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PAPER

Camphor-based Schiff base ligand SBAIB: an enantioselective catalyst for addition of phenylacetylene to aldehydes†

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A series of Schiff base ligands were synthesized from (1*R*)-camphor. Under the optimal conditions, (+)-SBAIB-a, **10** was found to be an excellent catalyst for the enantioselective addition of phenylacetylene to various aldehydes without utilizing either achiral additives or $Ti(O^iPr)_4$. This approach yielded (*R*)-propargylic alcohols in extremely high yields (up to 99%) and excellent enantioselectivities (up to 92%). The corresponding (*S*)-propargylic alcohols were synthesized in good to high enantioselectivities (up to 91%) and excellent yields (up to 99%) using (−)-SBAIB-a, **41**.

Introduction

The synthesis of enantioenriched propargylic alcohols is an area of intense research in asymmetric synthesis due to the usefulness of propargylic alcohol as versatile building blocks for a large number of pharmaceutically significant molecules and natural products.[1] This synthesis generates a new C–C bond and a stereogenic alcoholic center simultaneously. In the last two decades, considerable development has surfaced for the enantioselective nucleophilic addition of alkyne to carbonyl compounds to construct chiral propargylic alcohols.[2–6] Among them, an addition of alkynylzinc, which has been generated *in situ* from alkyne and either zinc salt or dialkylzinc to prochiral aldehyde,[3–5] is a widely preferred method due to its mildness for the wide range of functional groups and easy preparation of alkynylzinc. Despite there being numerous catalytic systems for the enantioselective addition of phenylacetylene to aldehyde, many require a long reaction time of up to 1–2 days, high catalyst loading, an extra addition of achiral additives[5,6] and elevated temperature to generate alkynylzinc. Therefore, the search for an ideal catalyst, which is either readily available in both enantiopure forms or easily synthesizable in a few steps in high yields, capable of providing very high enantiomeric excesses (ees) and yields for a wide range of substrates without the requirement of any extra additives, is still an ongoing process for enantioselective phenylalkynylation reactions.

Camphor derivatives are one of the most efficient chiral catalysts in asymmetric synthesis.[7,8] To date, four camphor-based ligands **1**,[7a] **2**,[7b] **3**[7c] and **4**[7d] are used as catalysts for the enantioselective alkynylation of aldehydes (Fig. 1). Among the four ligands, however, camphorsulfonamide **1**, reported by Wang *et al.*, was the only ligand that catalyzed this reaction successfully to achieve various propargylic alcohols in excellent ees and yields. Nevertheless, this catalytic system also has limitations, such as the need for an additional Lewis acid, $Ti(O^iPr)_4$, excesses of diethylzinc and phenylacetylene and yielding only moderate ees for aliphatic aldehydes.

This study hypothesized that camphor-based tridentate Schiff base ligands of 3-*exo*-aminoisoborneol [SBAIB] (Scheme 1) would generate a bifunctional catalytic system with dialkylzinc and phenylacetylene (Fig. 3), which would also circumvent the necessity of additional Lewis acids and achiral additives that are commonly required for many catalytic systems of this reaction.[5,6] Herein, this study reports the synthesis of a series of SBAIB ligands and their catalytic efficiency toward the enantioselective addition of phenylacetylene to various aldehydes.

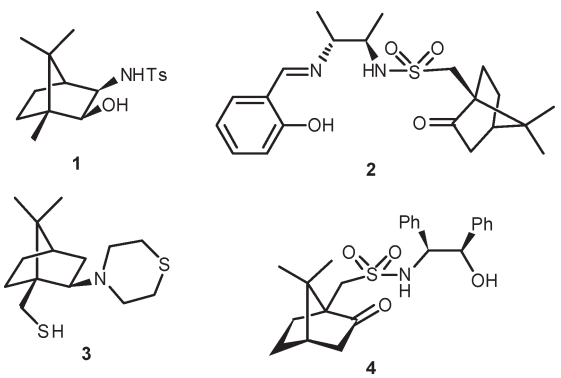

Fig. 1 Camphor-based ligands for enantioselective alkynylation to aldehydes.

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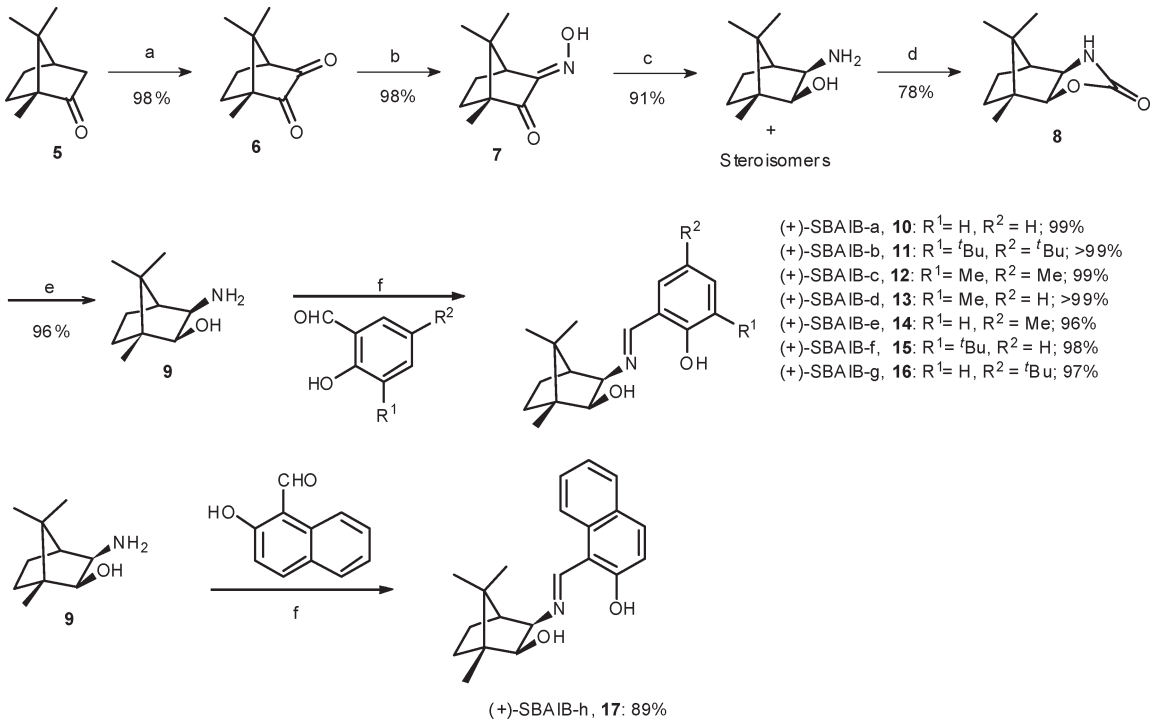
† Electronic supplementary information (ESI) available: Crystallographic data of (+)-SBAIB-a, **10**, NMR, MASS, IR, HPLC spectra for all SBAIB and propargylic alcohols. CCDC reference number 823886. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c1ob06683h



Scheme 1 The synthesis of SBAIB Ligands. *Reagents and conditions*: (a) SeO_2, Ac_2O, reflux, 17 h, 98%; (b) $H_2NOH.HCl$, NaOAc, EtOH/H_2O, reflux, 15 min, 98%; (c) $LiAlH_4$, THF, reflux, 20 h, 91%; (d) $(Cl_3CO)_2CO$, 6 M NaOH, DCM, −5 °C, 1 h then rt, 2.5 h, 78%; (e) 3 M NaOH, EtOH/H_2O, reflux, 6h, 96%; (f) Anhy. Na_2SO_4, EtOH/DCM, reflux, 12 h.

Results and discussion

Synthesis of tridentate Schiff base ligands from (1*R*)-camphor

Eight tridentate Schiff base ligands, (+)-SBAIB-a–h, **10–17**, were synthesized from commercially available and inexpensive (1*R*)-camphor **5** in six steps (Scheme 1).[9] Each ligand varies at aromatic rings by substituents and their positions. Firstly, the Riley oxidation of (1*R*)-camphor **5** produced camphorquinone **6**,[9a] which was subsequently converted to (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol ((−)-AIB), **9**, according to Zaidelwicz's procedure.[9b] The (−)-AIB successively underwent a condensation reaction with 2-hydroxybenzaldehydes in MeOH/CH_2Cl_2 (1 : 3) in the presence of anhydrous Na_2SO_4 at reflux temperature to produce (+)-SBAIB-a–g, **10–16**[10] in extremely high yields (up to 99%, overall yields: up to 65% from (1*R*)-camphor). The (1*R*,2*S*,3*R*,4*S*)-(−)-AIB, **9**, also reacted with 2-hydroxynaphthaldehyde to yield (+)-SBAIB-h, **17**. An X-ray crystallographic analysis of (+)-SBAIB-a, **10** (Fig. 2) verified the general structure of these tridentate (N, O, O) Schiff base ligands.

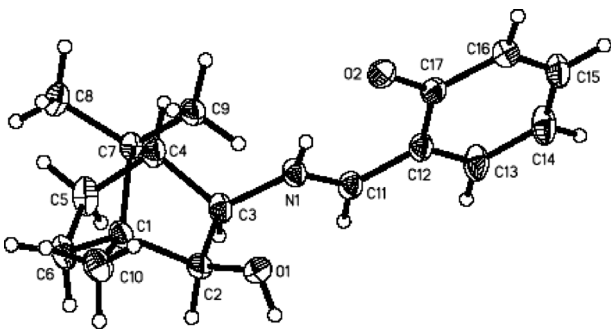


Fig. 2 X-ray crystallographic structures of (+)-SBAIB-a, **10** (CCDC 823886†).

Optimization of reaction conditions using (+)-SBAIB-a, 10

In the optimization of the reaction conditions, benzaldehyde **18** was utilized as a benchmark aldehyde and **10** was employed as a chiral promoter. Using Protocol A, toluene was the optimal solvent (Table 1, entries 1–4). A superior enantioselectivity (82% ee) of (*R*)-1,3-diphenylprop-2-yn-1-ol **18a** was found when 20 mol% **10**, phenylacetylene (2 eq), diethylzinc (1 M in hexane) (2 eq) reacted at room temperature in 2 mL of toluene (Table 1, entry 7). To further increase the ee and yields, the reaction was carried out with dimethylzinc (Table 1, entry 8) and tried with various additives, such as alcohols, polyethylene glycolic ethers and even $Ti(O^iPr)_4$ in various equivalents (not shown in Table 1). However, none of them improved the ees and yields. In an effort to enhance the enantioselectivity of this reaction, Protocol A was modified into protocols B, C and D, in which **10** (10 mol%), diethylzinc (2 eq., 1 M in hexane) and phenylacetylene (2 eq.) were mixed and stirred for 1 h, 3 h and 5 h, respectively, before the addition of benzaldehyde **18**. Despite a lack of high enrichment in ees compared to Protocol A, a regular increment was present in the ees of the products of 66%, 72% and 78% (Table 1, entries 9–11) in reduced reaction time (15 h, 13 h and 11 h, respectively). When the solvent of diethylzinc was changed from hexane to toluene, the ee was

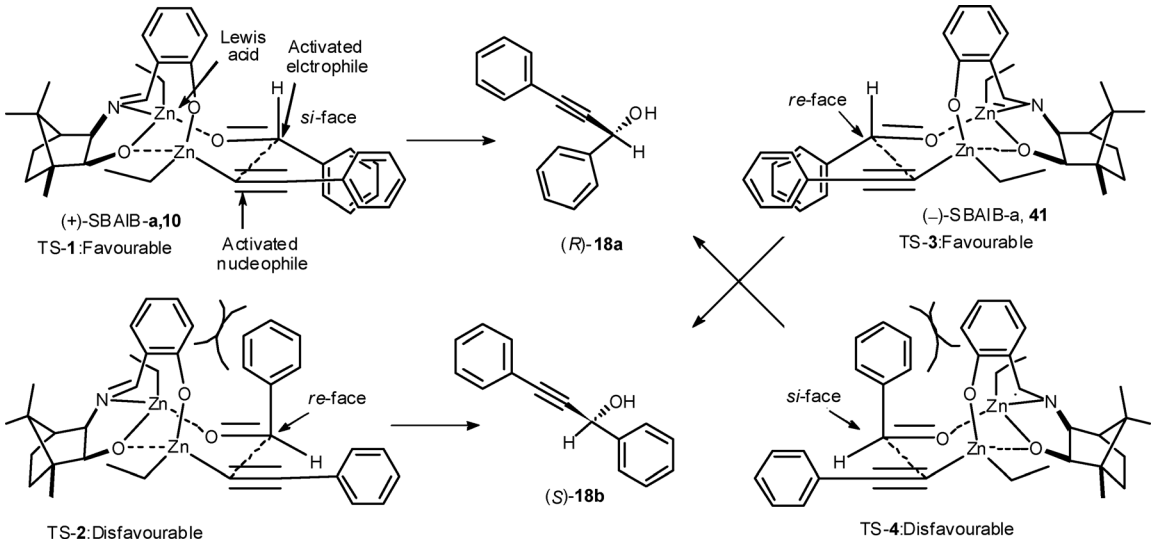
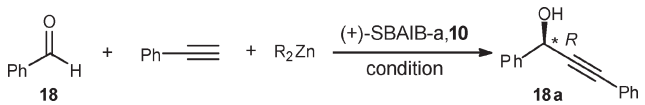


Fig. 3 The proposed mechanism.

