Chiralcel OD-H), hexane:*i*-PrOH 90:10, 1 mL/min, major enantiomer $t_r = 5.8$ min, minor enantiomer $t_r = 4.7$ min, to be 67%; $[\alpha]_D^{25} +18.8$ (c 0.51 in CHCl_3).

(*R*)-4,4-Dimethyl-1-(4-fluorophenyl)-2-pentyn-1-ol (8cd)

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) $t_r = 5.0$ min, minor enantiomer (*S*) $t_r = 4.6$ min, to be 65%; $[\alpha]_D^{25} +20.3$ (c 0.57 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3358, 2970, 2231, 1606, 1508, 1262, 1157, 1067, 985, 860, 836 and 771; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.51 (dd, J 8.4 and 5.4, 2H), 7.05 (t, J 8.4, 2H), 5.42 (s, 1H), 2.14 (br s, 1H), 1.26 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 162.5 (C, $J_{\text{C-F}}$ (d) 244.4), 137.1 (C, $J_{\text{C-F}}$ (d) 2.8), 128.5 (2CH, $J_{\text{C-F}}$ (d) 7.8), 115.3 (2CH, $J_{\text{C-F}}$ (d) 21.1), 96.1 (C), 78.2 (C), 64.0 (CH), 30.9 (3 CH_3), 27.5 (C); m/z (EI) 206.1115 (M^+ , 100%, $\text{C}_{13}\text{H}_{15}\text{FO}$ requires 206.1107), 123 (42) and 69 (36).

(*R*)-4,4-Dimethyl-1-(4-methylphenyl)-2-pentyn-1-ol (8ce)

Ee was determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*R*) $t_r = 5.9$ min, minor enantiomer (*S*) $t_r = 5.2$ min, to be 66%; $[\alpha]_D^{25} +20.1$ (c 0.56 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3374, 2969, 2231, 1512, 1363, 1262, 1066, 982, 817 and 759; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.43 (d, J 8.4, 2H), 7.18 (d, J 8.4, 2H), 5.41 (s, 1H), 2.36 (s, 3H), 2.08 (br s, 1H) and 1.27 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 138.5 (C), 137.9 (C), 129.1 (2CH), 126.7 (2CH), 95.5 (C), 78.5 (C), 64.5 (CH), 30.9 (3 CH_3), 27.5 (C) and 21.1 (CH_3); m/z (EI) 202.1539 (M^+ , 91%, $\text{C}_{14}\text{H}_{18}\text{O}$ requires 202.1358), 187 (100), 172 (27) and 145 (58).

(*S*)-1-(Furan-2-yl)-4,4-dimethyl-2-pentyn-1-ol (8cr)¹⁵

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*S*) $t_r = 5.6$ min, minor enantiomer (*R*) $t_r = 5.3$ min, to be 85%; $[\alpha]_D^{25} +16.8$ (c 0.53 in CHCl_3).

(*S*)-1-(Furan-3-yl)-4,4-dimethyl-2-pentyn-1-ol (8cs)¹⁵

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 0.5 mL/min), major enantiomer (*S*) $t_r = 9.5$ min, minor

enantiomer (*R*) t_r = 9.1 min, to be 90%; $[\alpha]_D^{25}$ +16.2 (*c* 0.56 in CHCl_3).

(*S*)-4,4-Dimethyl-1-(tiophen-2-yl)-2-pentyn-1-ol (8ct)¹⁵

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*S*) t_r = 5.7 min, minor enantiomer (*R*) t_r = 5.1 min, to be 90%; $[\alpha]_D^{25}$ +38.4 (*c* 0.51 in CHCl_3).

(*S*)-4,4-Dimethyl-1-(tiophen-3-yl)-2-pentyn-1-ol (8cu)¹⁵

Ee was determined by HPLC (Chiralcel OD-H, hexane:*i*-PrOH 90:10, 1 mL/min), major enantiomer (*S*) t_r = 5.5 min, minor enantiomer (*R*) t_r = 5.0 min, to be 77%; $[\alpha]_D^{25}$ +17.7 (*c* 0.57 in CHCl_3).

(*R*)-3-(Trimethylsilyl)-1-phenyl-2-propyn-1-ol (8da)^{6b,10l}

Ee was determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 95:5, 1 mL/min), major enantiomer (*R*) t_r = 7.4 min, minor enantiomer (*S*) t_r = 6.5, to be 52%; $[\alpha]_D^{25}$ +11.2 (*c* 0.58, CHCl_3).