Table 1 Optimization for catalytic enantioselective addition of phenylacetylene to benzaldehyde[a,d]



Entry	Ligand (mol %)	Solvent	Alkyl zinc/solvent (eq)[b]	Protocol[c]	*T*/°C	Time (h)	Yield (%)	ee (%)[e]
1	10	THF	Et_2Zn/hexane (2)	A	0–rt	34	92	11
2	10	toluene	Et_2Zn/hexane (2)	A	0–rt	20	99	74
3	10	Et_2O	Et_2Zn/hexane (2)	A	0–rt	20	97	70
4	10	CH_2Cl_2	Et_2Zn/hexane (2)	A	0–rt	20	98	69
5	10	toluene	Et_2Zn/hexane (2)	A	0	30	54	78
6	10	toluene	Et_2Zn/hexane (2)	A	rt	18	88	79
7	20	toluene	Et_2Zn/hexane (2)	A	rt	17	88	82
8	10	toluene	Me_2Zn/heptane (2)	A	rt	20	93	78
9	10	toluene	Et_2Zn/hexane (2)	B	rt	15	94	66
10	10	toluene	Et_2Zn/hexane (2)	C	rt	13	90	72
11	10	toluene	Et_2Zn/hexane (2)	D	rt	11	82	78
12	10	toluene	Et_2Zn/toluene (2)	C	rt	9	96	84
13	10	toluene	Et_2Zn/toluene (2)	E	rt	7	>99	86
14	20	toluene	Et_2Zn/toluene (2)	E	rt	6	97	91
15	25	toluene	Et_2Zn/toluene (2)	E	rt	6	96	89
16	30	toluene	Et_2Zn/toluene (2)	E	rt	6	98	90
17	20	toluene	Et_2Zn/toluene (1.2)	F	rt	20	90	85
18	20	toluene	Et_2Zn/toluene (3)	G	rt	4	97	90

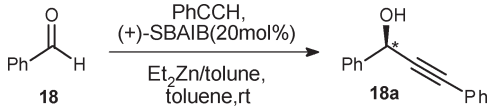
[a] For all of the reactions benzaldehyde (50 mg, 1 eq.). [b] Phenylacetylene/R_2Zn ratio = 1 : 1 unless mentioned. [c] Protocol A: phenylacetylene (2 eq.), solvent (2 mL), dialkylzinc (2 eq.), stir 1 h, ligand/solvent (2 mL), stir 1 h then benzaldehyde (1 eq.) at mentioned temperature; Protocol B: ligand, phenylacetylene (2 eq.), solvent (2 mL), dialkylzinc (2 eq.), stir 1 h then benzaldehyde (1 eq.); Protocol C: same as Protocol B except stir 3 h before benzaldehyde (1 eq) addition; Protocol D: same as Protocol B except stir 5 h before benzaldehyde (1 eq.) addition; Protocol E: same as Protocol B except stir 4 h before benzaldehyde (1 eq.) addition; Protocols F and G: Same as Protocol B except equivalents of diethylzinc 1.2 and 3, respectively. [d] The absolute configuration was based on determination of specific rotation and its comparison with the literature. [e] The enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H column).

amplified to 84%, with a high yield of 96% in a short time period of 9 h (Table 1, entry 12). The homo solvent (the reaction solvent and the solvent of dialkylzinc are same) played a significant role compared to the homogeneous mixture of hetero solvents in the proposed asymmetric catalytic system. A slight enhancement in ee (86%) with a quantitative yield in 7 h was present with the addition of benzaldehyde after 4 h (Table 1, entry 13). The optimal ee of 91% with a high yield (97%) was achieved in a short time (6 h) (Table 1, entry 14) when the amount of **10** increased from 10 to 20 mol%. This study also examined the reaction with a higher molar ratio of ligands (Table 1, entries 15 and 16), as well with a molar ratio lower than 10 mol%, though no significant increments emerged in the ee. Upon decreasing the amounts of diethylzinc and phenylacetylene (Table 1, entry 17), the ee decreased while the amounts of diethylzinc were increased and the ee remained constant, with no

change in yield (Table 1, entry 18). Thus, entry 14 in Table 1 was chosen as the optimal condition for phenylacetynylation of benzaldehyde using **10**.

To find out the optimal Schiff base ligand and study the substituent effects on the aromatic ring of the ligand, this study applied all other SBAIB ligands to this reaction. It was obvious from the results (Table 2, entries 2–8) that the substitution, mainly *ortho*-substitution, in the aromatic ring decreases the enantioselectivity. This is possibly due to the resulting steric hindrance for the aromatic hydroxy group that would be participating in the transition state of the reaction. Thus, among all of the catalysts, the simple salicylaldehyde derivative **10** was found to be an optimal catalyst for this reaction.

Table 2 Screening of ligands[a]



Entry	Ligand	Time (h)	Yield (%)	ee (%)
1	(+)-SBAIB-a, **10**	6	97	91
2	(+)-SBAIB-b, **11**	4	90	14
3	(+)-SBAIB-c, **12**	4	93	53
4	(+)-SBAIB-d, **13**	4	90	49
5	(+)-SBAIB-e, **14**	5	93	86
6	(+)-SBAIB-f, **15**	5	99	17
7	(+)-SBAIB-g, **16**	5	87	84
8	(+)-SBAIB-h, **17**	4	81	52

[a] Reaction conditions: ligand (20 mol%), phenylacetylene (2 eq), solvent (2 mL), dialkylzinc (2 eq), stir for 4 h then benzaldehyde (1 eq).

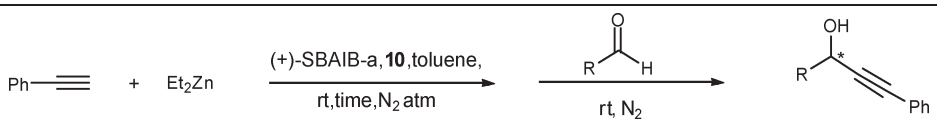
Catalytic enantioselective addition of phenylacetylene to various aldehydes

The scope of this catalytic system was studied for various aromatic and aliphatic aldehydes (Table 3). Both the electron-donating and electron-withdrawing groups that substituted benzaldehydes (Table 3, entries 2–14) produced propargylic alcohols (**19a–31a**) with excellent enantioselectivities (up to 92%) in excellent yields (up to 98%) within a short reaction time (4 h).

The ees were slightly lower for *meta*-halo-benzaldehydes; for instance, 3-chloro- and 3-fluorobenzaldehyde (entries 10 and 13) yielded **27a** and **30a** with slightly lower ees (85% and 83%, respectively). The best enantioselectivity (92%) was obtained for 2-anisaldehyde **23**. For the heteroaromatic aldehydes, high ees of **34a** (88%) and **35a** (91%) were achieved (entries17 and 18).

Aliphatic aldehydes also offered propargylic alcohols with moderate to good ees in excellent yields under the same optimal

Table 3 Enantioselective addition of phenylacetylene to aldehydes catalyzed by (+)-SBAIB-a, **10**



Entry	Aldehyde[a]	Product	Time (h)	Yield (%)	ee (%)[b]	Sign/config.[c]
1	benzaldehyde **18**	**18a**	6	97	91	+/*R*
2	2-tolualdehyde **19**	**19a**	4	98	90	−/*R*
3	3-tolualdehyde **20**	**20a**	4	98	87	+/*R*
4	4-tolualdehyde **21**	**21a**	4	96	86	+/*R*
5	4-*tert*-butylbenzaldehyde **22**	**22a**	4	95	89	+/*R*
6	2-anisaldehyde **23**	**23a**	4	98	92	−/*R*
7	3-anisaldehyde **24**	**24a**	4	93	91	+/*R*
8	4-anisaldehyde **25**	**25a**	4	94	91	+/*R*
9	2-chlorobenzaldehyde **26**	**26a**	4	91	91	−/*R*
10	3-chlorobenzaldehyde **27**	**27a**	4	92	85	+/*R*
11	4-chlorobenzaldehyde **28**	**28a**	4	97	88	+/*R*
12	2-bromobenzaldehyde **29**	**29a**	4	93	88	−/*R*
13	3-fluorobenzaldehyde **30**	**30a**	4	88	83	+/*R*
14	4-fluorobenzaldehyde **31**	**31a**	4	92	88	+/*R*
15	1-naphthaldehyde **32**	**32a**	4	99	84	−/*R*
16	2-naphthaldehyde **33**	**33a**	4	98	85	−/*R*
17	2-furfural **34**	**34a**	4	98	88	+/*R*[e]
18	2-thiophen-carboxaldehyde **35**	**35a**	4	95	91	+/*R*[e]
19	(2*E*)-cinnamaldehyde **36**	**36a**	4	94	64	+/*R*
20	(2*E*)-2-methyl-cinnamaldehyde **37**	**37a**	4	99	88	−/*R*
21	cyclohexanecarboxaldehyde **38**	**38a**	4	93	66	−/*R*
22	isobutyraldehyde **39**	**39a**	4	84(86)[d]	73(72)[d]	−/*R*[e]
23	pivaldehyde **40**	**40a**	4	83(87[d]	87(86)[d]	−/*R*[e]

[a] Phenylacetylene : Et_2Zn in toluene : ligand : aldehyde ratio = 2 : 2 : 0.2 : 1, all of the reactions were done with 50 mg aldehydes. [b] The enantiomeric excess was determined by HPLC analysis on a Chiralcel OD-H column. [c] The absolute configuration was based on determination of specific rotation and its comparison with the literature. [d] The reactions were carried out on a 250 mg scale and the obtained ees and yields are in parentheses. [e] The confusion that exists in the literature about the relationship between the absolute configuration and sign of specific rotation for these propargylic alcohols was addressed and clarified.

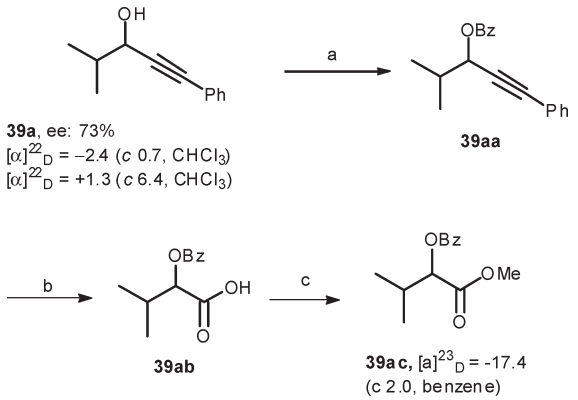
conditions. Entries 19 and 20 apparently indicate that α-substituted α,β-unsaturated aldehydes would yield significantly superior ees compared to simple α, β-unsaturated aldehydes. The aliphatic aldehyde with a higher substitution at the α-carbon yielded higher ees than the less substituted. For example, one additional methyl substitution of pivaldehyde **40** (entry 23) in comparison to isobutyraldehyde **39** (entry 22) causes an increased steric hindrance and, thus, the ee of propargylic alcohol, **40a**, rose to 87%.

The clarification of the absolute configuration of propargylic alcohols

All of the propargylic alcohols produced by the **10** catalyzed reaction (Table 3) possess *R* configuration compared with their specific rotation in the relevant literature. The propargylic alcohols **39a** and **40a** misled us initially to state that their configuration is *S*, based on their sign of specific rotation. However, this became controversial due to chiral HPLC data. Hence, the magnitude of the specific rotations of **39a** and **40a** are small and confusion is present in the literature regarding the relationship between their absolute configuration and sign of specific rotation. This study conducted a thorough analysis of all of the literature related to these alcohols, clarified the misunderstandings and proved that their absolute configuration is *R*, as shown below.

4-Methyl-1-phenyl-pent-1-yn-1-ol 39a

The specific rotation of **39a** was found to be $[\alpha]_D^{22} = -2.4$ (*c* 0.69, $CHCl_3$, 73% ee) (lit.[7a] $[\alpha]_D^{15} = -2$ (*c* 0.69, $CHCl_3$, 75% ee)) and its peak retention times in chiral HPLC were t_r (major): 5.83 min and t_r (minor): 10.11 min (column: Chiralcel OD-H). The absolute configuration of the title compound was first confirmed by Noyori *et al.*[13a] for *S* enantiomer ($[\alpha]_D^{23} = -1.6$ (*c* 6.26, $CHCl_3$), 99% ee)) and the retention times of peaks in chiral HPLC were *R*-isomer: 12.8 min, *S*-isomer: 21.3 min. Therefore, **39a** should have an *S* configuration as per the specific rotation and an *R* configuration as per the order of the peaks in the chiral HPLC. To find the absolute configuration, this study synthesized 1-methoxy-3-methyl-1-oxobutan-2-yl-benzoate **39ac** from **39a** (Scheme 2), which has a specific rotation of $[\alpha]_D^{23} = -17.4$ (*c* 2.00, benzene). The reported specific rotation for (*S*)-1-methoxy-3-methyl-1-oxobutan-2-yl-benzoate[13a] is



Scheme 2 The synthesis of **39ac** to confirm the absolute configuration of **39a**. Reagents and conditions: (a) BzCl, Et_3N, DCM; (b) OsO_4, $NaIO_4$, HMTA, THF/H_2O; (c) catalytic conc. H_2SO_4, MeOH.

$[\alpha]_D^{23.2} = +26.2$ (*c* 1.91, benzene), proving that **39a** has an *R* configuration.

In addition, this study synthesized **39a** on a larger scale and tested the specific rotation at high concentration, which was $[\alpha]_D^{22} = +1.3$ (*c* 6.4, $CHCl_3$, 73% ee) [*S* enantiomer: lit.[13a] $[\alpha]_D^{23} = -1.6$ (*c* 6.3, $CHCl_3$, 99% ee)]. This proves that the magnitude and even sign of the specific rotation could change with concentration, which was possibly the chief reason for the confusion in the literature. Thereafter, this study checked the HPLC of **39a** on the Chiralcel OD column, which showed that t_r (major): 13.6 min and t_r (minor): 22.97 min. The *R* enantiomer of 4-methyl-1-phenyl-pent-1-yn-1-ol is derived earlier, followed by the *S* enantiomer in both Chiralcel OD-H and Chiralcel OD columns. Therefore, to state the configuration of a molecule, not only does the sign of specific rotation require analysis, but the order of the major and minor peaks in the chiral HPLC also needs to be checked. Therefore, this study tabulated (Table 4) the confusions in existing literature for 4-methyl-1-phenyl-pent-1-yn-1-ol and their corrections.

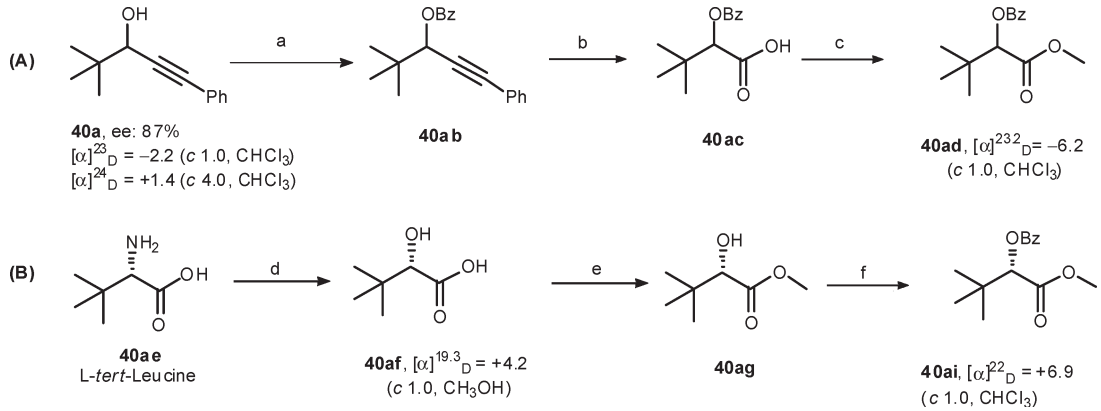
4,4-Dimethyl-1-phenyl-pent-1-yn-1-ol 40a

This study came to a conclusion with this molecule as well, that initially the compound **40a** (87% ee) has an *S* configuration since the specific rotation was checked in a low concentration $[\alpha]_D^{22} = -2.2$ (*c* 1.0, $CHCl_3$). However, this was not true with

Table 4 The corrections of 4-methyl-1-phenyl-pent-1-yn-1-ol's absolute configuration

Entry	Literature	Column	t_r major	t_r minor	$[\alpha]$	ee	Reported configuration	Re-assigned configuration
1	ref. 13*a*	Chiralcel OD	21.3	12.8	−1.6 (c 6.3, $CHCl_3$)	99	*S*	proved as *S*
2	ref. 3*a*	Chiralcel OD	7.9	16.0	+3.2 (c 6.8, $CHCl_3$)	90	*R*	*R*
3	ref. 7*a*	Chiralcel OD	6.1	10.7	−2.0 (c 0.7, $CHCl_3$)	75	NA/*S*[a]	*R*
4	ref. 5*c*	Chiralcel OD	12.6	6.8	+1.5 (c 0.6, $CHCl_3$)	47	NA/*R*[a]	*S*
5	ref. 3*e*	Chiralcel OD	5.5	9.2	+3.1 (c 1.1, $CHCl_3$)	95	*R*	*R*
6	ref. 6*f*[b]	Chiralcel OD	5.8	4.3	+2.7 (c 2.9, $CHCl_3$)	88	*S*[b]	*S*
7	this study	Chiralcel OD-H	5.8	10.1	−2.4 (c 0.7, $CHCl_3$)	73	*S*[a]	*R*[c]
					+1.3 (c 6.4, $CHCl_3$)	73	*R*[a]	*R*[c]

[a] These are the expected configurations from the sign of rotation. [b] Like us, ref. 6*f* also had the same problem with the sign of specific rotation, however they haven't clarified this; instead they simply state that it possess *S* configuration. [c] This is also confirmed by HPLC analysis on Chiralcel OD (t_r (major): 13.6 min and t_r (minor): 22.97 min).



Scheme 3 Syntheses of **40ad** and **40ai** to confirm the absolute configuration of **40a**. Reagents and conditions: (a) BzCl, Et_3N, DCM; (b) OsO_4, $NaIO_4$, HMTA, THF/H_2O; (c) catalytic conc. H_2SO_4 MeOH; (d) 2 M $NaNO_2$, 2 N H_2SO_4; (e) catalytic conc. H_2SO_4; (f) BzCl, Et_3N, DMAP, DCM.

high concentrations; the specific rotation was $[\alpha]_D^{24}$ = +1.4 (*c* 4.0, $CHCl_3$). The absolute configuration of 4,4-dimethyl-1-phenyl-pent-1-yn-1-ol was first reported by E. J. Corey *et al.*[14b] However, their back reference is ref. 14*a*, which failed to report the absolute configuration of the titled compound, instead mentioning only the specific rotation. Therefore, we wanted to have solid proof to state the absolute configuration of this molecule. This study thus synthesized 1-methoxy-3,3-methyl-1-oxobutan-2-yl benzoate **40ad** from **40a** (Scheme 3, A), and compared its specific rotation with (*S*)-1-methoxy-3,3-methyl-1-oxobutan-2-yl benzoate **40ai**, which was synthesized from L-*tert*-leucine[14c] (Scheme 3, B). This revealed that **40a** has an *R* configuration. The *R* enantiomer of 4,4-dimethyl-1-phenyl-pent-1-yn-1-ol was revealed to come first, followed by *S* enantiomers in all chiral columns (Chiralcel OD,[3a,3e,13a,14b] our result and Chiralcel OD-H column our result), with the eluent isopropanol/hexane. By thorough literature analysis of propargylic alcohols **34a**[11] and **35a**,[12] their configuration was confirmed as *R*.

Proposed mechanism for asymmetric induction

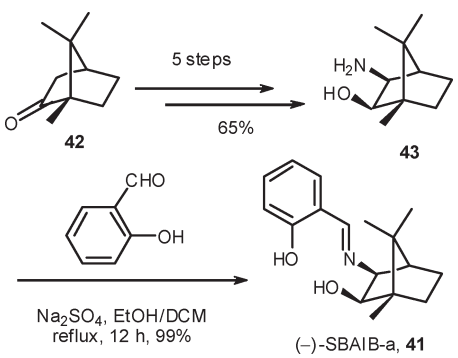
The absolute configuration of the newly generated stereogenic centre regarding benzaldehyde and **10** is predicted by the proposed model (Fig. 3). For this bifunctional catalyst system, TS-**1** is favorable due to less steric hindrance between the phenyl rings of the aldehyde and ligand. The alcoholic oxygen and imine's nitrogen can coordinate to zinc, which would act as a Lewis acid to activate the electrophilicity of the carbonyl group. Alcoholic oxygen and phenolic oxygen can coordinate to alkynylzinc; the alkynyl group can thus become activated nucleophiles. The addition of phenylacetylide to the *si*-face of carbonyl carbon consequently leads to the generation of (*R*)-propargylic alcohol, **18a**. The addition of phenylacetylide to the *re*-face of carbonyl carbon is unfavored (Fig. 3, TS-**2**) due to the steric hindrance between the phenyl rings of the aldehyde and the ligand. If this reaction is done with levo isomer (−)-SBAIB-a, **41** instead of dextro isomer (+)-SBAIB-**1**, the steric hindrance and face of the addition of the carbonyl group would seemingly experience an exact reversal. Therefore, regarding benzaldehyde, (*S*)-propargylic alcohol, **18b**, would be the enantioenriched alcohol, as shown in Fig. 3 (TS-**3**). Synthesizing (*S*)-propargylic alcohols of various aldehydes would be possible if the aforementioned proposed model is true. Thus, this study synthesized another Schiff base ligand, **41** (Scheme 4), and applied it to this asymmetric reaction.

Synthesis and application of (−)-SBAIB-a, 41

The **41** was synthesized from (1*S*)-camphor **42**, (Scheme 4) in an overall 65% yield by implementing the same procedure of (+)-SBAIB-a, **10**. (−)-SBAIB-a, **41** is catalyzed in this asymmetric reaction to produce various (*S*)-propargylic alcohols in good to excellent yields and ees. The experimental conditions and the results are shown in Table 5. The maximum enantioselectivity (91%) was obtained for pivaldehyde.

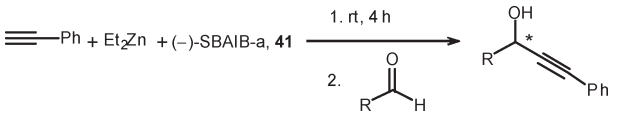
Conclusions

In summation, this study demonstrated the efficient synthesis of camphor-based Schiff base ligands, including (+)- and (−)-SBAIBs in very high yield. Among the Schiff base ligands, the (+)-SBAIB-a, under mild conditions, promotes the enantioselective addition of phenylacetylene to various aldehydes in a short reaction time (4 h). Various (*R*)-propargylic alcohols are consequently obtained in excellent enantiomeric excess (up to 92%) and in extremely high yields (up to 99%). This process also circumvents the requirements for either metallic additives/Lewis acids, such as titanium alkoxide and copper triflate, or nonmetallic/achiral additives, including DiMPEG, amine bases



Scheme 4 The synthesis of (−)-SBAIB-a, **41** from (1*S*)-camphor.

Table 5 (−)-SBAIB-a, **41**-catalyzed asymmetric addition of phenylacetylene to aldehydes[a,b]



Entry	Aldehyde	Product	Yield (%)	ee (%)[c]	Sign/config.[d]
1	**18**	**18b**	99	89	−/*S*
2	**19**	**19b**	99	90	+/*S*
3	**21**	**21b**	95	88	−/*S*
4	**23**	**23b**	99	90	+/*S*
5	**25**	**25b**	98	88	−/*S*
6	**26**	**26b**	95	87	+/*S*
7	**29**	**29b**	91	86	+/*S*
8	**35**	**35b**	91	89	−/*S*
9	**37**	**37b**	97	82	+/*S*
10	**40**	**40b**	99	91	+/*S*

[a] The reaction conditions were the same as in Table 3. [b] Phenylacetylene : Et_2Zn in toluene : ligand : benzaldehyde ratio = 2 : 2 : 0.2 : 1. [c] The enantiomeric excess was determined by HPLC analysis of the products (Chiralcel OD-H column). [d] The absolute configuration was based on a comparison of the retention time HPLC peaks and sign of specific rotation with the literature.

and alcohols. In addition, under the same reaction conditions, this study synthesized good to highly enantioenriched various (*S*)-propargylic alcohols (up to 91%) by employing **41** as a catalyst. This method represents the use of first camphor-based ligands for the enantioselective phenylacetylene addition reaction without use of any other extra additive. As a part of this work, we clarified the confusion in the scientific literature related to the absolute configuration of the propargylic alcohols **34a**, **35a**, **39a** and **40a** by thorough literature analysis. The applications of these ligands to other asymmetric reactions are in progress.

Experimental section

General remarks

All reactions were carried out in anhydrous solvents. THF and diethyl ether were distilled from sodium–benzophenone under argon. Toluene, CH_2Cl_2 and hexane were distilled from CaH_2. The aldehydes, dialkylzinc and phenylacetylene were used as purchased. All asymmetric reactions were carried out in dry glassware under nitrogen using a standard glovebox. Reactions were monitored by thin-layer chromatography using pre-coated silica gel 60 glass plates with F_{254} indicator. Visualization was accomplished by UV light (254 nm) in combination with iodine, potassium permanganate staining solutions. The products were purified by neutral column chromatography on 70–230 mesh silica gels. Yields refer to chromatographically and spectrographically pure material, unless otherwise noted. ^{1}H NMR and ^{13}C NMR spectra were obtained from 400 and 100.6 MHz NMR spectrometers, respectively. Chemical shifts (δ) are reported in parts per million (ppm) relative to $CDCl_3$ (7.26 and 77.0 ppm), the coupling constants are reported in Hertz (Hz) and the multiplicities are indicated as br = broad, s = singlet, d = doublet, dd = doublet of doublet, t = triplet, m = multiplet. Infrared spectra were recorded using a FT/IR spectrometer. Mass spectra (EI-MS) and high resolution mass spectra (HRMS-EI) were determined on a Thermo Quest MAT 95XL mass spectrometer. Melting points are checked by the use of melting point instrument. Melting point of the compounds might not be correct. Enantiomeric excesses were determined using high performance liquid chromatography (HPLC) with a Chiralcel OD-H chiral column and also with Chiralcel OD. Optical rotations were measured using a polarimeter at the indicated temperature using a sodium lamp (D line, 589 nm).

(1*R*,2*S*,3*R*,4*S*)-(−)-3-Aminoisoborneol, 9

This was prepared by the literature procedures from (1*R*)-Camphor.[9] mp 199–201 °C; $[\alpha]_D^{25} = -14.3$ (*c* 1.20, MeOH); lit.[9b] $[\alpha]_D^{22} = -8.2$ (*c* 1.15, MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 3.37–3.35 (d, J = 7.4 Hz, 2H), 3.05–3.03 (d, J = 7.4 Hz, 2H), 2.40 (br, s, 3H), 1.73–1.65 (m, 1H), 1.54–1.53 (d, J = 4.5 Hz, 1H), 1.43–1.37 (m, 1H), 1.06–0.95 (m, 2H), 1.05 (s, 3H), 0.94 (s, 3H), 0.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 79.0, 57.3, 53.4, 48.7, 46.6, 33.1, 26.9, 21.9, 21.2, 11.3.

(1*S*,2*R*,3*S*,4*R*)-(+)-3-Aminoisoborneol, 43

This was synthesized from (1*S*)-camphor using same literature procedures as for compound **9**. mp 201–203 °C; $[\alpha]_D^{20} = +5.9$ (*c* 1.15, MeOH).

General procedure for Schiff base ligands synthesis

Under an argon atmosphere, 2-hydroxy-1-aromaticaldehydes and 3-aminoisoborneol were mixed together in MeOH/CH_2Cl_2 (1 : 3) in the presence of anhydrous Na_2SO_4 at room temperature and refluxed for 12 h to complete either of one starting material. Then, it was filtered through an anhydrous Na_2SO_4 plug and the filtrate was evaporated to offer a yellow solid. The Schiff base ligands were purified by a proper solvent wash; washed with pentane to remove traces of 2-hydroxy-1-aromatic aldehyde and dissolved with hexane, cooled and filtered to remove traces of insoluble 3-aminoborneol.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(2-Hydroxybenzylidene)amino]-isoborneol, (+)-SBAIB-a, 10[10]

The condensation of salicylaldehyde (390 mg, 3.19 mmol) and (1*R*,2*S*,3*R*,4*S*)-3-aminoisoborneol **9** (450 mg, 2.65 mmol) was done in 18 mL of MeOH/CH_2Cl_2 (1 : 3) in the presence of anhydrous Na_2SO_4 (900 mg). Yield: 720 mg (99%); yellow solid, mp 135–137 °C; $[\alpha]_D^{24.5} = +157.7$ (*c* 1.00, MeOH); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.28 (br, 1H), 8.36 (s, 1H), 7.33 − 7.24 (m, 2H), 6.96–6.94 (d, J = 8.1 Hz, 1H), 6.89–6.85 (m, 1H), 3.83–3.81 (d, J = 7.6 Hz, 1H), 3.59–3.57 (d, J = 7.6 Hz, 1H), 1.85–1.77 (m, 3H), 1.60–1.54 (m, 1H), 1.27 (s, 3H), 1.20–1.08 (m, 2H), 1.10 (s, 3H), 0.87 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 165.7, 161.7, 132.6, 131.6, 118.7, 118.4, 117.3, 81.7, 76.5, 53.3, 49.3, 47.2, 33.5, 26.4, 21.6, 21.5, 11.4; IR (KBr) 3400, 2951, 2879, 1631, 1526, 1480, 1389, 1281, 1218, 1149, 1092, 1052, 755, 735 cm^{-1}; LRMS-EI (*m*/*z*) 273 (M^+, 100), 244 (22), 230 (34), 202 (25), 18 (26), 161 (55), 133 (36), 122 (72), 107 (37), 77