(*R*)-1-Fluorophenyl-3-(trimethylsilyl)-2-propyn-1-ol (8dd)^{10l}

Ee determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 95:5, 1 mL/min), major enantiomer (*R*) t_r = 6.8 min, minor enantiomer (*S*) t_r = 6.1 min, to be 57%; $[\alpha]_D^{25}$ +13.7 (*c* 0.54 in CHCl_3).

(*R*)-1-Methylphenyl-3-(trimethylsilyl)-2-propyn-1-ol (8de)

Ee determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 95:5, 1 mL/min), major enantiomer (*R*) t_r = 8.2 min, minor enantiomer (*S*) t_r = 6.7 min, to be 51%; $[\alpha]_D^{25}$ +13.3 (*c* 0.52 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3375, 2960, 2899, 2173, 1513, 1411, 1250, 1043, 983, 843 and 761; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.43 (d, *J* 8.4, 2H), 7.19 (d, *J* 8.4, 2H), 5.42 (s, 1H), 2.36 (s, 3H), 2.15 (br s, 1H) and 0.20 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 138.2 (C), 137.5 (C), 129.3 (2CH), 126.7 (2CH), 105.1 (C), 91.3 (C), 64.8 (CH), 21.2 (CH₃) and -0.2 (3CH₃); MS (EI) 218.1130 (*M*⁺, 100%, $\text{C}_{13}\text{H}_{18}\text{OSi}$ requires 218.1127), 203 (86) and 175 (43).

(*S*)-1-(Furan-2-yl)-3-(trimethylsilyl)-2-propyn-1-ol (8dr)^{5g}

Ee determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 95:5, 0.5 mL/min), major enantiomer (*S*) t_r = 13.2 min, minor enantiomer (*R*) t_r = 12.8 min, to be 74%; $[\alpha]_D^{25}$ +16.2 (*c* 0.52 in CHCl_3).

(*S*)-1-(Furan-3-yl)-3-(trimethylsilyl)-2-propyn-1-ol (8ds)

Ee determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 93:7, 1 mL/min), major enantiomer (*S*) t_r = 5.9 min, minor enantiomer (*R*) t_r = 5.4 min, to be 73%; $[\alpha]_D^{25}$ +11.3 (*c* 0.59 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3363, 2960, 2173, 1503, 1410, 1251, 1160, 1204, 943, 845 and 760; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.52 (m, 1H), 7.40 (t, *J* 1.6, 1H), 6.50 (m, 1H), 5.38 (s, 1H), 2.12 (br s, 1H), 0.20 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 143.6 (CH), 140.3 (CH), 126.1 (C), 109.2 (CH), 104.4 (C), 90.0 (C), 57.7 (CH) and -0.2 (3CH₃); MS (EI) 194.0773 (*M*⁺, 100%, $\text{C}_{10}\text{H}_{14}\text{O}_2\text{Si}$ requires 194.0763), 179 (58), 161 (30), 104 (86) and 73 (54).

(*S*)-3-Trimethylsilyl-1-(tiophen-2-yl)-2-propyn-1-ol (8dt)

Ee determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 95:5, 0.5 mL/min), major enantiomer (*S*) t_r = 14.8 min, minor enantiomer (*R*) t_r = 13.0 min, to be 63%; $[\alpha]_D^{25}$ +28.7 (*c* 0.57 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3394, 2960, 2899, 2174, 1410, 1251, 1041, 844, 794 and 761; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.30 (dd, *J* 5.0, 0.9, 1H), 7.18 (unresolved dt, *J* 3.5, 1H), 6.98 (dd, *J* 5.0 and 3.5, 1H), 5.64 (s, 1H), 2.40 (br s, 1H) and 0.22 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 144.3 (C), 126.7 (CH), 126.2 (CH), 125.7 (CH), 104.0 (C), 91.2 (C), 60.6 (CH) and -0.3 (3CH₃); *m/z* (EI) 210.0532 (*M*⁺, 100%, $\text{C}_{10}\text{H}_{14}\text{OSi}$ requires 210.0535), 195 (9), 167 (97) and 120 (91).

(*S*)-3-Trimethylsilyl-1-(tiophen-3-yl)-2-propyn-1-ol (8du)

Ee determined by HPLC (Chiralpack AD-H, hexane:*i*-PrOH 95:5, 1 mL/min), major enantiomer (*S*) t_r = 8.0 min, minor enantiomer (*R*) t_r = 6.8 min, to be 69%; $[\alpha]_D^{25}$ +13.9 (*c* 0.56 in CHCl_3); $\nu_{\text{max}}(\text{film})/\text{cm}^{-1}$ 3363, 3105, 2959, 2173, 1419, 1251, 1041, 844, 794 and 761; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.40 (m, 1H), 7.32 (dd, *J* 5.1 and 3.0, 1H), 7.18 (dd, *J* 5.1 and 1.2, 1H), 5.48 (s, 1H), 2.25 (br s, 1H), 0.21 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 141.7 (C), 126.5 (CH), 126.4 (CH), 122.8 (CH), 104.7 (C), 90.7 (C), 60.9 (CH) and -0.2 (3CH₃); *m/z* (EI) 210.0535 (*M*⁺, 100%, $\text{C}_{10}\text{H}_{14}\text{OSi}$ requires 210.0535), 195 (3), 167 (36), 120 (13).

Synthesis of carbamates 9 and 10

A solution of (*R*)-4,4-dimethyl-1-phenyl-2-pentyn-1-ol (**8ca**, 83.4 mg, 0.44 mmol, Table 5, entry 1, 67% *ee*), (*S*)-phenylethyl isocyanate (113 μL , 0.72 mmol) and a catalytic amount of 4-dimethylaminopyridine (DMAP) in toluene (1.7 mL) was stirred at 80 °C under nitrogen atmosphere for 24 h. The solvent was removed under reduced pressure and the concentrated was dissolved in dichloromethane and washed with saturated aqueous NaHCO_3 and brine. The organic layer was dried over MgSO_4 and concentrated under reduced pressure. Column chromatography eluting with hexane-EtOAc gave a mixture of two diastereomeric carbamates (121.5 mg, 85%). The major diastereomer (43 mg) could be obtained pure after crystallization from toluene (0.4 mL). A second crystallization allowed to obtain suitable crystals for X-ray analysis.

Major diastereomer (*R,S*)-9: mp 128–129 °C (toluene), $[\alpha]_D^{25}$ -13.2 (*c* 0.55 in CHCl_3); $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3038, 2969, 2241, 1690, 1541, 1224, 1053, 914, 698; $\delta_{\text{H}}(300 \text{ MHz}; \text{CDCl}_3)$ 7.54 (unresolved d, 2H), 7.40–7.20 (m, 8H), 6.42 (s, 1H), 5.03 (br d, *J* 6.6, 1H), 4.84 (qd, *J* 7.2 and 6.6), 1.44 (d, *J* 7.2, 3H) and 1.23 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{CDCl}_3)$ 154.5 (C), 143.4 (C), 138.2 (C), 128.6 (CH), 128.5 (CH), 128.4 (CH), 127.7 (CH), 127.3 (CH), 125.9 (CH), 96.2 (C), 75.4 (C), 66.6 (CH), 50.8 (CH), 30.7 (CH₃), 27.5 (CH₃) and 22.4 (C); $\delta_{\text{H}}(300 \text{ MHz}; \text{dmsO}-d_6)$ 7.98 (d, *J* 8.1, 1H), 7.50–7.20 (m, 10H), 6.28 (s, 1H), 4.63 (dq, *J* 8.1 and 6.9, 1H), 1.29 (d, *J* 6.9, 3H) and 1.17 (s, 9H); $\delta_{\text{C}}(75 \text{ MHz}; \text{dmsO}-d_6)$ δ 154.2 (C), 144.8 (C), 138.3 (C), 128.5 (CH), 128.2 (CH), 127.2 (CH), 126.6 (CH), 125.7 (CH), 95.3 (C), 76.3 (C), 64.9 (CH), 50.1 (CH), 30.4 (CH₃), 27.0 (CH₃) and 22.6 (C); *m/z* (FAB) 335.1889 (*M*⁺, 0.5%, $\text{C}_{22}\text{H}_{25}\text{NO}_2$ requires 335.1885) and 171 (100).

Minor diastereomer (*S,S*)-10, significative peaks taken from the diastereomeric mixture: $\delta_{\text{H}}(300 \text{ MHz}; \text{dmsO}-d_6)$ 7.98 (d, *J* 8.1,

1H), 7.50–7.20 (m, 10H), 6.30 (s, 1H), 4.67 (dq, $J = 8.1$ and 6.9 , 1H), 1.33 (d, $J = 6.9$, 3H), 1.21 (s, 9H).

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Notes and references

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