(21); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{17}H_{23}NO_2$ 273.1729, found 273.1723.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(3,5-Di-*tert*-butyl-2-hydroxybenzy-lidene) amino]isoborneol, (+)-SBAIB-b, 11

The condensation of 3,5-di-*tert*-butylsalicylaldehyde (200 mg, 0.85 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (173 mg, 1.02 mmol) was done in 8 mL of $MeOH/CH_2Cl_2$ (1 : 3) in the presence of anhydrous Na_2SO_4 (400 mg). Yield: 330 mg (quantitative); yellow solid, mp 66–68 °C; $[\alpha]_D^{17.3}$ = +59.6 (*c* 1.00, $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.15 (br, 1H), 8.41 (s, 1H), 7.39–7.38 (d, *J* = 2.4 Hz, 1H), 7.11–7.10 (d, *J* = 2.4 Hz, 1H), 3.82 – 3.79 (m, 1H), 3.59–3.57 (d, *J* = 7.6 Hz, 1H), 3.48 (s, 3H), 1.95–1.93 (d, *J* = 4.9 Hz, 1H), 1.83–1.75 (m, 2H), 1.62–1.53 (m, 1H), 1.43 (s, 9H), 1.30 (s, 9H), 1.27 (s, 3H), 1.14–1.13 (m, 2H), 1.02 (s, 3H), 0.87 (s, 3H);^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 167.4, 157.8, 140.2, 136.7, 127.2, 126.2, 118.0, 81.7, 53.3, 50.9, 49.3, 47.1, 35.0, 34.1, 33.5, 31.5, 29.4, 26.5, 21.7; IR (KBr) 3418, 2954, 1626, 1478, 1440, 1390, 1361, 1273, 1250, 1203, 1173, 1093, 1055, 876 cm^{-1}; LRMS-EI (*m*/*z*): 385 (M^+, 83), 370 (100), 342 (49), 203 (33), 131 (36), 105 (71), 91 (57), 77 (53); HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{25}H_{39}NO_2$ 385.2981, found 385.2974.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(3,5-Dimethyl-2-hydroxybenzylidene)-amino]isoborneol, (+)-SBAIB-c, 12

The condensation of 3,5-dimethylsalicylaldehyde (50 mg, 0.33 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (173 mg, 0.38 mmol) was done in 2 mL of $MeOH/CH_2Cl_2$ (1 : 3) in the presence of anhydrous Na_2SO_4 (100 mg). Yield: 99 mg (99%); yellow solid, mp 117–119 °C; $[\alpha]_D^{23}$ = +89.2 (*c* 1.00, $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.03 (br, 1H), 8.31–8.30 (d, *J* = 3.6 Hz, 1H), 7.01 (s, 1H), 6.89 (s, 1H), 3.81–3.79 (d, *J* = 5.4 Hz, 1H), 3.56–3.55 (d, *J* = 7.2 Hz, 1H), 2.26 (s, 3H) 2.24 (s, 3H), 1.87–1.86 (br, 1H), 1.81–1.77 (m, 2H), 1.59–1.53 (m, 1H), 1.29 (s, 3H), 1.19–1.07 (m, 2H), 1.01 (s, 3H), 0.86 (s, 3H);^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 166.3, 157.1, 134.6, 129.2, 127.1, 125.7, 117.8, 81.8, 77.0, 53.2, 49.2, 47.2, 33.6, 26.5, 21.7, 20.3, 15.5, 11.3; IR (KBr) 3468, 2952, 1630, 1540, 1477, 1389, 1337, 1268, 1093, 1046, 858, 786 cm^{-1}; LRMS-EI (*m*/*z*) 301 (M^+, 100), 258 (19), 189 (29), 150 (28); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{19}H_{27}NO_2$ 301.2042, found 301.2052.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(2-Hydroxy-3-methylbenzylidene)-amino] isoborneol, (+)-SBAIB-d, 13

The condensation of 3-methylsalicylaldehyde (49 mg, 0.35 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (50 mg, 0.29 mmol) was done in 2 mL of $MeOH/CH_2Cl_2$ (1 : 3) in the presence of anhydrous Na_2SO_4 (100 mg). Yield: 85 mg (quantitative); yellow solid, mp 153–155 °C; $[\alpha]_D^{23.6}$ = +94.3 (*c* 1.00, $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.40–13.38 (br, 1H), 8.32 – 8.30 (d, *J* = 8.0 Hz, 1H), 7.19–7.17 (d, *J* = 7.3 Hz, 1H), 7.10–7.08 (d, *J* = 7.4 Hz, 1H), 6.79– 6.76 (t, *J* = 7.4 Hz, 1H), 3.80 (br, 1H), 3.55–3.53 (d, *J* = 7.2 Hz, 1H), 2.27 (s, 3H) 2.04–1.98 (br, 1H), 1.81–1.76 (m, 2H), 1.60–1.53 (m, 1H), 1.29 (s, 3H), 1.15–1.07 (m, 2H), 1.01 (s, 3H), 0.87 (s, 3H);^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 166.0, 159.9, 133.5, 129.3, 126.1, 118.0, 81.7, 76.6, 53.2, 49.3, 47.2, 33.5, 26.5, 21.6, 15.6, 11.4; IR (KBr) 3436, 2951, 1628, 1541, 1457, 1271, 1235, 1093, 1052, 850, 774, 747, 617 cm^{-1}; LRMS-EI (*m*/*z*) 287 (M^+, 100), 258 (19), 244 (32), 216 (26), 202 (29), 175 (52), 147 (34), 136 (75), 121 (44), 91 (59), 77 (32); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{18}H_{25}NO_2$ 287.1885, found 287.1891.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(2-Hydroxy-5-methylbenzylidene)-amino] isoborneol, (+)-SBAIB-e, 14

The condensation of 5-methylsalicylaldehyde (45 mg, 0.32 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (50 mg, 0.29 mmol) was done in 2 mL of $MeOH/CH_2Cl_2$ (1 : 3) in the presence of anhydrous Na_2SO_4 (100 mg). Yield: 82 mg (96%); Yellow solid, mp 145–147 °C; $[\alpha]_D^{24.5}$ = +90.9 (*c* 1.00, $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.02 (br, 1H), 8.25 (s, 1H), 7.11–7.09 (d, *J* = 8.4 Hz, 1H), 7.01 (s, 1H), 6.85–6.83 (d, *J* = 8.4 Hz, 1H), 3.81–3.80 (d, *J* = 7.5 Hz, 1H), 3.54–3.52 (d, *J* = 7.5 Hz, 1H), 2.28 (s, 3H) 2.06 (br, 1H), 1.82–1.76 (m, 2H), 1.59–1.53 (m, 1H), 1.25 (s, 3H), 1.17–1.07 (m, 2H), 1.00 (s, 3H), 0.85 (s, 3H);^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 165.8, 159.3, 133.5, 131.5, 127.4, 118.4, 116.9, 81.7, 76.6, 53.2, 49.2, 47.2, 33.5, 26.5, 21.6, 21.5, 20.3, 11.4; IR (KBr) 3436, 2952, 1634, 1590, 1494, 1389, 1281, 1225, 1093, 1053, 820, 757 cm^{-1}; LRMS-EI (*m*/*z*): 287 (M^+, 100), 244 (29), 216 (24), 200 (21), 175 (44), 136 (68), 121 (37), 91 (28), 77 (15). HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{18}H_{25}NO_2$ 287.1885, found 287.1892.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(2-Hydroxy-3-*tert*-butyllbenzylidene)-amino]isoborneol, (+)-SBAIB-f, 15

The condensation of 3-*tert*-butylsalicylaldehyde (58 mg, 0.32 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (50 mg, 0.29 mmol) was done in 2 mL of $MeOH/CH_2Cl_2$ (1 : 3) in the presence of anhydrous Na_2SO_4 (100 mg). Yield: 95 mg (98%); yellow solid, mp 126–128 °C; $[\alpha]_D^{24.5}$ = +65.17 (*c* 1.00, $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz) δ 13.52 (br, 1H), 8.38 (s, 1H), 7.34–7.33 (d, *J* = 6.4 Hz, 1H), 7.12–7.11 (d, *J* = 6.2 Hz, 1H), 6.84–6.80 (t, *J* = 7.6 Hz, 1H), 3.82–3.81 (d, *J* = 7.5 Hz, 1H), 3.58–3.56 (d, *J* = 7.5 Hz, 1H)) 2.46 (br, 1H), 1.85–1.80 (m, 2H), 1.61–1.53 (m, 1H), 1.44 (s, 3H), 1.30 (s, 3H), 1.17–1.07 (m, 2H), 1.00 (s, 3H), 0.88 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 166.8, 160.4, 137.4, 130.0, 129.6, 118.8, 117.9, 81.6, 76.9, 53.3, 49.3, 47.2, 34.9, 33.5, 29.3, 26.5, 21.7, 21.6, 11.4; IR (KBr) 3435, 2953, 1736, 1628, 1434, 1388, 1362, 1265, 1202, 1111, 1052, 855, 796, 751, 618 cm^{-1}; LRMS-EI (*m*/*z*) 329 (M^+, 100), 286 (88), 178 (38), 91 (40), 77 (22); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{21}H_{31}NO_2$ 329.2355, found 329.2348.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(2-Hydroxy-5-*tert*-butyllbenzylidene)-amino]isoborneol, (+)-SBAIB-g, 16

The condensation of 5-*tert*-butylsalicylaldehyde (58 mg, 0.32 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (50 mg,

0.29 mmol) was done in 2 mL of MeOH/CH_2Cl_2 (1 : 3 ratio) in the presence of anhydrous Na_2SO_4 (100 mg). Yield: 93 mg (96%); yellow solid, mp 133–135 °C; $[\alpha]_D^{24.5}$ = +76.2 (*c* 1.00, $CHCl_3$);^{1}H NMR ($CDCl_3$, 400 MHz) δ 12.97 (br, 1H), 8.37 (s, 1H), 7.37–7.34 (m, 1H), 7.24–7.23 (d, *J* = 2.4 Hz, 1H), 6.90–6.88 (d, *J* = 8.7 Hz, 1H), 3.82–3.80 (d, *J* = 7.6 Hz, 1H), 3.57–3.55 (d, *J* = 7.6 Hz, 1H), 2.08 (br, 1H), 1.84–1.74 (m, 2H), 1.62–1.53 (m, 1H), 1.31 (s, 9H), 1.26 (s, 3H), 1.18–1.07 (m, 2H), 1.00 (s, 3H), 0.86 (s, 3H);^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 166.3, 159.1, 141.2, 130.0, 127.9, 118.0, 116.7, 81.7, 76.7, 53.3, 49.2, 47.2, 33.9, 33.5, 31.4, 26.5, 21.7, 21.5, 11.3; IR (KBr) 3435, 2954, 1634, 1494, 1390, 1362, 1289, 1266, 1210, 1093, 1054, 827, 620 cm^{-1}; LRMS-EI (*m*/*z*) 329 (M^+, 100), 314 (76), 286 (29), 178 (58), 147 (27); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{21}H_{31}NO_2$ 329.2355, found 329.2350.

(1*R*,2*S*,3*R*,4*S*)-(+)-3-[(2-Hydroxynaphthen-1-yl)methylene-amino]isoborneol, (+)-SBAIB-h, 17

The condensation of 2-hydroxyl-1-naphthaldehyde (56 mg, 0.32 mmol) and (1*R*,2*S*,3*R*,4*S*)-(−)-3-aminoisoborneol **9** (50 mg, 0.29 mmol) was done in 2 mL of MeOH/CH_2Cl_2 (1 : 3) in the presence of anhydrous Na_2SO_4 (100 mg). Yield: 85 mg (89%); yellow solid, mp 247–249 °C (decomposed); $[\alpha]_D^{24.8}$ = +139.5 (*c* 1.00, MeOH);^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.44–8.42 (d, *J* = 10.7 Hz, 1H), 7.64–7.60 (t, *J* = 9.5 Hz, 2H), 7.56–7.54 (d, *J* = 7.7 Hz, 1H), 7.32–7.28 (m, 1H), 7.18–7.15 (t, *J* = 7.5 Hz, 1H), 6.86–6.84 (d, *J* = 9.3 Hz, 1H), 3.94–3.92 (d, *J* = 7.3 Hz, 1H), 3.58–3.55 (t, *J* = 6.9 Hz, 1H)) 3.07 (br, 1H), 1.92–1.90 (d, *J* = 4.5 Hz, 1H), 1.85–1.80 (m, 1H), 1.63–1.55 (m, 1H), 1.27 (s, 3H), 1.18–1.11 (m, 2H), 1.02 (s, 3H), 0.85 (s, 3H);^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 156.4, 137.7, 134.1, 129.1, 127.9, 125.7, 122.4, 119.9, 117.5, 106.5, 79.9, 69.3, 52.8, 49.2, 47.3, 33.2, 26.5, 21.4, 21.1, 11.3; IR (KBr) 3151, 2920, 2865, 2756, 1741, 1631, 1617, 1516, 1491, 1341, 1309, 1189, 1163, 1105, 1079, 994, 862, 832, 750, 617, 493 cm^{-1}; LRMS-EI (*m*/*z*) 323 (M^+, 100), 280 (25), 182 (43), 170 (43), 128 (28); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{21}H_{25}NO_2$ 323.1885, found 323.1880.

(1*S*,2*R*,3*S*,4*R*)-(−)-3-[(2-Hydroxybenzylidene)amino]-isoborneol, (−)-SBAIB-a, 41

The condensation of salicylaldehyde (173 mg, 1.41 mmol) and (1*S*,2*R*,3*S*,4*R*)-(+)-3-aminoisoborneol **43** (200 mg, 1.18 mmol) was done in 8 mL of MeOH/CH_2Cl_2 (1 : 3) in the presence of anhydrous Na_2SO_4 (400 mg). Yield: 320 mg (99%); yellow solid, mp 133–135 °C; $[\alpha]_D^{20.2}$ = −129.2 (*c* 1.00, MeOH);^{1}H NMR (400 MHz, $CDCl_3$) δ 13.23 (br, 1H), 8.36 (s, 1H), 7.33–7.24 (m, 2H), 6.96–6.94 (d, *J* = 8.1 Hz, 1H), 6.89–6.85 (m, 1H), 3.83–3.81 (d, *J* = 7.6 Hz, 1H), 3.59–3.57 (d, *J* = 7.6 Hz, 1H), 1.85–1.77 (m, 3H), 1.60–1.54 (m, 1H), 1.27 (s, 3H), 1.20–1.08 (m, 2H), 1.10 (s, 3H), 0.87 (s, 3H);^{13}C NMR (100.6 MHz, $CDCl_3$) δ 165.7, 161.7, 132.6, 131.6, 118.7, 118.4, 117.3, 81.7, 76.5, 53.3, 49.3, 47.2, 33.5, 26.4, 21.6, 21.5, 11.4; IR (KBr) 3391, 2951, 1630, 1526, 1480, 1389, 1281, 1209, 1149, 1052, 917, 755, 562 cm^{-1}; LRMS-EI (*m*/*z*) 273 (M^+, 100), 244 (29), 230 (34), 202 (27), 18 (26), 161 (55), 133 (40), 122 (72), 107 (35), 77 (25); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{17}H_{23}NO_2$ 273.1729, found 273.1726.

General procedure of enantioselective addition of phenylacetylene to aldehydes (Table 3 and 4)

THF (2 mL) was added to a vial containing (+)-SBAIB-a, **10** or (−)-SBAIB-**1** (20 mol %) in an inert atmosphere box. To this solution, Et_2Zn (2 equiv., 1.1 M in toluene) and phenylacetylene (2 equiv.) were added successively. After stirring for 4 h to generate the alkynylzinc–ligand complex aldehyde (50 mg, 1 equiv.) was added, then it was stirred till reaction finish, as checked by TLC. Saturated NH_4Cl was added (CAUSION! Gas evolution) and it was extracted with Et_2O (3 × 25 mL). The combined Et_2O layer washed with brine, dried (Na_2SO_4), filtered and concentrated. This was then purified by column chromatography (silica gel 70–230 mesh, eluent: 12 to 15% EtOAc/hexane). The enantiomeric excess of all propargylic alcohols were determined by Chiral HPLC (condition for all propargylic alcohols: Chiralcel OD-H, 10% 2-propanol/hexane, 1 mL min^{-1}, 254 nm; except the flow rate for compounds **29a** and **29b**: 0.25 mL min^{-1}).

(*R*)-1,3-Diphenylprop-2-yn-1-ol, 18a,[2f,4h,5a,5d,7a]

Yield: 95 mg (97%), oil; ee: 91%; Retention time: $t_{r(major)}$: 11.25 min, $t_{r(minor)}$: 20.54 min; $[\alpha]_D^{26}$ = +1.72 (*c* 1.67, $CHCl_3$); lit.[5d] $[\alpha]_D^{27}$ = +2.4 (*c* 1.67, $CHCl_3$, 96% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.64–7.62 (d, *J* = 7.2 Hz, 2H), 7.49–7.26 (m, 8H), 5.71–5.69 (d, *J* = 6.2 Hz, 1H), 2.29–2.27 (d, *J* = 6.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 140.7, 131.8, 128.7, 128.6, 128.4, 128.3, 126.8, 122.4, 88.8, 86.6, 65.1; IR (KBr) 3338, 3063, 2925, 2872, 2229, 1598, 1489, 1279, 1189, 1030, 961, 916, 757, 619 cm^{-1}; LRMS-EI (*m*/*z*) 208 (M^+, 100), 191 (25), 145 (65), 129 (38), 102 (29), 77 (37); HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{15}H_{12}O$ 208.0888, found 208.0884.

(*R*)-1-(2-Methylphenyl)-3-phenylprop-2-yn-1-ol, 19a[4h,5a]

Yield: 91 mg (98%), white solid; mp 57–59 °C; ee: 90%; retention time: $t_{r(major)}$: 9.32 min, $t_{r(minor)}$: 21.13 min; $[\alpha]_D^{26}$ = −7.9 (*c* 1.13, $CHCl_3$); lit.[5a] $[\alpha]_D^{27}$ = −10.0 (*c* 1.13, $CHCl_3$, 96% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.76–7.74 (m, 1H), 7.49–7.44 (m, 2H), 7.34–7.21 (m, 6H), 5.84 (s, 1H), 2.61 (s, 1H), 2.51 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.4, 136.0, 131.7, 130.8, 128.5, 128.4, 128.3, 126.6, 126.3, 122.6, 88.7, 86.4, 62.9, 19.0; IR (KBr) 3337, 3262, 3056, 2969, 2862, 2224, 2602, 1448, 1460, 1445, 1279, 1174, 1109, 1029, 259, 754, 690 cm^{-1}; LRMS-EI (*m*/*z*) 222 (M^+, 12), 207 (100), 190 (3.8), 145 (17), 129 (21), 115 (23), 91 (33), 77 (19); HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{16}H_{14}O$ 222.1045, found 222.1085.

(*R*)-1-(3-Methylphenyl)-3-phenyl-prop-2-yn-1-ol, 20a[4h,5a]

Yield: 91 mg (98%), oil; ee: 87%; retention time: $t_{r(major)}$: 10.89 min and $t_{r(minor)}$: 27.23 min; $[\alpha]_D^{22.7}$ = +5.1 (*c* 1.6, $CHCl_3$); lit.[5d] $[\alpha]_D^{27}$ = +6.0 (*c* 1.6, $CHCl_3$, 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52–7.49 (m, 2H), 7.45–7.43 (d, *J* = 6.5 Hz, 2H), 7.34–7.29 (m, 4H), 7.19–7.17 (d, *J* = 7.5 Hz, 1H), 5.67 (s, 1H),

2.71 (s, 1H), 2.41 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 140.6, 138.4, 131.8, 129.2, 128.6, 128.6, 128.4, 127.4, 123.8, 122.5, 89.0, 86.5, 65.1, 21.1; IR (KBr) 3350, 3054, 3024, 2971, 2923, 2865, 2232, 1598, 1489, 1442, 1375, 1313, 1260, 1151, 1032, 910, 794, 756, 690 cm^{-1}; LRMS-EI (*m*/*z*) 222 (M+, 72), 207 (100), 189 (13), 145 (13), 129 (38), 91 (27), 77 (24); HRMS-EI (*m*/*z*): $[M]^+$ calcd for $C_{16}H_{14}O$ 222.1045, found 222.1041.

(*R*)-1-(4-Methylphenyl)-3-phenyl-prop-2-yn-1-ol, 21a[2f,4h,5d]

Yield: 89 mg (96%), pale yellow solid; mp 68–70 °C; ee: 86%; retention time: $t_{r(major)}$: 9.58 min, $t_{r(minor)}$: 20.52 min; $[\alpha]_D^{22.7}$ = +3.7 (*c* 1.0, $CHCl_3$); lit.[5d] $[\alpha]_D^{27}$ = +4.8 (*c* 1.0, $CHCl_3$, 92% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53–7.48 (m, 4H), 7.34–7.32 (m, 3H), 7.23–7.21 (d, *J* = 7.9 Hz, 2H), 5.67 (s, 1H), 2.68 (s, 1H), 2.39 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.2, 137.8, 131.8, 129.3, 128.5, 128.3, 126.8, 122.5, 89.0, 86.4, 64.9, 21.2; IR (KBr) 3351, 3054, 2921, 2865, 2228, 1597, 1513, 1489, 1442, 1414, 1305, 1261, 1177, 1031, 819, 756, 691 cm^{-1}; LRMS-EI (*m*/*z*): 222 (M^+, 60), 207 (100), 178 (33), 129 (25), 91 (13), 77 (8); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{14}O$ 222.1045, found 222.1038.

(*R*)-1-(4-*tert*-Butylphenyl)-3-phenylprop-2-yn-1-ol, 22a[15]

Yield: 77 mg (95%), oil; ee: 89%; retention time: $t_{r(major)}$: 7.54 min, $t_{r(minor)}$: 25.63 min; $[\alpha]_D^{20.7}$ = +2.0 (*c* 1.15, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.59–7.57 (d, *J* = 8.3 Hz, 2H), 7.52–7.44 (m, 4H), 7.34–7.32 (m, 3H), 5.69–5.68 (d, *J* = 5.0 Hz, 1H), 2.57–2.56 (d, *J* = 5.5 Hz, 1H), 1.36 (s, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 151.5, 137.7, 131.8, 128.6, 128.3, 126.6, 125.6, 122.5, 88.9, 86.5, 64.9, 34.6, 31.4; IR (KBr) 3368, 3056, 2962, 2867, 2228, 2197, 1738, 1599, 1509, 1489, 1409, 1363, 1268, 1203, 1108, 1017, 963, 839, 756, 690, 578 cm^{-1}; LRMS-EI (*m*/*z*) 264 (M^+, 8), 249 (30), 207 (100), 179 (16), 129 (42), 91 (14) 77 (12); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{19}H_{20}O$ 264.1514, found 264.1505.

(*R*)-1-(2-Methoxyphenyl)-3-phenyl-prop-2-yn-1-ol, 23a[4h,5a,5d,7a]

Yield: 86 mg (98%), pale yellow solid; mp 55–57 °C; ee: 92%; retention time: $t_{r(major)}$: 13.54 min, $t_{r(minor)}$: 17.12 min; $[\alpha]_D^{20.7}$ = −10.5 (*c* 1.20, $CHCl_3$); lit.[5d] $[\alpha]_D^{27}$ = −11.8 (*c* 1.22, $CHCl_3$, 92% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68–7.66 (d, *J* = 7.4 Hz, 1H), 7.50–7.48 (m, 2H), 7.35–7.32 (m, 4H), 7.03–7.00 (t, *J* = 7.4 Hz, 1H), 6.95–6.93 (d, *J* = 8.2 Hz, 1H), 5.96 (br, 1H), 3.91 (s, 3H), 3.21 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 156.8, 131.8, 129.7, 128.8, 128.4, 128.2, 128.0, 122.8, 120.9, 110.9, 88.5, 86.1, 61.6, 55.6; IR (KBr) 3400, 3059, 2935, 2835, 2232, 1600, 1490, 1463, 1439, 1286, 1109, 1029, 962, 823, 754, 691 cm^{-1}; LRMS-EI (*m*/*z*) 238 (M^+, 23), 223 (100), 207 (29), 178 (20), 135 (12), 115 (21), 91 (12), 77 (24); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0993.

(*R*)-1-(3-Methoxyphenyl)-3-phenyl-prop-2-yn-1-ol, 24a[4h,5a,5d,7a]

Yield: 81 mg (93%), oil; ee: 91%; retention time: $t_{r(major)}$: 16.21 min, $t_{r(minor)}$: 28.93 min; $[\alpha]_D^{21.3}$ = +13.0 (*c* 1.03, $CHCl_3$); lit.[5d] $[\alpha]_D^{28}$ = +15.7 (*c* 1.03, $CHCl_3$, 96% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49–7.46 (m, 2H), 7.33–7.29 (m, 4H), 7.21–7.19 (d, *J* = 8.1 Hz, 2H), 6.90–6.88 (m, 1H, 5.66 (s, 1H), 3.82 (s, 3H), 2.88 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 159.8, 142.3, 131.8, 129.7, 128.6, 128.3, 122.4, 119.0, 114.1, 112.2, 88.8, 86.5, 5.0, 55.3; IR (KBr) 3392, 3056, 2938, 2835, 2228, 1599, 1489, 1454, 1435, 1318, 1258, 1156, 1037, 997, 972, 870, 790, 756, 691 cm^{-1}; LRMS-EI (*m*/*z*) 238 (M^+, 100), 223 (21), 207 (29), 179 (22), 137 (28), 109 (52), 86 (28), 77 (36); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0990.

(*R*)-1-(4-Methoxyphenyl)-3-phenyl-prop-2-yn-1-ol, 25a[4h,5d,7a]

Yield: 82 mg (94%), white solid; mp 91–93 °C; ee: 91%; Retention time: $t_{r(major)}$: 13.56 min, $t_{r(minor)}$: 30.01 min; $[\alpha]_D^{21.3}$ = +3.6 (*c* 0.90, $CHCl_3$); lit.[7a] $[\alpha]_D^{15}$ = +3 (*c* 0.93, $CHCl_3$, 92% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.55–7.53 (d, *J* = 8.7 Hz, 2H), 7.49–7.47 (m, 2H), 7.33–7.30 (m, 3H), 6.94–6.92 (d, *J* = 8.6 Hz 2H), 5.64 (s, 1H), 3.82 (s, 3H), 2.41 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 159.7, 133.0, 131.7, 128.5, 128.3, 128.2, 122.5, 114.0, 88.9, 86.5, 64.7, 55.3; IR (KBr) 3368, 3063, 2958, 2839, 2228, 1612, 1514, 1488, 1414, 1278, 1255, 1172, 1107, 1028, 960, 828, 754, 689 cm^{-1}; LRMS-EI (*m*/*z*) 238 (M^+, 100), 223 (23), 207 (51), 178 (38), 135 (25), 91 (8), 77 (24); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{16}H_{14}O_2$ 238.0994, found 238.0989.

(*R*)-1-(2-Chlorophenyl)-3-phenyl-prop-2-yn-1-ol, 26a[4h]

Yield: 78 mg (91%), white solid; mp 65–67 °C; ee: 91%; Retention time: $t_{r(major)}$: 9.07 min, $t_{r(minor)}$: 10.74 min; $[\alpha]_D^{22}$ = −49.3 (*c* 0.50, $CHCl_3$); lit.[4h] $[\alpha]_D^{25}$ = −37.9 (*c* 0.51, $CHCl_3$, 64% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85–7.83 (m, 1H), 7.49–7.47 (m, 2H), 7.41–7.39 (m, 1H), 7.35–7.26 (m, 5H), 6.05 (s, 1H), 2.81 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.0, 132.8, 131.8 129.8, 129.7, 128.7, 128.5, 128.3, 127.3, 122.3, 87.7, 86.7, 62.4; IR (KBr) 3368, 3063, 2914, 2228, 1739, 1596, 1572, 1497, 1469, 1441, 1373, 1267, 1121, 1031, 964, 755, 690 cm^{-1}; LRMS-EI (*m*/*z*) 242 (M^+, 12), 207 (100), 179 (20), 139 (8), 129 (11), 77 (11); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{15}H_{11}ClO$ 242.0498, found 242.0494.

(*R*)-1-(3-Chlorophenyl)-3-phenyl-prop-2-yn-1-ol, 27a[4h,5a]

Yield: 79 mg (92%), oil; ee: 85%; retention time: $t_{r(major)}$: 9.45 min, $t_{r(minor)}$: 27.71 min; $[\alpha]_D^{22.3}$ = +11.6 (*c* 0.60, $CHCl_3$); lit.[5a] $[\alpha]_D^{27}$ = +12 (*c* 0.61, $CHCl_3$, 92% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.49–7.39 (m, 2H), 7.37–7.30 (m, 6H), 7.06–7.01 (m, 1H), 5.68 (s, 1H), 2.88 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 143.1, 143.0, 131.8, 130.2, 130.1, 128.8, 128.4, 122.4, 122.3, 122.1, 88.1, 86.9, 64.3; IR (KBr) 3338, 3063, 2874, 2227, 1614, 1593, 1489, 1443, 1316, 1247, 1133, 1033, 916, 897, 875, 792, 756, 690 cm^{-1}; LRMS-EI (*m*/*z*) 244 (12), 242 (M^+, 35), 207 (100), 189 (17), 179 (40), 178 (60), 139 (11), 129 (35), 89 (11), 77 (21); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{15}H_{11}ClO$ 242.0498, found 242.0505.

(*R*)-1-(4-Chlorophenyl)-3-phenyl-prop-2-yn-1-ol, 28a,[2f,4h,5a,5d,7a]

Yield: 83 mg (97%), white solid; mp 61–63 °C; ee: 88%; retention time: $t_{r(major)}$: 9.38 min and $t_{r(minor)}$: 29.49 min; $[\alpha]_D^{22}$ = +7.2 (*c* 1.25, $CHCl_3$); lit.[5d] $[\alpha]_D^{28}$ = +7.2 (*c* 1.25, $CHCl_3$, 94% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54–7.52 (d, *J* = 8.4 Hz, 2H), 7.48–7.45 (m, 2H), 7.36–7.29 (m, 5H), 5.65 (s, 1H), 2.92 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 139.1, 134.2, 131.8, 128.8, 128.8, 128.4, 128.1, 122.1, 88.3, 87.0, 64.3; IR (KBr) 3350, 3054, 2918, 2861, 2227, 1734, 1597, 1579, 2489, 1442, 1407, 1294, 1238, 1179, 1090, 1014, 960, 847, 801, 749, 688 cm^{-1}; LRMS-EI (*m*/*z*) 244 (8), 242 (M^+, 24), 207 (100), 178 (48), 129 (30), 77 (15); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{15}H_{11}ClO$ 242.0498, found 242.0503.

(*R*)-1-(2-Bromophenyl)-3-phenyl-prop-2-yn-1-ol, 29a[13c,16]

Yield: 73 mg (93%), white solid; mp 65–67 °C; ee: 88%; Retention time: $t_{r(major)}$: 41.27 min, $t_{r(minor)}$: 44.53 min; $[\alpha]_D^{22.1}$ = −53.9 (*c* 1.05, $CHCl_3$); lit.[13c] $[\alpha]_D^{23}$ = −55.7 (*c* 1.475, $CHCl_3$, 77% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86–7.84 (d, *J* = 7.7 Hz, 1H), 7.59–7.58 (d, *J* = 7.9 Hz, 1H), 7.49–7.47 (m, 2H), 7.40–7.36 (m, 1H), 7.34–7.29 (m, 3H), 7.23–7.18 (m, 1H), 6.02 (s, 1H), 2.82 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 139.5, 133.0, 131.8, 131.8, 130.0, 128.7, 128.3, 127.9, 122.8, 122.3, 87.7, 86.7, 64.6; IR (KBr) 3351, 3062, 2923, 2857, 2230, 1738, 1597, 1569, 1489, 1467, 1440, 1375, 1313, 1190, 1120, 1027, 965, 815, 755, 690, 630 cm^{-1}; LRMS-EI (*m*/*z*) 287 (6), 285 (M^+, 6), 207 (100), 129 (11), 77 (13); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{15}H_{11}BrO$ 285.9993, found 285.9998.

1-(3-Fluorophenyl)-3-phenyl-prop-2-yn-1-ol, 30a[13b]

Yield: 81 mg (88%), oil; ee: 83%; retention time: $t_{r(major)}$: 9.76 min, $t_{r(minor)}$: 35.24 min; $[\alpha]_D^{22.3}$ = +11.3 (*c* 1.0, $CHCl_3$); lit.[13b] $[\alpha]_D^{25}$ = +10 (*c* 1.0, EtOH, 85% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.61 (s, 1H), 7.49–7.47 (m, 3H), 7.37–7.30 (m, 5H), 5.66 (s, 1H), 2.82 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 142.5, 134.5, 131.8, 129.9, 128.8, 128.5, 128.4, 126.9, 124.9, 122.1, 88.1, 87.0, 64.3; IR (KBr) 3338, 3059, 2923, 2870, 2230, 1596, 1576, 1473, 1489, 1427, 1313, 1278, 1188, 1095, 1033, 998, 969, 789, 756, 711, 690 cm^{-1}; LRMS-EI (*m*/*z*): 226 (M^+, 100), 225 (79), 209 (31), 207 (24), 196 (48), 77 (23); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{15}H_{11}FO$ 226.0794, found 226.0790.

(*R*)-1-(4-Fluorophenyl)-3-phenyl-prop-2-yn-1-ol, 31a[4h,5a,7a]

Yield: 84 mg (92%), yellow solid; mp 40–42 °C; ee: 88%; retention time: $t_{r(major)}$: 8.92 min, $t_{r(minor)}$: 24.97 min; $[\alpha]_D^{22.3}$ = +4.8 (*c* 1.0, $CHCl_3$); lit.[7a] $[\alpha]_D^{15}$ = +3 (*c* 0.94, $CHCl_3$, 93%ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.60–7.57 (m, 2H), 7.49–7.46 (m, 2H), 7.37–7.30 (m, 3H), 7.10–7.05 (t, *J* = 8.7 Hz, 2H), 5.67 (s, 1H), 2.69 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 164.0–161.5 (d, $J_{C,F}$ = 246.5 Hz), 136.5–136.5 (d, $J_{C,F}$ = 3.0 Hz), 131.8, 128.8, 128.7–128.6 (d, $J_{C,F}$ = 9.1 Hz), 128.4, 122.3, 115.6–155.4 (d, $J_{C,F}$ = 22.1 Hz), 88.5, 86.9, 64.4; IR (KBr) 3350, 3065, 2874, 2228, 1893, 1738, 1605, 1508, 1489, 1413, 1295, 1225, 1096, 1031, 1015, 963, 837, 856, 691 cm^{-1}; LRMS-EI (*m*/*z*): 226 (M^+, 100), 225 (97), 209 (43), 197 (66), 183 (32), 148 (37), 129 (45), 102 (22), 77 (20); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{15}H_{11}FO$ 226.0794, found 226.0790.

(*R*)-1-(Naphthalen-1-yl)-3-phenyl-prop-2-yn-1-ol, 32a[4h,7a,13c]

Yield: 83 mg (99%), white solid; mp 82–84 °C; ee: 84%; retention time: $t_{r(major)}$: 16.91 min, $t_{r(minor)}$: 36.97 min; $[\alpha]_D^{23.1}$ = −23.4 (*c* 1.84, $CHCl_3$); lit.[7a] $[\alpha]_D^{19}$ = −26 (*c* 1.84, $CHCl_3$, 91% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.39–8.37 (d, *J* = 8.4 Hz, 1H), 7.95–7.86 (m, 3H), 7.61–7.49 (m, 5H), 7.35–7.30 (m, 3H), 6.34 (s, 1H), 2.79 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 135.7, 134.0, 131.8, 130.6, 129.4, 128.8, 128.3, 126.5, 125.9, 125.3, 124.7, 124.0, 122.5, 88.6, 87.3, 63.3; IR (KBr) 3367, 3051, 2918, 2852, 2228, 1738, 1597, 1509, 1489, 1366, 1228, 1162, 1008, 954, 912, 802, 779, 756, 690 cm^{-1}; LRMS-EI (*m*/*z*) 258 (M^+, 100), 257 (92), 241 (47), 229 (85), 228 (51), 181 (47), 129 (64), 77 (36); HRMS (*m*/*z*) $[M]^+$ calcd for $C_{19}H_{14}O$ 258.1045, found 258.1037.

(*R*)-1-(Naphthalen-2-yl)-3-phenyl-prop-2-yn-1-ol, 33a,[2f,4h,5d,7a,13c]

Yield: 81 mg (98%), white solid; mp 111–113 °C; ee: 85%; retention time: $t_{r(major)}$: 15.25 min, $t_{r(minor)}$: 56.14 min; $[\alpha]_D^{24.3}$ = −11.2 (*c* 1.30, $CHCl_3$); lit.[5d] $[\alpha]_D^{28}$ = −7.8 (*c* 1.30, $CHCl_3$, 96% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.05 (s, 1H), 7.89–7.86 (m, 3H), 7.75–7.73 (m, 1H), 7.54–7.51 (m, 4H), 7.36–7.32 (m, 3H), 5.87 (s, 1H), 2.86 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 138.0, 133.3, 133.2, 131.8, 128.7, 128.6, 128.4, 128.3, 127.7, 126.3, 125.6, 124.7, 122.4, 88.8, 86.9, 65.2; IR (KBr) 3245, 3054, 2918, 2852, 2668, 2224, 1737, 1598, 1488, 1366, 1282, 1168, 1123, 1012, 997, 960, 944, 862, 830, 754, 690 cm^{-1}; LRMS-EI (*m*/*z*) 258 (M^+, 100), 257 (44), 241 (31), 229 (71), 127 (34), 77 (17); HRMS (*m*/*z*): $[M]^+$ calcd for $C_{19}H_{14}O$ 258.1045, found 258.1036.

(*R*)-1-(Furan-2-yl)-3-phenyl-prop-2-yn-1-ol, 34a,[11,2f,4e,4h,5d]

Yield: 101 mg (98%), brown semi-solid; ee: 88%; retention time: $t_{r(major)}$: 10.30 min, $t_{r(minor)}$: 19.18 min; $[\alpha]_D^{26}$ = +18.4 (*c* 1.12, $CHCl_3$); lit.[5d] $[\alpha]_D^{28}$ = +10.4 (c 1.12, $CHCl_3$, 96% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50–7.48 (m, 2H), 7.44–7.43 (d, *J* = 0.7 Hz, 1H), 7.34–7.30 (m, 3H), 6.53–6.52 (d, *J* = 3.2 Hz, 1H), 6.38–6.37 (m, 1H), 5.71–5.70 (d, *J* = 4.0 Hz, 1H), 3.01–3.00 (d, *J* = 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 152.9, 143.1, 131.8, 128.8, 128.3, 122.1, 110.5, 107.9, 86.3, 85.7, 58.6; IR (KBr) 3379, 3054, 2918, 2861, 2280, 1631, 1598, 1489, 1443, 1384, 1308, 1223, 1180, 1142, 1071, 1009, 969, 916, 816, 756, 690 cm^{-1}; LRMS-EI (*m*/*z*) 198 (M^+, 46), 197 (44), 196 (66), 181(80), 168 (53), 152 (46), 129 (84), 115 (100), 105 (58), 77 (42); HRMS-EI (*m*/*z*) $[M]^+$ calcd for $C_{13}H_{10}O_2$ 198.0681, found 198.0688.

(*R*)-3-Phenyl-1-(thiophen-2-yl)prop-2-yn-1-ol, 35a[12,4e,5d]

Yield: 91 mg (95%), pale brown solid; mp 79–81 °C; ee: 91%; Retention time: $t_{r(major)}$: 11.06 min, $t_{r(minor)}$: 21.20 min; $[\alpha]_D^{25}$ = +18.7 (*c* 1.07, $CHCl_3$); lit.[5d] $[\alpha]_D^{28}$ = +20.7 (*c* 1.07, $CHCl_3$, 96%

ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51–7.49 (m, 2H), 7.36–7.31 (m, 4H), 7.26–7.25 (m, 1H), 7.01–7.00 (m, 1H), 5.90–5.88 (d, J = 6 Hz, 1H), 2.95–2.93 (d, J = 6.5 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 144.7, 131.8, 128.8, 128.4, 126.8, 126.2, 125.7, 122.1, 88.1, 86.0, 60.7; IR (KBr) 3400, 3063, 2918, 2861, 2224, 1738, 1596, 1489, 1441, 1383, 1225, 1121, 1028, 942, 851, 838, 757, 689, 570 cm^{-1}; LRMS-EI (m/z) 214 (M^+, 84), 213 (79), 197 (75), 185 (100), 152 (51), 129 (64), 111 (46), 102 (49), 97 (41), 77 (28); HRMS-EI (m/z) $[M]^+$ calcd for $C_{13}H_{10}OS$ 214.0452, found 214.0444.

(*R*,*E*)-1,5-Diphenylpent-1-en-4-yn-3-ol, 36a[3d,5d,7a]

Yield: 84 mg (94%), white solid; mp 77–79 °C; ee: 64%; Retention time: $t_{r(major)}$: 16.64 min, $t_{r(minor)}$: 56.07 min; $[\alpha]_D^{22}$ = +1.7 (*c* 1.25, $CHCl_3$); lit.[5d] $[\alpha]_D^{26}$ = +0.5 (*c* 1.25, $CHCl_3$, 92% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53–7.51 (m, 2H), 7.45–7.42 (m, 2H), 7.38–7.27 (m, 6H), 6.87–6.83 (d, J = 15.8 Hz, 1H), 6.45–6.39 (dd, J = 15.8, 6.0 Hz, 1H), 5.33–5.32 (d, J = 5.6 Hz, 1H), 2.70 (br, 1H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 136.1, 132.0, 131.8, 128.6, 128.4, 128.2, 128.1, 126.9, 122.4, 88.1, 86.4, 63.4; IR (KBr) 3350, 3026, 2857, 2224, 1738, 1594, 1489, 1442, 1375, 1088, 1066, 1011, 963, 754, 690 cm^{-1}; LRMS-EI (m/z) 234 (M^+, 47), 233 (61), 215 (55), 205 (47), 129 (100), 115 (39), 102 (67), 91 (52), 77 (46); HRMS-EI (m/z): $[M]^+$ calcd for $C_{17}H_{14}O$ 234.1045, found 234.1051.

(*R*,*E*)-2-Methyl-1,5-diphenylpent-1-en-4-yn-3-ol, 37a[2f,5b]

Yield: 84 mg (99%), low melting solid; ee: 88%; retention time: $t_{r(major)}$: 9.62 min, $t_{r(minor)}$: 41.74 min; $[\alpha]_D^{22.4}$ = −25.3 (*c* 1.02, $CHCl_3$); lit.[5b] $[\alpha]_D^{27}$ = −23.2 (*c* 1.02, acetone, 99%ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50–7.48 (t, J = 4.3 Hz, 2H), 7.39–7.33 (m, 7H), 7.28–7.26 (m, 1H), 6.79 (s, 1H), 5.18 (s, 1H), 2.46 (br, 1H), 2.09 (s, 3H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 137.1, 136.8, 131.8, 129.1, 128.6, 128.3, 128.2, 127.3, 126.8, 122.5, 88.1, 86.3, 68.8, 14.2; IR (KBr) 3339, 3056, 2918, 2852, 2224, 1737, 1598, 1489, 1442, 1364, 1280, 1176, 1070, 1007, 919, 755, 691 cm^{-1}; LRMS-EI (m/z) 248 (M^+, 11), 247 (23), 231 (91), 215 (88), 191 (12), 129 (44), 115 (47), 105 (100), 91 (28), 77 (38); HRMS-EI (m/z) $[M]^+$ calcd for $C_{18}H_{16}O$ 248.1201, found 248.1205.

(*R*)-1-Cyclohexyl-3-phenyl-prop-2-yn-1-ol, 38a[5d,13c,13d]

Yield: 88 mg (93%), oil; ee: 66%; retention time: $t_{r(major)}$: 6.04 min, $t_{r(minor)}$: 11.98 min; $[\alpha]_D^{22.3}$ = −7.6 (*c* 1.29, $CHCl_3$); lit.[5d] $[\alpha]_D^{27}$ = −8.8 (*c* 1.29, $CHCl_3$, 86%ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45–7.43 (m, 2H), 7.31–7.29 (m, 3H), 4.38 (s, 1H), 2.23 (s, 1H), 1.94–1.91 (d, J = 11.5 Hz, 2H), 1.81–1.78 (d, J = 12.0 Hz, 2H), 1.71–1.62 (m, 2H), 1.33–1.26 (m, 5H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 131.7, 128.3, 128.2, 122.8, 89.3, 85.6, 67.6, 44.3, 28.7, 28.2, 26.4, 26.0, 25.9; IR (KBr) 3350, 2935, 2852, 2228, 1738, 1598, 1489, 1449, 1375, 1082, 1028, 983, 755, 690 cm^{-1}; LRMS-EI (m/z) 214 (M^+, 60), 213 (3), 131 (100), 103 (15), 77 (14), 55 (15); HRMS-EI (m/z) $[M]^+$ calcd for $C_{15}H_{18}O$ 214.1358, found 214.1360.

(*R*)-4-Methyl-1-phenyl-pent-1-yn-1-ol, 39a,[3a,3e,5c,6f,7a,13a]

Yield: 102 mg (84%), oil; ee: 73%; retention time: $t_{r(major)}$: 5.83 min, $t_{r(minor)}$: 10.11 min; $[\alpha]_D^{22}$ = +1.3 (*c* 6.30, $CHCl_3$); lit.[3a] $[\alpha]_D^{23}$ = +3.2 (*c* 6.8, $CHCl_3$, 98% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45–7.43 (m, 2H), 7.31–7.29 (m, 3H), 4.41 (s, 1H), 2.34 (s, 1H), 2.02–1.94 (m, 1H), 1.09–1.05 (m, 6H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 131.7, 128.4, 128.3, 122.7, 89.0, 85.5, 68.3, 34.7, 18.2, 17.5; IR (KBr) 3367, 2962, 2929, 2872, 2224, 1738, 1598, 1489, 1468, 1443, 1383, 1252, 1069, 1028, 987, 755, 690 cm^{-1}; LRMS-EI (m/z) 174 (M^+, 8), 173 (2), 145 (3), 131 (100), 103 (18), 77 (14); HRMS-EI (m/z) $[M]^+$ calcd for $C_{12}H_{14}O$ 174.1045, found 174.1041.

(*R*)-4,4-Dimethyl-1-phenyl-pent-1-yn-1-ol, 40a,[3a,3e,13a,14a,14b]

Yield: 91 mg (83%), oil; ee: 87%; retention time: $t_{r(major)}$: 5.63 min, $t_{r(minor)}$: 7.18 min; $[\alpha]_D^{24}$ = +1.4 (*c* 4.0, $CHCl_3$); lit.[14b] $[\alpha]_D^{23}$ = +1.56 (*c* 4.0, $CHCl_3$, 97% ee); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45–7.43 (m, 2H), 7.31–7.30 (m, 3H), 4.25–4.24 (d, J = 2.5 Hz, 1H), 2.11 (s, 1H), 1.07 (s, 9H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 131.7, 128.3, 128.3, 122.8, 89.0, 85.6, 71.8, 36.2, 25.4; IR (KBr) 3399, 3059, 2964, 2869, 2219, 1738, 1598, 1489, 1443, 1364, 1322, 1238, 1254, 1206, 979, 755, 690 cm^{-1}; LRMS-EI (m/z) 188 (M^+, 11), 173 (10), 145 (5), 131 (100), 115 (5), 103 (15), 77 (16); HRMS-EI (m/z) $[M]^+$ calcd for $C_{13}H_{16}O$ 188.1201, found 188.1196.

(*S*)-1,3-Diphenylprop-2-yn-1-ol, 18b[3d]

Yield: 97 mg (99%), oil; ee: 89%; retention time: $t_{r(minor)}$: 13.28 min, $t_{r(major)}$: 24.89 min; $[\alpha]_D^{20.7}$ = −1.4 (*c* 0.9, $CHCl_3$); lit.[3d] $[\alpha]_D^{25}$ = −1.6 (*c* 0.88, $CHCl_3$, 94% ee).

(*S*)-1-(2-Methylphenyl)-3-phenylprop-2-yn-1-ol, 19b[2f,7c]

Yield: 91 mg (99%), white solid; ee: 90%; retention time: $t_{r(minor)}$: 10.14 min and $t_{r(major)}$: 23.49 min; $[\alpha]_D^{22}$ = +12.5 (*c* 1.2, $CHCl_3$); lit.[7c] $[\alpha]_D^{27}$ = +12.2 (*c* 1.2, $CHCl_3$, 86% ee).

(*S*)-1-(4-Methylphenyl)-3-phenyl-prop-2-yn-1-ol, 21b[7c]

Yield: 89 mg (95%), pale yellow solid; ee: 88%; retention time: $t_{r(minor)}$: 10.21 min, $t_{r(major)}$: 22.47 min; $[\alpha]_D^{22}$ = −5.0 (*c* 1.2, $CHCl_3$); lit.[7c] $[\alpha]_D^{27}$ = −5.2 (*c* 1.2, $CHCl_3$, 86%ee).

(*S*)-1-(2-Methoxyphenyl)-3-phenyl-prop-2-yn-1-ol, 23b[6f]

Yield: 87 mg (99%), pale yellow solid; ee: 90%; Retention time: $t_{r(minor)}$: 15.67 min, $t_{r(major)}$: 19.72 min; $[\alpha]_D^{22}$ = +11.1 (*c* 0.53, $CHCl_3$); lit.[6f] $[\alpha]_D^{25}$ = +12.7 (*c* 0.53, $CHCl_3$, 95% ee).

(*S*)-1-(4-Methoxyphenyl)-3-phenyl-prop-2-yn-1-ol, 25b[7c]

Yield: 86 mg (98%), white solid;. ee: 88%; retention time: $t_{r(minor)}$: 15.40 min, $t_{r(major)}$: 35.43 min; $[\alpha]_D^{23}$ = −4.8 (*c* 1.7, $CHCl_3$); lit.[7c] $[\alpha]_D^{27}$ = −4.2 (*c* 1.7, $CHCl_3$, 80%ee).

(*S*)-1-(2-Chlorophenyl)-3-phenyl-prop-2-yn-1-ol, 26b[2f,7c]

Yield: 82 mg (95%), white solid; ee: 87%; Retention time: $t_{r(minor)}$: 10.29 min, $t_{r(major)}$: 12.29 min; $[\alpha]_D^{24}$ = +47.1 (*c* 1.4, $CHCl_3$); lit.[7c] $[\alpha]_D^{25}$ = +46.2 (*c* 1.4, $CHCl_3$, 83%ee).

(*S*)-1-(2-Bromophenyl)-3-phenyl-prop-2-yn-1-ol, 29b[16,13c]

Yield: 71 mg (91%), white solid; ee: 86%; retention time: $t_{r(minor)}$: 44.86 min, $t_{r(major)}$: 48.18 min; $[\alpha]_D^{22.5}$ = +54.2 (*c* 1.0, $CHCl_3$), lit.[13c,16] for *R* enantiomer $[\alpha]_D^{23}$ = −55.7 (*c* 1.48, $CHCl_3$, 77%ee).

(*S*)-3-Phenyl-1-(thiophen-2-yl)prop-2-yn-1-ol, 35b[12,4e,5d]

Yield: 87 mg (91%), pale brown solid; ee: 89%; Retention time: $t_{r(minor)}$: 12.06 min, $t_{r(major)}$: 24.14 min; $[\alpha]_D^{22.5}$ = −20.2 (*c* 1.00, $CHCl_3$); lit.[5d] $[\alpha]_D^{28}$ = +20.4 (*c* 1.07, $CHCl_3$, 96% ee); For *R* isomer see ref. 12.

(*S*,*E*)-2-Methyl-1,5-diphenylpent-1-en-4-yn-3-ol, 37b[7c]

Yield: 82 mg (97%), low melting solid; ee: 82%; retention time: $t_{r(minor)}$: 10.62 min, $t_{r(major)}$: 51.71 min; $[\alpha]_D^{22.5}$ = +32.0 (*c* 1.00, $CHCl_3$); lit.[7c] $[\alpha]_D^{27}$ = +31.6 (*c* 1.02, $CHCl_3$, 71% ee).

(*S*)-4,4-Dimethyl-1-phenyl-pent-1-yn-1-ol, 40b[13a]

Yield: 108 mg (99%), oil; ee: 91%; retention time: $t_{r(minor)}$: 5.94 min, $t_{r(major)}$: 7.75 min; $[\alpha]_D^{17}$ = −2.1 (*c* 5.20, $CHCl_3$); lit.[13a] $[\alpha]_D^{23}$ = −2.5 (*c* 5.13, $CHCl_3$, 97%ee).

Synthesis of 39ac from 39a for the confirmation of the absolute configuration of 39a

4-Methyl-1-phenylpent-1-yn-3-yl benzoate 39aa

39a (600 mg, 3.44 mmol) was dissolved in dry CH_2Cl_2 (12 mL), followed by the addition of Et_3N (522 mg, 5.17 mmol) and benzoyl chloride (0.16 g, 1.2 mmol) at 0 °C. The reaction mixture was warmed to room temperature over two hours, then quenched with saturated $NaHCO_3$ at room temperature and stirred for a further 30 min. The aqueous phase was extracted with CH_2Cl_2 (3 × 75 mL) and the combined organic layer was dried over anhydrous Na_2SO_4. The organic solvent was concentrated under vacuum to afford crude product, which was purified by flash column chromatography (silica gel 60–230 mesh, 10% ethyl acetate/hexane) to give products **39aa** as a colorless oil. Yield: 927 mg (97%); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.12–8.10 (d, *J* = 8.2 Hz, 2H), 7.59–7.56 (t, *J* = 7.3 Hz, 1H), 7.48–7.44 (m, 4H), 7.33–7.27 (m, 3H), 5.72–5.71 (d, 1H), 2.29–2.21 (m, 1H), 1.19–1.15 (m, 6H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 165.6, 133.1, 131.9, 130.1, 129.8, 128.5, 128.4, 128.2, 122.4, 85.9, 85.3, 69.9, 32.9, 18.3, 17.8.

2-(Benzoyloxy)-3-methylbutanoic acid, 39ab

The above **39aa** (750 mg, 2.69 mmol), $NaIO_4$ (5.75 g, 26.94 mmol), HMTA (1.88 g, 13.47 mmol) in THF/H_2O (30 mL, 1 : 1) was stirred for 15 min, after which time OsO_4 (1.3 mL, 0.13 mmol of a 2.5 wt. % solution in *t*-BuOH) was added. This was stirred for 15 h at room temperature then for 10 h at 50 °C. The reaction mixture was cooled to room temperature and quenched slowly with saturated $NaHSO_3$ solution. This was extracted with DCM (3 × 100 mL). The combined DCM layer was extracted with saturated $NaHCO_3$ solution (3 × 100 mL), then this aqueous layer was acidified and extracted with DCM (3 × 100 mL). The combined DCM layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated to give solid **39ab** (500 mg) with benzoic acid as a by-product. This was carried to the next step without further purification.

1-Methoxy-3-methyl-1-oxobutan-2-yl-benzoate, 39ac

The above solid mixture (**39ab**) was taken into methanol (20 mL) followed by the addition of catalytic amount of conc. H_2SO_4. The resulting mixture was refluxed for 20 h then cooled to room temperature and basified with saturated $NaHCO_3$. This was extracted with DCM (3 × 100 mL) and the combined organic layer was washed with brine, dried over anhydrous Na_2SO_4 and concentrated to get the crude product. This was purified by column chromatography (silica gel 70–230 mesh, ethyl acetate/hexane (1 : 9)) to get colorless oil **39ac**. Yield: 300 mg (47%, for 2nd step); $[\alpha]_D^{23}$ = −17.4 (*c* 2.00, benzene); lit.[13a] for *S* isomer $[\alpha]_D^{23.2}$ = +26.2 (*c* 1.91, benzene); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.10–8.07 (m, 2H), 7.60–7.56 (m, 1H), 7.47–7.43 (t, *J* = 7.9 Hz, 2H), 5.08–5.07 (d, *J* = 4.6 Hz, 1H), 3.76 (s, 1H), 2.41–2.33 (m, 1H), 1.10–1.08 (m, 6H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 170.2, 166.1, 133.3, 129.8, 129.6, 128.4, 77.2, 52.1, 30.3, 18.9, 17.4.

Synthesis of 40ad and 40ai to confirm the absolute configuration of 32a

1-Methoxy-3,3-methyl-1-oxobutan-2-yl benzoate, 40ad. The synthesis of **40ad** followed the same procedure as for **39ac**. $[\alpha]_D^{23}$ = −6.2 (*c* 1.00, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09–8.07 (t, *J* = 7.1 Hz, 2H), 7.60–7.56 (t, *J* = 6.0 Hz, 1H), 7.47–7.44 (t, *J* = 7.8 Hz, 2H), 4.82 (s, 1H), 3.75 (s, 3H), 1.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 169.6, 166.2, 133.3, 129.8, 129.5, 128.4, 80.4, 51.8, 33.9, 26.3.

(*S*)-2-Hydroxy-3,3-dimethylbutanoic acid, 40af. The preparation of **40af** followed the literature procedure.[14c] $[\alpha]_D^{19.3}$ = +4.2 (*c* 1.00, CH_3OH); lit.[14c] $[\alpha]_D$ = +3.9 (*c* 1.00, CH_3OH); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.26 (br, 2H), 3.89 (s, 1H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 178.5, 78.3, 35.1, 25.7.

(*S*)-1-Methoxy-3,3-methyl-1-oxobutan-2-yl benzoate, 40ai. Esterification of **40af** and benzoyl protection of **40ag** were done according to the same procedures as for the preparation of **39ac** and **39aa**, respectively. $[\alpha]_D^{22}$ = +6.9 (*c* 1.00,$CHCl_3$). ^{1}H and ^{13}C NMR were the same as those of **40ad**.

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Notes and references

1 (*a*) B. M. Trost and A. H. Weiss, *Org. Lett.*, 2006, **8**, 4461–4464; (*b*) B. M. Trost and A. H. Weiss, *Angew. Chem., Int. Ed.*, 2007, **46**, 7664–7666; (*c*) L. Lin, Q. Zhao, A. N. Li, F. Ren, F. Yang and R. Wang, *Org. Biomol. Chem.*, 2009, **7**, 3663–3665; (*d*) J. Wu and J. S. Panek, *Angew. Chem., Int. Ed.*, 2010, **49**, 6165–6168; (*e*) S. Archambaud, F. Legrand, K. A. Julienne, S. Collet, A. Guingant and M. Evain, *Eur. J. Org. Chem.*, 2010, 1364–1380.

2 Reviews: (*a*) D. E. Frantz, R. Fassler, C. S. Tomooka and E. M. Carreira, *Acc. Chem. Res.*, 2000, **33**, 373–381; (*b*) L. Pu, *Tetrahedron*, 2003, **59**, 9873–9886; (*c*) P. G. Cozzi, R. Hilgraf and N. Zimmermann, *Eur. J. Org. Chem.*, 2004, 4095–4105; (*d*) G. Lu, Y. M. Li, S. S. Li and A. S. C. Chan, *Coord. Chem. Rev.*, 2005, **249**, 1736–1744; (*e*) B. M. Trost and A. H. Weiss, *Adv. Synth. Catal.*, 2009, **351**, 963–983; (*f*) D. L. Usanov and H. Yamamoto, *J. Am. Chem. Soc.*, 2011, **133**, 1286–1289 and reference therein.

3 Selected examples for zinc triflate, base and chiral inducer mediated alkynylation: (*a*) D. E. Frantz, R. Fassler and E. M. Carreira, *J. Am. Chem. Soc.*, 2000, **122**, 1806–1807; (*b*) Z. Chen, W. Xiong and B. Jiang, *Chem. Commun.*, 2002, 2098–2099; (*c*) D. Boyall, D. E. Frantz and E. M. Carreira, *Org. Lett.*, 2002, **4**, 2605–2606; (*d*) M. Yamshita, K. I. Yamada and K. Tomioka, *Adv. Synth. Catal.*, 2005, **347**, 1649–1652; (*e*) D. P. G. Emmerson, W. P. Hems and B. G. Davis, *Org. Lett.*, 2006, **8**, 207–210.

4 Selected examples for dialkylzinc and chiral inducer mediated alkynylation of aldehydes: (*a*) Z. B. Li and L. Pu, *Org. Lett.*, 2004, **6**, 1065–1068; (*b*) S. Dahmen, *Org. Lett.*, 2004, **6**, 2113–2116; (*c*) Y. F. Kang, L. Liu, R. Wang, W. J. Yan and Y. F. Zhou, *Tetrahedron: Asymmetry*, 2004, **15**, 3155–3159; (*d*) C. Wolf and S. Liu, *J. Am. Chem. Soc.*, 2006, **128**, 10996–10997; (*e*) G. Blay, I. Fernandez, A. M. Aleixandre and J. R. Pedro, *J. Org. Chem.*, 2006, **71**, 6674–6677; (*f*) Z. B. Li, T. D. Liu and L. Pu, *J. Org. Chem.*, 2007, **72**, 4340–4343; (*g*) J. Ruan, G. Lu, L. Xu, Y. M. Li and A. S. C. Chan, *Adv. Synth. Catal.*, 2008, **350**, 76–84; (*h*) G. Blay, L. Cardona, I. A. M. Fernandez Aleixandre, M. C. Munoz and J. R. Pedro, *Org. Biomol. Chem.*, 2009, **7**, 4301–4308; (*i*) M. Rachwalski, S. Lesniak and P. Kielbansinki, *Tetrahedron: Asymmetry*, 2010, **21**, 2687–2689.

5 Selected examples for dialkylzinc, Ti(O^iPr)4 and chiral inducer mediated alkynylation of aldehydes: (*a*) D. Moore and L. Pu, *Org. Lett.*, 2002, **4**, 1855–1857; (*b*) G. Gao, D. Moore, R.-G. Xie and L. Pu, *Org. Lett.*, 2002, **4**, 4143–4146; (*c*) T. Fang, D. M. Du, S. F. Lu and J. Xu, *Org. Lett.*, 2005, **7**, 2081–2084; (*d*) H. Koyuncu and O. Dogan, *Org. Lett.*, 2007, **9**, 3477–3479; (*e*) Z. Xu, J. Mao and Z. Yhang, *Org. Biomol. Chem.*, 2008, **6**, 1288–1292; (*f*) Y. M. Li, Y. Q. Tang, X. P. Hui, L. N. Huang and P. F. Xu, *Tetrahedron*, 2009, **65**, 3611–3614.

6 Examples for the influence of achiral additives on alkynylation reaction: (*a*) G. Lu, X. Li, G. Chen, W. L. Chan and A. S. C. Chan, *Tetrahedron: Asymmetry*, 2003, **14**, 449–452; (*b*) Q. Yu, R. G. Xie and L. Pu, *Angew. Chem., Int. Ed.*, 2006, **45**, 122–125; (*c*) Z. Xu, L. Lin, J. Xu, W. Yan and R. Wang, *Adv. Synth. Catal.*, 2006, **348**, 506–514; (*d*) F. Yang, P. Xi, L. Yang, J. Lan, R. Xie and J. You, *J. Org. Chem.*, 2007, **72**, 5457–5460; (*e*) M. C. Wang, Q. J. Zhang, W. X. Zhao, X. D. Wang, X. Ding, T. T. Jing and M. P. Song, *J. Org. Chem.*, 2008, **73**, 168–176; (*f*) J. C. Zhong, S. C. Hou, Q. H. Bian, M. M. Yin, R. S. Na, B. Zheng, Z. Y. Li, S. Z. Liu and M. Wang, *Chem.–Eur. J.*, 2009, **15**, 3069–3071; (*g*) T. Xu, C. Liang, Y. Cai, J. Li, Y. M. Li and X. P. Hui, *Tetrahedron: Asymmetry*, 2009, **20**, 2733–2736; (*h*) B. M. Trost, V. S. Chan and D. Yamamoto, *J. Am. Chem. Soc.*, 2010, **132**, 5186–5192; (*i*) Y. Du, M. Turlington, X. Zhou and L. Pu, *Tetrahedron Lett.*, 2010, **51**, 5024–5027. Review on influence of additives in asymmetric reaction: (*j*) E. M. Vogal, H. Groger and M. Shibasaki, *Angew. Chem., Int. Ed.*, 1999, **38**, 1550–1557.

7 Camphor-derived ligands used in enantioselective alkynylation of aldehydes: (*a*) Z. Xu, C. Chen, J. Xu, M. Miao, W. Yan and R. Wang, *Org. Lett.*, 2004, **6**, 1193–1195; (*b*) J. Sun, X. Pan, Z. Dai and C. Zhu, *Tetrahedron: Asymmetry*, 2008, **19**, 2451–2457; (*c*) P. Y. Wu, H. L. Wu, Y. Y. Shen and B. J. Uang, *Tetrahedron: Asymmetry*, 2009, **20**, 1837–1841; (*d*) S. Gou, Z. Ye, Z. Huang and X. Ma, *Appl. Organomet. Chem.*, 2010, **24**, 374–379.

8 References for camphor-derived ligands in enantioselective alkynylation of ketones: (*a*) T. F. Briggs, M. D. Winemiller, B. Xiang and D. B. Collum, *J. Org. Chem.*, 2001, **66**, 6291–6298; (*b*) G. Li, X. Li, X. Jia, L. Chan and A. S. C. Chan, *Angew. Chem., Int. Ed.*, 2003, **42**, 5057–5058; (*c*) G. Lu, X. Li, Y. M. Li, F. Y. Kwong and A. S. C. Chan, *Adv. Synth. Catal.*, 2006, **348**, 1926–1933.

9 (*a*) P. F. Xu, Y. S. Chen, S. I. Lin and T. J. Lu, *J. Org. Chem.*, 2002, **67**, 2309–2314; (*b*) M. J. Bosiak, M. P. Krzeminski, P. Jaisankar and M. Zaidlewicz, *Tetrahedron: Asymmetry*, 2008, **19**, 956–963. Selected other references of synthesis of AIB: (*c*) *Organic Syntheses*, Wiley & Sons, New York, 2004; Coll. Vol.10, p 305; (*d*) *Organic Syntheses*, Wiley & Sons, New York, 2009; Coll. Vol. 11, p 702–707; (*e*) M. P. Bonner and E. R. Thornton, *J. Am. Chem. Soc.*, 1991, **113**, 1299–1308.

10 J. Hartung, S. Drees, M. Greb, P. Schmidt, I. Svoboda, H. Fuess, A. Murso and D. Stalke, *Eur. J. Org. Chem.*, 2003, 2388–2408 has reported 61% yield for the synthesis of (+)-SBAIB-a, **10** from (−)-AIB, which was improved to 99% yield for (+)-SBAIB-a, **10**, by our method.

11 (*a*) R. Takita, K. Yakura, T. Ohshima and M. Shibasaki, *J. Am. Chem. Soc.*, 2005, **127**, 13760–13761. Till today, there were only four reports (refs 2*f*, 4*e*, 4*h* and 5*d*), of which ref. 4*e* is the first report to specify the configuration of 1-(furan-2-yl)-3-phenyl-prop-2-yn-1-ol as the *S* enantiomer, which has $[\alpha]_D^{25}$ = +34 (*c* 0.58, $CHCl_3$, 83% ee). To assign the configuration of the same molecule, ref. 4*e* cited ref. 4*a* in which neither the absolute configuration nor specific rotation of this compound was mentioned. Thereafter, the reports ref. 2*f* and ref. 4*h* cited ref. 4*e* to specify the configuration of this compound. As all of the propargylic alcohols that we have got by (+)-SBAIB-a, **10**, catalyzed reaction were in the *R* configuration, we had a doubt about the earlier report. As a proof, the ref. 4*e* wrongly assigned the configuration of 1-(3-furyl)-3-phenyl-2-propyn-1-ol as the *S* enantiomer, which has $[\alpha]_D^{25}$ = +3.0 (*c* 0.53, $CHCl_3$, 89% ee). This is revealed from their back reference, ref. 11*a*, which reported that the same compound with *R* configuration, specific rotation $[\alpha]_D^{24}$ = +1.8 (*c* = 2.10, $CHCl_3$) (99% ee) and with same order of major and minor peaks in the HPLC. This confirms to us that the configuration of 1-(furan-2-yl)-3-phenyl-prop-2-yn-1-ol in ref. 4*e* would have been wrongly assigned. Therefore, compound **34a** should have *R* configuration.

12 The ref. 4*e* also has the same controversy, as that above, for 1-(2-thiophenyl)-3-phenyl-2-propyn-1-ol. It mentioned that the *S* isomer has $[\alpha]_D^{25}$ = +20 (*c* 0.53, $CHCl_3$, 90% ee), however, it doesn't have any back reference for this compound. As all of our propargylic alcohols possess *R* configuration, we suspected that our compound **35a** should also have *R* configuration.

13 (*a*) K. Matsumura, S. Hahiguchi, T. Ikariya and R. Noyori, *J. Am. Chem. Soc.*, 1997, **119**, 8738–8739; (*b*) E. Tyrrell, K. H. Tesfa, A. Mann and K. Singh, *Synthesis*, 2007, 1491–1498; (*c*) J. Ito, R. Asai and H. Nishiyama, *Org. Lett.*, 2010, **12**, 3860–3862; (*d*) in ref. 13*c*, the major and minor peaks for (*R*)-1-cyclohexyl-3-phenyl-prop-2-yn-1-ol are wrongly written as compared to their HPLC data.

14 (*a*) P. V. Ramachandran, A. V. Teodorovic, M. V. Rangaishenvi and H. C. Brown, *J. Org. Chem.*, 1992, **57**, 2379–2386; (*b*) E. J. Corey and K. A. Cimprich, *J. Am. Chem. Soc.*, 1994, **116**, 3151–3152; (*c*) N. A. Van Draane, S. Arseniyadis, M. T. Crimmins and C. H. Heathcock, *J. Org. Chem.*, 1991, **56**, 2499–2506.

15 1-(4-Tert-butylphenyl)-3-phenylprop-2-yn-1-ol **22a** has the first peak in HPLC as a major peak like all other propargylic alcohols, which are *R* in configuration, generated by (+)-SBAIB-**1**-catalyzed reactions. With the support of our proposed mechanism, we are proposingthat compound **5a** should possess *R* configuration.

16 The similarities of 1-(2-bromophenyl)-3-phenylprop-2-yn-1-ol **29a** with all other *ortho*-substituted propargyl alcohols ((*R*)-1-(2-methylphenyl)-3-phenylprop-2-yn-1-ol **19a**, (*R*)-1-(2-methoxyphenyl)-3-phenyl-prop-2-yn-1-ol **23a**, (*R*)-1-(2-chlorophenyl)-3-phenyl-prop-2-yn-1-ol **26a**) are as follows; 1) The first peak is the major peak in HPLC data; 2) It has (−) sign of specific rotation like all other *ortho*-substituted propargylic alcohols. Hence as there is no report for the configuration of this compound, we are proposing that 1-(2-bromophenyl)-3-phenylprop-2-yn-1-ol **29a** could have *R* configuration.

